



Journal on Biomedical Radioelectronics

Proceedings of the 13th Russian German Conference on Biomedical Engineering
23-25 May 2018, Aachen, Germany



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Proceedings of the 13th Russian German Conference on Biomedical Engineering

23-25 May 2018, Aachen, Germany

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Introductory Words from the Editorial Board

The Russian Bavarian Conference on Biomedical Engineering (RBC) was founded 2005 in Munich. Thereafter, the conference established itself as a fruitful information exchange platform for researchers from Russia and Germany. The conference location alternated equally between cities in Russia and the southern part of Germany. After the successful 8th RBC conference in Moscow the steering committee decided to broaden the focus and establish a new conference: the Russian German Conference (RGC) on Biomedical Engineering. The goal is to serve as meeting point for information exchange and as venue for initiating bilateral Russian German research projects within the conference's scope. The first RGC on Biomedical Engineering took place in 2013 Hanover, Germany. Then, following the idea of an alternating conference location, the 10th RGC took place in 2014 in St. Petersburg, Russia. In 2015, the 11th RGC came to Aachen, Germany, for the first time, and, finally, the 12th RGC has been held in Suzdal, Russia, in 2016.

This year, we are very happy to welcome all participants to the 13th Russian German Conference on Biomedical Engineering in Aachen, Germany. In 2018, the RGC will be jointly held together with the 11th International Conference on Bioelectromagnetism (ICBEM) hosted by the Philips Chair for Medical Information Technology (MedIT) at RWTH Aachen University. Both conferences follow the idea to provide a platform for researchers all over the world to share their experience regarding their work in the broad field of biomedical engineering. Therefore, we would like to thank all participants contributing to RGC & ICBEM 2018 with their research and hope the conference to be a great experience for all participants.

The Editorial Board:

Prof. Sergey I. Shchukin,

Prof. Steffen Leonhardt

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Effect of temperature on electrical cell conductivity of human erythrocytes

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Introduction

The electrical conductivity (σ in units of S m^{-1}) of an electrolyte is determined by the concentration and mobility of its ions. Therefore, the electrical conductivity of the cell interior should provide information about the state of the ions within the cell, i.e., whether or not they are free moving or bound by ion exchanger mechanisms to components of the cytoplasm such as proteins. It is a key measurement for dielectric studies on cells. One of the most thoroughly investigated cells is the red blood cell of mammals. This cell exhibits a simple architecture, and its composition of proteins and lipids is well known. Pauly and Schwan, (1966) measured the internal conductivity of erythrocytes and found a value of 0.518 S m^{-1} at 25°C ($\sigma_{25} = 0.518 \text{ S m}^{-1}$). They concluded that the internal conductivity is largely due to the inorganic ionic content composed primarily of K^+ , Na^+ , Mg^{++} , Cl^- , and HCO_3^- whose concentrations are relatively easy to measure experimentally. The concentration of ions of haemoglobin due to their net charge was reported to be $+45 \text{ mmol charge/l}$ (cell H_2O) from a total concentration of haemoglobin of 7 mM (cell H_2O) and so the mean effective +ve charge per haemoglobin molecule was $+6.4$ (Pauly and Schwan, 1966). The calculation of cytoplasmic conductivity from the ionic concentration of ions present in the cytoplasm multiplied by their limiting ionic conductance according to Kohlrausch's law gave a value of $\sigma = 1.45 \text{ S m}^{-1}$ which is 2.7 times higher than that obtained from experimental measurements by Pauly and Schwan, (1966) ($\sigma_{25} = 0.518 \text{ S m}^{-1}$). They concluded that the discrepancy between ideal specific conductivity and the measured value was due to the ionic mobility being hindered by cytoplasmic viscosity (Pauly and Schwan, 1966). However, since most mammalian cells regulate their volumes, after the initial passive swelling (stomatocytogenic) or shrinking (echinocytogenic) as a result of changes in the bathing electrolyte and/or temperature, cells usually return to a near-normal volume (Glaser, 1979). Red blood cells quickly change their cell volumes because water moves quickly into them through water channel proteins called aquaporins which do not allow charged ions to pass through them (Murata et al., 2000). Several mechanisms are involved in the slower process of adjusting their cell volume back to normal, in most cases involving the loss and gain of K^+ and Cl^- and to a lesser extent Na^+ (Glaser, 1979; Bernhardt, 1991; Parker, 1993; O'Neill, 1999). A perturbation of cell volume

will certainly disturb the concentration of ions present in the cytoplasm as described by Glaser and Donath, (1984) and consequently cause the cytoplasmic conductivity to shift from the normal physiological state.

In this investigation, the cytoplasmic conductivity of human red blood cells (HRBCs) at different temperatures was observed. The cell volumes and cell water contents in the cells were measured experimentally. The cytoplasmic conductivity (σ_c) was calculated according to the Debye - Hückel – Onsager equation combined with Walden's rule (Laidler and Meiser, 1995) and its temperature coefficient was then estimated.

Materials and Methods

Red blood cells

HRBCs were obtained from the blood bank (Suratthani Hospital, Thailand) and used within 3 days. The cells were first separated from the blood plasma by centrifugation at 2000 g for 8 min . The supernatant plasma and buffy coat was removed. The sedimented cells were used for the experiments.

Preparation of the cell suspension

A 157 mM NaCl solution ($300 \text{ mOsmol kg}^{-1}$) containing 1 mM Sodium Phosphate buffer ($\text{pH } 6.8$) was used to resuspend the cells and the conductivity of the suspending medium was adjusted to a conductivity of 1.48 S m^{-1} . The standard conductivity of the bathing electrolyte suspensions at 20°C (σ_{20}) was measured in the temperature compensation mode ($\sigma_{20} = \sigma_T(1 - 0.0214(T - 20))$), where σ_T is the measured conductance at temperature T ($^\circ\text{C}$) in a constant temperature bath using a conductivity meter (Mettler-Toledo, Switzerland).

Volume experiments

The haematocrit volume (Hct) of the red-cell sediment was determined in haematocrit-capillaries by centrifugation at 10000 g for 8 min (Cence, China). From the Hct , the amount of measuring solution was calculated that was needed for the dilution of $50 \mu\text{l}$ of the sedimented cells to a final cell concentration of 10% (v/v). The cells were incubated in the measuring solution for 5 min and the Hct of the suspensions were determined by haematocrit-centrifugation at 10000 g for 8 min . In parallel, the cell number was microscopically determined using a standard haemocytometer (Improved Neubauer). From the cell count and the Hct after 5 min in suspended solutions, the mean cell

volume (MCV) was determined following standard clinical methods (Gedde and Huestis, 1979; Harris, 1984; Sudrisi, 2009; Glaser, 2000). A trapped water volume correction constant of 3% was assumed in all *Hct* calculations (Gedde and Huestis, 1979).

Determination of cell water

Red blood cells in a standard 1.5 ml Eppendorf tube were spun down (10 000g) after 5 min of suspension in the experimental medium. 300 μ l of the packed cell volume was then pipetted into a pre-weighed test tube (Gedde and Huestis, 1979; Harris, 1984; Sudrisi, 2009). In parallel, the *Hct* was determined experimentally. The tube was weighed before and after drying at 80 °C for 24 hours. The cell water determination (*W_c*) was calculated from the wetted cells weight (*W_t*) and dried cells weight (*W_d*) as follows (Harris, 1984)

$$\% W_c = \frac{W_t - W_d}{W_t} * 100 - (100 - Hct) * \frac{100}{Hct} \quad (1)$$

Results

Cell volume

The data set of volume changes as well as water content of HRBCs after suspension for 5 min in the measuring solutions. The changes in cell water were found to be proportional to volume changes: the HRBC volume increases with rising of temperature. To further characterize the nature of the volume changes depending on temperature, the data on cell volume change were plotted over a range of experimental temperatures (Figure 1) and fitted to the Arrhenius-relation as a suitable model (Glaser, 2000).

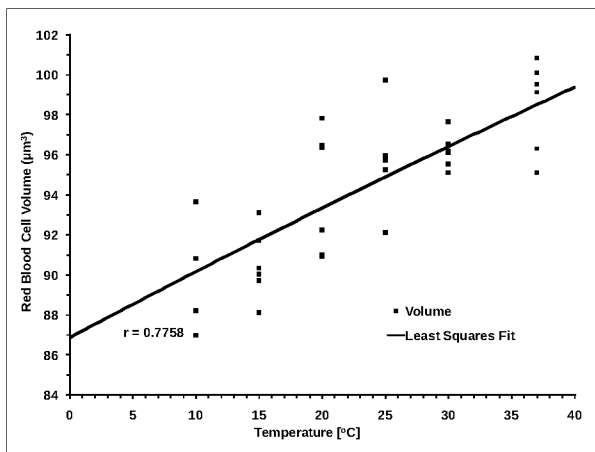


Figure 1: Volume changes over temperature in six different external conductivities. The Arrhenius relation

$(V_T = Ae^{\frac{-E_A}{RT}})$ was used to fit the experimental points and fitted using non-linear least squares fitting and the asymptotic errors were calculated by matrix inversion. At the standard experimental temperature of 25 °C the cell volume was found to be $96.18 (\pm 0.356) \times 10^{-18} \text{ m}^3 (\pm \text{SE}, n = 6)$ and the cell water content was $67.55 (\pm 0.824) \times 10^{-18} \text{ m}^3 (\pm \text{SE}, n = 6)$ and at the normal human body temperature of 37 °C, cell volume = $98.52 (\pm 0.926) \times 10^{-18}$

$\text{m}^3 (\pm \text{SE}, n = 6)$ and cell water $69.95 (\pm 0.658) \times 10^{-18} \text{ m}^3 (\pm \text{SE}, n = 6)$.

Cytoplasmic conductivity

A Plot of calculated cytoplasmic conductivities over a range of temperatures is shown in Figure 2. The data were fitted to an exponential relation using non-linear least squares methods and the asymptotic errors of the fitted parameters calculated by matrix inversion. A temperature coefficient value of $k = 0.06239 \pm 0.00202 (\pm \text{SE}, n = 24)$ was obtained (Figure 2). The intracellular conductivities increased by a factor of $1.866 \pm 0.0377 (\pm \text{SE})$ for every increase in temperature of 10°C and hence the Q_{10} of cytoplasmic conductivity vs. temperature is a typical value of ≈ 2 found in many biological systems (Glaser, 2000; Nobel, 2009).

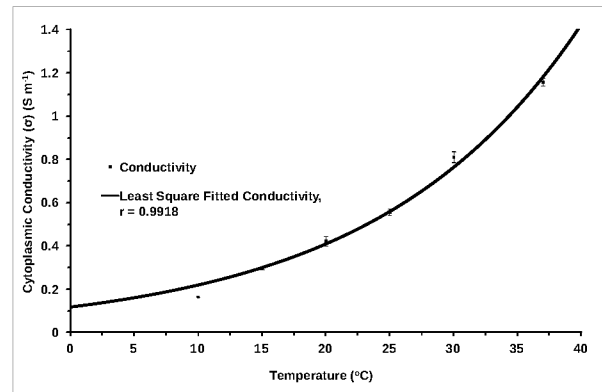


Figure 2: Cytoplasmic conductivity of HRBCs suspended in external conductivities of 1.48 S m^{-1} at six different temperatures. Data points are means $\pm \text{SE}$ ($n = 4$) so total $n = 24$. The line was fitted by non-linear least squares methods and the errors of the fitted parameters calculated by matrix inversion.

Discussion

Cell volume

The activation energy obtained from the fit in Figure 1 indicates the electrical energy required to provide a driving force for net movements of ions across the membrane plotted over the ionic concentrations of the suspending solution. Highly negative activation energy means there is a high ionic concentration difference across the cell membrane. The fits using the direct non-linear and log-transform methods both give an activation energy of about -2.4 kJ mol^{-1} . This means that there was little or no ionic concentration difference across the membrane and hence change in cell volume depends only on temperature. There are two major reasons for an influence of temperature on water influx. The first is an alteration of external hydrostatic pressure as predicted by the Van't Hoff relation. The hydrostatic pressure depends strongly on temperature and increases when the temperature is raised. The increase in external hydrostatic pressure will destroy the balance of the pressures between the two sides of the membrane. To re-balance the system, water moves down its chemical potential gradient and enters to the cell. The

cell swells. Secondly, increase in temperature will decrease the viscosity of external medium and consequently increase in the hydraulic conductivity, L_p , which is a parameter determined by the viscosity of the fluid (η) and membrane characteristics including the membrane pore of radius (r), pore number ($n \text{ m}^{-2}$), membrane thickness (δ), which are related as follows (Sperelakis, 1995):

$$L_p = \frac{n\pi r^4}{8\eta\delta} \quad (2)$$

Cytoplasmic conductivity

The experimentally measured HRBC conductivity value at 25 °C ($\sigma_{25} = 0.5566 \pm 0.0146 \text{ S m}^{-1}$, $\pm \text{SE}$, $n = 4$) shown in Fig. 2 agrees very well with the value of $\sigma_{25} \approx 0.5$ to 0.6 S m^{-1} found experimentally in other studies on red blood cells using quite different methods (Seidlet al., 1999; Fuhr et al., 1986; Sudsiri, 2002; Krupa and Terlecki, 1976; Asami, 1992) and is similar to theoretical estimates by Glaser and Donath (1984). For comparison, the conductivities of the cytoplasm of bacteria, plant protoplasts and yeast cells using dielectric methods have been reported to vary from 0.1 to 1.2 S m^{-1} at 25°C and so the conductivity of red blood cells appears to be representative for the cytoplasm of most cells (Hölzel and Lamprecht, 1992, 1997; Suehiro et al., 2003) despite the HRBC having a large amount of haemoglobin inside the cell which might lead to the belief that its conductivity would be unrepresentative. Of more physiological relevance is the HRBC conductivity at 37°C; $\sigma_{37} = 1.156 \pm 0.0188 \text{ S m}^{-1}$ ($\pm \text{SE}$, $n = 4$) in the present study which is very nearly twice the value found at the standard measuring temperature of 25 °C. Conductivity information on HRBC cells is useful information because the conductivities of most cells are not practically measureable whereas the conductivity of the HRBC is easily measured by very simple techniques and by more than one method.

Conclusions

Our study has shown that the cytoplasmic electrical conductivity of red blood cells can be estimated from very simple experimental observations *independently* of dielectric methods. This ability to estimate conductivity independently is important in validating dielectric experiments and for modelling the electrical behaviour of the HRBC. Cell volume of human erythrocytes is sensitively affected by both external ionic concentrations and to temperature. It was found experimentally that the conductivities increased by a factor of 1.866 ± 0.0377 for every increase in temperature of 10°C and hence the Q_{10} of cytoplasmic conductivity vs. temperature has a value of ≈ 2 . The alteration of cell volume induces changes in the cytoplasmic conductivities which depend exponentially on temperature. The convention of quoting conductivities at 25 °C can be misleading physiologically because conductivity is exponentially related to temperature (Fig. 2): the conductivity at normal body temperature (37 °C) is $1.18 \pm 0.02 \text{ S m}^{-1}$, $\pm \text{SE}$, $n = 4$) based on the curve fit. The conductivity of HRBC in a patient with a severe fever

(40 °C) would have a conductivity exceeding 1.4 S m^{-1} . The experimentally determined Q_{10} of ≈ 1.866 is a typical Q_{10} value found in many biological systems, including cation transport in red blood cells (Laidler and Meiser, 1995). A Q_{10} of 2 implies surprisingly large effects of small errors in temperature in biological systems: for example an error of 1°C in the experimental temperature will result in a greater than 7% error in a conductivity determination of a living cell but only a 2% error in that of a NaCl solution. However, this temperature effect would be easy to allow for in an experiment if the experimental temperature is carefully monitored. The results suggest that in future experiments on cellular mobility in strong electric fields (Gimsa et al., 1996; Sudsiri et al., 2002, 2007) special attention to the temperature will have to be made since a temperature increase will be induced by Joule heating, especially at high media conductivities as already reported by Sudsiri et al. (2007).

References

- [1] H. Pauly, H.P. Schwan, Dielectric properties and ion mobility in erythrocyte, *Biophys. J.*, 6: 621-639, 1966.
- [2] R. Glaser, The shape of red blood cells as a function of membrane potential and temperature, *J. Membrane Biol.*, 51: 217-228, 1979.
- [3] K. Murata, K. Mitsuoka, T. Hirai, T. Walz, P. Agre, J.B. Heymann, A. Angel, Y. Fujiyoshi, Structural determinants of water permeation through aquaporin-1, *Nature*, 407: 599-605, 2000.
- [4] I. Bernhardt, A.C. Hall, J.C. Ellory, Effects of low ionic strength media on passive human red cell monovalent cation transport, *J. Physiol.-London*, 434: 489-506, 1991.
- [5] J.C. Parker, In defence of cell volume, *Am. J. Physiol.-Cell Ph.*, 265: C1191-C1200, 1993.
- [6] C.W. O'Neill, Physiological significance of volume-regulatory transporters, *Am. J. Physiol.-Cell Ph.*, 276: C955-C1011, 1999.
- [7] R. Glaser, J. Donath, Stationary ionic states in human red blood cells, *Bioelectroch. Bioener.*, 13: 71-83, 1984.
- [10] L.K. Laidler, J.H. Meiser, *Physical Chemistry*, Houghton Mifflin, Boston, 1995.
- [11] M.M. Gedde, W.H. Huestis, Membrane potential and human erythrocytes shape, *Biophys. J.*, 72: 1200-1233, 1997.
- [12] A.L. Harris, C.C. Guthe, F. Van't Veer, D.F. Bohr, Temperature dependence and bi-directional cation fluxes in red blood cells from spontaneously hypertensive rats. *Hypertension*, 6: 42-48, 1984.
- [13] J. Chuaibamrung (Sudrisi), Influence of cell shape and cell volume on cytoplasmic conductivity of human red blood cells, *Journal of Microscopy Society of Thailand*, 23: 1-6, 2009.
- [14] R. Glaser, *Biophysics*, Springer, Berlin, Germany, 2000.

- [15] P.S. Nobel, Physicochemical and Environmental Plant Physiology, fourth ed., Academic Press, Amsterdam & Boston, 2009.
- [16] N. Sperelakis, Cell physiology, Academic Press, San Diego, USA, 1995.
- [17] J. Seidl, R. Knuechel, L.A. Kunz-Schughart, Evaluation of membrane physiology following fluorescence activated or magnetic cell separation, Cytometry, 36:102-111, 1999.
- [18] G. Fuhr, R. Glaser, R. Hagedorn, Rotation of dielectrics in a rotating electric high-frequency-field: Model experiments and theoretical explanation of the rotation effect of living cells, Biophys. J., 49: 395, 1986.
- [19] J. Sudsiri, D. Wachner, J. Donath, J. Gimsa, Can molecular properties of human red blood cells be accessed by electrorotation? Songklanakarin J. Sci. Technol., 24: 785-789, 2002.
- [20] J. Krupa, J. Terlecki, A Nondestructive Method for Measuring Electrical Conductivity of intracellular Matter of Tissue *in situ*, Rad. and Environm. Biophys., 13: 79-88, 1976.
- [21] K. Asami, T. Yamaguchi, Dielectric spectroscopy of plant protoplasts, Biophys. J., 63:1493-1499, 1992.
- [22] R. Hölzel, I. Lamprecht, Dielectric properties of yeast cells as determined by electrorotation, Biochim. Biophys., Acta 1104:195-200, 1992.
- [23] R. Hölzel, Electrorotation of Single Yeast Cells at Frequencies Between 100 Hz and 1.6 GHz, Biophys J., 73: 1103-1109, 1997.
- [24] J. Suehiro, R. Hamada, D. Noutomi, M. Shutou, M. Hara, Selective detection of viable bacteria using dielectrophoretic impedance measurement method, J. Electrostat., 57:157-168, 2003
- [25] J. Gimsa, T. Mueller, T. Schnelle, G. Fuhr, Dielectric spectroscopic of single human erythrocytes at physiological ionic strength: dispersion of cytoplasm, Biophys. J., 71: 495-506, 1996.
- [26] J. Sudsiri, D. Wachner, J. Gimsa, On the temperature dependence of the dielectric membrane properties of human red blood cells, Bioelectrochemistry, 70: 134-140, 2007.

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Development of the infrared images processing algorithm for the automatic detection of the early stage of periodontal disease

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Introduction

According to the WHO, inflammatory periodontal diseases occur in 90-95% of the adult population and lead to pathological changes in the dentoalveolar system [1].

Diagnosis is more based on visual examination of the oral cavity and index evaluation of the soft tissue periodontal conditions and is subjective. In most cases, patients already diagnosed with signs of inflammatory diseases are diagnosed, diagnosis at an early stage of inflammation causes significant difficulties, since there are no clinical manifestations of the inflammatory process [2-5].

As a result of previous studies, the possibility of visualization of the foci of inflammation of soft periodontal tissue (hereinafter – SPT) at an early stage has been established [1-8].

The purpose of this study is the development and testing of an algorithm for the automatic detection of foci of inflammation in the IR images of SPT. In the course of the research, the following tasks were set and solved:

- the effectiveness of segmentation algorithms is investigated when inflammation foci are detected at various stages of the inflammatory process;
- an assessment of the quality of the algorithm for automatic detection of inflammatory foci on the IR images of SPT was carried out.

Materials and Methods

The study was carried out using a verified database of 150 IR images of SPT at various stages of the inflammatory process, formed as a result of previous studies [7]. The Database contains of 20 IR images of Intact SPT, 70 IR images of the stage of the SPT early inflammation and 60 IR images of the stage of the SPT severe inflammation.

The choice of informative parameters of inflammatory foci is expedient to be carried out taking into account the laws of visual perception. High contrast of the object with the background is easier to perceive with the eye, which allows to identify the primary symptoms of the inflammatory process on the IR images of the SPT. The contrast in its turn is due to the intensity differences in the image. Thus, to determine the distinctive features of the inflammatory foci, the parameters characterizing the spatial dis-

tribution of the energy of inflammatory foci in the IR images of the SPT are analyzed, see tab. 1.

Table 1: Contents of the IR image of SPT database

№	The parameter (pi)	Formula for calculation	Notation
1	Average intensity	$I_m = \frac{1}{N} \sum_{i=1}^N I_i$	I _i – intensity of the i-th element of the image
2	Selective SD	$S_I = \frac{1}{N} \sum_{i=1}^N (I_i - I_{cp})^2$	
3	Coefficient of contrast at the border of the focus of inflammation of SPT	$C_a = \frac{I_{max} - I_{min}}{I_{max} + I_{min}}$	I _{max} , I _{min} – the maximum and minimum modes of intensity histogram
4	Modulus of gradient on the border of the inflammatory focus of SPT	$G = \sqrt{G_x^2 + G_y^2}$	G _x =dI/dx, G _y =dI/dy are the intensity gradients in the horizontal and vertical directions, respectively
5	The ratio of average intensities	$r = \frac{I_m}{I_o}$	I _o is the average intensity of the image

In the course of the studies it was established that the IR images of the SPT at the stage of early and severe inflammation differ from intact tissues by the mean intensity I_m , the selective mean square deviation S_I , the contrast coefficient at the border of the inflammatory focus of the SPT C_a , the gradient modulus at the border of the inflammatory focus of the SPT G and the ratio average intensities r , see tab. 2.

Table 2: Values of informative parameters of inflammatory foci on IR images of SPT

№	Parameters			
		Intact tissues	early inflammation	severe inflammation
1	I_m	0,39± 0,04	0,36± 0,01	0,71± 0,02
2	S_I	0,03± 0,01	(70± 1)10 ⁻³	(60± 1)10 ⁻³

3	Ca	$0,33 \pm 0,02$	$0,54 \pm 0,02$	$0,55 \pm 0,15$
4	G	$(18 \pm 3)10^{-4}$	$(50 \pm 1)10^{-4}$	$(48 \pm 1)10^{-4}$
5	r	$1,18 \pm 0,18$	$1,82 \pm 0,18$	$3,68 \pm 0,78$

There were threshold segmentation with the parameters C_a , G , and a watershed method applied for automatic segmentation of the centers of an inflammation on IR images of SPT.

The calculation of I_m , S_I and r were carried out within the investigated area of the potential focus of inflammation, and for G and Ca – outside. If the obtained values of informative parameters belong to the confidence intervals of the foci of inflammation, then the region was classified as a foci of inflammation, if not, then intact tissues.

The evaluation of the segmentation quality was carried out by calculating the relative error of the detection of foci for each of the algorithms:

$$k = 100 - \frac{S_a}{S_m} \cdot 100 \quad (1)$$

where k is the relative error, S_a – the area of the focus of inflammation, obtained in the mode of automatic allocation using the considered segmentation algorithms, S_m – the area of the focus of inflammation, allocated manually. The S_a and S_m were determined by counting overall pixels quantity of the segmented areas. The smaller the relative error of the two areas, the more accurately the area of the focus of inflammation of the SPT is segmented.

Results

The results of the segmentation quality estimation are presented in tab. 3.

Table 3: The value of the relative error

Algorithm	Stages of inflammation	
	Stage of early inflammation	Stage of severe inflammation
Threshold segmentation using C_a	6,2%	3,15%
Threshold segmentation using G	16,1%	32,3%
Watershed method	–	15,3%

Discussion

The segmentation algorithm modulating the gradient on the boundary of the focus of inflammation with the use of a sliding mask showed the highest relative segmentation error, because at the time of registration, artifacts, such as salivation, with a high modulus of the gradient appear on the IR images of the SPT, which in turn leads to the detection of regions that do not correspond to the centers of inflammation of the SPT.

The algorithm for segmentation of inflammatory foci on the basis of the watershed method showed good results when a stage of severe inflammation was detected on the

IR images of SPT. Foci of early inflammation of SPT by the watershed method are not segmented, which makes it impossible to apply this algorithm as a universal method for segmentation of inflammatory foci for various stages of the inflammatory process of SPT.

The segmentation algorithm based on the contrast ratio at the boundary of the SPT inflammation focus with the use of a sliding mask is the best and provides the lowest relative segmentation error.

Conclusions

As a result of the study, it was established that the least relative error of segmentation of inflammatory foci on IR images of SPT provides an algorithm for automatically detecting inflammatory foci by the contrast ratio at the border of the SPT inflammation focus using a sliding mask.

References

- [1] Gazhva S.I., Guluev R.S. Prevalence and intensity of inflammatory periodontal diseases (literature review) // Obozrenie. 2012. №1(75). P. 13-14
- [2] Zorina O.A., Aimadinova H.C., Rebrikov D.V. Early diagnosis of periodontitis on the basis of the analysis of the relationship between clinical signs and molecular markers. News of science Proceedings of materials the international scientific conference. 2015. P. 374-376.
- [3] Zorina O.A., Berkutova I.S., Sych M.Y. Monitoring the state of the microbiocenosis of the periodontal pocket in patients with chronic generalized and aggressive periodontitis. Actual directions of scientific research of the XXI century: theory and practice. 2013. № 1. P. 26-33.
- [4] Grudyanov A.I., Dmitrieva N.A., Kurchaninova M.G., Krishtop V.V. Changes in the composition of the microflora of the dentogingival sulcus in the process of orthodontic treatment. In the collection: From the Faculty of Advanced Medical Education - to the Institute of Postgraduate Education: History and Achievements Materials of the Jubilee Scientific and Practical Conference on the 30th Anniversary of the Institute of Postgraduate Education IvGMA. Executive Editor A.E. Baklushin. 2015. P. 101-102
- [5] Grudyanov A.I., Fomenko E.V. Methods of conservative treatment of inflammatory periodontal diseases. Moscow, 2013.
- [6] Kolpakov A.V., Makarov A.L., Spiridonov I.N. The use of the method of infrared diaphanoscopy for assessing the state of soft tissues of the oral cavity in stomatology // Science and education: electronic scientific and technical publication. 2013. №12. P.297-306.
- [7] Kolpakov A.V., Makarov A.L., Spiridonov I.N. Investigation of the absorption of optical radiation by soft periodontal tissues // Science and education: electronic scientific and technical edition. 2014. №11. P.444-457
- [8] Kolpakov A.V., Ydin I.N., Zorina O.A., Spiridonov I.N. Early detection of foci of inflammation in soft periodontal tissues with the help of infrared diaphanoscopy // Medical technology. 2016. №2. P.10 – 13
- [9] Bobkova A.O., Porshnev S.V., Zuzin V.V., Bobkov V.V., Investigation of methods for removing speckle noise on ultrasound images. 23rd International Conference "Computer Graphics and Sight - GraphCon 2015" - Vladivostok, Russia, Reports.

Computational modelling of electroaerosol flows during external therapy

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Introduction

Burn injuries are one of the most important modern social and medical issue due to its prevalence, high death rate and considerable rate of temporary inability of working and primary disability [1]. Extensive burns cause huge losses of blood and weakness of the body therefore making sick man vulnerable to the infections which lead to inflammation [2].

Electroaerosol therapy is one of the methods of burns treatment. Exposing the burn wound to negatively charged medical aerosol particles. Under the impact of negative charge, the improvement of absorbability and pharmacologic properties of medical aerosols is occurred. It is known that thanks to negatively charged medical aerosols the perfusion is increased that helps with regeneration [3]. Moreover, electroaerosols have distinct bactericidal effect, they are able to inhibit the growth of various bacteria and fungi [4].

Unlike pharmacologic methods, electroaerosol therapy is less toxic and dangerous to body, and it is considered to be effective in burns treatment and allows considerably lower the dose of medicamental burden.

The aim of this study is the research of flow rates of electroaerosols in the workspace of the device of electroaerosol therapy.

Materials and Methods

Solving stated task, the geometrical model of device's workspace chamber, shown on fig. 1, was suggested. This model consists of air space (surfaces 5 and 6) between biological object (surface 7) and workspace chamber (surfaces 1 and 2), and ionizing electrode (surfaces 3 and 4).

To compute this model, we did assume that the flow of electroaerosols is laminar, it is modelled as Newtonian incompressible fluid, there are no particle coagulation and recombination of charges. We consider that the velocity of particles and air flow are equal, and electroaerosols are water spheres.

Flow rates of electroaerosols in workspace were computed using the following equations:

- Fick's convection and diffusion [5]:

$$\nabla \cdot (-D_i \nabla c_i - z_i \cdot \text{mob} \cdot F \cdot \nabla V) + \vec{U} \cdot \nabla c_i = R_i, \quad (1)$$

$$N_i = -D_i \nabla c_i - z_i \cdot \text{mob} \cdot F \cdot \nabla V + \vec{U} c_i; \quad (2)$$

where c – concentration (mol/m³), D – diffusion coefficient (m²/s), z – ion's charge, mob – ion's mobility in an electric field (s·mol/kg), F – Faradey constant, R – reaction rate constant (mol/(m³·s));

- Navier-Stokes' laminar flow [6]:

$$\frac{\partial \vec{U}}{\partial t} = (-\vec{U} \cdot \nabla) \vec{U} + \nu \Delta \vec{U} - \frac{1}{\rho} \nabla P + \vec{f} + \vec{g}, \quad (3)$$

$$\nabla \vec{U} = 0, \quad (4)$$

where $\vec{U}$ – velocity (m/s), ν – kinematic viscosity (m²/s), ρ – density (kg/m³), P – pressure (Pa), $\vec{f}$ – vector field of mass forces, $\vec{g}$ – gravitational acceleration;

- Electrostatics [7]:

$$\vec{E} = \nabla V, \quad (5)$$

$$\nabla \cdot \vec{D} = \rho_v, \quad (6)$$

where $\vec{D}$ – electric displacement field (C/m²), ρ_v – spatial charge density (C/m³), $\vec{E}$ – electric field (V/m), V – electric potential (V).

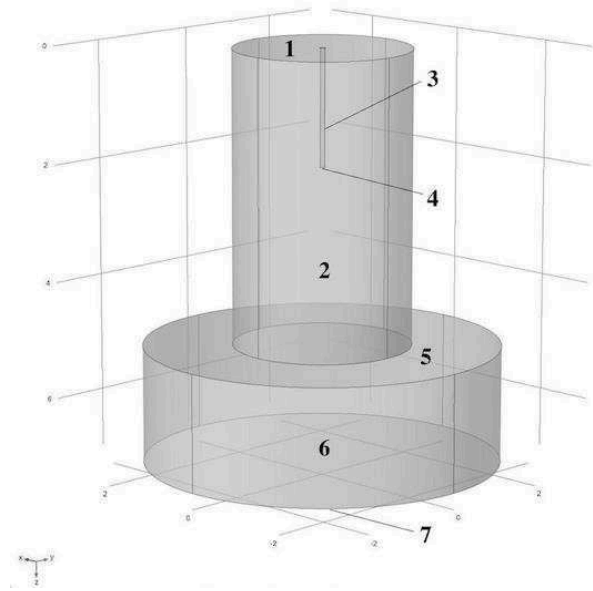


Figure 1: Geometrical model of device's workspace

To compute the ratio of electroaerosol particles on the bioobject's surface the following equations of forces affecting particles in the air flow were used [5, 6, 7]:

- Newton's law:

$$\frac{d(m_p v)}{dt} = F_t, \quad (7)$$

- Friction force:

$$F_D = \left(\frac{18\mu}{\rho_p d_p^2} \right) m_p (u - v), \quad (8)$$

- Brownian force

$$F = \zeta \sqrt{\frac{12\pi k_B \mu T r_p}{\Delta t}}, \quad (9)$$

- Electrostatic force

$$F = eZ(-\nabla V), \quad (10)$$

- Gravitational force

$$F_g = m_p g \frac{(\rho_p - \rho)}{\rho_p}, \quad (11)$$

where m_p – particle mass (kg), v – particle velocity (m/s), t – time (s), F_t – force affecting particle (N), u – airflow velocity (m/s), ρ_p – air density (kg/m³), ρ_p – particle density (kg/m³), d_p – particle diameter (m), μ – air dynamic viscosity (Pa·s), k_B – Boltzmann constant, T – absolute temperature (K), r_p – particle radius (m), ζ – proportionality coefficient.

All these equations were solved concurrently using finite-element methods.

To study the electroaerosol flow rates we did set the following boundary conditions: walls (surface 2) of workspace chamber and bioobject's surface (surface 7) are no slip; relative pressure at the inlet (surface 1) of workspace chamber P_{in} ; relative pressure at the outlet (surfaces 5 and 6) of workspace chamber $P_{out}=0$; side walls (surface 2) of workspace chamber and bioobject's surface have zero potential (ground); potential on ionizing electrode (surfaces 3 and 4) is $UI=-25$ kV; zero charge on inlet and outlet (surfaces 1,5 and 6); initial particle concentration in an entire model is 0 mol/m³; Inflow – surface 1 – concentration $Caer=0$ mol/m³; concentration $Caer_m=1,5 \cdot 10^{-16}$ mol/m³ on the edge (surface 4) of ionizing electrode; walls (surface 2) of workspace chamber and bioobject's surface (surface 7) are perfectly adsorbing walls – concentration $Caer=0$ mol/m³; Outflow – surfaces 5 and 6.

Results

Trajectories of particles with diameters 10 μ m and 40 μ m while the workspace chamber is parallel to gravity force vector $\vec{g}$ were obtained, which are shown on figures 2 and 3. It is considerable that the bigger the diameter of particles is the greater quantity of them reaches the bioobject's surface.

The effect of gravity force and particle diameter on electroaerosol flow particles ratio on bioobject's surface was studied in two workspace chamber's positions: vertical (chamber's axis was parallel to gravity force vector $\vec{g}$) or horizontal (chamber's axis was perpendicular to gravity force vector $\vec{g}$). We studied the dependence of diameter of electroaerosol particles and the part of electroaerosol particles reaching the bioobject's surface (particle ratio). The dependence is shown on figures 4 and 5.

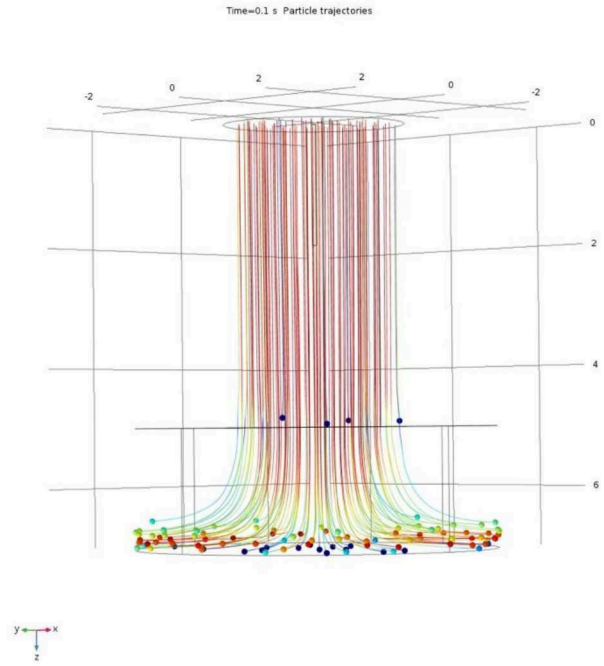


Figure 2: Trajectories of particles with diameter 10 μ m while the workspace chamber is parallel to gravity force vector $\vec{g}$

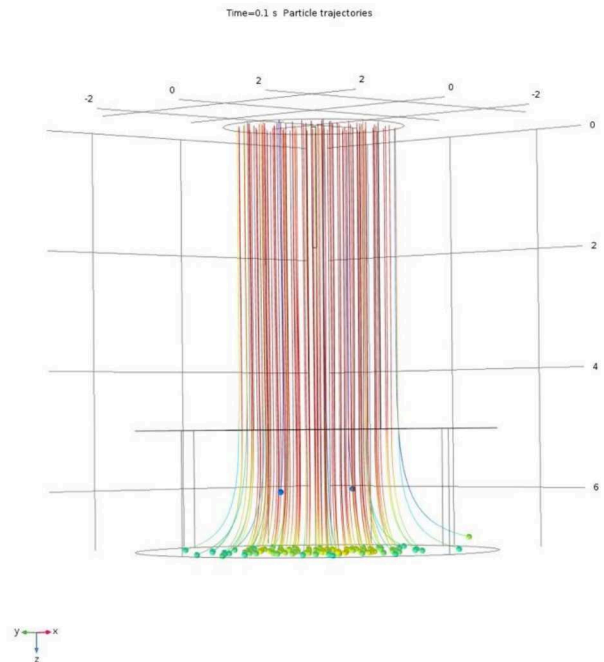


Figure 3: Trajectories of particles with diameter 40 μ m while the workspace chamber is parallel to gravity force vector $\vec{g}$

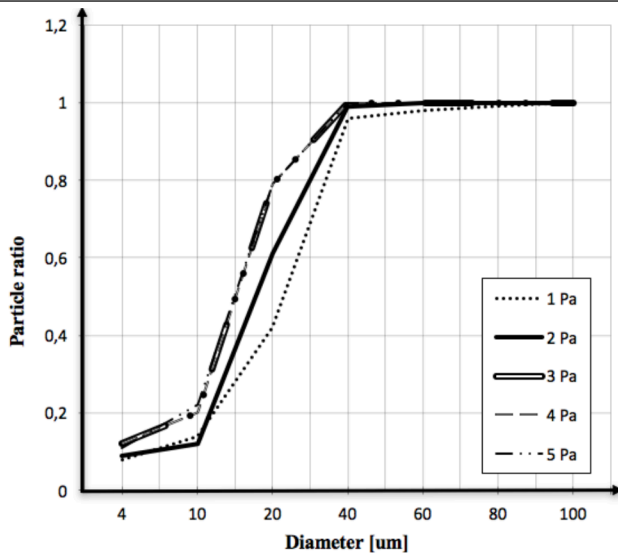


Figure 4: The dependence of particle ratio and diameter while the workspace chamber is parallel to gravity force vector $\vec{g}$

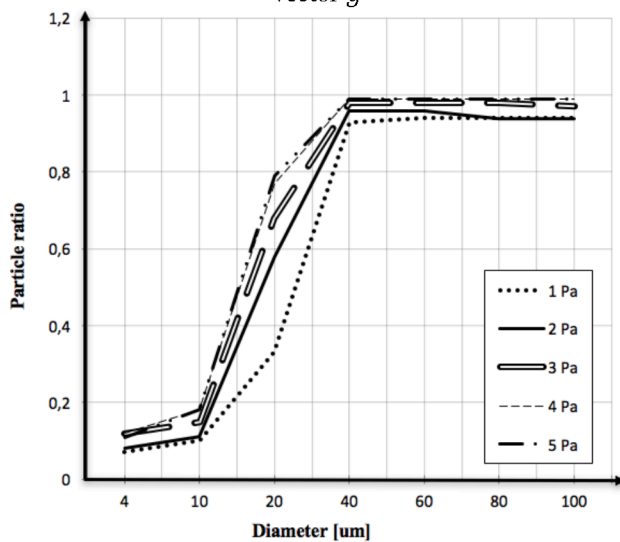


Figure 5: The dependence of particle ratio and diameter while the workspace chamber is perpendicular to gravity force vector $\vec{g}$

Conclusions

During the research, it was confirmed that electroaerosol particles with the diameter 40 μm and more reach the burned bioobject's surface the most effectively independently of the workspace chamber position. Recommended input pressure is 3 and more Pa because it provides greatest quantity of electroaerosol particles on burned bioobject's surface.

References

- [1] T. A. Spanholtz, P. Theodorou, P. Amini, G. Spilker. Severe burn injuries. Acute and long-term treatment. *Deutsches Arzteblatt Int*, 106(38): 607–613, 2009.
- [2] M. G. Jeschke, D. L. Chinkes, C. C. Finnerty et al. The pathophysiologic response to severe burn injury. *Ann Surg*, 248(3): 387–401, 2008.
- [3] A. N. Sheina. *Aerosolterapiya. Kremlyovskaya medicina (klinicheskiy vestnik)*, 1: 154–160, 2014.
- [4] Xiaoxia Xie, Lei Chen, Zhao-Qiang Zhang et al. Clinical study on the treatment of chronic wound with negatively-charged aerosol. *Int J Clin Exp Med*, 6(8): 649–654, 2013.
- [5] E. M. Harding Jr., E. J. Berg, R. J. Robinson. Diffusion in replica healthy and emphysematous alveolar models using computational fluid dynamics. *ISRN Biomedical Engineering*, 2013.
- [6] M.S. El-Genk, Yang In-Hwan. A numerical analysis of laminar flow in micro-tubes with a slip boundary. *Energy Convers Manag*, 50: 1481–1490, 2009.
- [7] H. Labair, S. Touhami, A. Tilmatine et al. Study of charged particles trajectories in free-fall electrostatic separators. *J. Electrostat.* 2017.
- [8] G.M. Hidy. *Aerosols. Encyclopedia of Physical Science and Technology (Third Edition)*. 2003.

Experimental study of the mechanical properties of materials for physical modelling of biological tissues

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Introduction

Testing of the different modes of surgical devices includes tests on autopsy material. In this case, the major limitations are difficult biological samples acquisition, the heterogeneity of tissue properties and the dependence of mechanical properties on storage time and temperature.

An alternative to testing on autopsy materials is the modeling of surgical intervention. Modeling can be physical, analytical and computer-simulated.

Computer-simulated modeling (finite element analysis) has the advantage of unlimited ranges of parameter changes in the study. However, the parameters for the analysis are rarely fully described for biological tissues. Also, the computer modeling is a solution to a simplified task, which do not reflect all processes occurring in a real operation. Analytical modeling offers investigation of mathematical models of biological tissues, but the modeling of surgical exposure is also simplified.

Physical modeling offers a possibility to study the effect of surgical intervention on the physical model of tissue (phantom). The physical model simulates the target tissue. It is made from material that fits best the required criteria, for example the Young's modulus. Therefore, in tests on blood vessels, for example, it would be much easier to have a model that could mimic the physical vascular properties.

A paper review of the values of the Young's modulus for various vessels and their layers showed that according to [1], the static Young's modulus of the coronary artery is 2.3 MPa with a tensile pressure of 100 mm Hg. For the abdominal aorta the Young's modulus lies in the range from 0.1 MPa to 1.2 MPa at a tensile pressure from 1 mm Hg. to 90 mm Hg. [2]. According to [3], the Young's modulus of the coronary artery in men, depending on age, lies in the range from 0.9 MPa to 5 MPa. For women, the range is from 0.9 MPa to 4 MPa.

Physical models allow tests on large volumes of samples, in comparison with the autopsy material. Homogeneity of phantom properties increases the repeatability of results. The method of physical modeling allows to more accurately estimate the influence on tissue comparing to analytical and finite element modeling.

Materials used for physical modeling are often made by mixing two components: the main component (MC) and the supplementary one. When the ratio of MC in the mixture changes, the mechanical properties of the model also change. In this paper, the criterion for the similarity of material and biological tissue are mechanical characteristics. The main mechanical characteristic of the material is the Young's modulus, so the selection of the material is based

on the correspondence of the Young's modulus to the real tissues.

For some materials, there is a wide range of values. It is due to the dependence of the mechanical properties on the ratio of mixing components in it. Ranges of possible values of the Young's modulus for some materials are presented in Fig. 1. [4]

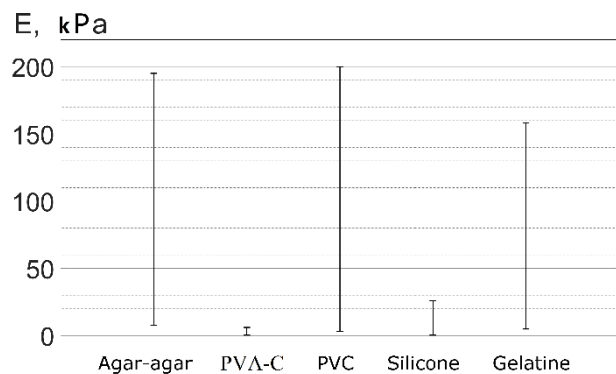


Figure 1: Mechanical properties of phantom materials

In [5] the Young's modulus for pure gelatin with concentrations of 25-30% was calculated. The range of values is 0.07-0.1 MPa. In [6] the values of the Young's modulus for gelatin mixtures are 0.4 kPa for gelatin-water mixture, 0.8 kPa for gelatin-water-sugar, 0.6 kPa for gelatin-water-sugar-citric acid.

In [7], there are dependences of the Young's modulus of gelatin and agar-agar on their concentrations $E_{gel} = 0,349 \cdot C^{1,87}$, $E_{agar} = 0,0034 \cdot C^{2,09}$, where C is the concentration in g/l of gelatin and agar-agar, respectively. Although, the chosen ranges of concentrations were not justified and these equations are applicable only within these ranges.

Taking into account the dependence of the mechanical properties on the ratio of mixing components, the most accurate simulation of the mechanical properties of biological tissue is possible by choosing the material of the most suitable concentration.

It is useful to cover the widest possible range of material properties to be able to mimic any type of biological tissue using chosen materials. According to the data shown in the Fig. 1, it is wise to choose gelatin and silicone for the current study. Gelatin is the most widely used material for physical models and therefore its mechanical properties at different concentrations are very useful to compare and refine the results of other studies. PVA-C could also be used

in this study but its drawback is a complex and long preparation procedure, especially for multi-layer structures. Unfortunately, biological tissues usually require multi-layer physical models.

However, as it was shown previously, in existing studies of the mechanical properties of materials for physical models, there is no clear dependence of the mechanical properties on the concentration under compression and stretch over the entire range of concentrations.

In this paper, we investigated the widest ranges of possible ratios of the components to be mixed when testing materials for compression and stretch. The dependence of the Young's modulus on concentration was investigated.

Materials and Methods

Materials

In the current work studies were conducted on gelatin and silicone. The dependence of the mechanical properties of these materials on the value of the mass fractions of their MC: gelatin and silicone gel, respectively, was investigated.

Mass fraction of MC can be expressed as:

$$\omega = \frac{m_{MC}}{m_{Mixture}} \times 100\% \quad (1)$$

where m_{MC} is the mass of MC, $m_{Mixture}$ is the mass of the mixture.

The solution for the samples was made from gelatin ("Dr. Oetker" brand) by adding water at a temperature of 60-70°C. It was poured into cylindrical containers (for compression tests) or flat containers (for tension tests) and placed in the refrigerator (temperature + 4°C) for 6 hours until complete solidification. To facilitate the extraction of samples, the forms were pre-lubricated with petroleum jelly.

Gelatin was tested for compression with a mass fraction ranging from 2% to 50%. The tensile samples were tested with a mass fraction of MC ranging from 10% to 40%.

The types of silicones vary significantly from soft to hard ones, the latest can be used for example for tires production. To simulate biological tissue, that is rather fragile, we searched the softest silicone. To measure the hardness of low-modulus materials (plastics, elastomers, rubbers, etc.),

From fig. 2 the softest silicone (Extra soft) is type 00. But silicones of this type are too expensive, therefore, type A was chosen for the tests. Among this type, a silicone compound Alcorsil 315 based on tin was chosen, its technical characteristics are given in the tab. 1. Compound consists of two parts - silicone gel (part A) and hardener (part B).

Table 1: Parameters of Silicone Alcorsil 315

Parameters	Values
Ratio by weight	100 A: 5 B
Viscosity of the mixture, cP	10,000 ± 2000
Life time	20-40 min
Curing time, at 23 ° C	4-6 hours
Shore A / D hardness	15 ± 2 A
Density, g / cm ³	1.08
Tensile strength, MPa	≥2.75
Breaking strength, MPa	≥1.77
Elongation at break,%	≥363
Linear shrinkage,%	<1

From tab. 1, the recommended ratio of weight parts (A:B) is 20:1. the upper and lower limits of silicone hardening were investigated within ± 900%, which is from 1:1 to 200:1.

For ease of mixing, the mass ratio was converted into a volume ratio. Corresponding component densities: $\rho_A = 1,125 \text{ g / cm}^3$, $\rho_B = 0,96 \text{ g / cm}^3$.

The solidification threshold ratio was investigated in droplets of small volumes. The suitable lower limit of volume ratio was 2:1 and the upper limit was 40:1. At lower ratios, a homogeneous compound was impossible to achieve due to instant solidification. At larger ratios no solidification occurred even after 24 hours. The later studies showed that samples with ratios 2:1 and 3:1 did not solidify in the syringe, but only in air and therefore were also excluded from the experiment.

Thus, Alcorsil 315 was tested within the range of a mass fraction of 75 - 97.6% for tensile and 80 - 97.6% for compression.

All samples were divided into groups by material, type of test and mass fraction of MC. Each group contained 3-5 samples.

Methods

For compression, the samples were made in form of cylinders 10 mm long. The nature of the destruction of gelatin samples in compression tests depended on the concentration of MC. Low concentration samples typically split into 3-5 pieces, while high concentrations samples crushed. Dumbbell samples for tensile tests were cut with a die. During the stretching, the wide part of the sample slipped out of the clamps; therefore, to increase the friction pieces of insulating tape were glued for the gelatin samples and adhesive tape for the silicone samples (figure 3). The rupture of the silicone samples occurred layer by layer.



a Shore hardness scale is used (fig. 2) [8].

Figure 2: Shore hardness scale



Figure 3: Stretching test of gelatin (left) and silicone (right) samples.

The thickness of the samples was measured with a micrometer. In the test on the Instron 3365 test machine, the dependence of the force on elongation was recorded. Then, from the experimental data, the dependence of the stress on the deformation was calculated as follows:

$$\sigma = \frac{F}{S}; \varepsilon = \frac{\Delta l}{l} \quad (2)$$

where F is the registered force, S - initial cross-sectional area of the sample, Δl - elongation, l - initial length.

The Young's modulus was calculated in the linear section of the stress-strain curve.

Results

The dependence of the average values of the Young's modulus on the mass fraction of MC for each group is shown in figures 4-7. There were 4 different groups for two types of materials and two types of tests: tension and compression.

The average value of the Young's modulus for each mass fraction is showed by an asterisk. The exact values are shown by red crosses. The error bars show the confidence interval of 95% for each mass fraction.

The average values for each group were approximated for best visualization. The lowest possible order of approximation was chosen. The order of approximation varies between different groups.

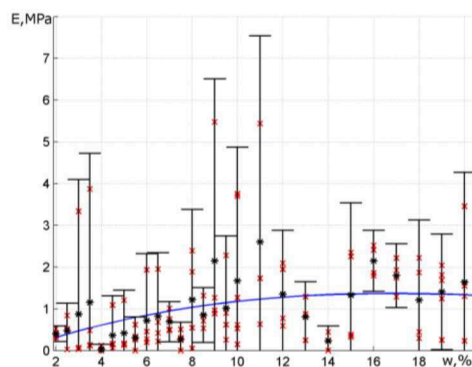


Figure 4: Dependence of the Young's modulus on gelatin concentration under compression

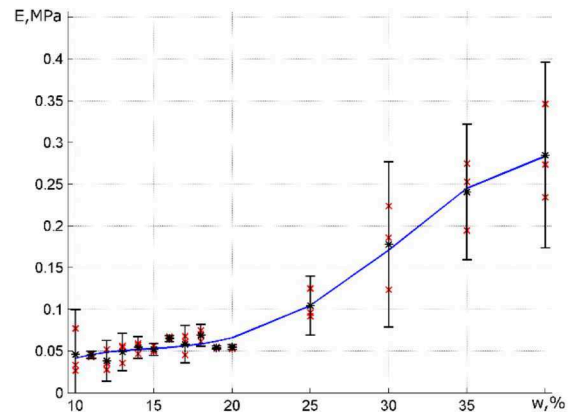


Figure 5: Dependence of the Young's modulus on gelatin concentration in tension

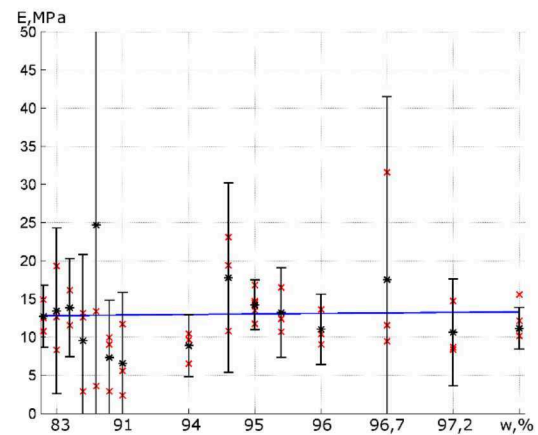


Figure 6: Dependence of the Young's modulus on silicone concentration under compression

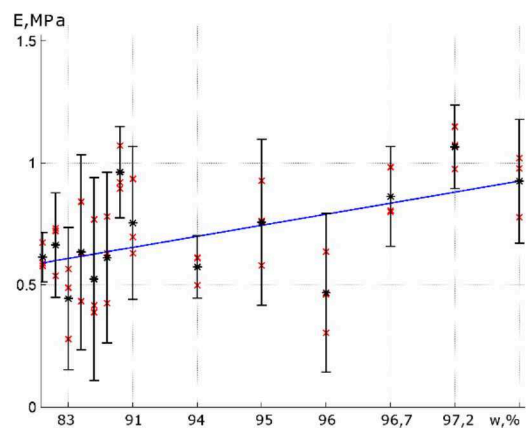


Figure 7: Dependence of the Young's modulus on silicone concentration in tension

Discussion

In this work materials for the physical modelling of biological tissues were tested under compression and stretch to find the strength properties, depending on the mass fraction of MC. The results for each group of samples were approximated.

This work allows to choose to the right concentration of material to get the physical model with exact physical properties of the target tissue.

As expected, the dependence of the Young's modulus on the mass fraction of silicone is more linear than for gelatin, which conforms well the literature review. Its Young's modulus is closer to vascular tissue so for vascular physical models it fits better. Also, silicone characteristics do not change with time and, most importantly, do not depend on temperature changes. This fact confirms the expediency of using silicone for modeling biological tissues.

According to the graphic results, we conclude that the dependence of the Young's modulus on the mass fraction for silicone is insignificant. Thus, it is necessary to choose a silicone with the Young's modulus that closely matches the parameters of the target tissue.

Gelatin required not only the exact conditions of storage and preparation, but it also quickly lost its properties due to drying or melting. Gelatin is good for model making because of its high variability of parameters. This makes it suitable for modeling a wide range of materials.

However, it should be noted that these materials are not suitable for vascular models. If we develop a blood vessel model we should use harder silicones or gelatin mixtures. These mechanical properties were investigated only in the linear portion of the stress-strain curves. This does not fully describe the nonlinear behavior of the material. Materials for physical modeling behave nonlinearly, like biological tissues [9]. Thus, it is also planned to study nonlinear mechanical properties of materials for physical modeling for the fine selection of material concentration to model specific tissues.

References

- [1] Gow, B. S., & Hadfield, C. D. The elasticity of canine and human coronary arteries with reference to postmortem changes. *Circulation research*, 45(5):588-594, 1979.
- [2] Drangova, M., Holdsworth, D. W., Boyd, C. J., Dunmore, P. J., Roach, M. R., & Fenster, A. Elasticity and geometry measurements of vascular specimens using a high-resolution laboratory CT scanner. *Physiological measurement*, 14(3): 277, 1993
- [3] Kasjanovs, V., Ozolanta, I., & Purina, B. Features of biomechanical properties of human coronary arteries. *Mechanics of composite materials*, 35(2):155-168, 1999
- [4] Hungr, N., Long, J. A., Beix, V., & Troccaz, J. A realistic deformable prostate phantom for multimodal imaging and needle-insertion procedures. *Medical physics*, 39(4):2031-2041, 2012
- [5] Cheremnykh, A. V., Gladkov, A. S., Afonkin, A. M., Potekhina, I. A., Serebryakov, E. V., Kuzmin, I. V. Modeling of the stress-strain state in the vicinity of the fault node of the kimberlite pipe area "Mir" (the Yakut diamond-bearing

- province) (Моделирование напряженно-деформированного состояния в окрестностях разломного узла района кимберлитовой трубки «Мир»). *Izvestiya SO RANS. Geology, prospecting and exploration of ore deposits*. 1, 2014.
- [6] Tsyusupova, B. B., Artykova, D. M., Tazhibaeva, S. M., Musabekov, K. B., Esimova, O. A. Structurization in pectin-containing food systems (Структурообразование в пектинсодержащих пищевых системах). *Kazakh National University named after al-Farabi, Almaty, Kazakhstan*
- [7] Hall, T. J., Bilgen, M., Insana, M. F., & Krouskop, T. A. (1997). Phantom materials for elastography. *IEEE transactions on ultrasonics, ferroelectrics, and frequency control*, 44(6), 1355-1365.
- [8] Taylor R. A Guide to Shore Durometers. Albright Silicone [Internet]. 2015 Jan [cited 2018 March 28];[about 1 p.]. Available from: <https://albrightsilicone.com/a-guide-to-shore-durometers>
- [9] Fung, Yuan-cheng. *Biomechanics: mechanical properties of living tissues*. Springer Science & Business Media, 2013.

Neural network approach to cell segmentation in immunocytochemical study

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Introduction

Immunocytochemical (ICH) study has a great importance in the evaluation of some predictive and prognostic factors in breast cancer (BC). The degree of C-erbB-2 oncoprotein expression is important for BC treatment strategy choice, because C-erbB-2 is a receptor for HER2/neu epidermal growth factor [6]. Overexpression of this oncoprotein is a risk factor of BC recurrence. The degree of membrane staining (qualitatively from 0 till 3+) represents tumor HER2 status in ICH study.

Now tumor HER2 status is evaluated manually by oncologist, doctor should check about 100-200 images of the specimen before giving the final assessment. Thus, the automation of determining tumor HER2 status is an urgent task, because it will allow to free an oncologist from routine work.

Automatization of tumor HER2 status assessment is divided into 2 subtasks: cells segmentation and automatic determining the degree of membrane staining. This work is devoted to the problem of cell segmentation.

For classical methods of computer vision the problem of cell segmentation is difficult due to the frequent presence of erythrocytic background and non-cellular elements at specimen image. In addition, the process of feature engineering for these algorithms is a time consuming and non-trivial. We propose segmentation algorithm, based on deep convolutional neural networks (CNN), which are very popular in image processing [1,5]. Using this approach, we got better results, than using classical computer vision algorithms.

Materials and Methods

Data

As input data for training algorithm we used biomedical images, obtained by hardware-software complex "Granat". Each color image has 1600 pixels at vertical and 1200 pixels at horizontal dimension. We prefer images with high and medium quality for manual segmentation. Images with bad quality were filtered from training dataset.

Selected images from different patients were manually segmented by an expert. Thus, for each image in training dataset we obtain binary image mask with correct result of cells segmentation. Training set contains about 300 manually segmented images. We use random crops and random angle rotations for training set augmentation.

Baseline segmentation algorithm

As a rule for algorithms comparison we need a simple algorithm, that successfully solves our segmentation task. After that we evaluate this algorithm and use these results as a baseline to construct algorithm with better quality. Baseline segmentation algorithm has the following steps:

- image normalization;
- adaptive histogram equalization;
- Otsu binarization;
- morphological operations (remove small holes, remove small objects, image opening);
- connected components detection.

Neural network approach for cells segmentation

We train deep CNN with U-net like architecture for task of cells segmentation, because this architecture proved itself very useful for segmentation problems with limited amounts of data [4]. In general, the U-Net architecture consists of an encoder to capture context and a decoder that enables precise localization (Fig.1).

The contracting path follows the typical architecture of a CNN with convolution and pooling operations and progressively downsampled feature maps. Every step in the expansive path consists of an upsampling of the feature map followed by a convolution [4]. Hence, the expansive branch increases the resolution of the output. In order to localize, upsampled features in the expansive path are combined with the high-resolution features from the contracting path via skip-connections.

We also employ batch normalization technique to improve convergence during training. As encoder we use VGG-11 CNN [5] pretrained at Imagenet dataset [2].

We deploy CNN with this architecture on its own at python language in Pytorch framework.

This U-net-like CNN was trained during 100 epochs using stochastic gradient optimization method called "Adam" [3]. We check training progress at labeled validation dataset.

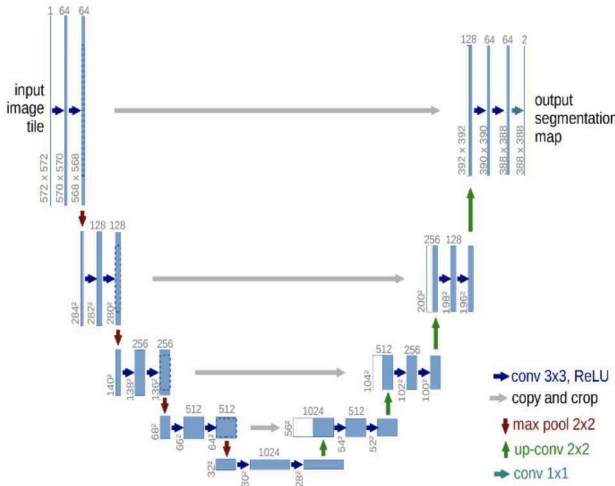


Figure 1: U-net architecture

Metric

We use Sørensen-Dice coefficient as metric. This metric shows similarity measure between true and predicted segmentation masks, like Jaccard coefficient.

$$Dice = \frac{2 * |True \cap Pred|}{|True| + |Pred|} \quad (1)$$

It's worth noting that typically total cells' area at image is far fewer that total background area. The task of CNN is high accuracy cells' segmentation, not background segmentation. So, it's important to note that when we compute intersection and union in Dice coefficient formula (1), we take in consideration only masks for cells only (not total masks for image).

Additionally, we check relative frequencies of true negative and false positive cells detection. This information gives us more intuition about algorithm's weak points and helps for further improving of segmentation quality.

Results

The quality of the resulting model was evaluated on validation data set consisting of 60 images (by 15 images of each membrane coloring degree).

During results exploration we found that trained CNN frequently segment small objects as false positive cells. This problem can be solved by two ways: training set extension or removing small connected components. Training set extension requires additional time for manual labeling of images by expert. So, we decide to remove connected components that have area less than some empirically determined threshold. This trick enables to increase Dice coefficient a little bit (from 0.81 to 0.83 in average for validation set), because area of false positive cells is relatively small. But at the same time relative frequency of false positives decreased from 16.8% to 10.8%.

Final average value of Sorensen–Dice coefficient for neural network segmentation model at validation set is 0.83 ± 0.09 . An example of image segmentation by CNN model is shown in Fig. 2.

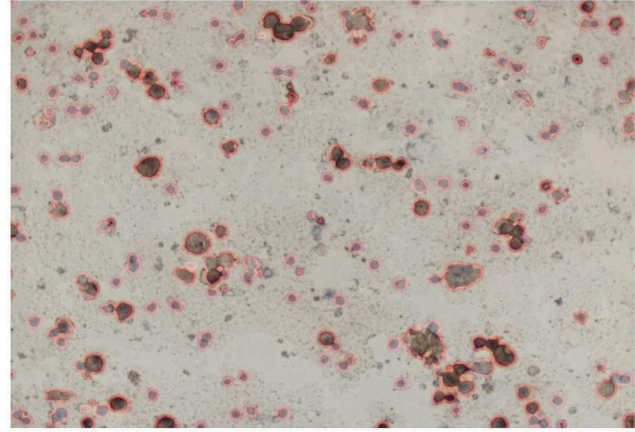


Figure 2: Image segmentation result

Simple baseline segmentation algorithm has 0.68 ± 0.16 average Dice coefficient on the validation data set.

Below you can see table with false positive and false negative rates for baseline and neural segmentation methods (Table 1).

Table 1: False Positive And False Negative Rates

Object	False positive rate	False negative rate
Baseline	$23.8 \pm 8.3\%$	$2.7 \pm 0.8\%$
Neural	$10.8 \pm 4.7\%$	$2.5 \pm 0.7\%$

Here we can see that CNN can significantly reduce false positive cells detection rate. The main reason is that CNN implicitly learns geometric and color features, which are specific just for cells.

Cell with complex background near it is another difficult case for baseline segmentation method. As a rule, it segments all «trash» area with cells inside it (Fig.3). In contrast, neural segmentation method can distinguish cell from difficult background around it (Fig.4).

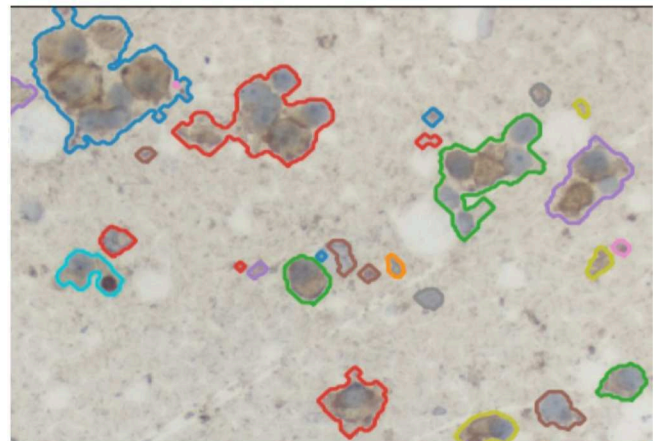


Figure 3: Segmentation result, obtained by baseline algorithm

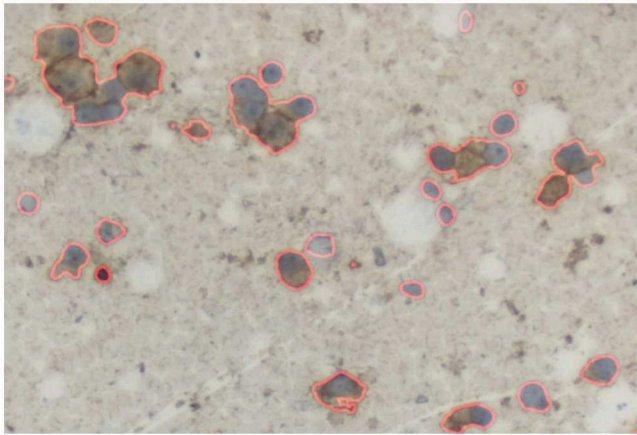


Figure 4: Segmentation result, obtained by neural network algorithm

- [3] Kingma, D., Ba, J.: Adam: A method for stochastic optimization. arXiv preprint arXiv:1412.6980 (2014)
- [4] C. J. De Luca. The use of surface electromyography in biomechanics. *J Appl Biomech*, 13(2):135–163, 1997.
- [4] Ronneberger, O., Fischer, P., Brox, T.: U-net: Convolutional networks for biomedical image segmentation. In: *International Conference on Medical Image Computing and Computer-Assisted Intervention*. pp. 234–241. Springer (2015)
- [5] Simonyan, K., Zisserman, A.: Very deep convolutional networks for large-scale image recognition. arXiv preprint arXiv:1409.1556 (2014)
- [6] Volchenko N.N., Slavnova E.N., Gladunova Z.D. and others. *Current cytological diagnostics of breast diseases*. Moscow: Publishing house of Bauman Moscow State Technical University, 2014

Conclusions

In this paper, we propose a neural network approach for cells segmentation that solves the problem of tumor HER2 status assessment. Our model is based at U-net CNN with pretrained VGG-11 encoder.

It has been shown that CNN-based model works significantly better than classical computer vision segmentation algorithms, especially on difficult cases of images with complex background. In case of high quality images without non-cellular elements both kinds of algorithms work well with similar precision.

The main advantages of CNN-based model are:

- lower false positive cell detection rate;
- more precise cell segmentation at images with complex background;
- robustness to noise and image artifacts.

The main reason that CNN-based model works better than classical segmentation algorithm is that neural net implicitly learns geometric and color features specific just for cells. At the same time baseline model operates only with information at color and intensity levels, and this is not enough for high-quality segmentation in complex cases.

Thus, implementation of neural network segmentation algorithm can reduce false positive cell detection rate from 23.8 % to 10.8 % and improve Dice coefficient from 0.68 to 0.83. Deploying this model into production can simplify the routine work of oncologist for determining HER2 status of breast cancer tumors.

References

- [1] Ching, T., Himmelstein, D.S., Beaulieu-Jones, B.K., Kalinin, A.A., Do, B.T., Way, G.P., Ferrero, E., Agapow, P.M., Xie, W., Rosen, G.L., et al.: Opportunities and obstacles for deep learning in biology and medicine. *bioRxiv* p. 142760 (2017)
- [2] J. Deng, W. Dong, R. Socher, L.-J. Li, K. Li and L. Fei-Fei, *ImageNet: A Large-Scale Hierarchical Image Database*. IEEE Computer Vision and Pattern Recognition (CVPR), 2009

Display Interfaces for the Control Unit of an Implantable Cardiac Pump

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Introduction

A cardiac pump consists of the implanted module providing monitoring of a heart rate and the external block providing processing and visualization of the logged data. One of basic elements of the external block is the graphic display. Coming from the sizes of device and quantity of displayed information, LCD and OLED displays are used as an output information device.

Presently the digital interfaces of image transferring are used for the small-size displays. The bit depth of information transmission depends on the depth of color of the image that we want to give. In black and white displays each pixel has from one to eight digits. In color displays it has from eight (RGB332) to 24 (RGB888) bits [1]. Figure 1 shows the type structure of graphic display control.

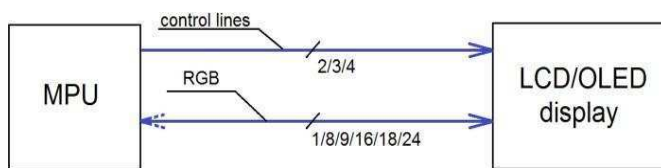


Figure 1: Typical connection of graphic displays

In the process of development restrictions and requirements, such as energy consumption, size, reliability, volume of the output information, cost etc., are imposed on a device. According to problem a developer make an optimal decision about the choice of hardware components. An interface, which will be used for data transmission, is chosen during work with graphic displays.

INTERFACES DESCRIPTION

A. Parallel interfaces

1. RGB interface:

Digital RGB interface has three timing signals - DOTCLK (PIXELCLK), HSYNC and VSYNC with frequencies of one pixel, line and frame transmission. Figure 2 shows the RGB transmission timing [2].

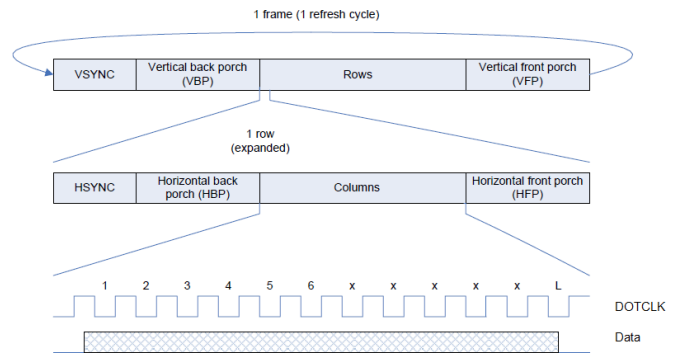


Figure 2: Frame and line timing parameters

To transmit a pixel color the parallel digital data bus is used. Width of bus is determined by colorize that we want to pass, or by restrictions of terminals. At the using of RGB interface, a width of data bus is 24 bits (RGB888). The feature of RGB interface work is transmission of full image frame. This method of image display is useful when it is necessary to change a picture on the screen constantly, for example, in the video transmission to screen.

2. System parallel interfaces.

For data transmission to a GPU it isn't always required to pass a full image. It is mostly necessary to change a small area of image on the screen. For this purpose Motorola and Intel companies created their own interfaces of graphic images transfer, which use registers of data transmission control in the RAM of GPU. The features of such interfaces are work with registers and delivery of control signal lines. The main difference between interfaces of Motorola and Intel companies is in the control signals. For the transmission of different color depth the different data bus width is used. We shall consider in detail every interface [3].

Intel 8080: Fig. 3 shows 8080-series bus interface [4]



Figure 3: 8080-series Bus Interface

The /WR and /RD signals are for indication writing to register and reading from register. The DC signal is used for designation of transmitted word type: command word (log.0) or data (log.1). The /CS signal is used for selecting chip of required device. There are timing performances of 8080 interface in the Table 1 [4]. Figure 4 shows the timing diagram of command/data writing [4].

Table 1: Parallel 8080, 6800 Timing Characteristics

Parameter	Min	Max	Unit
Clock Cycle Time (write cycle)	75	—	ns
Clock Cycle Time (read cycle)	450	—	ns
Pulse Width $\overline{CS}$ low (write cycle)	40	—	ns
Pulse Width $\overline{CS}$ high (write cycle)	25	—	ns
Data Access Time (READ)	250	—	ns
Output Hold time (READ)	100	—	ns
Pulse Width $\overline{CS}$ low (read cycle)	500	—	ns
Pulse Width $\overline{CS}$ high (read cycle)	500	—	ns
Rise time	—	4	ns
Fall time	—	4	ns

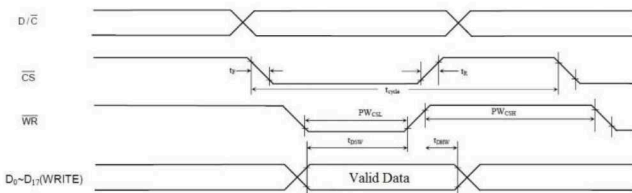


Figure 4: Parallel 8080-series Interface Timing Characteristics (write)

Motorola 6800: Fig. 5 shows 6800-series bus interface [1].

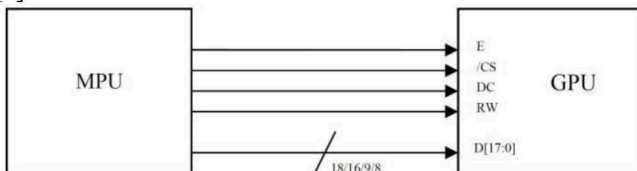


Figure 5: 6800-series Bus Interface

Unlike the Intel 8080 this interface is synchronous. For synchronization the E line, which latch data at the falling edge, is used. The RW control line is used for designation of read (log.1) or write (log.0) cycles. The DC signal is used for designation of transmitted word type: command word (log.0) or data (log.1). The /CS signal is used for selecting chip of required device. There are timing performances of Motorola 6800 interface in the Table 1 [4]. Figure 6 shows the timing diagram of command/data writing [4].

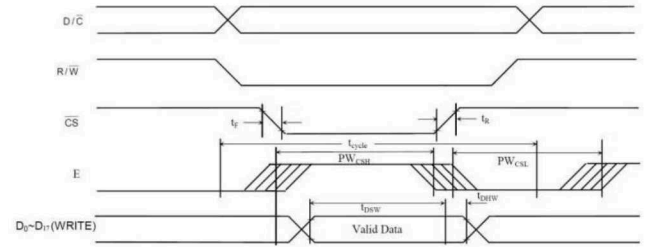


Figure 6: Parallel 6800-series Interface Timing Characteristics (write)

B. Serial system interface SPI

All considered interfaces had a parallel data bus. During resource lack the serial SPI interface is used for graphic data transmission. More often all this interface is used for black and white displays, which have a 1bpp capacity. There are 4-wire and 3-wire ways of data transmission by SPI.

4-wire SPI: Four flow lines are used for an information transfer. The SCLK signal is for data transmission clocking. The CS signal is used for selecting chip of required device. The SDI signal is used for data transmission. The SDC signal is used for designation of transmitted word type: command word (log.0) or data (log.1). In the process of one command word or data transmission 8 bits are used. There are timing performances of 4-wire SPI interface in the Table 2 [4]. Figure 7 shows the timing diagram of command/data writing [4].

Table 2: Serial Timing Characteristics

Parameter	Min	Max	Unit
Clock Cycle Time	75	—	ns
Chip Select Setup Time	2	—	ns
Chip Select Hold Time	10	—	ns
Clock Low Time	38	—	ns
Clock High Time	38	—	ns
Rise time	—	4	ns
Fall time	—	4	ns

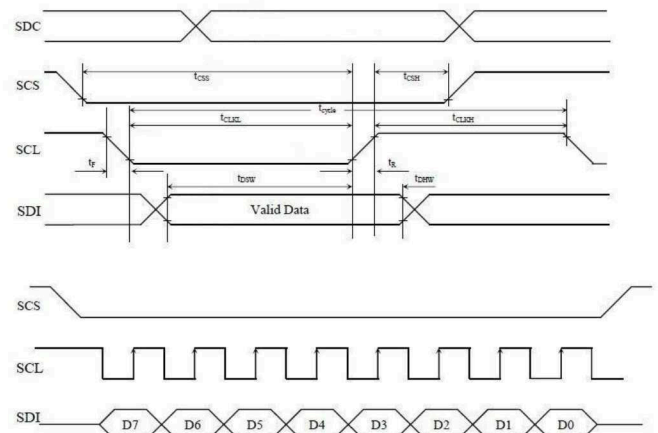


Figure 7: 4-wire Serial Timing Characteristics

3-wire SPI: Three flow lines are used for an information transfer. The SCLK signal is for data transmission clocking. The CS signal is used for selecting chip of required device. The SDI signal is used for data transmission. In the process of one command word or data transmission, 9 bits are used, and also the first bit points to a transmitted word type (command word or data). Figure 8 shows the timing diagram of command/data writing [4].

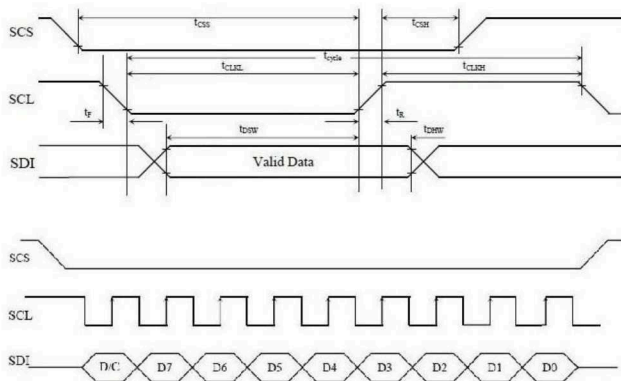


Figure 8: 3-wire Serial Timing Characteristics

Comparison of interfaces

Developing a device, it is necessary to understand, what interface will be optimal for this task. The basically criteria of interfaces comparison are memory, CPU time, number of wires and frame rate. There is comparing of interfaces in the Table 3.

Table 3: Comparison of interfaces

Interface	RGB	Parallel 8/9 bpp	Parallel 16/18 bpp	SPI 4-wire
Criteria				
Memory	Bad	Good	Good	Good
CPU time	Good	Bad	Bad	Very bad
Number of wires	Bad	Middle	Bad	Good
Frame rate	Good	Good	Good	Bad

In considering each interface it is possible to select a few groups of the under development devices where its application will be optimal. The small-size devices with small output information scope are in the first group. Using of the internal MPU SPI unit is typical for such systems. The large-size devices with big output information scope are in the second

group. Using of the parallel interface with the 16/18-bit data bus is the best variant for such systems. The small-size devices with big output information scope are in the third group. Using of the parallel interface with 8/9-bit data bus is typical for such systems. It should be taken that video controllers support transmission of bigger quantity of colors per pixel (16/18 bpp) in case of the 8/9-bit data bus. For this purpose we do two data sending instead of one, but we give up MPU time.

The classification given earlier is applicable to displays with internal video controller. In the absence of the internal GPU the RGB interface is used.

Conclusions

Comparing interfaces, we can note that everyone has advantages and disadvantages. When using parallel interfaces critical parameter is the MPU time. In the presence internal the MPU DMA unit we can transfer information to the display practically without using CPU time. The storage area which the DMA unit will transfer to a video controller is necessary for using this unit.

On the basis of the conducted research it has been decided to use for visualization of data of the Cardiac Pump the 8-bit Parallel Intel 8080 interface and color LCD with a 320x240 pixels screen resolution. Experiments were carried out and the MPU time was measured with and without using DMA. For display one-color rectangle at full screen size without using the DMA unit 15ms of MPU time and 1 byte of a memory were required. When using DMA $\approx 3\mu s$ of MPU time and 75 Kbytes of a memory were required.

References

- [1] LCD Module Protocol Interfaces at <http://www.lxdinc.com/>
- [2] Introduction to graphics and LCD technologies at <http://www.nxp.com/>
- [3] TFT LCD interfacing with the high-density STM32F10xxx FSMC at <http://www.st.com/>
- [4] Solomon Systech Limited (2009) SSD2119 Advance Information. 320 RGB x 240 TFT LCD Driver. Integrated Power Circuit, Source and Gate Driver and RAM.

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A Closed-loop system for blood glucose level control

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Introduction

Diabetes mellitus type 1 is a metabolic disease characterized by chronic increase of blood glucose concentration (BG) that occurs when pancreas is no longer available to produce enough amount of insulin. Patients with diabetes mellitus need continuous control of BG.

One of the most widespread methods for type 1 diabetes compensation is pump insulin therapy based on the exogenous insulin infusion combined with special physical activity treatments.

Closed-loop system for BG control may improve efficiency of insulin therapy and, furthermore provides an opportunity to compensate diabetes mellitus automatically.

Almost all up-to-date commercial BG meters and monitoring systems are invasive. A portable noninvasive glucometer development is an important task for modern science.

In the paper, we present a closed-loop system for blood glucose level control on the basis of a noninvasive glucometer, an insulin pump and model predictive control.

Elements and applications

Closed-loop operation is in maintaining BG in physiological range and preventing hypo- and hyperglycemia. A continuous glucose monitor measures BG noninvasively. An analyzing system is based on model-predictive control.

An insulin pump (IP) provides precision subcutaneous insulin infusion and control of an actual infused dose. The IP experimental embodiment comprises of a control unit, a mechanical drive based on a micro motor with a reduction gear system 1:1024, and an infusion system with a 3 ml reservoir. Tab.1 presents main parameters of the developed pump.

The experimental embodiment of portable non-invasive glucometer (PNG) comprises of a control unit and an earlap clip, connected to each other by an opto-electrical cable. Noninvasive BG measurement is based on absorption spectroscopy method. Infrared radiation from a laser diode is transmitted through an earlap and is registered by a photodiode. Transmitted radiation is analyzed and BG is calculated. The algorithm for calculating the concentration is based on the iterative methods.

The clip consists of a housing, a transmitter, a receiver (InGaAs photodiode) and optical elements (lenses, mirrors, windows). Infrared radiation goes from the control unit to the earlap via the optical fiber. Tab.2 presents main parameters of the developed glucometer.

Table 1: Insulin Pump
Experimental Embodiment Parameters

Parameter	Value
Reservoir volume	3 ml (300 u)
Basal insulin discretization	0.025 u
Bolus insulin discretization	0.2 u (2 ml)
Amount of daily basal profiles	48
Infusion accuracy	±2,6%
Energy supply	1 AAA battery
Run time (continuous work time)	3 days
Connection	Bluetooth
Control	autonomous/ by smartphone
Indication	3.5" TFT resistive touch screen

Table 2: Glucometer Experimental
Embodiment Parameters

Parameter	Value
Measurement object	earlap
Laser power	30 mW
Time of a single measurement	5 min
Amount of measurements during monitoring	12 mes/h
Energy supply	2xICR18650
Run time (continuous work time)	> 6 h
Connection	Bluetooth
Control	by smartphone
Indication	LED

IP and PNG can be controlled by a smartphone connected to them via Bluetooth interface. Smartphone application allows user to:

- input data about food intake and calibration data;
- input of personal and physiological data affecting on BG dynamics;
- create of basal and bolus insulin patterns creation and launching;
- visualize current BG and its dynamics track;

- save and show statistics data of the patient by certain day, week or month;
- signalize on appearance of system messages, warnings or errors.

In order to organize an effective feedback between IP and PNG we propose a short-term prediction algorithm [1]. Tasks of the algorithm are the following:

- patient BG prediction;
- calculation of the required bolus insulin dose;
- infusion subsystem or glucometer faults alarms;
- detecting user incorrect information input;
- alarms for hypo- and hyperglycemia;
- correcting the mathematical model parameters;
- detecting wrong BG measure results;
- detecting the need of glucometer to be recalibrated.

The algorithm is based on mathematical model of BG dynamics [2, 3]. The model assumes that glucose dynamics is regulated by insulin, amylin, epinephrine and glucagon secretion. Ascents of BG are mainly caused by food intake as well as glycogenolysis and gluconeogenesis activated by glucagon and epinephrine. Descents of BG are caused by glycolysis and glycogenesis activated by insulin and amylin. Thus, the general equation of BG dynamics can be represented as follows:

$$G = G_0 + G_f(m_{carb}, \zeta) + G_{gls}(v_{gn}, v_{epn}) + G_{gng}(v_{gn}, v_{epn}) - G_{glg}(v_{ins}, v_{am}) - G_{gs}(v_{ins}, v_{am}) \quad (1)$$

where G is current BG, G_0 is initial BG, m_{carb} is meal carbohydrates mass, ζ is food glycemic index, v_{gn} , v_{epn} , v_{ins} , v_{am} are concentrations of glucagon, epinephrine, insulin and amylin.

The closed-loop system comprises of two data sets – the measured BG from PNG and the predicted BG. The difference between them determines its further operation.

When a patient enters meal/insulin data or bolus insulin data is received from the pump, the model and the prediction are recalculated. After the prediction is made, several intervals are calculated for the current prediction. These ranges are used to classify the measured value into one of the following categories: reliable, reasonable reliable and unreliable. They are taken into consideration for error determination if appeared.

Results

Experimental trials of the closed-loop system were performed using the special test bench [4]; the scheme of the one is presented in the Fig.1. The test bench allows adjusting necessary glucose concentration in a model solution circulating in a flowthrough cuvette. Glucose level increasing simulates food intake while decreasing simulates insulin infusion. Blood-model solution contained glucose, water and such blood plasma components as albumin, urea, creatinine etc. A controlled hydraulic system provides smooth and accurate setting of target concentration in the cuvette.

Current glucose concentration in the cuvette was measured by the developed noninvasive glucometer and HemoCue Glucose 201+ as a reference. For relative error estimation 20 experiments were performed (36 measurements/experiment with BG in range 75–400 mg/dl, step 5–10 mg/dl). An average error in hyperglycemia is 13,41 %, in normoglycemia is 17,85 %, in hypoglycemia is 24,89 %. Adequacy of glucose meters is acceptable to be estimated using Clarke Error Grid Analysis (EGA). EGA of developed noninvasive glucometer is represented on the Fig.2. On the X axis are reference measurements; on the Y axis are developed glucometer measurements.

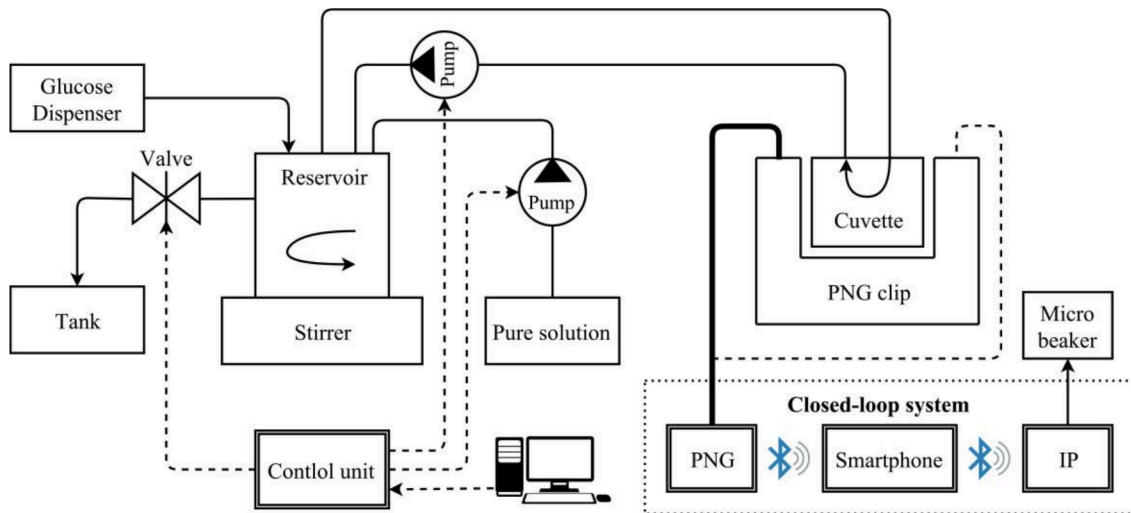


Figure 1: The scheme of the test bench for the closed-loop system experimental trials

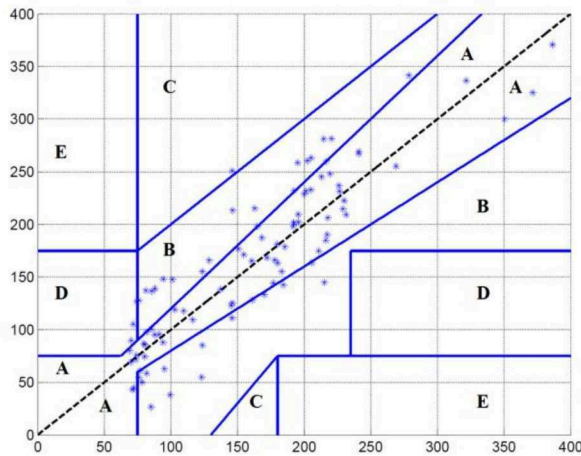


Figure 2: EGA of developed glucometer.
95.8% of measurements are in the A- and B-zone,
in C-zone is 1%, in D-zone – 3.1%, in E-zone – 0%

Series of experiments were performed in order to estimate the accuracy of the developed insulin pump. The amount of infusing insulin was changed from 0.1 ml to 2 ml, by 0.1 ml once an hour. Actually infused value was estimated by a micro beaker. As a result, the insulin infusion error averaged for one hour is 2.6%, while the maximum error is in the test range of 3.1%.

The short-term prediction algorithm was designed and tested *in silico* using Matlab. The input data sets for the algorithm were formed using the processed [5] DirecNet clinical protocols [6]. Two studies were performed: the accuracy study and the functional one. The functional study was aimed to test PNG and IP faults, incorrect data, hypo- and hyperglycemia alarms adequacy. During the study data from 30 patients was used. It included tracks for two consecutive days. For each patient, the day 1 track was used for mathematical model training and the day 2 track - for prediction system tests.

As measured BG in accuracy tests, we use actual patient track values with 5–25 % normal noise added. The algorithm was tested on every patient with different noise levels. Tests show that the difference between predicted values and patient BG values was less than 10%. During functional tests in every BG track, we deleted some data about food intake or insulin injections. As a result, the predicted track differed from real and measured ones. The algorithm analyzed the nature of the discrepancy of tracks and indicated relevant message. In every test the algorithm detected incorrect/absent data or displayed the necessary timely warnings.

The example of the prediction algorithm operation is presented in the Fig. 3.

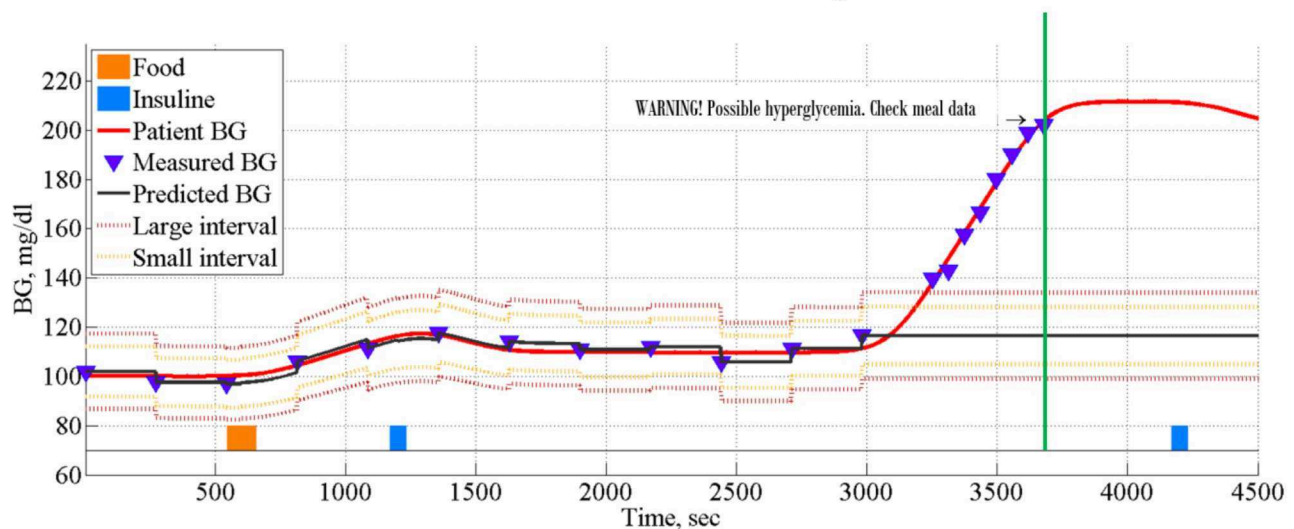


Figure 3: Prediction testing example. Patient BG is unknown for algorithm.
Predicted track is shifted to measured point if the latter is inside the reliable interval (small interval), measurement frequency 1 in 300s. If measured values are aside the reliable zone measurement frequency increased (1 in 60s).
If a divergent trend is detected, the algorithm cautions user.

Conclusions

The closed-loop system for BG level control is aimed to automate BG maintaining in physiological range with patient minimal involvement. The key feature of the system is a model predictive control and noninvasive BG measurements. The developed closed-loop elements (the optical noninvasive glucometer, the insulin pump and the model-based prediction algorithm) tests show high efficiency of proposed methods. The prediction algorithm

detects incorrect data, faults of the glucometer and the pump. The implemented model predictive control allows reduction of measurement errors.

References

- [1] Bazaev N.A., Pozhar K.V. Blood Glucose Prediction for “Artificial Pancreas” System. Gluconeogenesis. Rijeka, Croatia: InTech, 55–73, 2017.

- [2] N. Bazaev, K. Pozhar, E. Litinskaya, P. Rudenko. Mathematical Model of Blood Glucose Dynamics. The International Journal of Artificial Organs, 40(8), 437, 2017.
- [3] N.A. Bazaev, K.V. Pozhar, P.A. Rudenko. Mathematical Modeling of Blood Glucose Concentration Dynamics. Biomedical Engineering, 48(6), 292–296, 2015.
- [4] N.A. Bazaev, V.M. Grinvald, A.N. Zhigailo, E.L. Litinskaya, K.V. Pozhar, P.A. Rudenko. A Test bench for performance validation of an artificial pancreas system. Biomedical Engineering, Vol. 51, No. 6, March, 2018, pp. 422–426.
- [5] P.A. Rudenko, N.A. Bazaev, K.V. Pozhar, E.L. Litinskaya, V.M. Grinvald, A.I. Chekasin. Getting day blood glucose tracks using clinical protocols of the DirecNet database. Biomedical Engineering, Vol. 51, No. 5, January, 2018, pp. 346–349.
- [6] Ruedy K.J., Beck R.W., Xing D. and Kollman C. For the Diabetes Research in Children Network (DirecNet) Study Group Diabetes Research in Children Network: Availability of Protocol Data Sets // J Diabetes Sci Technol. – 2007. – Vol. 1(5). – pp. 738–745.

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Effect of thrombus formation on heat emission in Sputnik RBP

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Introduction

End-stage heart failure (HF) is a major cause of mortality, morbidity and disability worldwide. Nowadays, a surgical and medical treatment of HF has a positive trend. But heart transplantation remains an optimal treatment of end-stage HF. A shortage of donor organs has made this therapy available only for limited number of patients (1). This problem required a development of ventricular assist devices (VADs) for critically ill patients. The first devices had large dimension, but by the aid of engineering and technology developers have the opportunity to reduce the dimensions of VADs (2, 3). This feature allows the use of VADs for treatment of patients with small body surface area. However, the miniaturization of pump components may lead to a high hemolysis level (4, 5). Thrombus formation remains a serious problem of axial and centrifugal ventricular assist devices (6-8).

A typical construction of axial VAD consists of a flow straightener, an inlet bearing, an impeller, an outlet bearing and a diffuser in series, and a stator (9, 10). Mechanical friction between the pump components in such devices is accompanied by heat generation, which depends on the pump design (11).

Conversion of electrical energy to thermal energy is inherent for any motor under normal operation mode (12). Heat dissipation occurs due to thermal emissions from pump housing and heat transmission of blood moving through a device. Herewith excessive heat generation can adversely affect the blood hemolysis level and the protein denaturation increasing the probability of thrombus formation (13). As a result the pump failure probability increases. This problem can be solved only by emergency surgery with full replacement of implanted VAD (14, 15). Currently, the influence of thrombosis on a rotary blood pump heat generation is not fully investigated. Therefore, in vitro tests were conducted in hydraulic closed loop using the rotary blood pump of the Sputnik VAD to determine the nature of heat generation for different conditions which are typical for implantable systems. Since 2012 the Sputnik VAD successfully used to replace of left ventricular function for patients with HF. This VAD is the axial and continuous flow pump.

Materials and Methods

The Sputnik VAD construction is comprised of movable element (impeller) and stationary elements (flow straightener, diffuser, inlet and outlet bearings). An electrical motor allows you to rotate the pump at a speed from 5000 to 10000 rpm, providing a flow of up to 10 L/min (16).

Sputnik VAD produces necessary head pressure-flow rate (H-Q) curves (17). This blood pump has a length of 82 mm, outside full diameter of 34 mm and weight of 246 g. Experiments to compare the influence of thrombus formation on the VAD heat generation was carried out under following conditions: non-thrombosis, inlet (flow straightener) thrombosis, outlet (diffuser) thrombosis. The platinum-based silicone Ecoflex 00-10 (Smooth-On, USA) was used as a material for simulation of thrombus formation. For thrombus formation manufacture silicone components A and B was mixing in equal amounts. Degassing of resulting compound was conducted in vacuum chamber during 10 minutes. Further the silicone was applied on inner surface of flow straightener and diffuser. By hot air gun at 200 °C silicone instantly fixed. After complete polymerization the Ecoflex silicone is a very soft, durable and stretchable material without tacky surface. Thrombus with a volume of 0.5 cc was used in tests. Figure 1 shows an artificial clot in the diffuser (A, B) and flow straightener (C, D) before and after the tests. In total 27 hours of tests were performed for each thrombus formation.

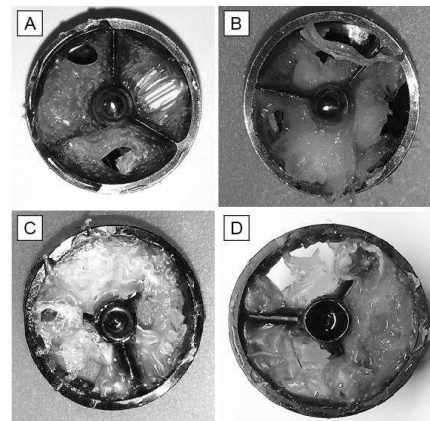


Figure 1: Image of the diffuser (A, B) and flow straightener (C, D) thrombosis at the beginning (A, C) and at the end of all tests (B, D).

The experiments were conducted on a special test bench, which consists of a hydraulic loop, temperature measuring and recording devices (infrared camera and thermocouple unit) and control units including pump controller, power source and personal computer. The pump body during the tests was placed inside a viscoelastic silicone cover with a volume of 1400 cc, which properties are similar to the soft tissues properties (18). Pump location inside the cover limits the heat dissipation into environment during the tests.

Temperature change of the Sputnik VAD body surface was measured by thermocouple-thermometer TPI 343 (TPI, USA). The data was recorded every 2 minutes. Temperature sensors were fixed tightly for more accurate recording of the pump surface temperature: one sensor – on the pump body at the stator location, and another sensor – at the pump outlet. This location of sensors allowed recording the heat emission level during stator operation and the temperature change at the pump outlet.

As an additional device for temperature change measurement a thermal imaging camera THT-47 (HT Italia, Italy) was used. This infrared camera is designed for rapid detection of heat map emitted by the test unit. THT Link software was used to analyze the obtained data.

Different test fluids were used to analyze viscosity influence on the pump heating. On the initial test stage distilled water with dynamic viscosity of 0.00085 Pa·s at 23 °C was taken. Aqueous glycerol solution (dynamic viscosity of 0.003 Pa·s at 23 °C) was used as fluid with blood viscosity. The test fluid volume in hydraulic loop was 6150 cc. On the second test stage test fluid was heated up to 37 °C during 90 minutes in a special bath by a heat regulator. Constant bath temperature was maintained for the duration of the experiment. Aqueous glycerol solution with dynamic viscosity of 0.006 Pa·s at 23 °C was used. It is noted that viscosity of fluid being heated decreases. Thus, aqueous glycerol solution with dynamic viscosity of 0.006 Pa·s at 23 °C after heating to 37 °C has viscosity equal to blood viscosity (19).

The experiments by test bench were carried out for each system configuration separately. Differences consist in four parameters: the pump speed (5000, 7000 and 9000 rpm), the viscosity of test fluid (distilled water or aqueous glycerol solution), the presence or absence thrombosis and its location and the test fluid temperature (room temperature – 23 °C or body temperature – 37°C). When using the aqueous glycerol solution with dynamic viscosity of 0.003 Pa·s at 23 °C, diffuser thrombosis and test fluid heating to body temperature the system configuration is «blood viscosity, outlet thrombosis, 37 °C».

Results

Experiments without heating the test fluid

The thermal map of the Sputnik VAD surface was obtained by infrared camera with aqueous glycerol solution with dynamic viscosity of 0.003 Pa·s as test fluid, pump reference speed of 5000 rpm and non-thrombosis (Fig. 2A). Figure shows areas with high temperature corresponding to the stator area. Also the output bearing was slightly heated in compare to the input bearing. There was no zone of excessive heat generation at the flow straightener area. Heat map of the pump surface is shown in Figure 2B for the pump inlet thrombosis case. The maximum temperature of the pump surface was located in the area between the inlet bearing and stator and amounted to 25.8 °C. In this case the heat emission level at the pump inlet is higher compared to the pump outlet. This pattern is

caused by thrombus location on the flow straightener. It should be noted the difference of the pump surface heat map in absence and presence of thrombus formation: hot spots in Figure 2A are shifted to the left (the pump inlet), whereas hot spots in Figure 2B are located at the pump center. Heat map obtained in the experiments with diffuser thrombosis is shown in Figure 2C. The minimum temperature of the pump surface was 24.1 °C, maximum temperature was achieved at the diffuser area and equal to 29.1 °C. In addition, there is a driveline cable connection in this pump body area, which emits a small amount of heat during pump operation.

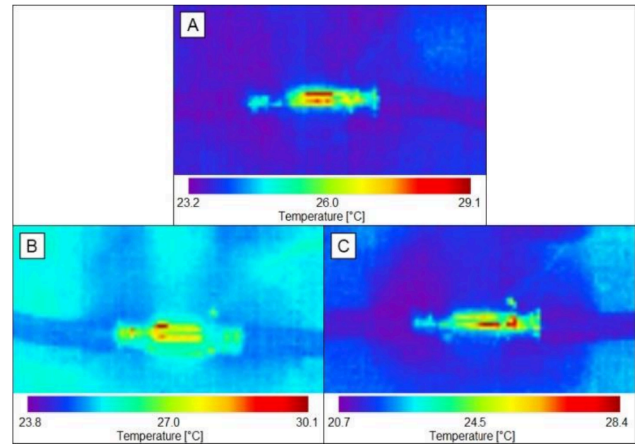


Figure 2: Thermal map of the Sputnik VAD surface at speed of 5000 rpm, using test fluid with blood viscosity and different thrombus clamping; where A – non-thrombosis, B – inlet thrombosis, C – outlet thrombosis.

For the same system configuration a temperature increase at the stator area surface and at the pump outlet measured using thermocouple sensors was equal to 0.7 °C for non-thrombosis, 1.2 °C for the inlet thrombosis and 1 °C for the outlet thrombosis. Consequently, for 5000 rpm the influence of the stator thermal energy to the total pump heat generation is minimized. Temperature change curves increase gradually, without spikes during 50 minutes, and then curves change to linearity range with a constant temperature value.

The temperature distribution obtained along the pump axis for reference speed of 9000 rpm is shown in Figure 3. For clarity the location of main pump components relative to coordinate origin is shown by vertical lines and numbers. Nature of the distribution is similar to the same data at the pump speed of 5000 and 7000 rpm. The differences are in maximum and average temperature values. For non-thrombosis case measured maximum temperature value of 26.7 °C is in the stator area. Conversion of stator electrical energy to thermal energy had a major influence on the total heat map of the pump. For inlet thrombosis case maximum temperature value was located in the area between the inlet bearing and stator, moreover characteristic temperature rise is observed before the thrombus, which is accompanied by a further sharp drop of meas-

ured temperature value. For outlet thrombosis case maximum temperature value of 27.9 °C was located in the thrombosis area. The temperature average at 9000 rpm for non-thrombosis system configuration was 24.4 °C, for inlet thrombosis – 24.6 °C and for outlet thrombosis – 24.5 °C.

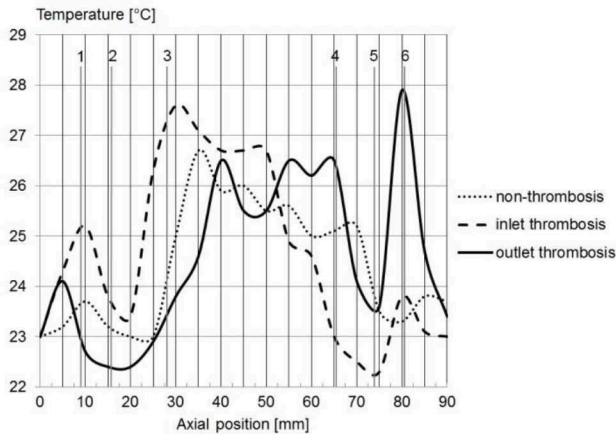


Figure 3: Temperature distribution along the pump axis for 9000 rpm, using test fluid with blood viscosity and different thrombus clamping; where 1-2 – flow straightener zone, 2-5 – impeller zone, 3-4 – motor zone, 5-6 – diffuser zone.

Curves obtained by thermocouple at 9000 rpm have different shape: temperature change curves of the stator area at the test start are compact and linearly increases with time, but the outlet temperature curves have a sharp discontinuity of temperature at the test start. At the reference pump speed of 9000 rpm maximum outlet temperature was higher than the stator temperature. Therefore, test fluid temperature was higher than the stator area surface temperature. As a result, electric stator energy is converted to thermal energy and contributes to heating of the test fluid.

Experiments with heating the test fluid

To determine the pump heat generation nature at human body temperature the test fluid was heated to 37 °C. After changing a single parameter of system configuration each subsequent experiment was started only after test fluid and pump body cooling to room temperature followed by heating to 37 °C. The pump outlet temperature change obtained by thermocouple is shown in Figure 4. The minimal temperature increase was 1.6 °C for «distilled water, outlet thrombosis, room temperature» configuration, maximum temperature increase was 5.1 °C for «blood viscosity, non-thrombosis, room temperature» configuration. Temperature increase is typical for all curves in the first 40-50 minutes of testing, further growth was slowing down and curves moved to flat area with a constant temperature spans.

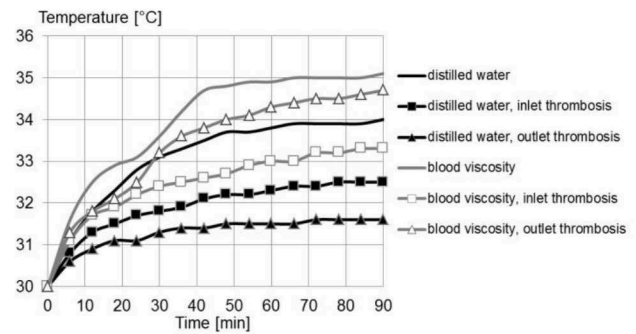


Figure 4: Temperature change curves at the pump outlet for different system configuration at the pump speed of 7000 rpm.

Temperature distribution curves for various reference speeds and thrombus presence at the inlet part of the pump are shown in Figure 5. The curves have a similar structure: temperature decreases first and then increases, reaching a maximum value in zone 1-2; in the stator area there is a decline up to diffuser reaching a minimum value; in zones 5-6 curves sharply increase and converge on the same parallel at 80 mm point; outlet temperature falls again. By reference to previously results it can be inferred that zone with maximum temperature includes a thrombus formation.

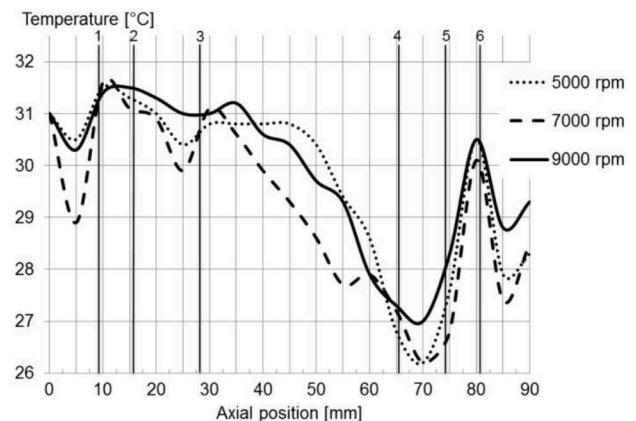


Figure 5: Temperature distribution along the pump axis for inlet thrombosis, using test fluid with blood viscosity and at different pump speeds; where 1-2 – flow straightener zone, 2-5 – impeller zone, 3-4 – motor zone, 5-6 – diffuser zone.

Conclusion and discussion

To determine relationship between the Sputnik VAD thrombosis and the pump heat generation numerous and continuous tests were conducted at in vitro bench. Temperature of the pump surface was increased in all trials regardless of reference pump speed, test fluid viscosity or thrombosis presence. At 5000 rpm conversion of stator electric energy to thermal energy provides the main contribution to the total pump heat emission. Whereas at

7000 and 9000 rpm pump surface temperature value depends more on pump rotational speed and test fluid viscosity. Results obtained at room temperature with great probability allow determining the presence and location of thrombosis. Pump surface areas with high temperature corresponded to thrombus presence in this pump part.

When the test fluid is heated up to human body temperature, identification of thrombus formation by visual analysis of heat map is complicated. This problem is associated with excessive test fluid heating and, therefore, elastic tubes surface heating. Temperature distribution curves along the pump axis were constructed to solve this task. Sites of pump, in which maximum temperature was measured, corresponds to thrombosis areas.

Data obtained on the laboratory bench gives an insight into the nature of released pump heat. However, a living organism is a very complex structure with many nuances. Therefore, understanding of human body heat transfer will allow developing a precise experimental model that will make possible obtaining accurate data of interaction with VAD. Most likely the overall blood temperature of the human organism does not increase during the VAD operation. But short-term or localized heat emission inside the pump with blood moving through it may cause thrombosis. In this case temperature value is the most important parameter. There is an increase of hemolysis rate consequently resulting to thrombus formation and potential death of patient already at the temperature of 40 °C (20). In spite of numerous studies on pump thrombosis detection (21), main causes and possible solutions (21), this problem remains important in the development of ventricular assist devices. Furthermore, study of the thrombosis problem is extremely important in implantation of tissue engineering structures based on carbon nanotubes in the area of defects in heart tissues and blood vessels.

Understanding of the pump heat generation will allow improving the design of axial and centrifugal VADs and reducing the probability of thrombosis.

References

- [1] Y. Ohashi, A. Andrade and Y. Nose. Hemolysis in an electromechanical driven pulsatile total artificial heart. *Artif Organs*, 27(12):1089-1093, 2003.
- [2] A. Cheung, K. Chorpennig and et al. Design concepts and preclinical results of a miniaturized HeartWare platform: The MVAD System. *Innovations (Phila)*, 10(3):151-6, 2015.
- [3] I. Adachi, S. Burki, F. Zafar and D.L. Morales. Pediatric ventricular assist devices. *J Thorac Dis*, 7(12): 2194–2202, 2015.
- [4] J. Garbade, H.B. Bittner, S. Lehmann, F.W. Mohr and M.J. Barten. Miniaturization of left ventricular assist devices: the ongoing trend. *Expert Rev Med Devices*, 9(1):49-58, 2012.
- [5] T. Takano, S. Schulte-Eistrup and et al. Impeller inner diameter in a miniaturized centrifugal blood pump. *Artif Organs*, 26(1):67-71, 2002.
- [6] V. Tchanchaleishvili, F. Sagebin, R.E. Ross, W. Hallinan, K.Q. Schwarz and H.T. Massey. Evaluation and treatment of

pump thrombosis and hemolysis. *Ann Cardiothorac Surg*, 3(5):490-495, 2014.

- [7] D.J. Goldstein, R. John and et al. Algorithm for the diagnosis and management of suspected pump thrombus. *J Heart Lung Transplant*, 32(7):667-70, 2013.
- [8] J.K. Kirklin, D.C. Naftel and et al. Pump thrombosis in the Thoratec HeartMate II device: an update analysis of the INTERMACS Registry. *J Heart Lung Transplant*, 34:1515-26, 2015.
- [9] F.H. Sheikh and S.D. Russell. HeartMate II continuous-flow left ventricular assist system. *Expert Rev Med Devices*, 8(1):11-21, 2011.
- [10] M.P. Macris, S.M. Parnis, O.H. Frazier, J.M. Fuqua Jr and R.K. Jarvik. Development of an implantable ventricular assist system. *Ann Thorac Surg*, 63(2):367-70, 1997.
- [11] T. Kink and H. Reul. Concept for a new hydrodynamic blood bearing for miniature blood pumps. *Artif Organs*, 28(10):916-20, 2004.
- [12] L. Chen, Y. Pei, F. Chai and S. Cheng. Investigation of a novel mechanical to thermal energy converter based on the inverse problem of electric machines. *Energies*, 9(7):1-19, 2016.
- [13] K. Araki, Y. Taenaka and et al. Hemolysis and heat generation in six different types of centrifugal blood pumps. *Artif Organs*, 19(9):928-32, 1995.
- [14] J.K. Kirklin, D.C. Naftel and R.L. Kormos. The fourth INTERMACS annual report: 4,000 implants and counting. *J Heart Lung Transplant*, 31:117–126, 2012.
- [15] M.S. Slaughter, J.G. Rogers and et al. HeartMate II Investigators: Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med*, 361:2241-2251, 2009.
- [16] S.V. Selishchev and D.V. Telyshev. Ventricular Assist Device Sputnik: Description, technical features and characteristics. *Trends Biomater Artif Organs*, 29(3):207-210, 2015.
- [17] S.V. Selishchev and D.V. Telyshev. Optimisation of the Sputnik-VAD design. *Int J Artif Organs*, 39(8):407-414, 2016.
- [18] T.K. Yasar, T.J. Royston and R.L. Magin. Wideband MR elastography for viscoelasticity model identification. *Magn Reson Med*, 70(2): 479-489, 2013.
- [19] J.B. Segur and H.E. Oberstar. Viscosity of glycerol and its aqueous solutions. *Ind Eng Chem*, 43(9):2117-2120, 1951.
- [20] N.L. Gershfeld and M. Murayama. Thermal instability of red blood cell membrane bilayers: temperature dependence of hemolysis. *J Membr Biol*, 101:67–72, 1988.
- [21] F. Kaufmann and T. Krabatsch. Using medical imaging for the detection of adverse events ("incidents") during the utilization of left ventricular assist devices in adult patients with advanced heart failure. *Expert Rev Med Devices*, 13(5):463-74, 2016.
- [22] A. Blitz. Pump thrombosis - a riddle wrapped in a mystery inside an enigma. *Ann Cardiothorac Surg*, 3(5):450-471, 2014.

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Surgery in the year 2030: Surgery 4.0?

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Introduction

Future developments in surgery are not only interesting for surgeons but also an issue for biomedical engineers and computer scientists in order to focus their own work and energy to areas which most probably become relevant. Surgery of the next decade may be described best by the keyword “surgery 4.0”.

The term and its meaning are as yet even unfamiliar to most surgeons and most probably even less known by engineers. We coined it in 2016 [Feußner 2016] to describe a vital development in surgery, which could conceivably become as disruptive in interventional medicine as the current trend toward economic and industrial digitalization. To make the parallels and contrasts more evident, a reflection on the Fourth Industrial Revolution is helpful.

The global economy is assumed to move forward to the Fourth Industrial Revolution. Commonly, the mechanization of production using water and steam power is considered to have driven the First Industrial Revolution. The next “revolutionary” impact on industrial productivity came from mass production facilitated by the availability of electrical energy and improved workflow organization (assembly line, etc.). This was followed by the Third Industrial Revolution, which is characterized by the use of information technology (IT) and robots to automate production.

Today, a systematic transformation of industrial production is under way, which can be grossly defined as the comprehensive computerization of manufacturing.

The vision is some type of self-organizing or autonomous production: the factory with its production lines “understands” what has to be produced and autonomously carries out all necessary steps and adjustments. This strategy, originally propagated by the German Government as the Industry 4.0 initiative, is evidenced in the customization of products under the condition of highly flexibilized production. This highly automated technology is enabled by the introduction of methods of self-optimization, self-configuration, self-diagnosis, cognition and intelligent support of the few human beings who are still required to master this complex process. The main pillars are as follows:

1. Interoperability: The ability of machines, devices, sensors, and people to connect and communicate with each other via the Internet of Things (IoT) or the Internet of People (IoP).
2. Information transparency: The ability of information systems to create a virtual copy of a physical world by digital models with sensor data. The very dense net of information is available for all

stakeholders. A huge amount of raw data have to be collected and interpreted in a higher context.

3. Technical assistance: Decision-making has to be facilitated by preparing all necessary information. Humans have to decide all necessary preconditions (information) that have already been provided.
4. Decentralized decisions: The ability of lower-level systems to make decisions on their own and to perform their tasks as autonomously as possible. Only in the case of exceptions and/or conflicting goals are tasks to be escalated to a higher level.

Autonomous decision-making by mechatronic support devices is the real disruptive element of Industry 4.0. Humans will need to be confident that machines are able to act and react reasonably, reliably, and as fast and as safely as a human worker.

There are, however, some necessary preconditions for this vision to become reality.

1. The IoT must support direct communication or dialogue with the technical equipment. If one device alters its functionality, the whole technical environment is informed.
2. Data/information must be provided wherever it is needed in real-time and by a high-quality, reliable service (5G telecommunication).

Surgery and the 4.0 development

What then has all this to do with surgery? Some context in the form of a brief review of modern surgical history may be helpful.

The beginning of scientific surgery dates back about 150 years. Retrospectively, this comparatively short period of time can be subdivided into three different eras. In the beginning, surgeons learned to master the specific challenges of the different anatomical regions – beginning with the abdomen and ending with the brain. In the next phase, surgery was not any longer confined to resection/amputation, but the focus was now laid on substituting deficits. Destroyed joints were replaced by artificial implants, and functional reservoirs were developed to accommodate for the roles of the stomach or rectum, for example, after their resection. The ultimate highlight of the era was the transplantation of whole organs (the heart, liver, kidneys, etc.).

The trend today is to further minimize the surgical trauma – collateral damage to other organs, functional impairment, and pain due to the operative intervention. This third era of

surgery started with the introduction of laparoscopic surgery. Laparoscopy was, however, only the beginning of a broad development in many medical disciplines toward minimally invasive therapy.

We are now arguably on the threshold of a new era. This does not mean that further advances in reconstruction (phase II) or trauma reduction (phase III) should no longer be pursued, but the innovative impact comes now from another discipline: information/digitalization.

Although surgery is often considered a manual or technical discipline, it will not remain unaffected by the general trend toward the information age development.

On the contrary, surgery in the information age is more or less a synonym of “surgery 4.0”. Surgery will soon adapt new technologies and methodologies, such as the IoT, process modeling, cooperative learning machines, and new approaches to the generation of knowledge that will affect surgery – all with the aim to improve the quality, efficiency, and outcomes of surgical care. Surgery 4.0 might be the chance to master the difficult situation surgery is currently in.

Surgery is forced to maximize quality and value of surgical in a highly competitive environment. Surgery 4.0 or “information-based surgery” might be the best chance to respond to these needs. Some practical aspects of “surgery 4.0” are delineated.

The fully integrated, “cognitive” OR workplace

Today, the surgical OR is a workplace comprehending the OR table, the surgical lamps and a plethora of peripheral devices working completely independent of each other. The OR of the future will be a highly integrated environment of smart intraoperative assistance systems collaborating with each other via the IoT.

Model-based surgery

A fully integrated OR, however, is only conceivable if the surgical activities – the workflow – is known and can be “understood” by the system. The precondition is a modeling of the surgical workflow.

A “surgical model” is an evidence-based, detailed plan of a particular surgical intervention with a clear description of the workflow from skin incision to closure. It not only includes the normal course of an operation but considers potential modifications and deviations as well. To create “surgical models” either bottom-up or top-down approaches may be considered [Neumuth 2017]. Modern IT methodologies such as machine learning will become extremely helpful to establish “model-based surgery”. However, even the most advanced computer technology cannot substitute for surgical expertise – an urgent challenge for the surgical community to engage and scientifically collaborate in the development of Surgery 4.0.

Knowledge extraction

Since the preoperative diagnostic workup and the whole treatment as well as the postoperative care will be meti-

culously documented in each individual case, these easily accessible data will become very valuable for gaining new insights retro- or prospectively (data mining). For surgical decision making, hundreds or thousands of similar cases can easily be identified as a fundament of evidence-based treatment.

The key: Surgical Data Science

As shown above, the future transformation in surgical care will be driven by data/information. The key elements on the path toward evidence-based surgery are new tools to measure, model, and quantify surgical processes including intraoperative decision-making and knowledge extraction. An intelligent collaboration between care providers and devices/technologies will be enabled. A new scientific domain is, thus, gradually emerging: Surgical Data Science. It is defined as follows: “Surgical Data Science is an emerging scientific field with the objective of improving the quality of interventional healthcare and its value through capturing, organization, analysis, and modeling of data. It encompasses all clinical disciplines in which patient care requires intervention to manipulate anatomical structures with a diagnostic, prognostic, or therapeutic goal, such as surgery, interventional radiology, radiotherapy, and interventional gastroenterology. Data may pertain to any part of the patient care process (from initial presentation to long-term outcomes), may concern the patient, caregivers, and/or technology used to deliver care, and is analyzed in the context of generic domain-specific knowledge derived from existing evidence, clinical guidelines, current practice patterns, caregiver experience, and patient preferences. Data may be obtained through medical records, imaging, medical devices or sensors that may either be positioned on patients or caregivers or integrated into the instruments and technology used to deliver care. Improvement may result from understanding processes and strategies, predicting events and clinical outcome, assisting physicians in decision-making and planning execution, optimizing ergonomics of systems, controlling devices before, during and after treatment as well as from advances in prevention, training, simulation and assessment. Surgical Data Science builds on principles and methods from other data-intensive disciplines such as computer science, engineering, information theory, statistics, mathematics, and epidemiology, and complements other information-enabled technologies such as surgical robotics, smart operating rooms, and electronic patient records.” [Maier-Hein 2017] It also includes a significant impact on surgical education and training. Surgical Data Science (SDS) not only enables objective computer-aided skill evaluation but also automated coaching.

Discussion

Surgery of the next decades will certainly gain a new profile due to the vast use of information. Self-evidently surgery 4.0 is not only confined to a more or less abstract utilization of information but will also have a massive impact

upon the use of a new hardware: Intelligent, cognitive surgical assistance systems (“robots”) will reduce the surgical workload by (semi-) autonomous manipulations like camera navigation or suturing. Integrated, precisely navigated percutaneous or endoscopic puncture probes could replace conventional surgical cancer resection by local ablation. Based upon an “intelligent” OR environment even completely new surgical approaches like combined laparoscopic/endovascular interventions are becoming conceivable. From the surgical viewpoint, these options would be highly attractive, but this also means that technology will play an increasing role in modern surgery. Simply accepting this fact is not enough what surgeons can do. They are even summoned up to contribute actively to technical progress by identifying currently existing deficits, by careful evaluation and improvement of prototypes and generally by providing their domain knowledge. Hopefully, this will lead to a new “culture of cooperation” between basic scientists, computer scientists, engineers and clinically active surgeons.

Conclusions

Surgery 4.0 does not mean that robots will perform surgery on their own in the future. This can neither be the vision of surgeons nor would it be accepted by the majority of patients in societies with a highly developed healthcare system, as one very recent study [Arnold 2017] has shown. However, artificial intelligence, robotics, model-based surgery, and many additional principles of Surgery 4.0 will certainly help to make surgery more evidence-based, safer, and easier, all with the goal of a better outcome and experience for the patient.

References

- [1] Arnold D, Wilson T. What doctor? Why AI and robotics will define new health. 2017. Available at: https://www.pwc.de/de/gesundheitswesen-und-pharma/assets/30597_healthcare_ai_ipad_interactive_v10.pdf. Accessed 16 August 2017.
- [2] Feußner H, Wilhelm D. Minimally invasive surgery and robotic surgery: surgery 4.0? *Chirurg* 2016;87:189–94.
- [3] Maier-Hein L, Vedula S, Speidel S, Navab N, Kikinis R, Park A, Eisenmann M, Feussner H, Forestier G, Giannarou S, Hashizume M, Katic D, Kenngott H, Kranzfelder M, Malpani A, März K, Neumuth T, Padoy N, Pugh C, Schoch N, Stoyanov D, Taylor R, Wagner M, Hager GD, Jannin P. Surgical Data Science: Enabling next-generation surgery. *arXiv:1701.06482*, 2017
- [4] Neumuth T. Surgical process modeling. *Innov Surg Sci* 2017;2:123–37.

Acknowledgements

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Intraoral Microfocus X-ray radiography in veterinary medicine

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Introduction

The provision of veterinary dental care is becoming an increasingly urgent task, for example, in dog breeding. So, for a thoroughbred exhibition animal, the loss of even one tooth can lead to the termination of a career.

In medicine in the vast majority of cases, diagnosis of the maxillofacial department is carried out with the help of specialized X-ray devices: traditional dental units, orthopantomographs and cone-ray tomographs [1]. Traditional dental devices (radioviographs) are designed to produce images of individual teeth or jaw areas, orthopantomographs for two-dimensional, and cone-ray tomographs for three-dimensional images of the full dentition of both jaws, including adjacent anatomical structures.

For a number of reasons - differences in the anatomy and physiology of the maxillofacial department of man and dog, as well as the language barrier, these devices cannot be directly used in veterinary dentistry. The flexibility and mobility of the fingers, paws, neck, and back of the dog are fundamentally lower than that of the corresponding human organs. The dog cannot fix the detector of the X-ray image with a finger or sit motionlessly in the chair of the cone-ray tomograph for a long time. The dog also cannot understand and fulfill the specific requirements of the X-ray assistant during the X-ray shooting.

Obviously, to solve the problems of diagnosis of veterinary dentistry in full, it is necessary to develop the appropriate technology.

Materials and Methods

At the present time for diagnostics in veterinary stomatology is used:

- sighting (traditional) dental units for taking pictures of individual teeth or jaw areas on an X-ray detector measuring 30×40 mm, which is placed in the oral cavity of the animal (Fig. 1)

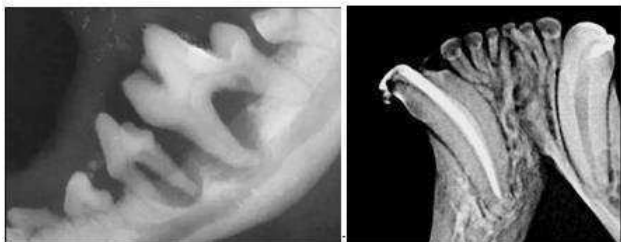


Figure 1. Examples of obtained images using standard sighting dental devices.

- stationary X-ray apparatus for obtaining images of the entire head of the animal on an X-ray detector of 240×300 mm or more (Fig. 2, 3).



Figure 2. Scheme of shooting using powerful stationary X-ray apparatus.



Figure 3. Example of obtained images using powerful stationary X-ray apparatus.

The main disadvantages in the first case.

The size of the image detector does not allow:

- get a complete picture of even one tooth of a large dog;
- placement the image detector in the oral cavity of a small dog.

The probability of damage to the image detector by a dog of any size is great.

The main disadvantages in the second case:

- on the picture of the dog's head, images of all the teeth, bones of the skull and soft tissues are superimposed on

each other. This greatly complicates the description of the picture and the diagnosis

- the additional dosage for the animal and personnel.

At the beginning of the 21st century in Russia was offered a technique of Microfocus X-ray radiography. Unlike the currently known methods, this method allows to obtain:

- sighting images of individual teeth or jaw areas;
- panoramic images of the full dentition of both jaws, including adjacent anatomical structures [2].

To implement the technique, an X-ray tube with a hollow outside anode and a massive target 0.01BD57-90 (Fig. 4) was developed [3]. The length of the anode pipe is 120 mm, diameter 12 mm, and material - aluminum. The tube generates a panoramic X-ray beam with a solution angle of $135 \times 360^\circ$. The direction of the radiation output is opposite to the direction of motion of the electrons in the accelerating gap of the cathode-anode (tube target). On its basis, the sighting-panoramic dental X-ray apparatus PARDUS-02 was also developed [4].

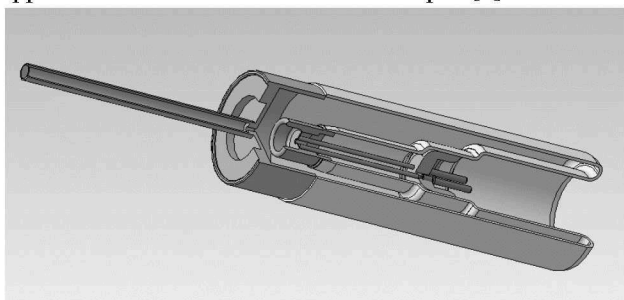


Figure 4. 3D drawing of the X-ray tube with a hollow outside anode and a massive target 0.01BD57-90.

Results

Studies conducted based on the city veterinary clinic №1 of St. Petersburg showed that the sighting device of the PARDUS family in portable design can be successfully used in veterinary dentistry for the direct dental studies. In the course of the tests, specialists highly appreciated the quality of the obtained X-ray images (Fig. 5), as well as the prospects for the development of a sight-panoramic technique for performing X-ray studies in veterinary medicine.



Figure 5. Dental pictures, obtained with portable X-ray device of the family "PARDUS".

A fundamental difference between the technique of panoramic X-ray radiography in veterinary medicine, in contrast to the standard methods, is the location of the anode of the X-ray tube directly inside the oral cavity of the animal. The X-ray generated by the tube passes through the teeth, jawbones, soft tissues and get to the X-ray detector, which is located outside the head of the dog opposite the diagnosed area (Fig. 6). In the course of further planned studies, the methods of installation will be tested, the shooting regimes will be improved, the dose of irradiation of the animal and the X-ray assistant will be estimated.

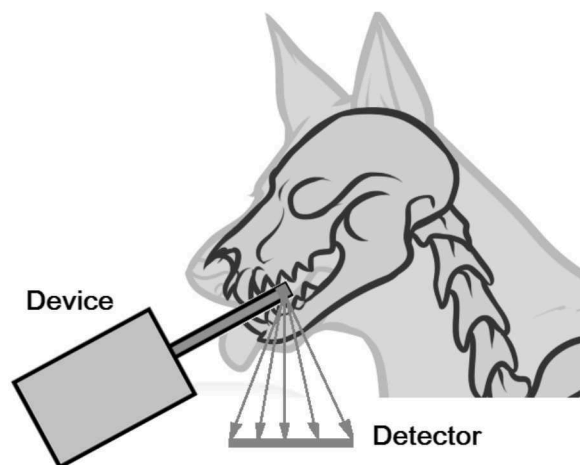


Figure 6. Scheme of the intraoral panoramic X-ray survey in veterinary medicine.

The main advantages of the method of the intraoral survey in veterinary medicine:

- small diameter and long length of the anode pipe allow placing the target of the X-ray tube anywhere in the oral cavity of an animal of any size;
- the reverse panoramic direction of X-ray radiation excludes the imposition of teeth belonging to different branches of the jaws;
- high informativeness of the images is provided by a small focal spot at an extremely low current tube (0.1 mA) and, accordingly, very low the exposure dose;
- the source of X-ray radiation is located inside the mouth, so the intensity of unused radiation is fundamentally lower due to absorption of the tissues of the head;
- ensured safe conditions for the X-ray assistant when shooting "from the hand" without the use of a traditional tripod;
- shooting "from the hand" greatly facilitates the laying of the animal and improves the efficiency of the diagnosis, primarily in non-specialized and non-stationary conditions.

Conclusions

As a result of a complex of design, technological and clinical research, a new technology for performing X-ray diagnostics in veterinary dentistry was proposed. The technology includes the method of the sight-panoramic survey

of the maxillofacial department of the animal and a set of digital technical means for its implementation. Conducted tests have shown expediency of carrying out of the further practical development in the field an X-ray survey of the maxillofacial department of the animals.

References

- [1] Fundamentals of X-ray diagnostics / Ed. N.N. Blinov. Tutorial. - Moscow: Medicine, 2002.
- [2] Potrakhov N.N. Microfocus X-ray radiography in dentistry and maxillofacial surgery. St. Petersburg: Technomedia Ltd., Page 184, 2007.
- [3] Author's Certificate No. 1793491 of the USSR, MKI H01J35 / 08. X-ray tube / Potrakhov N.N. and others; Application 25.06.91; registered 08.10.92.
- [4] Potrakhov N.N., Potrakhov E.N., Gryaznov A.Y. Portable X-ray diagnostic devices of the family "PARDUS" for sighting and panoramic research in stomatology and maxillofacial surgery // Medical technology, pages.45-46 - 2008. - №5.

Specialized x-ray machine for neonatology

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Introduction

The usage of X-ray radiation in modern neonatology makes a significant contribution to the quality of medical care for newborns with pathologies. High-quality image of the baby allows to quickly diagnose the problem or to prevent future possible complications.

The method of contact diagnostics (see fig.1) gives satisfactory results, however, to obtain informative images should take into account the following restrictions:

1. *A large distance between the radiation source and the object of study.* This condition is dictated by the need to distance the radiation source to reduce the blurring of the edges. It is necessary to use sufficiently powerful sources to work around the dynamic range of the receiver (which leads to the maximum contrast of the image). Increased tube current causes an increase of the focal spot. Its size directly affects the degree of outer edges blur on the image, which is unacceptable in the case of medical diagnosis. Compensation for this phenomenon is increasing the distance between source and receiver. This can lead to unwanted additional exposure of medical staff and others patients.

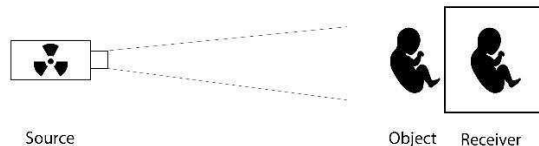


Figure 1: Contact X-ray diagnostics of newborns

2. *High resolution X-ray detector.* Upon contact of an object and a radiation receiver, the image quality depends on resolution of the receiver. However, increasing resolution naturally reduces sensitivity of pixels (by reducing their geometry sizes). This eventually leads to the necessity of increasing power of the radiation source.

3. *High power X-ray radiation.* Increased distance source-object and high resolution of the receiver lead to significant increase in power of X-ray diagnostic machine. Traditionally, the radiological diagnosis in neonatology and pediatrics using radiation sources with power up to 5 kW, which is directly related to their size and weight. From the point of view of stationary use it's not a big deal. However, for portable options, which work in conditions of constant transportation, this factor is essential.

Thus, of use of X-ray machines in non-specialized conditions, for example when you need to do diagnostic immediately after the procedure of childbirth is in the room of the maternity ward, the use of classical X-ray machines, described above, is not optimal. The basic idea, which is based on an alternative approach to the diagnosis of new-

borns is the use of smaller power sources with reduced size of the focal spot of the radiation source. The decrease in its value up to 0.3 mm or below will allow to diagnose newborns under appropriate conditions with scaling method (see fig. 2). Decrease focal spot is achieved with a small current of the tube and using additional focusing electrodes. The lack of dose is compensated by minor (20 – 30%) increasing of operating voltage and decreasing of shooting distance. As a result, while maintaining the quality of the image this approach provides the following benefits:

- Resolution of the receiver can be reduced. This leads to the best sensitivity.
- Source-object distance is reduced, which minimizes exposure of staff and others, and also reduces requirements on the output power.
- Relatively low power (360 – 500 W) of radiation source reduces weight and size of the device, which greatly simplifies its use in unsteady conditions [1].

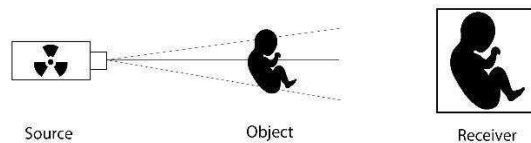


Figure 2: X-ray diagnostics of newborns with scaling

In this paper, the circuit and structural features of low-power portable apparatus for neonatology, its internal structure and organization of electronic modules are introduced.

Materials and Methods

Interconnection of electronic modules built on the centralized control principle (see fig.3). For the implementation of sensing functions and heat supplying, the subsidiary module is used. The high-voltage part comprises a generator and a voltage multiplier.

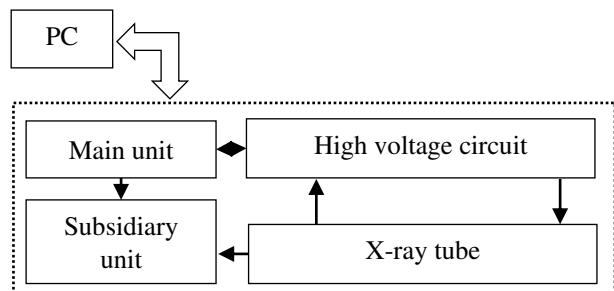


Figure 3: The generalized structure of electronic modules

Fig. 4 represents the organization of the main control module. Its basic functions are:

- control of X-ray tube supply power generator;
- management of data flow between PC and device;
- monitoring of the central module: the temperature of the inductive element, the average temperature of the power transistors, the average power consumption;
- X-ray dose control.

The Central MCU communicates with the Ethernet controller that have hardware support for the TCP/IP protocol. All data transmission is handling through specialized Ethernet PHY controller by SPI interface. The use of specialized chip simplifies the interaction of the microcontroller with a PC and partially offloads the core and the peripheral modules, however, the cost of such solution is considerably higher than MII/RMII chip. The power supply is controlled by 16-bit timer with push-pull signal with a pulse width modulation (PWM) [2]. The module is located on the outside of the case and is not in contact with an insulating filler (transformer oil). Inside casing the subsidiary module, all high voltage components (transformer, multiplier and divider, the X-ray tube) are located. From the Central unit to the internal elements a power line (the transmission of energy to the transformer) and two differential signal lines are routed. To ensure independent transmission in both directions of the communication channel a full duplex is implemented.

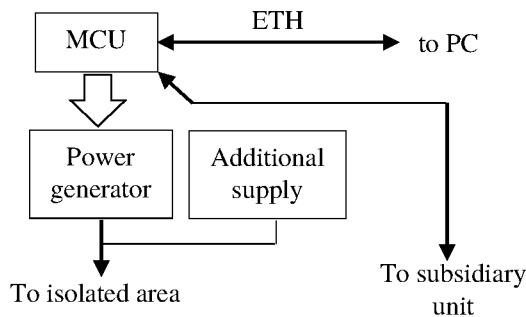


Figure 4: Structural diagram of control board

A subsidiary module (a structural diagram is represented in fig. 5) is placed inside the case in the vicinity of high-voltage circuits. The unit performs following functions:

- control of filament current;
- measurement of electrical parameters of the X-ray tube, such as voltage, tube current, filament current;
- calibration of measurement data and control of electrical parameters of the X-ray tube searching in a given workspace;
- control of ambient temperature (temperature of transformer oil);
- flexible converting input analog signals.

The main module node is the MCU, which controls the filament current and measures circuit parameters using the 4-channel 12-bit internal ADC. The temperature of the environment is controlled by sensor, which integrated into MCU package. Communication with the control board is realized via the RS-485 interface. This solution provides the most optimal ratio of communication speed to noise immunity.

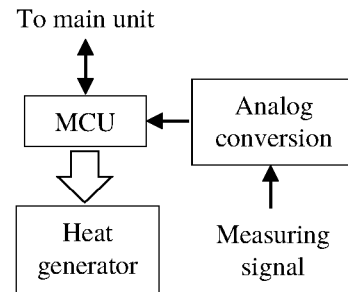


Figure 5: Structural diagram of the subsidiary module

When controlling the filament current is important to consider that the resistance of the filament is substantially depends of temperature. Standard approach uses the pulse-width modulation; full voltage amplitude is applied to the filament. In the case of low temperature (it happens at first turn on) initial current intensity may be significant (exceed the maximum to 1.5 times). This eventually may lead to its thermal destruction. A solution to this problem is the combination of pulse-width modulation and frequency control [3]. Fig. 6 represents a simplified circuit of the filament supply. The pins of the X-ray tube cathode form a parasitic inductance which at high frequency limits start current equal to:

$$I_{\text{start}} = \frac{U_s}{R_{\text{heat}} + Z_{\text{leak}}}, \quad (1)$$

where U_s is the amplitude of the voltage of the filament supply, V; R_{heat} – the resistance of the filament in Ohms; Z_{leak} – impedance of the parasitic inductance of pins on the current frequency, Ohms.

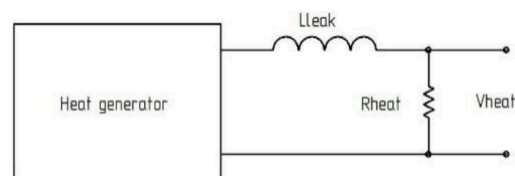


Figure 6: The equivalent circuit of circuit the heated filament

Thus, the combination of a gradual increase of duty cycle and frequency can be used to achieve amplitude modulation of the heat voltage that will provide a smooth increase of operating current and significantly extend the service life of the machine.

The machine construction design (see fig. 7) is based on several ribs formation of the carrier frame. This is done by perpendicularly arranged walls that provide a rigid positioning of the device in space relative to the outer aluminum case. This aspect is especially important because of the strict requirements for maintaining a minimum displacement of the apparatus. The change in the position in the process of exploitation can lead to the risk of voltage breakdown. Therefore, special attention was paid to make the structure as rigid as possible [4].

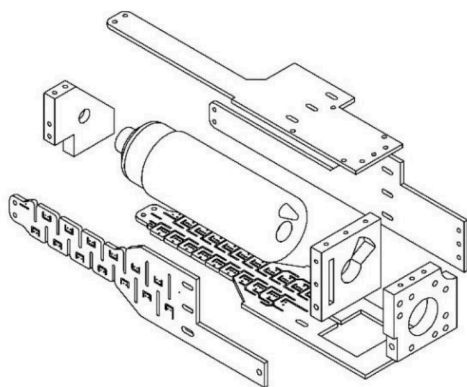


Figure 7: Sketch of the internal nodes construction of X-ray machine

Load-bearing walls are made of FR4. The products made of this material is technologically advanced and has a stable surface breakdown voltage of about 1.5 kV/mm (assuming storage material is isolated from dirt and moisture). The transverse plate is made of PTFE and in addition to quality insulation provide rigid fixation of all structural elements.

Results

Eventually, fully functioning layout portable, low power apparatus for neonatology with the ability to control from PC or control panel, were designed and constructed. Main characteristics are introduced below:

- operating voltage: 120 kV;
- operating voltage ripple: < 3%;
- maximum power: 360 W;
- efficiency: > 75%;
- output raise time: < 20 ms;
- weight: 5 kg;
- controlled by PC or portable console;
- size: 380 × 130 × 180 mm.

The present design provides a quick assembly, which increases the manufacturability of serial production. A modular approach to the design of electric circuits allows to make fast replacement of units and perform a local update of specific parts of the scheme. Testing the model sample of the device was carried out in laboratory conditions.

The closest analog is portable X-ray machine EcoRay 9020HF. Comparison (see tab. 1) demonstrates, that new design uses tube with lower focal spot, which allows to decrease power of machine and its weight. Lower power is compensated by higher voltage (120 kV against 90 kV) and decreased distance (0.35 m).

Table 1: Characteristics of apparatus in comparison with nearest analog on the market

Item	Introduced machine	Analog
Focal spot size, mm	0.4 × 0.4	1.2 × 1.2
Power, W	360	1200
Operating voltage, kV	120	90
Shooting distance, m	0.35	0.66
Weight, kg	5	7

Discussion and Conclusions

Modern medical X-ray machines allow to obtain high-quality images for accurate diagnosis of patients. However, medical staff are always at risk of extra exposure. This is especially true for portable applications, when medical worker holds the apparatus or stands near it. Introduced machine greatly reduces extra radiation in comparison with similar ones having large focal spot. Small focal spot allows to decrease power of the apparatus and distance between source and receiver. Dimensions and weight are also decreased, portability is improved. Moreover, X-ray diagnostic complex based on microfocus tube can perform images with higher quality than classic apparatus does. Implementing local net between machine, PC and receiver allows to expand possibilities of constructing specialized X-ray complexes. Several sources and receivers could be combined under single or distributed control.

References

- [1] Potrakhov N N. Journal of new medical technologies, 2007, vol. 14, no. 3 167-9.
- [2] V. V. Klonov., I. A. Larionov, V. B. Bessonov. Modification of circuit and investigation of operating modes of the high-frequency pulse resonance converter for the X-ray tube power supply. In IV all-russian scientific and practical conference for manufacturers of X-ray technology, pages 42–46, nov 2017.
- [3] Philips semiconductors. Power semiconductor applications, chapter 2 – Switch mode power supplies. URL: <http://educyclopedia.karadimov.info/library/APPCHP2.pdf>.
- [4] G. Pisarenko 1988. Handbook on strength of materials.

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Computer program for setting up a medical X-ray apparatus

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Introduction

Distribution of digital equipment, including the production of medical X-ray apparatuses, allows to control various devices using a computer software. At present, this mechanism is a widespread practice.

The vast majority of power sources of medical X-ray apparatuses are built according to the scheme with amplitude or pulse-width modulation (PWM). At the same time, the resonance control scheme of the X-ray tube is also promising. In comparison with PWM control, the resonance circuit allows to obtain greater efficiency and to provide a more exact adjustment of operating parameters of the apparatus. The adjustable parameters are: resonance frequency, heating current and duty cycle. The most convenient way to establish the values of these quantities is their software setting. Thus, the aim of the work is to create graphic user interface (GUI) for setting up an X-ray apparatus.

Materials and Methods

A model sample of medical X-ray machine for neonatology was compiled on the basis of the EPU department of ETU «LETI» [1]. Due to the features of a scope of the apparatus it is necessary to provide high efficiency of his work that is achieved by applying a resonant control circuit.

Parameters of the X-ray apparatus

The parameters of the power supply (excluding the voltage multiplier), which define the mode of operation of the X-ray tube (current and voltage on the tube) include filament current, resonant frequency and duty cycle. A specific set of values for these parameters will yield the desired current and voltage of the tube.

In order to determine possible combinations of these parameters for establishment the required values of current and voltage on the X-ray tube, the characteristic curves for current and voltage were obtained experimentally. The received dependences are qualitatively reflected in figure 1, 2 and 3 (in Fig. 1, the ratio of currents is as follows $I_4 < I_3 < I_2 < I_1$; in Fig. 3, the ratio of the filament currents is as follows $I_{h4} > I_{h3} > I_{h2} > I_{h1}$).

Experiments have shown that at different currents of heat, the current of the X-ray tube is guaranteed to reach saturation at a voltage of 40 kV (V_{min}). This feature allows to receive calibration points as follows: to expose the minimum level of filling (about 5%); to shift the frequency before obtaining voltage on the tube of 40 kV; when this

value is reached, record the calibration point parameters. Increasing the filling coefficient with a given step, it is possible to receive a set of calibration points. In order to set certain operating parameters, the machine takes the values of the obtained calibration points as a basis during operation and, if necessary, calculates the value at the interval between them.

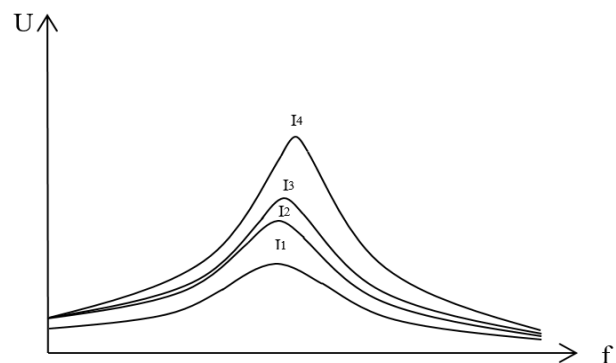


Figure 1: Dependence of the X-ray tube voltage on the generator frequency

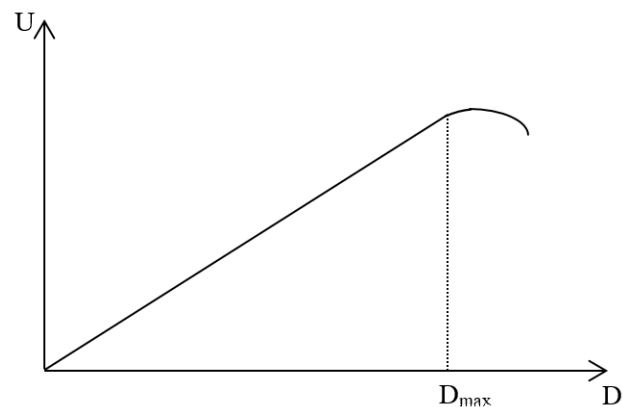


Figure 2: Dependence of the X-ray tube voltage on duty cycle

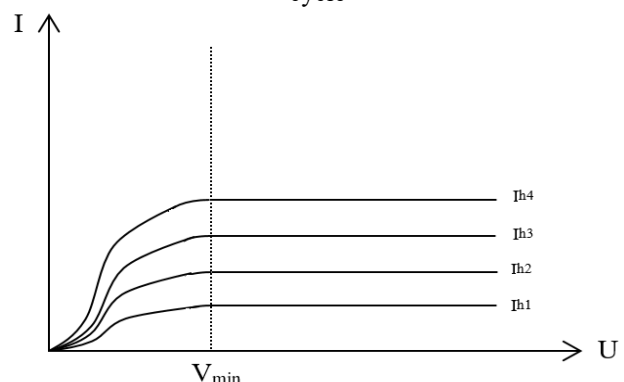


Figure 3: Volt-ampere characteristic of the X-ray tube

Features of the apparatus control and their software implementation

Due to the fact that the X-ray radiation belongs to ionizing, special attention should be given to matters of radiation safety when carrying out all types of work. If it is necessary to control the X-ray machine remotely using a computer program, first of all there is a question about the reliability of the communication line. In addition, the reliability of the received and sent data, which can affect the operation of the machine, is also an important point. At the same time all data can be sent and received only according to a certain protocol of interaction.

Reliability of the communication line: Taking into account the aforesaid, communication of the apparatus with a personal computer can be performed through the Ethernet line. There may be situations when the apparatus stops responding to commands due to the loss of physical connection between the cables. In that case, if the generation of X-ray has been started, then it will continue that is undesirable. To monitor the situation of loss of communication software implemented the constant data exchange between the personal computer and the x-ray apparatus. The need for constant monitoring of the operational parameters of the apparatus justifies the existence of such a constant connection. If necessary to send a command that differs from request parameters, corresponding to the command packet simply replaces the send queue of the request packet.

Accuracy of the data: The TCP / IP Protocol stack was selected as the top-level protocols. This ensures that the data packet is delivered to the recipient. For a possibility of management under the TCP/IP protocol a specialized chip of w5100 is used. In this chip, the use of standardized protocols is implemented by hardware, which eliminates the need to control the delivery and check the checksum (this factor is important in the X-ray t equipment as ensuring the reliability of the transmitted data will protect the machine from possible errors and emergency uncontrolled user modes).

Protocol of interaction: Any interaction between the control device and the operated device is performed according to certain rules, usually described in the so-called protocols. The first version of the protocol of interaction XRTMP (X-ray tube management protocol) between the x-ray apparatus and the external controller was developed to simplify the interaction of developers when writing software for the PC and for the microcontroller. In accordance with the protocol, all packets have a fixed length, which is 20 bytes. Figure 4 shows a block diagram of the interaction levels between the control device and the X-ray apparatus. The drafted protocol is responsible for the interpretation of transmitted data packets and the organization of interaction between internal nodes of the apparatus. In accordance with the communication protocol, besides control commands (these include turning the machine on and off with the set parameters), there are al-

so special commands for apparatus settings (for example, setting generator parameters such as frequency and duty cycle, etc.).

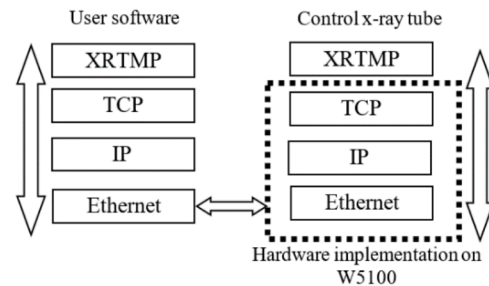


Figure 4: Organization of a protocol stack

Setup of the apparatus: Values of the operational parameters, though weakly, but vary from device to device in connection with dissimilarity of the electronic components used to build these devices. For this reason, at the first inclusion tuning of the apparatus has to be performed surely. Otherwise, the parameters stated in the documentation may not fully correspond to reality. Program and circuit control implementation provides a possibility of various calibrations types and settings:

- calibration of sensor;
- adjustment of emergency thresholds;
- setting operation modes of the tube;
- control of the working dose.

Calibration of sensors is intended for increase the accuracy and reliability of the data about current and voltage on X-ray tube, about heat current and also a radiation dose received from them. Depending on which components were used to assemble the apparatus, the emergency threshold values may vary. In order to take into account this feature, it is possible to update the threshold values. Setting of the operation modes allows to correct the current and voltage values for modes which are already written down in the machine. Special attention among the possible calibrations and settings deserves to control the working dose.

Structurally inside the apparatus there is a possibility of placement a special sensor, which is capable to register a relative dose of X-ray radiation. Under normal operating conditions, the dose level will coincide with the calibrated values (with allowance for minor fluctuations). In the case when the mode of operation of the apparatus is incorrect, the program will be able to track this by changing the working dose of radiation. All settings occur at the level of the microcontroller, which receives instructions for calibration from the host computer.

Results

To control the model of the X-ray apparatus, a program for a personal computer has been developed. As a development tool the framework Qt [2] was applied, and the program was under construction on the basis mentioned above data exchange protocol. With the help of this development environment, the interface of the control program was designed and implemented, the main window of

which is represented in the Fig. 5. The program is written on the C++ language.

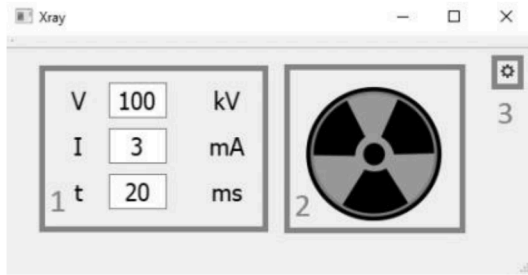


Figure 5: Main window of the program

The main window of the program can be conditionally divided into 3 parts: first block is the unit for setting exposure parameters (voltage, current and time); second block is the immediate start-up of apparatus (inclusion of X-ray radiation); third block is the configuration icon. Almost always the operator needs to use only the first two blocks. However, there are situations when it is necessary to change the machine settings (for example, to rebuild the resonant frequency). Circuitry and software implementation allow performing this action by simply changing the value in the corresponding field of the program by the operator. Despite such apparent simplicity of adjustment, all controls for calibration, advanced setting and connection of the machine are taken out into separate window, which is accessed after entering the correct password. Part of the advanced program settings window is shown in Fig. 6.



Figure 6: Part of advanced settings window

The presented part of the advanced settings allows changing the resonance frequency, duty cycle, starting and stopping the generator, and also checking the communication by the signal LED.

In general, advanced settings allow the attendants to perform the following actions:

- change IP-addresses and ports as needed to establish the connection between the personal computer and the apparatus;
- open and close the corresponding TCP connection;
- send a special request to the apparatus;
- receive and visualize response from the apparatus to corresponding request;

- start and stop pulse generator;
- change frequency and duty ratio of the generator;
- monitor the connection and operation of apparatus by means from signal LED;
- perform calibration for following parameters: voltage, tube current, filament current and temperature of tube;
- to monitor the above parameters in real time.

Indication of the current values of the main parameters of the apparatus is also contained in a separate part of the extended settings window of the apparatus. The parameter display field is shown in Fig. 7.

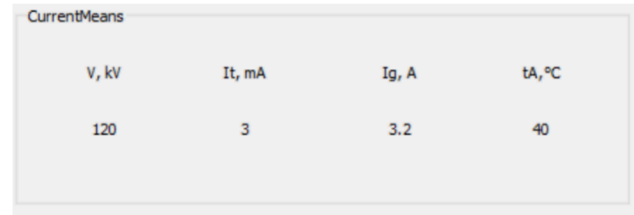


Figure 7: Indication of the current parameters of the apparatus

It should be noted that the program requires a computer with an installed operating system of the Windows family (Windows XP SP3 or higher), as well as the ability to use the computer TCP/IP connection. As for the rest, the program does not impose special requirements on the used computer.

Conclusions

The computer program created in the course of operation allows to adjust the X-ray apparatus for neonatology to improve its performance characteristics. In the future we plan to expand the ability program to control several satellites simultaneously, and also to find the optimal calibration algorithm for the apparatus and to implement it programmatically.

References

- [1] V. V. Klonov., I. A. Larionov, V. B. Bessonov. Modification of circuit and investigation of operating modes of the high-frequency pulse resonance converter for the X-ray tube power supply. In IV all-russian scientific and practical conference for manufacturers of X-ray technology, pages 42 – 46, nov 2017.
- [2] M. Summerfield. Advanced Qt programming: creating great software with C++ and Qt 4. Courier in Westford, Massachusetts, 2010.

Acknowledgements

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Digital X-ray image processing with using the adaptive histogram equalization and adaptive background correction

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Introduction

Microfocus X-ray is a combination of methods for receiving X-ray images using radiation sources with focal spots size less than 100 μm . Using these sources gives the opportunity to obtain images with a direct geometric image magnification 5-20 times. Today microfocus X-ray is widely used in medicine, industrial non-destructive testing and quality assessment of agricultural crops. [1,2,3].

In the list of cases, microfocus X-ray images could not be authentically analyzed because of insufficient quality of images. More often main disadvantages of microfocus X-ray images are irregular background, distorted brightness characteristics, the presence of noises. Therefore, the development of algorithms for digital processing of microfocus X-ray images is a relevant task.

Materials and Methods

In the paper, two algorithms of digital X-ray images processing are considered: the algorithm for correcting the uneven image background based on the subtraction of the distorting function and the algorithm for locally-adaptive histogram equalization.

Algorithm for correcting the image background

During the X-ray examination according to the scheme with the direct geometric magnification uneven image background arises, complicating visual analysis and subsequent digital image processing. A distorting function is introduced to eliminate irregular background of the image. It is considered that the receiver registers an image that can be represented as the sum of the image and the distorting function, which creates the uneven background. The distorting function in microfocus X-ray is usually described by a function of the form:

$$g(x, y) = C \left[\left(x - \frac{x_{\max}}{2} \right)^2 + \left(y - \frac{y_{\max}}{2} \right)^2 \right], \quad (1)$$

where C – is a constant, whose value depends on the microfocus X-ray apparatus mode and the shooting conditions, $x_{\max}$ and $y_{\max}$ – is the vertical and horizontal size of the image respectively.

This form of distorting function follows from shooting peculiarities with image enlarging, as X-ray radiation intensity decreases proportionally to the square of the distance.



Figure 1: Image for the analysis

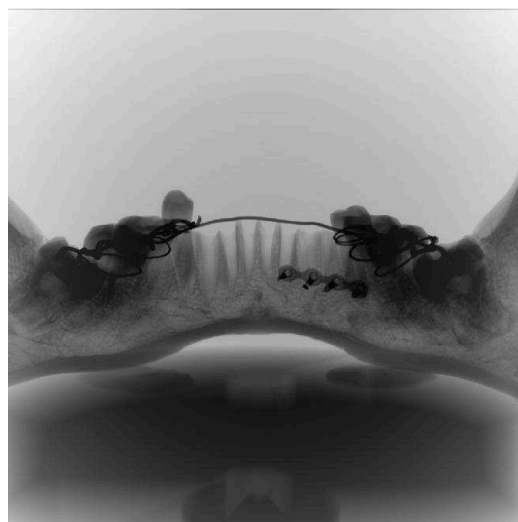


Figure 2: The result of image background correction

For every single profile, its minimum and maximum are determined and the difference between them is found. The constant C is determined by the expression (2) as the medium difference between minimum and maximum of the profiles.

$$C = \frac{\sum_k^N (a_{k \max} - a_{k \min})}{N}, \quad (2)$$

where N – the number of profiles, $a_{k \max}$ and $a_{k \min}$ – respectively maximum and minimum brightness values. In case of the big difference between profiles minimums and maximums the number of the analysed profiles should be increased to get the correct constant.

On figure 3 profile built along the upper edge of the image is presented.

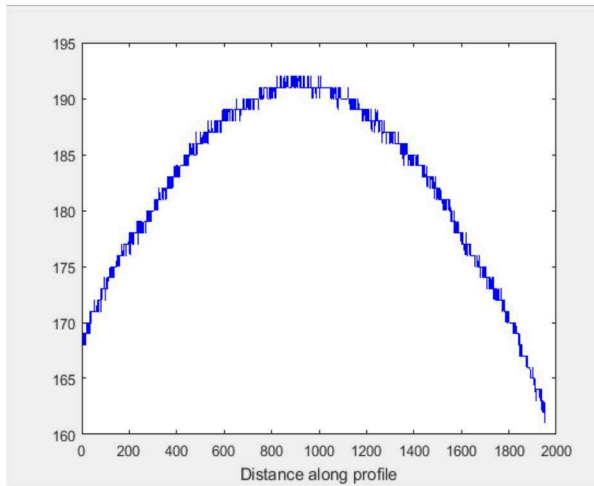


Figure3: Profile of the upper edge of the image

The resulting image $f(x,y)$ is obtained by the way of subtraction $g(x,y)$ from image registered by the receiver:

$$f(x,y) = h(x,y) - g(x,y) \quad (3)$$

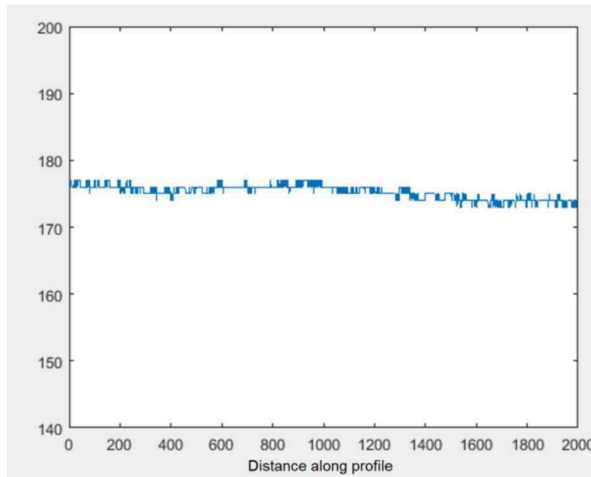


Figure4: Profile of the upper edge of the image after correction

On the figure 4 profile built along the upper edge of the image after the correction of the tone is presented. As it's shown in the figure 3 profile of the image is aligned, uneven background illumination is removed. After image background correction, it's much more convenient for automatic analysis. Visual analysis also becomes easier. So, for teeth image selection on the image primitive threshold transformation can be used, while in a case of uneven background it is ineffective.

The algorithm of local-adaptive equalization of the histogram

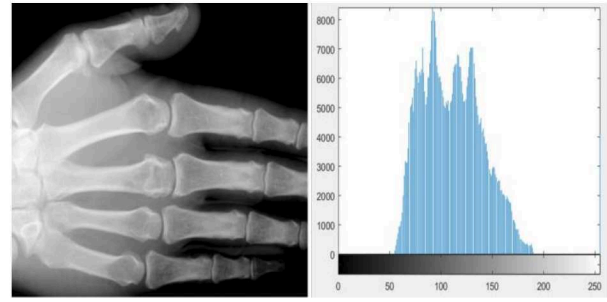


Figure5: The original image and its histogram

The method of the local-adaptive histogram equalization can be also used for the image's contrast improving.

Histogram of the image is a function defined as:

$$h(r_k) = n_k, \quad (4)$$

where r_k – k - is a level of brightness on the image, n_k – number of pixels, belonging to this level of brightness. If the image has a low contrast, this means that the histogram values are concentrated in a certain region of the brightness range [5]. For improving contrast it's necessary for non-zero levels of the histogram to overlap the bigger part of the range of brightness. Equalization of the histogram is a transformation that can be described by the formula:

$$s_k = T(r_k) = \sum_{j=0}^k \frac{n_j}{n}, \quad (5)$$

where s_k – k -level of the brightness of the processed image, n – the common number of pixels on the image, n_j – number of pixels that have brightness r_k .

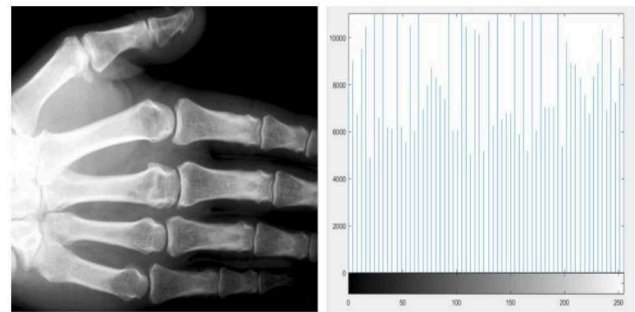


Figure6: The image and its histogram after using the method of histograms' equalization

This method allows you to significantly increase the contrast of X-ray microfocus images without the operator's participation. However, the method of the histogram equalizing does not lead to the desired result if the image has an uneven background or if the image has a wide histogram.

To overcome listed limitations method of local-adaptive histogram's equalization is applied: at first in the method of local-adaptive histogram's equalization the image is splitted into a number of non-crossing areas (usually from

16 to 128) and then every single area is subjected to the histogram's equalization. On the next step, all the areas are combined into a single image with the bilinear interpolation. For removing artificial borders, which appear in the combining areas, the interpolation is used. In this way, there is a local increase in the contrast of the main image details.

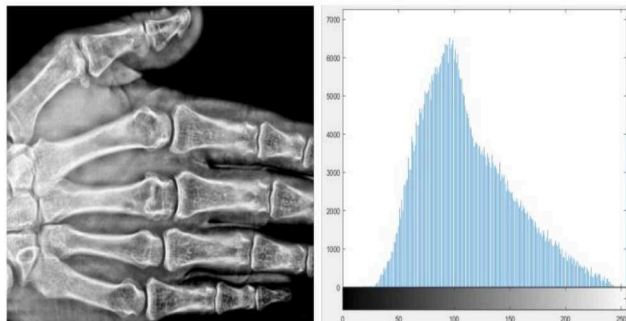


Figure7: Image and its histogram after using the method of the local-adaptive equalization of the histogram

Results and discussion

To check the quality of method of the background correction a sample of 100 medical microfocus X-ray images obtained using different radiation receivers was used.

As the result of the developed method backgrounds of the 73% of the images were fully leveled (pixel brightness values difference between the edges and the center has become less than 5 points), for 27% of the images pixel brightness values difference between the edges and the center has become less than 10 points.

Every single wrong case of the background correction was considered in details. In all the cases error was caused by the fact that objects in the image occupied more than 80% of the length of the profile, so there wasn't enough information to determine the background.

To check the quality of method of the background correction a sample of 50 medical microfocus X-ray images was used. As the result of the application of the method of histogram's adaptive equalization to all images from the sample for 80% of the images, a notable contrast increase was fixed. It also became possible to distinguish the details of tissues and bones. If the traditional method of histogram equalization is applied to the same images, significant improvement in contrast, without deterioration of contrast in other areas of the image, was achieved only in 40% of cases.

Conclusions

As the result the algorithm for image background correction and algorithm of the local-adaptive histogram equalization was developed.

On the samples of microfocus X-ray images, investigations of developed methods were done. Both of the methods gave satisfactory results.

Also, it was determined that while doing the local-adaptive equalization of the histogram, contrast image of both soft and osseous tissues can be reached on the same shot.

References

- [1] Potrakhov N N. Journal of new medical technologies, 2007, vol. 14, no. 3 167-9.
- [2] Potrakhov N N, Gryaznov A Yu Zhamova K K , Bessonov V B, Obodovski A V, Staroverov N E, Kholopova E D, 5 46-54 Biotechnosphere
- [3] Gryaznov A Yu Methods and systems microfocus phase contrast X-ray medical. Doct. Diss., Saint Petersburg, 2010. 245 p.
- [4] Sobel and G. Feldman, "A 3x3 Isotropic Gradient Operator for Image Processing," Pattern Classification and Scene Analysis, 1973, p. 271-272.
- [5] Gonzalez R C, Woods R E. Digital Image Processing. Prentice Hall Publ., 2008, 976 p.

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The advantages of background correction of microfocus X-ray images are presented.

Methods of investigation parameters of plasma of glow discharge lasers

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Introduction

Gas-discharge devices are used widely in various fields of science and technology. The high prevalence of such devices is due to the wide variety of design solutions associated with the type of discharge flowing in the device. Among of such devices a special place is occupied by instruments with an extended positive column of a glow discharge. Glow discharge lasers belong to such devices. Glow discharge lasers are used actively for technological, metrological and medical purposes.

Gas-discharge lasers, including glow discharge lasers, are not only widespread but also quite complex devices in structure and manufacturing technology. From this point of view and taking into account the economic reality, it is quite logical to find ways to increase the service life of the gas-discharge lasers used, and to restore active elements in the event of complete loss of generation. The relatively short life of lasers makes this problem even more urgent. Possible reasons for the complete or partial failure of gas-discharge lasers are: a disturbance in the operation of the power source; increase in the level of losses in the optical resonator; reduction of amplifying in the active element of the laser. The service life of power supplies is much higher than that of active elements. In optical resonators, the main causes of a noticeable reduction in radiation power are the degradation and contamination of mirrors and Brewster's windows. The main reason for the failure of the active element is the degradation of the active medium due to the leakage of atmospheric gases, gas desorption by elements of construction, the absorption of the working gas by the shell, by the electrodes and their spray products, and the diffusion of the working gas through the envelope.

Glow discharge lasers, which include CO₂ and He-Ne lasers, are used in surgery, ophthalmology, laser therapy. For the effective use of such lasers, one must know their behavior in dynamics. Also, due to the limited lifetime of such lasers, the question of replacing the gas mixture is very relevant.

Determination of the plasma parameters of a glow discharge is an important task in the design and analysis of the gas discharge devices [1]. Of particular interest is the determination of the parameters of the discharge occurring in long tubes, for example, in gas discharge lasers. One of the main characteristics that defines the behavior of the discharge gap in the circuit is the current-voltage characteristic (CVC). The CVC allows judging the state of the active environment, in particular, the degree of leakage of the atmospheric gases. In addition, the form of the

CVC has a significant influence on the dynamic properties of the discharge.

Due to physical and constructive features, the laser radiation has a temporary instability due to the influence of various factors. Therefore glow discharge lasers are used in along with radiation power stabilization systems.

Instability of laser radiation parameters

Methods for stabilizing the power of laser radiation are classified on passive and active. In practice are used often active methods. Passive methods stabilizing do not take into account all the factors affecting the instability of the laser radiation power. Active stabilization methods assume negative feedback. One of the options for stabilizing the power of laser radiation is adjustment the pump level. In glow discharge lasers this process reduces to modulating the discharge current. Let us assume that at the time t the laser had a power level P_0 at a current I_0 , which corresponds to the point A (fig. 1). Due to external influences, the energy characteristic of the laser can shift and this current will correspond to the power $P_0 + \delta P$ (point B). The principle of current stabilization of power consists in forced changing the discharge current by such a value δI so that the radiation power level again is equal to P_0 (point C).

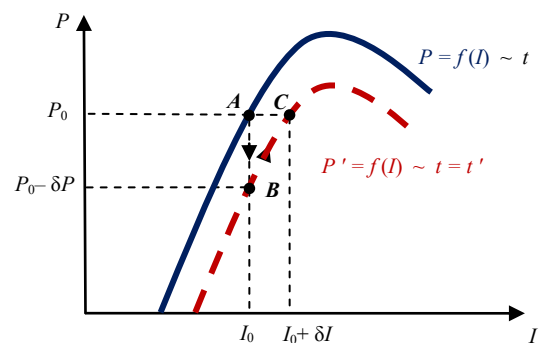


Figure 1: Explanation of the operation principle of the radiation power stabilization system

Method and equipment of experiment

To increase the accuracy of calculations of the plasma parameters of a positive column in this work was taken an attempt to refine the values of the accommodation coefficient. The idea of refining χ is based on the use of half experimental approach to the problem. Initially it was conducted a series of experiments to study the CVCs of the discharge gaps. In the experiments we used two models.

Layout 1 consisted of four discharge tubes with inner diameters of 1,1; 2; 3,4 and 5,2 mm, with movable anodes, transported by means of the magnetic actuators within the length of positive column 0,1...0,25 m (fig. 2).

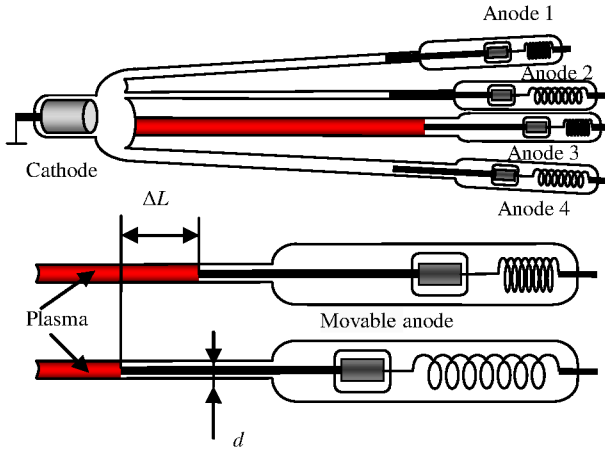


Figure 2: Layout 1 with a movable anodes

Layout 2 is a multianode tube with an inner diameter of 6,5 mm with the possible values of the active medium length 1,3; 1,12; 0,98; 0,78, 0,61; 0,47 and 0,35 m. In addition, layout 2 has an optical resonator and therefore the discharge gap can be used as the active medium of a He-Ne laser (fig. 3).

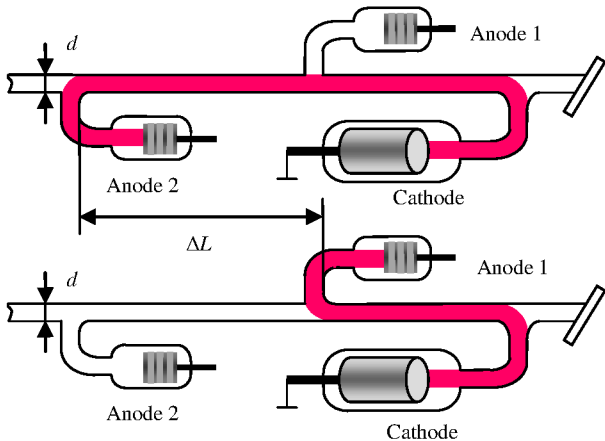


Figure 2: Layout 2 with several anodes

Layout 3 consisted of four discharge tubes with inner diameters of 3; 5; 10 and 15 mm, with fixed anodes (fig. 4).

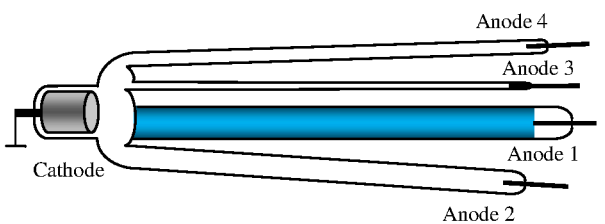


Figure 4: Layout 3 with fixed anodes

Layouts are connected with a vacuum pumping and filling system, which allows varying the gas content and operating pressure.

Equations of plasma parameters

The condition of the balance of charges for such a cylindrical plasma column can uniquely associate the average ionization frequency with coefficient of the ambipolar diffusion. Taking into account the expression for the ambipolar diffusion, frequency of ionization is defined as

$$\nu_i = \frac{b_i k (2,405)^2 T_e}{R^2 e}.$$

The average ionization rate can be written as

$$\nu_i = n_a \int_0^{\infty} q_i(U) \nu(U) f(U) dU,$$

where n_a – is the concentration of atoms; q_i – ionization cross section; $f(U)$ – Maxwell distribution function for electrons over energies. Approximations of the cross section of ionization for atoms and molecules were assumed linear. Thus, after integrating, was obtained an expression for the frequency of ionization [2]:

$$\nu_i = n_a \left(\frac{8kT_e}{\pi m_e} \right)^{0,5} \cdot \alpha_i \exp \left(\frac{-eU_i}{kT_e} \right) \left(U_i + \frac{2kT_e}{e} \right). \quad (1)$$

The transcendental equation (1) is applicable for the single component active media of the gas discharge lasers. For multicomponent gas mixtures the sum of ionization frequencies of all gases within the mixture should be used:

$$\sum_j \nu_i(j) = \frac{(2,405)^2 b_i k T_e}{R^2 e} = \frac{23,1 b_i k T_e}{ed^2}.$$

In these conditions, the average ion mobility of the gases can be calculated using the Blanc law.

Discharge CVC determines the behavior of the longitudinal potential gradient. The longitudinal potential gradient E_z in the positive column (PC) of a glow discharge is proportional to the square root of the accommodation coefficient χ of the electrons, which refers to the total energy of the electron W_e . The value of χ is important in the theory of a glow discharge PC: it characterizes the energy balance of the PC and connects the longitudinal potential gradient E_z with electronic temperature T_e [3]:

$$E_z = \frac{1,5kT_e \sqrt{\chi}}{e\lambda_e},$$

where $\lambda_e = \lambda_{e0}/p$ – is the average free path length for electrons; p – gas pressure.

Function $\chi = f(T_e)$ can be found taking into account shares of energy lost by electrons in elastic and inelastic collisions:

$$\chi = \chi^* + \chi_a + \chi_w,$$

where $\chi^* = 2m_e/M$ – is the average fraction of the energy lost by electron in the elastic collision; χ_a – average fraction of energy loss due to the excitation; χ_w – share of energy losses at the walls.

The described above technique was used as the basis for the program to calculate T_e . The program allows the choice of the laser type or the required gas mixture, and the display mode for the calculated information, definition of the constants and ranges of changes in the diameter of the discharge channel, the total and partial pressures of the gas components and gas temperature.

An important role in the analysis of the dynamic discharge resistance is played by the static CVC. As was said above, for the glow discharge lasers conditions the CVC has a decreasing character. In this case, the CVC can be approximated by an expression that includes the length of the discharge gap L and the longitudinal gradient of the potential E_z :

$$U_0 = U_k + aE_z L I^b,$$

where U_k is the cathode voltage drop, which is determined by the pair of gas-cathode material; a, b – constants, depending on the kind of gas and discharge conditions. In this case, it is possible to introduce a static slope of the current-voltage characteristic:

$$\rho = dU / dI = abLE_z I^{b-1}.$$

The discharge conditions realized in glow discharge lasers correspond to the region of sharp drop in the CVC of the discharge gap. In such a case there is a transition stage from the electrons free diffusion to the ambipolar. To obtain expressions for the total dynamic resistance, one can use the method of small perturbations. In accordance with this method, the current and voltage of the discharge will, respectively, have the form: $U = U_0 + u$, $I = I_0 + i$. In these expressions I_0, U_0 are stationary values of the current and voltage at the discharge i, u are the variable components of the discharge current and voltage, where $u \ll U_0, i \ll I_0$.

Then the dynamic resistance will be determined by solving:

$$\frac{1}{I_0} \frac{\partial^2 i}{\partial t^2} + \frac{1}{I_1} \frac{di}{dt} + \frac{i}{I_2} = \frac{1}{U_0} \frac{\partial^2 u}{\partial t^2} + \frac{1}{U_1} \frac{du}{dt} + \frac{u}{U_2}.$$

Solution (1) was sought in the form:

$$Z_d = \frac{u_0}{i_0} e^{j\omega} = \frac{I_0^{-1} (j\omega)^2 + I_1^{-1} j\omega + I_2^{-1}}{U_0^{-1} (j\omega)^2 + U_1^{-1} j\omega + U_2^{-1}}. \quad (2)$$

Results

Using layouts, it is possible to carry out an experimental study of the current-voltage characteristics of a discharge for conditions characteristic of glow discharge lasers (fig. 5). The CVC characteristic is closely related to the longitudinal gradient potential of the discharge positive column.

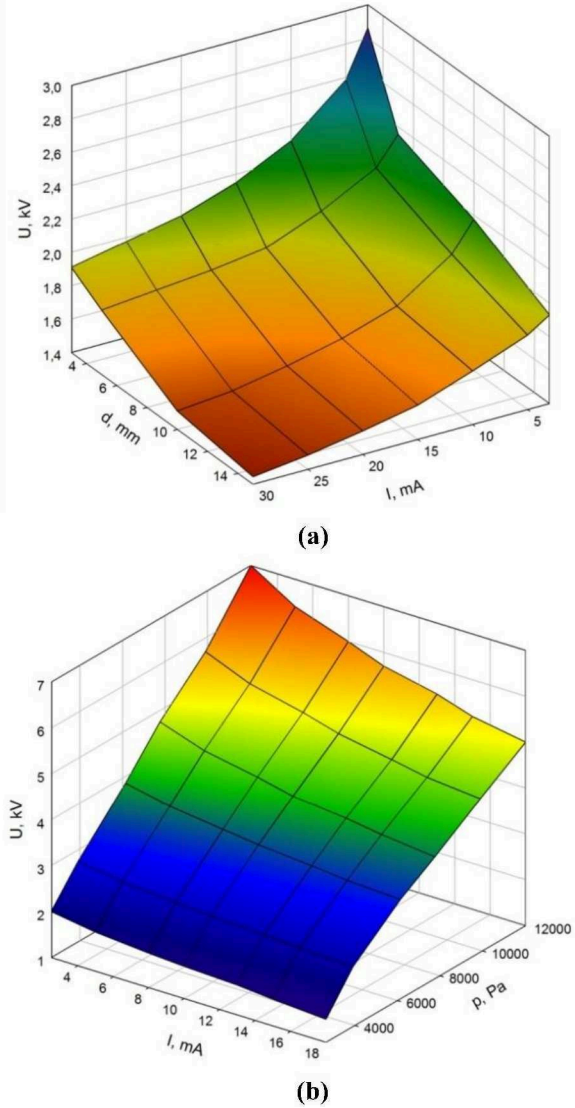


Figure 5. 3D-plots of current-voltage characteristics of the discharge: **(a)** in a carbon dioxide; **(b)** in a gas mixture $\text{CO}_2:\text{N}_2:\text{He}=1:1:6$

After transformation (2), an expression for the dynamic resistance of the glow discharge lasers is obtained, as the total AC resistance

$$Z_d = R(\omega) + jX(\omega) \quad (3)$$

$$R = \frac{(I_2 U_2)^{-1} + \omega^2 \left[(I_1 U_1)^{-1} - (I_2 U_0)^{-1} - (I_0 U_2)^{-1} + \frac{\omega^2}{I_0 U_0} \right]}{U_2^{-2} - 2\omega^2 (U_0 U_2)^{-1} + \omega^2 U_1^{-2} + \omega^4 U_0^{-2}},$$

$$X = \frac{\omega \left[(I_1 U_2)^{-1} + \omega^2 (I_0 U_1)^{-1} - (I_2 U_1)^{-1} + \omega^2 (I_1 U_0)^{-1} \right]}{U_2^{-2} - 2\omega^2 (U_0 U_2)^{-1} + \omega^2 U_1^{-2} + \omega^4 U_0^{-2}},$$

where R and X is the active and reactive components of the impedance of the positive column; ω is the angular frequency. The remaining parameters depend on the discharge conditions.

To automate the process of analyzing the discharge impedance behavior, a program was developed in the MS Visual C # programming environment (fig. 6). It makes it

possible to calculate the active, reactive constituent, the impedance module, and also construct a hodograph of impedance. Before calculating the user, it is possible to select the type of gas mixture, specify the discharge conditions, the range of the discharge current and the frequency of the signal. The result of the calculation is the family of dependences of the impedance components on the frequency for different discharge currents. Each dependency family is located on a separate tab. The technique based on the use of expression (3) is the basis of the technique for modeling the impedance of plasma of glow discharge lasers.

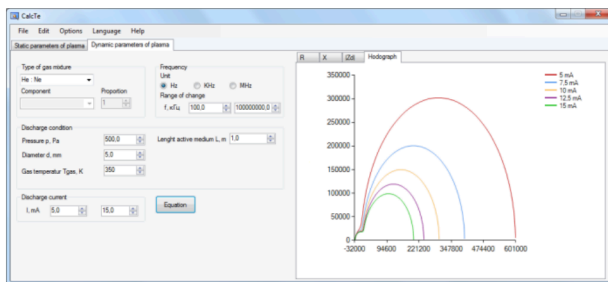


Figure 6: Program for modeling the dynamic resistance of glow discharge lasers

The results of calculating the dynamic resistance of the plasma obtained by using the developed program was analyze. At low modulation frequencies, the discharge plasma exhibits weakly inductive properties, and the impedance has a purely active value. Since under these conditions the CVC is of a falling nature, the active component of the discharge resistance $R(f, I)$ will have a negative value, and be determined by the operating point on the characteristic. With increasing frequency, the active resistance of the discharge reaches a constant value equal to the static discharge resistance. The dependence of the reactive component of the resistance $X(f, I)$ has a resonance character. At high modulation frequencies, the plasma does not have time to respond to external influences, so the reactive component of the impedance tends to zero. The advantage of the proposed method for calculating the impedance of the discharge of laser tubes is that it allows one to correctly assess the nature of the reactivity of the discharge, the presence of active resistance of both signs [4].

Conclusions

The result of the work is a set of experimental data, and theoretical models that allow calculating plasma parameters for glow discharge lasers. The calculation procedure was implemented in the form of a software package that allows performing analysis of static and dynamic plasma parameters. The results obtained can be used to develop systems for stabilizing the power of laser radiation. Also, the obtained data can be used to select the parameters of the gaseous mixture of glow discharge lasers when they

are restored. These lasers can be used in medical equipment.

References

- [1] Privalov V.E., Smirnov E.A. Stabilization of radiation power of glow discharge lasers and their application (review). Optical and mechanical industry. 1986. № 11, pages 52-60.
- [2] Kiselev A.S., Smirnov E.A. Technique for calculating the parameters of a glow discharge plasma. Vacuum Technology and Technology. Vol. 24. No. 1, pages 56-59, 2014.
- [3] Granovskii V.L. Electric current in a gas. Moscow: Science, 1971.
- [4] Smirnov E.A. Dynamic characteristics of glow discharge in long tubes. News of SPbGETU "LETI". SPb.: Publishing house SPbGETU "LETI", 2013, №10, p. 6-10.

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Study of the influence of the installation angle of the pedicular screw on its resistance to axial traction

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Introduction

Different spine diseases and injuries can damage the neural structures, leading to neurologic complications up to paresis and paralysis. According to competent authors (Plane, 1988; Dove, 1989; Riebel, 1993; Crawford, 1994), unstable spinal fractures need a surgical treatment using ventral access and occur more than 20% of the total number of occasions. In current surgical practice, in order to reduce the pressure, the damaged spine are getting immovably fixed with a metal transpedicular system (TS), which consists of screws, beams, or plates. Screws are inserted in the body of a spinal bone above and below the damaged area along the lateral surface. After installing the required amount of components, screws are getting fastened together to form a stabilizing system. This method allows patients to sufficiently rehabilitate and return to an active full life.

This kind of restraint deteriorates due to periodic stress during its exploitation. There are several reasons: osteoporosis of the bone tissue; material of the implant system does not match the requirements for biocompatibility and bioinerticity; young's modulus of bone tissue and the young's modulus of the material of the implant structure are different.

In order to determine the maximum force of the screw's resistance during its axial extension, biomechanical tests were carried out using the pull-out scheme. Also, the goal was to determine the dependence of the traction load of the angle of inclination of the screw, installed in the spinal bone, and to evaluate the destruction of the spinal bone's body.

Materials and methods

For this study, pedicle Stryker screws (USA) were chosen; they have different geometric characteristics. The screws are an integral part of the TS, they are made of titanium alloy Ti-6Al-4V, it's composition is regulated by ISO 5832-3:1996. The vertebrae of the animals were selected as a bioobject. Structure and properties of bone tissue of the spinal bones of animals and human are similar [1-3], so the thoracic spine bone of the ram were prepared for the test - thawed at room temperature for 4-5 hours and treated with salt. To obtain the most comparable test results, vertebrae of the thoracic spine were used.

A dense cortical layer from the ventral side of the spinal bone of the ram was 1.20 mm thick, with the dorsal side of 0.88 mm thick. So that, the needle holes were made in the spinal bone bodies. The depth of breakdown was not more than 2-2,5 mm with a diameter of 1-1,5mm. The screw was installed into the hole and screwed into the spinal bone for the entire length of the thread of the leg, punching the cortical layer from the opposite side. The spinal bone with the screw was fixed in the grips of the Instron 3365 test machine so that the axis of the screw formed an angle with the axis of the load application - it was determined by means of its construction on the photo (Figure 1). Traverse speed 2mm / min.

Instron 3365 - universal testing system. We can use it to perform static testing, including tensile and compression applications.

According to ASTM F543 - 02 [4], the stress was applied vertically upwards along the X axis (Figure 2). Figure 3 shows the spinal bone in the grips of the test machine.

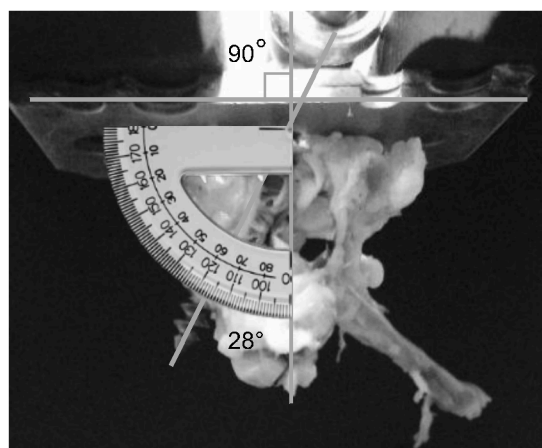


Figure 1: Position of the spinal bone with the screw in the grips of the test machine, determination of the angle of inclination.

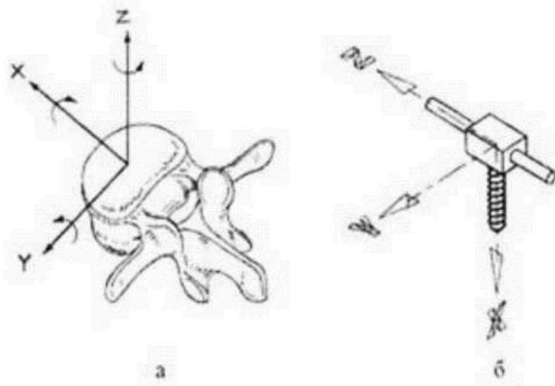


Figure 2: Global (a) and local (b) coordinate systems, which were used in the tests

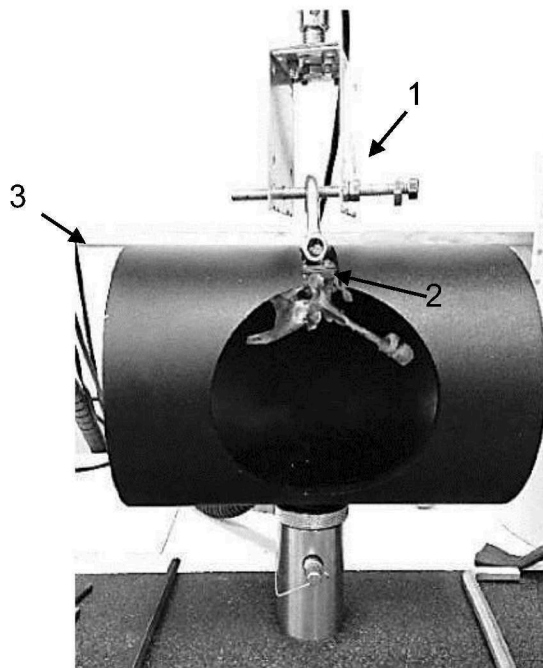


Figure 3: Vertebrae with a screw installed in the Instron grips before testing

1. – the clamp for pull-out the screws
2. – the screw inside the vertebra of an animal
3. – the clamp for fixation of vertebrae

Results

The dependence of the maximum load of traction on the angle of inclination of the screw relative to the axis of the applied force was determined. The screw is tested in the pull-out circuit. And the study of the influence of the geometric features of screws, which were mounted in the vertebra at an angle of $16 \pm 2^\circ$, on their resistance to axial extension was held.

The results of the study were listed in the table 1. It shows the maximum forces for the axial extension of the screw and the inclination angles. So we can see that the strength of the resistance to axial traction decreases with an increase in the angle of inclination of the screw

Table 1: Angle of screw installation and maximum force for the screw

Characteristics / Test Number	1	2	3	4	5
Angle, deg.	$28 \pm 0,5$	$18 \pm 0,5$	$14 \pm 0,5$	$13 \pm 0,5$	$5 \pm 0,5$
Load, N	303 ± 2	938 ± 5	965 ± 5	1073 ± 5	1208 ± 6

Conclusions

As a result of experimental studies it was found that the strength of the resistance to axial traction decreases with an increase in the angle of inclination of the screw. An increase in the angle of the screw installation by 9° led to a deterioration in the fixation and removal by 20% of the resistance to axial traction. The formed angle between the axis of the screw and the axis of its extension led to an increase in bone tissue damage.

An increase in the outer diameter of the screw leads to an increase the trauma of the vertebrae - vertebrae were cracked in tests when the screws were installed at an angle of more than 5° .

References

- [1] Chavassieux P. Effects of sodium fluoride on bone remodelling in ewes. / P. Chavassieux, P. Pastoureaux, G.Boivin et. al. // Bone Miner Res, 1987. - №2: abstract 359.
- [2] Pastoureaux P. Effects of oophrectomy on biochemical and histological indices of bone turnover in ewes. / P. Pastoureaux, M.E. Arlot, F. Caulin et. al. // J Bone Miner Res, 1989. - №4: S237.
- [3] Wallach S. The bone «Quality» Problem. / Wallach S, Feinblatt J.D., Avioli L.V. // Calcified tissue international, 1992. - №51- p. 169-172.
- [4] ASTM F 543 - 02 «Standard Specification and Test Methods for Metallic Medical Bone Screws». / 100 Barr Harbor Drive, PO Box C700, West Conshohocken, PA 19428-2959.

The study of biomechanical characteristics of the venous wall after ultrasound exposure

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Introduction

Ultrasound ablation is one of the most perspective methods of surgical treatment of lower limbs varicose veins (LLVV). Currently, the ultrasound method is successfully used for hemorrhoids sclerosis [1].

Study of the structure of pathological venous wall after ultrasound exposure is an essential stage of ultrasound ablation technological parameters tests. The goal of this work is studying the possibility of using biomechanical characteristics as assessment criterion for evaluation of differences in pathological venous wall structure before and after ultrasound ablation.

Materials and Methods

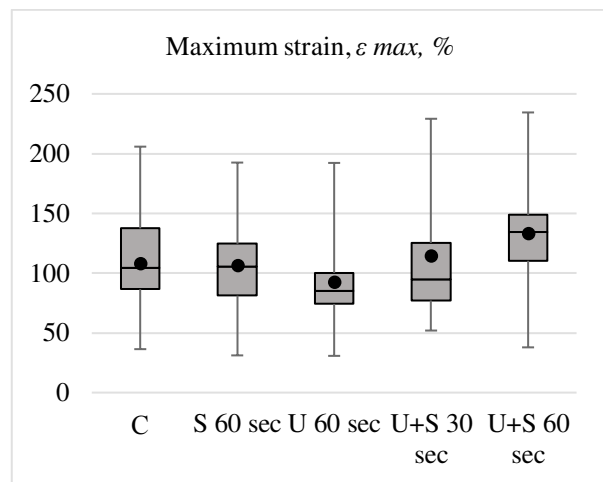
Ultrasound ablation technological parameters tests was carried out on the samples prepared from the segments of the great saphenous vein (GSV) trunk, taken during saphenectomy in the Vascular Surgery Department of the Russian Scientific Surgery Center n.a. B. V. Petrovskiy. For the experiment were identified four groups with different modes of exposure to venous wall samples and a control group. Five groups were formed in total:

- a) control group (C);
- b) treatment with sclerosant solution for 60 seconds (S 60 sec);
- c) contact ultrasound treatment for 60 seconds (U 60 sec);
- d) ultrasound treatment with sclerosant solution for 30 seconds (U+S 30 sec);
- e) ultrasound treatment with sclerosant solution for 60 seconds (U+S 60 sec).

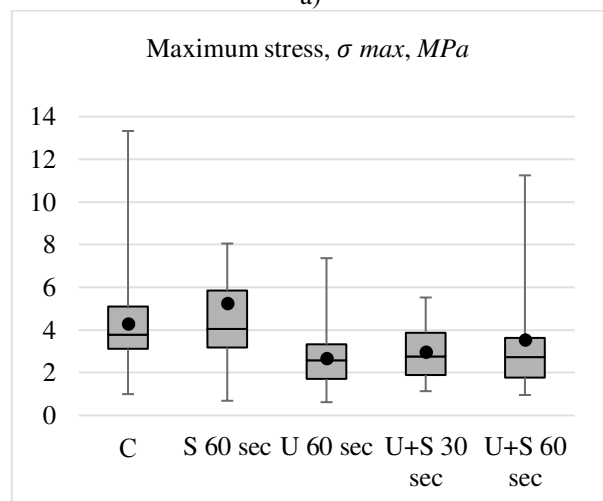
After the stage of ultrasound ablation, the samples of the venous wall were tested for uniaxial stretching using the INSTRON 3365 machine in accordance with the method described in [2]. A series of experiments was performed in total on 110 samples of the venous wall in accordance with the developed technology, and also the histological research of the treated specimens in the Pathomorphological Department of the Russian Scientific Surgery Center n.a. B.V. Petrovskiy.

Biomechanical tests results processing was carried out in Matlab software package. During processing, the values of the maximum strain, ϵ_{max} , the maximum stress, σ_{max} , and the Young modulus, E , were determined for each sample (fig. 1).

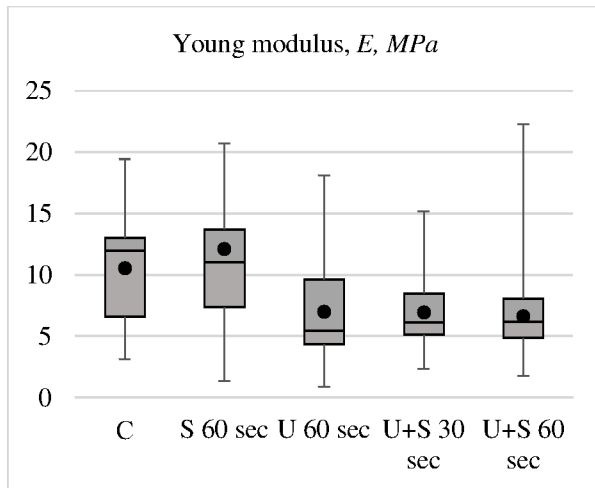
Based on the presence of several comparison groups, the nonparametric tests of Kruskal-Wallis and Newman-Keuls were chosen as the statistical method of data analysis [3]. For the null hypothesis, it was assumed that the various modes of processing the GSV samples do not affect the biomechanical characteristics and the resulting differences are random.



a)



b)



c)

Figure 1: Trends in the variation of biomechanical characteristics of the venous wall in dependence to exposure modes (see explanations in the text): a) the maximum strain; b) the maximum stress; c) the Young modulus.

Results

As a result of a multiple comparison of the GSV samples biomechanical characteristics under different modes of exposure by the Newman-Keuls test, statistically significant differences were found with p -value < 0.01 between groups with different parameters of ultrasound exposure to the venous wall, a group of samples treated only with a sclerosant solution and a control group. Statistically significant differences were not found for the Young modulus of samples, treated by the contact ultrasound for 60 seconds (U 60 sec) and samples, treated by the ultrasound together with the sclerosant solution for 30 seconds (U+S 30 sec).

Conclusions

In the course of experimental studies, the influence of ultrasound on the biomechanical characteristics of the venous wall was evaluated. Based on the results of analysis of the obtained experimental data, it was shown the expediency of using biomechanical characteristics as a criterion for assessing the differences in the structure of the pathological venous wall before and after ultrasound ablation.

Using the obtained experimental data, ranges of biomechanical characteristics corresponding to different modes of exposure to venous wall can be determined. Thereby, biomechanical tests can be used as an alternative to histological studies.

References

- [1] Soloviev O.L., Savrasov G.V., Soloviev A.O. Sclerosing treatment of hemorrhoids with ultrasound effect - 2002. - P. 1-10.
- [2] Savrasov G.V., Bashlai A.P., Belikov N.V. Features of biomechanical studies in the pathological lesion of

the blood vessels wall. // Digest of the 15th scientific and technical conference "Medico-technical technologies for the protection of health" (Portugal, Madeira Island, September 20-27, 2013). M: Publishing House: SRI RL Bauman Moscow State Technical University, 2013. P. 133-137.

- [3] Glanc S. Medicobiological statistics. M.: Praktika 1999; 429 p.

Animal Trials of Wearable Apparatus for Peritoneal Dialysis

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Introduction

Chronic kidney failure (CKF) is a pathological condition which can be characterized by lowering metabolite and water removal rate and insufficient organism's homeostasis [1]. In 2010 the number of patients suffering from end-stage kidney failure (ESKF) excided two million people [2], [3]. Nowadays kidney transplantation is the only method of ESKF treatment. Alas, the amount of donor kidneys is not enough to supply all patients with donor organs. Organ rejection is another problem which can occur after kidney transplantation. In view of problems listed above renal replacement therapy (RRT) is vital necessity for patient with CKF. Blood purification and ultrafiltration are the main functions of RRT. There are two widespread RRT modalities commonly used nowadays: hemodialysis (HD) and peritoneal dialysis (PD). Although both methods provide sufficient blood purification, they have the following disadvantages: hemodialysis requires about 150 liters of dialysate per procedure, thus this therapy can be performed only in specialized dialysate centers. Moreover HD can cause low blood pressure and blood clots in dialysis access. Peritoneal dialysis requires frequent (4-6 per day) exchange of spent solution for peritoneal dialysis which increases the probability of peritoneal cavity contamination. Peritonitis is the main issue of PD which causes inflammation of peritoneal cavity and makes further PD procedures impossible.

Dialysate regeneration is method of spent solution purification which can potentially solve issues listed above. One of the major challenges of dialysate regeneration is urea elimination, since this metabolite is poorly removed by sorbent materials. Alternative dialysate regeneration methods such enzymatic and electrochemical methods can be use as alternative methods for urea removal; however chemical byproducts of electrolysis and urea hydrolysis are the main disadvantages of these methods. In this case different dialysate regeneration approaches can be combined to overcome these issues. For example combination of enzymatic and sorbent methods provides adequate urea and ammonia elimination and at the same time allows maintaining dialysate ion concentration in wearable artificial kidney (WAK) [4]. Therefore different variations of dialysate regeneration methods can be potentially used in WAK technology.

In this work combination of sorption and electrochemical methods was applied as dialysate regeneration approach. Sorption method can clean waste dialysate from different organic products of patient's metabolism including nitrogen bound substrate such as uric acid and creatinine and aromatic substrates such as phenol and p-cresol [5]. This method can also control ion concentration and

pH of the dialysate. However most sorbents including ion exchange resins and majority of activated carbon modification have low capacity for urea, which is the main downside of sorption method. For purpose of urea elimination electrochemical method can be applied. This method can continuously eliminate urea from the solution by means of direct anode oxidation. Urea oxidation rate depends on different parameters such as current density, active anode surface, electrode type, solution ion composition, pH of the solution etc. Ability to regenerate working electrodes and urea elimination effectiveness are the main advantages of this method. However free-chloride and chloride-bound substrates generate during electrolysis. In addition electrochemical method acidifies solution during electrolysis and changes its ion composition. Intensive gas generation should also be taken into consideration. Therefore dialysate regeneration system based on this method requires additional degassing unit, post-treatment sorbent column and pH stabilizer for a proper and save functioning. Preliminary studies of this method were performed in the following papers: [6], [7].

In this study WAK with regeneration unit based on sorbent and electrochemical methods was tested on animals.

Materials and Methods

In this work dialysate regeneration by means of sorbent and electrochemical methods was applied in animal trials. Animal trials were performed with usage of the following solutions for peritoneal dialysis: Fresenius Balance (glucose 1.5 %) and Extraneal (Baxter). Initial pH of both solutions was 5.4. Fresenius contains glucose as an osmotic agent (glucose concentration – 1.5%). Extraneal contains icodextrin as an osmotic agent. Composition of the solutions is presented in tables 1 and 2.

Table 1: Fresenius Balance (glucose 1.5 %)

Ion	Concentration, mmol/l
Calcium (Ca^{++})	1,75
Sodium (Na^+)	134,0
Magnesium (Mg^{++})	0,5
Chloride (Cl^-)	103,5

Table 2: Extraneal (icodextrin – 75 g/l)

Ion	Concentration, mmol/l
Calcium (Ca^{++})	1,75
Sodium (Na^+)	133,0
Magnesium (Mg^{++})	0,25
Chloride (Cl^-)	96

Peritoneal WAK system with described dialysate regeneration unit was tested on two dogs with weight 15 kg. Dialysate solution changed every 12 hours. Concentration of ions and nitrogen-bound substrates in dialysate was measured every hour. Scheme of the experiment is presented on figure 1.

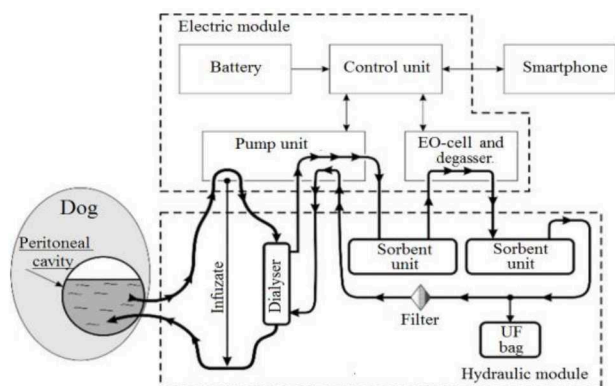


Figure 1: Experimental scheme of animal trials (UF – ultrafiltrate, EO-cell – electrochemical cell)

Experimental set-up included WAK system with dialysate regeneration module connected to dog's peritoneal cavity through catheter, control unit and receiving device (smartphone) for WAK-system control. Dialysate regeneration unit included dialyzer, sorbent units and electrolyzer. Dialyzer blocked protein and high-molecular substrates, thus preventing protein contamination of pumps and electrochemical cell. Sorbent units eliminated uric acid, creatinine and electrolysis byproducts, while electrochemical cell oxidized urea. Regenerated solution then came back to peritoneal cavity. The following materials were used in dialysate regeneration unit: sorbent units were filled with activated carbon FAS (100 g per unit); for urea elimination Ti/Pt electrodes with cumulative surface 300 cm² were added in EO-cell. Obtained results were compared with the following referent values [8]: urea 4–6 mmol/l, creatinine up to 176 μmol/l, uric acid up to 160 μmol/l.

Biotechnical system was divided on two parts. The first part was animal peritoneal cavity connected to dialyzer through the catheter (intracorporeal circuit). Fresh dialysate pumped into cavity. Wasted solution then came in the dialyzer where uremic metabolites diffused through the membrane to the dialysate in extracorporeal circuit. In extracorporeal circuit solution circulated through the dialysate regeneration unit. Dialysate circulation was performed by three peristaltic pumps: one in the intracorporeal circuit and two in the extracorporeal circuit.

Acute kidney disease (AKD) was provoked by infusion of mixture of 3 ml Diclophenac and 15 ml Ultravist. AKD was lately confirmed by blood test. To prevent catheter damage and animal injury the subject animal was sedated during the experiment.

Concentration of nitrogen-bound substrates, ion composition and pH were measured on biochemical analyzer Stat Fax 3300. Control of dialysate regeneration unit

functioning was performed through the laptop. In particular electrochemical cell performance (such as current density and time of electrolysis) was controlled manually through laptop software.

Results

The main results of medical trials are presented on figures 2 and 3

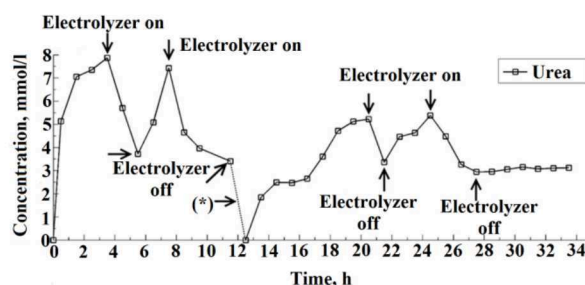


Figure 2: Urea concentration dynamics in the dialysate during WAK animal trials

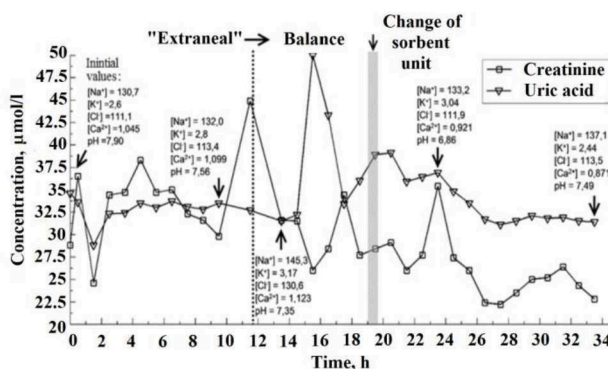


Figure 3: Creatinine and uric acid concentration dynamics in the dialysate during WAK animal trials

Developed dialysate regeneration unit effectively eliminated nitrogen-bound metabolites due to their adsorption on activated carbon and direct anodic oxidation. While creatinine and uric acid concentrations in dialysate solution did not exceed 50 μmol/l, urea concentration increase was observed during the experiment. To prevent intensive chloride byproduct generation EO cell worked only when urea concentration was close to 10 mmol/l. Overall nitrogen-bound substrates concentration stayed on physiological level during the trials and did not exceed critical values.

Necessity of electrolysis time control was the main issue of tested dialysate regeneration unit. In case of low urea concentration free-chloride and chloride-bound substrate generation becomes the main anode reaction. To eliminate these byproducts additional sorbent units are needed [9]. Moreover additional electrodes for urea detection have to be developed and applied to the system. Electrochemical cell functioning thus has to be automated. As a result electrochemical cell should work only if urea concentration in the solution gets close to or exceeds 10 mmol/l.

Another main obstacle of dialysate regeneration was poor potassium elimination. During animal trials potassium concentration increasing was observed. During the first hour of experiment potassium concentration in dialysate drastically increased from 0 to 2.6 mmol/l. After that potassium concentration steadily increased during peritoneal dialysis procedure. Twelve hours later potassium end concentration was 3.17 mmol/l. Next twelve hours after dialysate change potassium concentration continued increasing. In future version of dialysate regeneration unit specialized ion exchange resins will be needed for potassium elimination.

During dialysate regeneration chloride concentration increased which was also observed which can be explained by the following processes: ion diffusion through peritoneal membrane in the solution; ion generation during anode electro-oxidation process. The second phenomena can be explained by low urea concentration in the solution. As urea concentration drops below 6–8 mmol/l, generation of chloride gas, chloride-bound byproducts and chloride ion become the main anode process on anode surface. Thus electrochemical method can be effective in case of high urea concentrations (15 mmol/l and higher). Chloride-bound substrates generation can be decreased by EO-cell working mode control. For that development of specific urea sensor is essential.

Discussion

Overall presented dialysate regeneration unit eliminated nitrogen-bound substrates from spent dialysate and maintained their concentration on physiological level. Activated carbon and sorbent materials in general are effective in case creatinine and uric acid elimination. In addition specific types of activated carbon maintain pH and ion concentration on appropriate level. However sorbent method was ineffective in case of urea elimination. For urea concentration control electrochemical method was applied. Despite of its efficiency this method had following restrictions: chloride gas and chloride-bound substrates are the main byproducts of electrolysis, thus additional dialysate treatment was required; electrochemical method is ineffective on urea concentrations below 5 mmol/l ergo additional urea sensor for EO-cell work is needed. The main disadvantage of presented system – lack of fine-dispersed sorbents for protein elimination, which have to be added in the next step of WAK development. System also requires additional ion-exchange resins for potassium and chloride elimination

Conclusions

Presented dialysate regeneration unit for WAK-system effectively removed nitrogen-bound substrates. It did not affect dog's physiological state; however additional biocompatibility tests are required. For effective electrochemical cell functioning additional urea sensor might be needed. To remove proteins, protein-bound substrate and high-molecular substrates fine-dispersed sorbents are

needed. Presented dialysate regeneration unit can be used in further WAK development.

References

- [1]. Robert Thomas, Abbas Kasno, John R. Sedor. Chronic Kidney Disease and Its Complications. *Prim Care* // 2008. – Vol.35. – №2 – P.329–344.
- [2]. Maintenance dialysis throughout the world in years 1990 and 2010. Thomas B. [et al.]. *Journal of the American Society of Nephrology*. 2015. Vol. 26. №11. P/ 2631–2633.
- [3]. Maria Jafaar. Horizon Scanning Report. Wearable Dialysis Device. // Report No: 006/2016.
- [4]. Gura V., Macy A., Beizai M., Ezon C., Golper TA. Technical Breakthroughs in the Wearable Artificial Kidney (WAK) / *Clinical Journal of the American Society of Nephrology* // 2009 – Vol.4. – №9. – P.1441-1448.
- [5]. V. M. Grinval'd, G. M. Leshchinskii, V. V. Rodin, S. I. Strelkov, A. A. Yakovleva. Development and testing of Unit for Electrochemical Oxidation of Products of Hemodialysis. *Biomedical Engineering*, Vol. 37, No. 2, 2003, pp. 67–72.
- [6]. Bazaev N., Grinval'd V., Putrya B. Research of dialysis fluid regeneration methods. *Proceedings of the 12th Russian-German Conference on Biomedical Engineering*. – Suzdal.– 2016.– P. 289-292
- [7]. Bazaev N.A. et al. Mathematical model of a biotechnical system for extrarenal blood purification using portable artificial kidney apparatus. *Biomedical Engineering*. 2016. Vol. 49. № 5. P.322–326
- [8]. W.J. O'Connor. *Normal Renal Function: The Excretion of Water, Urea and Electrolytes Derived From Food and Drink*. Springer. 2001. P. 249 – 251.
- [9]. Removal of urea in wearable dialysis device: a reappraisal of electro-oxidation / Maarten Wester [et al.] // *Artificial Organs*. 2014. P.1–17

The control method of peripheral venous catheters automatic insertion using force measurement

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Introduction

The aim of this work is to develop a feedback unit based on a strain gage force sensor integrated into a robot-assisted venipuncture system to control the rectilinear catheter insertion in order to minimize post-injection complications caused by mechanical damage to vessel wall [1-3].

When the carriage of an automated system with a installed catheter moves, the catheter exerts pressure on the strain gage force sensor, which changes its own resistance in proportion to the force acting on it.

Materials and Methods

To obtain the characteristic signals at the moment of vessel wall puncture, a laboratory stand was designed. The mechanical and electrical part of the stand includes: a carriage with guides, a rack gearing, a DC motor with GM12-N20VA gearbox (500: 1 ratio), an L293D motor driver and a signal recording unit. The signal recording unit consists of the following main elements:

- FlexiForce A201 strain gage force sensor (maximum applied force 4 N) from the Tekscan manufacturer, which is attached to the carriage [4];
- inverting voltage converter ICL7660;
- MCP602 operational amplifier for realizing an inverting amplification stage;
- Arduino Nano platform with ATmega 328 microcontroller with built-in 10-bit ADC module.

Experimental studies were conducted on different biological phantoms. A strain-gage force sensor was installed between the carriage, which drives the catheter and the catheter itself. This position allows to achieve the maximum sensitivity of the strain gage sensor to the catheter at the moment of puncture of the phantom. The used biological phantom in the first series of experimental studies is presented in Figure 1, the biological phantom is a gelatin, which simulate the soft tissues and an artificial tissue vessel as well as a sealed food layer in a gelatin. The food sheath was chosen to simulate the vessel wall, because it is structural similarity. In the second and third series of experimental studies, the soft tissues were simulated by a pork meat fragment; the blood vessel in the first

case was simulated by a soft rubber tube with an internal pressure of 136 mm of water. (Mean venous pressure), in the second case - using a thin-walled tube made of polyvinyl chloride. The main principle of the three types of phantoms is to simulate the transition from soft tissue to the vascular bed with a higher density border.

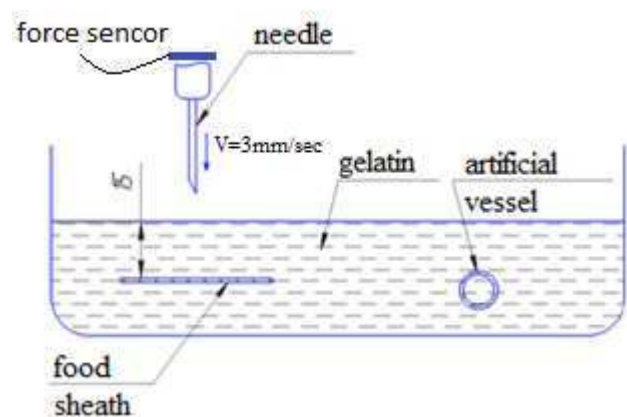


Figure 1: The image of the phantom

Analyzing the obtained signals during the third series of experiments (the characteristic form of signal is shown in Figure 2), it was difficult to uniquely determine the moment of vessel wall puncture. Therefore, it was decided not to use these signals to estimate the characteristic parameters of the signal as well as during the algorithm designing.

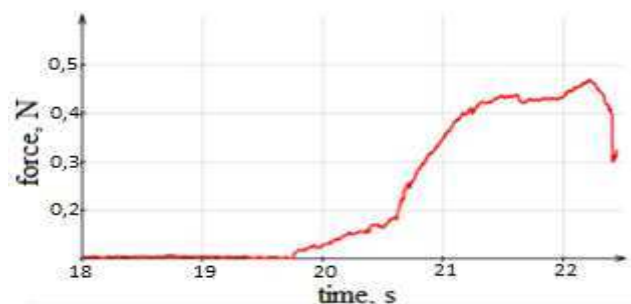


Figure 2: Characteristic signal form

The obtained signals in the first and second series of experiments had a similar shape, which is shown in Figure 3. The following signal characteristic parameters were selected for their further analysis:

- punching duration (ΔT), s;
- peak value, N;
- local minimum after puncture, N;
- the ratio of the maximum and minimum.

The results of the experiments are shown in Tables 1-3.

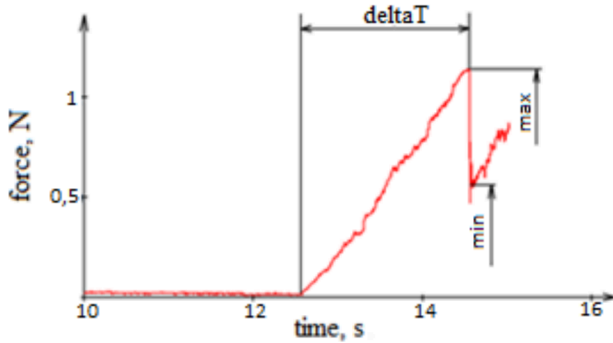


Figure 3: Selected characteristic signal parameters

Table 1: The results of the first series of experiments, the phantom: food sheath

No.	peak value (max), N	local minimum after puncture (min), N	ratio $\frac{max}{min}$	Punching duration (ΔT), sec
01:01	0,97	0,45	2,15	1,96
01:02	1,14	0,55	2,07	1,94
01:03	1,32	0,8	1,65	2,35
01:04	1,19	0,6	1,98	2,17
01:05	1,24	0,61	2,03	1,97
Average	1,17	0,6	1,98	2,08
Deviation	0,131	0,127	0,192	0,178

Table 2: The results of the second series of experiments, the phantom: artiftion vessel

No.	peak value (max), N	local minimum after puncture (min), N	ratio $\frac{max}{min}$	Punching duration (ΔT), sec
02:01	0,43	0,25	1,72	1,4
02:02	1,08	0,37	2,92	1,67

02:03	0,76	0,39	1,95	1,38
Average	0,76	0,34	2,2	1,48
Deviation	0,32	0,07	0,64	0,16

Table 3: The results of the third series of experiments, the phantom: a rubber tube with an internal pressure of 136 mm of water article

No.	peak value (max), N	local minimum after puncture (min), N	ratio $\frac{max}{min}$	Punching duration (ΔT), sec
03:01	0,35	0,17	2,06	1,61
03:02	0,48	0,25	1,92	1,76
03:03	0,4	0,2	2	2,312
03:04	0,48	0,33	1,45	2,28
Average	0,43	0,24	1,86	1,99
Deviation	0,064	0,07	0,28	0,36

Results

Based on the results of the experimental studies, discrete signals were obtained, which were used to develop an algorithm for recognizing the vessel wall puncture. The algorithm is based on the analysis of the amplitude-time parameters of the obtained signals. It is shown that the applied electrical circuit for signal recording satisfies the assigned task. It is established that the received signals are qualitatively similar to the signal from the literature sources [5] and have a coincidence in order of the measured value (force acting on the force sensor). Based on the literature data, a conclusion about the permissible adjustment of the measuring equipment was made.

Conclusions

As a result of this study, a feedback module was developed to control the introduction of a peripheral catheter on the basis of a strain gage force sensor capable of detecting the moment of vessel wall puncture.

References

- [1] Portable robot for autonomous venipuncture using 3D near infrared image guidance. [Electronic resource] – Access mode: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4482475/#FD7>.
- [2] The System Design and Evaluation of a 7-DOF Image-Guided Venipuncture Robot. [Electronic resource] – Access mode: <https://www.ncbi.nlm.nih.gov/pubmed/26257588>

- [3] Real-time Needle Steering in Response to Rolling Vein Deformation by a 9-DOF Image-Guided Autonomous Venipuncture Robot. [Electronic resource]. – Access mode: <https://www.ncbi.nlm.nih.gov/pubmed/26779381>
- [4] Datasheet FlexiForce A201 Sensor. [Electronic resource] URL: <https://www.tekscan.com/sites/default/files/resources/FLX-A201-A.pdf>
- [5] Saito H., Togawa T. Detection of needle puncture to blood vessel using puncture force measurement //Medical and Biological Engineering and Computing. – 2005 –№. 2 – P. 240-244.

The influence of the antennas geometry on the stability of the inductive wireless power transfer systems

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Introduction

Implantable medical devices (IMD) are an important part of modern medicine. Such devices are used to replace, support or restore the functions of human organs, such as the organs of the cardiovascular system, the musculoskeletal system, the digestive system, the central nervous system, etc. [1]. Progress in the field of electronics, micro- and nanotechnology has significantly expanded the scope of IMD, allowed to reduce the size of devices and increase their stability and reliability of work [2].

The development of energy supply methods is one of the key directions for the improvement of IMD technologies. Strict requirements for reliability, safety, biocompatibility and size significantly complicate the development of the power supply systems. At the same time, the characteristics of a particular system are largely determined by the characteristics of the IMD for which it is intended [3]. In this regard, the borrowing of existing industry solutions is virtually impossible, and the choice of energy supply method is becoming one of the main stages of IMD development [4].

Nowadays, many suitable methods of power transfer for supplying IMD have been discovered. The use of wireless transmission systems helps to avoid unnecessary surgical procedures, the risk of infection through the transdermal wires and allows to reduce the size of the implanted device. High reliability and efficiency, the ability to integrate with other devices [5] and the continuing interest of the world scientific community for more than 10 years has led to the choice of inductive energy transfer systems. The main value of the inductive energy transfer is mutual inductance M . Its calculation can be carried out according to the Neumann formula:

$$M = \frac{\mu_0}{4\pi} \oint \oint \frac{dl_t dl_r}{R_{tr}}; \quad (1)$$

where dl_t and dl_r are the filament elements, R_{tr} is the distance between them, and μ_0 is the magnetic constant of the vacuum.

It follows from the Neumann formula that the mutual inductance is determined by the mutual arrangement of the antenna pair. It should be noted that the misalignments of the antennas relative to each other is a characteristic feature of the inductive energy transfer systems. Therefore, one of the main tasks in the development of power supply systems of IMD is to compensate for the misalignments of antennas. A rather promising way to compensate for displacements of flat round antennas is to optimize the geometry of the antenna pair [6].

The aim of this work is to investigate the influence of geometry of antennas with the same inductance on the stability of the main output value of inductive energy supply systems - output power.

Materials and Methods

Stand review

One of the main output characteristics of inductive wireless power systems is the power transferred to the load (output power P_L). This characteristic depends both on the operating frequency of the system and on the mutual arrangement of the antennas.

To ensure high values of output power, a pair of LC oscillation circuits tuned to one resonance frequency [7], which can be calculated by the following formula:

$$f_{res} = \frac{1}{2\pi\sqrt{L_T C_T}} = \frac{1}{2\pi\sqrt{L_R C_R}}; \quad (2)$$

where L_R and L_T , are the inductances of the receiving and transmitting antennas, C_R and C_T are the capacities of the receiving and transmitting boards.

When a certain value of the coupling coefficient k_{crit} , called the critical coupling coefficient, is reached, the maximum output power of the system is ensured. The magnitude of the critical coupling coefficient k_{crit} can be determined using the following expression [8]:

$$k_{crit} = \frac{1}{\sqrt{Q_T Q_R}}; \quad (3)$$

where Q_T and Q_R are the Q-factors of the receiving and transmitting circuits:

$$Q_T = \frac{1}{R_T} \sqrt{\frac{L_T}{C_T}}; \quad (4)$$

$$Q_R = \frac{1}{R_L} \sqrt{\frac{L_R}{C_R}}; \quad (5)$$

R_T , R_L - the resistance of the transmitting board and the load resistance of the receiving board, respectively.

Simulation of the system of inductive wireless energy transmission, working in the frequency of resonance and critical coupling of antennas for an axial distance between them equal to 5 mm was carried out. The equivalent circuit of the system is shown in fig. 1. The parameters of the modeled system are presented in tab. 1.

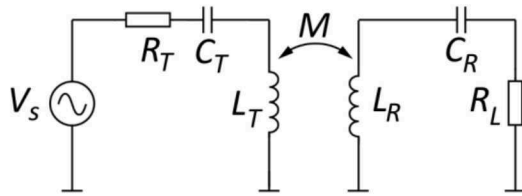


Figure 1: The scheme of the experimental stand

As can be seen in fig. 1, the system uses SS-compensation. Therefore, the output power can be calculated by the following expression:

$$P_L = \frac{\omega^2 M^2 V_s^2 R_L}{(Z_T Z_R + \omega^2 M^2)^2}; \quad (6)$$

where ω is the angular operating frequency of the system, Z_T and Z_R are the impedances of the transmitting and receiving boards:

$$Z_T = j\omega L_T + \frac{1}{j\omega C_T} + R_T; \quad (7)$$

$$Z_R = j\omega L_R + \frac{1}{j\omega C_R} + R_L. \quad (8)$$

Table 1: Stand parameters

Parameter	Value
V_s, V	5
R_T, Ohm	8.33
R_L, Ohm	20
$L_T=L_R, H$	1.5
$C_T=C_R, nF$	4.5

Analysis of the effect of antenna geometry

To determine the effect of the antenna geometry, two sets of parameters as shown in fig. 2 were taken:

- 1) Antennas with 5 turns, outer diameter 50 mm, inner diameter 30 mm, and pitch between turns 2.5 mm;
- 2) Antennas with 4 turns, outer diameter 112 mm, inner diameter 40 mm, and pitch between turns 12 mm.

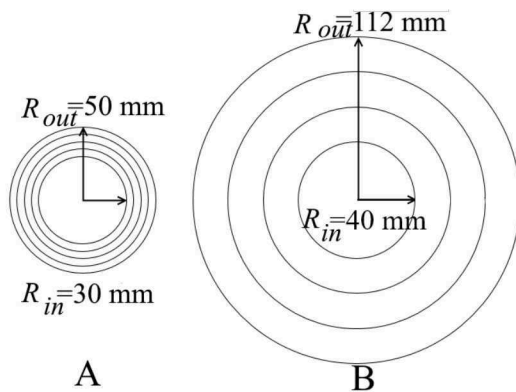


Figure 2: The first (A) and second (B) set of antenna geometric parameters

The antenna parameters were chosen so that the inductance values were close to the value given in tab. 1. The calculated resonant frequency of the system is 2 MHz. The critical coupling factor is 0.7. Therefore, the point of critical coupling of the antennas is located at a close distance between the antennas (≈ 3 mm of the axial distance).

Results

Fig. 3-6 show the results of numerical modeling of inductive wireless power transmission systems for two sets of antenna parameters. Fig. 3 and 4 show the dependence of the output power on the axial distance between the antennas and the operating frequency, fig. 5 and 6 show the dependence of the output power on the lateral misalignment and the operating frequency with axial distance 5 mm. As can be seen from fig. 3 and 4, with a small distance between the antennas, the system can operate over a wide frequency range, providing sufficiently high output power.

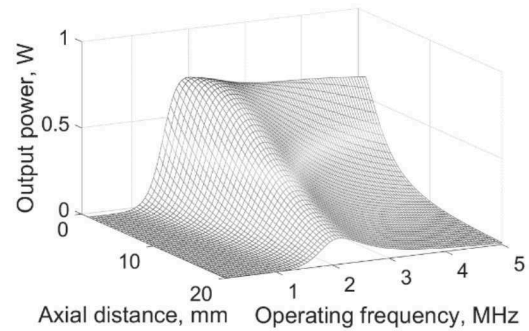


Figure 3: The dependence of the system output power on the axial distance between the antennas and the system operating frequency for antennas with 5 turns, outer diameter 50 mm, inner diameter 30 mm, and pitch between turns 2.5 mm

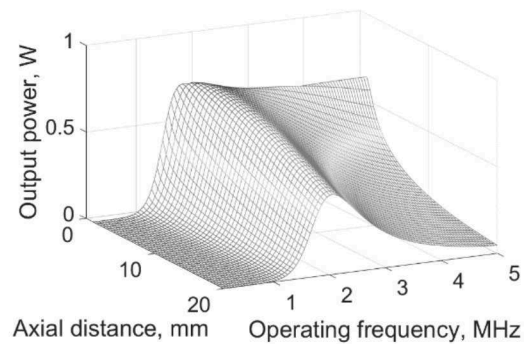


Figure 4: The dependence of the system output power on the axial distance between the antennas and the system operating frequency for antennas with 4 turns, outer diameter 112 mm, inner diameter 40 mm, and pitch between turns 12 mm

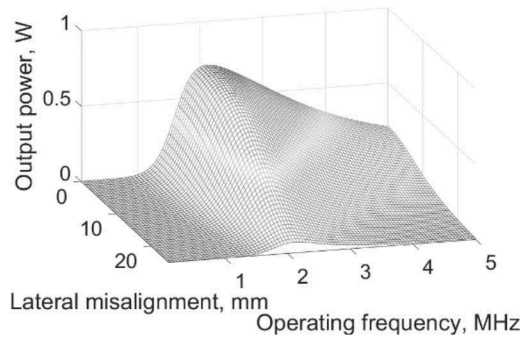


Figure 5: The dependence of the system output power on the lateral misalignment of the antennas with axial distance 5 mm and the system operating frequency for antennas with 5 turns, outer diameter 50 mm, inner diameter 30 mm, and pitch between turns 2.5 mm

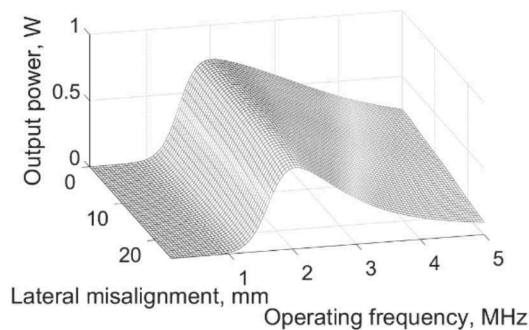


Figure 6: The dependence of the system output power on the lateral misalignment of the antennas with axial distance 5 mm and the system operating frequency for antennas with 4 turns, outer diameter 112 mm, inner diameter 40 mm, and pitch between turns 12 mm

However, already at an axial distance of more than 5 mm, the working frequency width is greatly reduced to a frequency range close to the resonant frequency. Therefore, to reduce the sensitivity of the system to misalignments, it is necessary to ensure operation at the resonant frequency.

Discussion

As can be seen from fig. 3 and 5, antennas with the first set of parameters are fairly sensitive to axial and lateral displacements. Even with a 15-millimeter displacement (axial and transverse), there is a noticeable drop in output power. At the same time, according to fig. 4 and 6 it can be seen that antennas with a second set of parameters give more stable output values to the misalignments.

Using antennas with a larger pitch and/or larger outer diameters allows to increase the stability of inductive wireless power transmission systems. Usually increasing the size of the device is undesirable for IMDs. Thus, first of all it can be said that implantable (receiving) antenna should be as big as possible from the medical point of

view. Furthermore, external antenna should have the same or some bigger size.

It is also should be noted, that high-stable output is more important in the case of continuous powering of IMD, than in the case of recharging. Stable output is even more important in the case of life-critical IMD, such as ventricular assist devices. So, in this case medical restrictions for antennas size should be not so strong.

Conclusions

In order to investigate the influence of geometry of antennas on the stability of inductive energy supply systems we perform numerical modelling. We have compared two sets of antennas with relatively close inductance values and significantly different pitch (namely, 2.5 and 12 mm). It was shown that antennas with greater pitch and diameter have much stable output characteristics. The output power in the range of the axial distance from 3 to 20 mm for antennas with the first set of parameters is reduced by 80% (from 0.74 W to 0.15 W). With lateral misalignments up to 25 mm and an axial distance of 5 mm, this characteristic decrease by a factor of 10 (from 0.71 W to 0.071 W). For antennas with a second set of parameters, the output power for axial misalignments decreases by 39% (from 0.74 W to 0.46 W), with lateral misalignments decreases by 15% (from 0.74 to 0.63).

Our results are mainly applicable in the case of continuous powering of IMD, especially life-critical IMD. Our future works will be focused on the incorporation of presented results in the optimization algorithm for design of inductive powering unit.

References

- [1] J.S. Ho, S. Kim and A.S.Y. Poon. Midfield wireless powering for implantable systems. *Proceedings of the IEEE*, 101(6): 1369–1378, 2013.
- [2] A.B. Amar, A.B. Kouki and H. Cao. Power Approaches for Implantable Medical Devices. *Sensors*, 15(11): 28889–28914, 2015.
- [3] K.N. Bocan and E. Sejdić. Adaptive Transcutaneous Power Transfer to Implantable Devices: A State of the Art Review. *Sensors*, 16(3): 393, 2016.
- [4] D.C. Galbraith, M. Soma and R.L. White. Radio-frequency coils in implantable devices: misalignment analysis and design procedure. *IEEE Transactions on Biomedical Engineering*, 34(4.): 276–282, 1987.
- [5] M. Catrysse, B. Hermans and R. Puers. An inductive power system with integrated bi-directional data-transmission. *Sensors and Actuators, A: Physical*, 115(2–3): 221–229, 2004.
- [6] Y. Cheng and Y. Shu. A New Analytical Calculation of the Mutual Inductance of the Coaxial Spiral Rectangular Coils. *IEEE Transactions on Magnetics*, 50(4): 6, 2014.
- [7] C. M. Zierhofer and E. S. Hochmair. Geometric approach for coupling enhancement of magnetically coupled coils. *IEEE Trans. Biomed. Eng.*, 43(7.): 704–714, 1996.
- [8] K. Van Schuylenbergh, R. Puers, *Inductive Powering*. Springer Netherlands, 2009.

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Calculation method for the class E power amplifier parameters for transcutaneous inductive energy transfer systems

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Introduction

Improvement in wireless power supply technology is a promising direction for the development of implantable medical devices (IMDs). The rejection of implantable chemical elements and percutaneous wires for powering the device can reduce the risk of postoperative complications, reduce the cost of treatment, and also can help to downsize the system [1]. A possible way to realize wireless powering is to use inductive energy transfer (IET) systems. Wireless powering technologies based on IET are widely used [2, 3]. Among the main advantages of IET over other methods of wireless powering (such as ultrasound or optic methods) is the weak absorption of electromagnetic radiation by biological tissues, which makes it possible to provide the required level of output power for a wide range of IMPs [4].

Powering of IMD imply the use of mobile chemical energy sources. In the case of IET systems it means that the DC power source signal is applied to the DC/AC converter, which has high power losses. After this, the alternating current is applied to the power amplifier and then to the transmitting coil.

The equivalent circuit diagram of the IET system where the influence of the receiving part of the system on the transmitting part is included as the equivalent impedance of the receiving part of the Z_{eq} , is shown in Figure 1.

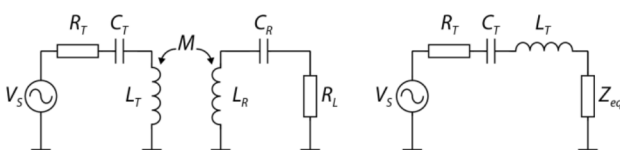


Figure 1: Equivalent circuit diagrams of the IET system

Because of high power losses on stages of converting signal and of transmitting power, it is necessary to use the most effective power amplifier (PA). Theoretically class E amplifier's efficiency equals 100% [6]. High efficiency is achieved by the absence of simultaneous non-zero current and voltage signals on the switch transistor S : when the voltage has a non-zero value, the current is zero and vice versa. However, the class E PA is extremely sensitive to changes in the parameters of the circuit [8]. At the same time, the mutual misalignment of the coil pair is a significant problem of the IET systems [5]. The source of the misalignments is the motor performance of the patient and also the postoperative edema of the tissues. Misalignments lead to changes in the mutual inductance of the

coil pair, which reduces the efficiency of the class E PA. The purpose of this work is to develop an algorithm for calculating the parameters of the class E PA, which used in the IET system.

Materials and Methods

Circuit diagram of the class E PA is shown in Figure 2. When using an amplifier as part of the IET system, the L_T coil, which enters the load network, acts as a transmission coil. For compensating the reactive power of the transmitter coil a pair of C_{TS} and C_{TP} capacitors are used. The load is the reflected impedance of the receiving part of the IET system Z_{eq} .

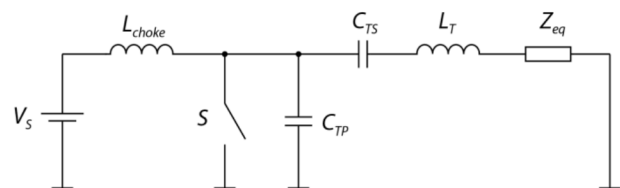


Figure 2: Class E power amplifier circuit diagram [7]

Methods for calculating the parameters of class E PA for a fixed resistive load are exist [7, 8, 9]. But in the IET system, a resonant circuit with a variable value of the equivalent impedance, depending on the mutual inductance of the coils. This impedance acts as a load of the PA, which changes when the mutual position of the coils changes.

In this paper, an algorithm for calculating and selecting the circuit parameters of the IET system with the class E PA, considering the misalignment of the coil pair, is proposed.

1. Defining design constraints

Since the class E PA is calculated for a IMD having certain load characteristics that are expressed through R_L , it must be tuned to a fixed value of the mutual inductance, which in turn corresponds to a certain misalignment of the coil pair. The range of misalignment were chosen for the use of IET systems with the auxiliary circulation systems [10]. For this IMD the axial and lateral misalignments has a range from 5 to 25 mm. The operating point of the IET system was chosen for 15 mm of axial misalignment and 0 mm of lateral misalignment. A number of features must be taken into account during designing of the IET system. The size of the implantation area for the receiving part of

the system is limited by anatomic features. Accordingly, restrictions are imposed on the geometric parameters of the coils (usually on the outer diameter of the implanted coil).

2. Calculation of the internal Inductances

After the geometrical parameters of the coil pair are determined, it is necessary to calculate the internal inductance of the transmitting and receiving coils (L_T and L_R , respectively), as well as the mutual inductance of the coils M for a certain range of misalignments. For this the Neumann formula can be used [11].

3. Choosing frequency

For the operation of the IET system, frequencies in the range from 100 kHz to 10 MHz are considered optimal due to the electromagnetic properties of the human body tissues. Accordingly, the operating frequency of the system f is selected within this range.

4. Calculation of the receiver total impedance

Series reactive compensation for the receiving part of the IET was chosen. The impedance of the secondary circuit Z_R in this case is calculated using the following expression:

$$Z_R = R_L + j\omega L_R + \frac{1}{j\omega C_R}, \quad (1)$$

where C_R is the compensating capacitance, ω is the angular frequency of the system. The value of this capacitance is chosen such that the resonant angular frequency of the receiving contour ω_{res} coincides with the working angular frequency of the circuit ω . In this case, the reactive components of the receiving loop completely compensate each other, and the impedance of the receiving loop becomes equal to the load resistance R_L . The resonant angular frequency is determined by the following equation:

$$\omega_{res} = \frac{1}{\sqrt{L_R C_R}}. \quad (2)$$

5. Determination of the choke inductance

There are no equations calculating of the choke inductance L_{choke} in the literature devoted to the class E PA. The existing experience in designing shows that the inductance of the choke is selected 20-100 times more than the inductance of the transmitting coil. The choice of the choke inductance value depends on the required purity of the signal. If the insignificant presence of harmonics in the signal is permissible, then the inductance of the choke must be 20-50 times greater than the inductance of the transmitting coil. If a signal with maximal purity is required, the inductance of the choke must be 50-100 times greater than the inductance of the transmitting coil. Further increasing of the choke inductance, as a rule, does not improve the purity of the signal and can lead to loss of power of the main signal.

6. Calculation of the reflected impedance

The analytical expression for the reflected impedance of the receiving part can be obtained by analyzing the equivalent circuit diagram of the IET system using the Kirchhoff rules:

$$Z_{eq} = \frac{\omega^2 M^2}{Z_R}. \quad (3)$$

Taking into account the transformations for the impedance of the receiving circuit in the clause 1, the expression for the reflected impedance of the receiving part of the IET system takes the following form:

$$Z_{eq} = \frac{\omega^2 M^2}{R_L}. \quad (4)$$

7. Calculation of the class E PA capacitors, the choice of power supply and control signal

Substituting the obtained expression for the reflected impedance of the receiving part of the IET system into the formulas for Q and capacitances of the class E PA [6], the values of the series and parallel capacitances for a given mutual inductance can be obtained:

$$Q = \frac{L_2 R_L}{\omega M^2}, \quad (5)$$

$$C_1 = \frac{R_L}{\omega^3 M^2 \left(\frac{\pi^2}{4} + 1 \right)} \left(0,99866 + \frac{0,91424}{Q} - \frac{1,03175}{Q^2} \right) + \frac{0,6}{\omega^2 L_{choke}}, \quad (6)$$

$$C_2 = \frac{R_L}{\omega^3 M^2 \left(Q - 0,104823 \right)} \left(1,00121 + \frac{1,01468}{Q - 1,7879} \right) - \frac{0,2}{\omega^2 L_{choke}}. \quad (7)$$

The power supply voltage is selected based on the required output power, taking into account the power losses in the system. A transient signal is applied to the base (gate) of the transistor with a duty cycle of 0.4-0.5 of such amplitude that the transistor operates in a switch mode.

8. Adjustment of the transmission coil internal inductance

When calculating the capacitances values, a situation may arise where negative values of the capacitances are obtained. In this case, the quality factor Q turned out to be too low and it is necessary to take the transmitting coil with a lower inductance. This will lead to a decreasing of the mutual inductance value at the selected operating point of the IET system, and, consequently, to an increasing of the quality factor, which will allow to obtain positive values of the capacitances during calculations.

9. Assessment of system characteristics and adjustment of parameters

It should be noted that the characteristics of the output signal of the class E PA are influenced by the output parameters of the transistor. At the same time, the analytical expressions presented in the literature do not take into account their influence in explicit form. A possible way to

account for them is to manually adjust the components using the method of N. Sokal [6]. As a control characteristic, the voltage U_{DS} (U_{CE}) is used.

Testing the calculation method for the class E PA

Calculating method for the class E PA parameters in the IET systems was tested using LTspice XVII electronic circuit simulator. Sets of transmitting and receiving coils (L_T and L_R , respectively) whose geometric parameters correspond to the values of internal inductance 3.4 μH , 4.21 μH , 7.29 μH were chosen. The load R_L is 20 Ohm, the inductance of the L_{choke} choke is 75 μH , the capacitance of the compensating capacitor C_R in the secondary circuit is 4.5 nF. The duty ratio of the control pulse signal is 0.5. Voltage V_S 10 V. The values of the operating frequencies f , the capacitors of the C_{TP} and C_{TS} for each system are shown in Table 1.

Table 1: Class E PA parameters for different coil pairs

3.4 μH	
C_{TP} , nF	2.85
C_{TS} , nF	15.15
f , kHz	1280
7.29 μH	
C_{TP} , nF	1.32
C_{TS} , nF	14.3
f , kHz	879
12.27 μH	
C_{TP} , nF	2.7
C_{TS} , nF	15.32
f , kHz	677

Results

As a result of the simulation, for each coil pair a sine signal on the output was obtained, the maximum efficiency value of each circuit is observed with the value of the mutual inductance corresponding to 15 mm of the axial misalignment and 0 mm of the lateral misalignment of the coils. The work of the of the class E PA changes due to changes in the mutual inductance value. It is worth noting that both increasing and decreasing mutual inductance leads to a drop in the efficiency of energy transfer in the IET system. Figures 3-8 show the dependencies of the IET system coupling factor, efficiency and the output power from axial and lateral misalignments.

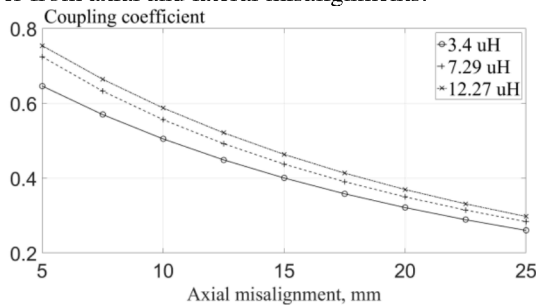


Figure 3: Dependence of the IET system coupling coefficient on the axial misalignment

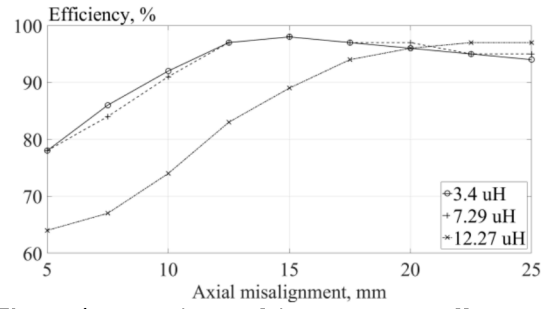


Figure 4: Dependence of the IET system efficiency on the axial misalignment

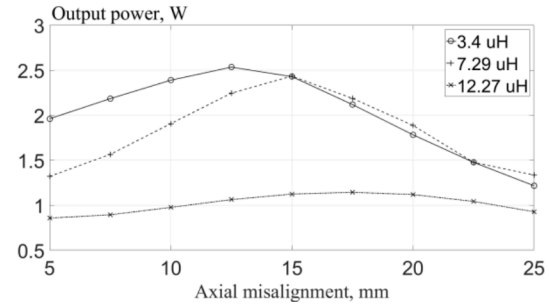


Figure 5: Dependence of the IET system output power on the axial misalignment

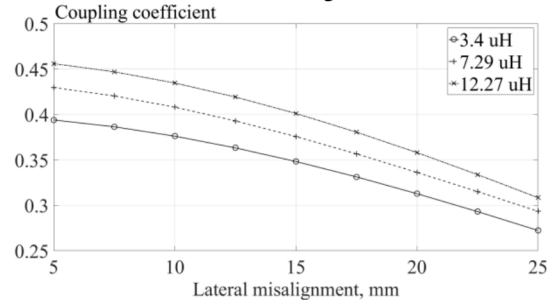


Figure 6: Dependence of the IET system coupling coefficient on the lateral misalignment

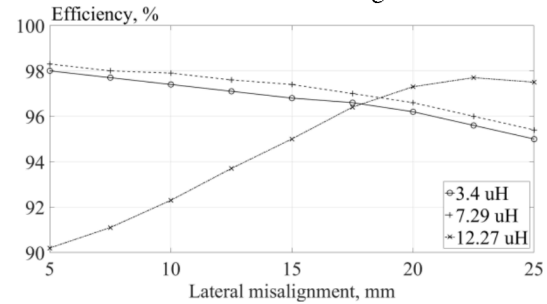


Figure 7: Dependence of the IET system efficiency on the lateral misalignment

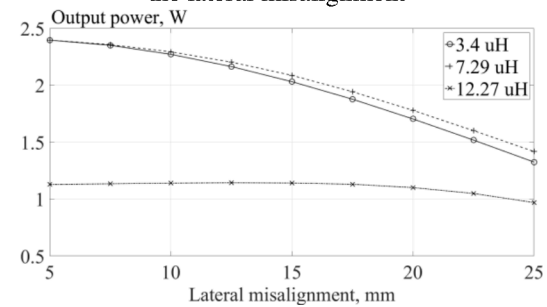


Figure 8: Dependence of the IET system output power on the lateral misalignment

Discussion

It was found that the dependencies of overall efficiency on axial misalignments (figure 4) can be divide into two areas: one with relatively high drop due to changes in the distance between coils (for axial misalignments lesser than 15 mm), and other, with relatively stable output. Based on this the misalignment values for the operating point should be chosen lesser than the middle point of the misalignment range. That will make system working in the flat area and increase its stability. Also the output power for the 12.27 μH coils is lower than for the 3.4 and 7.29 μH , but has less spread in values and acts more stable within all ranges of the axial misalignments (figure 5). A similar statement can be made for the dependencies of the efficiency and output power on the lateral misalignment (figures 7, 8). The operating point shifted for 3.4 and 12.27 μH both for axial misalignments, and for 12.27 μH operating point shifted for lateral misalignments due to fixed value of the load resistance R_L and adjusting only the amplifier's capacitances. With the fixed value of the load resistance R_L and inductance L_T , it is impossible to completely adjust the amplifier for some coil sets only changing capacitors. For large values of the lateral misalignment, where the reflected impedance Z_{eq} of the system with 12.27 μH coils approaches the value of the reflected impedance Z_{eq} of the systems with 7.29 and 3.4 μH coils, the dependences of efficiency and output power take the same form as the other coil sets.

That's why during calculating the IET system with class E PA the value of the optimal internal inductance must be chosen according the load resistance and desired operation mode of IMD. If IMD needs regular recharges it is relevant to use lower inductances due to its high output power values. For IMD which works permanently and needs continuous powering it is relevant to chose coils with higher inductances due to its stable total efficiency despite its low output power parameter (in comparison with coils with lower inductances for the same load resistance).

Conclusions

This article presents a method for calculating and further adjusting the IET system using a class E power amplifier. The method is based on an understanding of the specifics of the operation of the IET system, the mutual inductance calculation procedures developed by the research team, and the algorithm for calculating the parameters of the class E PA, known for the works of N. Sokal. The verification of the presented method for the geometric parameters of the coil pair characteristic of the auxiliary circulation system is demonstrated. The system's performance was verified by computer simulation in the LTspice envi-

ronment. The maximum values of power on the load and overall efficiency are observed at the operating point of the IET system with the class E PA for the 7.29 μH coil pair, to which the amplifier was tuned (in the example shown corresponds to an axial misalignment of 15 mm) and shifted for the 3.4 and 12.27 μH coil pairs. IET system efficiency and output power decreases both during increasing and decreasing mutual inductance of the coil pair.

References

- [1] P. Eldridge, B. Simpson, J. Gilbert. The Role of Rechargeable Systems in Neoromodulation. *European Neurological Review*, 6(3): 187-192, 2011.
- [2] B.A. Achfar, B.K. Ammar, C. Hung. Power approaches for implantable medical devices. *Sensors*, 15: 28889 – 28914, 2015.
- [3] N.K. Bocan, E. Sejdic. Adaptive transcutaneous power transfer to implantable devices: a state of art review. *Sensors*, 16, 2016.
- [4] A.A. Danilov, G.P. Itkin, S.V. Selishchev. Progress in methods for transcutaneous wireless energy supply to implanted verticular assist devices. *Bioedical Engineering*, V. 44, Issue 4, 125-129, 2010
- [5] K.V. Schuylenbergh and R. Puers. *Inductive powering*. Springer Science + Business Media, 2009.
- [6] F. H. Raab. Effects of Circuit Variations on the Class E Tuned Power Amplifier. *IEEE Journal of solid-state circuits*, SC-13(2): 239 – 247, 1978.
- [7] Sokal N.O. Class-E RF power amplifier. *QEX*, Jan/Feb: 9–20, 2001.
- [8] M. A. A.-R. Firas. Design of input matching networks for class-E RF power amplifier. *High frequency electronics*, Jan: 40–48, 2011.
- [9] K. Chen, D. Peroilis. Design of high efficient broadband class-E power amplifier using synthesized low-pass matching networks. *IEEE Transactions on microwave theory and techniques*, 59(12): 3162–3173, 2011.
- [10] O. Knecht, R. Bosshard, J.W. Kolar. High Efficiency Transcutaneous Energy Transfer for Implantable Mechanical Heart Support Systems. *IEEE Transactions on Power Electronics*, 30(11): 6221–6236, 2015.
- [11] A.A. Danilov, E.A. Mindubaev, S.V. Selishchev. Design and Evaluation of an Inductive Powering Unit for Implantable Medical Devices Using GPU Computing. *Progress In Electromagnetics Research*. 69: 61–73, 2016.

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Diamond and Platinum Electrodes For Urea Electrochemical Oxidation

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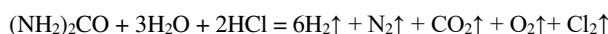
Introduction

Dialysate regeneration process can be potentially used in wearable artificial kidney (WAK) development as a method of uremic toxins removal [1–3]. These toxins and metabolites include nitrogen-bound substrates (urea, uric acid, creatinine etc), aromatic substrates (such as p-cresol), phosphates, nitrates etc. For purpose of dialysate regeneration the following approaches can be used: sorbent method [4], electrochemical method [5, 6], enzymatic method [7] etc. Each of them has its own advantages and disadvantages and overall different combinations of methods listed above can be used for effective dialysate regeneration. Nitrogen-bound substrates removal is one of the main issues of dialysate regeneration. While sorbents can effectively remove creatinine and uric acid, they are not effective in case of urea elimination. Thus alternative solution has to be found. In this paper urea electrochemical oxidation on diamond and platinum electrodes was investigated.

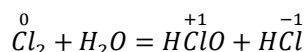
This paper is dedicated to electrochemical urea oxidation method. All experiments were performed in acidified solution (pH = 5.4). The following reactions might take place on anode and cathode surfaces and in the solution during electrolysis of acidified solution:

Cathode:		Anode:
$H^+, Ca^{2+}, Na^+, Mg^{2+}, Cl^-, H_2O$		$(NH_2)_2CO, H_2O, Cl^-$
Reduction of H^+ and water		Oxidation of urea, Cl^- and water
C	3	$2H^+ + 2e^- = H_2 \uparrow$ $2H_2O + 2e^- = H_2 \uparrow + 2OH^-$
A	1	$(NH_2)_2CO + H_2O - 6e^- = N_2 \uparrow + CO_2 \uparrow + 6H^+$ $2Cl^- - 2e^- = Cl_2 \uparrow$ $2H_2O - 4e^- = O_2 \uparrow + 4H^+$

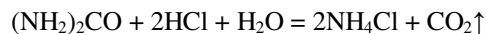
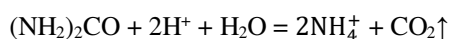
Molecular formula for anode urea oxidation:



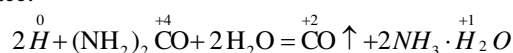
The following reaction might take place in the solution:



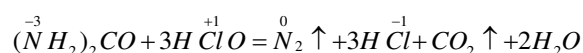
Urea hydrolysis in acidified medium can be presented by the following reaction:



Urea reduction can also take place due to urea's reaction with atomic hydrogen during its generation on cathode surface:



Urea oxidation can take place in the solution due to its reaction with hypochlorous acid:



It should be emphasized that during urea electrochemical oxidation different toxic byproducts (including sodium hypochlorite) are generated and accumulated in the solution. To resolve this problem different types of materials can be used including ion-exchange resins and non-selective sorbents such as activated carbon.

Materials and Methods

In this work dialysate regeneration by means of electrochemical oxidation method has been investigated. Effectiveness of electrochemical dialysate regeneration depends on multiple factors, such as initial ion composition of dialysate solution, initial concentration of nitrogen-bound substrates, pH of solution, solution initial temperature, current density, electrode surface, electrode material etc [8–13]. In this article all experiments were performed in a solution for peritoneal dialysis Fresenius Balance (glucose 1.5 %). Initial pH of the solution was 5.4. The solution contains glucose as an osmotic agent (glucose concentration – 1.5%). Composition of the solution is presented in table 1.

Table 1: Fresenius Balance (glucose 1.5 %)

Ion	Concentration, mmol/l
Calcium (Ca^{++})	1,75
Sodium (Na^+)	134,0
Magnesium (Mg^{++})	0,5
Chloride (Cl^-)	103,5

The model solution contained 30 mmol l^{-1} of urea. Solution was recirculated through hermetic electrochemical cell with rate 50 ml/min. Cumulative anode surface for each electrode type was 150 cm^2 . The volume of the model solution was 500 ml.

The following electrode types were chosen for experiment: smooth-platinum films deposited on titanium sub-

strate and boron-doped diamond films deposited on titanium substrate.

Preliminary cyclic voltammetry (CV) for electrode samples was studied. Experimental three-electrode cell for CV is presented on figure 1.

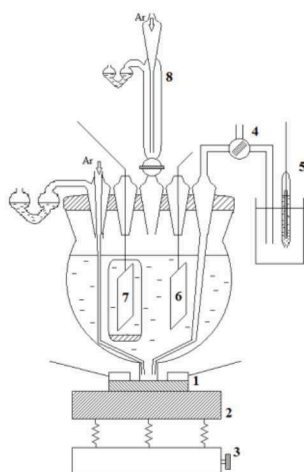


Figure 1: Three-electrode experimental cell for CV studies: 1 – electrode sample; 2 – table; 3 – lifting mechanism; 4 – salt bridge; 5 – reference electrode Ag/AgCl; 6, 7 – auxiliary electrodes; 8 – argon purge system

Cell top had five polished outlets for electrodes and argon flow system. Auxiliary electrode was separated from anode space with glass filter. Argon gas to provide inert medium inside the system was circulating through electrochemical cell. Reference electrode Ag/AgCl was linked to worked electrode through salt bridge filled with saturated solution of potassium chloride.

Experimental set-up is presented on figure 2.

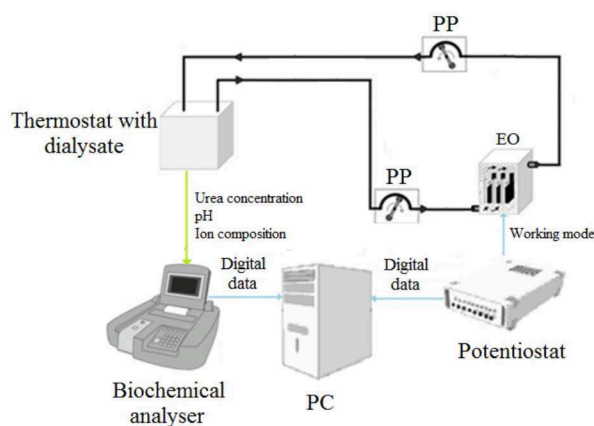


Figure 2: Experimental set-up for electrode samples testing: PP – peristaltic pump; EO – electro-oxidation cell

Urea concentration, pH and ion composition of the solution were controlled on biochemical analyzer Stat Fax 3300. Potentiostat PI-50-Pro controlled electrochemical cell working mode. All gathered data was processed and stored on personal computer. 1 ml of dialysate sample was taken every hour for urea and pH concentration measurement. Current density was 5 mA cm^{-2} .

Results

Cyclic voltammetries for platinum and diamond electrodes were studied.

Figures 3 and 4 present the cyclic voltammetries obtained with diamond and Pt electrodes in the solution for peritoneal dialysis with a scan rate of 10 mV s^{-1} for different urea concentrations.

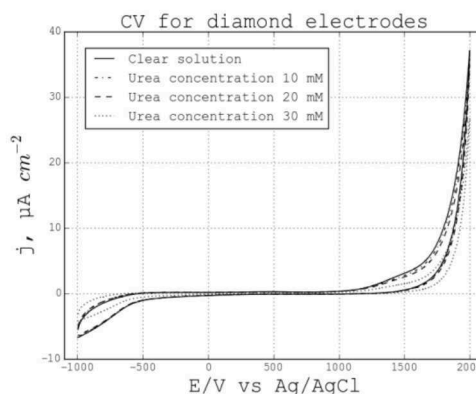


Figure 3. Cyclic voltammetry obtained with diamond electrode in the solution for peritoneal dialysis (Fresenius) for different urea concentrations (scan rate – 10 mV s^{-1})

In case of diamond electrodes, the presence of urea decreases current density in potential regions from -1000 to -500 mV vs Ag/AgCl and from 1000 to 2000 mV vs Ag/AgCl.

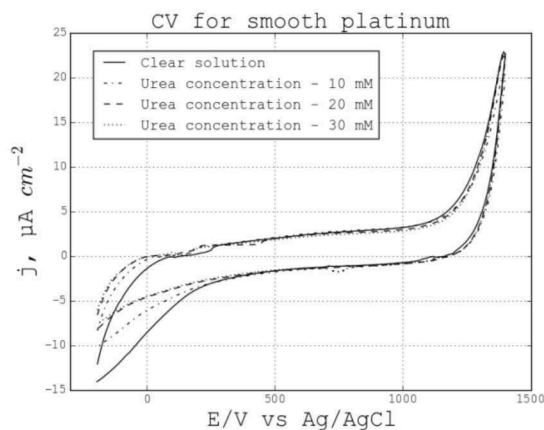


Figure 4. Cyclic voltammetry obtained with smooth platinum electrode in the solution for peritoneal dialysis (Fresenius) for different urea concentrations (scan rate – 10 mV s^{-1})

In case of cyclic voltammetry for smooth platinum electrode urea presence also altered the curve shape. Urea presence changed current density in the potential regions from -400 to 200 mV vs Ag/AgCl. At the same time, no current density change was observed on potential region from 1100 to 1400 mV vs Ag/AgCl. Observed phenomenon on both electrodes can be explained by electrode surface blockage due to urea adsorption on electrodes.

In the next stage urea oxidation rate for different electrode types was studied. Diamond and Ti/Pt electrodes were selected for this purpose. The main results of the experiment are presented on fig. 5.

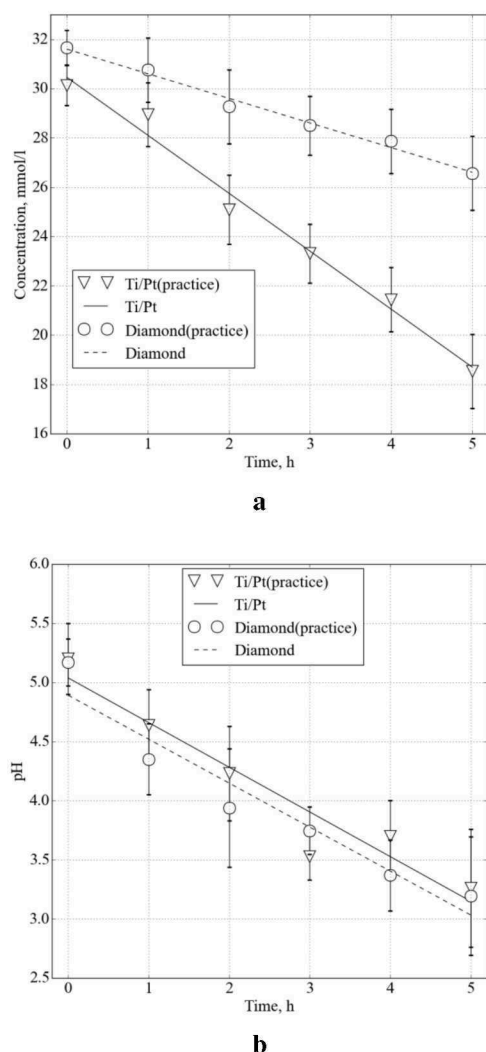


Figure 5. Results of experiment: a) urea concentration as a function of time; b) pH as a function of time

For Ti/Pt electrode urea oxidation rate was $69.54 \pm 4.3 \text{ mg h}^{-1}$, while for boron-doped diamond electrodes - $30.60 \pm 4.1 \text{ mg h}^{-1}$. The fact that platinum electrodes had higher urea elimination rate in comparison with diamond can be explained by catalytic properties of platinum.

Both diamond and platinum electrodes decreased pH of dialysate from 5.2 to 3.2. Increase of chloride was observed for both electrode samples. The highest chloride increase rate was observed for platinum electrodes ($5 \pm 1 \text{ mM h}^{-1}$). For diamond electrodes chloride the increase rate was $2 \pm 1 \text{ mM h}^{-1}$. Ti/Pt produced $0.142 \pm 0.02 \text{ mg}$ of sodium hypochlorite during the experiment, while sodium hypochlorite production was not observed for diamond electrodes.

Discussion

Cyclic voltammetries for both platinum and diamond electrodes in the solution for peritoneal dialysis have shown the tendency of urea to be adsorbed by electrode surface, which led to decrease of current density and change of the curve shape. At the same time, it was impossible to estimate what anode potential was preferable for potentiostatic urea oxidation. According to [14] experiments of potentiostatic urea oxidation mode demonstrated that this mode was ineffective due to low reaction kinetics. During the experiment, low urea oxidation rate was observed.

Galvanostatic urea-oxidation mode proved more effective than galvanostatic mode; however, it affected solution ion composition and pH and increased sodium hypochlorite generation in case of Ti/Pt. It is remarkably that hypochlorite generation was not observed for diamond electrodes. It should be also noted that ion chloride concentration increase on diamond was less intense in comparison with Ti/Pt, although diamond acidified solution with the same rate as platinum. These properties could possibly compensate low urea-oxidation rate; however, diamond electrodes were not stable and degraded during electrolysis due to high current density (5 mA cm^{-2}), which excluded diamond electrodes as a candidate for dialysate regeneration.

Ti/Pt electrodes was approved as more stable material with higher urea oxidation rate, but high sodium hypochlorite generation rate, electrolysis influence on ion composition and pH of the solution should be taken into consideration. These issues can be resolved by adding ion exchange resins, activated carbon and degasser in dialysate regeneration unit.

Conclusions

Titanium diamond electrodes had lower oxidation rate and did not produce sodium hypochlorite, and at the same time they were unstable and dissolved during electrolysis which made this electrode type inappropriate for dialysate regeneration unit. Ti/Pt was the most stable material in case of electrolysis with higher urea oxidation rate and thus it is still the most prominent material for renal replacement therapy with regeneration.

Urea electro-oxidation on platinum electrodes may be potentially used in case of dialysate regeneration. However, pH stabilization of the solution is required. This issue can be resolved by adding activated carbon column. Future research will be warranted to investigate the possibilities of ion composition and pH control in closed-loop dialysate regeneration system during the process of urea electrochemical oxidation.

References

- [1]. Maria Jafaar. Horizon Scanning Report. Wearable Dialysis Device. // Report No: 006/2016.
- [2]. A wearable artificial kidney for patients with end-stage renal disease / Gura V. [et al.] // JCI Insight. 2016. P. 1–15.
- [3]. Maintenance dialysis throughout the world in years 1990 and 2010. Thomas B. [et al]. Journal of the

- American Society of Nephrology. 2015. Vol. 26. №11. P/ 2631–2633.
- [4]. John WM Agar. Review Understanding sorbent dialysis systems // Nephrology. 2010. Vol. 15. P.406–411.
- [5]. W. Simka, J. Piotrowski, G. Nawrat. Influence of anode material on electrochemical decomposition of urea // Electrochim. Acta. 2007. Vol. 52. P.5696–5703.
- [6]. Removal of urea in wearable dialysis device: a reappraisal of electro-oxidation / Maarten Wester [et al.] // Artificial Organs. 2014. P.1–17.
- [7]. A wearable haemodialysis device for patients with end-stage renal failure: a pilot study / Andrew Davenport [et al.] // Lancet. 2007. Vol. 370. P. 10
- [8]. J.C. Wright, A.S. Michaels, A.J. Appleby Electrooxidation of urea at the ruthenium titanium oxide electrode // AIChE J. 1986. Vol. 32. P.1450–1458.
- [9]. Electrocatalytic oxidation of urea on a sintered Ni–Pt electrode / W. Simka [et al.] // J. Appl. Electrochem. 2009. Vol. 39. P.1137–1143.
- [10]. B.K. Boggs, R.L. King and G.G. Botte. Urea electrolysis: direct hydrogen production from urine. Chem // Commun. 2009. Vol. 32 P.4859–4861.
- [11]. A.T. Miller, B.L. Hassler, G.G. Botte. Rhodium electrodeposition on nickel electrodes used for urea electrolysis // Appl. Electrochem. 2012. Vol. 42. P. 925–934.
- [12]. V. Vedharathinam, G.G. Botte. Understanding the electro-catalytic oxidation mechanism of urea on nickel electrodes in alkaline medium // Electrochim. Acta. 2012. Vol. 81. P.292–300.
- [13]. V. Vedharathinam, G.G. Botte. Direct evidence of the mechanism for the electro-oxidation of urea on Ni(OH)₂ catalyst in alkaline medium // Electrochim. Acta. 2013. Vol.108. P.660–665.
- [14]. Electrochemical Removal of Urea from Physiological Buffer as the Basis for a Regenerative Dialysis System / Richard W. Keller [et al.] // J.Electroanal. Chem. 1980. Vol. 116. P.469–485.

Acknowledgements

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Algorithm of physical activity detection according to the accelerometer data of implantable pacemaker with rate-adaptive pacing.

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Abstract

The number of implantable pacemakers increases every year. Rate-adaptive pacing improves the quality of life of patients with implantable pacemakers. The accuracy of current algorithms is not sufficient for a productive life of patients. The object of this article is to demonstrate new algorithm of physical activity detection according to the accelerometer data.

Keywords

Rate adaptation, pacemaker, accelerometer.

1. Introduction

There is a trend towards improvement in quality of life in today's world. Rate adaptation allows patients with implantable pacemakers to bring their life as close to normal as possible. Rate responsive pacemakers allow to increase the heart rate, depending on the patient's physical load. Figure 1 illustrates how pacemaker works without rate adaptation. The frequency of the stimulating pulses remains constant during the day with changes of the physical activity intensity. Figure 2 shows the operation of a pacemaker with frequency adaptation, in this case the frequency of the stimulating impulses is adjusted to the change in physical activity.

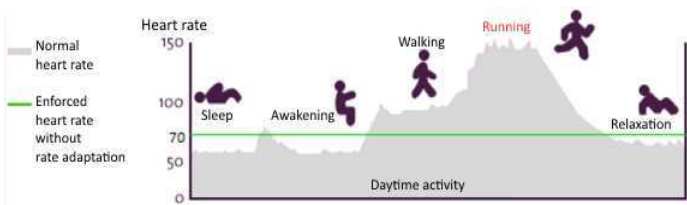


Figure 1 – Enforced heart rate without rate adaptation



Figure 2 – Enforced heart rate with rate adaptation

This article describes the development of algorithm of physical activity detection according to the accelerometer data of implantable pacemaker. Rate adaptation is achieved by using sensors that determine the parameters related to the load and associate them with the frequency of stimulation. Methods of stimulating impulses frequency adaptation depending on various parameters were examined in the article [1]. Incorrect interpretation of passive movements continues to be a disadvantage of the developed algorithms.[2]

2. Methods and materials

2.1 Experiment description

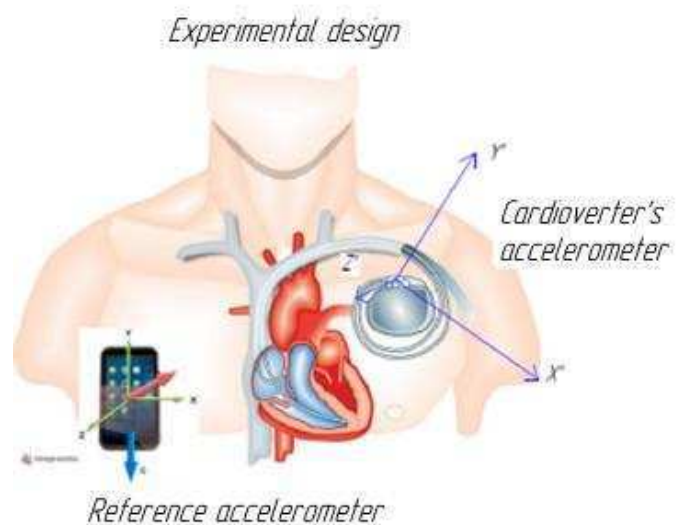


Figure 3 – Experiment setup

The accelerometer sensor was chosen for the experimentation because it directly measures physical activity, unlike other sensors, which measure only the parameters affected by physical activity. The experiment was conducted with the aim of obtaining physical activity data that was used to develop an algorithm.

Two accelerometers were used in the experiment. The first sensor required for accelerometer axes reorientation was fixed on the subject's abdomen so that its axes were directed according to the human body axes. The second sensor, which simulated the accelerometer of implantable pacemaker, was also fixed on the abdomen, but was located at an arbitrary angle in the range of 0 to 90 degrees, the axes of the second accelerometer didn't coincide with the human body axes. (Figure 3)

Accelerometers of the LIS302DL type built into a mobile phone were used for carrying out the experiment. Basic technical specifications of LIS302DL accelerometer are presented in Table 1.

Table 1

Technical characteristic	Value
Sampling frequency	50 Hz
Supply voltage	2.16 V to 3.6 V
Amplitude range of g	$\pm 2g/\pm 8g$

2.2 Database

A database was created according to the results of the experiment for three motion types: running, walking and stair climbing. The experiment was conducted on eight volunteers. Each database file contains data obtained from the accelerometer (time and acceleration in three axes) and the necessary parameters for the information analysis: the motion type, sex, age, weight and height of the test subject.

2.3 Accelerometer axes reorientation procedure

Axes of the implanted pacemaker accelerometer should coincide with the human body axes in order to implement the algorithm of physical activity detection. Calibration is performed by means of external accelerometer during the implantation. The direction of the vector of gravity has to coincide with the vertical axis of the implantable pacemaker accelerometer. For this purpose three experiments were carried out using the external accelerometer, whose data was taken as a reference.

The following matrix equation is used to convert the data obtained from the accelerometer:

$$A = \begin{bmatrix} X1 & X2 & X3 \\ Y1 & Y2 & Y3 \\ Z1 & Z2 & Z3 \end{bmatrix} \begin{bmatrix} X'1 & X'2 & X'3 \\ Y'1 & Y'2 & Y'3 \\ Z'1 & Z'2 & Z'3 \end{bmatrix}^{-1} \quad [3]$$

Where A - coordinate transformation matrix

X,Y,Z – reference accelerometer data

X',Y',Z' – pacemaker accelerometer data.

Computing matrix A is calculated once and loaded into the pacemaker.

Each signal from the collected database contains information from both accelerometers. All signals pass primary processing of accelerometer axes reorientation, which is necessary for further application of the algorithm of physical activity detection.

2.4 Algorithm of physical activity detection.

Threshold algorithms are used to detect the physical activity using an accelerometer sensor.

The data processing begins with dividing the signal received from the accelerometer during the experiment into 3-second intervals in order to reduce the delay time. 3-second delay is optimal, because the change in heart rate after exercise is normal within 3 seconds. [4] The threshold value determined by the experimental data for the sensor signals is 0.25g. The quantity of peaks above the threshold value is calculated. Figures 4 and 5 show peak detection signal processing at the 3-second interval.

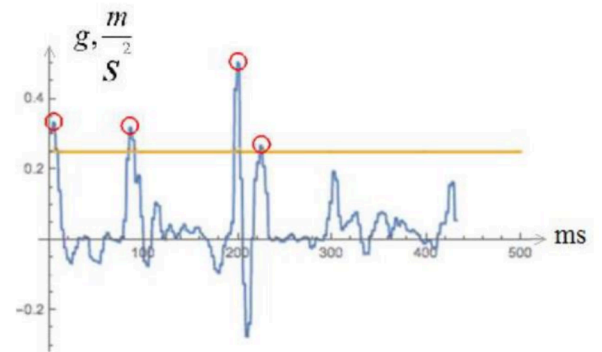


Figure 4 – Quantity of peaks for slow walking motion

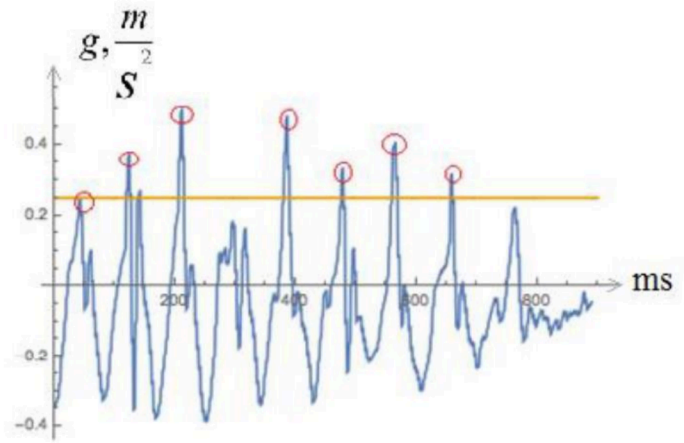


Figure 5 – Quantity of peaks for running motion

The percentage of signal counts over the threshold value to the total number of samples is calculated. This percentage describes the intervals duration above the threshold value and the acceleration increase.

Based on the results of the experiment, a space of attributes was formed for each type of physical activity.

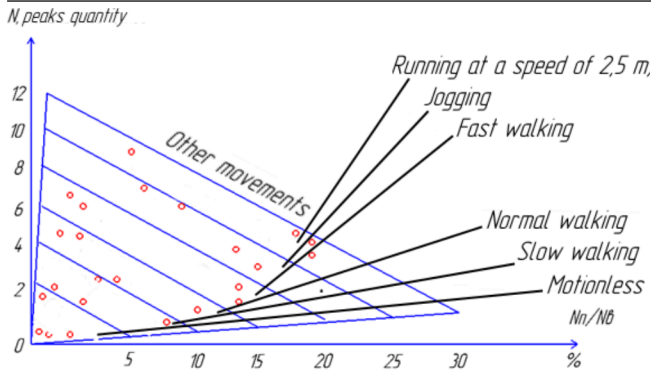


Figure 6 - Diagram of the physical activity detection
The stimulating heart rate is selected in accordance with Table 2.

Table 2 — Dependence of heart rate on physical activity [5]

Motion type	Heart rate, BPM
Slow walking	86
Normal walking	104
Fast walking	122
Jogging	135
Running at a speed of 2,5 m/s	155

3. Results

The space of attributes was formed for each type of physical activity. Another outcome of this work is the generated database. The algorithm of accelerometer axes reorientation was created, that was necessary for application of the physical activity detection algorithm. Algorithm of the physical activity detection was developed.

Table 3. Results of applying the physical activity detection algorithm

Motion type	Total intervals	Intervals recognized	Correctly recognized intervals
Relaxation	4	4	4
Slow walking	4	4	3
Normal walking	4	3	3
Fast walking	4	2	1
Jogging	4	6	4
Running at a speed of 2,5 m/s	4	5	4

The developed algorithm was tested on the collected database.

4. Discussion

As a result of the algorithm application for physical activity detection, 5 out of 24 intervals were determined incorrectly. This may be associated with small difference in the number of peaks above the threshold value for walking fast and jogging motion types. Furthermore, algorithm application errors may be related to the presence of passive movements. At the present time, the possibility is being considered of analyzing the third criterion included into the algorithm with the aim of creating a three-dimensional space of attributes model. It is also planned to add the possibility of recognizing passive movements to the algorithm.

Conclusion

This article describes the development of the physical activity detection algorithm applied with help of accelerometer sensor when using the implantable pacemaker rate adaptation. Preprocessing the data using the algorithm of accelerometer axes reorientation is explained. The features of the experiment for data collection and database formation are described. In the future, it is planned to increase the amount of movements in the database and the number of physical activity detection algorithms.

Reference list

- [1] Materialy Vtorogo Vserossiyskogo s"yezda aritmologov [Materials of the Second All-Russian Congress of Arrhythmologists]. Moscow, BSCCS Publ., 2007
- [2] Wilfried Mullens , W. H. Wilson Tang. Telemonitoring and Sensor Technologies in Chronic Heart Failure Matthias Du- pont .2014
- [3] Armin Bolz. Cardiac Pacemaker Systems. Springer-Verlag Berlin Heidelberg 2011
- [4] Varma N, et al. Evaluation of ef fi cacy and safety of remote monitoring for ICD follow-up: the TRUST trial. Circulation. 2008
- [5] Duperron G.A. Teoriya fizicheskoy kul'tury [Theory of physical culture]. Leningrad, 1927. 210 p.

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Multidiagnostics study of postoperative cognitive disorders

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Introduction

The analysis of works of domestic and foreign scientists shows that the results of anesthesia frequently, especially for elderly patients, negatively affect the state of cognitive functions in the postoperative period [1]. Therefore, the modern diagnosis of post-operative cognitive dysfunction (POCD) in the early stages, when changes are potentially reversible, and to develop methods for preventive and corrective cerebroprotective therapy on the background of adequate correction of homeostasis acquire important practical significance.

Objective methods for the assessment of violations of cognitive functions available to the anesthesiologist in everyday practice, does not currently exist. Such methods include electrophysiological assessment of psychomotor functions (the ability to create, save and execute motor program) with the help of stabilography.

As integral characteristics for quantifying the anesthetic component of the operating aggression, the authors propose to use the results of stabilographic studies of the patient in combination with the assessment of his cardiac rhythm, especially with the detection of ventricular extrasystoles (VE). The urgency of the problem of diagnosis is not in doubt due to their high prevalence (more than 62 % of all extrasystoles) and the most important role in the development of sudden cardiac death (SCD), therefore, it is necessary to improve algorithms for the detection of ventricular arrhythmias based on analysis of electrocardiosignals (ECS).

The aim of this work is the search for adequate anesthesia, based on the study of the manifestations of postoperative cognitive dysfunction using the system of «WebMultiMedic» providing a comprehensive assessment of the dynamics stabilographic and electrocardiographic indicators.

Materials and Methods

In result of cooperation authors with LLC «BIOSOFT-M» (Moscow, www.biosoft-m.ru) is developed a unique system of remote multidagnostic of patients with dysfunctions of the locomotor system during the postoperative period. Technique, implemented in the system allows passing on the empirical, approximate recommendations to the exact values calculated on the basis of multifactori-

al characteristics of each patient and synchronous recording of the results of complex research of patient by means of computer stabilography, electrocardiography, electromyography, electroencephalography with remote multidagnostic system «WebMultiMedic» [2, 3]. Rising of the quality of diagnosis is achieved through an integrated synchronous registration, processing and analysis of diagnostic signals of multiple research techniques of body functions as well as through the implementation of remote examination of patients on the basis of mobile data communications via Internet. Force plate, electrocardiograph, electromyograph and electroencephalograph combined on the basis of specialized hardware and software into a single system that performs remote examination of patients outside hospitals or in other places. Authorization of doctor and patient on Web-server is performed automatically by means of the keys that contain identifier codes and licenses for the types of data operations and modes of examination of a patient. Web-server of functional diagnostics implements the infrastructure to support remote communications in online and offline examinations, a set of operations performed by a physician in during the analysis and processing the results of diagnostics, storage of patient data and real-time video communication for remote consultations.



Figure 1

The main software includes the Romberg test, psychological tests, and special research tests designed by original techniques. [4].

The system provides a detailed analysis of the stabilometric parameters and the frequency measurement of heart rate and the amplitude-time parameters of the ECS; performs analysis of heart rate variability, however does not allow to detect ventricular extrasystoles.

Developed an original method of detecting ectopic cardio pulses [5], based on the analysis of the physical nature of the formation of ventricular extrasystoles. Upon detection of ectopic cardio pulses joint processing of the two ECG leads S is performed so that the same QRS-T complexes are mutually compensated. If you experience ectopic complexes the ratio of signals 1 and 2 lead changes, and thus on the signal S appears a surge, which is detected by the threshold device.

One of the variants of implementation of the method is the partitioning of the ECS in each of the leads on the positive and negative components S, and the choice of four weighting factors $k1+$, $k1-$, $k2+$, $k2-$, so that in the time intervals corresponding to the appearance of the typical complexes, the value of the signal S tends to zero:

$$S = k_1^+ \sum_{i=1}^N X_{1i}^+ + k_1^- \sum_{i=1}^N X_{1i}^- + k_2^+ \sum_{i=1}^N X_{2i}^+ + k_2^- \sum_{i=1}^N X_{2i}^-$$

A study of the software implementation of the method showed certain shortcomings:

- not in all cases possible to compensate for typical QRS-T complexes,
- selection of 4 coefficients is complicated and takes a long time.

It is proposed to use the a single factor for what it is expedient for each of the cardiac complex to form mono impulse (monopulse). QRS complexes detection algorithm is based on the ranking procedure MSM (MaxSubMin), performed in a sliding window [6]. This procedure just creates a monopulse signal. MSM procedure is to perform three sequential steps:

- finding the maximum value of a discrete reference ECG signal in a sliding size $2s + 1$ window;
 - finding the minimum value of the discrete reference ECG signal in a sliding size $2s + 1$ window;
 - subtracting the minimum value from the maximum value.
- Formally MSM procedure is written as follows:

$$y_{\max}(t) = \max(x(t-s), x(t-s+1), \dots, x(t-1), x(t), x(t+1), \dots, x(t+s-1), x(t+s));$$

$$y_{\min}(t) = \min(x(t-s), x(t-s+1), \dots, x(t-1), x(t), x(t+1), \dots, x(t+s-1), x(t+s));$$

$$MSM(t) = y_{\max}(t) - y_{\min}(t).$$

Examples of the formation of MSM procedure of monopulse signal and subsequent integration into the sliding window (MSMI) are shown in Figure 2. The blue line represents the input ECG signals, and the red line represents a monopulse signal. Monopulse signal can uniquely detect the QRS complexes in all four cases (ECG signals with high-amplitude T wave, ECG signals with the drift of isoline, ECG signals from motion artifacts, ECG signals with negative QRS complexes).

Figure 3 procedure MSMI window size is 11 samples ($s = 5$), the size of the integration window 21 samples (frequency for sampling ECG signals $fd = 500$ samples per second).



Figure 2

The combination of methods described above allowed to create a method of differential detection of ECG complexes

$$Z(t) = MSMI1(t) - K \cdot MSMI2(t),$$

where K is a tuning factor, which is set at the beginning of the research.

The structure illustrating the proposed method, shown in figure 3.

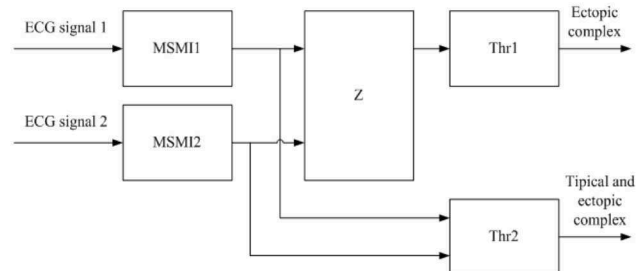


Figure 3

Example of the formation of pulses corresponding to ectopic complexes, shown in figure 4 (output Z).

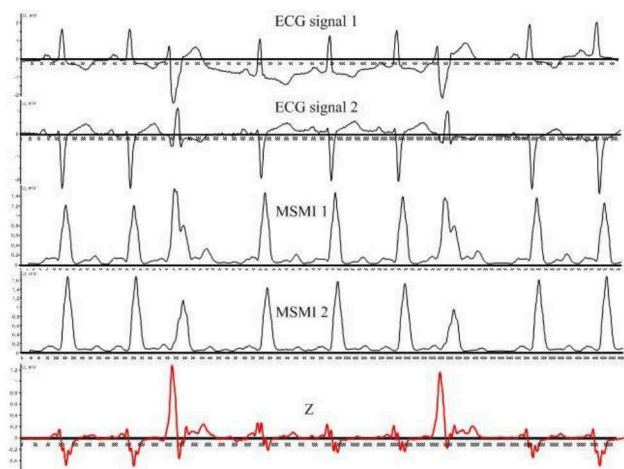


Figure 4

The developed method of differential detection of the QRS complexes is simple and has high performance, it can be implemented in real time. It does not use complex algorithms based on pattern recognition (recognition of many classes with their further classification into normal and ectopic).

Testing the developed method on signals from MIT-BIH Arrhythmia Database showed that the probability of correct detection of QRS complexes (sensitivity), even without pre-filtering is 0,97-0,98.

The application before the procedure MSMI the «hard» filtering with a bandwidth of 2-30 Hz, and the introduction of adaptive threshold improves the probability of correct detection of QRS complexes to 0.99 (when you test on the same signals). The characteristics of detection of ectopic complexes are about the same.

Method recommended for use in the system «WebMulti-Medic» with the aim of improving the quality of ECG-diagnosis.

Results

For analysis of postoperative cognitive dysfunction using stabilographic monitoring of patients operated on for chronic cholecystitis, the study on 29 patients operated at the Penza clinical hospital № 6 named after G. A. Zakharin.

Studies were conducted with the approval of the Local ethics Committee, and written consent from each patient for the surgery, anesthesia and research.

The choice of patients contingent for the study was determined by the fact that in laparoscopic cholecystectomy a direct impact on the musculoskeletal system is considered to be minimal compared to other interventions, which allows to put the patient on his feet in the first day of the postoperative period.

All patients were divided into 2 groups: group 1 (23 patients in the perioperative period received antioxidant therapy with mafusol and cardioksipin); control group 2 (6 patients, the perioperative period, this therapy was not used).

The surgery was performed under endotracheal anesthesia (a common method of anaesthesia induction and supporting anesthesia with nitrous oxide).

Stabilographic examination of patients was performed before surgery, 24 hours and 48 hours after surgery. The majority of patients were discharged to outpatient treatment within 3-4 days.

In addition to the common in the clinic of the research was determined stabilographic parameters: X is the average position of the center of pressure (CD) on the X-axis (mm); Y – middle position CD along the Y-axis (mm); V – average speed of displacement of the CD (mm/s); S – area of statokinesigram (mm²) [7] (figure 5).

Revealed the difference of the indices of stabilography: in the control group, the rate of displacement of the center of pressure (V) and area of the stabilogram (S) have a larger spread of values for all modes of study (with open and closed eyes) than in the group of patients who received antioxidant therapy in the perioperative period.

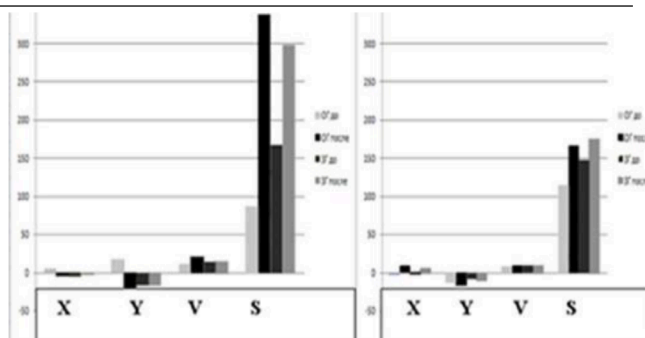


Figure 5

In the course of further studies, we studied in more detail the dynamics of changes in the stabilographic parameters in 120 patients in the perioperative period with laparoscopic cholecystectomy, as a result, a method was patented to reduce the anesthetic risk during laparoscopic cholecystectomy [7].

Discussion

To identify cognitive disorders in clinical practice most commonly used short scale assessment of mental status (MMSE) proposed by M. F. Folstein co-authors in 1975 and represents a short questionnaire of 30 items, widely used for the primary assessment of cognitive function and screening of their violations. The diagnostic sensitivity of this technique is not absolute, but is too selective.

Another method for neuropsychological evaluation of cognitive disorders that have a higher sensitivity in comparison with the test ME is MoCA test – the Montreal scale assessment of cognitive disorders (2004) [1].

However, these techniques have a substantial component of subjectivity offer only the qualitative characteristics of the patient.

The sensitivity of the stabilometric method and the quality of information allowed to use this method to determine the current functional state of the patient, the researcher receives information about static and locomotor functions of the patient which cannot be obtained by any other means [8].

In this regard, there is reason to assume that the used during anesthesia medication and other means, affect the static and locomotor functions of the patient and can be measured quantitatively, which may serve as an objective safety criteria conducted anesthesia.

Another important and objective criterion for assessment of postoperative condition of the patient can serve as the parameters characterizing the violation of his heart rate, especially the presence of dangerous ectopic ventricular complexes in the ECS.

Therefore, we believe a promising integrated research stabilographic and cardiological criteria for the assessment of anesthesia that is given undeservedly little attention, by both domestic and foreign researchers.

Conclusions

Thus, the results of the conducted research we can draw the following conclusions.

1. Instrumental method of monitoring based on computerized of stabilography and channel ECG diagnosis system «WebMultiMedic» can serve as a complementary tool of the anesthesiologist in the optimization of General anesthesia in patients during laparoscopic cholecystectomy.
2. The modernization of the ECS channel analysis system «WebMultiMedic», namely, the introduction of differential detector complexes of the ECS, allows high accuracy to detect PVCS and assess the risk of sudden cardiac death.
3. According to the study most informative stabilographic parameters are the velocity of center of pressure on the platform and the area of the stabilogram. It is important that in the control group, the variation rate of displacement of the center of pressure and area of the stabilogram were significantly greater than in the group of patients who received antioxidant therapy in the perioperative period (for all modes of study).
4. The results of these studies quantitatively confirm the feasibility of the use of stabilography as a tool to optimize anesthesiological treatment of patients with laparoscopic cholecystectomy.
5. The research results confirm the feasibility multidagnostic survey and research of all groups of postoperative patients with a view to detection of postoperative cognitive disorders.

References

- [1] Postoperative cognitive dysfunction and the principles of cerebroprotective in modern anesthesiology: a training manual for physicians / ed. by A. M. Ovezova. – Moscow, 2015. – 76 c.
- [2] V.V. Istomin, T.V. Istomina, A.V. Kireev and A.I. Safronov, "Methodical software of the system for remote multi-diagnostic and rehabilitation of patients after hip replacement," Scient. and Tech. Bull. of the Volga, 1, 113 (2011).
- [3] T.V. Istomina, A.V. Kireev, A.I. Safronov, V.V. Istomin and T.V. Karamysheva, Patent for useful model number 122009. Stabilometric simulator, (Russian Federation, 2011).
- [4] Istomina T. V., Filatov I. A., Safronov A. I., Istomin V. V., Karpitskaya S. A., and others. Modern equipment for remote Multidiagnostic and rehabilitation of patients with postural deficits // «XXI century: results of the past and challenges of the present plus»: a scientific Periodical. – Penza: Publishing house PenzGTU, 2013. – №09(13). T.I. – C. 64-70.
- [5] Patent № 1616600 of the USSR. Detector ventricular extrasystoles / T. V. Istomina, L. Yu. Krivonogov, Yu.V. Polubabkin; publ. 30.12.1990, Newsletter № 48.
- [6] Krivonogov L. Yu. System for electrocardiographic diagnosis of critical conditions in terms of the free activity of the patients. Diss. ... Ph. D.: Penza, 2017.
- [7] Patent № 2594976 of the RF. A method of reducing anesthetic risk during laparoscopic cholecystectomy» Safronov A. I., Kireev V. A., Vasil'kov V. G., Karpitskaya S. A. egistered in State register of inventions of the Russian Federation of 28 July 2016.
- [8] Skvortsov D. V. Stabilometric study: a brief guide / by D. V. Skvortsov, M.: Mask, 2010. — 172 c.

A Database with face video images of patients with schizophrenic disorders and control healthy group

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Introduction

Schizophrenia is characterized by various negative and positive symptoms and specific incremental changes in personality. Negative symptoms are manifested in behavior, especially in facial expressions. Actual problems today are predicting disease course, evaluation of the effectiveness of treatment, and diagnosis of schizophrenia in preclinical stage of the disease. Development of the automated system of analysis will allow us to study flat affect – one of the negative symptoms of schizophrenia. Consequently, automated facial expressions analysis will make progress in addressing actual problems.

In recent works are reported about using an automated approach to the assessment of facial movements by images for tracking disease course and treatment effectiveness [1, 2, 3]. However, most studies aimed at identifying the differences between healthy group and patients.

The result of different studies (in Canada, India, European countries, Iran) was the discovery of specific anomalies of facial expressions in schizophrenia. Interest in such studies has grown significantly during the last 5 years. In Russia, such studies are still very few.

Patients with schizophrenia have specific anomalies such as a low frequency of positive emotions on certain stimuli and typical movements [4, 5].

Materials and Methods

A database of video images of patients with schizophrenic disorders and in the psychosis high-risk state [6] has been being collected in Mental Health Research Center. A database of control healthy group has been being collected in Bauman Moscow State Technical University.

Stimulant material for the study of facial expressions were three demonstration videos, intended to product emotions of sadness and joy, duration is about 4-5 minutes, and questions on the subject of videos. The first video is neutral, the second one is sad and the last one comprises two parts: neutral part and subsequent funny part. After video demonstration respondents are also asked to estimate their emotional state. A person can choose one or more of the following emotions: happiness, delight, sorrow, worry, sadness, fear, indifference, shame and disgust, – or propose his own variant of emotion. For chosen emotions a respondent has to estimate intensity in the range from one (the weakest intensity) to five (the strongest intensity).

The respondents with schizophrenic disorders first read the text, then watch the video and estimate their emotional state. Thus, following steps of our study were recorded: reading the text, watching the video 1, discussion of the video 1, watching the video 2, discussion of the video 2.

Respondents with schizophrenic disorders were recorded at two time points: the first point is on hospitalization, the second point is on discharge from the hospital.

Medical advisers of our research group conducted standard procedures for evaluating the mental state of patients with schizophrenic disorders on various scales: Positive and Negative Symptoms Scale (PANSS), The Scale of Prodromal Symptoms (SOPS), The Hamilton Rating Scale for Depression (HDRS), Scale of side effects assessment (Udvald for Kliniske Undersogelser Side-Effect Rating Scale, UKU).

Before the first video a respondent of control healthy group is asked to fill out a questionnaire on trait anxiety from state-trait anxiety inventory (STAI-40). After the last video a respondent is asked to fill out a questionnaire on state anxiety from STAI-40, Toronto alexithymia scale questionnaire (TAS-26) and gelotophobia, gelotophilia and katagelasticism questionnaire (PhoPhiKat<30>).

During demonstration respondent's facial image is recorded. For recording we use Logitech C922 Pro Stream webcam. Recorded videos has full HD resolution (1 920 x 1 080 pixels) at 30 frames per second. For each respondent a video of about 2 GB have been recorded.

Conditions of registration is limited to the hospital environment. The patient sits at the table in front of the window while recording the video. Lighting in the room is top and diffused. The patient's face is illuminated evenly, there are no shadows.

The patient sits in front of the laptop with a webcam attached to the top of the screen. Distance from person to camera is from 30 to 90 cm. Face takes up 60% of the image.

Participants

Medical advisers of our research group separated patients into two groups according to clinical observation: patients with schizophrenia and patients in the psychosis high-risk state. 13 respondents are with schizophrenia in the age from 17 to 25 (the average age 20 years), duration from 1 to 24 months, the mean duration is 9 months with normal

or corrected vision, exclusion criteria: severe somatic and neurological diseases, hearing impairment, alcohol and drug addiction in the anamnesis. 30 patients are in the psychosis high-risk state (age from 16 to 25 years, the average age 20 years, disease duration from 3 to 96 months, mean duration of the disease 33 months). 20 respondents aged 20 to 25 years from control healthy group are recorded. Among them six persons are women and fourteen persons are men.

Results

Primary processing of the video images data was performed manually with facial action coding system (FACS) [7]. We made annotation of two intervals: watching the video 1 and watching the video 2. Motion acts over the FACS (yawning, swallowing, tremor, tears) are included during the annotation.

Annotation include the list of action units and motion acts and the number of the beginning and the end of the act. The beginning and the end of our intervals are also marked in the annotation. Furthermore, there are asymmetrical action units and motion acts in the annotation.

Annotation is made by two authors of the thesis. To verify the homogeneity of the annotations obtained, we tested the hypothesis that distributions of each action unit belong to the same distribution. To test the hypothesis, we use the Kolmogorov-Smirnov test. The null hypothesis is that the data in two vectors are from the same continuous distribution. We performed a test with a 5% significance level.

We used such features:

- frequency of action unit η is the ratio of the number of action unit per interval to the duration of the interval;
- percentage of action unit π is the ratio of the sum of the durations of the action unit during an interval to the duration of the interval.

The analysis showed that there are no differences with the 5% significance level. Features without differences are showed with «+» in the table, e.g. see tab. 1. Features are grouped according to the area of the face. Furthermore, appearance of asymmetric action units is marked with letters «R» and «L» corresponding to right and left action units, «n/a» means the absence of asymmetry in video images.

Conclusions

Our first estimation confirms the possibility of solving different tasks with this database and its annotation:

1. Study differences between groups of healthy persons and patients with schizophrenia.
2. Study differences between groups of patients with schizophrenia and patients in the psychosis high-risk state.
3. Investigation of the dynamics of mimic manifestations at the beginning and at the end of treatment.

4. Identification of the relationship between the results of psychological scaling and the severity of psychopathological disorders of facial expressions.

5. Development of an automated approach to the evaluation of facial movements for the study of changes in various time points of the course of a mental illness.

Table 1: Verified Action Units

Action Unit	η	π	η R	π R	η L	π L
Up Face Action Units						
au01	+	+	+	+	+	+
au02	+	+	+	+	+	+
au04	+	+	+	+	+	+
au05	+	+	n/a	n/a	n/a	n/a
au06	+	+	+	+	+	+
au07	+	+	+	+	+	+
Middle Face Action Units						
au09	+	+	n/a	n/a	n/a	n/a
au10	+	+	+	+	+	+
Down Face Action Units						
au11	+	+	+	+	+	+
au12	+	+	+	+	+	+
au13	+	+	n/a	n/a	n/a	n/a
au14	+	+	+	+	+	+
au15	+	+	+	+	+	+
au16	+	+	+	+	+	+
au17	+	+	+	+	+	+
au18	+	+	n/a	n/a	n/a	n/a
au20	+	+	n/a	n/a	+	+
au24	+	+	n/a	n/a	n/a	n/a
au25	+	+	n/a	n/a	n/a	n/a
au26	+	+	n/a	n/a	n/a	n/a
au28	+	+	n/a	n/a	n/a	n/a
au31	+	+	n/a	n/a	+	+
au35	+	+	n/a	n/a	n/a	n/a

References

- [1] Benson P.J. et al. Simple viewing tests can detect eye movement abnormalities that distinguish schizophrenia cases from controls with exceptional accuracy. *Biological psychiatry*, 72(9):716-724, 2012.
- [2] Hamm J. et al. Dimensional information-theoretic measurement of facial emotion expressions in schizophrenia. *Schizophrenia research and treatment*, 2014.
- [3] Tron T. et al. Automated facial expressions analysis in schizophrenia: A continuous dynamic approach. In *International Symposium on Pervasive Computing Paradigms for Mental Health*, pages 72-81, Springer International Publishing, 2015.
- [4] Tron T. et al. Facial expressions and flat affect in schizophrenia, automatic analysis from depth camera data. In *IEEE-EMBS International Conference on Biomedical and Health Informatics (BHI)*, pages 220-223, IEEE, 2016.
- [5] Dudek A. et al. Analysis of facial expressions in patients with schizophrenia, in comparison with a healthy control-case study. *Psychiatria Danubina*, 29(3):584, 2017.
- [6] Fusar-Poli P. et al. The psychotic high-risk state. *JAMA Psychiatry*, 70(1):107-120, 2013.
- [7] Ekman P., Friesen W.V. *Facial action coding system*, 1977.

Determination of the coupling-loss distance between the inductive coils in a transcutaneous energy transfer system

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Introduction

Improving the methods of power supply is one of the most important areas for implantable medical devices (IMD) development [1], [2]. Wireless energy transfer by means of inductive coupling represents one of the possible solution. This technology is currently the main method of feeding cochlear implants [3], [4] and of the spinal cord stimulators [5], [6]. The prospective areas of application include energy supply systems for mechanical support of blood circulation [2], [7], visual prostheses [8], [9] and active orthopedic implants [10].

There are areas of research on transcutaneous energy transfer using inductive coupling, an example is the development of formal design and optimization methods developing to this day [11]. Important for solving problems in the implementation of such methods is to ensure the stability of energy transfer, when the receiving and transmitting coils are offset relative to each other, as well as increasing the efficiency of energy transmission [12], [13].

The formal rules for determining the boundary and initial conditions must be defined in order to optimize the geometry of the coils. One of these rules can be the determination of the optimal distribution of the turns in the inductive coil, at which the coupling between them is stable, and the energy transfer efficiency is sufficient for power supply of the device.

Materials and Methods

One of the key problems in the use of inductive coupling for transcutaneous energy transfer is accounting for and compensating for the effect of coil bias on the system output characteristics [1]. Misalignments are usually divided into axial (d , change in the longitudinal distance between the coils), lateral (ρ , misalignments of the coils in a plane perpendicular to the axis of the receiving coil) and angular (φ , change in the angle between the axes of the coils). In this case, the greatest influence on the system characteristics is caused by lateral misalignments, since the magnitude of the axial and angular misalignments is to a considerable extent limited by the system geometry. Numerical simulation of the energy transmission system allows to investigate this problem with the aim of solving it. With the help performed calculations, it is possible to realize the energy transfer system with various geometrical parameters of the coil pair and their misalignments.

In the course of theoretical study, points of zero mutual inductance (M_{zero}) were located. In this case, both the axial misalignments and the geometric configurations of the coil couple were changed. Thus, using the numerical simulation, the graphs shown in figures 1, 3, 5 were obtained.

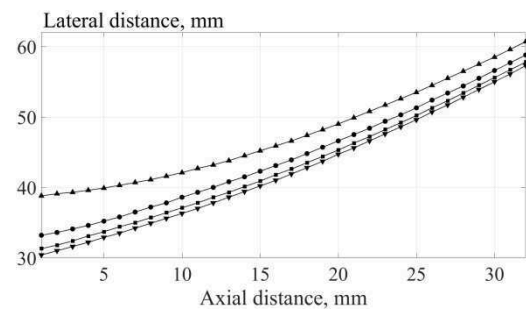


Figure 1: The ratio of axial to lateral misalignments for points of zero mutual inductance as a function of one- (▲), two- (•), three- (■) and four- (▼) coils. Fixed outer diameter 50 mm, internal diameter 50 ... 25 ... 16.6 ... 12.5 mm, winding pitch 0 ... 12.5 ... 8.3 ... 6.25 mm, the number of revolutions is 1 ... 2 ... 3 ... 4, respectively.

Figures 1 and 3 shows a graphs of the dependence of the axial misalignments of the lateral for the zero point of the mutual inductance. The calculation was performed for four symmetrical coil couple with a value of the number of turns from 1 to 4. The outer diameter (D_{out}) was fixed at a value of 50 mm (Fig. 1) or 100 mm (Fig. 3) for all four simulated coils. The pitch between turns was chosen in such a way that it was equal to $D_{out} / 2n$, where n is the number of turns.

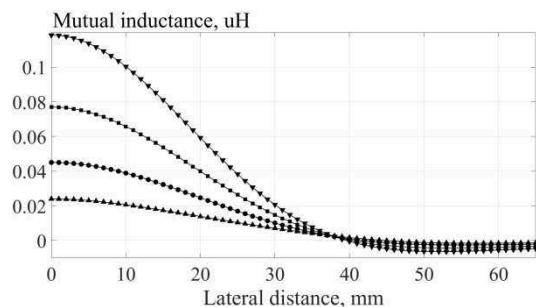


Figure 2: Mutual inductance versus lateral misalignments. Fixed outer diameter 50 mm, internal diameter 50 ... 25 ... 16.6 ... 12.5 mm, winding pitch 0 ... 12.5 ... 8.3 ... 6.25 mm, the number of turns 1 (▲) ... 2 (•) ... 3 (■) ... 4 (▼), respectively. Axial misalignments 15 mm.

In the course of another theoretical study, the mutual inductance was found to depend on lateral misalignments.

In this case, the point of maximum (M_{max}) (the lateral misalignments is zero) and the point of zero mutual inductance (M_{zero}) were analyzed. This analysis is presented in figures 2, 4 and 6.

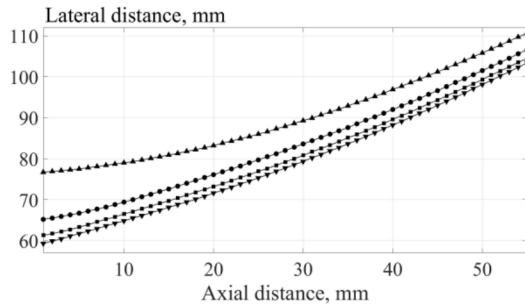


Figure 3: The ratio of axial to lateral misalignments for points of zero mutual inductance as a function of one- (▲), two- (●), three- (■) and four-turn (▼) coils. Fixed outer diameter 100 mm, internal diameter 100 ... 50 ... 33.3 ... 25 mm, winding pitch 0 ... 25 ... 16.6 ... 12.5 mm, the number of revolutions is 1 ... 2 ... 3 ... 4, respectively.

Figures 2 and 4 show the graphs of the mutual inductance versus the lateral misalignments of a symmetrical coil couple. The calculation was carried out for four symmetrical coils with a speed of 1 to 4. The outer diameter (D_{out}) was fixed at a value of 50 mm (Fig. 2) or 100 mm (Fig. 4) for all four simulated coils. The pitch between the turns was chosen in such a way that it was equal to $D_{out} / 2n$, where n is the number of turns. The axial misalignments was selected taking into account the average skin thickness between the inductance coils in the energy transfer system, which is 15 mm.

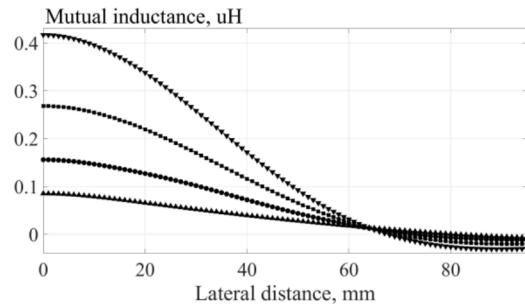


Figure 4: Mutual inductance versus lateral misalignments. Fixed outer diameter 100 mm, internal diameter 100 ... 50 ... 33.3 ... 25 mm, winding pitch 0 ... 25 ... 16.6 ... 12.5 mm, the number of turns 1 (▲) ... 2 (●) ... 3 (■) ... 4 (▼), respectively. Axial misalignments 15 mm.

The last study was the numerical simulation of four coil couples with a fixed outer diameter of 50 mm, and the number of turns 2. The value of the internal diameter varies from 30 to 15 mm (30 ... 25 ... 20 ... 15 mm), the pitch between the turns, respectively changed from 2.5 mm (10 ... 12.5 ... 15 ... 17.5 mm). The graphs obtained from the calculations are shown in figures 5 (the ratio of the zero point of the mutual inductance to the axial misalignments)

and 6 (the ratio of the mutual inductance to the lateral misalignments).

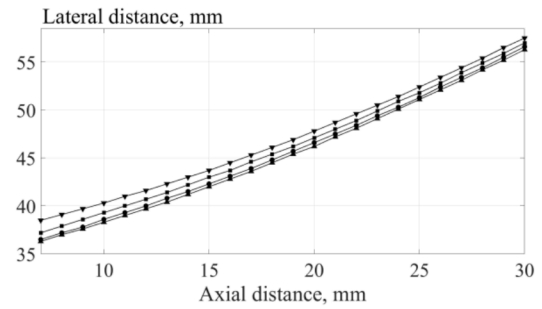


Figure 5: The ratio of axial to lateral misalignments for points of zero mutual inductance. Fixed outer diameter 50 mm, internal diameter 30(▲) ... 25(●) ... 20 (■) ... 15(▼) mm, winding pitch 10 ... 12.5 ... 15 ... 17.5 mm and fixed the number of turns 2.

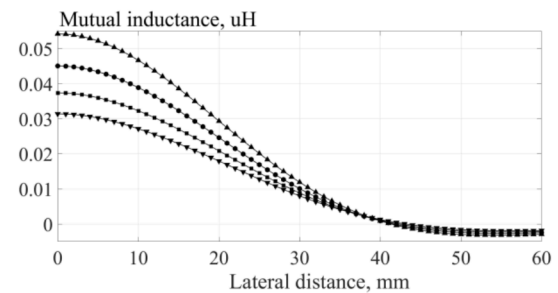


Figure 6: Mutual inductance versus lateral misalignments. Fixed outer diameter 50 mm, internal diameter 30(▲) ... 25(●) ... 20 (■) ... 15(▼) mm, winding pitch 10 ... 12.5 ... 15 ... 17.5 mm and fixed the number of turns 2. Axial misalignments 15 mm.

Results

The main characteristics of a couple coil, which can change when using the design algorithm, include the outer and inner diameters, as well as the winding pitch / number of turns. According to the graph shown in figure 2, it is seen that as the value of n increases in the coil, the zero point of the mutual inductance shifts to the left closer to zero ρ . So the lateral misalignment at M_{zero} for a one-turn coil is 44.6 mm, and for a four-turn this value drops to 39.6 mm, with a fixed D_{out} of 50 mm. Thus, the zero point shift was changed by 11% from the value for a one-turn coil. It follows that the coil with a smaller number of turns has a greater stability, in terms of loss of coupling. As shown in figure 1, this decrease with increasing n is exponential.

A similar exponential dependence (Fig. 3) is observed with an increase in D_{out} up to 100 mm. The lateral misalignment at M_{zero} increases in 1.65 ... 1.8 times, in comparison with coils, whose outer diameter is 50 mm. Figure 4 shows that ρ at a zero point of the mutual inductance for a one-turn coil is 80.1 mm, and for a four-turn coil this value drops to 65.5 mm, with a fixed D_{out} of 100 mm. Thus, the M_{zero} shift has changed by 18% from the value

for a one-turn coil. The axial misalignments of 15 mm for the numerical simulation of the graphs presented in figures 2 and 4 was chosen as the average value of the thickness of the skin layer between the coils in the energy transfer system.

It should be noted that the curves for lateral misalignments at the zero point of mutual inductance have a stable linear character after $d \approx D_{out} / 2.5$ (Fig. 1, 3).

The drop M_{max} with decreasing n from 4 to 1 occurred from value 0.4165 to 0.0848 (Fig. 4), at D_{out} 100 mm. With D_{out} 50 mm, the drop M_{max} with decreasing n from 4 to 1 occurred from value 0.1184 to 0.0240 (Fig. 2). In both cases, the maximum value of the mutual inductance decreased by approximately 80%. In this case, M_{max} ($D_{out} = 100$ mm) on 71% or 3.5 times larger than M_{max} ($D_{out} = 50$ mm). This difference is explained by the length of the wire needed to fill two coils with the same number of turns, but differing D_{out} . Because of the difference in the length of the wire, the self-inductance of the coil with a large D_{out} is obtained more, and, consequently, the mutual inductance will increase. This drop in M_{max} with decreasing D_{out} can be reduced by increasing the number of turns close to the outer edge.

Adjustment of the M_{max} and M_{zero} values can be performed by changing the pitch between turns. However, the smaller the pitch the more difficult it is to adjust the values due to the exponential fall (Fig. 5).

As shown in figure 6, the location of the turns closer to the outer edge of the coil allows to increase M_{max} . The increase in the value of M_{max} is 42% (from 0.0542 to 0.0314), the diameter of the inner turn of 30 mm and 15 mm, respectively, with a fixed D_{out} of 50 mm and the number of turns 2. However, in this case, the location of the turns, a large increase in M_{max} leads to a slight decrease in ρ at M_{zero} by 4% (from 43.1 mm to 41.3 mm).

Discussion

Increased number of turns lead to reducing the stability of energy transfer (Fig. 2, 4). Moreover, such a decrease in M_{zero} to zero value of lateral displacement occurs according to the exponential dependence even with an increase in the outer diameter of the coil (Fig. 1, 3). It is assumed that in order to achieve greater stability of energy transfer, it is necessary to reduce the number of turns in the coil.

For coils with the same number of turns D_{out} and M_{max} are positively associated (Fig. 4): drops in D_{out} lead to drops in M_{max} . This is due to the difference in the length of the wire, and, consequently, of the intrinsic inductance, which affects M_{max} . It is possible to reduce the drop of the M_{max} by increasing the length of the wire in the coil (Fig. 5, 6). This is achieved by increasing the winding density of the wire from the inner to the outer edge of the coil while the original number of turns keeps constant.

Conclusions

With the help performed calculations, various configurations of coils were analyzed to determine their optimal

geometry. It was found that increasing the number of turns in the symmetrical coils leads to the shift of the zero point of mutual inductance is to the zero value of lateral misalignment. Such a shift occurs on an exponential curve and with an increase in the outer diameter of the coil an exponential shift of the zero point is also observed, however it has large lateral misalignment values.

The difference in the values of the maximum mutual inductances with a fixed number of turns, but with a different external diameter, results from the length of the wire necessary to fill two coils with the same number of turns.

It should be noted that the curves for lateral misalignments at the zero point of mutual inductance have a stable linear character after $d \approx D_{out} / 2.5$.

Adjustment of the M_{max} and M_{zero} values can be performed by changing the pitch between turns. However, the smaller the pitch the more difficult it is to adjust the values due to the exponential fall.

References

- [1] Agarwal K., Jegadeesan R., Guo Y.-X., Thakor N. Wireless Power Transfer Strategies for Implantable Bioelectronics: Methodological Review // IEEE Reviews in Biomedical Engineering, 2017. Vol.10. PP. 1-28.
- [2] Danilov A.A., Itkin G.P., Selishchev S.V. Progress in methods for transcutaneous wireless energy supply to implanted ventricular assist devices // Biomedical Engineering. 2010. Vol. 44. № 4. PP. 125-129.
- [3] Zeng F.-G., Rebscher S., Harrison W., Sun X., Feng H. Cochlear implants: system design, integration, and evaluation // IEEE Reviews in Biomedical Engineering. 2008. Vol. 1. PP. 115-142.
- [4] Clark G. Cochlear implants: Fundamentals and applications // Springer. 2003. 831 p.
- [5] North R. Neural interface devices: spinal cord stimulation technology // Proceedings of the IEEE. 2008. Vol. 96. PP. 1108-1119.
- [6] Eldridge P., Simpson B.A., Gilbert J. The Role of Rechargeable Systems in Neuromodulation // European Neurological Review. 2011. Vol. 6. № 3. PP. 187-192.
- [7] Pelletier B., Spiliopoulos S., Finocchiaro T., Graef F. et al. System overview of the fully implantable destination therapy—ReinHeart-total artificial heart // European Journal of Cardio-Thoracic Surgery. 2015. Vol. 47. № 1. PP. 80-86.
- [8] Weiland J.D., Humayun M.S. Visual Prosthesis // Proceedings of the IEEE. 2008. Vol. 96. № 7. PP. 1076-1084.
- [9] Li X., Yang Y., Gao Y. Visual prosthesis wireless energy transfer system optimal modeling // Biomedical Engineering Online. 2014. Vol. 13. № 3. PP. 1-11.
- [10] Burny F., Donkerwolcke M., Moulart F. et al. Concept, design and fabrication of smart orthopedic implants // Medical Engineering & Physics. 2000. Vol. 22. PP. 469-469.
- [11] Cheng, Yuhua, Gaofeng Wang, and Maysam Ghovanloo. Analytical modeling and optimization of small solenoid coils for millimeter-sized biomedical implants // IEEE Transactions on Microwave Theory and Techniques. 2017. Vol. 65. № 3. PP. 1024-1035.
- [12] Danilov A., Mindubaev E., Selishchev S. Space-frequency approach to design of displacement tolerant transcutaneous energy transfer system // Progress In Electromagnetics Research M. 2015. Vol. 44. PP. 91-100.
- [13] Danilov A.A., Mindubaev E.A., Selishchev S.V. Methods for Compensation of Coil Misalignment in Systems for In-

ductive Transcutaneous Power Transfer to Implanted Medical Devices // Biomedical Engineering, 2017. Vol. 51, Is. 1. PP. 56-60.

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Artificial Muscles with the Possibility of Application in Medical Practice

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Introduction

Movement reproduction and control in medical practice is an important technological and engineering task. Recently, the development of artificial muscles (AMs), which are in demand in many fields of medicine, has been in focus of medical professionals and engineers. The research in this direction include concerns creating artificial heart muscle patches and sphincter cuffs for different body parts (urethra, anal canal, and lower esophagus). The AMs are widely used as executive mechanisms (actuators) in prostheses, exoskeletons, implanted drug delivery tools, etc. Medical engineers face the problem of designing light, biocompatible, and reliable AMs, which would be safe for humans and characterized by the low power consumption and acceptable operating temperature. In view of the aforesaid, the properties of various materials, including polymers and nanocomposites, promising for fabricating AMs have been studied. One of the fundamental properties of such materials is their high biocompatibility. It is proposed to use mainly electroactive polymers and nanocomposites containing carbon nanotubes (CNTs). The latter deserve much attention, since they are characterized by the combination of the high strength, flexibility, elasticity, and electrical conductivity.

Here, we made a brief literature review of the current state of research and development in the field of AM drives and prototypes and discuss prospects of their application in medical practice.

Artificial Muscles

A. Pneumatic artificial muscles

The McKibben mechanical drive operates by pumping a fluid or gas under pressure into a chamber bounded by a rigid braid [1]. A new-type McKibben muscle uses paraffin as an expandable material, which is heated to a temperature of 95°C. This type of muscles has certain advantages over the liquid type, but is not compact, hard to control, has a high operating temperature, and, thus, inapplicable in medicine.

A pneumatic artificial muscle (PAM) drive offers great potential for prosthetics, since it is characterized by the high power density ($P_m \geq 4$ kW/kg) and exhibit other properties of natural human muscles [2]. A PAM prosthesis provides a torque sufficient for the knee joint in performing the high-energy human motor functions (fast

walking, climbing stairs, etc.) and imitating normal gait parameters [3].

The trigger mechanism for a hydraulic artificial muscle (HAM) is similar to that of a PAM, but the HAM has several advantages, e.g., ductility, low weight, easy maintenance, and low cost [4]. The PAMs and HAMs are designed as drives for robotics and various engineering products. Sometimes, they can be used for external strengthening of human limb movement, but are not intended for invasive use as artificial human muscles.

B. Electroactive polymers

Electroactive polymers (EAPs) have some characteristics similar to those of natural muscles. In particular, they are driven by electric pulses [5]. Usually, the EAP materials are divided into two main groups: electronic (activated by the electrostatic field) and ionic (activated by ion transport). The group-I EAPs are high-voltage (≥ 1 kV), develop a low power ($P_m \leq 0.1$ kW/kg), and exhibit the high efficiency ($CE \geq 90\%$). The group-II EAPs are considered to be low-voltage (≤ 5 V) and have high power and low efficiency ($CE \leq 20\%$).

Obviously, the group-I EAP materials are inapplicable for use in artificial muscles (prosthesis and implants) because of the high-voltage breakdown danger. The EAPs contained in ionic polymer composites and metals are promising for creating various medical products, including electroactive AMs, distributed biomimetic nanoactuators, nanoconverters, nanorobots, and nanosensors. They are characterized by the combination of high load force and low electric voltage (1–3 V) [6]. Ion EAPs is, in fact, functional materials for the development of AMs. Their low-voltage power supply ensures the high safety; the polymer surface electrodes made of noble metals (Au, Pd, Pt, etc.) provide the acceptable biocompatibility and make these materials suitable for use in invasive medical implants. For example, the ionic EAP-based AM is designed to fabricate artificial sphincters of the lower esophagus, anal canal, urinary canal urethra, and heart muscle patches [7]. The EAPs based on the elastic ionic polymers and electrodes are immersed in an electrolyte and all parts are encapsulated in an elastic hermetic. Such a system represents an AM prototype and, depending on its characteristics (mechanical, power, and others), can be used in medical practice [8]. However, this direction is still at the stage of intense research and a practical AM prototype for medical applications has not been fabricated yet.

C. Other artificial muscle materials

The most accessible and simplest is a drive in which nylon and polyethylene fibers woven in a certain way (in spiral springs) contract in length and expand in diameter upon heating. Such drives are controlled using the Joule heat induced by the current transmitted through a conductive coating on the filament surface. The attained drive parameters are a volume energy density of 840 kJ/m^3 , an energy density per unit mass of $E_m \sim 530 \text{ J/kg}$, and a power per unit mass of $P_m \sim 1.0 \text{ kW/kg}$ [9]. These values are at a level of the human heart muscle parameters, i.e., $P_m \sim 0.33 \text{ kW/kg}$. The inexpensive AMs are fabricated from highly oriented nylon threads [10, 11]. A twisted nylon bundle can lift a load exceeding tenfold the load lifted by a human muscle of the same length. An artificial finger has been demonstrated. However, drives of this type are not suitable for use in AMs for invasive prosthetics in a human body because of their strong overheating. The high performances are typical of niobium nanofibers; specifically, their conductivity is $\sim 3 \cdot 10^6 \text{ S/m}$, the tensile strength is up to $\sim 1 \text{ GPa}$, and the Young's modulus is 20 GPa .

The twisted nanofiber yarn impregnated with a paraffin wax is strained upon heating and can work as a drive [12]. During the transmission of electric current, the wax melts, expands, and unwinds; the yarn drive does a torsion work. Numerous actuators based on heating and cooling of intermetallic materials employ the shape memory effect. They develop the high powers ($P_m \sim 4 \text{ kW/kg}$) and are widely used in robotics [13]. However, despite the very high specific powers developed by the shape memory alloys, their elastic strain limit is 4% [14], while the value for the human muscle tissue is about 20% .

The available AM prototypes cannot simultaneously perform complex deformations (bending, contraction, extension, etc.) attributable to natural muscles. Recently, it has been established that a single-layered lattice microstructure of onion epidermal cells in applied electric voltages of $50\text{--}1000 \text{ V}$ can simultaneously participate in complex deformations [15, 23]. Currently, this research direction is at the initial stage and its future prospects are still obscure.

D. Carbon nanotube-based artificial muscles

The unique mechanical and electrical properties of CNTs make them excellent candidates for application in AMs for medicine.

The CNT airgel, sometimes referred to as frozen smoke is an ultralow-density solid material [16]. Nanotubes in the airgel layers are arranged parallel and form a sort of framing. In high voltages ($1\text{--}5 \text{ kV}$), the layers are expanded at a straining rate of $3.7 \cdot 10^4 \text{ \% / s}$, which exceeds many times the known values. The advantages of this material are an energy density per unit mass of $E_m \sim 30 \text{ J/kg}$ and an attainable strain stress reduced to the material density of $\sim 15 \text{ kPa} \cdot \text{m}^3/\text{kg}$. In addition, they have a very wide operating temperature range ($80\text{--}1900 \text{ K}$) and can develop a force that exceeds that developed by natural muscles with the same cross section by a factor of 30 . Undoubtedly, the main mechanical, energy, and temperature parameters

of the investigated CNT layers are acceptable for creating AMs, but, to use them in practice, it is necessary to solve the problems concerning the high power-supply voltage, encapsulation, and insufficient safety level and biocompatibility.

The biological polymer chitosan (nanocomposite) films saturated with single-walled CNTs (SWCNTs) exhibit a strain of $\leq 5 \text{ V}$ under the action of a voltage pulse [17]. The electrothermal generation of mechanical movements, simplicity of controlling, and biocompatibility make these nanomaterials promising for application in AMs. The complication of a nanomaterial composition aimed at increasing its specific conductivity will help significantly reduce an existing SWCNT concentration of $25 \text{ wt.}\%$ and, consequently, further enhance the safety and biocompatibility of the proposed AMs. Test drives from multi-walled CNTs (MWCNTs) and niobium nanowires were fabricated [18]. The muscular structure matrix used is made of a heat-sensitive paraffin wax. As metal fillers, tungsten or NiTi alloy nanowires are used, which induce the Joule heating of the matrix. The proposed drives have the higher mechanical characteristics as compared with nylon filament-based actuators, but their drawback is the high operating temperature.

A nanocomposite consisting of a nanogel, which contains boric acid, hyaluronic acid, and MWCNT nanowire strands, was used for creating a drive [19]. A MWCNT strand immersed in the nanogel swells and execute a torsion motion due to the internal anion charge variation. Such a drive can be used for implementing torsion movements, is sensitive to glucose, and has the high potential for application in AMs. In addition, such an AM can work as a glucose sensor (in the range of $(55\text{--}100) \cdot 10^{-3} \text{ M}$), which automatically releases the medication when needed.

In a liquid electrolyte, the twisted CNT strands can generate rotational motion and length shortening. Owing to these properties, the novel materials are capable of lifting loads that are heavier than those lifted by a human skeletal muscle of the same size by a factor of 25 [20–22]. To control their operation, low voltages ($\leq 5 \text{ V}$) can be used. With these materials, a rotational speed of 590 rpm and a maximum reversible rotation angle of 15000° were attained. The high developed power, fast response, and low supply voltage are positive indicators for creating AMs; however, it remains difficult to convert the rotational motion into other motion forms.

In an electrolyte consisting of KOH in a concentration of 1 M , the SWCNTs coated with platinum nanoparticles ensure a desired deformation in low applied electrical voltages ($\leq 1.5 \text{ V}$) and currents ($\leq 0.08 \text{ A}$) [23]. The proposed principle of generating the mechanical deformation due to the charge redistribution in the electrolyte is promising for the development of AMs, including those for medical applications.

A new-type AM with artificial absorption of a solvent is highly efficient without changing the temperature [24]. Such AMs are driven by rubber swelling in a nonpolar solvent. The calculated CE value is $\sim 16\%$, which is similar to an CE value of $\sim 20\%$ of the human muscle tissue [25].

Polyhydroxylated fullerene added to the sulfonated polyetherimide matrix increases the ionic conductivity

and this effect can be further enhanced by coating nanotubes with platinum particles [26]. The obtained energy of $E_m \leq 10$ J/kg is lower than the energy $E_m \sim 40$ J/kg generated by a human skeletal muscle [25]. The developed power ($P_m \sim 0.1$ kW/kg) is also lower than a value of $P_m \sim 0.3$ kW/kg of the human heart muscle tissue.

The operational principles of AMs discussed in reviewed works [18–23, 26] are common and analogous to those of natural muscles. These are the redistribution of ions under the action of current pulses in an electrolyte, straining a CNT filament, and plate motion. Therefore, these research directions are promising for creating AMs for use in medicine.

Conclusions

The analysis of available literary data allowed us to draw the following conclusions:

- Artificial muscles operating on the basis of the flow dynamics laws (pneumatics and hydraulics [1–4]) can develop extremely high specific powers ($P_m \geq 4$ kW/kg) and are suitable for robotics and external prosthetics of human limbs. However, it is hard to use them as invasive implants because of their unacceptable energy supply and insufficient biocompatibility.
- The AMs made of electroactive ionic polymers ([1–8]) are characterized by a power of $P_m \sim 1.0$ kW/kg, an energy of $E_m \sim 530$ J/kg, and an efficiency of $CE \leq 20\%$, which are analogous to the human muscle tissue parameters ($P_m \sim 0.33$ kW/kg, $E_m \sim 39$ J/kg, and $CE \sim 20\%$). However, the structural components used (electrolytes, polymers, electrodes, etc.), high cost, and limited durability of the available AM prototypes do not meet the medical requirements.
- The actuators based on the laws of conversion of the electrical energy into mechanical one (nylon and polyethylene fibers [10,11], niobium nanofibres [12], and shape memory materials [13]) have operating temperatures of $\geq 60^\circ\text{C}$ and, certainly, cannot be used in invasive medical implants.
- Carbon nanotubes and their layers immersed in an electrolyte deform in the course of the chemical reaction and generate mechanical movement [18–23, 25], analogously to mammal muscles. To date, the test parameters of an AM artificial muscle prototype are inferior to the natural muscles.

Thus, the intense research and development directed to improving the characteristics of drives based on ionic electroactive polymers and composite nanomaterials containing carbon nanotubes will make it possible to create invasive muscles for medical purposes. Solving the existing problems in this way is claimed by the modern state of medicine and, especially, the need for treating the heart diseases. Now, heart failure is a cause of about 10 million people die around the world and the creation of an artificial muscle as an auxiliary part instead of a damaged heart site will save numerous lives.

References

- [1] D. Sangian, S. Naficy, and G. Spinks. Thermally activated paraffin-filled McKibben muscles. *Journal of Intelligent Material Systems and Structures*, 27(18): 2508–2516, 2016.
- [2] G. Waycaster, S. Wu, X. Shen. A pneumatic artificial muscle actuated above-knee prosthesis. *Dynamic Systems and Control Conference*, 1: 12–15, 2010.
- [3] Y. Park, B. Chen, D. Young. Bio-inspired active soft orthotic device for ankle foot pathologies. *International Conference on Intelligent Robots and Systems*, 2011.
- [4] R. Tiwari, M. Meller, K. Wajcs, C. Moses, I. Reveles, E. Garcia. Hydraulic artificial muscles. *Journal of Intelligent Material Systems and Structures*, 23(3): 301–312, 2012.
- [5] F. Carpi, R. Kornbluh, P. Sommer-Larsen and G. Alici. Electroactive polymer actuators as artificial muscles: are they ready for bioinspired applications? *Bioinspiration & Biomimetics*, 6: 045006 (10 pp), 2011.
- [6] V. Palmre, D. Pugal, K. Kim, K. Leang, K. Asaka, A. Aabloo. Nanothorn electrodes for ionic polymer-metal composite artificial muscles. *Scientific Reports*, 4: 6176 (10 pp), 2014.
- [7] M.S. Banik. Electroactive polymer based artificial sphincters and artificial muscle patches. Patent US #7128707.
- [8] L. Rasmussen. Electrically driven mechanochemical actuators that can act as artificial muscle. Patent US #7935743.
- [9] S. Mirvakili, A. Ravandi, I. Hunter, C. Haines, and et al. Simple and strong: Twisted silver painted nylon artificial muscle actuated by Joule heating. *Electroactive Polymer Actuators and Devices*, 9056: 905601–10, 2014.
- [10] S. Mirvakili, I. Hunter. Multidirectional Artificial Muscles from Nylon. *Advanced Materials*, 201604734 (7 pp), 2016.
- [11] S. Aziz, S. Naficy, J. Foroughi, H. Brown, G. Spinks. Characterisation of torsional actuation in highly twisted yarns and fibres. *Polymer Testing*, 46: 88–97, 2015.
- [12] S. Mirvakili, A. Pazukha, W. Sikkema, C. Sinclair, and et al. Niobium Nanowire Yarns and their Application as Artificial Muscles. *Advanced Functional Materials*, 23(35): 4311–4316, 2013.
- [13] A.P. Kamantsev, A.M. Zhikharev, V.V. Kolodov, E.V. Morozov, S.V. Von Gratovsky, R.A. Antonov, V.G. Shavrov, A.V. Shelyakov. Actuator based on functional material. Patent RU #2539605.
- [14] A. Villanueva, C. Smith, S. Priya. Shape memory alloy (sma) actuators and devices including bio-inspired shape memory alloy composite (bismac) actuators. Patent US 20120174571.
- [15] C. Chen, W. Shih, P. Chang, H. Lai, and et al. Onion artificial muscles. *Applied Physics Letters*, 106: 183702 (5 pp), 2015.
- [16] A. Aliev, J. Oh, M. Kozlov, A. Kuznetsov, and et al. Giant-Stroke, Superelastic Carbon Nanotube Aerogel Muscles. *Science*, 323(5921): 1575–1578, 2009.
- [17] Y. Hu, W. Chen, L. Lu, J. Liu, C. Chang. Electromechanical Actuation with Controllable Motion Based on a Single-Walled Carbon Nanotube and Natural Biopolymer Composite. *ACS Nano*, 4(6): 3498–3502, 2010.
- [18] S. Mirvakili, I. Hunter. Fast Torsional Artificial Muscles from NiTi Twisted Yarns. *Appl. Mater. Interfaces*, 9(19): 16321–16326, 2017.
- [20] J. Lee, S. Ko, C. Kwon, M. Lima, R. Baughman, S. Kim. Carbon Nanotube Yarn-Based Glucose Sensing Artificial Muscle. *Small*, 12(15): 2085–2091, 2016.
- [21] J.A. Lee, Y.T. Kim, G.M. Spinks, D. Suh, X. Lepró, M.D. Lima, R.H. Baughman, S.J. Kim. All solid state carbon

- nanotube torsional and tensile artificial muscles. *Nano Lett.*, 14: 2664–2669, 2014.
- [22] J. Lee, Y. Kim, G. Spinks, D. Suh, and et al. All-solid-state carbon nanotube torsional and tensile artificial muscles. *Nano Letter*, 14(5): vol. 14, no. 5, 2664–2669, 2014.
- [23] S. Lu, B. Panchapakesan. Hybrid platinum/single-wall carbon nanotube nanowire actuators: metallic artificial muscles. *Nanotechnology*, 17(3): 888–894, 2006.
- [23] M. Lima, M. Hussain , G. Spinks , S. Nafi, and et al. Efficient, Absorption-Powered Artificial Muscles Based on Carbon Nanotube Hybrid Yarns. *Small*, 11(26): 3113–3118, 2015.
- [24] R.K. Josephson. Contraction Dynamics and Power Output of Skeletal Muscle. *Annual Review of Physiology*, 55: 527–546, 1993.
- [25] J. Helmer, K. Hughes. Artificial muscle. Patent US # 3882551.
- [26] J. Foroughi, G. Spinks1, G. Wallace, J. Oh, and et al. Torsional Carbon Nanotube Artificial Muscles. *Science*, 334(6055): 494–497, 2011.

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Apnea Detection in a Contactless Multisensor System using Deep Learning Algorithm

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Introduction

Obstructive sleep apnea (OSA) is an ordinary breathing disorder, causing a temporary blockage of the upper airway during sleep. It usually stops breathing for 10 seconds or longer and the apnea episodes may regularly happen from 5 to 100 times an hour. The severity criteria can be assessed by Apnea-Hypopnea Index (AHI) or Respiratory Disturbance Index (RDI) in three main categories: mild (5-15 events an hour), moderate (15-30 events an hour), and severe (more than 30 events an hour) [1]. The signs include loud snoring, restless sleep, or daytime sleepiness. If it remains untreated, OSA can lead to many possible serious health complications, such as depression, mood disorders, and heart disease. It can also bring about drowsiness with the uprising risk of accidents while driving and working.

In this work, a prototype of contactless multisensor chair was set up in order to detect vital parameters and a deep learning algorithm based on a hybrid model of convolutional neural network (CNN) and recurrent neural network (RNN) was applied for the detection of apnea in a sitting position, simulated scenarios such as in a pilot seat, in a seat of truck driver or in any types of passenger seat, where a big data can be collected during a flight or a journey, processed in real-time for prewarning or alarms, and transmitted to a cloud storage at a medical center. The main objective of this work is to set up a new software architecture for data acquisition and vital parameter extraction and to demonstrate the integration of deep learning algorithm for the detection of apnea.

To realise this system for the digital lifestyle, a modified λ architecture is proposed with a compromise between real-time processing and restricted computational resources. This software structure offers the benefits not only to a real-time stream processing but also a batch or a large volume of collected data processing. Typically, this approach tries to balance throughput, fault-tolerance, and latency (or time interval) in batch processing.

This contribution is organized as follows. In the section of “Materials and Methods”, it begins with a hardware configuration for data acquisition based on multiple devices for the monitoring of heart and lung activities. It also provides a software architecture using λ architecture as well as a deep learning algorithm. The results of our experiments

are then given in a subsequent section, namely “Results”, followed by a section of “Discussion”. The article ends in the last section with the conclusions and future works.

Materials and Methods

Hardware Configuration

A hardware system consists of a number of unique contactless sensors mainly produced in the Chair of Medical Information Technology (MedIT), including a magnetic induction (MI) sensor for the monitoring of breathing [2], a cECG system for the monitoring of heart activity [3], a smart photoplethysmography (PPG) [4], ballistocardiography (BCG) [5], and a thermal camera (Seek Thermal Compact) with a micro-USB connector. The additional analog/digital (A/D) converter was set up by using NI USB-6259 as an interface for cECG and BCG measurements with a sampling frequency of 1,000 Hz. All devices are then connected to a FUJITSU desktop computer (Intel® Core™ i5-3470 CPU @3.20 GHz, 4 cores with 14 GB random access memory (RAM)).

Data Flow with System Interface

All signals are acquired through different communication ports and socket. Signal processing and feature extraction were carried out in all channels and passed directly to Kafka producer. The producer consists of a pool of buffer space, which can hold records that have not been transmitted to the server. Apache Kafka is able to handle these big data with very low time interval or latency with a range in milliseconds. The data flow of system interface is shown in Figure 1.

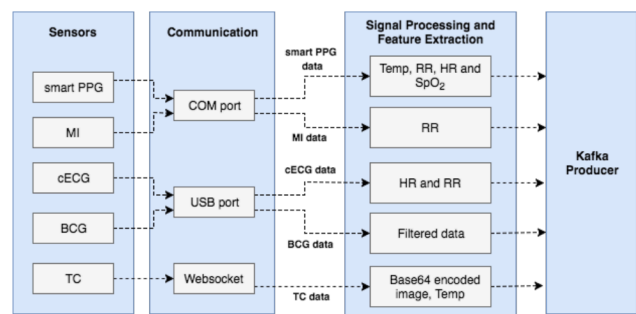


Figure 1: Data flow with system interface in a contactless multisensor system [6].

However, in this article, we mainly focus on the signal acquired from a MI sensor, where respiratory rate (RR) is extracted and the preprocessed signals are used for the detection of apnea.

Software Architecture

To process and analyse big data, the state-of-the-art λ architecture [7] is proposed as demonstrated in Figure 2. The software is programmed by Java programming language for data acquisition. With the proposed architecture, Apache Kafka and Apache Spark worked underground to manage the data in two main layers, namely speed layer and batch layer. The speed layer supports stream processing where fast data is being processed in real-time. While batch layer handles all stored records for batch or large collection processing. The deep learning model can use both data from speed layer and batch layer for apnea detection. With limited computational resources, the full functionality of deep learning algorithm in the batch layer had not been implemented in this work. The visualisation of real-time data and apnea detection was set up using Kibana with the aid of AngularJS, which integrated into a serving layer. In our configuration, Elasticsearch was used as a search engine or a master database in this work.

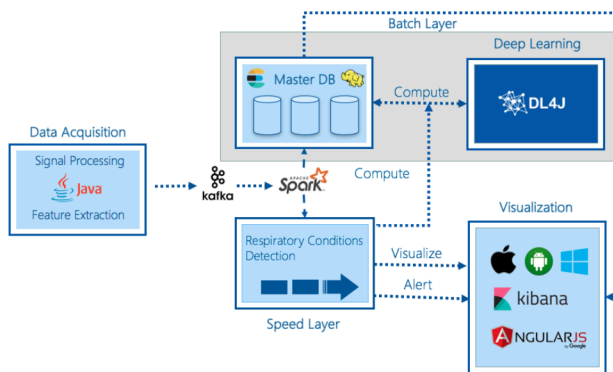


Figure 2: λ architecture for apnea detection using a deep learning algorithm [6].

Deep Learning Model for Apnea Detection

In this work, two different structures of deep learning models have been implemented, namely convolutional neural network (CNN) [8] and a hybrid model of CNN and long short-term memory (LSTM). This was implemented under a Java-based framework using Deeplearning4j, which is a deep learning library for integration, vectorisation, modeling, and evaluation. Since the performance of the hybrid model is significantly better than the proposed CNN model, only the hybrid deep learning model is presented in this article. LSTM can be classified as a recurrent neural network (RNN) [9]. It offers a feedback structure of neural network whilst CNN provides a feedforward neural network. LSTM is explicitly designed to prevent the long-term dependency problem. However, it might have a

convergence issue during model training. The designed hybrid deep learning model with 9 layers is given in Figure 3. It contains 3 CNN layers, 3 max subpooling layers, 1 dense layer, 1 LSTM layer and 1 last RNN output layer.

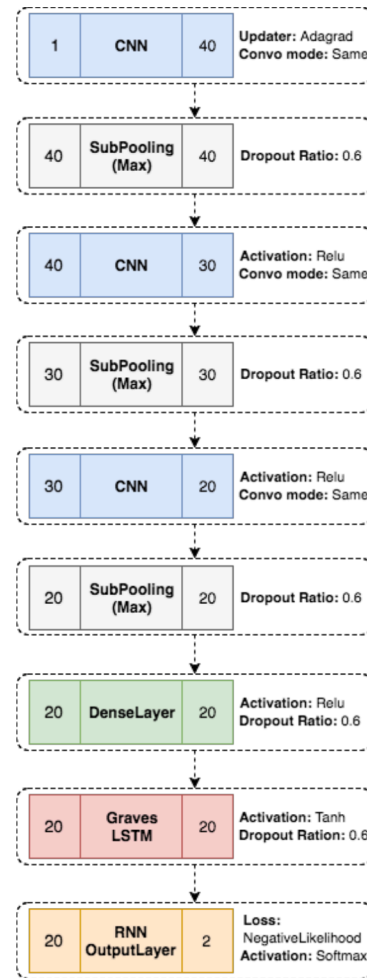


Figure 3: Deep learning model based on the multi-layer hybrid architecture [6].

The MI input signals were divided into chunks of 2,000 points or 20 seconds. The classification was carried out in order to detect normal breathing or apnea from a machine perspective. In this particular system, Xavier weight initialisation method was defined with adaptive gradient algorithm [10] as an update strategy, negative log likelihood as a loss function, softmax activation function in the final RNN output layer with 0.01 learning rate.

The apnea data were collected mainly by a MI sensor from five healthy male subjects at the rest position and they were requested to mimic central apnea by holding their breathing for short periods irregularly. These generated the database of breathing patterns over seven hours. The starting and stopping periods of mimic apnea were labels as used as a supervised learning. 70% of the dataset (976 records) were used for training the deep learning model for detection of

apnea based on the MI sensor and 30% of the dataset (416 records) were applied for validation purpose.

Results

Data Acquisition

The primary signals were acquired from three main sensors i.e. photoplethysmography (PPG) sensor, magnetic induction (MI) sensor, and cECG system. All of these signals can be used for the extraction of respiratory signals [11], [12], [13]. The original signals were acquired and given in Figure 4. These signals can be preprocessed using appropriate filters or techniques for feature extraction. In this work, only a second-order Butterworth bandpass filter was applied to the processing of MI signals. The passband was designed in the range between 0.1 Hz and 1 Hz, corresponding to the breathing frequency of 6 bpm to 60 bpm.

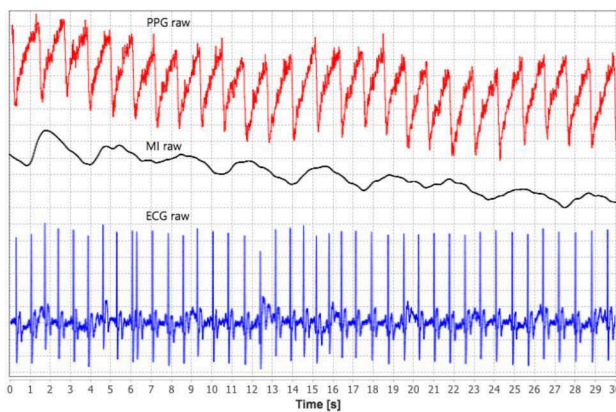


Figure 4: A sample set of primary sensors acquired from MI, cECG, and PPG sensors for 30 s [6].

In this work, a peak detection algorithm was performed in order to estimate the respiratory rate (RR) based on a moving window of 10 s [14]. The estimation of RR was mainly for data representation and this feature was not used for training the hybrid deep learning model.

Training Performance of the Deep Learning Model

The overall 1,392 breathing records were applied for the evaluation of the proposed hybrid deep learning model. Each record contained the breathing data of 20 s. 70% of the dataset was used for training the CNNs and RNNs. The training was performed to update the model parameters, resulting in one cycle or an epoch. The repetitive training was activated one after another to update the new model parameters in order to achieve higher accuracy with no overfitting. In this particular work, the training was carried out for 34 epochs with the highest accuracy of 92% and the performance of the model is shown in Figure 5. The rest 30% of the dataset was utilized for validation purpose and its highest accuracy in the validation dataset was 90% at the 34th epoch. These two datasets were selected randomly.

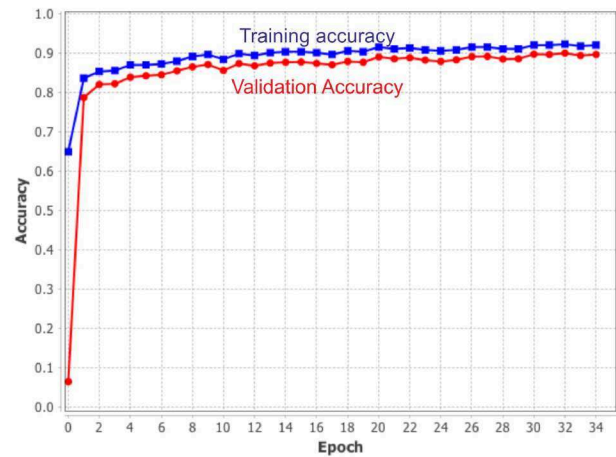


Figure 5: Training performance of the model [6].

Visualisation of Apnea Detection

The data from the speed layer were stored in a database, handled by Elasticsearch. For visualisation of streaming data, Kibana dashboard was designed for real-time visualisation of all acquired signals and AngularJS was used as a platform for building web applications. In Figure 6, the upper curve showed the original MI signal for 60 s, which contained mimic apnea and the respiratory rate of 12 bpm was shown at the top right corner, which was computed based on the peak detection algorithm during feature extraction.



Figure 6: Visualisation of magnetic induction (MI) signal based on Kibana visualisation plugin for Elasticsearch and AngularJS platform [6].

The middle curve in Figure 6 represented a filtered MI signal based on the designed second-order Butterworth filter. The red part is highlighted using Java programming for the detection of apnea episode in real-time processing. Therefore, the system can effectively recognise the mimic apnea and it should be able to detect apnea in various scenarios for

real-time warning and for investigation of historical records in batch processing.

Discussion

Due to the fact that typical respiratory rate for a healthy adult at rest is approximately 12-18 bpm, one breathing cycle thereby takes 3.3-5 s. Since a fixed 20-s window was implemented for the evaluation of apnea episode, 4-6 breaths are contributed to this timeframe. The detection of apnea based on this window size can be activated when the state of stopping breath minimally takes longer than 10 s. In other words, this system can detect apnea whenever there was no breathing cycle for 2-3 breaths. The adjustment of window size may be made for the notification of an apnea episode, however, the proposed window size was reasonable for the implementation of apnea detection.

Because there was no data available for the detection of respiratory patterns using a MI sensor, we, therefore, set up the measurement with a random mimic of apnea and only 1,393 breathing records were acquired and stored in the database. They included normal breathing as well as the mimic apnea. They were used for the training of the proposed deep learning model with the highest accuracy of 92% in the training dataset and 90% in the validation dataset. These accuracies should be improved by collecting a larger quantity of data.

Convolutional neural network (CNN) is a type of feed-forward artificial neural network and is usually applied to two-dimensional signals i.e. images. However, it can also be applied to time series like in this case. While long short-term memory (LSTM) network is a special kind of recurrent neural network (RNN) with a smart dynamical feedback structure to form short memory in the networks. Based on the dataset, the hybrid model of CNN and LSTM provided much better performance for the apnea detection than a CNN model. In this article, the hybrid model was therefore presented.

Conclusions and Future Works

A hybrid deep learning model based on CNN and LSTM has been implemented for the detection of apnea with the dataset measured from 5 healthy volunteers. The highest accuracy was 92% and 90% in the training dataset and in the validation dataset, respectively. With the aid of λ architecture, streaming data and batch data can be processed in real-time and apnea detection can be realised in the proposed contactless multisensor system, which can be used for an immediate alarm or long-term medical diagnostics.

There are many aspects in which this contactless multisensor system can be extended. The following points should be implemented in the future:

1. Classification of apnea into three main categories, namely mild, moderate, and severe
2. Comparison and evaluation of different deep learning models (i.e. CNN, LSTM, and a hybrid model of CNN and LSTM) with other classification algorithms such as random forests, decision trees, or nearest neighbors.
3. Implementation of robust sensor fusion for the detection and classification of apnea.

References

- [1] V. Tsara, A. Amfilochiou, M.J. Papagrigorakis, D. Georgopoulos, and E. Liolios. Definition and classification of sleep related breathing disorders in adults. *Hippokratia*, 13(3):187–191, 2009.
- [2] D. Teichmann, J. Foussier, J. Jia, S. Leonhardt, and M. Walter. Noncontact monitoring of cardiorespiratory activity by electromagnetic coupling. *IEEE Transactions on Biomedical Engineering*, 60(8):2142–2152, 2013.
- [3] B. Eilebrecht, J. Henriques, T. Rocha, M. Walter, S. Paredes, P. de Carvalho, M. Czaplik, and S. Leonhardt. Automatic parameter extraction from capacitive ecg measurements. *Cardiovascular Engineering and Technology*, 3(3):319–332, 2012.
- [4] D.U. Uguz. Design of a multipurpose photoplethysmography sensor to assist cardiovascular diagnosis. In *Proceedings of the International Student Scientific Conference Poster 2017*, May 2017.
- [5] C. Brüser, S. Winter, and S. Leonhardt. Unsupervised heart rate variability estimation from ballistocardiograms. *International Journal of Bioelectromagnetism*, 15(1):1–6, 2013.
- [6] M.S. Sayani. Deep learning of respiratory-related conditions using a non-contact multisensor system. Master thesis, RWTH Aachen University, 2018.
- [7] N. Marz and J. Warren. *Big Data: Principles and best practices of scalable realtime data systems*. Manning Publications, 2013.
- [8] J. Patterson and A. Gibson. *Deep Learning: a practitioner's approach*. O'Reilly Media, Inc., 2017.
- [9] S. Hochreiter and J. Schmidhuber. Long short-term memory. *Neural Computation*, 9(8):1735–1780, 1997.
- [10] J. Duchi, E. Hazan, and Y. Singer. Adaptive subgradient methods for online learning and stochastic optimization. *Journal of Machine Learning Research*, 12:2121–2159, 2011.
- [11] D. Teichmann, A. Kuhn, S. Leonhardt, and M. Walter. The main shirt: A textile-integrated magnetic induction sensor array. *Sensors*, 14:1039–1056, 2014.
- [12] R. Ruangsawana, G. Velikic, and M. Bocko. Methods to extract respiration information from ecg signals. In *IEEE International Conference on Acoustics Speech and Signal Processing*, March 2010.
- [13] M.V. Madhav, M.R. Ram, E.H. Krishna, N.R. Komalla, and K.A. Reddy. Estimation of respiratory rate from ecg, bp and ppg signals using empirical mode decomposition. In *IEEE Instrumentation and Measurement Technology Conference*, May 2010.
- [14] J. Six, O. Cornelis, and M. Leman. Tarsosdsp, a real-time audio processing framework in java. In *Proceedings of the 53th AES Conference*, 2014.

A Noninvasive Glucose Estimation based on Near Infrared Spectroscopy and Pulse-Echo Ultrasound

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Introduction

Management of Diabetes has become a world-wide issue affecting patients of wide age ranges. To avoid diabetes induced complications from hyper and hypo-glycemia, patients need to frequently monitor their blood sugar levels multiple times. However, the most prevalent method of blood glucose monitoring is invasive [1, 2], which is uncomfortable to patients, carries risk of skin infections, and is inconvenient for long-term usage. As has been mentioned in multiple review articles [3, 4], the development of a reliable noninvasive glucose meter (NGM) has vast market potential and is urgently needed. Currently, major challenges to overcome in NGM are the low signal to noise ratio and poor accuracy: introduced by variable temperatures and skin surface humidity etc., necessitating additional calibration among individuals [5]. Fortunately, recent studies found that the efficiency of NGM could be significantly improved by integrating multiple sensing techniques [6, 7].

In this study, we combine two technologies: namely the Pulse-Echo Ultrasound (PEU) and Near-Infrared Spectroscopy (NIRS), to measure blood glucose level non-invasively. These technologies are based on the essential properties of light and ultrasound transmission in tissue. For PEU, an ultrasound pulse is generated using an ultrasound pulser and transmitted through the tissue. A smooth metal disk reflects this signal and transmits the sound back to the source where it is detected by a transducer. The echo arrival time is dependent on the speed of sound in the tissue. As the speed of sound now depends on the glucose concentration, the time of arrival of the reflected signal (also referred to as time lag) becomes a proxy variable for glucose concentration [8]. For NIRS, light attenuation in tissue can be expressed as: $F_{out} = F_{in}e^{-\mu_{eff}d}$ where F_{in} & F_{out} are the incident and output light fluencies, $\mu_{eff} = \sqrt{3\mu_a(\mu_a + \mu'_s)}$ is the effective attenuation coefficient, μ'_s is the reduced scattering attenuation coefficient and μ_a is the absorption attenuation coefficient [9]. Scattering and absorption varies with glucose concentration for near infrared light [10]. It is also known from Kirill's work that transmitted optical signal intensity decreases when glucose concentration increases [2]. Hence by monitoring attenuation of an optical signal through a tissue, we can potentially determine glucose concentration levels.

Since both these methods use distinct measures (time of arrival and effective optical transmission) to estimate blood

glucose level, PEU and NIRS in conjunction provide a reliable method to estimate glucose levels non-invasively. In vitro experiments are done to collect data, two modelling techniques are investigated to estimate glucose levels and resulting prediction results are presented.

Experimental Setup

Figure 1 shows a schematic of the system. For ultrasound detection, the sound wave is detected by a piezoelectric disk whose central frequency is 4.25 MHz (7×0.5 mm R Wire Leads, Steminc). An ultrasound pulser (5055 PR, Panametrics) is connected to disk to generate the ultrasound pulse. An oscilloscope is used to acquire the PEU data (TDS5054 digital phosphor oscilloscope, Tektronix). For the NIRS part: a laser diode of 950 nm is used. The laser diode is controlled by a Laser Diode Combi Controller (ITC510, Thorlabs) which is modulated by a function generator (SDG2042X, Siglent) with a 100 Hz sine wave output. Transmitted near infrared light is detected by a InGaAs Switchable Gain Amplified Detector (PDA10CS, Thorlabs). Glucose solution is contained in a lab made tank (blue block in the schematic) of dimensions $200 \times 100 \times 20$ mm, with a window size of 100×70 mm. The window is covered with plastic membrane whose thickness is 0.3 mm. The laser detector and piezoelectric disk are placed on one side of the tank, whereas the ultrasound reflector for ultrasound and laser diode is placed on the other side. Gel is used to couple the piezoelectric disk to the tank to facilitate efficient acoustic transmission. To reduce system size, the laser output is routed through an optical fiber. During the in-vitro experiments, the tank was filled with serum-glucose solution with a pre-determined glucose concentration and was maintained at a constant 20°C temperature. The setup can easily be adapted for in-vivo experiments by switching the arrangements shown in the red dotted boxes.

Data

PEU Dataset

PEU data is collected in the following way. An ultrasound signal is sent from the transducer (from one side of the tank). This signal is reflected back from the other side of the tank and is detected after a specific time interval. This time interval is now dependent on the speed of sound inside the tank medium which in turn is dependent on the glucose concentration inside the tank. Therefore, by ob-

The first two authors contributed equally to this work.

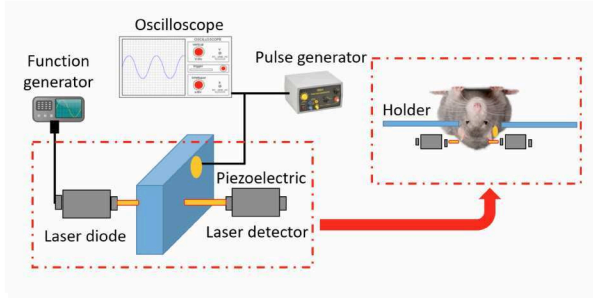


Figure 1: Experimental Setup Schematic

serving the time intervals, it is potentially possible to determine the glucose concentration.

For illustration, 13 different glucose levels were selected at which the time intervals are determined. At each of these glucose levels the experiment was repeated 15 times. By observing the cross correlation data between the emitted signal and the reflected signal, it was possible to determine values of the time lags.

Figure 2 presents the collected data, i.e. the value of the mean time lags at each glucose level. It is evident that there is a clear unique relationship between the glucose level and the time lags.

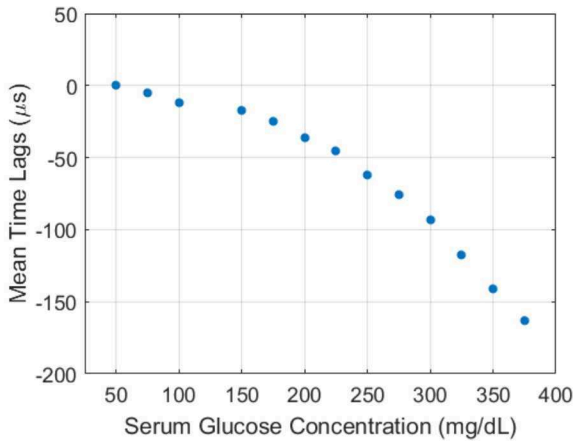


Figure 2: Mean Time Lags vs Glucose Concentration

NIRS dataset

NIRS data was collected in the following way. At each of the glucose concentration levels, an optical signal (with the help of a laser) was emitted from one side of the tank. This signal was then detected at the other end of the tank. Since the attenuation in the detected signal is known to be dependent on the glucose concentration, the RMS value of the attenuated signal can now serve as a modelling parameter for glucose concentration. The collected data has been presented in Figure 3. Once again, we observe a unique relationship between glucose concentrations and the RMS values.

It is interesting to note from Figures 2 and 3 that the two

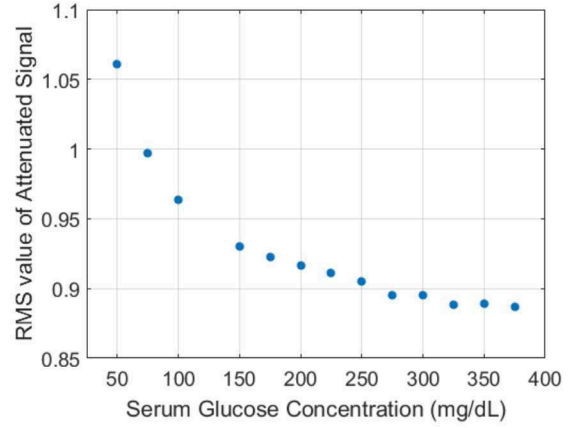


Figure 3: RMS value vs Glucose Concentration

methods PEU and NIRS are most sensitive to different regions of the glucose spectrum. This is evident in the slope of the plots. PEU is seen to be most sensitive in the high glucose region while NIRS is seen to be most sensitive in the low glucose concentration region. In fact, this complementing sensitivity makes these two techniques suitable for combined use. It should be noted that the data for PEU as well as NIRS was collected simultaneously on the same serum samples.

Modelling and Prediction

The in-vitro experiment yielded $N = 13$ data points. This dataset is divided into two groups: namely the training data (S_{train} where $|S_{train}| = n_{train}$) and the testing data (S_{test} where $|S_{test}| = n_{test}$). The idea now is to develop a prediction model using the training dataset and validate its performance on the testing dataset. Note that $n_{train} + n_{test} = N$. Independent prediction models are developed for PEU and NIRS which estimate the respective glucose levels ($\hat{G}_{PEU}, \hat{G}_{NIRS}$) as well as their uncertainties in terms of variances ($\hat{\sigma}_{PEU}^2, \hat{\sigma}_{NIRS}^2$). The final glucose estimate ($\hat{G}$) is evaluated simply using an inverse variance weighted technique

$$\hat{G} = \frac{(\hat{\sigma}_{PEU}^2)^{-1} \hat{G}_{PEU} + (\hat{\sigma}_{NIRS}^2)^{-1} \hat{G}_{NIRS}}{(\hat{\sigma}_{PEU}^2)^{-1} + (\hat{\sigma}_{NIRS}^2)^{-1}}. \quad (1)$$

Two modelling techniques have been investigated in this work: Linear Regression and Gaussian Process Model.

Linear Regression Model (LRM)

In this work, a linear regression cubic polynomial model of the form

$$\hat{G}_{PEU/NIRS} = a_0 + a_1x + a_2x^2 + a_3x^3 \quad (2)$$

is sought where x denotes the independent variable. For PEU, x is the mean time lags and for NIRS is the RMS value of the attenuated signal. For brevity, subsequent development will not include the subscripts PEU/NIRS.

The coefficients ($\mathbf{a} = [a_0, a_1, a_2, a_3]^T$) are determined by minimizing the sum of squared errors (or residues) in the

dataset S_{train} . The final well known expression is

$$\mathbf{a} = (\mathbf{V}^T \mathbf{V})^{-1} \mathbf{V}^T \mathbf{G} \quad (3)$$

where $\mathbf{V}$ is the Vandermonde matrix. The i^{th} row of the Vandermonde matrix is given by $V(i,:) = [1, x_i, x_i^2, x_i^3]$ and the i^{th} element of $\mathbf{G}$ vector is given by G_i where $(x_i, G_i) \in S_{train}$.

The covariance of the estimated coefficients are then given by $\hat{\sigma}_a^2 = s^2 (\mathbf{V}^T \mathbf{V})^{-1}$ where $s^2 = \frac{\sum_{i=1}^{n_{train}} r_i^2}{n_{train} - |\mathbf{a}|}$ and r_i is the residue for the i^{th} data point in S_{train} , i.e.

$$r_i = G_i - (a_0 + a_1 x_i + a_2 x_i^2 + a_3 x_i^3). \quad (4)$$

It should be noted that $|\cdot|$ operator represents cardinality and in this case $|\mathbf{a}| = 4$.

Finally, the prediction of glucose at an unknown point x_0 can be made simply using the model, i.e.

$$\hat{G}_{PEU/NIRS} = a_0 + a_1 x_0 + a_2 x_0^2 + a_3 x_0^3. \quad (5)$$

The uncertainty in prediction $\hat{\sigma}_{PEU/NIRS}^2$ is given by:

$$\hat{\sigma}_{PEU/NIRS}^2 = \mathbf{V}_0^T \hat{\sigma}_a^2 \mathbf{V}_0, \quad (6)$$

where $\mathbf{V}_0 = [1, x_0, x_0^2, x_0^3]^T$. A prediction $\hat{G}$ at x_0 can now be made by using equation (1).

Gaussian Process

In this method of prediction, it is assumed that the output variable (i.e. glucose concentration in our case) for the training data set (S_{train}) as well as the point at which a prediction is to be made (for example a sample point in S_{test}) are both part of a joint Gaussian probability distribution function. A linear predictor is then designed such that the predicted output ($\hat{G}_{PEU/NIRS}$) is a linear combination of the observations in the training dataset (i.e. $G_i \in S_{train}$).

It can be shown that the predicted output ($\hat{G}_{PEU/NIRS}$) at an unknown point x_0 is given by:

$$\hat{G}_{PEU/NIRS} = \mathbf{V}_0^T \hat{\mathbf{a}} + \mathbf{R}_0^T \mathbf{R}^{-1} (\mathbf{G} - \mathbf{V} \hat{\mathbf{a}}) \quad (7)$$

and the associated uncertainty is given by:

$$\hat{\sigma}_{PEU/NIRS}^2 = \hat{\sigma}_a^2 (1 - \mathbf{R}_0^T \mathbf{R}^{-1} \mathbf{R}_0 + \mathbf{u}_0^T (\mathbf{V}^T \mathbf{R}^{-1} \mathbf{V})^{-1} \mathbf{u}_0), \quad (8)$$

where $\mathbf{u}_0 = \mathbf{V}^T \mathbf{R}^{-1} \mathbf{R}_0 - \mathbf{V}_0$. $\mathbf{G}$, $\mathbf{V}$ and $\mathbf{V}_0$ are defined as mentioned previously. The matrix $\mathbf{R} \in \mathbb{R}^{n_{train} \times n_{train}}$ is introduced to capture spatial correlations between sample points in S_{train} . The elements of $\mathbf{R}$ are determined using various spatial correlation kernels studied throughout the Gaussian Process literature. In this work, a squared exponential autocorrelation function kernel was used, i.e. the elements of $\mathbf{R}$ were calculated using the relation

$$R_{ij} = e^{-\left(\frac{x_i - x_j}{l}\right)^2} \quad (9)$$

for all $i = [1 : n_{train}]$ and $j = [1 : n_{train}]$; where R_{ij} represents the i^{th} row j^{th} column element of $\mathbf{R}$, $x_i \in S_{train}$ and $x_j \in S_{train}$ and l is a scale parameter that needs to be determined. The vector $\mathbf{R}_0$ whose i^{th} element ($\mathbf{R}_0(i)$) is defined through

$$\mathbf{R}_0(i) = e^{-\left(\frac{x_i - x_0}{l}\right)^2} \quad (10)$$

represents the spatial correlation of the training set to x_0 .

Before the final expressions (in equations (7) and (8)) can be calculated, the values of $\hat{\mathbf{a}}$, $\hat{\sigma}_a^2$ and parameter l needs to be evaluated. Once again, there are a number of ways outlined in the literature by which they can be determined. The approach used in this work is that of a Maximum Likelihood estimator (MLE). The MLE algorithm can be shown to yield closed form expressions for $\hat{\mathbf{a}}$ and $\hat{\sigma}_a^2$ and an optimization problem to determine l . The results have been presented in equations (11) through (13):

$$\hat{\mathbf{a}} = (\mathbf{V}^T \mathbf{R}^{-1} \mathbf{V})^{-1} \mathbf{V}^T \mathbf{R}^{-1} \mathbf{G} \quad (11)$$

$$\hat{\sigma}_a^2 = (\mathbf{G} - \mathbf{V} \hat{\mathbf{a}})^T \mathbf{R}^{-1} (\mathbf{G} - \mathbf{V} \hat{\mathbf{a}}) / n_{train} \quad (12)$$

$$l = \arg \min_l \hat{\sigma}_a^2 (\det(\mathbf{R}))^{1/n_{train}}. \quad (13)$$

Once the above values are known for PEU and NIRS, a prediction $\hat{G}$ at x_0 can now be made using equations (7), (8) and (1). Details of the Linear Regression method as well as the Gaussian Process prediction can be found in [11].

Results

In this work, n_{train} was selected to be 10 (therefore $n_{test} = 3$). The division of the data points between the two groups was done randomly. Then the datapoints in S_{train} were used for modelling and the models were used to predict the glucose levels at the datapoints in S_{test} . The predicted values were then compared to the true values. Performance of both the prediction algorithms were tested and compared. Figures 4 and 5 show the PEU and NIRS model developed using linear regression on a sample training set respectively. The red squares bordering the blue circles represent the training set. The black curve denotes the predicted line (or the regression line). The grey band shows a $3 - \sigma$ band about the prediction line.

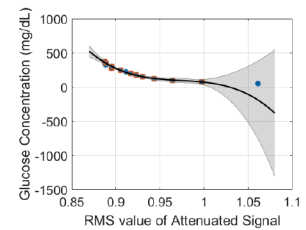
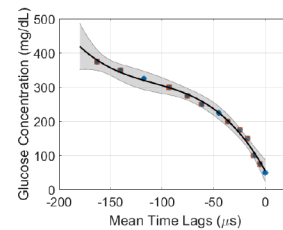


Figure 4: PEU LR Model Figure 5: NIRS LR Model

Figure 6 shows the PEU model developed using Gaussian Process modelling on the same sample training set. A similar plot of NIRS Gaussian Process model has been presented in Figure 7. It should be mentioned that the models

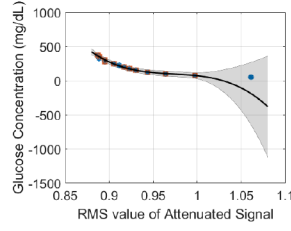
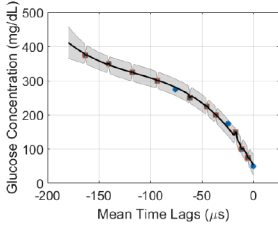


Figure 6: PEU GP Model Figure 7: NIRS GP Model

are seen to predict negative values (for NIRS) at the edges. This is primarily due to poor extrapolation capacity of the models and should be ignored.

The linear regression models are then combined (using equation (1)) to predict the glucose levels at the n_{test} points. The same predictions are also made by combining the Gaussian process models. Table 1 lists the corresponding results. Columns 4 and 5 in the table represent the percentage error in prediction from both the methods.

True Glucose	LR	GP	% Var (LR)	% Var (GP)
50	62.25	52.58	24.50	5.16
225	219.64	220.65	2.38	1.93
325	336.59	333.47	3.57	2.61

Table 1: Prediction results from Linear Regression (LR) and Gaussian Process (GP) Modelling

We can see from the table that, in this particular example both the algorithms are successfully able to predict the glucose concentration within an error of 25mg/dL .

In order to determine quantitatively which algorithm performs better on average, a Monte Carlo based simulation was done. The division of the data set into the training set and testing set was repeated 1000 times. For each of these cases the prediction errors from Linear Regression and Gaussian Process modelling were recorded. The results were organized into two matrices E_{LR} and E_{GP} . $E_{LR} \in \mathbb{R}^{n_{test} \times 1000}$ where each column represents the Linear Regression prediction error from each Monte Carlo trial. Similarly each column of E_{GP} represents the Gaussian Process model prediction error from each Monte Carlo trial. Finally to compare the two methods, the following metric

$$J_{LR/GP} = \sqrt{\sum_i^{n_{test}} \sum_j^{1000} E_{LR/GP}(i, j)^2} \quad (14)$$

was defined to evaluate which algorithm did better on average. $E_{LR/GP}(i, j)$ represents the i^{th} row j^{th} column of the error matrices E_{LR} and E_{GP} . It was found that $J_{LR} = 650.4864$ and $J_{GP} = 452.5926$. Hence, we can conclude from the values that the Gaussian Process model performs better and should be used for all successive predictions.

Conclusions

In this paper, combining two modes of non-invasive glucose concentration sensing to improve accuracy of predic-

tion has been investigated. In-vitro experiments were done to establish that this method is not only possible but could also be potentially state of the art. Two different modelling techniques (Linear Regression and Gaussian Process modelling) are explored and variance weighted data fusion is used to make final predictions. Both methods have shown promise although a Monte Carlo based simulation suggested the Gaussian Process works better on average. This work provides the foundation to go further and perform in-vivo experiments and address the issues associated with that.

References

- [1] Sandeep Kumar Vashist. Non-invasive glucose monitoring technology in diabetes management: A review. *Analytica chimica acta*, 750:16–27, 2012.
- [2] Kirill V Larin, Mohsen S Eledrisi, Massoud Motamedi, and Rinat O Esenaliev. Noninvasive blood glucose monitoring with optical coherence tomography: a pilot study in human subjects. *Diabetes care*, 25(12):2263–2267, 2002.
- [3] Timothy M Dall, Wenya Yang, Pragna Halder, Bo Pang, Marjan Massoudi, Neil Wintfeld, April P Semilla, Jerry Franz, and Paul F Hogan. The economic burden of elevated blood glucose levels in 2012: diagnosed and undiagnosed diabetes, gestational diabetes mellitus, and prediabetes. *Diabetes care*, 37(12):3172–3179, 2014.
- [4] Ilana Harman-Boehm, Avner Gal, Alexander M Raykhman, Jeffrey D Zahn, Eugene Naidis, and Yulia Mayzel. Noninvasive glucose monitoring: a novel approach, 2009.
- [5] Sandeep Kumar Vashist. Continuous glucose monitoring systems: a review. *Diagnostics*, 3(4):385–412, 2013.
- [6] Praful P Pai, Arijit De, and Swapna Banerjee. Accuracy enhancement for noninvasive glucose estimation using dual-wavelength photoacoustic measurements and kernel-based calibration. *IEEE Transactions on Instrumentation and Measurement*, 67(1):126–136, 2018.
- [7] Zhihong Gao, Mitsuru Taniwaki, Hiromi Shimada, Sayaka Ishihara, Makoto Nakauma, Takahiro Funami, and Kaoru Kohyama. Ultrasound analysis of the effects of food bolus volume on tongue movement at the initiation of swallowing. *Journal of texture studies*, 44(5):387–396, 2013.
- [8] Graham H Thomas, Roger M Watson, and J Oakey Noell. Method and apparatus for non-invasive monitoring of blood glucose, June 9 1992. US Patent 5,119,819.
- [9] Omar S Khalil. Spectroscopic and clinical aspects of noninvasive glucose measurements. *clinical chemistry*, 45(2):165–177, 1999.
- [10] Praful P Pai, Pradyut K Sanki, and Swapna Banerjee. A photoacoustics based continuous non-invasive blood glucose monitoring system. In *Medical Measurements and Applications (MeMeA), 2015 IEEE International Symposium on*, pages 106–111. IEEE, 2015.
- [11] Vincent Dubourg. *Adaptive surrogate models for reliability analysis and reliability-based design optimization*. PhD thesis, Université Blaise Pascal-Clermont-Ferrand II, 2011.

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Tissue layers three-dimensional structure formation by nanosecond laser pulses

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Introduction

Carbon nanotubes (CNTs) attract the attention of researchers due to their electronic, optical, thermal and mechanical properties [1]. Thus, there is a tendency to increase the applicability of CNTs for the nanomaterials creation for various purpose, including medical ones.

This work is devoted to the creation of three-dimensional tissue-engineered structures based on albumin and collagen proteins with an inner scaffold made of CNTs. Such structures are well suited as implants for the cardiovascular system due to their high biocompatibility, ability to biodegradation [2] and ensuring the germination of blood vessels net.

Therefore, it is obvious that it is necessary to obtain detailed information on the structural changes that occur during laser radiation influence. Under the influence of this kind of high-intensity radiation on the local area of protein dispersion with CNTs, phase transformations with the formation of a three-dimensional tissue-engineered structure take place. And in the case of using laser beams of nanosecond duration, nonlinear effects arise. That is why it is necessary to conduct Z-scan and fixed sample location experiments to determine the dependence of the total absorption coefficient on the intensity, which is important to consider during the formation of the tissue-engineered structure [3].

As a result of this work, nonlinear properties of protein aqueous dispersions with CNTs were determined using a method based on the radiation transfer equation [4]. The beam radius values were measured depending on the location of sample relative to the focus of the lens and a comparison of these data with the theoretical ones was made. In this way, the values of the input light fluence which fell on the local region of the sample during the formation of the tissue-engineered structure were determined.

Materials and Methods

Aqueous dispersions of bovine serum albumin (BSA) with a concentration of 25% and bovine collagen (BC) with a concentration of 2% and similar dispersions with single-walled carbon nanotubes (SWCNTs) were investigated in the study.

To prepare the dispersion with CNTs, they were premixed in a homogenizer with water with a mass concentration of 0.03% until a homogeneous solution was obtained. This solution was then mixed with the protein water dispersion and processed in an ultrasonic bath for 40 minutes.

Results

As shown in fig. 1, as the input energy density increases, the BSA dispersion with CNTs exhibits strong nonlinear effects (fig. 1b). This is reflected in the sharp weakening of the normalized transmission and, correspondingly, in the increase of the laser radiation absorption. An absorptivity increase is also observed for the dispersion without CNTs, but it is insignificant (fig. 1a). The theoretical curves were plotted from the results of optical parameters calculations.

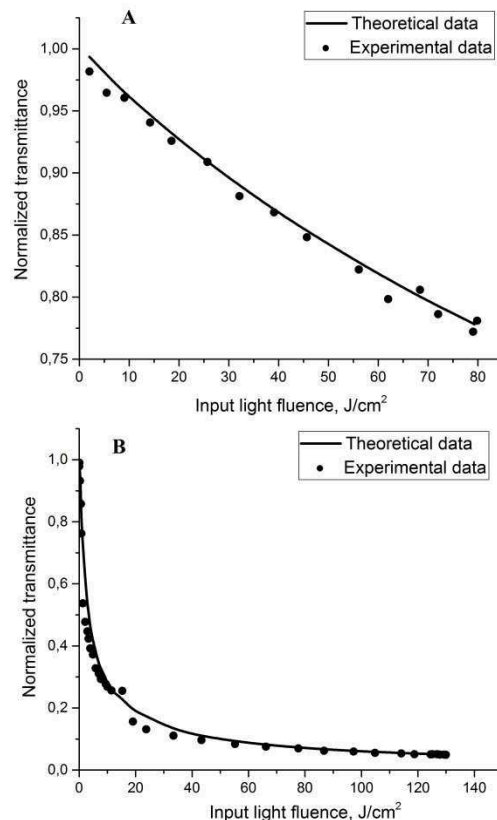


Figure 1: Normalized transmittance dependence on input light fluence for: A – BSA, B – BSA+SWCNT

Fig. 2 shows the normalized transmittance for collagen dispersions without nanotubes (fig. 2a) and with nanotubes (fig. 2b). To better trace the behavior of the sample at low values of the input light fluence, the dependence data are presented on a logarithmic scale. Collagen dispersion also show an increase of the laser radiation absorption when CNTs were added, but it is weaker than for BSA dispersions. The nonlinear properties of protein dis-

persions with single-walled carbon nanotubes are also confirmed by the calculated calculations.

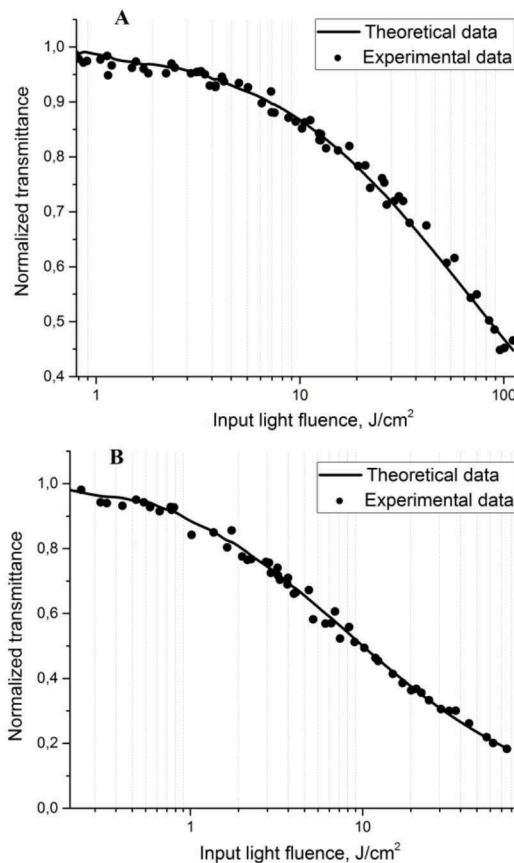


Figure 2: Normalized transmittance dependence on input light fluence for: A – BC, B – BC+SWCNT

Calculations were made using a method based on the radiation transfer equation. When carbon nanotubes were added, the value of the linear absorption coefficient increased however, this growth was insignificant. Albumin and collagen water dispersions without CNTs showed values of the linear absorption coefficient $\alpha = 1.92 \text{ cm}^{-1}$ and $\alpha = 2.16 \text{ cm}^{-1}$ respectively, and the same dispersions with carbon nanotubes showed $\alpha = 2.7 \text{ cm}^{-1}$ and $\alpha = 2.94 \text{ cm}^{-1}$.

Unlike linear absorption, the value of the nonlinear absorption coefficient increased significantly with the addition of carbon nanotubes. For dispersions without CNTs, the nonlinear absorption coefficient β was 4 cm/GW and 5.9 cm/GW for albumin and collagen respectively, and for similar dispersions with CNTs $\beta = 345 \text{ cm/GW}$ and $\beta = 66.9 \text{ cm/GW}$.

Also, for the suspensions studied, the threshold light fluence values, at which nonlinear effects begin to occur were calculated for studied dispersions. For pure aqueous dispersions of albumin and collagen, this values were 6 mJ/cm^2 and 8.5 mJ/cm^2 respectively, and for dispersions with nanotubes they were 51 mJ/cm^2 and 25.5 mJ/cm^2 .

The calculated values of the waist radius for all the experiments were $23 \pm 3 \text{ }\mu\text{m}$. Knowing the value of the radius of

the beam in the neck, the beam radius values at any point can be calculated as:

$$\omega(z) = \omega_0 \sqrt{1 + \left(\frac{\lambda z}{\pi \omega_0^2}\right)^2} \quad (1)$$

where ω_0 – laser beam waist, $\omega(z)$ – laser beam radius at any point of the optical axis Z.

To verify the correspondence of the used laser beam to the Gaussian beam, the beam radius depended on the distance from the focus of the lens was studied. To do this, the CCD camera was placed on a mechanized ruler and similarly to the Z-scan experiment was moved relatively to the focus of the lens. As a result, experimental values of the beam radius at different points were obtained, which correlate well with the theoretical values (fig. 3).

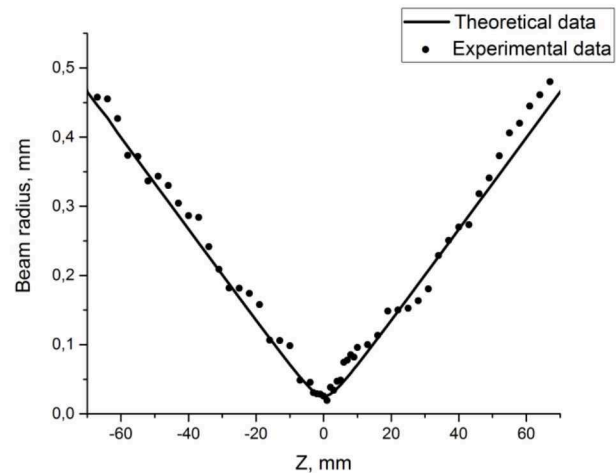


Figure 3: Beam radius dependence on optical axis Z displacement

Conclusions

An increase of the nonlinear absorption coefficient with the addition of CNTs suggests that it is the nanotubes that absorb most of the laser radiation as its light fluence increases, and thus reduce the effect of the laser on the proteins. Absorbing laser radiation, nanotubes heat up and transfer heat to the medium, which leads to the creation of a solid composite. Thus, proteins are less damaged in the formation of three-dimensional structures by laser printing methods.

References

- [1] S. Iijima. Helical microtubules of graphitic carbon, *Nature* 354: 56–58, 1997.
- [2] A. Parag, J.B. Hall, C.B. McLeland, M.A. Dobrovolskaia, S.E. McNeil. Nanoparticle interaction with plasma proteins as it relates to particle biodistribution, biocompatibility and therapeutic efficacy, *Advanced drug delivery reviews* 61: 428–437, 2009.
- [3] Balu M. White-light continuum Z-scan technique for nonlinear materials characterization, *Optics Express* 12(16): 3820–3826, 2004.
- [4] Tereshchenko S.A., Podgaetsky V.M. Determining the parameters of the laser radiation intensity limiter based on a time-dependent equation of radiative transfer in a nonlinear medium, *Quantum electron.* 41(1): 26–29, 2011.



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Biotechnical system for automatic assessment of facial nerve dysfunction rate

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Introduction

Recently in the field of maxillofacial surgery there is a growing number of patients with facial palsy. Assessment of the facial nerve dysfunction rate is needed for planning of treatment, for monitoring of rehabilitation efficiency and for prediction of patient's state [1]. In clinical experience and research studies to estimate facial nerve dysfunction rate scaling systems are implemented (House-Brackmann, Sunnybrook, Yanagihara, Nottingham, eFACE [2]). As follows from the analysis of the existing methods, all of them have two crucial disadvantages: biased approach and nonuniversality [1].

It is determined that facial nerve dysfunction severity is related to facial muscles dysfunction, which means that it is related to facial lateral asymmetry level. Consequently, it is possible to estimate facial nerve dysfunction rate by applying biometric facial video analysis, based on the measuring of anthropometric features of the facial region. Therefore, development of the biotechnical system for automatic assessment of facial nerve dysfunction rate based on biometric facial video analysis is relevant.

Materials and Methods

In the framework of the present research biotechnical system for automatic assessment of facial nerve dysfunction rate based on biometric facial video analysis is proposed. Figure 1 shows the structure of the system.

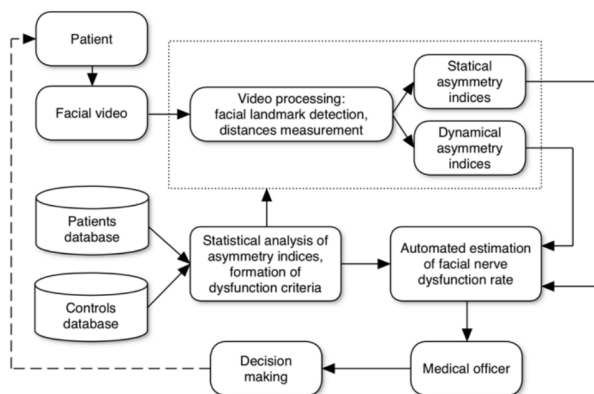


Figure 1: Structure of biotechnical system for automatic assessment of facial nerve dysfunction rate

In the framework of the proposed method, video, containing patient's facial movements, is to be captured, facial video processing (including 2 stages: facial landmark detection and distances measurement) is to be performed,

statical and dynamical asymmetry indices, based on relative shift of facial landmarks, are to be estimated. Based on databases of patients and control set, statistical analysis of asymmetry indices is to be held, resulting in formation of dysfunction criteria. Therefore, based on asymmetry indices, automated estimation of facial nerve dysfunction rate is to be performed.

Within this research data recording technique is developed. In its framework, the experimental subject is positioned at a distance of 1 meter to camera (Logitech HD, 1920×1080, 15 fps) against the homogenous background. The face position is frontal. The experimental subject is asked to perform the following movements: demonstration the face at rest, eye squeeze, raising the eyebrows, smiling, forcefully smiling, combining lips a tubule, cheeks puffing, articulating, forced articulating (with overacting amplitude of lips movements).

Facial landmarks detection is implemented with dlib library [3] with 42 enabled facial landmark points of the 68 points MultiPIE/IBUG face model [4] (is shown on Figure 2).

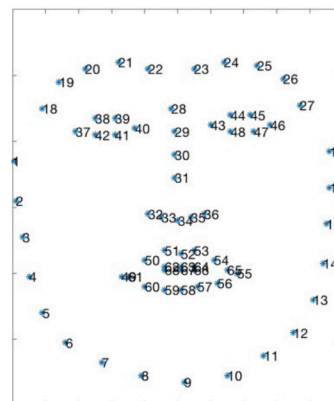


Figure 2: Facial landmarks configuration of the MultiPIE/IBUG face model

Facial asymmetry rate estimations are based on evaluation of relative shift of groups of landmarks. Preliminary facial asymmetry rate estimation (point and integral) is performed for 20 patients and 20 representatives from control set. Point asymmetry rate estimations include asymmetry indices of forehead and mouth regions [5] ("0" corresponds to totally asymmetrical movement, "1" corresponds to totally symmetrical movement).

Forehead asymmetry rate is based on estimation of the rate of relative shift of eye and eyebrow points from left and

right forehead regions (points P_{18} - P_{22} respective to points P_{37} - P_{42} and points P_{23} - P_{27} respective to points P_{43} - P_{48}). The basic principles are described below:

a) estimation of mean eyebrow points LEB and REB :

$$LEB = \frac{1}{5} \sum_{i=18}^{22} P_i, REB = \frac{1}{5} \sum_{i=23}^{27} P_i,$$

b) estimation of mean eye points LEC и REC :

$$LEC = \frac{1}{6} \sum_{i=37}^{42} P_i, REC = \frac{1}{6} \sum_{i=43}^{48} P_i,$$

c) estimation of distances D_{REB} and D_{LEB} between mean eye and eyebrow points on the left and on the right sides:

$$D_{LEB} = d(LEB, LEC), D_{REB} = d(REB, REC),$$

where d – distance measure,

d) estimation of relative shifts Δ_L^f and Δ_R^f of the forehead region points on the left and on the right sides:

$$\Delta_L^f = \left| \max_i(D_{LEB_i}^{test}) - \bar{D}_{LEB}^{rest} \right|,$$

$$\Delta_R^f = \left| \max_i(D_{REB_i}^{test}) - \bar{D}_{REB}^{rest} \right|,$$

where $\bar{D}_{LEB}^{rest}$ and $\bar{D}_{REB}^{rest}$ – distances between mean eye and eyebrow points on the left and on the right sides at rest, $D_{LEB_i}^{test}$ and $D_{REB_i}^{test}$ – distances between mean eye and eyebrow points on the left and on the right sides during the facial movements, i – number of videoframe,

e) estimation of indice r_f , which reflects the shift between left and fight parts of forehead region:

$$r_f = \begin{cases} \frac{\Delta_R^f}{\Delta_L^f} & \text{if } \Delta_L^f > \Delta_R^f \\ \frac{\Delta_L^f}{\Delta_R^f} & \text{otherwise.} \end{cases}$$

Mouth asymmetry rate is based on estimation of the rate of relative shift of mouth corners points from left and right sides and mouth center points (points P_{49} and P_{55} respective to points P_{52} , P_{63} , P_{67} , P_{58}). The basic principles are described below:

a) estimation of mean distances D_{LM} and D_{RM} between mouth corners points P_{49} and P_{55} and mouth center points P_{52} , P_{63} , P_{67} , P_{58} :

$$D_{LM} = \frac{1}{4} (d(P_{49}, P_{52}) + d(P_{49}, P_{63}) + d(P_{49}, P_{67}) + d(P_{49}, P_{58})),$$

$$D_{RM} = \frac{1}{4} (d(P_{55}, P_{52}) + d(P_{55}, P_{63}) + d(P_{55}, P_{67}) + d(P_{55}, P_{58})),$$

b) estimation of shifts Δ_L^m and Δ_R^m from the left and from the right sides:

$$\Delta_L^m = \left| \max_i(D_{LM_i}^{test}) - \bar{D}_{LM}^{rest} \right|,$$

$$\Delta_R^m = \left| \max_i(D_{RM_i}^{test}) - \bar{D}_{RM}^{rest} \right|,$$

where $\bar{D}_{LM}^{rest}$ and $\bar{D}_{RM}^{rest}$ – mean distances between mouth corners points and mouth center points at rest, $D_{LM_i}^{test}$ and $D_{RM_i}^{test}$ – distances between mouth corners points and mouth center points during the facial movements, i – number of videoframe,

c) estimation of indice r_m , which reflects the shift between left and fight parts of mouth region:

$$r_m = \begin{cases} \frac{\Delta_R^m}{\Delta_L^m} & \text{if } \Delta_L^m > \Delta_R^m \\ \frac{\Delta_L^m}{\Delta_R^m} & \text{otherwise.} \end{cases}$$

Integral asymmetry rate estimations include distances between relative shift curves (“0” corresponds to totally symmetrical movement).

Results

Table 1 shows the results of experimental evaluation of asymmetry indices of forehead region during eye squeeze, raising the eyebrows, smiling, forcefully smiling, combining lips a tubule, cheeks puffing. The median and also lower and upper quartiles are presented. The presented asymmetry indices correspond to point asymmetry rate estimation.

Table 1: Asymmetry indexes of forehead region

Exercise	Control	Patients
Eye squeeze	0.94	0.88
Raising the eyebrows	0.95	0.68
Smiling	0.86	0.09
Forcefully smiling	0.94	0.74
Combining lips a tubule	0.72	0.47
Cheeks puffing	0.08	0.39

Table 2 shows the results of experimental evaluation of areas between relative shift curves of forehead regions during articulating, forced articulating. The presented values of areas correspond to integral asymmetry rate estimation.

Table 2: Areas between relative shift curves of forehead regions (pixels per frame)

Exercise	Control	Patients
Articulating	75	94
Forced articulating	98	122

Discussion

Performed point asymmetry rate estimations are based on peak amplitudes acquired from series of videoframes. Therefore, in general, peak amplitudes from different videoframes can be used for single asymmetry rate estimation. This results in upward bias of asymmetry rate estimation and downward bias of test-sensitivity in case of facial nerve dysfunction. Consequently, it is reasonable to use integral asymmetry rate estimations based on dynamical features acquired from each frame.

Conclusions

According to results of preliminary facial asymmetry rate estimation, it's reasonable to develop integral facial asymmetry rate based on dynamic features. At this moment set of these features is under exploration.

References

- [1] T. Hadlock, L. Urban. Toward a universal, automated facial measurement tool in facial reanimation. Arch Facial Plast Surg, Vol. 14(4), 277-282, 2012.
- [2] A.Y. Fattah et al. Facial nerve grading instruments: systematic review of the literature and suggestion for uniformity. Plastic and Reconstructive Surgery, Vol. 135(2), 569-579, 2015.
- [3] D.E. King. Dlib-ml: A machine learning toolkit. Journal of machine learning research, Vol. 10, 1755-1758, 2009.
- [4] C. Sagonas. et al. Incremental face alignment in the wild. 300 faces In-the-wild challenge: Database and results, 2016.
- [5] H.S. Kim et al. A smartphone-based automatic diagnosis system for facial nerve palsy. Sensors, Vol. 15, 26756-26768, 2015.

Variation in Local Pulse Wave Velocity over the Cardiac Cycle: *In-Vivo* Validation using Dual-MPG Arterial Compliance Probe

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Introduction

The biomechanical characteristics of arterial vessels assessed from a short segment (local estimates) are key cardiovascular clinical markers [1]. Local measurement of artery condition has the potential to quantify the prognostic value for the prediction of cardiovascular morbidity and mortality. The elastic properties of large arteries affect locally during the pathophysiological process of various vascular disease such as atherosclerosis [2]. Pulse wave velocity assessed from a short vessel segment (local PWV) has been considered as an indicator of arterial stiffness. Local PWV is shown to correlate well with the mechanical characteristics of an artery over a wide physiological range [1, 3]. Researchers have demonstrated the potential of local PWV to evaluate blood pressure (BP) parameters locally from an artery without using the conventional bladder-type pressure cuff (cuffless technique) [4 – 6]. Simultaneously measured local PWV, arterial dimensions and local BP parameters are essential to accurately characterize and quantify the elastic behavior of central and peripheral arteries [1].

A standard approach for local PWV measurement relies on simultaneous acquisition of the propagating blood pulse waves from two distinct locations at a known separation distance (ΔX) within a small arterial segment. Time taken for the blood pulse wave to travel ΔX distance (pulse transit time [ΔT]), is obtained as the time delay between an identifiable point (fiducial point) on the proximal and distal pulse cycle pair. Following the fundamental distance-time equation, local PWV is then calculated as; Local PWV = $\Delta X / \Delta T$. Typically, only one measure of local PWV per cardiac cycle obtained from the reflection-free period is used for the quantitative characterization of an artery. However, local PWV is not a constant within a cardiac cycle, which otherwise varies proportionally to the instantaneous change in arterial pressure. Recently, we have proposed a calibration-free technique for cuffless BP measurement by tracking the variation in local PWV over the cardiac cycle [7]. This approach requires simultaneously measured local PWV and arterial dimensions from multiple points over the cardiac cycle. Such a methodology has the potential to revolutionize the conventional subject- and/or population-specific calibration-based cuffless BP evaluation techniques.

In this work, a method and system for direct measurement of local PWV variation over the cardiac cycle have been

presented. A novel dual-element magnetic plethysmograph (MPG) arterial compliance probe was developed. An application-specific dual channel blood pulse signal acquisition electronics hardware and fully automated pulse wave analysis algorithms were used for accurate measurement. An *in-vivo* validation study was conducted on 15 healthy volunteers to demonstrate the feasibility of local PWV evaluation from multiple fiducial points. Measurements were performed from the carotid artery using the dual-MPG probe in a beat-by-beat manner. Design of the arterial compliance probe, hardware implementation, and measurement algorithms are discussed in detail. *In-vivo* validation study results and observations are also summarized in the following sections, along with the limitations of the current study and recommended future research direction.

Pressure Dependency of Local PWV

The pulse wave initiated by blood ejection from the heart represents a propagating wave (in a fluid) through an elastic vessel. The velocity of traveling waves through an arterial segment (local PWV; henceforth denoted as ‘C’ in the equations/expressions) depends on physical characteristics of the vessel and blood density (ρ). A theoretical model describing the propagation of blood pulse wave in a cylindrical elastic vessel with an incremental modulus of elasticity E, inner radius R and wall thickness h was introduced by Moens and Korteweg [8], which can be expressed as in (1).

$$C = \sqrt{\frac{Eh}{2\rho R}} \quad (1)$$

The product of E and h is proportional to the ratio of tension acting on the vessel’s wall to the fractional amount of circumferential stretching, caused by the transmural pressure (P). Therefore, an increment in the lumen radius (dR) due to a small rise in pressure (dP) is given by the following expressions [9],

$$\begin{aligned} dR &= dP \frac{R^2}{Eh} \\ \Rightarrow \frac{Eh}{2R} &= A \frac{dP}{dA} \end{aligned} \quad (2)$$

where dA is the instantaneous change in arterial cross-sectional area A. Substitution of (2) into (1) yields the well-known Bramwell-Hill equation of the form:

$$C = \sqrt{\frac{A}{\rho} \frac{dP}{dA}} \quad (3)$$

Further, an empirical relationship for incremental modulus of elasticity E developed by Hughes et al. through heuristic modeling is given by [10]:

$$E = E_0 e^{\alpha P}, \quad (4)$$

where E_0 is the theoretical zero-pressure modulus, and α is an arbitrary constant that depends on the vessel property (typically $0.016 \text{ mmHg}^{-1} \leq \alpha \leq 0.018 \text{ mmHg}^{-1}$). Thus, (1) and (4) can be combined to derive an empirical relationship between local PWV and arterial pressure as described in the following expression. Here, $\eta = \sqrt{E_0/\rho}$ is a constant that depends on the particular artery.

$$C = \eta \sqrt{\frac{h}{2R}} e^{\frac{\alpha}{2} P} \quad (5)$$

Both the equations (3) and (5) illustrate that the local PWV is a function of arterial dimensions and instantaneous pressure level. Equation (5) suggests that the local PWV increases exponentially over a cardiac cycle with respect to BP variation during the systolic phase.

Measurement System

Design of Dual-MPG Arterial Compliance Probe

A dual-MPG arterial compliance probe (fig. 1) was designed and developed for blood pulse detection from superficial arteries. The probe holder was machined with custom parts (face diameter = 30 mm) to fit two identical Hall-effect permanent magnet-based MPG transducers [5]. As shown in fig. 1, two disc-shaped permanent magnets (D032A – Amazing Magnets LLC, CA, USA; diameter = 3.175 mm) were fixed on the probe face with a center-to-center distance of 25 mm. When the probe is placed on the skin surface above an artery, the magnetic lines of force encompasses two distinct arterial sites within a small section. Fluctuations in this field caused by blood pulse waves propagating through the artery were detected using highly-sensitive Hall-effect ICs (SS49E T3 – SEC Electronics Inc., NY, USA). The Hall-effect ICs were fixed at a distance of 3.6 mm away from the center of respective magnets. Their output voltage was proportional to blood pulse signals at the measurement sites. The sensor separation distance and design features were optimized based on our initial experiments, such that the MPG probe could acquire dual pulse waveforms without any cross-coupling. Pulse propagation distance ΔX was taken as the center-to-center distance between proximal and distal MPG modules ($\Delta X = 25 \text{ mm}$).

Hardware and Software Architecture

Shielded three-core cables with a wire gauge of 28 AWG were used to interface the MPG transducers with the electronics hardware. A dedicated dual-channel analog front-end (AFE) was developed for the precise acquisition of proximal and distal blood pulse cycles. The inherent inter-channel delay between the AFE channels was minimized ($< 0.1 \text{ ms}$) using a custom electronic circuit design by avoiding capacitors in the principal signal path. Subtractor

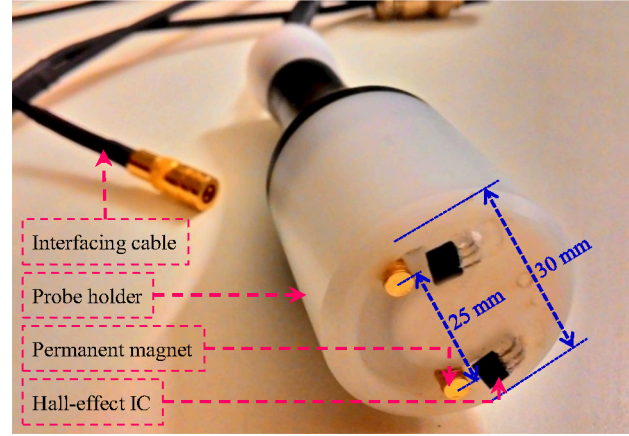


Figure 1: Dual-MPG arterial compliance probe

circuit with an instantaneous feedback of subtrahend [5] was used to remove static components from the acquired MPG signals (voltage $\approx 2.8 \text{ V}$, frequency $< 0.05 \text{ Hz}$). The extracted pulsatile components (in the order of millivolts) were amplified with an approximate gain of 40 dB, using a dual channel instrumentation amplifier (INA2126P – Texas Instruments Inc.). A commercially available simultaneously sampling data acquisition card (PXIe-6368 – National Instruments, TX, USA) was used to digitize the amplified MPG signals (sampling rate = 100 kS/s/ch).

Dual-channel MPG signal acquisition, post-processing, and pulse wave analysis were performed via a custom computer program developed using LabVIEW (Version 2014, National Instruments, TX, USA). MPG signals from both the channels were processed instantaneously in the digital domain. Initially, a 2nd order Butterworth low-pass digital filter with a cutoff frequency of 10 Hz was applied to smoothen the waveforms. Zero phase-shift filters were preferred to overcome phase difference between the unfiltered and the filtered signals. Any baseline drift caused by respiration or other artifacts were removed using a baseline wander elimination technique. Processed MPG pulse cycles were segregated with the same time interval from the pulse wave train using a cycle-cutting algorithm. Each proximal-distal cycle pairs were normalized between 0 and 1 to overcome any amplitude difference occurred during real-time acquisition.

Pulse Wave Analysis

Identification of multiple fiducial points within a pulse cycle is essential to assess local PWV variation over the cardiac cycle. Two characteristic identification points were defined near the foot and peak of the measured blood pulse cycles. These fiducial points were derived by applying a second-order differentiator to each pulse cycles. Fig. 2 exhibits an example blood pulse cycle and its second-derivative waveform (normalized to equal amplitude), illustrating the relative position of two critical points in the blood pulse cycle. The fiducial point near the waveform foot (Ψ_{Foot} ; resembles the systolic rising point) and the one near the systolic peak (Ψ_{Peak}) represent the

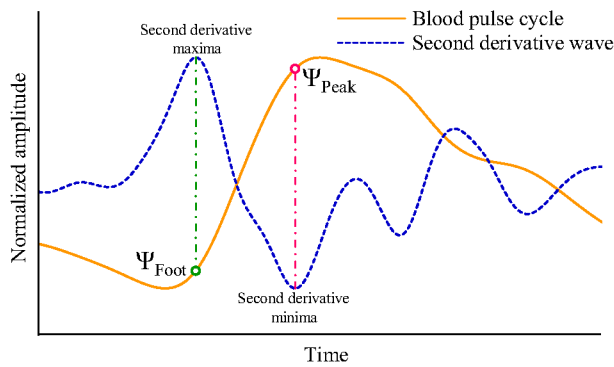


Figure 2: Fiducial points Ψ_{Foot} and Ψ_{Peak} defined in a blood pulse cycle from the second derivative wave

locations in pulse cycle corresponding to the maxima and minima of the second derivative waveform respectively. The time delay between Ψ_{Foot} of the proximal and distal pulse cycles was taken as the pulse transit time at diastolic BP level (ΔT_D), and a similar measure from Ψ_{Peak} represented pulse transit time at systolic BP level (ΔT_S). Local PWV was then evaluated from the systolic rising point and neighborhood of systolic peak using ΔX and corresponding transit time estimates, denoted as C_D and C_S respectively.

Validation Materials and Methods

An *in-vivo* study was conducted on 15 volunteers (age = 27 ± 4 years) to investigate the feasibility of the proposed method and system. The study objective and measurement protocol were explained to each volunteer, and written informed consent was obtained. They were requested to relax in sitting posture for 3 – 5 minutes before starting the measurement in order to stabilize BP and heartrate.

Once the anthropometric parameters were recorded, BP was measured from the left brachial artery with a clinical grade automatic BP monitor (SunTech 247 – SunTech Medical Inc. NC, USA). Local PWV values were then measured from the left carotid artery by placing the arterial compliance probe over the neck. The carotid artery was preferred since it is close to the skin surface, easily accessible and provides a straight vessel segment of sufficient length before the bifurcation. The operator adjusted the probe placement and orientation after locating the carotid pulse by palpation to acquire quality signals from both the proximal and distal MPG transducers. Signal acquisition and real-time local PWV evaluation were continued for 20 – 25 cardiac cycles from each volunteer.

Results and Discussion

Reliability of Carotid MPG Signal Acquisition

The developed prototype device was capable of detecting high-fidelity blood pulse signals from the carotid artery. Fig. 3 depicts a sample of simultaneously acquired proximal and distal MPG signals (after post-processing) from 25 mm distance apart. The peak-to-peak amplitude of the

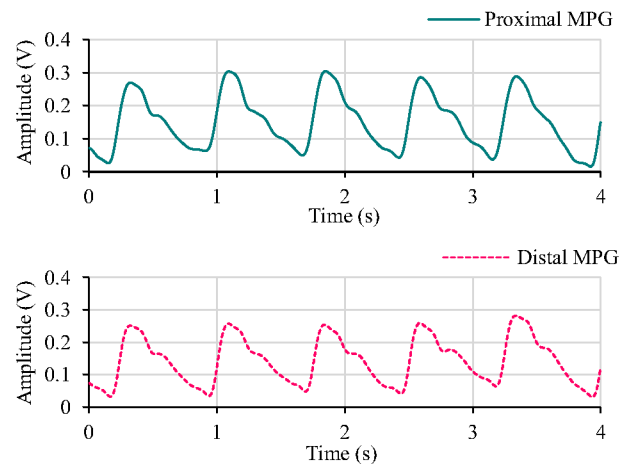


Figure 3: Simultaneously acquired proximal and distal MPG waveforms using arterial compliance probe

MPG signals was subjective, the typical range was between 1.5 mV_{PP} and 3.5 mV_{PP}. Spectral analysis of the acquired MPG signals revealed an approximate signal-to-noise ratio of 29 dB. It was sufficient for resolving pulse transit time estimates ΔT_D and ΔT_S (on the order of milliseconds) using the developed algorithms. However, degraded signal quality and/or an intense baseline drift caused by body movement yielded an error in critical point identification. Measurements obtained from such non-ideal cases were manually eliminated. In future, real-time signal quality indicators will be implemented in the measurement software to quantify the quality of acquired MPG signals. Such an automated instant feedback system could potentially guide the operators to archive more accurate and reliable measurements.

Variation in Local PWV Over the Cardiac Cycle

Carotid local PWV values were evaluated from both systolic rising point and neighborhood of systolic peak in a beat-by-beat manner. Fig. 4 presents continuously measured C_D and C_S from the left carotid artery of a particular volunteer (age = 28 years). Consistent with the theory, measured C_S values were higher than the corresponding C_D values, that was observed in continuous cardiac cycles from all recruited volunteers (tab. 1). The coefficient of variation (CoV) of C_S to C_D ratio evaluated from continuous cardiac cycles was less than 7%, indicating the reliability of measurement. Beat-to-beat variation in C_D and C_S measurement was between 4% to 7% and 6% to 9.5% respectively. Relatively high beat-to-beat variation observed in C_S measurement could be due to the wave reflection and confounding factors that influence Ψ_{Peak} locus and/or MPG waves from a small arterial segment. Further works are in progress to develop improved pulse wave analysis algorithm, and to optimize the probe design and sensing modality for accurate evaluation of C_D and C_S from various arterial sites.

Consistent with previous studies [4, 5], the absolute values of C_D were lower than the conventional carotid-femoral regional PWV estimates. Pearson's correlation

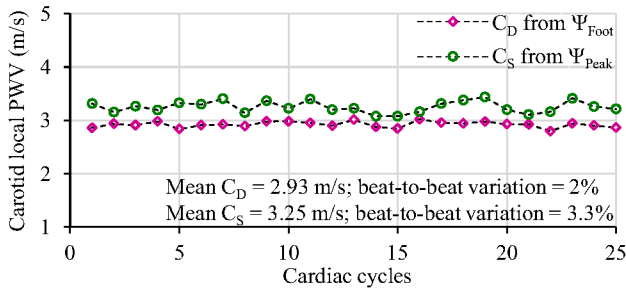


Figure 4: Carotid local PWV obtained from two distinct fiducial points within a cardiac cycle (C_D and C_S), illustrating measurement reliability and beat-to-beat variation

Table 1: Measurements Recorded from Volunteers

Volunt eer ID	Brachial BP (mmHg)		Local PWV (m/s)		Cs/Cn CoV
	Systolic	Diastolic	C_D	C_S	
22y/F	115	70	2.98	3.12	4.2%
25y/M	121	69	2.79	2.94	5.1%
28y/M	110	73	2.93	3.25	3.2%
26y/F	106	76	2.89	3.11	5.5%
27y/M	100	78	3.03	3.21	2.8%
29y/M	130	89	4.2	4.46	6.3%
33y/M	104	70	3.41	3.71	2.9%
30y/M	120	75	3.4	3.63	5.0%
25y/M	117	60	2.78	2.96	4.3%
28y/F	110	79	3.24	3.46	3.8%
31y/F	112	84	3.28	3.61	4.1%
27y/F	103	71	2.72	2.83	6.6%
36y/M	138	77	3.81	4.08	3.3%
25y/F	98	72	2.4	2.61	6.7%
21y/M	101	66	2.04	2.24	3.6%

coefficients (r) obtained from the regression analysis of BP parameters versus mean C_D and C_S pooled over all the volunteers were statistically significant ($p < 0.0001$). The r -value was 0.71 and 0.68 for diastolic BP versus C_D , and systolic BP versus C_S respectively. Results of this *in-vivo* study demonstrated the feasibility of dual-MPG arterial compliance probe to acquire local PWV variation over the cardiac cycle. This probe can be potentially used in cuffless BP monitoring techniques that utilize variations in local PWV to realize a calibration-free approach [7].

Study Limitations and Future Research Direction

A major limitation of the present *in-vivo* study concerns the small sample size of young, healthy volunteers. However, the current study was conducted to demonstrate the practical feasibility of a novel technique. An extensive validation study in a large population with pathophysiological sub-populations is needed to confirm the validity of proposed method and system over a wide physiological range. Variation in local PWV obtained by the proposed technique did not compare with that obtained by a reference method since commercial devices which can measure carotid local PWV from multiple points over the cardiac cycle are not available at present. Further research is underway to assess the variation in local PWV over the cardiac cycle via single-site measurement techniques.

Simultaneously acquired arterial dimensions and pressure wave can be utilized to realize such systems with the help of Bramwell-Hill equation.

Conclusions

The proposed arterial compliance probe and associated measurement system was experimentally validated on 15 human volunteers and demonstrated the expected functionality. Blood pulse signals were continuously acquired from the carotid artery using dual MPG transducers positioned 25 mm apart. Carotid local PWV was evaluated using the proximal and distal cycles, from two distinct fiducial points within a cardiac cycle in a beat-by-beat manner. Consistent with the theoretical models, local PWV obtained from the neighborhood of the systolic peak was higher than that obtained from the systolic rising point; illustrating the variation in local PWV over the cardiac cycle. This was consistently observed in all recruited volunteers with high reproducibility. An extensive clinical study in a large population is required to further validate the proposed approach. The potential application of accurate measurement of variation in local PWV over the cardiac cycle has been established in calibration-free BP evaluation techniques. Hence, the proposed arterial compliance probe could provide an opportunity for cuffless, calibration-free evaluation of BP parameters from superficial arteries in a beat-by-beat manner.

References

- [1] G. G. Raymond and M. B. Marc. Terminology for describing the elastic behavior of arteries. *Hypertension*, 41(6):1180–1182, 2003.
- [2] R. S. Reneman et al. Non-invasive ultrasound in arterial wall dynamics in humans: what have we learned and what remains to be solved. *Eur Heart J*, 26(10):960–966, 2005.
- [3] T. Pereira et al. Novel methods for pulse wave velocity measurement. *J Med Biol Eng*, 35(5):555–565, 2015.
- [4] P. M. Nabeel el al. Single-source PPG-based local pulse wave velocity measurement: a potential cuffless blood pressure estimation technique. *Physiol Meas*, 38(12):2122–2140, 2017.
- [5] P. M. Nabeel el al. A magnetic plethysmograph probe for local pulse wave velocity measurement. *IEEE Trans Biomed Circuits Syst*, 11(5):1065–1076, 2017.
- [6] J. Vappou et al. Non-invasive measurement of local pulse pressure by pulse wave-based ultrasound manometry (PWUM). *Physiol Meas*, 32(10):1653–1662, 2011.
- [7] J. Joseph et al. Method and system for cuff-less blood pressure (BP) measurement of a subject. US Patent US20170156706 A1, 2017.
- [8] W. W. Nichols and M. F. O'Rourke. McDonald's Blood flow in arteries: theoretical, experimental, and clinical principles. 4th ed., Hodder Arnold Publication, 1998.
- [9] J. C. Bramwell and A. V. Hill. The velocity of the pulse wave in man. *Proc. Roy. Soc. Lond. Ser. B*, 93(652):298–306, 1922.
- [10] D. J. Hughes et al. Measurements of Young's modulus of elasticity of the canine aorta with ultrasound. *Ultrason Imaging*, 1(4):356–367, 1979.

Hemodynamic Interventions for Inducing Blood Pressure Variation in Laboratory Settings

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Introduction

Arterial blood pressure (BP) parameters are key hemodynamic indices often used for screening and diagnosis of various pathophysiological conditions. Brachial artery BP measurement using a bladder-type pressure cuff and sphygmomanometer (auscultatory or oscillometric technique) is a routine part of clinical assessments. Over the past few years, the interest in methods that allow non-invasive, cuffless evaluation of BP parameters has increased to overcome the fundamental limitations of cuff-based techniques [1]. Cuffless techniques rely on exploring the relationship between BP and BP-dependent non-invasively measurable physiological parameters. Such theoretical or heuristic mathematical models generally require subject- and/or population-specific calibration procedure to quantitatively convert the acquired physiological parameters into pressure. Pulse transit time estimates, arterial vessel characteristics, and various hemodynamic indices are typically utilized to implement cuffless BP evaluation techniques [2]; these parameters are subject specific. Hence, a calibration curve and/or BP prediction model that is tailored to each subject would be optimal for accurate measurement [3]. Further, these calibration curves/models would have to be updated at regular intervals for accurate and reliable BP evaluation [2].

In order to develop subject-specific calibration curves or data-driven prediction models, the desired input physiological parameters should be recorded over a wide range of BP values from the subject. For this, resting BP level should alter via suitable BP perturbing interventions. Calibration curves or prediction models obtained through data recorded from a single intervention may not be effective for accurate BP evaluation [2]. Subject-specific data obtained from multiple interventions that perturb BP through different physiologic mechanisms could potentially provide reliable prediction models. Hemodynamic interventions such as drug-induced methods, anesthesia induction, and intensive care unit (ICU) therapies are typically followed to produce major BP changes over a wide physiological range [4]. However, these approaches are technically demanding, highly invasive, require well-trained physicians with clinical and/or research experience, and limited to hospitalized subjects. Therefore, subject-specific calibration curve/model construction and recalibration via invasive interventions cannot be adopted to realize cuffless BP techniques for wearable devices and routine screening applications. Practically feasible non-

invasive interventions are needed to perturb BP parameters during the design, validation and recalibration phases of cuffless BP devices.

In this work, we evaluated the variation in brachial BP parameters during multiple hemodynamic interventions that change the BP level through different physiological mechanisms. Five non-invasive interventions namely; (i) cold pressor test, (ii) treadmill-running exercise, (iii) mental arithmetic, (iv) leg-raise test, and (v) sustained hand-grip test were preferred for the validation study. These BP perturbing interventions could be safely performed in laboratory/non-specialist settings without the assistance from a physician or a trained investigator. Further, they could mimic various daily life activities such as experiencing cold weather conditions, brisk walk or performing strenuous exercise, stressful situations et cetera. An *in-vivo* study was conducted on randomly recruited normotensive subjects in order to characterize the BP altering strategies of aforesaid interventions. Measurement protocol of the performed study, BP perturbing procedure, recommended experimental conditions, *in-vivo* study results and observations are discussed in the following sections.

Materials and Methods

Subject Selection

Fifteen normotensive subjects ranged in age from 22 to 34 years comprising of males and females (body mass index = $22 - 29 \text{ kg/m}^2$) were recruited for the present *in-vivo* study. The study objectives and measurement protocol were explained to each participant and their written informed consent was obtained. This study conforms to the principles outlined in the Declaration of Helsinki. Before data collection, participants were requested to relax for 5 – 10 min to reduce their anxiety and to bring the BP parameters and heartrate to the normal level.

Study Protocol

The *in-vivo* validation study was designed by including five hemodynamic interventions listed in tab .1. Systolic BP (SBP), diastolic BP (DBP), mean arterial pressure (MAP) and heartrate were repeatedly measured from the brachial artery under (i) physically relaxed condition, (ii) during an intervention, and (iii) post-intervention recovery period. Measurements were performed using a clinical grade automatic BP monitor (SunTech® 247™ – SunTech Medical Inc. NC, USA; resolution = 1 mmHg) with a bladder-type pressure cuff. During the study, resting BP

Table 1: Hemodynamic Interventions for Altering BP Parameters

Intervention	Protocol	Observations and comments
Cold pressor test 	Immerse both the hands into an ice water container for 2 – 4 min. Maintain the ice water temperature between 3 – 5°C.	• Minimum 2 min intervention required for moderate perturbation in BP • Trivial body movement/motion artifacts • Sensitive towards individual pain threshold and pain tolerance
Treadmill-running exercise 	Run on a treadmill for 7 – 10 min. Start with a low speed of 3 km/h, and increase the speed at a steady rate (maximum up to 10 km/h).	• Significant variation in SBP and heartrate • Maintain heartrate < 85% of (220 – Age) • Prone to body movement/motion artifacts during the intervention period • High breathing artifacts during post-intervention recovery period
Mental arithmetic 	Perform serial subtraction of a two-digit number from a four-digit number quickly and repetitively for 4 – 5 min.	• Recreation of real-life stressful situation • Trivial body movement/motion artifacts • Variations in BP may not be observed when the participant is an experienced public speaker or intellectually sound in mathematics
Leg-raise test 	By adopting the supine posture, raise and hold one leg without any support, for 2 – 3 min.	• Moderate variation in BP parameters and heartrate • Post-test BP recovery time < 1 min • Minimal body movement/motion artifacts • Not recommend in patients with sciatica
Sustained handgrip test 	Hold and clench handles of the spring-type handgrip in both the hands by putting in maximum effort for a sustained time until fatigued.	• Substantial variation in BP parameters and heartrate • Minimal body movement/motion artifacts • Strength deficit of the muscles associated with variation BP level

and heartrate (baseline values) of each subject were measured for 2 – 3 min. After the baseline measurement, the participants underwent a BP perturbing intervention task (protocols are summarized in the tab. 1), followed by a recovery phase, in which they rested until BP and heartrate returned to the baseline value or remained in steady level. It was preferred to conduct only one intervention task per day for an individual subject. This helped to investigate the physiological response and cardiovascular reactivity of each intervention independently.

Results and Discussion

Intervention Characteristic Curve for BP Variation

For each subject, the recorded brachial SBP, DBP, MAP, and heartrate were analyzed and compared in order to characterize the BP altering strategies of preferred interventions. The average time interval between two consecutive BP measurement was approximately 42 s, which is the time taken by the BP monitor to inflate, deflate, and report the measured values. The obtained discrete readings of each BP parameter was interpolated onto their successive readings to produce continuous curves showing the locus of instantaneous variation in BP parameters.

This interpolation allowed characterization of BP variation due to an external intervention.

Fig. 1 depicts typical intervention characteristic curve illustrating variation in BP level during the course of study, under increasing BP conditions. This projected curve was obtained by generalizing data recorded during the present study over all the subjects. However, an intervention characteristic curve for each BP parameter is subject-specific. As shown in fig. 1, the fiducial parameters of BP intervention characteristic curve were defined with re-

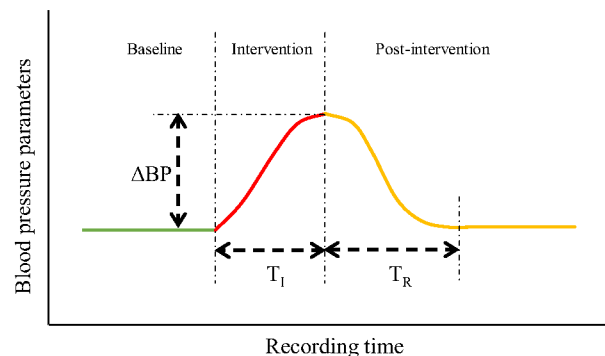


Figure 1: Typical BP intervention characteristic curve

spect to initial baseline and post-intervention measurements. The total time taken to perform an intervention task as per the protocol (tab. 1) is denoted as the intervention period (T_I). The post-intervention recovery period (T_R) is defined as the time taken to regain initial baseline values or a steady BP level after finishing an intervention task. The maximum increment yielded in the BP level from its baseline value is expressed as an absolute change (ΔBP), this quantitative metric for SBP, DBP and MAP are ΔP_S , ΔP_D , and ΔP_M respectively. Similarly, the maximum variation in heartrate (with respect to baseline heartrate) during the intervention task is denoted as ΔHR .

The proposed fiducial parameters were evaluated separately for all five interventions to investigate their individual effect. Representative characteristic curves (obtained from a subject with age = 17 years and body mass index = 24 kg/m^2) demonstrating the variations in BP parameters and heartrate during all five interventions has been presented in fig. 2. It may be noted that the treadmill-running exercise is subject to significant body movement and motion artifacts. As a consequence, measurements recorded while performing the treadmill-running task were not reliable, and hence those data points were removed from its characteristic curves.

Hemodynamic Variation due to External Intervention

All five interventions included in this study are known to increase BP parameters, however, the induced variations and post-intervention recovery are caused by the different physiological phenomenon. The proposed fiducial parameters defining hemodynamic variations due to external interventions have been summarized in fig. 3 using box-and-whisker diagrams pooled over all the subjects. The absolute values of T_I were limited by pre-defined study protocol as per the nature of interventions, however, the

absolute T_R values depended on physiological response and cardiovascular reactivity to an intervention task. Absolute T_R for each BP parameter was comparable ($< 5\%$ variation), and hence an average T_R has been depicted in fig. 3. Due to elaborated T_I and severity of the treadmill-running task, its mean T_R was higher (4.2 min) than the corresponding metrics offered by other intervention tasks. Both the leg-raise and sustained handgrip tests (means of $T_R = 0.6 \text{ min}$ and 0.9 min respectively) yielded rapid post-intervention recovery from the elevated BP level.

It may be observed from the box-and-whisker diagrams that the cold pressor test yielded a moderate increment in all BP parameters (mean values of $\Delta P_S = 22.5 \text{ mmHg}$, $\Delta P_D = 16.7 \text{ mmHg}$ and $\Delta P_M = 18 \text{ mmHg}$). These BP variations are mediated by a sudden increase in the peripheral vascular resistance due to vasoconstriction, the underlying mechanism being the autonomic neural pathways acting via sympathetic nervous system [5]. Cardiac output and heartrate typically increase during aerobic exercise like running on a treadmill, which leads to a significant increment in SBP (mean values of $\Delta P_S = 37.6 \text{ mmHg}$ and $\Delta HR = 67.2 \text{ bpm}$) with a moderate variation in DBP level (mean $\Delta P_D = 14.4 \text{ mmHg}$) during the post-exercise recovery period. However, in physical tasks such as sustained handgrip test, the static contraction of muscles against fixed mechanical spring load causes a marked increase in all the BP parameters with a relatively small heartrate variability [6]. The presented study also demonstrated substantial variation in the BP parameters (means values of $\Delta P_S = 28.5 \text{ mmHg}$, $\Delta P_D = 26.7 \text{ mmHg}$ and $\Delta P_M = 26.5 \text{ mmHg}$) with a mean heartrate increment of 17.6 bpm during the sustained handgrip test.

Consistent with the physiological theory, a moderate increment in SBP, DBP, and MAP was observed during the

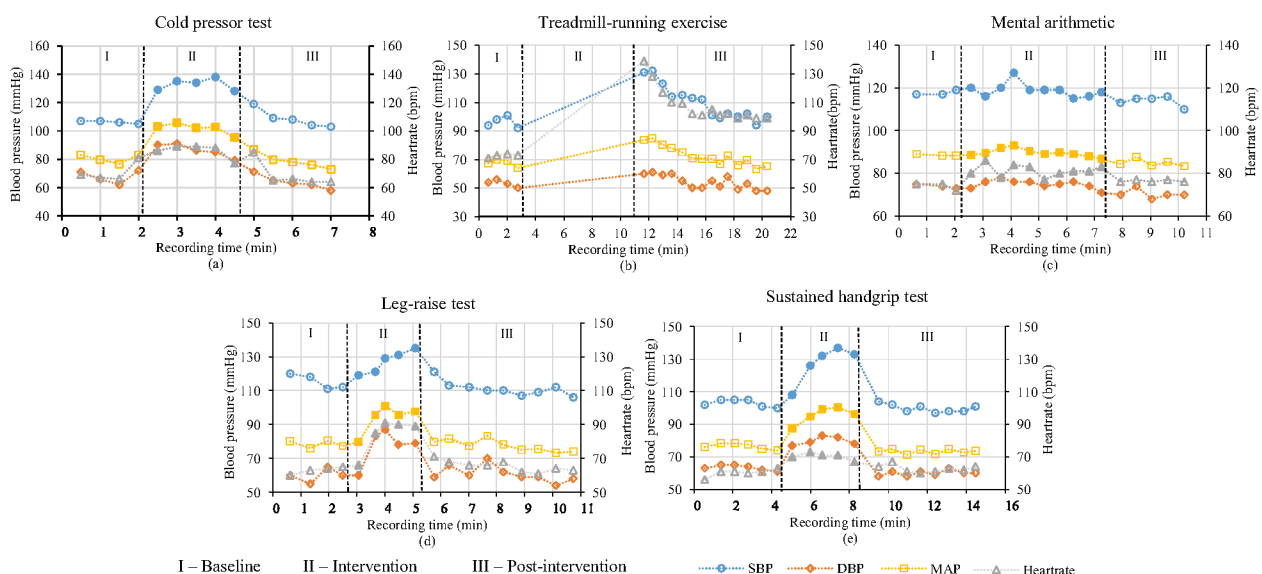


Figure 2: Subject-specific intervention characteristic curves obtained from a particular subject, illustrating the variation in SBP, DBP, MAP and heartrate during (a) cold pressor test, (b) treadmill-running exercise, (c) mental arithmetic, (d) leg-raise test, and (e) sustained handgrip test

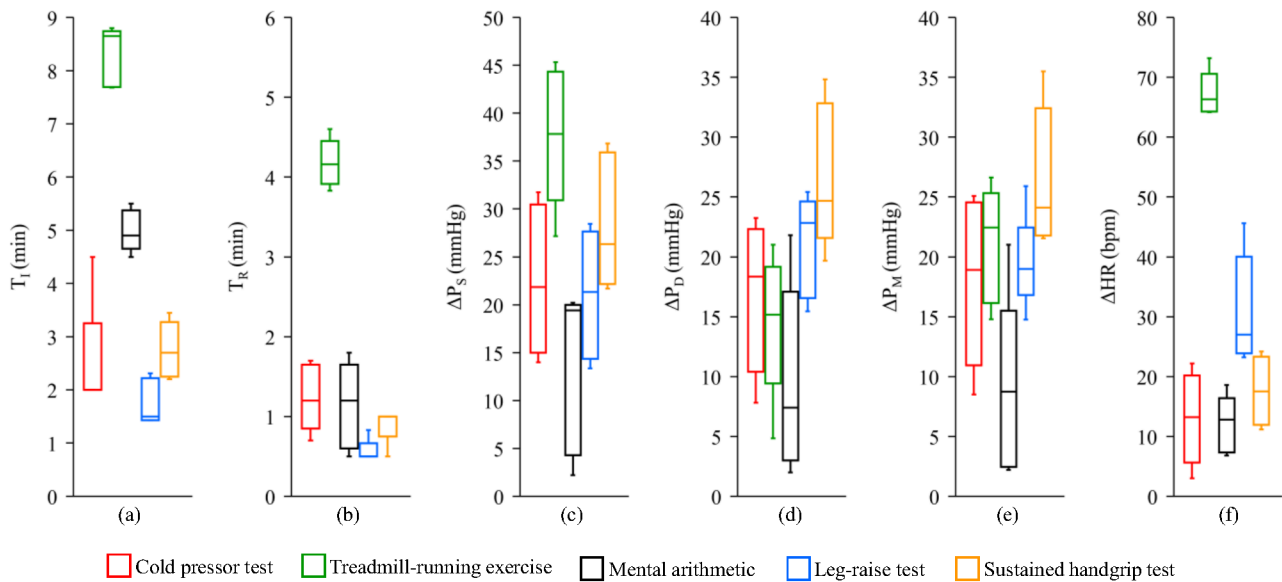


Figure 3: Box-and-whisker plots illustrating the measured fiducial parameters (a) T_I , (b) T_R , (c) ΔP_S , (d) ΔP_D , (e) ΔP_M , and (f) ΔHR pooled over all the subjects

active leg-raise test (mean values of $\Delta P_S = 21.1$ mmHg, $\Delta P_D = 21$ mmHg and $\Delta P_M = 19.5$ mmHg). These variations are induced when a subject is performing a voluntary leg-raise the lowered perfusion pressure to the sustained contracting leg muscles is being compensated with an increase in cardiac output and BP, acting via the central pressor response [7]. Hemodynamic variations observed during the mental arithmetic test were idiosyncratic and prone to psychological reactions. Short-term changes in BP parameters were observed for the recruited subjects during the mental arithmetic test due to increase in sympathetic activity and dumping of baroreflex. Mean values of ΔP_S , ΔP_D , and ΔP_M obtained from the mental arithmetic test were 13.6 mmHg, 9.5 mmHg and 8.9 mmHg respectively. Heart rate variations were also not prominent (mean $\Delta HR = 12$ bpm) during the mental arithmetic test in the recruited normotensive subjects.

Conclusions

This study demonstrated five hemodynamic interventions that perturb resting BP level in a safe and controlled manner. During the study, the BP parameters were found to vary at different levels in accordance with the physiological response, which mimics daily life activities of an individual. For each subject, brachial SBP, DBP, MAP, and heart rate were measured from three phases: baseline, during the intervention and post-intervention recovery period. BP altering strategies of the preferred interventions were evaluated using the proposed BP intervention characteristic curve and fiducial parameters. The treadmill-running exercise found to induce significant variations in SBP and heart rate. However, the measurements were susceptible to motion and breathing artifacts. A moderate variation in all BP parameters was observed during the cold pressor test, where no physical movements were in-

involved. Therefore, the cold pressor test may be a recommendable method for acquiring physiological signals under varying BP conditions with minimum error due to motion and breathing artifacts. Further validation study in a large population is in progress, in which BP and BP-dependent physiological parameters are recorded in a beat-by-beat manner during multiple interventions. Data recorded from such extensive studies can be used for developing BP prediction models through data-driven methods such as machine learning. Such models can be potentially used in wearable devices and cuffless 24-hour ambulatory BP monitors.

References

- [1] X. -R. Ding et al. Continuous blood pressure measurement from invasive to unobtrusive: celebration of 200th birth anniversary of Carl Ludwig. *IEEE J Biomed Health Inform*, 20(6):1455–465, 2016.
- [2] R. Mukkamala et al. Toward ubiquitous blood pressure monitoring via pulse transit time: theory and practice. *IEEE Trans Biomed Eng*, 62(8):1879–1901, 2015.
- [3] P. M. Nabeel el al. Single-source PPG-based local pulse wave velocity measurement: a potential cuffless blood pressure estimation technique. *Physiol Meas*, 38(12):2122–2140, 2017.
- [4] C. C. Young et al. Clinical evaluation of continuous noninvasive blood pressure monitoring: accuracy and tracking capabilities. *J Clin Monit*, 11(4):245–252, 1995.
- [5] M. J. Joyner et al. Sympathetic nervous system and blood pressure in humans: individualized patterns of regulation and their implications. *Hypertension*, 56(1):10–16, 2010.
- [6] R. Garg et al. The isometric handgrip exercise as a test for unmasking hypertension in the offsprings of hypertensive parents. *J Clin Diagn Res*, 7(6):996–999, 2013.
- [7] B. L. Luu et al. Blood pressure and the contractility of a human leg muscle. *J Physiol*, 591(21):5401–5412, 2013.

Non-Invasive Assessment of Arterial Incremental Elastic Modulus Variations within a Cardiac Cycle

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Introduction

Non-invasive assessment of arterial elastic properties is of high interest in cardiovascular research and screening of the vascular health. Over the last decades, a great emphasis has been placed on quantifying arterial stiffness, and its pathological significance is asserted in various epidemiological studies [1]. Typically used arterial elastic indices such as distensibility coefficient (DC), compliance coefficient (CC), and Peterson modulus (E_P) provide the measure of the functional stiffness of the artery. On the other hand incremental Young's elastic modulus (E_{inc}) quantifies material or intrinsic stiffness and hence properly characterizes the non-linear elastic behavior of the artery [2]. It has been recently demonstrated that the standard deviation in E_{inc} is an independent biomarker of coronary heart diseases [3]. The absolute value of E_{inc} varies within a cardiac cycle during diastolic to systolic phase. Accurate evaluation of these variations can be potentially used to quantify the degree of non-linearity in the elastic properties of an arterial section. Further, these variations can form a basis for tracking the variation in pulse wave velocity over the cardiac cycle [4], and cuffless evaluation of arterial blood pressure (BP) parameters without any calibration procedure [5].

Accurate evaluation of E_{inc} of a particular artery requires a local evaluation of arterial dimensions (diameter, wall thickness, distension) and transmural pressure simultaneously. High fidelity pressure and diameter waveforms are a mandate to efficiently track the variation of the E_{inc} over a cardiac cycle. State of the art techniques use B-mode or M-mode ultrasound modalities for estimation of arterial wall thickness and diameter waveforms [6, 7]. Local pressure waveforms required for the evaluation of E_{inc} are typically obtained using applanation tonometric transducers. However, for simultaneous acquisition of diameter and pressure waveforms using such modalities are prone to practical limitations due to the design form factor of the probes [8]. Further, the waveforms can be subject to inherent phase delays due to (i) the acquisition of the desired waveforms from two distinct arterial sites separated by a significant distance, and (ii) the lack of time synchronization between the acquisition modules of pressure and diameter waveforms. The devices realized using the aforementioned technique have not gained widespread applicability for large population screening due to the necessity of skilled operator and portability issues.

In this work, we propose a non-invasive measurement system for the evaluation of E_{inc} and its variation over a cardiac cycle in a beat-by-beat manner. The system uses a novel custom-designed probe which includes a single element ultrasound transducer and a tonometer for simultaneous measurement of arterial wall thickness, diameter, and pressure waveforms. The probe design was optimized to ensure that the measurements were localized over a small arterial segment, resembling single-site measurement. Online evaluation of the desired arterial dimensions without an ultrasound image was performed using our clinically validated ARTSENS[®] technology [9, 10]. The developed prototype system was experimentally validated by an *in-vivo* study of 10 subjects. The systolic and diastolic E_{inc} were evaluated from the left common carotid artery (LCCA). The proposed measurement system architecture, validation study protocol, results, and observations are discussed in the following sections.

Principle of E_{inc} Evaluation

The circumferential stress (σ) of an elastic artery with wall thickness (h) is developed due to the tension (T) acting on the arterial walls against the internal distending pressure (P), is given as in (1).

$$\sigma = \frac{T}{h} \quad (1)$$

Where, T is related to end-diastolic diameter (D_d) according to the Laplace law by considering thin wall assumption ($D_d \gg h$), which can be expressed as in (2).

$$T = \frac{P D_d}{2} \quad (2)$$

Using (1) and (2) the incremental stress ($d\sigma$) along the circumference due to a small increment in pressure (dP) can be obtained as follows;

$$d\sigma = \frac{dP D_d}{2h} \quad (3)$$

The resultant incremental circumferential strain ($d\epsilon$) due to the stress on the arterial walls can be expressed in terms of change in luminal diameter (dD) and D_d as in (4).

$$d\epsilon = \frac{dD}{D_d} \quad (4)$$

Further, E_{inc} can be evaluated as the ratio of $d\sigma$ and $d\epsilon$ and can be obtained by dividing (3) and (4), which can be expressed as is given in (5).

$$E_{inc} = \frac{D_d^2 dP}{2h dD} \quad (5)$$

Measurement System

Ultrasound-Pressure Probe Design

An application specific probe was designed and developed to facilitate simultaneous measurement of arterial dimensions and pressure from a small arterial section. The probe incorporates a single element ultrasound transducer (diameter = 5 mm, center-frequency 5 MHz, spatial half angle $< 1.3^\circ$) for tracking the dynamics of arterial dimensions, and a commercially available tonometer (SPT-301 – Millar Instrument) for capturing arterial pressure waveforms. A custom probe enclosure (probe holder) was 3D printed to integrate the ultrasound and tonometer transducers. Design schematic and assembly of the proposed ultrasound-pressure probe has been depicted in fig. 1. The separation between the transducers was kept minimal (2 mm) to perform a reliable single-site measurement.

Data Acquisition Hardware

The design architecture of the signal acquisition hardware is illustrated in fig. 2. The ultrasound transducer was interfaced to a dedicated analog front end (AFE) of the ARTSENS[®] device. The AFE consists of high-voltage pulse generation circuitry and a pulser-receiver module for operating the ultrasound transducer in pulse-echo mode. A high-speed digital input-output card (NI PXIe 6556 – National Instruments) was employed for controlling the pulser-receiver module. The ultrasound transducer was insonated to obtain an A-scan of 40 mm depth. The received A-scan radio-frequency (RF) frames were pre-conditioned using a 40 dB dual stage amplifier, and then digitized using a high-speed digitizer (NI PXI 5154 – National Instruments, sampling rate = 50 MHz). The hardware was configured to achieve a high frame rate of 1 kHz. The tonometer used for acquiring pressure signal was interfaced to ADInstruments' PowerLab and BrigdAmp, controlled using LabChart software. The pre-processed pressure waveform from the BridgeAmp was

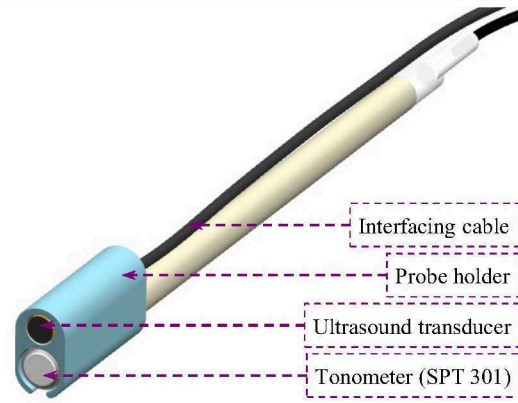


Figure 1: Proposed ultrasound-tonometer probe assembly digitized using a data acquisition card (DAQ; NI PXIe 6368 – National Instruments) at a sampling rate of 1 kHz. A digital trigger pulse (1 kHz pulse repetition rate) generated by NI PXIe 6556 was used for the synchronized acquisition of RF frames and pressure waveform from the independent hardware modules.

Signal Processing and Measurement Software

Simultaneously acquired pressure signal and RF echo frames were processed in the digital domain using dedicated semi-automated software developed on National Instruments' LabVIEW platform. The measurement software architecture has been depicted in fig. 2. The acquired RF frames were processed using intelligent algorithms of the ARTSENS[®] technology. The arterial proximal and distal walls were automatically identified and the wall motion was tracked using a correlation based technique [9]. High fidelity diameter waveform was captured using the software, and the end-diastolic diameter (D_d) and distension (ΔD) were obtained over continuous cardiac cycles. For reliable evaluation of h , distal wall echo was chosen and the measurement was done between the leading edges of the intima and adventitia. The discontinuities in the linearity of the unwrapped phase of the dis-

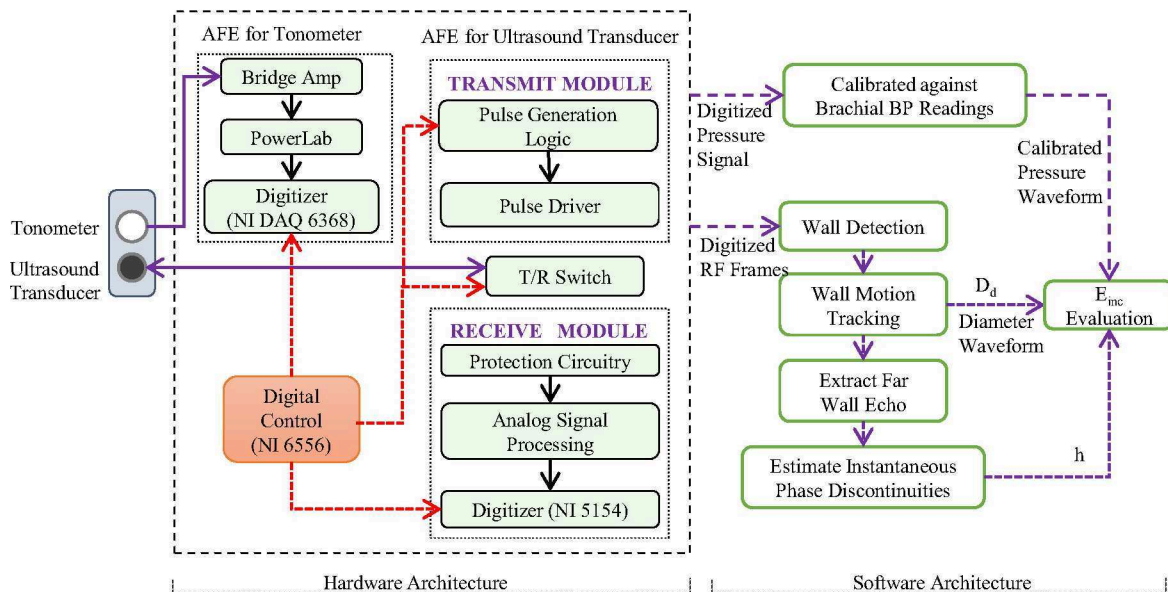


Figure 2: Schematic diagram illustrating the hardware and software architecture of the proposed measurement system

tal wall echo were used to find the leading edges of the intima and adventitia complex and estimate h [11]. The acquired raw tonometer pressure signal was filtered with a low-pass filter of 15 Hz cutoff frequency to remove high-frequency noise. The processed pressure signal was then calibrated against the measured brachial BP, considering end diastolic and mean arterial pressure to be approximately constant throughout the arterial tree when the subject is in supine posture.

For each cardiac cycle, the pressure-diameter loop (PD loop) was obtained by plotting diameter cycle along the abscissa and pressure cycle along the ordinate. For the investigation of variation in E_{inc} two fiducial points were defined; (i) second derivative maxima of the pressure cycle, a point (Ψ_d) at the neighborhood of end-diastolic point, and (ii) second derivative minima of the pressure cycle, a point (Ψ_s) at the neighborhood of systolic peak. Slope of the PD loop at these two points ($(dP/dD)|_{\Psi_d}$ and $(dP/dD)|_{\Psi_s}$ along with D_d and h were used for the estimation of E_{inc} at the Ψ_d and Ψ_s (E_{Ψ_d} , E_{Ψ_s} respectively) with the help of (5).

In-vivo Validation Study

Subject Selection for In-Vivo Validation

An *in-vivo* study was conducted on 10 healthy subjects to validate the functionality of the proposed ultrasound-pressure probe and the associated measurement system. The subjects recruited for the study were within 20 to 30 years of age (mean age = 25.6 ± 2.6 years).

Study Protocol

A written informed consent was obtained from the recruited subjects after briefing them the study objectives and the measurement protocol. Anthropometric measurements were performed and the subject was asked to relax for 5 minutes. The measurement of brachial BP and E_{inc} from the LCCA were performed by a single operator with subjects in supine posture. Clinical grade automatic BP monitor (SunTech® 247™ – SunTech Medical) was used to record the brachial BP parameters. The ultrasound-pressure probe was then placed on the left side of the neck, 2 cm below the carotid bulb to target the carotid artery. The probe was oriented to achieve good quality RF frames (with two strong echoes from the proximal and distal wall) and high fidelity pressure waveform. The probe was held steady and the signals were recorded continuously for a sufficient number of cardiac cycles.

Results and Discussion

Reliability of Continuous Signal Acquisition

The ultrasound-pressure probe and the prototype system developed for the evaluation of E_{inc} variation over the cardiac cycle demonstrated the expected functionality. The system could efficiently capture diameter and pressure variations over continuous cardiac cycles. A cycle of

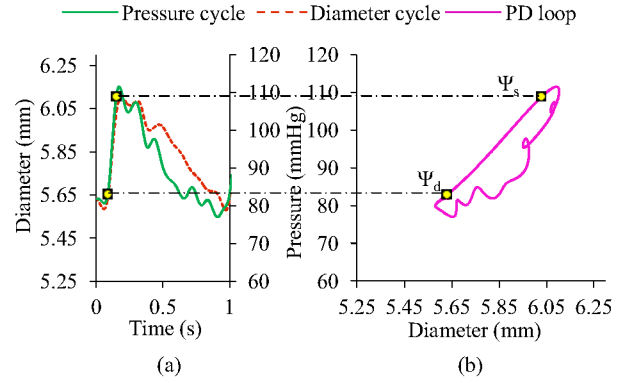


Figure 3: (a) A sample of simultaneously acquired pressure and diameter cycle from the LCCA, (b) Illustrating the construction of PD loop, the defined fiducial points are marked on the loop

Table 1: D_d , h , E_{Ψ_s} , and E_{Ψ_d} measured from the subjects

Subject ID	Age	D_d (mm)	h (mm)	E_{Ψ_s} (kPa)	E_{Ψ_d} (kPa)
P01	27	5.29 ± 0.08	0.72 ± 0.01	297.56 ± 5.17	167.58 ± 2.98
P02	24	5.76 ± 0.15	0.59 ± 0.03	372.50 ± 15.01	266.76 ± 11.80
P03	22	5.60 ± 0.09	0.53 ± 0.03	260.06 ± 13.9	179.80 ± 9.90
P04	27	6.07 ± 0.17	0.65 ± 0.02	255.43 ± 8.76	202.07 ± 7.60
P05	26	5.08 ± 0.16	0.55 ± 0.02	185.59 ± 7.12	133.62 ± 3.52
P06	28	5.49 ± 0.05	0.61 ± 0.03	158.45 ± 8.55	123.39 ± 6.43
P07	29	4.29 ± 0.08	0.37 ± 0.02	188.52 ± 6.24	143.79 ± 7.85
P08	22	6.01 ± 0.19	0.70 ± 0.01	440.92 ± 20.34	373.67 ± 16.33
P09	23	5.44 ± 0.17	0.46 ± 0.02	174.54 ± 11.51	156.29 ± 9.06
P10	28	5.52 ± 0.08	0.62 ± 0.04	150.76 ± 9.38	119.23 ± 6.76

both the diameter and pressure waveform obtained from a particular subject have been shown in fig. 3(a). It may be noted that the pressure and diameter waveforms follow a similar trend and are clearly correlated. Similar quality signals were captured from all other subjects. The temporal resolution of the pressure and diameter variations was 1 ms, enabling construction of high-resolution cycle-to-cycle PD loops. A PD loop obtained from the diameter and pressure cycle shown in fig. 3(a), is illustrated in fig. 3(b), and the fiducial points Ψ_s and Ψ_d are marked on it. It was observed that the slope of all the PD loops at Ψ_s is steeper than the slope at the Ψ_d , and increases nonlinearly from fiducial point Ψ_d to fiducial point Ψ_s exhibiting a non-linear stress strain relationship. The quality of the acquired signals and the PD loops were sufficient for reliable calculation of E_{Ψ_s} , and E_{Ψ_d} .

Variation of E_{inc} over a Cardiac Cycle

The measurements of D_d , h , E_{Ψ_s} , and E_{Ψ_d} were obtained from the subjects in a beat-by-beat manner. The beat-to-beat estimates of these parameters for a particular subject have been shown in fig. 4 (a) – (c). The measurement repeatability was evaluated by calculating the beat-to-beat variation – standard deviation (SD) to mean ratio of a finite number of cycles, expressed in percentage. Beat-to-beat variation observed for D_d , h , E_{Ψ_s} , and E_{Ψ_d} were less than 4%, 7.5%, 7%, and 7% respectively, indicating the reliability of measurements. E_{Ψ_s} , and E_{Ψ_d} obtained from

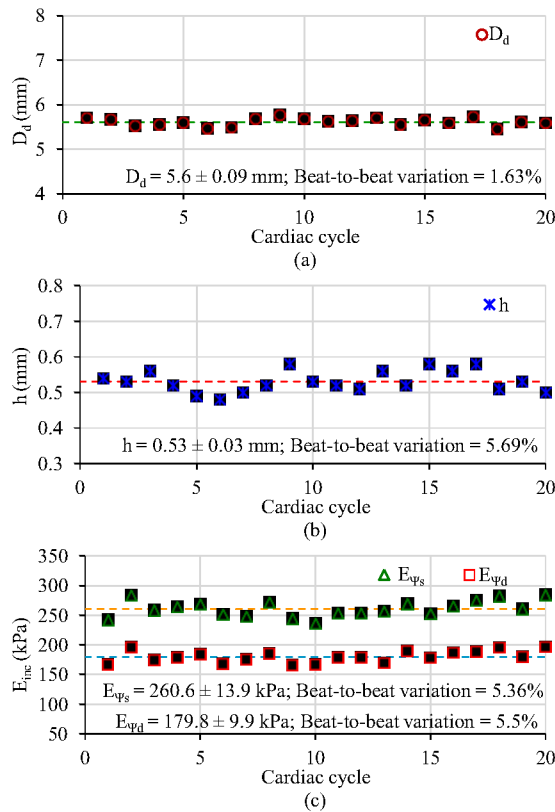


Figure 4: Beat-by-beat variations of (a) D_d (b) h (c) E_{inc} obtained from the LCCA for a particular subject

the recruited subjects are summarized in tab. 1, (values expressed as mean $\pm$ SD). The obtained values of E_{inc} concur with studies reported earlier [12]. A statistically significant ($p < 0.001$) variation between E_{ψ_s} and E_{ψ_d} was observed in all subjects over continuous cardiac cycles. Consistent with theory, the absolute values of E_{ψ_s} was greater than E_{ψ_d} . This indicates that the elastic characteristics of an arterial segment are not constant, which otherwise vary over the cardiac cycle as a function of distending arterial pressure.

Limitations of the Present Study

The validation study was conducted only on a small group of normotensive subjects. An extensive clinical study on a large population including hypo and hypertensive subjects is required to further validate the proposed technique. Simultaneous evaluation of beat-by-beat E_{ψ_s} and E_{ψ_d} using ultrasound-pressure probe of the proposed system and a reference ultrasound imaging system was not practically viable.

Conclusions

A non-invasive measurement system for the evaluation of E_{inc} and its variation over the cardiac cycle in a beat-by-beat manner was presented. A novel ultrasound-pressure probe was designed and developed for the simultaneous capturing of high fidelity diameter and pressure waveforms from the carotid artery. PD loops obtained from these waveforms exhibited a non-linear pressure-diameter

relationship. Beat-by-beat evaluation of arterial dimensions was performed using application-specific measurement software. E_{inc} at two distinct fiducial points in the neighborhood of systolic peak and end-diastolic region (E_{ψ_s} and E_{ψ_d}) were obtained from the recorded h , D_d measurements and PD loop. The functionality of the developed prototype system was validated by conducting an *in-vivo* study on 10 subjects. Observed beat-to-beat variation in D_d ($< 4\%$), h ($< 7.5\%$), E_{ψ_s} ($< 7\%$) and E_{ψ_d} ($< 7\%$) were in the acceptable range, indicating the reliability of the measurements. The absolute values of E_{ψ_s} were greater than E_{ψ_d} in all recruited subjects and showed a significant variation ($p < 0.001$), which was consistent with the theory. The present study results have demonstrated that the proposed system can reliably assess E_{inc} and its variation within a cardiac cycle in a non-invasive manner, which can be potentially used for the screening of various cardiovascular events. Further efforts are needed to translate the prototype system to a portable hand-held device with integrated ultrasound-pressure transducer in-order to make it to clinical practice for cardiovascular screening.

References

- [1] S. Laurent et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications. *Eur Heart J*, 27(21):2588–2605, 2006.
- [2] R. E. Shadwick. Mechanical design in arteries. *J Exp Biol*. 202(23):3305–3313, 1999.
- [3] L. Niu et al. Standard deviation of carotid young's modulus and presence or absence of plaque improves prediction of coronary heart disease risk. *Clin Physiol Funct Imaging*, 37(6):682–687, 2017.
- [4] A. Avolio. Arterial Stiffness. *Pulse*, 1(1):14–28, 2013.
- [5] J. Joseph et al. Method and system for cuff-less blood pressure (BP) measurement of a subject. US Patent US20170156706 A1, 2017.
- [6] A. P. Hoeks et al. Assessment of the distensibility of superficial arteries. *Ultrasound Med Biol*, 16(2):121–128, 1990.
- [7] F. Molinari et al. A state of the art review on intima-media thickness (IMT) measurement and wall segmentation techniques for carotid ultrasound. *Comput Methods Programs Biomed*, 100(3):201–221, 2010.
- [8] A. P. Hoeks et al. Effects of assessment and processing techniques on the shape of arterial pressure-distension loops. *J Vasc Res*, 37(6):494–500, 2000.
- [9] A. K. Sahani et al. Automatic measurement of end-diastolic arterial lumen diameter in ARTSENS. *J. Med. Devices*, 9(4):1-11, 2015.
- [10] J. Joseph, et al. Technical Validation of ARTSENS—An Image Free Device for Evaluation of Vascular Stiffness. *IEEE J Transl Eng Health Med*, 3:1–13, 2015.
- [11] V. K. Raj et al. An image-free ultrasound method to estimate artery wall thickness surrogate for screening. In *MeMeA 2017*, pages 326–33. IEEE Rochester, May 2017.
- [12] E. Urbina et al. Correlates of carotid artery stiffness in young adults: The Bogalusa Heart Study. *Atherosclerosis*, 176(1):157–164, 2004.

The patterning of biostructures with carbon nanoframe in protein matrix

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Introduction

The creation of three-dimensional frame materials is an urgent task for various fields, from biomedicine to emissive electronics. Creation of carbon nanotubes (CNTs) frame with strong heating by laser irradiation has been described [1]. The heating provides the connection of single-walled nanotubes to each other in defective areas of the carbon's structure. The purpose of this paper is to describe the mechanism of carbon nanotubes patterning under laser irradiation in a protein matrix to create a nanomaterial for tissue-engineering. To understand the nature of the nanotubes patterning in the frame, we considered the features of the interaction of defective regions and open ends of CNTs with laser radiation in the UV-visible-IR range. Defective areas inefficiently divert heat, so with a general heating of the nanostructure, these areas overheat more noticeably and can eventually collapse [2, 3]. Patterning of biostructures with a carbon nanoframe in protein matrix under the influence of pulsed laser radiation was studied. It was also experimentally confirmed that laser pulse of nanosecond duration has a structuring effect on an array of CNTs. These biostructures with a carbon nanoframe in protein matrix can be used as bulk biomaterials for restoration of defects in damaged tissues, due to their ability to enhance cell proliferation and tissue regeneration [4 - 6].

Materials and Methods

If we consider the energy absorption in the case of a normal incidence of a plane electromagnetic wave, then it is possible to calculate the absorption coefficient. Maxwell's theory and the quantum-mechanical approach are used in this case. The nanotube array acts as the interface between the two media. Both media are vacuum. We consider the process of interaction of a network of nanotubes with an incident wave that passes from vacuum through a network of nanotubes to vacuum again. We considered waves with a vector E directed along the nanotube axis and perpendicular to it. The absorption coefficient was determined by the formula:

$$A = 1 - |R|^2 - |T|^2, \quad (1)$$

where $|R|^2$ and $|T|^2$ are the squares of the modules of complex reflection and transmission coefficients. We have

taken the most frequently synthesized single-walled carbon nanotubes such as armchair and zigzag. Their diameter was 0.7 - 3 nm. We investigated nanotubes with defects of 1V type (one vacancy of the carbon atom), 2V (two vacancies of carbon atoms), SW (defect of the connection rotation) and mixed type 1V + SW. Nanotubes with open ends were also investigated. Laser radiation was considered in the wavelength range of 0.01-2 μm . Carbon nanotubes absorb energy depending on the chirality and polarization of the wave.

Based on the results of the study of the absorption of laser beam energy by defective parts of CNTs, we carried out a series of numerical experiments of the binding of nanotubes in an aqueous solution. In an aqueous solution, nanotubes can move relatively freely. The process of binding of two nanotubes with defects of 2V, 1V, SW and SW + 1V types was simulated. These defects, as it was shown above, allow the defective sections to absorb energy by $\sim 50\%$ more at a certain wavelength. Numerical experiments were carried out by the method of molecular dynamics using adaptive intermolecular reactive empirical bond order potential to describe the behavior of defect-free nanotube regions and the environment and the self-consistent charge density functional tightbinding method, which describes the appearance of covalent bonds between tubes. The simulation step was 0.1 fs.

For the experimental studies, we used single-walled nanotubes, which were synthesized by an electric arc method on a Ni-Y catalyst. They were further purified in air with washing in HCl and carboxylated in a mixture of $\text{HNO}_3 / \text{H}_2\text{SO}_4$, then washed with water until neutral reaction. Analysis of the results of Raman spectroscopy showed that the average diameter of CNTs was 1.8 ± 0.2 nm, and that there were defective structures in the array of tubes. As the protein matrix, an aqueous solution of albumin and collagen was used. For the patterning of protein biostructures with a carbon nanoframe, a Ti: Sa femtosecond laser of 810 nm with a pulse duration of 140 fs and a repetition rate of 80 MHz was selected.

In addition, the experimental studies of the interaction of pulsed laser radiation with an array of carbon nanotubes grown on a silicon substrate were carried out. The sample was located perpendicular to the laser beam at the lens focus $F=10$ cm. CNTs were grown by PE-CVD method with Ni-Ti (10/2 nm) catalyst in C_2H_2 , Ar and NH_3 at

mosphere and temperature of 550 °C. Nanotubes in array have average diameter of 40-50 nm and the length of 7.3-7.6 μm .

The source of laser radiation was a solid-state pulsed Nd:YAG laser with wavelength of 1064 nm and a pulse duration of 16 ns. The pulse energy of Nd:YAG laser depended on the optical pumping energy of the active element Nd:YAG and was controlled directly by the laser control unit. Leaving the laser, the beam hit the prism of Glan, transforming radiation with arbitrary polarization into a linearly polarized, parallelly regulating the energy of the beam with a given step. The pulse energy varied in the range of 1.21-4.158 μJ . The energy density of the pulse was in the range of 0.4-2.2 J / cm^2 . After leaving the Glan prism, the laser beam hit the wedge-shaped quartz prism, reflected from it (the energy of the reflected beam was $\sim 10\%$ of the original beam) and hit the energy meter based on the Ophir PD-10 sensor. The action was effected by single laser pulses at different areas of the sample.

Results

We performed one modeling experiment for 1V, 2V and 1V + SW defects single-walled carbon nanotubes. Using the finite-difference time-domain method we obtained the patterns of the distribution of the electromagnetic field's magnitude E over the volume of carbon nanotubes. Fig. 1a shows the maximum values of the intensity E , which are indicated in red. The distribution of temperature along the tube was initially uneven, taking into account the inhomogeneous absorption of the electromagnetic wave's

energy. In the defect area, the temperature was maintained at 50% more than in ideal sections of the tube. One of the results of the binding of nanotubes (12,12) with one 2V defect in each tube, perpendicular to each other is shown in Fig. 1b-d. The unevenness of temperature distribution during nanotubes binding is shown in Fig. 1b. The maximum values of the temperature (1600-1700 K) correspond directly to the close region to the 2V defect.

The distance between the nearest tubes in the solution was in the range of 3.2 to 4 Å. The binding time was determined by many factors, including the distance between the tubes. Figure 1d shows the atomic structure of the tubes when four stable bonds were formed.

We have established that uneven temperature heating leads to the formation of covalent bonds between the tubes even at an initial distance above 3.2 Å. We performed a numerical experiment that described the interactions of two nanotubes (12,12) with defects of 2V type. The change of energy during the formation of bonds in time (within 8 ps) varied in the range -7.43 – 7.36 eV / atom.

Fig. 2 shows an image of scanning electron microscopy of a nanoframe structured by laser radiation from carbon nanotubes in a protein matrix. The sample was located on a conducting silicon substrate and split in the center. Fig. 2 shows a branched tree-like structure of single-walled carbon nanotubes. Laser structuring and the formation of a branched framework under the action of covalent bonding are confirmed by high values of the nanohardness of the material ~ 300 MPa.

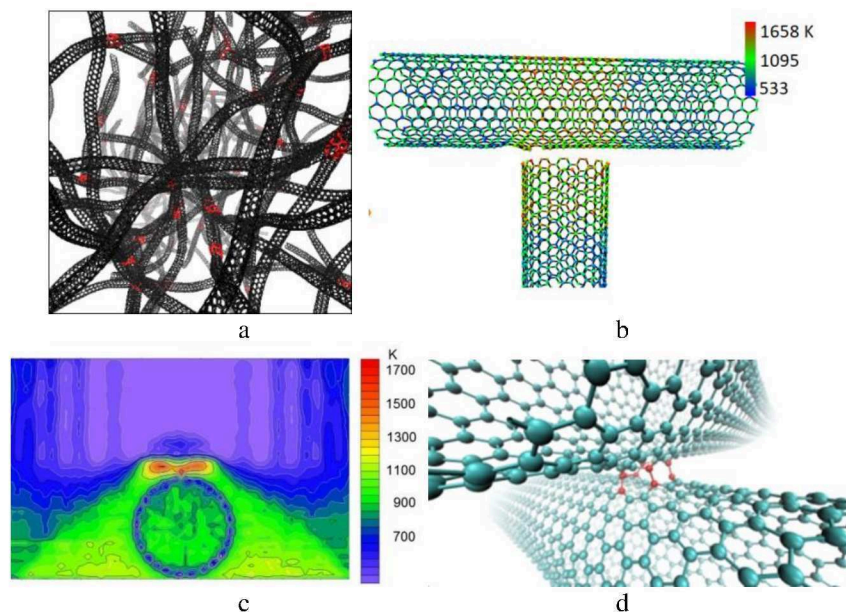


Figure 1: Binding of nanotubes into a carbon nanoframe (a shows the distribution of the maxima of the laser radiation electromagnetic field, b shows the uneven distribution of temperature in the tubes caused by uneven absorption of the energy of the incident laser radiation, c shows the temperature field near the nanotubes contact after cessation of laser irradiation, d shows the process of covalent bonds formation)

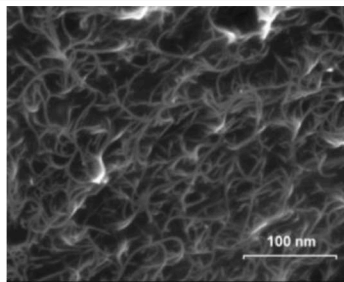


Figure 2: SEM image of a biostructure with a carbon framework in a protein matrix

The study of the CNTs before and after interaction with laser radiation was carried out using scanning electron microscopy (Fig. 3).

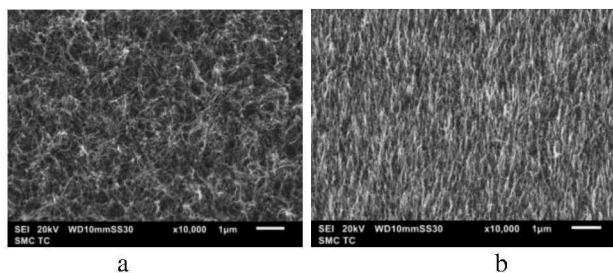


Figure 3: SEM image of a CNTs array before (a) and after (b) laser irradiation with energy of 180.4 μ J

The dependence of the alignment degree of the carbon nanotubes array on the energy of the laser pulse was observed. At energies of less than 100 μ J, the alignment effect was practically not observed. At an energy of 135 μ J, an alignment effect began, which reached a maximum at 180 μ J, and then decreased. At energies above 200 μ J, thinning of carbon nanotubes was observed, as well as partial destruction of their structure.

Conclusions

The mechanism of covalent bonding of single-walled carbon nanotubes under the action of laser heating was revealed. Its essence lies in the formation of hot spots in the areas of defects and open ends of nanotubes due to a strong uneven heating during absorption of laser radiation. It was shown that binding can be controlled by forming hot spots in the necessary tube regions by forming one or two defects of 1V, 2V, SW and 2SW + 1V type. In the regions of these defects, the absorption of the laser beam reaches 50% in comparison with 5% absorption of a nanotube without defects. The change in energy during the formation of bonds in time (within 8 ps) varies in the range -7.43 - 7.36 eV / atom. Self-formation of a frame nanomaterial from nanotubes dispersion predominantly formed by semiconductor tubes with diameter of 1.8 ± 0.2 nm, under irradiation of Ti:Sa femtosecond laser with wavelength of 810 nm was demonstrated experimentally. Samples of bioconstructions had a tree-like branched structure of carbon nanotubes frame with nanohardness up to 300 MPa. Also, it was shown that laser pulse of na-

nosecond duration has a structuring effect on an array of carbon nanotubes. As the energy of the pulse increased, the effect of cleaning and thinning carbon nanotubes was observed. It was associated with laser heating and covalent bonding of nanotubes in defective regions and near the ends of the tubes.

It is expected that the ordered structure of biostructures with carbon nanoframe in protein matrix should promote improved cells fixation. Thus, biostructures will be able to be used as a matrix for cell adhesion and growth, which will be confirmed by in vitro and in vivo studies.

References

- [1] A. Gerasimenko, O. Glukhova, G. Savostyanov, V. Podgaetsky. Laser structuring of carbon nanotubes in the albumin matrix for the creation of composite biostructures. *J Biomed Opt*, 22(6):65003, 2017.
- [2] J. Che et al. Thermal conductivity of carbon nanotubes. *Nanotechnology*, 11:65–69, 2000.
- [3] G. Zhang. *Thermal Transport in Carbon-Based Nanomaterials (Micro and Nano Technologies)*. Elsevier, 2017.
- [4] N. Zhurbina, et.al. Investigation of cell proliferative activity on the surface of the nanocomposite material produced by laser radiation. *Proc. SPIE* 9917: 991718-991724, 2016.
- [5] L. P. Zanello et al. Bone cell proliferation on carbon nanotubes, *Nano Lett.* 6(3):562–567, 2006.
- [6] O. Im, et.al. Biomimetic three-dimensional nanocrystalline hydroxyapatite and magnetically synthesized single-walled carbon nanotube chitosan nanocomposite for bone regeneration. *Int. J. Nanomedicine*, 7:2087-2099, 2012.

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Mixed Reality applications for the collaborative operating room – a prototypical study

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Introduction

The rapid development of medical technology enables new treatment methods and leads to a strong increase in minimally invasive surgical interventions. For this reason, more and more specific devices are constantly being added to the OR. At the same time the OR staff faces the challenge to manage the adjustment and timely provision of these devices during surgery [1]. Similarly, nursing teams in Germany are increasingly understaffed and are consequently filled with staff from other European countries that may have difficulties knowing the specific terms in the OR or understanding the requirements for each situation [2].

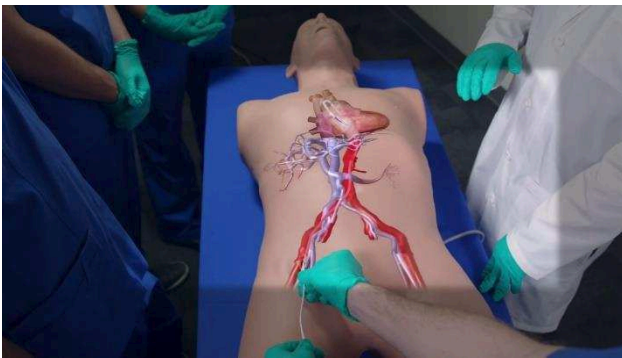


Figure 1: Exemplary application of the HoloLens for medical training (Source: caehealthcare.com)

Strategies and measures must therefore be developed to ensure and further improve efficiency, safety and outcome of the intervention. This requires solutions that bring staff and technology closer together in order to simplify system management of the OR, reduce communication issues and improve staff collaboration.

Mixed Reality (MR) applications may be a key technology to make this vision a reality. They are capable of providing information by more general means than pure language. At the same time, recent developments in machine learning allow enhanced image detection [3], workflow recognition [4] and natural language processing [5] in real time during surgery. In their combination these techniques may enable technical systems to robustly interpret the current surgical context, automatically provide the required information at the right time and react flexibly to changing demands.

In addition to providing solely information, MR application would further allow to sterily adjust most devices in the OR from a central entity. Previously, this technology has already been used for medical training [6] (also see Fig. 1) and specific surgical applications [7]. However, most developments have mainly focused on the surgeons and less on the remaining OR staff so far.

Under these assumptions this paper investigates the potential of mixed reality applications for sterile interaction within the collaborative operating room. An exemplary use case of an assistive device that supports the scrub nurse in selecting the correct instruments is presented and evaluated in an initial user experience experiment.



Figure 2: Image of the HoloLens (Microsoft, Redmond, WA, USA) as used in the presented mixed reality application (Source: microsoft.com)

Materials and Methods

To realize a simple prototype of the envisioned system, we employed a Microsoft HoloLens (see Fig. 2). The HoloLens is a wearable device that enables the augmentation of the physical world with virtual entities. It is equipped with a multitude of sensors that enable the device to localize itself within the environment (spatial mapping) and enable various modes for user interaction.

Spatial mapping is performed by means of 4 greyscale cameras and a time-of-flight (TOF) sensor that enhances the camera images with further depth information. An additional inertial measurement unit (IMU) may also measure acceleration and spatial orientation. By combining all different sensory data, the HoloLens is able to locate itself and project holograms at any desired location within the room. All necessary sensor fusion is directly processed on the HoloLens' proprietary computer.

Aside from the possibility to interact with the system via head movements and hand gestures, the HoloLens also include four microphones to allow voice control and binaural speaker for audio feedback.

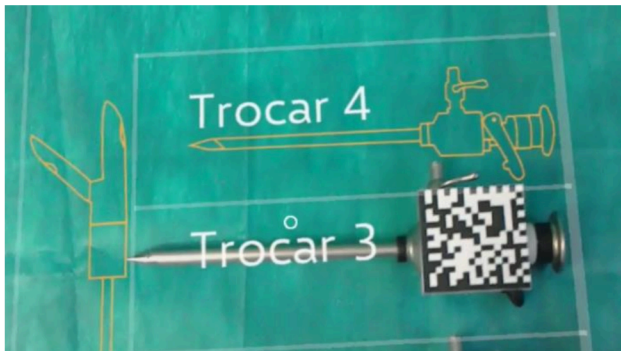


Figure 3: Segment of the grid that is projected onto the surgical tray

Included Functionalities

Our proposed assistive system supports the scrub nurse in identifying the instruments that are currently needed. It projects a grid onto the surgical tray (see Fig. 3). Each grid cell is reserved for one specific instrument and denoted by the instrument's name and contour sketch. With the integrated spatial mapping function, the grid cell pattern is automatically projected onto the surgical tray at a specified location. Through gestures the user is able to flexibly relocate the grid as desired within the plane of the surgical tray. Gestures are robustly recognized by the system even when the hands are covered with surgical gloves.

If an instruments has been placed in its corresponding grid cell, the contour sketch automatically disappears to give the user direct feedback about his or her action. The user may also interact with the system though verbal commands. By calling the name of an instrument the system clearly highlights the respective grid cell with a red box.

Currently, the integrated computer vision software of the HoloLens is not able to recognize and distinguish between the different surgical instruments in the scene. Particular problems arose due to the delicate and similar structure of some instruments. Furthermore, specular reflections from metallic surfaces highly reduced recognition accuracy. An integration of custom image processing algorithms that make use of the spatial information and could feed back their results to the HoloLens in real time are currently and to the authors' best knowledge not applicable within the API for the HoloLens. However, this functionality is crucial for the system to determine if an instrument has been correctly placed in its corresponding grid cell. For the first prototype we therefore attached QR-code markers to each instrument that were recognized within the HoloLens' video frames.

Experimental evaluation

Based on our prototype we performed a user experiment with 14 participants, some with prior OR experience. None had direct experience as a scrub nurse. During the test, participants first received a short introduction to the interaction modalities of the HoloLens such as gesture and voice control. Once participants were acquainted with the HoloLens in general, they were asked to set up the system and test out the assistive functions.

First off, users were presented the projected grid and were asked to relocate the grid to a desired position by means of gesture control. After the grid was in the right position, the participants had to place a total of 13 different surgical instruments in their respective grid cells as it is shown in Fig. 3. If the user had correctly placed the instrument in a grid cell, the contour sketch disappeared. If it did not disappear, the user had to pick up the instrument again, find the correct box and place the instrument there. Additionally, the participants were asked to interact with the system via voice commands in order to highlight the grid cells and contour sketches of specific instruments.

After successful completion the participants were all asked to fill out a User Experience Questionnaire (UEQ) [8], including a total of 26 statements that had to be rated with a 7-step Likert-scale. All statements fell into six different categories: "Attractiveness", "Perspicuity", "Efficiency", "Dependability", "Stimulation" and "Novelty".

To facilitate evaluation, we mapped the 7-step Likert-scale that takes values from 1 to 7, to values between -3 and 3 as it is also done in [9]. The resulting scale made it easier to directly tell if the user experience was rather positive (positive values) or rather negative (negative values).

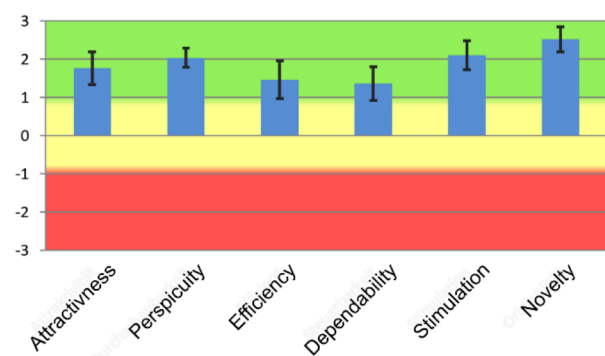


Figure 4: Results from the User Experience Questionnaire (UEQ) [8]

Aside from the user experiments voice recognition accuracy was tested for all 13 instruments by calling their respective name various times (n=30) and recording if the system recognized the command correctly.

Results

All participants were able to accomplish the task without major difficulties and therefore also completed the stand-

ardized questionnaire subsequent to the experiment. The detection of the QR code worked stable, was, however, sensitive to the distance and angle to the HoloLens' camera.

The system received mean ratings between 1.357 and 2.518. Fig. 4 shows the results as means and standard deviations over all participants and for all six categories. The scale is divided into three sections: -3 to -0.8 (very poor / poor), -0.8 to +0.8 (mediocre) and +0.8 to +3 (very good / good), marked by the respective colors red, yellow and green. Therefore, the ratings for all categories were considered as at least "good". The standard deviation takes values of less than 0.5 points in all categories. Specifically "Perspicuity", "Stimulation" and "Novelty", received the highest grades, where "Perspicuity" means how intuitive and clear the system is. Ratings for "Efficiency" and "Dependability" were the lowest, however, still fall into the highest of the three categories and were thus also considered as "good".

A relative comparison with benchmark results for typical UEQ ratings showed that for the categories "Attractiveness", "Perspicuity", "Stimulation" and "Novelty", the presented system ranks among the top 10% of the results contained in the benchmark [9]. The remaining categories "Efficiency" and "Dependability" still rank above average.

Voice detection also worked well for most instruments. Detection rates were above 70% for all instruments. All except the two keyword "PE Forceps" and "Scissors" were even detected with an accuracy of 90% or more.

Discussion

In this context, the results underline that the system was well received by most participants and its user experiences ranks well among other applications. The test clearly showed that the general concept of the system works well and that the interaction between the user and the system is intuitive. Since the test did not primarily include professional scrub nurses, this conclusion may only apply to the general usage of the system in an OR setup. Clear statements about the integration into the actual workflow and its further interaction with the additional OR team members cannot be made at this point.

Conclusions

Currently, the presented system could already be used for training, whereas a sterile application in the OR is hindered by the QR-code tags that are still necessary for instrument recognition. With further advancements in computer vision, however, a direct detection from the image may already be feasible, given that the HoloLens' API allows a practical integration of custom algorithms.

Although the HoloLens is already employed for real medical applications, its weight of 579g and its relatively

short battery life of 2 to 3 hours of active use might restrict their application during real surgery. Particularly for longer surgical interventions, the system might not be practical at its current state.

Future research will be devoted at its integration into the OR and the preexisting workflow. The system is planned to be coupled to a workflow recognition engine that aids at automatically highlighting the required instruments in each situation. We further work on enhancing the system's flexibility by integrating verbal information given by the surgeon. Further user experiments will put a stronger focus on OR staff members, particularly scrub nurses, and their collaboration with the remaining OR team.

References

- [1] Carpintero, E., Pérez, C., Morales, R., et al., Development of a robotic scrub nurse for the operating theatre. *3rd IEEE RAS & EMBS International Conference on Biomedical Robotics and Biomechatronics*, 2010
- [2] C. Schäfer. Risikofaktor Pflegekräftemangel. *Dialyse aktuell*, 16 (09): 483-483, 2012, in German
- [3] Ren, S., He, K., Girshick, R., & Sun, J. (2015). Faster r-cnn: Towards real-time object detection with region proposal networks. In *Advances in neural information processing systems* (pp. 91-99).
- [4] R. Stauder, N. Navab et al. Learning-based Surgical Workflow Detection from Intra-Operative Signals. *arXiv preprint arXiv:1706.00587*, 2017
- [5] Young, T., Hazarika, D., Poria, S., & Cambria, E. (2017). Recent trends in deep learning based natural language processing. *arXiv preprint arXiv:1708.02709*.
- [6] C. Kamphuis et al. Augmented reality in medical education? *Perspectives on medical education* 3.4: 300-311, 2014
- [7] N. Navab, T. Blum et al. First deployments of augmented reality in operating rooms. *Computer*, 45 (7): 48-55, 2012
- [8] B. Laugwitz, M. Schrepp et al. Construction and evaluation of a user experience questionnaire. *Symposium of the Austrian HCI and Usability Engineering Group*, 2008
- [9] M. Schrepp et al. User Experience Questionnaire Benchmark Praxiserfahrungen zum Einsatz im Business-Umfeld. *Usability Professionals*, 13: 348-353, 2013, in German

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Longterm high resolution manometry (HRM) challenges and pitfalls of an automated motility analysis

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Introduction

High resolution manometry (HRM) of the esophagus is the gold standard in the diagnosis of esophageal motility disorders[1]. However, it only measures a short period of time and allows only to distinguish between the most common esophageal motor abnormalities with the help of Chicago Classification[2]. As the measurements take place in clinic for a very limited period of time only little is known about circadian changes in esophageal motility. Especially for patients with intermittend symptoms conventional, short-term HRM cannot assess the underlying causes of the disease precisely.

Therefore, we prolonged the time of measurement to a full of 24 hours using a combined ambulatory impedance-manometry device consisting of 36 pressure channels and 15 impedance channels[3]. With this setting it is possible to examine esophageal motor function throughout a whole day whilst the patient is following her/his normal duties.

The aim of our project was to establish normal values for healthy persons and to identify patients with transient esophageal problems as only little is known about normal and pathological patterns when examining esophageal motor function and dysfunction throughout a whole day.

Materials and Methods

For the longterm high resolution manometry (HRM) we used a 10 French Solide State Manometry catheter designed for high resolution impedancomanometry studies (Unisensor, Attikon, Swiss). In the probe, the esophageal pressure values are already digitalized and sent to the portable recording unit MALT™ (Standard Instruments, Karlsruhe, Germany). With the power supply of two standard lithium AA-batteries the systems allows studies up to 26 hours.

The recording unit has an internal memory of 1 GB

size and can store pressure plots of 36 pressure channels with a rate of 50 Hertz without the necessity of data compression.

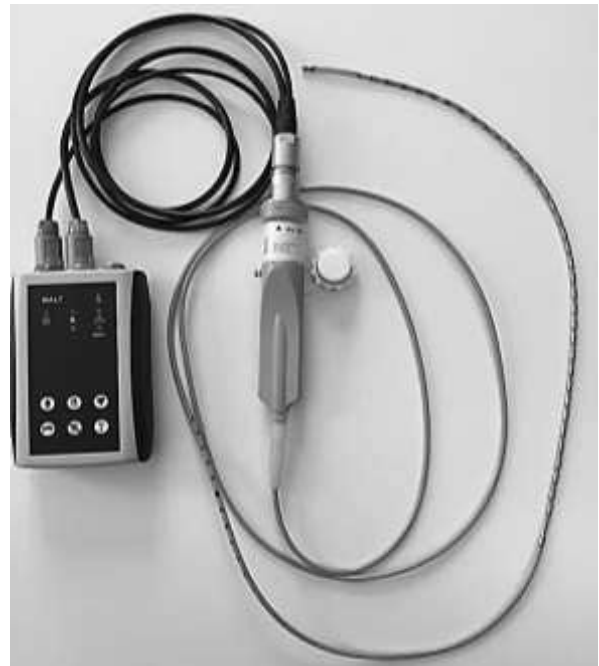


Figure 1: Device for ambulatory high resolution manometry of the esophagus

In addition to the huge amount of pressure raw data, complementary information on body position, eating and drinking habits as well as sleeping is integrated into the dataset.

With this newly developed device we have been recording more than 80 longterm high resolution manometries since the beginning of our project. Technical and clinical feasibility was documented prospectively and iteratively improved.

Evaluation

The 24 hour recordings of normal, healthy test persons were manually analysed. An extended Chicago classification system was used (Fig. 2).

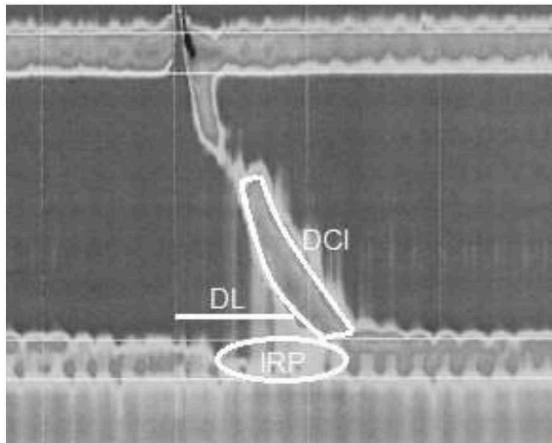


Figure 2: Important values for evaluation of esophageal motility according to Chicago Classification Version 3.0 (DL = distal latency, DCI = distal contraction integral, IRP = integrated relaxation pressure)

Parallely, an automated analysis program was developed, based upon the classical Chicago criteria. An act of swallow was assumed as soon as a relaxation of the upper esophageal sphincter (UES) was followed by sequential contractions measured by the more distal sensors. With the ongoing evaluations, it became clear that this rather rigid algorithm had to be changed as described below.

Results

Technical and organizational problems

Though the probe is quite rigid and has a diameter of about 3mm (10 French) the examination is accepted by our patients and in our healthy volunteers quite effortlessly. Only three measurements had to be stopped before time.

More problematical in the performance of longterm high resolution manometries are technical aspects. The used solid state probes are high end products and are designed for about 200 uses (about 600 operating hours). When extending the time of measurement to 24 hours, the guaranteed operating hours are reached within 25 measurements which rises the costs of a single measurement to around 720 €. Especially with the longterm use the probes need more reparationment and checking which adds additional costs to each examination.

Manual Evaluation

Up to now there is no program for automated computer analysis of HRM and especially non for long-term measurements available.

As expected, manual analysis of the pressure recordings was extremely tedious and time consuming. However, it yielded important new insights.

“Static” parameters

These so called static parameters represent the resting pressure of both high pressure zones in the esophagus: the upper and the lower esophageal sphincters.

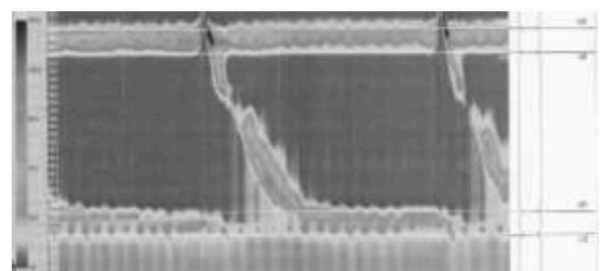


Figure 3: Color-coded HRM pressure plot of a normal swallow that starts with relaxation of upper esophageal sphincter, followed by a propulsive peristalsis and ends by contraction of the lower esophageal sphincter. (right: marking of pressure bands of upper and lower esophageal sphincter)

We found that physiological (complete) swallows as shown in the figure above (Fig. 3) do not at all represent the majority of all motor events of circadian esophageal motility. Depending upon posture (upright/prone) and food intake, a considerable number of incomplete swallows occurred. In these instances, a clear relaxation of the UES is not observed, but the distal contractile sequences show the typical pattern.

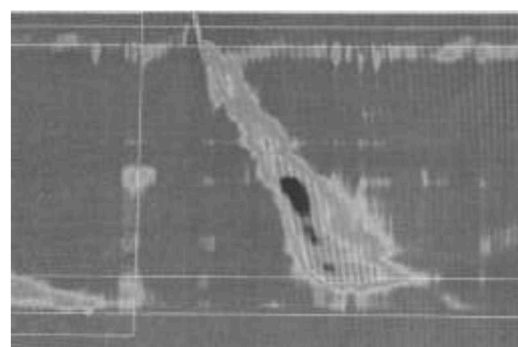


Figure 4: Relaxation of the UES is barely visible. Though a human analysist would recognize the act of swallowing, a machine based system would certainly not recognize this type of motor event

Even more surprisingly, irregular motor events could be detected in healthy people without any esophageal problems. Retropulsive contractile sequences could be observed as well as distal cramps (Fig. 4) or transient relaxations of the lower esophageal sphincter (TLESR) which were often followed by reflux (Fig. 5).

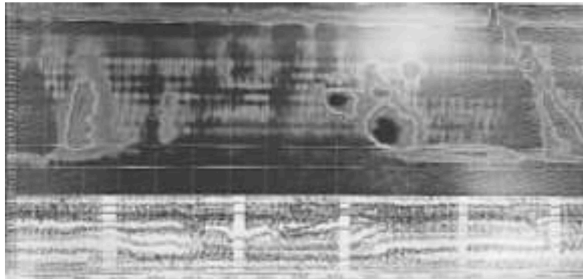


Figure 5: Transient sphincter relaxation, followed by fluid reflux (as seen in impedance measurement at below the HRM plot) and a distal contractile wave before an act of clearance swallowing

Systematic further classification of the normal motility pattern is currently conducted. Up to now, we are still unable to present a complete catalogue of physiological circadian pressure events. At any rate, “irregular” contractile events which were considered pathological in our previous analyses can be found frequently in normal test persons as well.

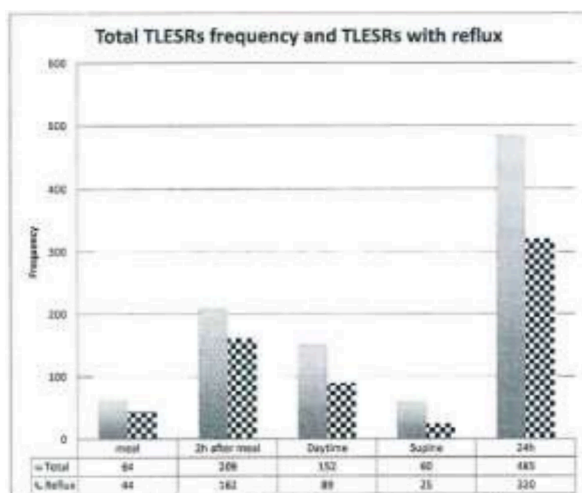


Figure 6: Total number of TLESR and TLESR with reflux

When analysing our patients with reflux disease it shows that the mean resting pressure of the lower esophageal sphincter underlies a slight modulation with an increase of resting pressure and the integrated relaxation pressure during nighttime. Whereas in the upper esophageal sphincter resting and relaxation pressure stay stable throughout the measurement. Most remarkably, the number of TLESR are appearingly dependent of the circadian cycle.

Dynamic parameters

Dynamic parameters is the preamble for all values that can only be measured during an act of swallowing (eg. transportation velocity, area under the curve).

In patients with known reflux disease significant changes in the cause of measurement can be seen in the value of DCI (distal) and PCI (proximal contraction integral), the intrabolus pressure (IBP), in distale latency (DL) and distal contraction velocity (DCV).

Problems of automated analysis

As manual analysis is not feasible in clinical practice it is by now possible to get a computer aided analysis according to the newest Chicago Classification. These computer aided programs tend to correctly mark pressure landmarks during swallowing whenever an act of swallowing is marked correctly beforehand. For an expert in analysis of HRM the analysis of a whole dataset can be performed in around 20 hours which excludes it from clinical routine.

Originally an algorithm for detecting an act of swallowing was developed which relied on the pressure changes in the UES. A swallow was assumed if a relaxation in the upper esophageal sphincter was followed by a characteristic postdeglutitive increase of pressure.

The rate of complete swallows that can be evaluated with measurements of the parameters shown in Fig. 1 was very high (>95%) but unfortunately these typical contractile sequences made up only about 1/3 of circadian motor events of the esophagus. Especially motility patterns without oropharyngeal triggering of a swallow (e.g. secondary peristalsis waves for esophageal clearance, ...) aren't considered for analysis at all [4]. Whilst typical motor events can be evaluated with computer-assisted programs the remnant has still to be evaluated manually.

Conclusion

Analysis of longterm high resolution manometry (HRM) is at the moment not yet feasible in clinical routine. It is essential to develop a computer program to bring longterm HRM into clinical practice. As shown above, automatic analysis is by far more complex than it is when performing short time analysis according to the Chicago Classification. As there are

up to now no bigger series on normal and pathological values with longterm manometry studies it is hard to define new, more suitable algorithms for computer analysis of HRM. Further studies will be necessary to build up a big database of normal and pathological

values as well as newer and more elaborated algorithms (eg. deep learning methods) will be necessary for a better understanding of circadian motility patterns of the esophagus.

Conflicts of interest:

No conflict of interests. The project was supported by Dr. Pflieger-Stiftung Bamberg, Germany.

References:

1. Roman S, Pandolfino J, Mion F. High-resolution manometry: a new gold standard to diagnose esophageal dysmotility? *Gastroenterologie clinique et biologique* 2009; 33: 1061-1067
2. Kahrilas PJ, Bredenoord AJ, Fox M et al. The Chicago Classification of esophageal motility disorders, v3.0. *Neurogastroenterol Motil* 2015; 27: 160-174
3. Jell A, Wilhelm D, Ostler D et al. Langzeit-HR-Manometrie der Speiserohre: Erste Beobachtungen aus dem klinischen Einsatz. *Zeitschrift fur Gastroenterologie* 2016; 54: 1069-1075
4. Samoilov A, Telyshev D. Determination of Heart Rate Variability from High-Resolution Esophageal Manometry Data. *Biomedical Engineering*, DOI 10.1007/s10527-018-9742-y:

Investigation of the spectral properties of media based on chitosan and carbon nanotubes

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Introduction

Common diseases of the cardiovascular system include pathological changes in connective tissue structures of the heart and large blood vessels due to atherosclerosis, inflammatory lesions, congenital inferiority or mechanical damage. These diseases led to the development of methods for creating tissue-engineered structures implanted in the area of damage to the tissues of the heart and blood vessels [1]. Such methods involve the formation of a three-dimensional biocompatible scaffold with its subsequent filling with living cells. One of the most effective and modern methods of creating such scaffolds is laser printing.

Biological and synthetic materials are used to create cellular and tissue engineering structures for the restoration of the cardiovascular system [2]. However, biological materials have deficiencies associated with the possibility of transmission of infections, and synthetic compounds do not provide the necessary mechanical and bioresorption characteristics. In view of this, there is a need for new materials for tissue engineering in the field of the cardiovascular system.

To create the considered structures it is proposed to use chitosan, basically this aminosugar is used as a matrix medium for fillers in the form of functional particles [3, 4]. The addition of carbon nanotubes to natural or synthetic polymer structures enhances the mechanical properties and enhances the electroconductive and physiological properties of the structure for restoring the tissues of the cardiovascular system [5].

In this paper, we present a study of chitosan-based samples with inclusions in the form of carbon nanotubes in order to use the composition as a starting material for the preparation of cellular and tissue-engineered structures used in cardiovascular surgery.

Materials and Methods

Two types of water-soluble chitosan, edible and succinate, were used in this study. Edible chitosan (EC) was obtained from high-molecular chitosan by chemical hydrolysis and was a cream colored powder with a main substance content of 88.4%, a moisture content of 3.13% and mineral substances of 0.53%. Chitosan succinate (CS) is derived from crab chitosan by interaction with succinic anhydride. The material was a pearl-cream powder with a residual moisture content of 4.79%, the pH of the aqueous solution was 7.7.

As a filler for the creation of samples, 2.7% aqueous paste based on single-walled carbon nanotubes (SWCNTs) was used. SWCNTs were obtained by gas-phase synthesis with a wash to 99% purity. The diameter of the tubes was 1-2 nm, the length exceeded 5 μm . The feature of nanoparticles was a high specific surface area – 420 m^2/g .

Water dispersion media (dispersions) based on SWCNTs with EC and CS were obtained. First, SWCNTs were mixed on a magnetic stirrer for 20 minutes with distilled water to obtain a concentration of $10^{-5}\%$. The resulting dispersions were then subjected to a powerful ultrasonic field with a power amplitude of $\sim 40\text{ W}$ for 50 min. Then a powder of EC and CS with a concentration of 1:49 was gradually added to the homogeneous dispersion of SWCNT. The mixture was then stirred in an ultrasonic bath with an operating frequency of 45 kHz for 40 minutes.

From the final dispersions obtained, film samples were prepared for the study by water evaporation upon the influence of laser radiation. A pulsed ytterbium laser (wavelength 1064 nm) and a semiconductor laser (970 nm wavelength) with a power of no more than 5 W were used as sources of laser radiation.

Raman spectra in the range 100-1800 cm^{-1} were measured using the LabRAM HR Evolution (Horiba) spectroscopic complex. As a source of exciting radiation, a HeNe laser with a wavelength of 633 nm was used.

Absorption spectra of samples in the IR range 4000-400 cm^{-1} (2.5-25 μm) were obtained by the method of attenuation total reflection using the Nicolet iS50 Fourier spectrometer (Thermo).

Results

To study the degree of binding of the aqueous dispersion components of chitosan to carbon nanotubes (CNTs), characteristic amide bands on IR and Raman spectra of film samples were analyzed. To compare the spectra, control samples from pure components are prepared separately.

IR Spectra

Peaks on the spectrum of pure chitosan turned out to be shifted relative to the peaks of films based on chitosan and SWCNT, and their intensity was sharply changed, which indicates the molecules connection of substances among themselves. From the spectrum of EC (see fig. 1), it is seen that the intense peak near 3350 cm^{-1} is due to stretching vibrations O–H and H–H (stretching of bonds);

the band of about 2868 cm^{-1} is connected with the valence vibrations of the C–H bonds.

A group of bands from 500 cm^{-1} to 1660 cm^{-1} is characteristic of the amide group (Amide I–Amide VI bands). Amide I (about 1550 cm^{-1}) characterizes the vibrational ability of the amide group, in which a periodic elongation of the C=O bond occurs, which can be used to judge the degree of acetylation. Comparing with the analogous peak in fig. 2b, we can conclude that the CS degree of acetylation is higher.

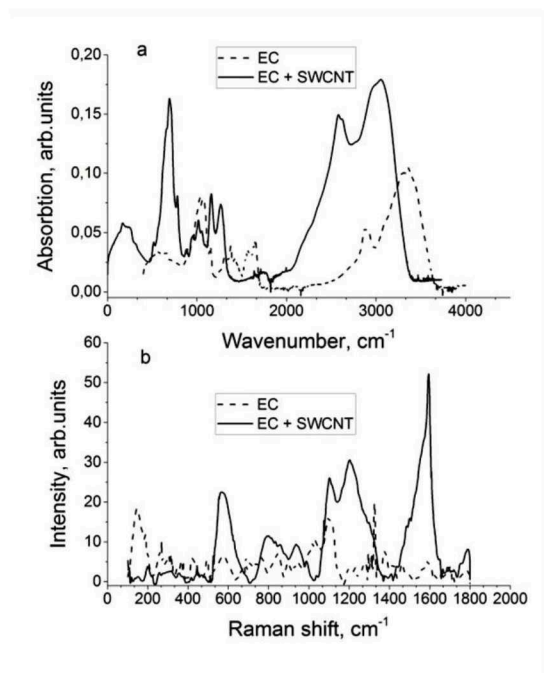


Figure 1: IR (a) and Raman (b) spectra of pure edible chitosan and with addition of CNTs

The absorption band of about 3450 cm^{-1} can be sensitive to adsorbed water, and an increase in the water content leads to an increase in the absorption band of about 1640 cm^{-1} , which was observed on the spectrum of EC with SWCNT. The difference in the intensity of the peaks near 3350 cm^{-1} and 1550 cm^{-1} in the CS spectrum is related to the degree of acetylation. Also, it is possible that the contribution of SWCNTs was more pronounced on the spectrum when connected to the EC.

A wider CS band of about 3350 cm^{-1} in comparison with EC could be associated with the stretching of the O–H bond, which overlaps the N–H stretching in the same region. It should be noted that intense peaks for CS with SWCNTs of about 1040 cm^{-1} and 1200 cm^{-1} are related to the stretching vibrations of C–C and C–O, which confirms the binding of the dispersion components to each other. A similar increase in intensity is observed for EC with SWCNT in the same region with respect to the spectrum of pure chitosan, however, the peak amplitudes are harsher than in the spectrum of CS. It is assumed that the penetration of SWCNTs into a more viscous gel-like

structure of EC with a concentration of 2% was weaker than in the more liquid CS sample.

Raman Spectra

As seen in fig. 1b and 2b, the spectrum of chitosan with SWCNT is shifted relative to the initial chitosan spectrum, which indicates changes in the structure of amino sugars and tubes. These shifts are responsible for connecting the components of the dispersion to each other.

The bands of about 1603 cm^{-1} correspond to the deformation symmetric vibrations of the amino group. The shape of the peaks in the spectrum of EC with SWCNT is similar to that of the spectrum of CS with SWCNT, which is mainly due to a stronger manifestation of the contribution of nanotubes to the Raman spectrum in comparison with the spectra of organic substances.

Peaks with frequencies of about 1200 cm^{-1} and 1120 cm^{-1} are responsible for the stretching vibrations of C–O and C–N, which were manifested in the spectra of EC and CS. These peaks shifted from their original position when chitosan was combined with the tubes, and their intensity increased sharply, which can be explained by the SWNT D mode that is strongly manifested in this region.

It should also be noted that SWCNTs exhibit semiconductor properties and do not have any structural damage, as can be seen from fig. 3b: the ratio of the intensity of the RBM mode (about 500 cm^{-1}), D and 2D modes (about 1200 cm^{-1} and 2800 cm^{-1}) with the G mode intensity (about 1594 cm^{-1}).

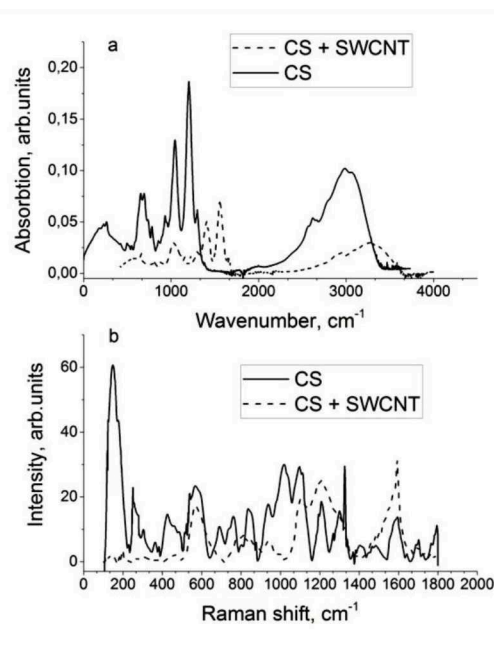


Figure 2: IR (a) and Raman (b) spectra of pure chitosan succinate and with addition of CNTs

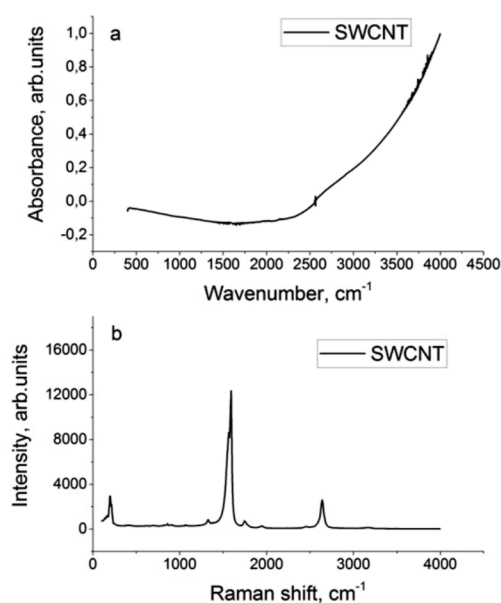


Figure 3: IR (a) and Raman (b) spectra of SWCNTs

Discussion

For the study water dispersions of chitosan and dispersion of chitosan with carbon nanotubes were made. To investigate the properties of materials obtained from these dispersions, film samples were obtained by evaporating the aqueous component under the influence of laser radiation. Based on the results of the study using IR spectroscopy and Raman spectroscopy, it was found that changes in the structure of a sample based on chitosan and SWCNT occurred due to the appearance of intermolecular bonds. It was found that a higher degree of acetylation of CS leads to its more homogeneous dissolution, while EC is prone to gelling. The addition of carbon nanotubes is due to an increase in the hardness of the resulting samples.

Conclusions

Thus, the conducted researches are useful for manufacturing of three-dimensional cellular and tissue engineering designs used for restoration of defects of cardiovascular system.

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References

- [1] H. Hong, et al. Fabrication of a novel hybrid heart valve leaflet for tissue engineering: an in vitro study. *Artificial organs*, 33(7):554-558, 2009.
- [2] S. Catros, et al. Laser-assisted bioprinting for creating on-demand patterns of human osteoprogenitor cells and nano-hydroxyapatite. *Biofabrication*, 3(2):025001, 2011.
- [3] P. V. Popryadukhin, et al. Composite materials based on chitosan and montmorillonite: prospects for use as a matrix for cultivation of stem and regenerative cells. *Cell and Tissue Biology*, 6(1):82-88, 2012.

- [4] P. Matteini, F. Ratto, F. Rossi, S. Centi, L. Dei, R. Pini. Chitosan films doped with gold nanorods as laser-activatable hybrid bioadhesives. *Advanced Materials*, 22(38):4313-4316, 2010.
- [5] M.D. Dozois, L.C. Bahlmann, Y. Zilberman, X.S. Tang. Carbon nanomaterial-enhanced scaffolds for the creation of cardiac tissue constructs: A new frontier in cardiac tissue engineering. *Carbon*, 120:338-349, 2017.

Piezoelectric properties of PVDF and PVDF-TrFE electrospun materials for nerve regeneration

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Introduction

Traumatic injuries and loss of functionality in peripheral nerves often lead to life-long physical restrictions. Currently, the tension-free reconstruction of longer nerve defects applying autologous nerve grafts is a gold standard in nervous tissue repair. However, the main disadvantage of this method - the complete loss of function of the donor nerve - has encouraged the scientific community to develop new tissue-engineered nerve conduits. Biosynthetic nerve guides with innovative material properties could offer alternatives to the available on the market tubular implants with very variable regeneration success. Among materials for designing of artificial nerve conduits, the ones with inherent piezoelectric properties are of high interest. Because of their proven biocompatibility, stimulation of cell ingrowth and piezoelectric properties [1, 2], polyvinylidene fluoride (PVDF) and trifluoroethylene (PVDF-TrFE) are promising materials for designing active implants for nerve regeneration. It is believed that the regeneration of severed nerves could be accelerated by these properties. The current work is based on our previous study [3] and aims to develop a measuring method to describe the electro-mechanical coupling parameter, so-called the piezoelectric module.

Materials and Methods

Preparation of materials for testing: The polyvinylidene fluoride and its copolymer polyvinylidene fluoride-co-trifluoroethylene were used as received without any purification. To prepare the polymer solutions, PVDF (Sigma-Aldrich, MW ~ 530,000 Da) and PVDF-TrFE (Piezotech Arkema, weight ratio 70/30, MW ~ 450,000 Da) were dissolved in N-Dimethylformamide (DMF) (Fluka Analytical) and acetone (AppliChem GmbH) in a weight ratio of 6:4. For the identification of favorable conditions for production of scaffolds, the solutions with PVDF concentrations of 10%, 15% and 20% as well as PVDF-TrFE of 10%, 15% and 20% were prepared at 50 °C and stored at room temperature overnight prior to electrospinning.

Electrospinning of solutions: The indicated above solutions were processed by means of electrospinning to form scaffolds (fiber mats) [4, 5]. With this method, fiber mats with different polymer mass contents were produced. The focus of the selected manufacturing process was to attain the most mechanically stable fiber mats possible. For this purpose, a preliminary study of the manufacturing parameters was carried out (data not shown). In the electrospinning process, a flow rate of 2 ml/h and voltages of 20-30

kV were applied as optimal process parameters to produce aligned fibers on a rotating aluminum cylindrical collector (300 rpm). The electrospinning time for each sample was 2.5 hours.

FTIR analysis: The Fourier Transform Infrared Spectroscopy (FTIR) was used to record the infrared spectra of the electrospun scaffolds. The spectra were compared to those of untreated/raw materials with respect to the presence of the nonpolar α - and piezoelectric crystalline β -phase. The FTIR spectra were recorded using a PerkinElmer 100 FTIR spectrometer (PerkinElmer, Norwalk, CT, USA) equipped with a triglycine sulfate detector and an attenuated total reflection accessory with a diamond/ZnSe crystal. The acquisition parameters were the following: 4 cm⁻¹ resolution, 8 co-added interferograms, and 4000–550 cm⁻¹ wavenumber range. An automatic CO₂/H₂O vapor correction algorithm was used during recording of the spectra. Spectra analysis and display were carried out using PerkinElmer software.

Measurements using the impact press machine: The developed method is based on the direct piezoelectric effect. For this, the fiber mats were mechanically stressed using the modified impact stress machine (fig. 1) and their induced electrical value was measured.

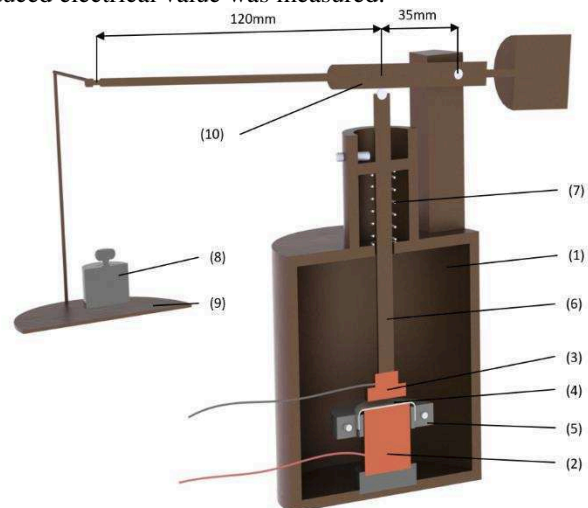


Figure 1: Section of the structure of the impact press machine: (1) measuring cell, (2, 3) electrodes, (4) test sample, (5) clamping device, (6) pressure rod, (7) spring, (8) applied weight, (9) shell, (10) lever

The measuring cell (1) is a closed shell of steel. Due to the influence in the electrical conductor, this shields the measurement against electromagnetic interference (Faraday cage). The lower electrode (2) is located in the meas-

uring cell on a polymer base which is insulated from the measuring chamber. The sample (4) is positioned in a clamping device (5) between the lower and the upper electrode (3). This consists of two rings between which the sample is clamped. The clamping device together with the sample is placed on the lower electrode, so that only the sample is in contact with the electrode surface. Due to the weight of the rings, the sample is evenly stretched over the electrode surface (fig. 2).



Figure 2: Sample without (left) and with the clamping device (right)

The upper electrode is connected to a rod (6), which projects from the measuring cell. The rod is held in position by a spring (7). On the tip of the rod there is a ball, which applies pressure uniformly to the rod and thus to the sample. The mechanical load is applied by means of a lever (10) via a weight (8), which is positioned in a shell (9). The electrodes from the measuring cell were connected to the voltage meter (610C, Keithley Instruments) during loading and unloading. The generated voltage measurement signal was then passed on to the oscilloscope (K8031, Velleman), digitized and graphically displayed on a computer via software. For capacitance measurement, the electrodes were connected to the capacitance meter (E7-20, MNIPI) in the loaded state of the sample after the voltage signal had been decayed. The measuring principle is based on the direct piezoelectric effect. During mechanical compression of the sample, a voltage difference can be measured on the surfaces. For the determination of the piezoelectric module, the capacitance of the sample C_p must be known. Afterwards, the module d_{33} can be calculated with the following equation:

$$d_{33} = \frac{Q}{F} = \frac{w \cdot U \cdot C_p}{W \cdot F} \quad (1)$$

where Q : induced charge in C, F : impact force in N, U : induced voltage in V, C : electric capacitance in F, w : area of the mechanical load in cm^2 , W : area of the electrodes in cm^2 .

Performing measurements: The samples were fixed in the clamping device and placed on the lower electrode in the measuring cell. The measuring cell was then closed and the pressure rod adjusted so that the upper electrode did not make contact with the sample during resting. A set of weights m_{app} of 48g, 99g, 170g and 363g was used to apply the pressure load on the sample. Considering the weight of the pressure rod (m_{rod}), the upper electrode ($m_{electrode}$), the pressure compensation by the tensioning energy of the spring (m_{spring}), the conversion factor from the arm ratio of the lever (1) and the gravitational acceleration (g), the actual acting force (F_{app}) applied on the sample can be calculated as follows:

$$F_{app} = (m_{app} - m_{rod} - m_{electrode} + m_{spring}) \cdot l \cdot g = (m_{app} - 40g) \cdot \frac{120\text{mm} + 35\text{mm}}{35\text{mm}} \cdot 9,81 \frac{\text{m}}{\text{s}^2} \quad (2)$$

Both the weight of the rod and the electrode as well as the pressure compensation of the spring were approximated with 40g since the contact between the upper electrode and the sample is ensured only at a weight of 40g in the shell. Tab. 1 shows the applied weights (m_{app}) in the shell and the forces (F_{app}) acting on the sample.

Table 1: Applied weights in the shell and the corresponding force on the sample

m_{app}	48 g	99 g	170 g	363 g
F_{app}	0,3 N	2,56 N	5,65 N	14,02 N

For the determination of the piezo modulus d_{33} , the voltage potentials at the surfaces and the capacitance of the samples were measured during the applied force on the sample. Fig. 3 shows the equivalent circuit diagram for the voltage measurement of the examined piezoelectric samples.

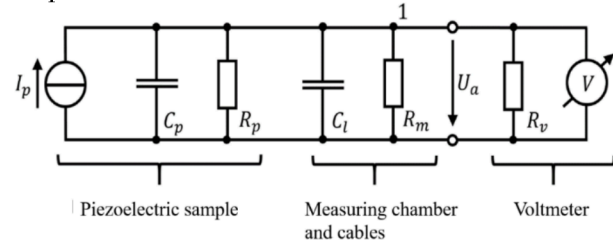


Figure 3: Electrical equivalent circuit diagram of the voltage measurement of the piezoelectric sample

In measuring the capacitance, the total capacitance (C_{tot}) has been recorded in the connected component. This included the capacitance of the sample (C_p) and the parasitic capacitance of the cables (C_l) (fig. 3). The capacitances were connected in parallel in this measurement setup. Thus, the total capacitance (C_{tot}) can be calculated using the following equation:

$$C_{tot} = C_p + C_l \quad (3)$$

Results

Effect of polymer concentration on the crystalline β -phase: Preliminary experiments showed that 10% PVDF solution resulted in generation of fiber mats with the presence of undesired beads. For this reason, this concentration of PVDF was not taken into consideration for further investigations. The study investigated the influence of the polymer concentration on the transformation process of the crystals from α - to the piezoelectric β -phase during electrospinning.

In fig. 4, the normalized FTIR absorption spectra of electrospun fiber mats from 15% and 20% PVDF polymer solution are compared with the spectrum of raw PVDF pellet. The analysis of FTIR data demonstrates that the spectra of both fiber mats from 15% and 20% PVDF solutions do not contain peaks at 796 cm^{-1} , 976 cm^{-1} and 1383 cm^{-1} of the α -phase, as compared to the raw pellet. The characteristic peaks at 840 cm^{-1} and 1275 cm^{-1} of the β -

phase have approximately the same intensity for both fiber mats.

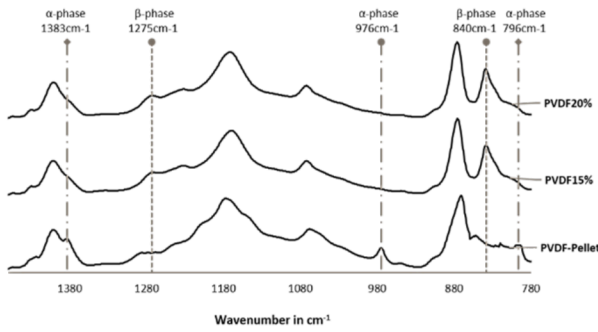


Figure 4: Normalized FTIR spectra of the raw PVDF pellet and PVDF fiber mat made of 15% and 20% polymer concentration in a DMF/acetone (6/4 ratio) solvent

Fig. 5 shows the unprocessed PVDF-TrFE powder as well as fiber mats made of 10%, 15% and 20% PVDF-TrFE solutions by means of electrospinning. In contrast to the PVDF, in which the crystals are converted into the piezoelectric β crystal phase during the electrospinning process, the PVDF-TrFE powder shows the characteristic peaks of the piezoelectric β -phase at 850 cm^{-1} , 1288 cm^{-1} und 1400 cm^{-1} [7]. Thus, the PVDF-TrFE, theoretically, does not require transformation processes for the conversion of crystallites into the β -phase. Furthermore, the three PVDF-TrFE fiber mats show nearly identical peaks at the β -phase-wavelengths.

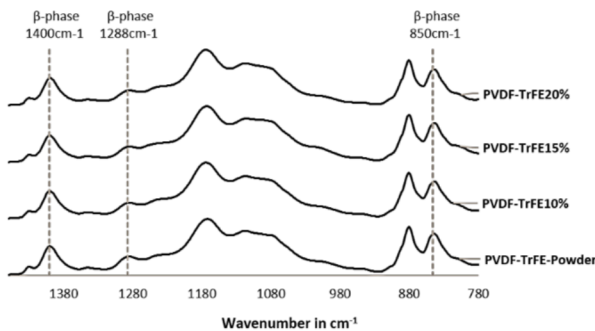


Figure 5: Normalized FTIR spectra of the raw PVDF-TrFE powder and PVDF-TrFE fiber mats made of 10%, 15% and 20% polymer concentration in a DMF/acetone (6/4 ratio) solvent

Effect of polymer concentration on the crystalline β -phase: Five fiber mats per polymer concentration were examined. Each fiber mat was manually loaded and unloaded six times, yielding 60 measuring points for each concentration. The quasi-static frequency of the measuring cycle was 0.2 Hz. Fig. 6 and 7 show measured voltages and sample capacities, respectively. Taking into account the relationship $d_{33} = (U \cdot C)/F$, fig. 8 represents the equivalent piezo modulus d_{33} of the fiber mats produced.

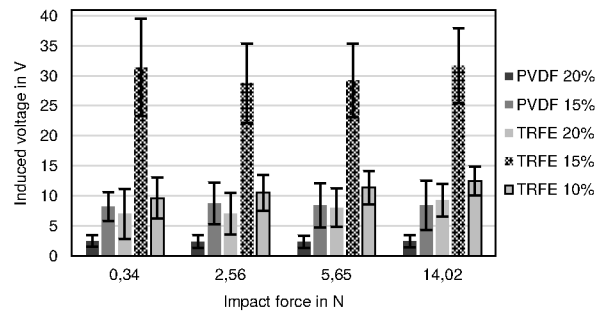


Figure 6: Measured voltages of PVDF and PVDF-TrFE fiber mats (n=6)

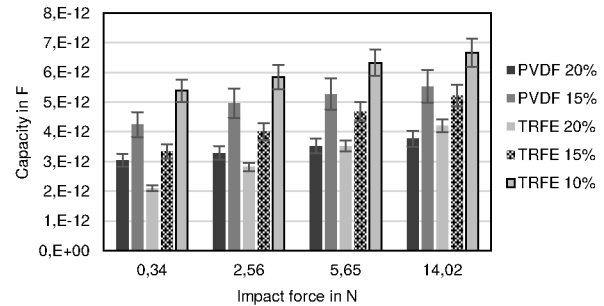


Figure 7: Measured capacities of PVDF and PVDF-TrFE fiber mats (n=6)

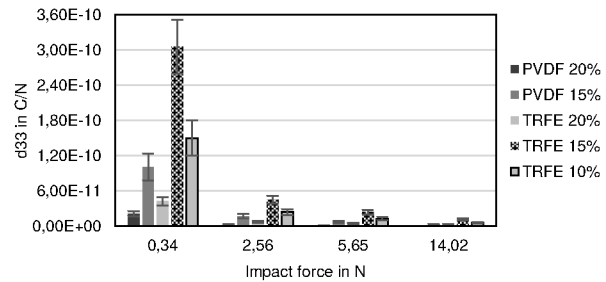


Figure 8: Piezoelectric module d_{33} of PVDF and PVDF-TrFE fiber mats (n=6).

Discussion

The piezomodule represents a geometry-independent parameter of a material, which is constant under different load profiles (by definition $d_{33} = Q/F$). If the piezomodule and the sample capacitance are known, the voltage induced at the sample surfaces during a load can be calculated with the relationship $U = (d_{33} \cdot F)/C$.

The structural transformation of α -phase into β -phase for PVDF was confirmed using FTIR analysis. This effect can be attributed to elongation of fibers during deposition onto grounded collector and simultaneous evaporation of DMF/acetone, which in turn affects orientation of dipole moments in the final PVDF electrospun fiber mat material.

For the piezoelectric investigation of the electro-spun fibrous mats from PVDF and PVDF-TrFE, an impact press machine was developed. In this method, the sample capacitance and the induced voltage were measured and then the induced charge was calculated. In order to reduce the measurement inaccuracies, the measuring charge was processed by a measuring amplifier (self-developed), taking into account the time behavior of the signal. The

measurement results showed a dependence of the piezoelectric modulus on the load, load frequency and fiber mat thickness. This behavior is due to the nonlinear viscoelasticity of the fiber mats. Since the piezoelectric modulus of the fiber mats did not behave uniformly under different load profiles, it is not possible to predict the induced voltage at a certain load.

The electrical response to a specific load profile must therefore be examined individually for different fiber mat geometries. For error-free detection of the induced voltage, a surface-covering contact between the sample surface and the measuring electrodes must be ensured. This can be performed using spinning conducting electrodes from the piezoelectric polymer and graphene oxide, as indicated elsewhere [8]. In addition, for a reproducible production of certain fiber mat geometries, a complete control of the electrospinning process has to be considered.

Conclusions

The aim of this work was to develop a measuring method to describe the electro-mechanical coupling parameter, so called piezoelectric module. The developed method is based on the direct piezoelectric effect. For this, the fiber mats were mechanically stressed and their induced electrical values were subsequently measured. In order to do this, a purely mechanical test cell for static measuring conditions was first constructed. However, the non-conductive surface structure of the fiber mats as well as the time response of the measuring signal were not considered. The measurement process on all fiber mats using the piezo module showed the same influence of the load and load frequency. As the load increased, the piezo module was reduced. Additionally, the increase in the load frequency led to an increase of the piezoelectric module. This behavior is attributed to the non-linear viscoelastic compliance of the fiber mats.

References

- [1] H. Kawai. The Piezoelectricity of Poly (vinylidene Fluoride). Japan J Appl Phys, 8: 975-976, 1969.
- [2] S.A.M. Tofail and J. Bauer. Electrically Active Materials for Medical Devices. World Scientific Publishing Company 2016.
- [3] F. AL Halabi, L. Freund, A. Repanas, P. Behrens, S. Knigge, K. Haastert-Talini, B. Glasmacher. Effect of different solvents on morphology and properties of piezoelectric PVDF scaffolds for nerve regeneration. Biomedical Engineering, 60(S1), 2015, doi: 10.1515/bmt-2015-5000.
- [4] S. Ramakrishna. An introduction to electrospinning and nanofibers. World Scientific 2005.
- [5] J. Doshi and D.H. Reneker. Electrospinning process and applications of electrospun fibers. J Electrostatics, 35(2-3): 151-160, 1995.
- [6] A. Szentivanyi, T. Chakradeo, H. Zernetsch, B. Glasmacher. Electrospun cellular microenvironments. Understanding controlled release and scaffold structure. Adv Drug Deliv Rev, 63(4-5): 209-220, 2011.
- [7] D. Mao, B.E. Gnade and M.A. Quevedo-Lopez. Ferroelectric Properties and Polarization Switching Kinetic of Poly (vinylidene fluoride-trifluoroethylene) Copolymer. In M. Lallart, editor, Ferroelectrics - Physical Effects, chapter 4, 2011, ISBN 978-953-307-453-5, doi: 10.5772/17147.
- [8] B. Li, F. Zhang, S. Guan, J. Zheng, C. Xu. Wearable piezoelectric device assembled by one-step continuous electrospinning. J Mater Chem C, 4(29): 6988-6995, 2016.

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Evaluation of the P300 parameters with photic stimulation

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Introduction

Modern rehabilitation methods for patients with musculoskeletal problems after stroke include the following: therapeutic physical training methods, massage, physiotherapy, high-tech methods, etc. [1] High-tech methods include: the creation of supportive and "stimulating" robotic devices, the use of virtual reality, transcranial magnetic stimulation and BCI is often used for rehabilitation tasks based on movement presentation [2, 3]. Currently, the use of BCI to control fingers movement based on the cognitive evoked potential (EP) P300 has been studied [4].

The purpose of this paper is to study the influence of spatial and temporal stimulation parameters on P300 detection.

Materials and Methods

Two volunteers have participated in experiment, the first one is a male at 23 years old and the second is a female at 22 years old. The volunteers had been placed in a comfortable armchair at a distance of 70 cm from square photic stimulation matrix (PSM). PSM consists of 9 LEDs with a 574 nm wavelength. The task for the participants was explained in detail, thus they had to follow certain target stimuli (TS). The TS number corresponded to the diode position in the PSM (Fig. 1).

The spatial interval was equal as:

$$X = \arctg(Xf/D) \quad (1)$$

Where Xf is the actual size between nearest LEDs in PSM (for each matrix interval is 1 cm, 2 cm and 3 cm relatively), D – distance between volunteers and PSM.

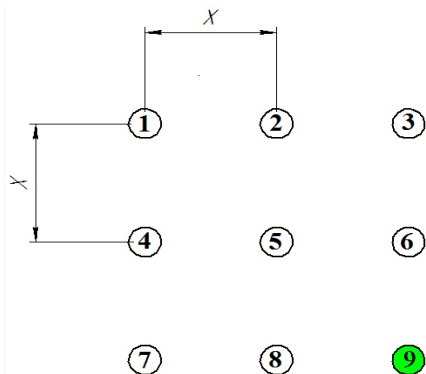


Figure 1: Scheme of PSM, «X» is spatial interval with nearest LED in PSM. LED with number «9» was highlighted

The experiment consisted of 6 experimental series (ES) for the first volunteers and 3 for the second (Table 1). Each experimental series consisted of 3 alternations of stimulation and relaxation intervals (Figure 2).

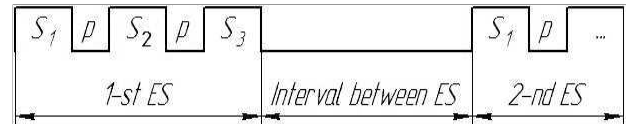


Figure 2: Time diagram of photic stimulation. S_i – interval stimulation in experimental series, i – serial number of TS, p – pause between stimulation probes S_{i+1} and S_i

Photic stimulation was performed using the oddball paradigm [5]. TS was given once in a 9 stimuli series, the rest were non-target stimuli (NTS). Thus, in a 9 stimuli series, each LED in the PSM was highlighted [6].

The volunteers should mentally count the number of TS highlights during stimulation, the stimulation follows by a 20 second rest (Figure 2) in which the subject had reported the TS counted number. Then the subject again counted the number of TS, so the procedure was repeated 3 times (3 numbers were counted).

After that, the stimulation parameters such as stimulation frequency, PSM size, and stimulation time were varied and the following experimental series was performed (see Table 1).

Table 1: Experimental procedures

Experimental procedure 1						
Number of stimulation mode	1A	1B	1C	1D	1E	1F
Numbers of TS	9,1,1	9,1,1	9,1,1	9,1,1	9,1,1	9,1,1
Frequency, Hz	1	5	3	5	1	5
Time, s	200	50	100	50	200	50
Spatial interval in PSM, °	2.4	2.4	1.6	1.6	1.6	0.8
Experimental procedure 2						
Number of stimulation mode	2A		2B		2C	
Numbers of TS	1,1,2		1,1,2		1,1,2	
Frequency, Hz	1		3		1	
Time, s	200		100		200	
Spatial interval in PSM, °	2.4		2.4		1.6	

Electrodes are placed according to the international system "10-20", ipsilateral ear electrodes were used as reference electrode; the earth electrode was installed on one cm above the nasion.

The EEG recording was performed using "Neuron-Spectrum-5". The sampling frequency is 500 Hz, the signal was filtered in the frequency band from 0.7 to 35 Hz. The electrode-skin impedance was measured at the beginning of the experiment and it was checked that electrode-skin impedance did not exceed 20 kΩ during the experiment. Table 2 shows the detailed parameters of the experiment.

Table 2: Parameters of experiment

	Conditions for 1-st subject	Conditions for 2-nd subject
Sound noise level, dB	50	45
Illumination of the room, lux	570	570
Experimental procedure	1	2
Room temperature, °C	24	24

Matlab R2011b software was used for experimental data processing. The coherent averaging method was used with an analysis period of 500 ms. for obtaining the EP.

Results

Figure 3 shows the graphs of typical EP in stimulation mode 1A. The signal 9 shows the EP response to TS. A positive peak is observed with amplitude in the order of 12 μV in the 350 ms region. The signal amplitude in response to the NTS in the region from 300 to 400 ms has not exceeded the value of 7 μV.

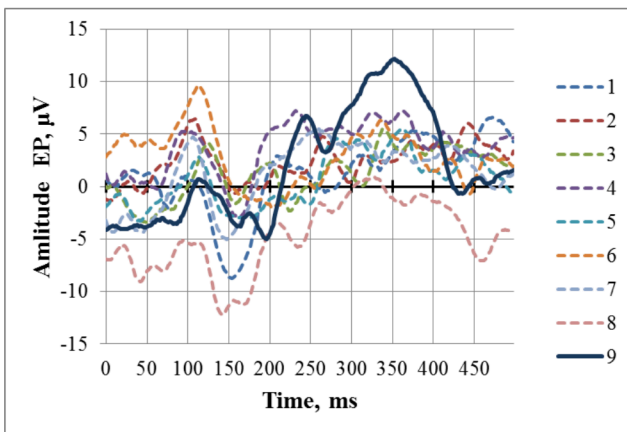


Figure 3: Typical EPs in PzA1 lead of photic stimulation. 1,2,3,4,5,6,7,8 – EPs response of number NTS, 9 – EP response of TS. Number of analyzed EEG epoch is 21 for average

Figure 4 shows the EP in stimulation mode 1B. The graphs have oscillations form. The EP on the TS is not significantly different from the response to the NTS.

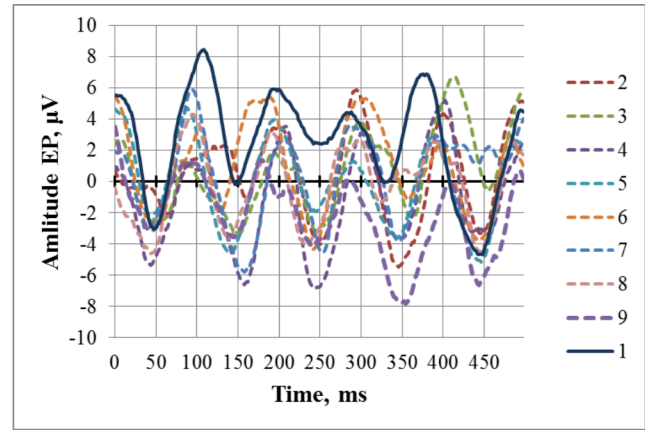


Figure 4: EPs in PzA1 lead of photic stimulation with 5 Hz frequency. 2,3,4,5,6,7,8,9 – EPs response of number NTS, 1 – EP response of TS. Number of analyzed EEG epoch is 27 for average

Based on the results of the experimental studies, the amplitudes and latencies of the EP P300, EP amplitudes in response to NTS were obtained under different stimulation modes (Table 3). The EP amplitude was defined as the maximum value of signal in the region from 300 to 400 ms. The average difference between the amplitudes of P300 and EP on the NTS is as follows:

$$\Delta A_{av} = \frac{1}{N} \sum_{i=1}^N f(A_{P300}^i, A_{EP}^i) \quad (2)$$

where N is the number of stimulations in the experimental series ($N = 3$), i – is the sequence number of the stimulation in experimental series, A_{P300}^i – is the amplitude of P300 for the i -th stimulation, A_{EP}^i – is the maximum amplitude of EP for the i -th stimulation in the time window from 300 up to 400 ms, $f(A_{P300}^i, A_{EP}^i)$ – is the amplitude difference function, equal to:

$$f(A_{P300}^i, A_{EP}^i) = \begin{cases} A_{P300}^i - A_{EP}^i, & \text{if } A_{P300}^i \geq A_{EP}^i \\ 0, & \text{if } A_{P300}^i < A_{EP}^i \end{cases} \quad (3)$$

Table 3: Experimental results with two subjects

N	Am- plitude P300, μV	Latency P300, ms	Ampli- tude EPs, μV	Stimu- lation mode	Δ <i>A</i> _{av} , μV
Subject 1					
1	12	354	7	1A	6,3
2	17	370	10		
3	17	372	10		
4	11	308	6	1B	3,7
5	7	382	7		
6	10	378	4		
7	8	348	2	1C	5,7
8	11	372	5		
9	8	390	3		
10	10	376	3	1D	2,3
11	4	370	5		
12	4	368	5		
13	15	338	8	1E	7,7
14	15	374	10		
15	20	368	9		
16	11	302	5	1F	4,3
17	9	302	5		
18	8	304	5		
Subject 2					
1	9	372	4	2A	3,7
2	7	362	4		
3	7	370	4		
4	1	386	2	2B	0,7
5	4	382	2		
6	2	282	4		
7	5	356	4	2C	1
8	2	390	5		
9	5	300	3		

The P300 was detected if its amplitude was greater than the EP amplitude on the NTS. Based on the values of Table 3, P300 detection dependencies for different stimulation modes were plotted (Figures 5 and 6).

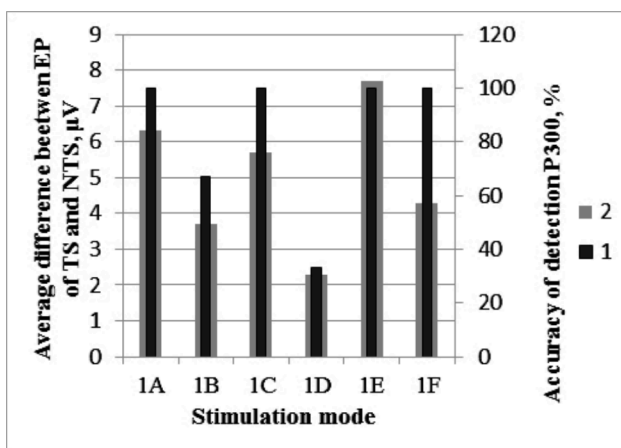


Figure 5: Evaluate of P300 detection with different stimulation mode for subject 1. 1 – The accuracy of P300 detection, 2 – The amplitude average difference value in different stimulation mode

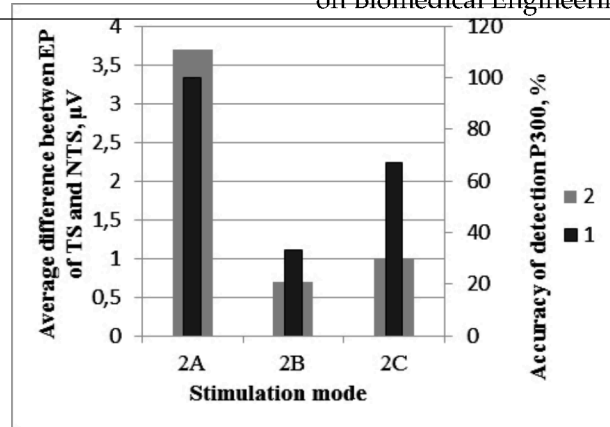


Figure 6: Evaluate of P300 detection with different stimulation mode for subject 2. 1 – The accuracy of P300 detection, 2 – The amplitude average difference value in different stimulation mode

Discussion

One of the most important stimulation parameters during P300 registration is the photic stimulation frequency. Figure 3 shows the typical EP. The graph shows the main peak, which corresponds to P300 presence in response to TS. The visual EP (VEPs) P100 and N145 are also presented on the graph. This EP form is typical for a photic stimulation with 1 Hz frequency. The P300 amplitude varies from 12 to 20 μV and the latency is approximately 360-370 ms.

The photic stimulation frequency increasing to 3 Hz leads the P300 amplitude to decrease and the latency variability to increases. However, the accuracy of P300 determination was not decreased for the first volunteer (Figure 5).

The photic stimulation frequency increasing to 5 Hz leads to the occurrence of oscillations with a 10 Hz frequency and an amplitude in the order of 7 μV . These oscillations are superimposed on the EP P300 and can mask it. The reason of these oscillations is associated with the appearance of steady-state VEPs with photic stimulation frequency increasing, which corresponds to the results of previous work [6]. Against the background of VEPs, the amplitude of P300 decreases and varies in the range from 4 to 11 μV , which in turn affects the P300 detection.

As for the second volunteer, EP P300 had a slightly smaller amplitude from 7 to 9 μV at a stimulation rate of 1 Hz. However, even a slight change in the stimulation modes (an increase in the frequency to 3 Hz or a decrease in spatial interval) significantly reduced the amplitude of P300 (Table 3). As a result, the detection accuracy of P300 decreased (Figure 6). Such a decrease in the P300 amplitude can be associated with fatigue and loss of attention concentration. Therefore, to take an objective account of the involvement degree of patient during study, additional independent measurements must be carried out. Spatial interval with photic stimulation frequencies of 1 and 3 Hz did not affect the accuracy of P300 determination. The amplitudes of VEPs and P300 were approximately in the same values range.

In previous work [6] it was shown that the spatial interval influence on the P300 detection in a 5 Hz photic stimulation and it was assumed that a decrease in spatial interval reduces the accuracy of P300 determination. However, based on the results of current experimental studies, it was found that at 5 Hz photic stimulation, the P300 recognition accuracy for spatial interval 2.4° , 1.6° and 0.8° was 67%, 33% and 100%, respectively.

Thus, the spatial interval influence on the accuracy of P300 detection is more complex.

Conclusions

It was shown that the accuracy of the EP P300 amplitude decreases and the latency becomes more variable during a 5 Hz frequency photic stimulation. The most stable high-amplitude P300 signals were allocated at 1 Hz photic stimulation. At spatial interval in the PSM, on the one hand, the amplitude of P300 increases, while the amplitude of the VEPs that can mask the signal increases in the other hand. During P300 registration, it is important to monitor the concentration of patient's attention within the limit of cognitive task performing.

References

- [1] O.A. Mokienko, N.A. Suponeva, G.A. Asiatskaya, A.S. Klotchkow etc. Clinical recommendation «Stroke in adult: central paresis of upper limb». Rehabilitation specialist's union of Russia, Moscow, 2017.
- [2] O.A. Mokienko, P.D. Bobrov, L.A. Chernikova, A.A. Frolov. Based on motor imagery brain-computer interface for rehabilitation patients with hemiparesis, J Byulleten Siberian medicine, 12: 30-35, 2013.
- [3] K. K. Ang, C. Guan, K. Sui Geok Chua, B. T. Ang etc. Motor imagery BCI for upper limb stroke rehabilitation: an evaluation. IEEE International Conference on Engineering in Medicine and Biology Society(EMBC), Tokio, 261 –264, 2017.
- [4] A.Ya. Kaplan, D.D. Zhigulskaya, D.A. Kirjanov. Research the possibility single fingers of human phantom arm management in brain computer-interface circuit. J Russian State Medical University messenger, Moscow, 2: 26-30, 2017.
- [5] V.V. Gnezditsky. Vyzvanyye potentsialy v klinicheskoy praktike. TRTU, Taganrog, 1997.
- [6] A.N. Dmitriev, I.K. Sergeev, S.I. Shchukin. Evaluation influence spatial distance between photostimulation's on detection P300. J Biomedicinskaya radioelektronika, 9: 19-22, 2017.

Telephone call management in the cognitive operating room

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Introduction

Mobile phones increase the reachability of surgeons and health care providers, thus facilitating decisions making and improving patient care [1,2]. Accordingly, phones are regularly taken into the operating room (OR).

On the other hand, any intraoperative interruption increases the workload and may lead to a negative influence on the outcome [3,4]. Incoming telephone calls are responsible for as much as 1/4 of all disturbing intraoperative events [5]. To avoid this type of interruption, strict interdiction of telephone calls could be a simple and effective means. However the majority of incoming calls is not time-critical and not important, the lack of reachability could be detrimental in some cases. Accordingly, a complete elimination of mobile phones out of the OR is not an option.

To solve this problem, a situational aware system could be helpful which is able to discriminate between “important” calls and those which can easily be postponed. This paper discusses if a cognitive OR system could be used for a situation-adapted preselection of incoming telephone calls for the members of the surgical team.

Materials and Methods

Cognitive OR

In our “cognitive OR”, a central control and steering system is established, which collects a wide range of incoming information in real time [6]. Through “intelligent” interpretation of these data, based upon highly grained patient and surgical workflow models, the system is always aware of the actual situation and even capable to predict forthcoming events including the time left to the end of the surgery. In addition, it even classifies the actual state of the surgery according to “normal”, “irregular” or “critical”. The system described here is a middle ware between the person on the telephone and the surgeon addressed.

Call routing

Incoming calls for the surgeon (in our case to a DECT phone) are not directly forwarded to his phone. Instead the calls are routed to a call handler (Fig. 1). The call handler is provided by an Asterisk based VOIP server. This VOIP server directly interacts with the cognitive OR to get information about the current status of the surgery including the remaining duration. In addition, the central database is informed about incoming calls and is therefore

able to display these calls on a central information unit or create a list of missed calls after the operation is completed. The VOIP server is also able to distinguish between calls from within the hospital network and calls from outside.

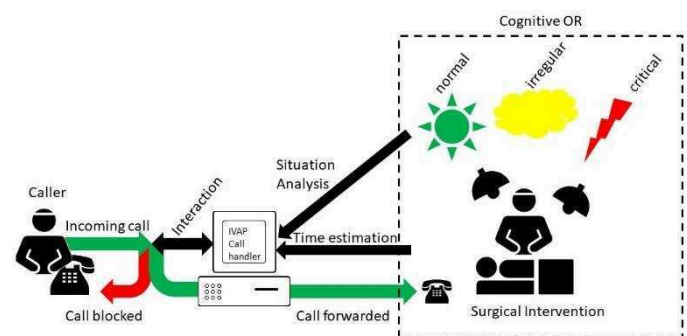


Figure 1: Call routing model

Caller interaction module

The decision whether the surgeon should be encountered with the call or not depends upon three different aspects:

- I) Significance of the request
 - II) Actual surgical situation
 - III) Time line
- I) Significance of the request

Many calls are neither time critical nor really important, but, of course, the system will be unable to classify the urgency of the call. This has to be left to the caller. The system, however, provides the necessary information to enable the caller to weigh up whether it is justified to contact the surgeon immediately or not.

- II) Actual surgical situation

The workload during a surgical operation varies. If it is a comparatively easy case and if everything is running smoothly, the surgeon should be more open to respond to a telephone call than under severe strain. The situational aware system is able to classify the workflow as either “normal” (green), “irregular” but not yet dangerous (yellow) or “critical” (red). Accordingly, answers A, B or C

are selected. The type of answer may vary in the course of the operation.

Accordingly, the caller will be informed as follows:

- A) "Dr. NN is currently doing a surgery which will probably be finished in ... minutes/hours. Nonetheless, you could be put through if required. In this case, please dial "2".

The threshold is, thus, comparatively low to contact the surgeon right now.

The next step is to make the caller a bit more hesitating to get connected:

- B) "Dr. NN is at the OR table at the moment. The surgery will last for another ... minutes/hours. Please, do not disturb unnecessarily. However, if your matter is urgent and cannot wait, please dial "2".

It is assumed that the caller rather refrains from being put through to the surgeon.

If the situation in the OR is really critical and any unnecessary distraction has to be avoided, the reply has to be very deliberate:

- C) "Dr. NN is currently doing a surgery. A call can only be accepted in vital cases. Can your call wait for another ... minutes/hours? Only if you are sure it cannot wait dial "2".

In this case, only really urgent calls should be connected.

III) Time line – estimated duration of the surgery

At the beginning of an operation it has to be expected that the surgeon will not be directly available on the phone for a considerable period of time. Accordingly, a better access should be granted to the caller as compared to later phases of the operation. If not determined otherwise, the system should routinely start with answer "A". After 2/3 of the estimated duration, the answer is automatically switched to "B". In any case, the caller will be informed about the expected duration of the operation.

Thus, the telephone management does not decide upon whether a caller is connected or not but it just modulates the threshold to contact the surgeon during the operation or not. To find out whether this method is effective in reducing the number of incoming calls without depriving the caller of the ability to reach the surgeon in critical cases, a study was conducted.

Survey

A list of different scenarios was presented to different healthcare providers of a surgical unit comprehending three different groups of matters of minor (class III), major (class II) or vital (class I) importance. Each test person was summoned up to call the respective doctor and got

either the answer A, B or C, each with 3 different time estimations (60, 30 or 15 min till the end of surgery). It was protocolled if he/she insisted about getting connected.

Class III scenarios:

1. A former patient visits the surgical floor and asks whether he could briefly see the doctor who had successfully done his surgery 3 weeks in order to express his thanks.
2. The administration calls and asks to transfer a message to the doctor which is not urgent but important.

Class II scenarios:

1. The relatives of a patient are just paying her a visit. Since the patient will be discharged within the next days, they would like to ask for the doctor to get information about the organization of the further care.
2. A patient waiting for her surgery which will take place in about 2 – 3 hours is very thirsty. It should be adequate to give her 500 or 1000 ml of saline

Class I scenarios

1. A patient with the signs of an acute secondary haemorrhage after a cholecystectomy
2. A patient with clear clinical signs of an acute pulmonary embolism

In addition, every test person was asked to judge upon the value of receiving the estimated time left till the end of the operation by using a modified Likert Scale (negligible=1 to very helpful=5). To test the overall acceptance of the system the same Likert Scale was used.

Results

A number of 46 different healthcare providers participated in the survey. The results show a clear correlation between the significance of the request and the number of calls passed through (Fig. 2). For a request of minor importance (class III) 99% of all test persons dispense with a connection of their call. Out of 414 calls only 4 calls were forwarded. For the scenario with a request of major importance (class II) 7% of all calls were forwarded to the surgeon (29 out of 414 calls), mostly in a normal OR situation. In case of a request of vital importance (class I) 78% of all test persons decided to be connect to the surgeon (324 out of 414 calls). The results of the Likert scale for the value of receiving the estimated time left till the end of the operation were 4.0 for a request of vital importance, 3.5 for major importance and 2.6 for minor importance. The remaining operation time only showed an influence to class I scenarios (Fig. 3). Most callers refrained from being put through for the case of 15 minutes remaining operation time (63%, 57 out of 90 blocked

calls). The overall acceptance of the system was resulted in a value of 3.5.

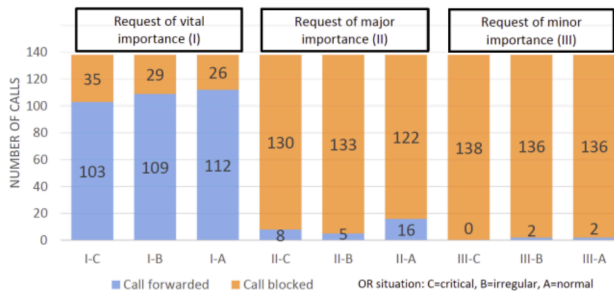


Figure 2: Calls blocked/forwarded by importance of the request and OR situation

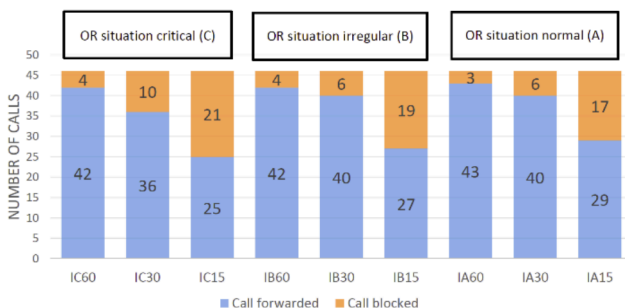


Figure 3: Calls blocked/forwarded in case of a vital request by OR situation and remaining time

Discussion

The result of the survey clearly shows the advantage of the telephone management system. Unnecessary calls (request of minor importance) can be blocked and the surgeon is not constantly interrupted during the surgery. On the other hand important calls are still forwarded into the OR. The definition of the three different thresholds in combination with the estimation of the time left till the end of the surgery deliver the caller a clear impression of the current situation in the OR. Not only the surgeon, but also the caller benefits from the system. The time estimation was considered very useful by the vast majority of the test persons. The estimation is an important hint for most callers to decide whether they want to be connect or not, especially in class I scenarios. The prognosis also avoids unnecessary further call attempts within the estimated time period.

Conclusions

In this paper we presented a concept for telephone call management within the OR. A survey under different healthcare providers showed a broad acceptance and the need for such a system. Telephone management in the OR has to potential to reduce unwanted interruption during surgeries as well as to reduce the workload of surgeons and nurses without blocking urgent or important calls. The next step is to adapt these findings and to evaluate the call management system under real surgical conditions.

References

- [1] Angarita, F. A., Strickland, M., Acuna, S. A. (2015). Incorporating smartphones into clinical practice. *Annals of Medicine and Surgery*, 4(2), 187.
- [2] Mentis, H. M., Chellali, A., Manser, K., Cao, C. G., Schwartzberg, S. D. (2016). A systematic review of the effect of distraction on surgeon performance: directions for operating room policy and surgical training. *Surgical endoscopy*, 30(5), 1713-1724.
- [3] Weigl, M., Stefan, P., Abhari, K., Wucherer, P., Fallavollita, P., Lazarovici, M., Catchpole, K. (2016). Intra-operative disruptions, surgeon's mental workload, and technical performance in a full-scale simulated procedure. *Surgical endoscopy*, 30(2), 559-566.
- [4] Arora, S., Sevdalis, N., Nestel, D., Woloshynowych, M., Darzi, A., Kneebone, R. (2010). The impact of stress on surgical performance: a systematic review of the literature. *Surgery*, 147(3), 318-330.
- [5] Weigl, M., Antoniadis, S., Chiapponi, C., Bruns, C., Sevdalis, N. (2015). The impact of intra-operative interruptions on surgeons' perceived workload: an observational study in elective general and orthopedic surgery. *Surgical endoscopy*, 29(1), 145-153.
- [6] Ostler, D., Kranzfelder, M., Stauder, R., Wilhelm, D., Feussner, H., & Schneider, A. (2015). A centralized data acquisition framework for operating theatres. In *E-health Networking, Application & Services (HealthCom), 2015 17th International Conference on* (pp. 1-5). IEEE.

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Translation Dynamics in Holistic Analysis of Functional Human-body System

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Introduction

The core tenet in system fault diagnostics is that behavior of the whole emerges from activity of functional components and coordination of their interaction. This motivates a *drill-down* approach in functional analysis of complex systems [1, 2].

Manned spacecraft, aircraft carriers, submarines, and the socio-biological system of human body with person's actions all impress by their complexity of interwoven detail as soon as one can look behind their encasement, and full comprehension of functional structures and of output in response to stimuli input will often deem impossible. A systematic approach may then start from construction principles that let the apparatus fulfill its mission: for example, components that allow the plane to fly (wings, propulsion), to take off and to land (wheels), and to carry goods and passengers (cabin). Next, the set of vital prerequisites, as energy supply, wiring, cabin air, to mention a few. Finally, all equipment, including human operators, to pilot the plane's operations – have orientation, decide on direction, and interact with outside world. Apart from disrupted material integrity of whole plane, review of these items for clues is witnessed, for example whenever an Airbus or Boeing disappears on a scheduled passenger flight over the oceans. Speculating about malfunction of said *productivity* sub-systems, *vital functions* sub-systems, *operational functions* sub-systems illustrates a scaling understanding that is equally seen in a doctor's scrutinizing first view of a patient as totality of person 'encased' in body system before deciding on an entry point for diagnostic work-up.

Definition 1 *Highly complex systems intended by design for purposeful action are called production systems.*

Principle 1 *Production systems share a tri-partite functional decomposition of their ensemble, the Whole, into vital functions, productivity functions, and operational functions, referred to as *wirk-components*, meaning components for effectuation, in German more precisely *Komponenten des Bewirkens*.*

Corollary 1 *The tri-partite functional decomposition is then canonical among all production systems.*

The decomposition is exhaustive and non-overlapping. Its components are referred to as *canonical wirk-components*.

Principle 2 *At any moment, the behavioral activity of the Whole is a complete translation of interaction between its three canonical *wirk-components* and their functional properties currently prevailing.*

These principles are to apply throughout though systems differ substantially in material realization and in designated environment. The present exposition then describes an equally canonical *configuration of effectuation dynamics*, a *wirkgefüge* independent of its physical realization, that first energizes the cooperation of *canonical wirk-components* - the *logical units* at tri-partite "function-level no.1" - and then translates this to whole-body "function-level 0" aggregate dynamics.

The configuration of control couplings that permits the human body system to energize required action of its *canonical wirk-components* in any situation and that is conceptually equally independent of its material realization, is referred to as *schaltgefüge*, which is considered as the mission of *Wiener* [3]-sense "*kybernetik*" in [4]. By their independence of material realization, *axiomatic wirkgefüge* and *kybernetik schaltgefüge* then require each other, which explains the level of abstraction in the present exposition.

Materials and Methods

Prerequisites

The design of *axiomatic wirkgefüge* exploits intuitive concepts from electric direct-current circuits: tension (voltage), accumulated charge, capacity, resistance, supply and consumer power (wattage) demand, that are basic – not to suggest that physical electricity is actually involved.

Definition 2 *The axiomatic *wirkgefüge* consists of a ubiquitous source with potential difference (voltage) U_0 , and for every single logical unit, of a supply condenser of capacity C for buffer storage of supply charge $Q_s(t)$ by time t , a resistor with resistance $R_s(t)$ for passage control of supply current (amperage) $I_s(t)$ to said condenser, and of another condenser for charge consumption, conceived as a mirror of the supply-part condenser, with current voltage $U_c(t)$ generated by its current charge $Q_c(t)$ as source for the demand part, another resistor with resistance $R_d(t)$ for passage control of demand current (amperage) $I_d(t)$ to an end consumer with demand wattage $P_e(t)$.*

Principle 3 (Sluggishness) *The exposition focuses on almost instantaneous charge increments and decrements on supply and demand part condensers, respectively, in any incremental time interval $[t, t + dt]$, $t > 0$; accumulated charges Q are assumed continuous functions $(Q(t))_{t>0}$ with derivative $(I(t))_{t>0}$ everywhere. Voltages, resistances, wattages, however are assumed to lag behind, shown in their pre- t values, $U(t-)$, $R(t-)$, $P(t-)$. They can then be*

assumed to have currently fixed values during an arbitrarily small amount of time while accumulated charge on the condensers changes.

Remark 1 The concept of a “mirror” condenser is introduced for use in the postponed control regimen, in particular to control access to available supply charge.

Assumption 1 Ohm’s law and Kirchhoff’s rules as known for direct electric current circuits do apply in the axiomatic *wirkgefüge*.

Remark 2 For human body system, source voltage may be thought of being generated by the cellular system, the body’s material base layer, while effectuation dynamics affect only the activity on function levels above the cellular system. That all functional activity is realized by ubiquitous living cells may ‘close the loop’ for the circuit.

Generic Single Circuit

The axiomatic *wirkgefüge* of Def. 2 applies; see Fig. 1 for illustration.

Single-circuit supply-part

Define the charge supply part through quadruple $[U_0, (R_s(t))_{t>0}, C, (Q_s(t))_{t\geq 0}]$. To determine supply current $I_s(t)$ explicitly, note that ohmic resistance $R_s(t)$ implies a voltage drop of $U_s^*(t) = R_s(t)I_s(t)$ that leaves an effective supply voltage $U_s(t)$ at the condenser of $U_s(t) = U_0 - U_s^*(t)$, that generates t -prevalent charge $Q_s(t)$ on the condenser through $Q_s(t) = CU_s(t)$. While $U_s(t) = U_0$ when $R_s(t) = 0$, $R_s(t) > 0$ permits re-arrangement such that $I_s(t) = U_0/R_s(t) - Q_s(t)/[CR_s(t)]$, and, by $dQ_s(t) = I_s(t)dt$, a supply-charge increment during $[t, t + dt]$ of

$$dQ_s(t) = \frac{U_0C - Q_s(t)}{CR_s(t)}dt \quad (1)$$

yields the first-order differential equation

$$U_0C = \dot{Q}_s(t)R_s(t)C + Q_s(t) \quad (2)$$

with $Q_s(0) = 0$. For constant resistance $R_s(t) \equiv R_s^* > 0$, a solution of (2) is

$$Q_s(t) = U_0C \left(1 - e^{-\frac{1}{R_s^*C}t} \right). \quad (3)$$

Single circuit demand-part

With Q_c differentiable, the quadruple

$$[(Q_c(t))_{t\geq 0}, C, (R_d(t))_{t>0}, (P_e(t))_{t>0}] \quad (4)$$

defines the charge demand part according to end-consumer power demand $P_e(t)$; demand-circuit current is $I_d(t) = \dot{Q}_c(t)$, voltage drop at demand-control resistor of resistance $R_d(t)$ then is $U_d(t) = R_d(t)\dot{Q}_c(t)$. With source voltage $U_c(t) = Q_c(t)/C$ for consumption according to t -prevalent condenser charge $Q_c(t)$, effective voltage $U_e(t)$ at

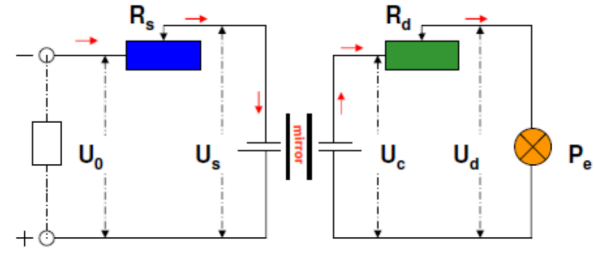


Figure 1: The motivation for the generic single-circuit according to Def. 2 is illustrated as if it were a pair of electric circuits.

the end consumer is then $U_e(t) = U_c(t) - U_d(t)$ with ohmic resistance $R_e(t) = U_e(t)/\dot{Q}_c(t)$ and power (wattage) $P_e(t)$, $P_e(t) = U_e(t)\dot{Q}_c(t)$, at any time $t > 0$. While $U_e(t) = U_c(t)$ when $R_d(t) = 0$, $R_d(t) > 0$ permits rearrangement that gives a first-order quadratic differential equation in Q_c ,

$$\dot{Q}_c^2(t) - \dot{Q}_c(t) \frac{Q_c(t)}{CR_d(t)} + \frac{P_e(t)}{R_d(t)} = 0, \quad (5)$$

which implies a decremental change in charge on the demand-part condenser. that depends on t -prevalent condenser charge $Q_c(t)$, end-consumer’s pre- t -power (wattage) demand $P_e(t)$, and pre- t demand-current control resistance $R_d(t)$, for a fixed capacity C .

When one absorbs the demand-control resistor’s and the end-consumer’s ohmic resistances into one resistor according to their serial connection, $R(t) = R_d(t) + R_e(t)$, one obtains the linear first-order differential equation in $Q_c(t)$,

$$\dot{Q}_c(t) = -\frac{Q_c(t)}{CR(t)}. \quad (6)$$

Results

A Triple Circuit

The triple-circuit *wirkgefüge* will have one copy of the generic single-circuit in Sect. “Generic Single Circuit” for each *Wirkkomponente*, set in a parallel connection which implies common source voltage U_0 for each while total current and moved charges split at the branching points into the partial circuits, see Fig. 2.

For each replication identified by a subscript i , for $i = 1, 2, 3$, one has (1) now as

$$dQ_{si}(t) = \frac{1}{R_{si}(t)C_i} (U_0C_i - Q_{si}(t))dt. \quad (7)$$

and (5) as

$$dQ_{ci}(t) = -\frac{Q_{ci}(t)dt}{C_iR_{ci}(t)} \quad (8)$$

$$\dot{Q}_{ci}(t)Q_{ci}(t) = R_{di}(t)C_i\dot{Q}_{ci}^2(t) + C_iP_{ei}(t). \quad (9)$$

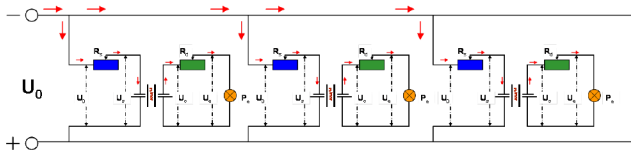


Figure 2: Schematic triple-circuit in parallel connection of three replicates of generic circuit in Fig. 1.

Up-scaling: triple- to single-circuit

For clarity of exposition, it is helpful to use superscripts FL0 and FL1 in order distinguish the appropriate function levels in notation, whenever both function levels are involved in a statement.

Up-scaling supply-parts

Here, it has to be shown that the configuration permits to re-obtain (2) from the triple in (7).

Capacities and t -prevalent charges on the three supply-part condensers add up as much as currents according to Kirchhoff's rule, $C_s = C_1 + C_2 + C_3$, $Q_s(t) = Q_{s1}(t) + Q_{s2}(t) + Q_{s3}(t)$, $I_s(t) = I_{s1}(t) + I_{s2}(t) + I_{s3}(t)$, while for supply-control resistances $((R_s)^{-1})(t) = R_{s1}^{-1}(t) + R_{s2}^{-1}(t) + R_{s3}^{-1}(t)$ holds.

Theorem 1 The FL1 triple-circuit supply-parts defined by

$$[C_i^{\text{FL1}}, Q_{si}^{\text{FL1}}(t), R_{si}^{\text{FL1}}(t)]_{i=1,2,3;t>0} \quad (10)$$

translate into a FL0 single-circuit supply-part

$$[C_s^{\text{FL0}}, Q_s^{\text{FL0}}(t), R_s^{\text{FL0}}(t)]_{t>0} \quad (11)$$

by summation of capacities, charges, and inverse resistances,

$$C_s^{\text{FL0}} = C_s^{\text{FL1}}, \quad (12)$$

$$Q_s^{\text{FL0}}(t) = Q_s^{\text{FL1}}(t), t > 0, \quad (13)$$

$$(R_s^{\text{FL0}})^{-1}(t) = (R_s^{\text{FL1}})^{-1}(t), t > 0. \quad (14)$$

Proof: Rewriting (7) for each i ,

$$dQ_{si}(t) = \frac{U_0}{R_{si}(t-)} - \frac{Q_{si}(t)dt}{R_{si}(t-)C_i} \quad (15)$$

and observing that $Q_{si}(t) = U_{si}(t)C_i$ for the supply-part condensers and $U_{si}(t-)/R_{si}(t-) = I_{si}(t)$, for every i , summation of (7) over $i = 1, 2, 3$ yields indeed

$$dQ_s(t) = \frac{1}{C_s} (R_s)^{-1}(t-) (U_0 C_s - Q_s(t)) dt \quad (16)$$

Up-scaling demand-parts.

It now has to be shown that the configuration permits to re-obtain (5) from the triple in (9), too.

Capacities C_i and t -prevalent charges $Q_{ci}(t)$ on the three demand-part (mirror) condensers, and end-consumers' power demands (wattages) $P_{ei}(t)$ are first added, $C_s =$

$C_1 + C_2 + C_3$, $Q_c(t) = Q_{c1}(t) + Q_{c2}(t) + Q_{c3}(t)$, and $P_e(t) = P_{e1}(t) + P_{e2}(t) + P_{e3}(t)$.

One then has to construct a demand-part circuit at FL0 with the desired properties that arise from summations across respective circuits at FL1. To organize the train of thought, a general lemma is helpful.

Lemma 1 For any single circuit with condenser of capacity C and t -prevalent charges $Q(t)$, $t \geq 0$, and with a consumer of power demand $P(t)$, $t \geq 0$, there exists a resistor of resistance $R(t)$, $t \geq 0$, such that

$$R(t) = \frac{\frac{Q(t)}{C} - \frac{P(t)}{Q(t)}}{\dot{Q}(t)} \quad (17)$$

for any t , $\dot{Q}(t) > 0$, $t \geq 0$.

Proof: On the condenser, t -prevalent charges $Q(t)$ imply t -prevalent voltages $U(t)$ and $U(t) = Q(t)/C$ for any $t \geq 0$. Voltage drop $U_P(t)$ at t according to a t -prevalent power demand $P(t)$ is $U_P(t-) = P(t-)/\dot{Q}(t)$, for any $t \geq 0$. For any residual voltage $U(t) - U_P(t) \geq 0$, there is a resistor in the circuit which implies a voltage drop $U_R(t) = U(t) - U_P(t)$ at t ; its resistance $R(t)$ is then $R(t-) = U_R(t-)/\dot{Q}(t)$, for any $t \geq 0$. Together, these results prove the Lemma.

It remains to identify FL0 capacity, charges, powers from the FL1 triple-circuits summaries, first, and then to apply the Lemma in order to finalize the up-scaling.

Theorem 2 The FL1 triple-circuit demand-parts defined by

$$[C_i^{\text{FL1}}, Q_{ci}^{\text{FL1}}(t), R_{di}^{\text{FL1}}(t), P_{ei}^{\text{FL1}}(t)]_{i=1,2,3;t>0} \quad (18)$$

translate into a FL0 single-circuit demand-part

$$[C_c^{\text{FL0}}, Q_c^{\text{FL0}}(t), R_d^{\text{FL0}}(t), P_e^{\text{FL0}}(t)]_{t>0} \quad (19)$$

by summations of capacities, charges, and power demands,

$$C_c^{\text{FL0}} = C_c^{\text{FL1}}, \quad (20)$$

$$Q_c^{\text{FL0}}(t) = Q_c^{\text{FL1}}(t), t > 0, \quad (21)$$

$$P_e^{\text{FL0}}(t) = P_e^{\text{FL1}}(t), t > 0; \quad (22)$$

and a derived resistance

$$R_d^{\text{FL0}}(t-) = \frac{\frac{Q_c^{\text{FL0}}(t)}{C_c^{\text{FL0}}} - \frac{P_e^{\text{FL0}}(t-)}{\dot{Q}_c^{\text{FL0}}(t)}}{\dot{Q}_c^{\text{FL0}}(t)} \quad (23)$$

for the demand-control resistor.

Proof: With $C = C_c^{\text{FL1}}$, $Q(t) = Q_c^{\text{FL1}}(t)$, and $P(t) = P_e^{\text{FL1}}(t)$, the assertion follows from Lemma 1.

Remark 3 Note that (23) is the quadratic first-order differential equation (5).

Discussion

Methodology

An axiomatic *wirkgefüge* is described as a mathematical framework for translation of dynamics from canonical tripartite “function-level no.1” to whole-body “function-level

0" aggregate. It splits the aggregate's functional activity according to the number of the aggregate's constituent logical units and distributes its charge according to their respective demands; but it also re-combines individual units' dynamics into the dynamics of their aggregate whole. This points to its use at other function levels: One may consider the liver organ as an aggregate whole at "function-level no. n " for some positive number n , say, and involve its *wirk-components* as logical units on "function-level no. $(n+1)$ ", taking care that the decomposition is exhaustive and non-overlapping. In this way, one can start to work downwards from any logical unit in a functional hierarchy; to work upwards, however, one has to take into account *all* logical-unit "neighbors" on the same function level before one can up-scale to upper level dynamics. Hence, drill-down appears to be the preferable direction.

The mathematics of *axiomatic wirkgefüge* is deliberately simple, and may seem too simplistic to be relevant, at first sight. However, it rapidly builds up complexity when decomposing functional aggregates into logical units way down - long before one gets to the bottom of 10^{14} living cells, each a burn chamber and base functional unit. It then reminds one of the wheat-chessboard problem.

This exposition merely describes the "firing" in the sense of energy transfer dynamics; specification of a control regimen of dynamics in single and in triple circuits is postponed. The differential equations were hence left without solutions, as the side conditions that are necessary to obtain specific solutions depend on an adequate "wiring" in the sense of a *kybernetik schaltgefüge* that permits the human body system to energize required action of its *axiomatic wirkgefüge* in any situation for preservation of its integrity and survival. Their common independence of physical realization is expected to permit to design both configurations by analogy with better understood complex engineered production systems.

Medical Perspective

Partition of whole-body's power demand into its canonical *wirk-components* - vital, productional, operational - marks an entry point for investigation of partitional variation in different stressing (by exposures or interventions) scenarios and of any discrepancy in power-demand partitioning from so-called "normal" population in various disorders; disablement, impairment, somatic or psychic chronic disease can be expected to imply partition shifts in either productivity (musculo-skeletal locomotor function, sexual reproductivity), or operational ability (communication with body's outside world, self-steering one's operations), or vital-functions activity (e.g. respiration, circulation, immune response, nervous control, hormonal regulation, food intake, digestion, waste ejection), and possibly in more than one. Detectable as deviations from "normal" whenever it manifests itself in person's behavior, evidence of persistent shifted partitioning may also be of interest in a context of unspecific screening for power-demand anomalies in human body system.

Specifically, among the first would be investigations in patients with manifest movement disorders and Parkinson's disease, as well as in patients in different stages of progressive recovery, functional rehabilitation, work and social-life re-integration, and life-balance restoration after an ischemic stroke with moderate to severe neurological deficits [5]; for healthy-subject controls, athletes will be first choice in these investigations.

The practical implementation poses challenging problems regarding technology for taking specific measurements of *wirk-components* power demands and methodology of its application. Relative assessments will be in foreground. Whole-body power demands when "sleeping", "awake lying still" of 77 cal/h, "sitting at rest", "standing relaxed", "walking slowly", and "running" of 65 cal/h, 77 cal/h, 100 cal/h, 105 cal/h, 200 cal/h, and 570 cal/h, respectively, [6], give first clues, e.g. to net walking-power demand against background upright posture, of 95 cal/h. (Note that an interface for exchange with outside world in total energy balances is not included.)

Conclusions

The axiomatic construct suggests a path into multi-scale modeling of human body system *wirkgefüge*, coherent by design, and progress will be made from top to bottom. This way, impact from health-compromising exogenous factors can be integrated at any level, but applicability in clinical context is still to be confirmed.

References

- [1] J. Mau. Systems Neuroergonomics. In R. Wang and X. Pan, editors, *Advances in Cognitive Neurodynamics* (V), chapter 59, pages 431–437. Springer Science+Business Media, Singapore, jan 2016.
- [2] J. Mau. Reducing complexity in modeling human body. In *Proceedings of The XVIII International Conference on Complex Systems: Control and Modeling Problems (CSCMP-2016)*, pages 23–28. Samara, Russia, sep 2016.
- [3] N. Wiener. *Cybernetics or Control and Information in the Animal and the Machine*. Massachusetts Institute of Technology, Boston, 1961.
- [4] H. Sachsse. *Einführung in die Kybernetik*. Vieweg, Braunschweig, 1974.
- [5] J. Mau. Kybernetic modeling of human body system. In *Proceedings of the 12th Russian German Conference on Biomedical Engineering (XII RGC'2016)*, Suzdal, Russia, pages 11–15. Vladimir, Russia, jul 2016.
- [6] J. E. Hall. *Guyton and Hall Textbook of Medical Physiology*. Saunders, Philadelphia, 12 edition, 2011.

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Enabling “Surgery 4.0”: 5G Data Transmission in Minimally-invasive Surgery

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Introduction

With the expansion of the digital functionalities in the OR in the sense of "Surgery 4.0" facilitating important applications such as real-time person or asset track- and tracing or tele-robotic surgery, the question of improved data transmission quality becomes more and more urgent (1). As the currently available technologies for data transmission in the OR (Ethernet/LAN, W-LAN, Bluetooth) are limited in terms of transmission rate, latency and signal stability (2), the upcoming mobile data transmission technology 5G seem to offer a high potential.

5G includes the following characteristics as compared to the current mobile transmission standard 4G/LTE: a 100 times higher data transmission rate (up to 10 Gbps), an extremely low latency (1ms) and 1000 times higher capacity (3). The possibility of transmitting a high data volume almost without delay with high precision and stability makes the 5G technology interesting for different medical applications.

It is not yet known whether the promising 5G mobile telecommunication performance is sufficient for the demanding medical applications such as person or asset track- and tracing, video data transmission for telemedicine and tele-robotic surgical operations, where fast, secure and ubiquitously available data transmission is essential.

The latter is the basic prerequisite for the emerging field of cognitive surgery (4), in which the surgical team is extensively supported in its work by the digitalized OR environment. It was the purpose of this research project to evaluate possible fields of applications for 5G to enable Surgery 4.0.

The manuscript comprehends of two different sections:

- a) A Delphi study evaluating the expectations and acceptance of 5G in the medical (surgical) field in general
- b) The evaluation of 5G technology for a surgical telepresence application (use-case tele-robotic surgery)

Materials and Methods

Delphi study

In order to first obtain an estimation of possible 5G applications in the medical field, necessary technical developments and comparison to currently available data transmission technologies (4G/LTE, WLAN), a Delphi study was carried out. The Delphi method is a structured communication method, which relies on a panel of experts. It is based on the principle that forecasts from a structured group of individuals are more accurate than those from unstructured groups (5).

In two rounds, a fixed panel of 12 experts (industry n= 9, small and medium size enterprises n= 2, academic institution n= 1) provided a written assessment of a list of 28 theses/questions related to the potential future developments of 5G, which was compiled as questionnaire by the authors. The theses/questions were grouped in five different sections: experience, trend, impact, promoting and detaining factors with/of 5G technology. For every thesis/question, probability was explored and in a second round, the results of the previous round were given as feedback. Subsequently, experts were asked to reassess the hypotheses and either confirm or revise their own opinion, where it diverges from the majority opinion.

Surgical Telepresence

Telepresence in general refers to a set of technologies allowing a person to feel as if they were present, to give the appearance of being present, or to have an effect (via tele-robotics) at a place other than their true location (6).

The term teleconsultation in the medical field means an image- or video-based consultation of a remote expert giving verbal advice during an operation or procedure. Whereas surgical telepresence reveals a (real) physical action at the

distant point of care by a consultant. In this case, a mechatronic support system (e.g. a surgical robot = slave) processes the haptic commands of a consultant entered into an interface (master) into precise manipulations at the remote surgical site (7). As compared to teleconsultation, the requirements of data transmission volume, rate and latency are significantly higher for telepresence, since any delay or interruption of the dataflow would be extremely hazardous.

To evaluate 5G performance for surgical telepresence, we set up an ex-vivo use-case using the robotic camera control arm SoloAssist® (AKTORMed, Barbing, Germany) as slave system maneuvering a laparoscope inside the abdominal cavity of the OR phantom ELITE (CLA Coburg, Germany). Data transmission characteristics were measured. Control commands for the slave system (move up-down-left-right, zoom-in and out) were manually entered into a graphical user interface (GUI, Fig. 1) and data transmission to the robotic camera control arm was conducted with 5G. Normally, data transmission from the input interface to the robot is tethered.

Communication with the SoloAssist® is bidirectional and was realized through a CAN-interface. It allows to send movement commands to and receive position information from the robotic camera control arm. The unidirectional (video) data exchange with the laparoscope unit (K. Storz, Tuttlingen, Germany) was realized through a frame grabber. It receives the analog signal from the laparoscope through a coaxial connection and converts it to digital format. Key capabilities of the 5G testbed (5G NR V2V oriented) are given in Table 1.

Latency	< 2ms
Data rate	Uplink 6 Mbps (HD), Downlink < 10kbps
Wireless range between terminal / sensor and 5G access point	Indoor < 20 m
Interface	1 Gigabit Ethernet (cat6)
Transfer mode	Ultra-reliable low latency communication (URLLC)
Terminal speed	0 kmph
Duplex Mode (LTE)	Time Division Duplex (TDD)
Frequency	2.6 GHz / 20MHz

Table 1. Characteristics of the Huawei 5G testbed (USRP X310). Versatile data interface configurable to support different 5G applications using low-latency (<1ms) machine-type communication.

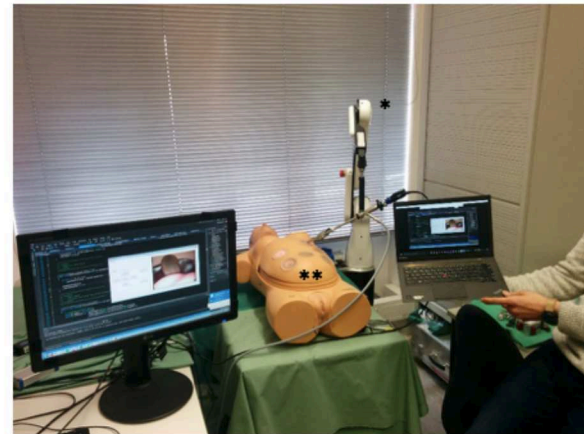


Figure 1. Upper figure: Graphical user interface (GUI) on a tablet computer. Touchscreen to enter the direction of movement for the robotic camera arm SoloAssist® (move up-down-left-right, zoom-in and out), display of the video image (gallbladder). Lower figure: The robotic camera arm (*), maneuvering the laparoscope inside the abdominal cavity of the operating phantom ELITE (**, CLA Coburg), is controlled via GUI by means of 5G data transmission.

Results

Delphi study

At time of abstract submission $n = 10$ experts (83 %) had completed two survey rounds. Principal points are: 5G technology is regarded as trend-setting for the future transfer of information in the healthcare domain (85.7% agree / 14.3% agree fully). The current mobile standard 4G/LTE is assessed not to be sufficiently suitable for the expected future data transmission requirements (57.1% agree fully). According to expert opinion, the financing of 5G-based services should be actively supported by healthcare politics (42.9% agree fully / 57.1% agree more likely) and potential industry partners should be involved as early as possible in the process of 5G integration in healthcare applications (71.3% agree fully / 28.7% agree more likely).

Preliminary study results confirm our use-case hypotheses that telepresence with 5G data transmission improves medical care in remote regions by actively including spe-

cialist knowledge and skill into patient diagnostic or treatment (85.7% agree with operation of 5G technology).

Uncertain yet is the question, whether the experience gained so far with mobile data technology (4G/LTE) allows a good assessment of which problems, requirements and opportunities arise with the implementation of the new 5G data technology or not (57.1% neutral / 28.6% hardly agree / 14.3% tend to agree).

Telepresence

The active involvement of an expert over a distance in the course of an operation was realized in the telepresence use-case. By implementation of the 5G data transmission module, the robotic camera-control arm SoloAssist® was successfully maneuvered wireless without any data transmission interruptions or data transmission delay. A prototype installation of the system was presented at the Mobile Broad Band Forum (MBBF) in London in December 2017.

5G technology allows different settings of the transmission parameters of the physical layer. Especially for the URLLC mode that is used in our setup, a careful parameter selection (e.g. subcarrier spacing and time transmission internal (TTI) length) is important to achieve a minimum of latency combined with a high robustness against transmission errors (Fig. 2).

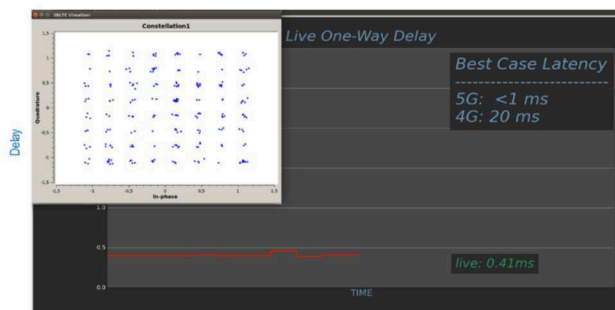


Figure 2. Latency of 5G data transmission can be reduced to < 1ms by carefully selecting the transmission parameters. The measured signal delay of the deployed 5G module including encoding and decoding was 0.41ms.

The evaluation of the transmission properties in terms of reliability is shown in Figure 3. Classic OFDM (Orthogonal Frequency-Division Multiplexing, used in 4G) was compared with a filtered variant (p/f- OFDM, used in 5G). Two different radio channels were used. Measurements showed that a minimum signal-to-noise ratio of 15dB is required to achieve a 99.999% reliability.

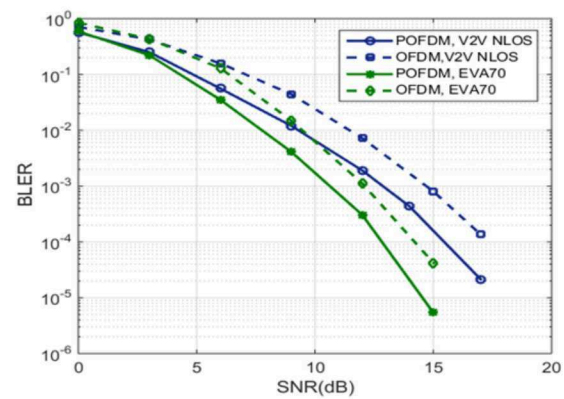


Figure 3. Reliability of radio transmission. OFDM (Orthogonal Frequency Division Multiplexing, used in 4G). p/f- OFDM are filtered variants used in 5G. Radio channels: V2V (Vehicle to vehicle), NLOS (Non line of sight pass) and EVA70 (Extended vehicular A). BLER = block error rate, SNR = signal to noise ratio.

Conclusion

Advanced mobile telecommunication technologies have the potential to enable future applications of “Surgery 4.0”. Preliminary results of the Delphi study reveal a positive perspective of 5G implementation in a clinical environment. 5G data transmission creates a future-oriented possibility of telepresence, which is not yet available in this form. For upcoming research, special focus should be put on medical real-time interaction applications, especially remote robotic surgery, as the future 5G standard will not only provide high data rates for the transmission of multimedia content up to virtual reality, but also an extremely reduced latency and simultaneously high reliability of data transmission.

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References

1. Feußner H, Park A. Surgery 4.0: the natural culmination of the industrial revolution? Innovative Surgical Sciences.
2. Li QC, Niu H, Papathanassiou AT, Wu G. 5G network capacity: Key elements and technologies. IEEE Vehicular Technology Magazine. 2014;9(1):71-8.

3. What is 5G? Characteristics and usages 2018.
Available from:
<https://www.gemalto.com/mobile/inspired/5G>.
4. Kranzfelder M, Schneider A, Fiolka A, Koller S, Reiser S, Vogel T, et al. Reliability of sensor-based real-time workflow recognition in laparoscopic cholecystectomy. *International journal of computer assisted radiology and surgery*. 2014;9(6):941-8.
5. Okoli C, Pawlowski SD. The Delphi method as a research tool: an example, design considerations and applications. *Information & management*. 2004;42(1):15-29.
6. Draper JV, Kaber DB, Usher JM. Telepresence. *Human factors*. 1998;40(3):354-75.
7. Kranzfelder M, Schneider A, Fiolka A, Koller S, Wilhelm D, Reiser S, et al. What Do We Really Need? Visions of an Ideal Human–Machine Interface for NOTES Mechatronic Support Systems From the View of Surgeons, Gastroenterologists, and Medical Engineers. *Surgical innovation*. 2015;22(4):432-40.

IVAP 2025 – Towards the collaborative operating room

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Introduction

The advances in digitalization and information processing are influencing interventional medicine. Medical devices include a growing number of functionalities, which provide more operational flexibility while increasing complexity of the OR environment [1]. Adapting to this development provides an essential challenge and opportunity to optimize modern surgery and therapy procedures. With the advancements of digital assistance systems, it can be ensured that the surgeon concentrates on the essential, namely the patient and the operation, rather than being distracted by the technical overflow of peripheral devices. In this work we present our vision and first results of a collaborative operating room that actively supports context-sensitive intra- and postoperative surgical therapy. To achieve this goal we enhanced a new Operating Room (OR) for comprehensive data acquisition, recognition of the OR team and computational tools for workflow analysis in order to achieve an understanding of the situational sequence and semi-automatic assistance and ensure an increased security level.

The functioning of the cognitive surgical environment is demonstrated by a typical example: the laparoscopic resection of the gallbladder for symptomatic gallstones. Such an operation is very common and is performed about 200,000 times a year in Germany. The procedure is highly standardized.

Materials and Methods

The basic idea of this concept relies on three pillars: First, precise analysis and comprehensive acquisition of all available information about the surgical situation, second, by the interpretation using comprehensive structured knowledge and third, the derivation of the relevant assistance functions and smart services. The system components involved, continually feedback to the IVAP OR-system and thereby verify the workflow, as illustrated in Figure 1. These main components are described in more detail in the following section.

Data acquisition

An important prerequisite for situational awareness of the cognitive-technical system is the actual ability of "understanding" similar to a surgeon. A robust interpretation of

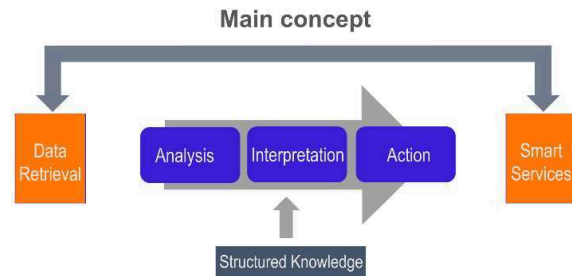


Figure 1: Main concept of the collaborative operating room is based upon three pillars: analysis of captured data, interpretation of comprehensive real-time information based on structured knowledge and the prediction of further activities and their execution (action) in the form of smart services.

the current surgical context requires a centralized continuous provision with real time data as shown in [2]. We implemented a central data acquisition framework as illustrated schematically in Figure 2.

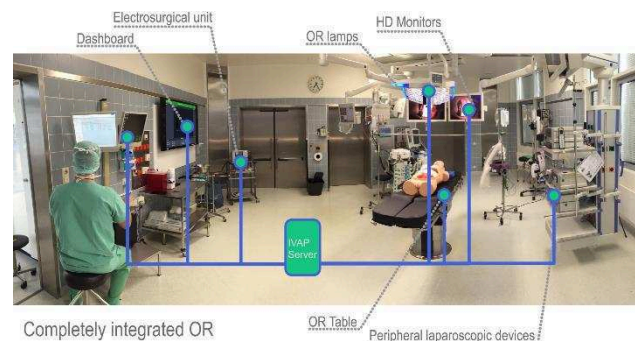


Figure 2: Schematic illustration of a centralized data acquisition within the OR

This broad variety of data is heterogeneous by nature and can be grouped as follows:

1. *Device data:* Status of installed and peripheral surgical components. In particular, we collect information about the operating table, room-, surgical- and endoscopic light, insufflation pressure and flow, aspiration and suction volume, usage of the electrosurgical devices, and surgical instruments in use.

2. *Data on the surgical team members:* The OR is equipped with four Bluetooth-Low-Energy (BLE) antennas, which allow capturing the presence of staff members and a coarse localization within in the OR. Subject to their permission, the level of experience of staff members is stored in a database.
3. *Pre- and intraoperative patient data:* previous diseases, laboratory values, anaesthesiological data. The clinical information system (CIS) provides a wide range of patient-relevant data. Statistical methods and machine learning are currently being evaluated in order to estimate the preoperative course of the operation.
4. *Image and video data:* pre- and intraoperative radiological imaging, endoscopic video data, overview cameras. Especially the video data contains a lot of information, which has to be extracted by suitable algorithms.

This categorization naturally involves overlaps, e.g. regarding information, which can be derived from the different video streams. For example, the overview camera can be used to track staff movement or to detect the use of special equipment (e.g. C-arm). The laparoscopic image is all the visual information the surgeon has from the surgical site inside the patient. Therefore, a lot of information about the surgical procedure and usage of instruments can be deduced by means of computer vision methods. We have applied Deep Learning methods on the laparoscopic video stream to perform an end-to-end surgical phase recognition from the laparoscopic video frames, as shown in [3]. Additionally a convolutional neural network (CNN) was trained to detect instruments in the laparoscopic image and autonomously controls a camera guidance robot [4].

All data – device, sensor and inferred from video frames – is collected centrally in real time and stored for further processing. Alongside the structured knowledge, this data forms the input for the determination of the surgical workflow.

Structured knowledge

In order to recognize the actual surgical process, which can deviate from the planned course, the system requires a detailed OR-model. The OR-model consists a systematic, finely granulated description of the course of action, including all conceivable variants and the description of alternative points. Regarding the case of laparoscopic Cholecystectomy, the model consists of eight phases, each of which is precisely modeled. The highly standardized procedure consists of 32 different surgical steps, about 1,600 actions and about 16,000 surgical manipulations. The modelling was done using the Business Process Model and Notation (BPMN) 2.0.

Based on these models, a rule-engine was designed, which performs the actual interpretation of the data in the central database and derives relevant actions and support functions.

Derived action: (semi-)autonomous support

The autonomous execution of actions by the IVAP OR-system in a closed loop would be desirable and technically feasible. However, this is currently prevented by regulatory barriers. Therefore, only entirely uncritical actions are performed automatically such as switching off the room lights or closing the window blinds. More critical support functions are implemented in a semi-autonomous i.e. human-in-the-loop manner. Decisions and actions are prepared by the system, but must always be acknowledged or carried out by a person. Hence, specific human machine interfaces were designed as part of the cognitive OR concept.

Human machine interaction

The communication between the system and the surgical staff is implemented in different ways. Since speech is one of the most natural forms of communication, a voice output (based on Microsoft Speech API) was integrated. Because this can easily lead to disturbance of the team, speech synthesis of messages and warnings is only used before the operation (greetings of the surgeons) or when a staff member's immediate attention is required. The display of messages on the central dashboard or small tablet screens close to the scrub nurse is much less disturbing. Those messages can be status updates, non-urgent messages or recommendations for actions. Additionally, the touchscreens can be used as backchannels for user input into the cognitive IVAP OR-system as shown in Figure 3.

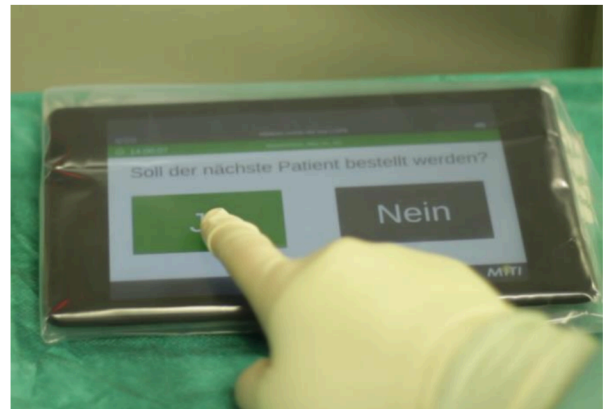


Figure 3: User-input on sterilely packed tablet. The IVAP OR-system asks, whether the next patient should be ordered and waits for approval by the user.

Results

Comprehensive networking of all OR components and the installation of a few additional sensors enabled an ordinary OR to be converted into a framework for surgical data acquisition and laid the foundations for an intelligent support of the OR team.

Since cognitive support needs situational awareness, a substantial amount of effort was invested into the recognition of surgical phases and actions. While the sensor driven recognition was shown by [5] we implemented a CNN for the detection of the surgical phase within the laparoscopic

video. The CNN performed with an average precision of 65.9% and an average Recall of 74.7% [3].

Based on the surgical phase recognition and the sensor- and device data driven rule-engine, we implemented a number of assistive functions. These functions can be categorized as follows:

1. *Room control*: control of window blinds and room lights
2. *Personalized setup*: recognition and greeting of the surgeon. Display of preferred settings (e.g. height of surgical table)
3. *Monitoring of device settings*: device parameters are cautiously monitored. In case of deviation from the specifications, warnings are given as visual display or voice output (e.g. insufficient brightness of the endoscopic light source, excessive patient pressure of the insufflator).
4. *Optimization of associated processes*: situational reminders for Team-Time-Out, ordering of the next patient and notification of cleaning staff at the end of surgery.

Conclusions

The passive conglomerate of different high-tech modules was transformed into an integrated collaborative assistance system. The successful implementation of this project represents the first major step in the direction of Surgery 4.0 [6]. While in the case of laparoscopic cholecystectomy, a manual “top-down” modelling was possible, methods for automatic abstraction of surgical models using statistical and machine learning approaches is the subject of our current research.

References

- [1] Kenngott H, Wagner M, Preukschas A et al. Der intelligente Operationssaal. *Der Chirurg* 87:1033-1038, 2016.
- [2] Ostler D, Kranzfelder M, Stauder R et al. A centralized data acquisition framework for operating theatres. In: *E-health Networking, Application & Services (HealthCom)*, 17th International Conference on. IEEE, p 1-5, 2015.
- [3] Stauder R, Ostler D, Kranzfelder M et al. The TUM LapChole dataset for the M2CAI 2016 workflow challenge. *arXiv preprint arXiv:1610.09278*, 2016
- [4] Marahrens N, Koller S, Ostler D et al. Deep learning-based robotic endoscope guidance. In: *Jahrestagung CURAC*, 2017.
- [5] Kranzfelder M, Schneider A, Fiolka A et al. Reliability of sensor-based real-time workflow recognition in laparoscopic cholecystectomy. *International journal of computer assisted radiology and surgery* 9:941-948, 2014.
- [6] Feussner H, Ostler D, Kranzfelder M et al., Surgery 4.0. In *Health 4.0: How Virtualization and Big Data are Revolutionizing Healthcare* (pp. 91-107). Springer, Cham, 2017.

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Creation of 3D nanocomposite bioconstructions using a layer-by-layer laser prototyping device

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Introduction

Nowadays a high demand for bioconstructions used for regeneration of tissue defects, including difficultly repaired osteochondral ones, is exist. One of the important factors for successful developing of them is production of three-dimensional biocompatible scaffolds that provide replacement of a damaged tissue site and maintain proliferation of the patient's cells. As a result of implantation, a healthy tissue is formed in the site of a defect, and a scaffold dissolves gradually as tissue grows.

Among current methods of scaffolds obtaining, an important place is given to methods of three-dimensional prototyping. Their advantages are unquestionable in case of preparation of scaffolds for regeneration of osteochondral defects: high resolution, the ability to get a scaffold with shape that exactly coincides with CT and MRI imaging of defect, and the possibility of controlling the internal structure of scaffold [1] However, not all materials suitable for using in 3D prototyping have required characteristics [2]. Often they are either not completely biocompatible, but also are not biodegradable, thus performing a kind of substitution and remaining a foreign material in the body.

In order to overcome the shortcomings of traditional methods, the laser device for the fabrication of nanocomposite bioconstructions by method of laser 3D prototyping was developed. In the work we created samples of 3D nanocomposite bioconstructions and carried out studies of their structural and biological properties.

Materials and Methods

Materials

Bovine serum albumin (BSA) and bovine collagen (BC) were selected as components of the protein matrix. BSA is one of the main proteins of blood performing a transport function. This protein also has the ability to be cross-linked under the action of laser radiation [3]. A lyophilized BSA purity of more than 99% was used. BC is one of the main proteins of the extracellular matrix. BC was taken in the form of suspension in water (2% wt. of pure collagen). The solvent for all components was water for cellular studies.

Single-walled carbon nanotubes (SWCNTs) of the types of 90A (length 0.5-1.5 μ m, diameter $\sim$ 1.5 nm) and 95TA (length - more than 5 microns, diameter -1-2 nm) were used for the production of nanobioconstructions. Nanotubes were in form of black paste in deionized water with a nanotube concentration of $\sim$ 2.5% wt.

Preparation of dispersion

The first step of the dispersion preparation was the dissolution of carbon nanotubes in water. The required amount of SWCNTs in water was mixed with a magnetic stirrer for 40 minutes. Then they were sonicated in a homogenizer with amplitude of no more than 30 W for 45-60 minutes to reduce the number of aggregated CNTs. Then BSA (25%) and collagen (1%) were added to the CNTs with water, it was mixed with the stirrer and then in an ultrasonic bath until the components were completely dissolved.

Device for making solid samples

The principle of the device operation is moving the focused laser beam along a planned trajectory above a container with the water-protein dispersion of carbon nanotubes. Under the action of laser radiation, evaporation of the water part occurs while laser radiation orients the nanotubes. Thereby they form a strong, porous scaffold that promotes the regeneration of bone and cartilage tissue cells [4-6].

Configuration of the device is shown in fig. 1. The main component of the device is the source of radiation (2) - semiconductor laser with a wavelength of 810 nm, which is controlled by the power supply (1). Radiation is transferred by means of optical fiber to a lens that is fixed to moving system, based on stepper motors (4).

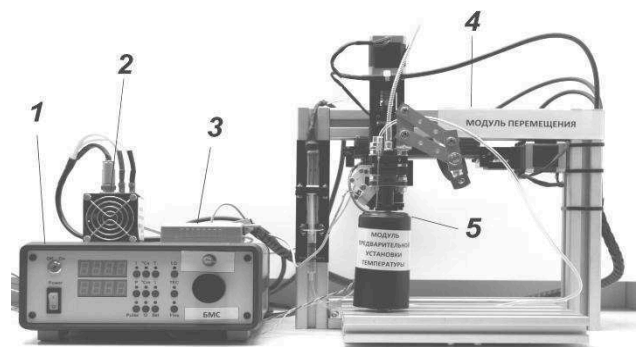


Figure 1: The device for making of samples using layer-by-layer laser prototyping method: 1 - power supply unit, 2 - semiconductor laser, 3 - thermostabilization system, 4 - moving system, 5 - container with the dispersion

The device is equipped with an IR-sensor that measures the temperature of the dispersion. The sensor is connected to the thermostabilization system (3). The main purpose of this system is to dynamically adjust the laser radiation power to maintain the established dispersion temperature.

The creation of bioconstructions takes place at a certain temperature of 40-55 °C at the bottom of the container (5) fixed on the preliminary heating table.

Focusing of laser radiation was carried out in a spot with a diameter of $\sim 0.1 \mu\text{m}$. The travel distance of the focused beam was also $\sim 0.1 \mu\text{m}$. The thin layer of water-protein dispersion of nanotubes was distributed at the bottom of the container using a syringe connected to the dosing system. Then the dispersion was irradiated by laser along a given trajectory. After the dispersion layer was cured, the amount of dispersion necessary to form the next layer was added to the container.

Analysis of samples surfaces

The surface structure of the experimental samples was studied using confocal microscopy. When scanning with this method, a focused laser beam was moved along the sample area. A laser confocal microscope Lasertech VL 2000 DX with a high numerical aperture (up to 0.95) and a short wavelength of laser radiation was used.

An atomic force microscope (AFM) was used for more detailed analysis of the morphology of the sample surface. In the PeakForce QNM mode, the power curve was taken at each point of the sample and immediately was analyzed. The study was conducted in a semi-contact mode in air. A probe with a tip diameter of 5 nm was used. The scanning was performed on an area of $10 \mu\text{m}^2$ and $30 \mu\text{m}^2$.

Study of the internal structure of samples

The internal volume structure of the samples was studied with the x-ray microtomograph. The maximum possible spatial resolution was selected. Using the intensity function, the voltage and current at the cathode (no more than 30 kV) were adjusted to obtain an average intensity value of 30-50%. The scan parameters were selected in accordance with the density and geometric dimensions of the sample.

Investigation of biocompatibility

To study the biocompatibility, experiments related to the proliferation of cells (osteoblasts and chondroblasts) were carried out on samples in culture plates in a CO_2 thermostat at 37 °C for 48 hours. After that, the number of cells was evaluated and their morphology was analyzed. The restoration of osteochondral defects was carried out on laboratory animals (rabbits).

Results and Discussion

Characterization of surface of samples

Samples obtained using the described method are shown in fig. 2. The power at which the dispersions solidify depended on the concentration of nanotubes and the trajectory which the laser beam moved along. Dispersions with a low concentration of nanotubes cured more slowly because of the high transparency of the layer. To form the next layers, a lower beam power was required compared to one for the first layers. Due to the varying of power and the number of passes of the trajectory to form one layer, it

is possible to achieve a structure of different hardness - from soft rubberlike to completely solid. It is successfully possible to obtain samples with grid structure that promotes cell growth on the surface by mimicking the structure of the natural extracellular matrix.



Figure 2: 3D nanocomposite bioconstructions obtained from a grid trajectory with a distance of 0.5 mm (a) and 1.5 mm (b) between parallel lines

To obtain the experimental samples, the distance to the container with dispersion was preliminarily chosen with the smallest diameter of the beam. The selected speed of the radiation source was 2.5 mm/s. The parameters of making of samples are given in tab. 1.

Table 1: Parameters of making

Sample	Type and concentration of SWCNTs	Current intensity	Number of trajectory passes
I	90A, 0,01 %	3.0-4.8	1-4
II	90A, 0,1 %	2.3-3.3	2-4
III	95TA, 0,01 %	3.3-4.8	1-4
IV	95TA, 0,1 %	2,5-3,0	1-2

Images of a top view of sample II obtained by laser confocal microscopy are shown on fig. 3. Dark and light bands correspond to the low and high areas of the sample. The average value of the band width for this sample was $\sim 20 \mu\text{m}$ and it depended on the focusing of the laser beam on the sample. Each of the bands contained basically perpendicular convexes in the form of "folds", whose size was $\sim 1 \mu\text{m}$ and depended on the laser radiation power.

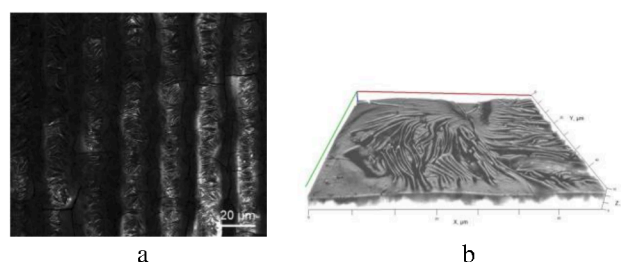


Figure 3: Surface topography of samples obtained by confocal microscopy (a - microimage, b - reconstructed image)

Figure 3 b shows the reconstructed three-dimensional image. It is clearly seen from the figure that the "folds" impart a relief surface to the sample, which subsequently establishes an interconnection between the structure of the

samples and their biological properties - an increased adhesion of the cells to the samples, because the size of the chondroblasts and osteoblasts is about 50 μm .

Analysis of surface using AFM

Fig. 4a shows the AFM topogram of sample I. It is a typical picture of the surface layer of protein material. The main characteristic of this image is the presence of pores on the surface. A network of shallow channels is visible, which apparently are fractures on the surface of the material, formed as a result of thermal effects on the protein component. The width of the channels is 30-70 nm.

Several types of pores with a diameter of 100-200 and 400-700 nm are observed on the AFM images of sample II (fig.4b). In this sample, the pores were uniformly distributed and had a small dispersion in size, in comparison with sample I. In sample II, formation of shallow cracks with a width of 200-500 nm and the absence of a network of channels were observed, as in sample I.

Sample III (fig.4c) also had a porous structure, with different pore sizes. The sample had a homogeneous structure and no large fractures on the surface of the material.

Sample IV (fig. 4d) had a large number of pores uniformly distributed over the entire surface of the sample with a diameter of 70-100 nm and 10-30 nm. In this sample there were no fractures, and there was also no network of channels.

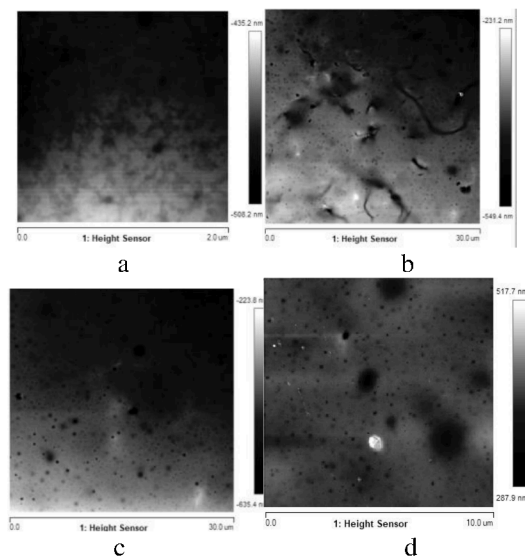


Figure 4: AFM images of the samples surface

The following was established as a result of studies of the structure of experimental samples by the AFM method. The surface of all samples is homogeneous porous material, the structure of which is typical for products based on proteins. Nanotubes on the surface could not be detected, which is due to the fact that all SWCNTs was under the layer of the protein matrix inside the material. The experimental samples had pores of various sizes. In samples I, III, IV there were large pores with a diameter of 500-5000 nm. These pores were distributed irregularly and were the result of air bubbles occurred during the formation of

samples. Because sample I had pores of smaller diameter than sample II and the pore diameter in sample III exceeded the pore diameter in sample IV, the porosity is directly dependent on the SWCNTs concentration for samples I and II based on SWCNTs 90A, and is on the inverse relationship for samples III and IV on the basis of SWCNTs 95TA. The concentration of CNTs affected the appearance of a network of shallow channels on the surface of samples I and III. When the concentration of CNTs increased from 0.01 to 0.1%, the channel network was not observed (samples III, IV). This may be due to the reinforcing effect of carbon nanotubes in the protein matrix, which prevents the formation of fractures on the surface of the material.

X-ray microtomography

The obtained images of the internal structure of large samples by the X-ray microtomography method are shown in fig. 5. Based on the results of studies of the structure of sample I, it was found that cavities occupying 50-70% of the sample area were observed in the upper and lower layers of the sample, but the central part of the sample had a homogeneous structure. In the structure of the sample there was a pore space with a radius of 0.2 mm and a crack of a size of 0.25 mm. The presence of individual large pores in the sample is due to the presence of air bubbles in the initial nanocomposite dispersion, which creates cavities in the structure of the material during laser prototyping. This problem can be solved by using additional ultrasonic treatment of the nanocomposite dispersion.

Two-dimensional visualization of sample II is shown in fig. 5b. Cavities with a diameter of 0.1-1.0 mm were observed in the structure of the sample. The number of micropores in this sample exceeds the amount of pores found in sample I, while the pores are uniformly distributed throughout the sample volume and have similar dimensions.

In sample III (fig. 5c), according to the results of microthomography, cavities with a diameter of 0.4 to 2.7 mm were found predominantly distributed around the central part of the sample. Such an inhomogeneous structure can be a consequence of some irregularity distribution of SWCNT in the volume of the initial dispersion and a large number of air bubbles and protein clots.

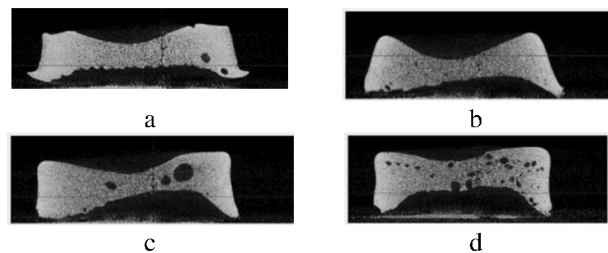


Figure 5: The internal structure of large samples, obtained with X-ray microtomography

In the case of sample IV, a series of cavities measuring from 0.2 mm to 0.9 mm were observed throughout the investigated section. The structure of the material looks more homogeneous. In general, the cavities are distributed evenly, with the exception of some sample areas. A much larger number of pores were observed than in sample III with a lower concentration of nanotubes.

The formation of a porous internal structure is most likely determined by laser heating of the nanocomposite dispersion. Carbon scaffold has high thermal conductivity, contribute to a strong heating of the areas nearby and resulting in the boiling of the water-protein solution and the formation of pores and cavities.

Biocompatibility studies

Seeding of cells on the obtained samples showed that the samples promoted the proliferation of osteoblasts and chondroblasts, maintaining a normal morphology.

Conclusions

A method for obtaining of 3D nanocomposite bioconstructions from water-protein dispersion of carbon nanotubes is described. The device for layer-by-layer laser prototyping was developed. The surface and internal structure of the created samples was characterized. The folded relief surface of the samples and the porous internal structure corresponds to the parameters of the natural extracellular matrix for supporting of cells. Bioconstructions demonstrated proliferation of cells (osteoblasts and chondroblasts). The osteochondral defects in the joints of laboratory animals were restored with the use of samples. Thus, the developed method can be used to restore defects of osteochondral joints with a various geometric shape.

References

- [1] S. M. Giannitelli. Current trends in the design of scaffolds for computer-aided tissue engineering. *Acta biomaterialia*, 10(2):580-594, 2014.
- [2] W. Y. Yeong, C. K. Chua, K. F. Leong, and M. Chandrasekaran. Rapid prototyping in tissue engineering: challenges and potential. *TRENDS in Biotechnology*, 22(12):643-652, 2004.
- [3] J. D. Pitts, P. J. Campagnola, G. A. Epling, and S. L. Goodman. Submicron multiphoton free-form fabrication of proteins and polymers: studies of reaction efficiencies and applications in sustained release. *Macromolecules*, 33(5):1514-1523, 2000.
- [4] A. Barrientos-Durán, E. M. Carpenter, N. I. Zur Nieden, T. I. Malinin, J. C. Rodríguez-Manzanique, and L. P. Zanello. Carboxyl-modified single-wall carbon nanotubes improve bone tissue formation in vitro and repair in an in vivo rat model. *International journal of nanomedicine* 9:4277, 2014.
- [5] N. O. Chahine, N. M. Collette, C. B. Thomas, D. C. Genetos, and G. G. Loots. Nanocomposite scaffold for chondrocyte growth and cartilage tissue engineering: effects of carbon nanotube surface functionalization. *Tissue Engineering Part A*, 20(17-18):2305-2315, 2014.
- [6] A. Yu. Gerasimenko, O. E. Glukhova, G. V. Savostyanov, V. M. Podgaetsky. Laser structuring of carbon nanotubes in

the albumin matrix for the creation of composite biostructures. *Journal of Biomedical Optics*, 22(6):065003-1 - 065003-8, 2017.

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Analysis of physiological data to quantify stress and workload of surgeons with different levels of training during a laparoscopic cholecystectomy

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Introduction

In a difficult and demanding environment such as the operating room, the individual effect of workload on surgeons is of particular importance. The increased stress and workload during an operation can lead to an impairment of technical skills and vigilance that causes an impact on memory and other cognitive processes. These facts can significantly influence our decisions and have an important effect on patient safety. (1)

Apart from the personal stress level of the surgeon, new technologies like robotic or robotic-assisted systems are increasingly finding the way into our operating theatres and will lead to an additional load of stress. Robots do not yet have the cognitive skills and experience of human assistants who can easily recognize, analyze and adapt to changing situations or even stress factors. For a safe human-robot interaction, and therefore a maximum of patients safety in intraoperative stress situations we must fulfill certain requirements. In order to reduce the arising workload of the human-machine interaction we should acquire knowledge of the surgical workflow. Critical situations during an operation should be identified and adapted by the robotic-assisted systems.

The first aim of this study was to examine the specific effects of intraoperative stress on the cardiovascular system at surgeons with different levels of training by measuring the respiratory rate (RR) and heart rate (HR). The second goal of our work was to examine a possible integration of our data into a workflow recognition system to recognize more complex and non-linear correlations by machine learning.

Materials and Methods

In a cross-sectional study during laparoscopic gallbladder resections (n=9) at the University Hospital Rechts der Isar, Munich, Germany the effect of intraoperative stress on autonomic balance, measured by the determination of heart rate (HR) and respiratory rate (RR) was studied.

The subject of the examination was a laparoscopic cholecystectomy performed by an experienced surgeon as well as an intern with less training on that operation. Difficult steps in this operation, that requires a high degree of concentration, are usually the preparation of the Calot triangle, the clipping of the vessels as well as the removal of the cystic duct.

The HRV was quantified by the analysis of the variation of beat-to-beat intervals in the electrocardiogram (ECG).

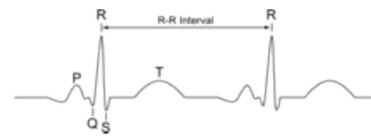


Figure 1: Standard figure of a QRS-Complex of the ECG. HRV can be calculated by the signal.

During the laparoscopic cholecystectomy we measured the respiratory rate, pulse and position of the upper body by using a specially designed chest belt with sensors that recorded the pulse rate and movement of the thorax during in- and expiration. Two experienced and three less experienced surgeons were enrolled as voluntary participants after given their written informed consent. Neither acute nor chronic illnesses within our test persons were present. Each participant was monitored over the course of a laparoscopic cholecystectomy. Data were analyzed with the statistical software SPSS Version 15.0 (SPSS, Inc., Chicago, IL, USA). Results are expressed as percent, median and total range.

Results

The median age of the participating surgeons was 39 years; the body mass index (calculated as weight in kilograms divided by height in meters squared) was in median 22.3 and all participants were in good physical conditions. The surgeons had 11.4 years of practice in middle and worked 49.2 h per week (**Table. 1**). No participant received any medication or had cardiovascular disease.

Characteristics	Median (range)
Age (years)	39 (28-62)
Height (m)	1.78 (1,73-1,85)
Weight (kg)	70.6 (58-84)
Physical activity rate	6.0 (3,0-9,0)
Years of experience (year)	11.4 (1-35)
Working hours per week (h)	49.2 (40-60)

Table 1: Characteristic of the study sample (n=5);
Physical activity rate: evaluation on a scale from 0(no activity)
to 10 (activity more than 8 h per week)

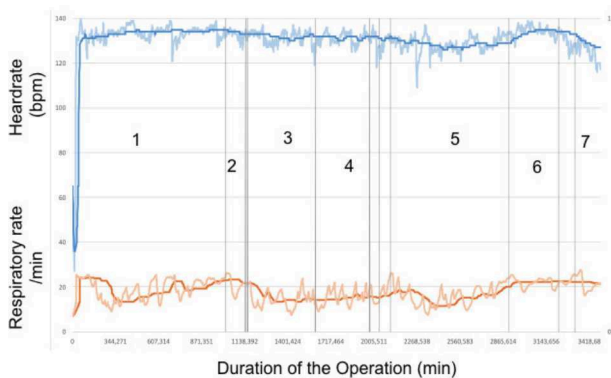


Figure 2: Median measure of the HR (dark blue line) and the respiratory rate RR (dark red line) of the experienced surgeons.

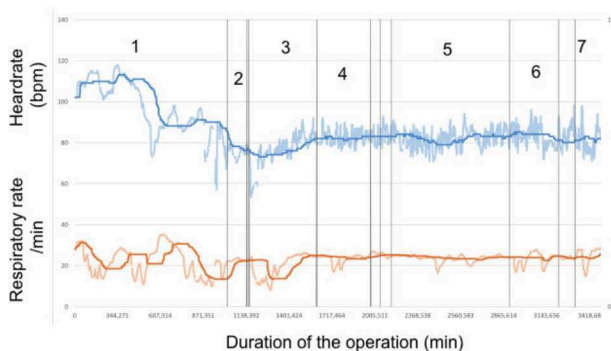


Figure 3: Median measure of the HR (dark blue line) and the respiratory rate RR (dark red line) of the non-experienced surgeons.

The two graphs above show the mean heart rate HR (dark blue line) and respiratory rate RR (dark red line) of the two experienced surgeons measured over the nine trials (**Figure 2**) and the three less experienced interns (**Figure 3**). To better display the variance in pulse and respiratory rate, the curves have been smoothed. The numbers in the graphs refer to the individual steps during the laparoscopic cholecystectomy. 1: prearrangement; 2: insertion of the individual trocars; 3: preparation of the Calot triangle; 4: clipping of the vessels and Ductus cysticus; 5: triggering the stacker; 6: gallbladder retrieval; 7: hemostasis.

The measured values of the experienced surgeons in Figure 2 show a slightly higher pulse but there is no great variance between the individual steps of the operation. Whereas the measurements on the interns with less experience (Figure 3) indicated that starting with a lower HR level, the different surgical steps produced a greater HR variance.

Discussion

In the present study we were able to show that there is an association of perceived stress at work and the cardiac autonomic control in surgeons. Regarding the outcome variables, the two groups of surgeons, divided according to their perceived stress levels, showed differences in the variation intraoperative HR and respiratory rate (RR).

Other research groups confirm to our findings that the analysis of the heart rate and the respiratory rate are very important marker of physical and mental stress as well as workload. (2,3) We postulate that the stress level, measured by HR and respiratory rate and the variation of both parameters, of a surgeon is reciprocally proportional to the level of education and training. Moreover, in general, young physicians are thought to experience more stress than veteran surgeons who are used to differ to different working conditions and follow their daily routine. (4) As we were able to show in our study, the experienced surgeons started with a bit higher HR level but the different steps of the operation with their different degrees of severity caused no big variance in HR or RR. In contrast, the less experienced surgeons showed a lower overall pulse level, but the individual surgical steps led to a greater variance in pulse (HR) and respiratory rate (RR). Therefor we claim that the analysis of the variance of HR shows a correlation on the occurrence of critical events during surgical procedure. However, this knowledge must be adapted to the surgeon's level of training. Moreover the integration of this data and knowledge into a workflow recognition system in order to recognize more complex, non-linear interrelationships by machine learning can lead to a safe human- robot interaction in intraoperative stress situations. This brings us closer to our goal of enabling robots or robotic-assisted systems to recognize problems and react to them independently.

There remain some potential biases of our study. Momentarily we have a small amount of participants in the study and just a few repetitions of the experiment. There are more different ways to gather and analyze physiological data of the participants. Beside the examined heart and respiratory rate, some groups postulate the use of biochemical indicators or eye tracking as well as EEG or EMG. Especially measuring the blink rate, the saccades, the pupil diameters and the duration of fixation with eye tracking seems to be another line leading approach. (5)

Conclusions

In our opinion the analysis of the workload of a surgeon and its effects are very important. According to the Yerkes Dodson law, performance increases with physical and mental stress, but only to a point. When the stress level become too high our performance decreases. But if we link our knowledge with technology in the future, we may be able to minimize the dangers arising from excessive workload and stress with the help of machines.

References

1. Arora S, Sevdalis N, Nestel D, Woloshynowych M, Darzi A, Kneebone R. The impact of stress on surgical performance: a systematic review of the literature. *Surgery* [Internet]. 2010 Mar;147(3):318–30, 330-6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20004924>
2. Rieger A, Stoll R, Kreuzfeld S, Behrens K, Weippert M. Heart rate and heart rate variability as indirect markers of surgeons' intraoperative stress. *Int Arch Occup Environ Health* [Internet]. 2014 Feb;87(2):165–74. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23370764>
3. Weippert M, Behrens K, Rieger A, Stoll R, Kreuzfeld S. Heart rate variability and blood pressure during dynamic and static exercise at similar heart rate levels. *PLoS One* [Internet]. 2013;8(12):e83690. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24349546>
4. Böhm B, Rötting N, Schwenk W, Grebe S, Mansmann U. A prospective randomized trial on heart rate variability of the surgical team during laparoscopic and conventional sigmoid resection. *Arch Surg* [Internet]. 2001 Mar;136(3):305–10. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/11231850>
5. Tokuda S, Obinata G, Palmer E, Chaparro A. Estimation of mental workload using saccadic eye movements in a free-viewing task. *Conf Proc. Annu Int Conf IEEE Eng Med Biol Soc IEEE Eng Med Biol Soc Annu Conf* [Internet]. 2011;2011:4523–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22255344>

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New Geometric Method of Heart Rate Variability Estimation based on the Multiscale Correlation Analysis Representation

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Introduction

The nature and characteristics of ECG signals have been the subject of research for more than 100 years. This is because ECG signals contain a valuable diagnostic information about the functioning of the heart and, indirectly, about some other organs. Now, despite the impressive track record of the diagnostics and recommendations already developed [1], ECG signals continue to be the subject of intensive study both in the field of cardiology and biomedical engineering. Cardiologists search for new diagnostic properties of ECG signals, while engineers are interested in new approaches and methods for such signals processing and analysing. New methods imply, in particular, new techniques of noise suppression, efficient signal representation and feature extraction.

Feature extraction is an essential step in ECG processing. It consists in formation of some feature patterns – a set of descriptors most adequately describing the signal. Among these features / descriptors the most important are those with diagnostic properties. As a rule, they represent time domain parameters, though sometimes they can be defined in the frequency domain. Basing on ECG patterns, one can make some initial diagnosis [1]. For example, an “irregular” QRS complex without P wave is the hallmark of atrial fibrillation, the shape of the QRS with a left bundle branch block indicates a risk of cardiomyopathy, etc.

ECG patterns, especially P–QRS–T complexes, are also the basis for the subsequent heart rate analysis. Usually it is a more complex phase of ECG signal processing. However, now there are many methods and approaches related, for example, to the heart rate variability (HRV) analysis [2]. Quantitative evaluation of the HRV is usually based on the calculation of some indices connected with the variability of sequential NN intervals (normal-to-normal intervals between adjacent QRS complexes). Some of these indices are determined in the time domain – SDNN, CV, RMSSD, PNN50, etc. Others – in the frequency domain – VLF, LF, HF spectral power components, IC index, etc. It should be noted that, due to the complexity of the ECG signal, its fractal-like nature, the values of almost all indices can essentially diverge for different lengths of time intervals analysed, even for the same record. Therefore, the European Society of Cardiology suggests differentiating the diagnostic methodologies based on HRV indices obtained from the short-term recordings (of 2 to 5 min) and from the long-term recordings (of entire 24-h period) [3].

The above discussion is illustrated in Figure 1 by cardioin-

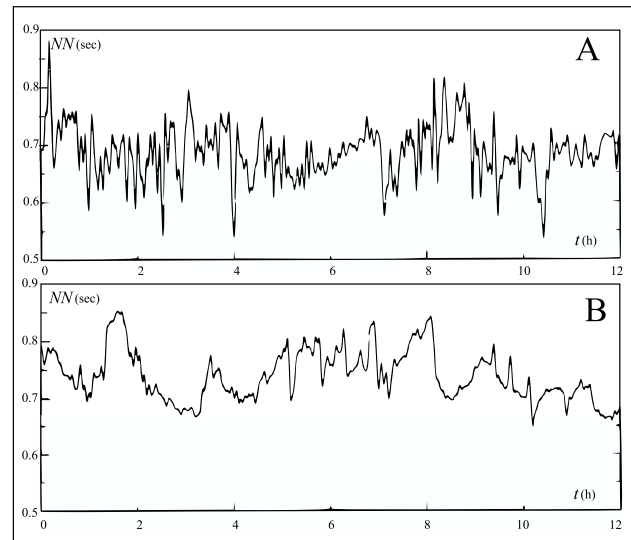


Figure 1: The interbeat interval NN after low-pass filtering for (A) a healthy subject and (B) a patient with severe cardiac disease (dilated cardiomyopathy). The healthy CIG shows more complex fluctuations compared to the more “smoother” diseased heart rate fluctuation pattern. Drawing is adapted from [4].

tervalograms (CIG, the NN interval dependences on time) for a healthy person (A) and a heart disease person (B). It is clear from the figure that both CIGs are qualitatively different. For example, at a small temporal scale, the variability (spread) of NN intervals in a healthy person is greater, which is a well known fact [5] – but on large scales the variability becomes equal in both cases. This observation suggests that the diagnosis based on HRV is adequate, but diagnostic procedures (automatic in particular) may be non-trivial. This circumstance gives high relevance to the development of new ECG processing methods based on long records – more than 10 minutes, for example, Holter.

Geometric Method of HRV Estimation

As it is mentioned above, variations in heart rate may be evaluated by a number of indices, which can be calculated by a number of methods. Perhaps the most popular and at the same time the simplest to perform are the so-called geometric methods [2], [3].

Geometric Methods

Geometrical methods include, as a rule, some geometric pattern formed by the sequence of NN intervals, such as the sample density distribution, sample density distribution of differences between adjacent intervals, Lorenz plot of NN or RR intervals, etc., and a simple formula, which judges the variability based on the geometric and/or graphic properties of the formed pattern. A number of popular geometric methods can be found in [3], [6].

The main advantage of geometric methods is their relative insensitivity to the accuracy of NN intervals measuring. The main drawback is the need for a large amount of NN intervals for constructing a geometric pattern. In practice, it takes at least 20 minutes (but preferably 24 hours) to ensure correct operation of geometric methods, that is, the measurements of not less than ~ 1500 NN intervals are necessary. In addition to the fact that this is hard routine work (which, however, with certain precautions can be assigned to a computer), it makes known geometric methods inappropriate to assess short-term changes in HRV.

MCA based Method

In order to avoid the limitations of classical geometric methods (but to inherit their attractive properties), we developed a new estimating HRV method based on the multiscale correlation analysis (MCA) representations [7]. The idea of this method springs in connection with the study of statistical characteristics of point processes and was first announced in [8].

Let's note from the beginning, that the main instrument of multiscale correlation analysis – the MCA representation (pattern) – is formed not on the basis of NN intervals, as in the classical methods, but on the basis of some special estimation of autocorrelation function (ACF) calculated directly by the ECG record. The basic definitions of MCA representations for analyzing the rhythm of the ECG in the general form can be found in [7].

Further, let's accept for ECG the special model $z(t')$ of a pulse process:

$$z(t') = \sum_{k=-\infty}^{\infty} A_k g(t' - t'_k) \quad (1)$$

where sequence $-\infty < \dots < t_0 < t < t_1 < \dots < \infty$ is the random time moments of pulse occurrences, specially numbered with respect to some fixed time t (the point of the current analysis), $\dots, A_0, A_0, \dots$ are the random amplitudes of the pulses, which we assume to be a stationary sequence of independent random variables with mean $\bar{A}$, and $g(t')$ is a non-random waveform, like the P-QRS-T complex, the same for all pulses. The statistics of the sequence $\{t_k\}$ is given by some point process (PP), whose model is specified below.

Within the model (1) framework, the general definition of MCA representation [7] takes the following special form:

$$\hat{R}(t, \tau) = \frac{1}{\tau} \sum_{k=-\infty}^0 \sum_{k'=1}^{\infty} A_k A_{k'} \int_{-\infty}^{\infty} |G(f)|^2 \times \\ \times \exp\{2\pi i f \tau\} \exp\{2\pi i f(t_k - t_{k'})\} df \quad (2)$$

where τ is the scale parameter of MCA representation and $G(f)$ is the Fourier spectrum of $g(t')$. The equation (2) expresses the MCA representation in terms of random variables $\{t_k\}$, $\{A_k\}$ and thereby fully determines the $\hat{R}(t, \tau)$ as a random value. However, even with the simplifications made (independence of the amplitudes and pulse intervals, stationarity, etc.), it is completely unrealistic to obtain a complete statistical description of $\hat{R}(t, \tau)$ in the form, for example, of its probability distribution. Therefore, it is necessary to confine the description of MCA representation to some simple characteristics, namely, to mathematical expectation of MCA $\langle \hat{R}(t, \tau) \rangle$, without taking into account possible random fluctuations around it. The corresponding formula for the mean MCA representation can be obtained by averaging (2) (over all random variables and under all assumptions made) and has the form announced in [8]:

$$\langle \hat{R}(t, \tau) \rangle = \frac{\bar{A}^2}{\tau} \int_{-\infty}^{\infty} |G(f)|^2 \exp\{2\pi i f \tau\} \times \\ \times \left(\sum_{k=-\infty}^0 \sum_{k'=1}^{\infty} \langle \exp\{2\pi i f(t_k - t_{k'})\} \rangle \right) df \quad (3)$$

Model Specification

As follows from (3), in order to obtain the final, suitable for analysis mean MCA representation, it is necessary to know the averages $\chi_{k'k}(f) = \langle \exp\{-2\pi i f s_{k'k}\} \rangle$, where $s_{k'k} = (t_{k'} - t_k)$ are the intervals between ECG pulses (P-QRS-T complexes) occurring in $t_{k'}$ and t_k . Let us note in this connection that $\chi_{k'k}(f)$ also represents the characteristic function of $s_{k'k}$, which, in turn, is the sum $s_{k'k} = s_k + \dots + s_{k'-1}$, where $s_j = (t_{j+1} - t_j)$ are the intervals between consecutive time moments. So, recalling that the characteristic function of the sum of independent random variables is the product of the characteristic functions of the terms, we arrive at the idea of choosing the cyclic renewal process – point process with independent intervals [9] – as associated with (1) PP.

As the concept of cyclic renewal process does not have widespread usage let's give here its exact definition with reference to [9]. Namely, consider a stochastic process $y(t')$ that cycles in some time moments $0 = t_0 < \dots < t_j < \dots < \infty$ through states $0 \rightarrow 1 \rightarrow \dots \rightarrow K-1 \rightarrow 0 \rightarrow \dots$ in that order, again and again. The time intervals $s_j = (t_{j+1} - t_j)$ with which the process remains in the states j are called sojourn times of these states. If all these sojourn times are independent, distributed with their own probability densities $\rho_j(s)$, then $y(t')$ is called the cyclic renewal process. It is clear that the process obtained by decimating $y(t')$ in such a way that the result contains only the moments of the

state 0 arrivals, then the resulting process will be the usual renewal process.

If we re-index the process time moments $\{t_j\}$ with respect to the current analysis time moment t in the same way as in the definition (1), then, it can be shown, that when t unlim- itedly increases, any set of intervals $s_k, \dots, s_{k'-1}$ becomes stationary, it is a well-known fact in the theory of (usual) re- newal processes. Moreover, in this asymptotically station- ary case the probability distribution density of the intervals is greatly simplified and its explicit expression becomes the following:

$$\rho(s_k, \dots, s_{k'-1}) = \sum_{l=0}^{K-1} P_l \prod_{j=k}^{k'-1} \rho_{(l+j) \bmod(K)}(s_j) \\ k \leq 0 < k', \quad P_l = \bar{s}_l / \bar{S}, \quad \bar{S} = \bar{s}_0 + \dots + \bar{s}_{K-1} \quad (4)$$

where $\bar{s}_l$ are the mean values of sojourn time intervals in the states l , i.e. mathematical expectations of $\rho_l(s)$. In this context $\bar{S}$ is the duration of the mean overall cycle or the mean period of the cyclic renewal process considered.

It follows from (4) that stationary joint distribution of in- tervals $s_k, \dots, s_{k'-1}$ does not decompose into a product of individual interval distributions. So, formally, stationary cyclic process ceases to be a renewal process (except for the case $K = 1$). At the same time, since (4) can be considered as a formula of total probability for alterna- tives $l = 0, 1, \dots, K-1$, conditional (provided that s_0 is dis- tributed in accordance with the distribution $\rho_l(s)$ of the l 'th alternative) distributions of intervals will continue to be represented by products. Thus, a process considered would be more correctly treated as a conditionally renewal cycli- cal process. Incidentally, we note that the probabilities of the alternatives P_l are determined by the relative sojourn times in the consequent states l .

Having a complete statistical description (4) of any set of intervals $s_k, \dots, s_{k'-1}$, it is possible, in the frames of the model accepted, to find all necessary for calculating (3) characteristic functions $\chi_{k'k}(f) = \langle \exp\{-2\pi i f s_{k'k}\} \rangle$:

$$\chi_{k'k}(f) = \langle \exp\{-2\pi i f \sum_{j=k}^{k'-1} s_j\} \rangle = \\ = \sum_{l=0}^{K-1} P_l \prod_{j=k}^{k'-1} \chi_{(l+j) \bmod(K)}(f) \quad (5)$$

where $\chi_j(f) = \langle \exp\{-2\pi i f s_j\} \rangle$ are the characteristic func- tions of sojourn time interval distributions in the states j – distribution densities $\rho_j(s)$.

For one important case, which is implied in the cardiac NN intervals modeling, expression (5) can be essentially simplified. This is the case of a narrow enough densities $\rho_j(s)$, where the narrowness is understood as the small $Q_j = \sigma_j / \bar{s}_j$ values – standard deviation to the mean value ratios. Since in this case $\chi_j(f) = \langle \exp\{-2\pi i f s_j\} \rangle$ are well approximated by Gaussian characteristic functions

$$\chi_j(f) \simeq \exp\{-2\pi i f \bar{s}_j\} \exp\{-\frac{1}{2} (2\pi f \sigma_j)^2\},$$

then formula (5) can be approximated by the expression:

$$\chi_{k'k}(f) = \\ = \sum_{l=0}^{K-1} P_l \exp\{-2\pi i f \bar{s}_{l+k}^{l+k'-1}\} \exp\{-\frac{1}{2} (2\pi f \Sigma_{l+k}^{l+k'-1})^2\} \quad (6)$$

where:

$$\bar{s}_{l+k}^{l+k'-1} = \sum_{j=k}^{k'-1} \bar{s}_{(l+j) \bmod(K)} \\ \Sigma_{l+k}^{l+k'-1} = \sqrt{\sum_{j=k}^{k'-1} \sigma_{(l+j) \bmod(K)}^2} \quad (7)$$

Geometric Pattern of mean MCA representation

To obtain the main instrument of the geometric method based on MCA, it only remains for us to substitute ex- pression (6) in mean MCA representation (3), calculate the sums of internal series and take the corresponding integral. The series in (3) can be calculated exactly:

$$\sum_{k=-\infty}^0 \sum_{k'=1}^{\infty} \langle \exp\{2\pi i f (t_k - t_{k'})\} \rangle = \sum_{n=1}^{\infty} H_n(f) \quad (8)$$

where:

$$H_n(f) = \frac{1}{\bar{S}} \sum_{l=0}^{K-1} \bar{s}_l^{l+n-1} \times \\ \times \exp\{-2\pi i f \bar{s}_l^{l+n-1}\} \exp\{-\frac{1}{2} (2\pi f \Sigma_l^{l+n-1})^2\} \quad (9)$$

The integral in (3) can not be calculated exactly, since we do not know the exact form of the spectrum $|G(f)|^2$. Nev- ertheless, it can be found approximately if we take into account the characteristic properties of ECG signals, that are prototypes of model (1) process. As HRV manifests itself in a noticeable change of NN intervals duration, the width of the distributions $\rho_l(s)$ is greater than the duration of the characteristic fragments of P–QRS–T complex. But this implies that in the frequency domain, on the contrary, $H_n(f)$ is much narrower than the spectrum $|G(f)|^2$. There- fore, taking $|G(f)|^2$ from the integral (3) as the constant $|G(0)|^2$ and calculating the remaining Gaussian integrals, we finally obtain:

$$\langle \hat{R}(t, \tau) \rangle = \frac{\bar{A}^2 |G(0)|^2}{\bar{S}} \sum_{n=1}^{\infty} \sum_{l=0}^{K-1} \frac{\exp\left\{-\frac{(\tau - \bar{s}_l^{l+n-1})^2}{2(\Sigma_l^{l+n-1})^2}\right\}}{\sqrt{2\pi} (\Sigma_l^{l+n-1})^2} \quad (10)$$

With regard to formula (10), let us make an almost obvious observation – although in the left-hand site of the MCA representation denotation there remains a formal depen- dence on t , it is absent on the right-hand side. This is a natural consequence of the assumption of model stationar- ity.

Illustrations

In order to illustrate the important characteristics of a synthesized instrument that can be used in ECG diagnostics, we calculated the mean MCA representation $\langle \hat{R}(t, \tau) \rangle$ (10) for the model case in which the sojourn time intervals are given by a simple sinusoidal formula:

$$\bar{s}_l = \frac{\bar{S}}{K} (1 + \delta \sin(2\pi l/K)), \quad 0 \leq l < K \quad (11)$$

where the value $\bar{S}/K$ determines the average level of all sojourn time intervals $\bar{s}_l$, and the dimensionless "modulation index" δ determines the degree of their variability. Figure 2 shows two graphs of $\langle \hat{R}(t, \tau) \rangle$ (10) – one (A) for the considerable variability index $\delta = 0.3$ and the other (B) for its small value $\delta = 0.03$. It is not difficult to see that in the first case (A) the noticeable "beats" of the $\langle \hat{R}(t, \tau) \rangle$ oscillations are clearly manifested, but in the second case (B) the dependence on τ of the mean representation envelope is practically monotonic. Thus, extracting the envelope of the mean representation and estimating its oscillations, one can detect the presence of rhythm variability, and even find the related to it parameters, for example, the process cycle.

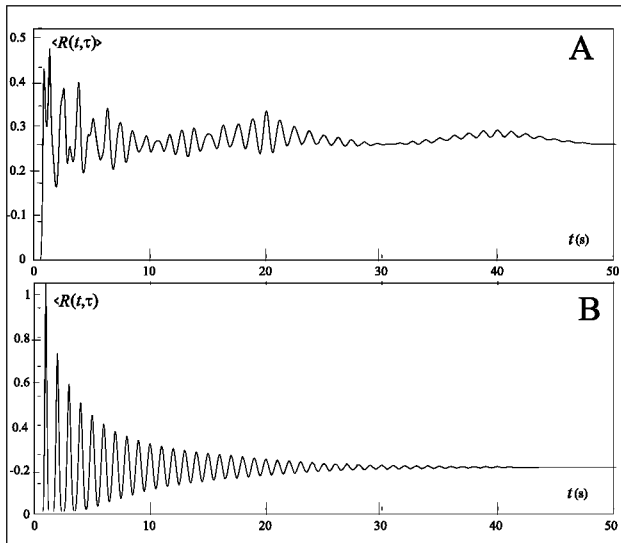


Figure 2: The graphics of mean MCA representation $\langle \hat{R}(t, \tau) \rangle$ (10) with the same parameters $\bar{S}/K = 1$, $\bar{A}|G(0)|/\bar{S} = 1$, but different heart variability parameter δ (A) $\delta = 0.3$ and (B) $\delta = 0.03$.

To illustrate how the discussed features of the synthesized instrument manifest themselves in the processing of real data, Figure 3 shows two graphs of the $\langle \hat{R}(t, \tau) \rangle$ (10) calculated and averaged over the ECG records from the Physionet portal databases NSRDB and SHAREE [10]. In both cases, with a time step $\Delta = 2$ sec a set of $N = 1000$ ACFs $\hat{R}(t, \tau)$ (2) were calculated along each record and resulting representation $\langle \hat{R}(t, \tau) \rangle$ was obtained as their arithmetic mean.

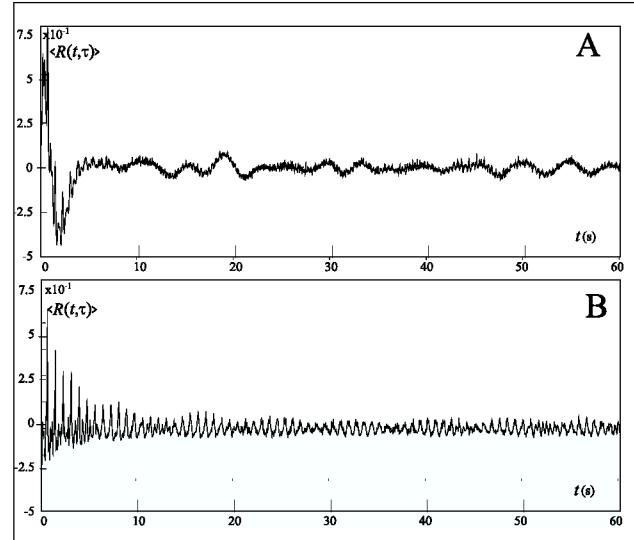


Figure 3: The graphics of mean MCA representation calculated and averaged over the real ECG records: (A) record of a healthy subject from NSRDB and (B) record of a patient with myocardial infarction from SHAREE [10].

The first graph (A) in Figure 3 is obtained from NSRDB ECG record and corresponds to the healthy person case. The second (B) is formed with the help of SHAREE data and shows the features of the disease person (myocardial infarction) representation. With the naked eye, we can see that the features of representations noted above for the model case also occur in the processing of real data. In particular, the shape of the envelope of representations allows us to accurately discriminate the case of a healthy patient from a patient with severe cardiac disease.

Conclusions

The synthesized instrument (10) showed very promising results on real records processed. Two types of ECG records from NSRDB and SHAREE databases [10] of a PhysioBank – the largest and growing archive of well-characterized digital recordings of physiologic signals were used. The proposed method made it possible to reliably discriminate the records from NSRDB, where no significant arrhythmias or any other HR disturbances were found from SHAREE records of hypertensive subjects at higher risk to develop vascular events.

Although there is still a lot of work to bring the method to the status of a useful and reliable tool for the analysis and diagnosis of heart disease, the first encouraging results suggest the optimistic prospects associated with it.

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References

- [1] J.S. Coviello. *ECG interpretation made incredibly easy!* Philadelphia: Wolters Kluwer, 3 edition, 2017.
- [2] R.M. Baevsky and A.G. Chernikova. Heart rate variability analysis: physiological foundations and main methods. *Cardiometry*, (10):66–76, 2017.
- [3] Task Force of the European Society of Cardiology, the North American Society of Pacing, and Electrophysiology. Heart rate variability. standards of measurement, physiological interpretation, and clinical use. *Eur Heart J*, 7(3):354–381, 1996.
- [4] A.L. Goldberger and H.E. Stanley et al. Long-range anticorrelations and non-gaussian behavior of the heartbeat. *Phys Rev Letters*, 70(9):1343–1346, 1996.
- [5] S.S. Yamamoto J.F. Thayer and J.F. Brosschot. The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. *Phys Rev Letters*, 141(2):122–131, 2010.
- [6] M. Malik. Geometrical methods for heart rate variability assessment. In M. Malik and A. Camm, editors, *Heart Rate Variability*, pages 47–61. Armonk, Futura Publishing Company -New York, 1995.
- [7] V.E. Antsiperov and I.V. Zabrosaev. New results for the pvc / spb detection using based on the mca heart rhythm estimation method. In *Proceedings of the 12th Russian-German Conference on Biomedical Engineering*, pages 182–186. Vladimir State University, jul 2016.
- [8] V.E. Antsiperov. Syclic renewal point processes for heart rate variability modeling. In *Extended abstracts of the second Russian Conference with international participation "Physics for Life Sciences"*, page 61. Ioffe Institute science-tech information department, sen 2017.
- [9] R. Serfozo. *Basics of Applied Stochastic Processes*. Springer, -Berlin, -Heidelberg, 2009.
- [10] L.A.N. Amaral A.L. Goldberger and et al. P.h. Ivanov. Physiobank, physiotoolkit, and physionet: Components of a new research resource for complex physiologic signals. *Circulation*, 101(23):e215–e220, 2000.

Tactile information analysis for forearm prosthesis feedback implementation

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Introduction

To date, the problem of bionic hand prostheses control is connected with the complexity of using such devices with small and fragile objects. One of the important element for precise control of prostheses is the feedback, which is either absent in the such devices on the market or does not transmit information to the user.

The lack of feedback in prosthetic devices creates inconvenience, similar to tactile sensitivity violations [1]. With such disorders people have difficulties in many types of daily activities due to a lack of information about the mechanical states of contact during various objects manipulation [2].

In this paper, aspects are considered to solve the problem of missing tactile information replenishment in bioelectrical prosthesis using. Kinematical and mathematical models of the prosthesis for feedback input parameters calculation is presented. Also, the realization of the unit for effort registration, which is developed by the prosthesis.

The task of feedback implementation

Using the reception for feedback

Contact events between the fingers and objects provide sensorimotor control points for the motion phase controller. Behavioral studies show that this information is important for accuracy of motion commands controlling [2].

In addition, the perception of the object shape and relief is carried out by touch, in which the skin and motor analyzers participate [3]. On the basis of these features of touch as feedback parameters, it is necessary for the user to transmit precisely the amount of fingers pressure and their position.

Various kinds of stimulation are used for transmitting information to the patient and creating feedback: electro-tactile sensory stimulation, vibration-tactile sensory stimulation, and information transfer using acoustic signals perceived by hearing [4].

The most common practice is vibration-tactile stimulation, which is realized by pressure and vibration on the patient's skin. This type of feedback is compatible with a one-time electromyogram recording (in contrast to electro-tactile stimulation) and does not depend on the background sound.

Biophysical feedback model

To ensure the feedback system functioning it is necessary to consider the following patterns [5]:

$$S = a \cdot \log(I) + b \quad (3)$$

(3): S - the amount of sensation; I - intensity of stimulation; a and b - constants that are different for stimulus modalities.

According to this formula, the sensation increases in proportion to the logarithm of the stimulus intensity. For different sensory systems, this ratio is different. For skin mechanoreception is characteristic [5]:

$$\frac{\Delta I}{I} = m \quad (4)$$

(4): ΔI - the change in intensity of stimulation recognized by a person; m - the ratio of the change in the intensity of stimulation recognized by a person to the intensity of stimulation;

For the informative nature of the system, each of the following impacts should look like this:

$$I = I_0(m + 1) \quad (5)$$

(5): m - the ratio of the change in the intensity of stimulation recognized by a person to the intensity of stimulation; I_0 - initial intensity of stimulation.

It follows that the informative effects are multiples of m values of the minimum perceived value. Consequently:

$$I = I_{\min}(m + 1)^n \quad (6)$$

(6): $I_{\min}$ - the minimum noticeable intensity of stimulation; n - the number of the difference threshold.

$$n = \log_{m+1} \frac{I}{I_{\min}} \quad (7)$$

In fact, n is the number of distinguished exposure levels within the dynamic range. Providing the greatest value of n means distinguishing effort with the greatest accuracy within the dynamic range of impact. This result can be achieved by varying the area and amplitude of the effect on the skin.

The finger position registration and force detection unit has a minimum resolution, which is taken as the minimally different exposure threshold $I_{\min b}$. Then the number of the difference threshold n_b :

$$n_b = \log_{m_b+1} \frac{I_b}{I_{\min b}} \quad (8)$$

(8): n_b - the number of the difference threshold; $I_{\min}$ - the minimum block resolution; I_b - the current value of the signal; m_b - the ratio of the change in the intensity of stimulation recognized by a person to the intensity of stimulation.

The numbers of the difference thresholds in the feedback signal recording unit and in the tactile stimulation unit must coincide:

$$n_b = n \quad (9)$$

From equations 7 and 8:

$$\log_{m+1} \frac{I}{I_{\min}} = \log_{m_b+1} \frac{I_b}{I_{\min b}} \quad (9)$$

Materials and methods

Measurement of the parameters of the opening width and the resulting effort for the feedback system in prosthetic tasks is preferably done indirectly by the signals from sensors inside the kinematic scheme. It is also preferable not to place pressure sensors directly on the tip of the finger, since the sensors themselves have a limited area, and points are located on the surface of the finger, the mechanical pressure of which will not be recorded by the sensor. For indirect force measurements at the tip of the finger, it is necessary to take into account the transfer functions of the mechanism parts. This will eliminate the misinterpretation of the received data, since the function may not be linear.



Figure 1: Prosthesis with an external power source manufactured by "Metallist"

The special stand was assembled to implement feedback in upper limb prostheses, thanks to which the test signals for feedback realization were recorded. In stand a functional-cosmetic prosthesis manufactured by "Metallist" was used (Fig. 1). The actuator is built into the mechanism of the

prosthesis and drives the prosthesis fingers and is movable relative to the body of the brush. One point of fixing the actuator is on the body of the brush, the second point is on the lever, which is the extension of the thumb. This fixing is used to save space inside the prosthesis and the weight of the product.

In the proposed prosthesis design, the position of the fingers is determined by counting the revolutions at the output of the prosthesis drive gear reducer using a digital monopolar Hall sensor. The measurement of the grasping motion developed by the prosthesis is carried out inside the kinematic chain (Figure 2), using a piezoelectric sensor built into the drive connection with moving parts of the prosthesis, and similarly recalculated at the fingertip through the transfer function.

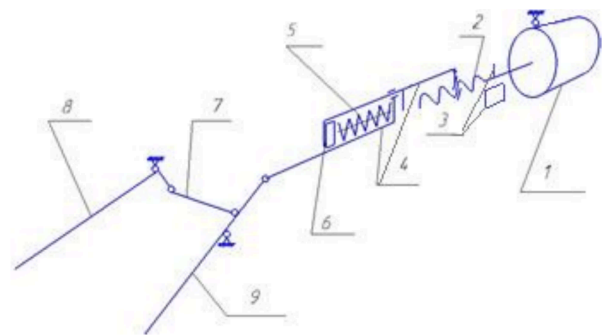


Figure 2: Kinematic scheme of the prosthesis: 1 - Prosthesis motor, 2 - Screw-nut transmission, 3 - Hall sensor and magnet on shaft, 4 - Sensor body, 5 - Spring, 6 - Silicon-sensitive resistor FSR400, 7 - Lever, 8 - II-V Fingers, 9 - I Finger

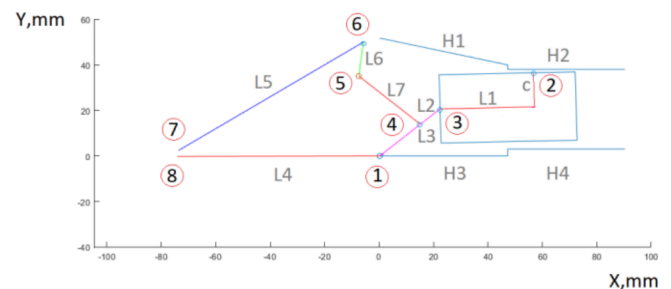


Figure 3: Mathematical model of prosthesis

For the proposed construction of the prosthesis in the Matlab a mathematical model of the kinematics of movement of the prosthesis mechanism details in the process of grasping-opening was created. In the model (Figure 3), the articulated connections are numbered with numbers, under the letter L the lengths of the arms are indicated, H - the dimensions of the prosthesis body for which the parts should not protrude, L5 and L4 - the prosthesis fingers, L1 - the current length of the actuator, c - the distance from the point hinged connection of the actuator with the body to the axis of the translational

motion of the actuator, L2, L6, L7 - the lever mechanism of the prosthesis which is transmitting the movement Δl_1 from the actuator of the prosthesis to the fingers. Points 1, 2, 6 - cylindrical joints of parts with the body of the prosthesis, points 3,4,5 - hinged cylindrical connections of the details of the linkage, and points 7 and 8 - the distance between the tips of the fingers. The blue rectangles indicate the dimensions of the actuator.

In the model, the distance between the fingertips (points 7 and 8), designated h , is calculated, which depends on the position of the actuator Δl_1 , and the force acting on the sensor F_d , also depending on the position of the actuator Δl_1 and the force at the tip finger F .

$$h = f_1(\Delta l_1)$$

$$F_d = f_2(F, \Delta l_1)$$

Both functions are nonlinear. It is noteworthy that the sensitivity of the sensor to the force at the tip of the finger F increases due to its conversion by the function f_2 . The results of the simulation are shown in Figure 4.

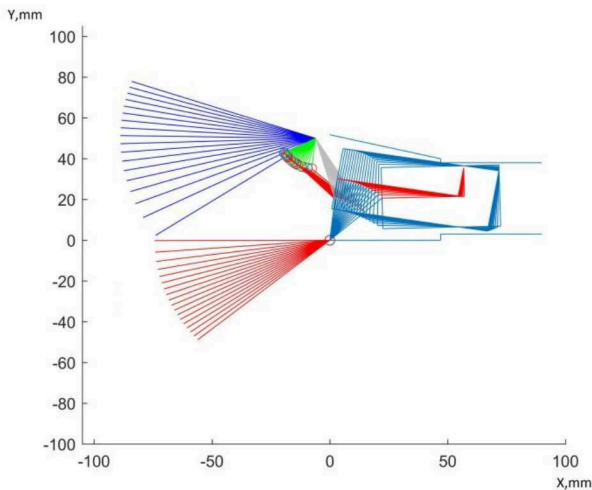


Figure 4: The motion of details of the prosthesis mechanism during the movement of the actuator with a step of 1 mm to the maximum extended

The design of transmission of traction from the drive to the fingers is spring-loaded - this is a necessary element of feedback. Upon contact with a solid surface, the force of interaction between the prosthesis fingers grows not spasmodically, but gradually, allowing the user to realize the touch and have time to react to it before the prosthesis develops maximum force.

To determine the position of the fingers, the speed at the output of the gear reducer of the prosthesis drive is calculated using a digital monopolar Hall sensor (Figure 5). To eliminate high-frequency noise after the Hall sensor, a passive low-pass filter was used.

Experimental part

Force signal at the end of the finger registration

As an example of a test signal, a signal was recorded in the process of chicken egg crushing by prosthesis. The chicken egg is fragile enough, so it is well suited to illustrate the operation of the feedback system. In the course of the experiment, the egg and prosthesis were placed on special supports.

The values of the voltage drop across the strain gage were calibrated using a set of laboratory weights of 20 g, 100 g, 200 g and 500 g, which made it possible to translate the values of the ADC readings into the values of the acting force. The data were recorded with a sampling frequency of 1000 Hz. To remove high-frequency noise, digital signal filtering was performed.

During the egg compression experiments, four series of measurements were made, resulting in a plot of the average strength of the egg shell destruction resistance with standard deviation (Figure 6). The signals recorded for each series of measurements were synchronized at the moment of breakage of the shell (at maximum force).

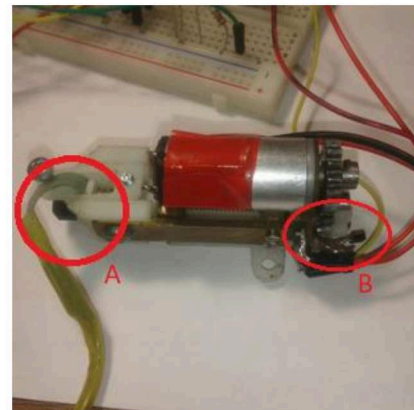


Figure 5: Location of the force-sensitive sensor (A) and the Hall sensor (B)

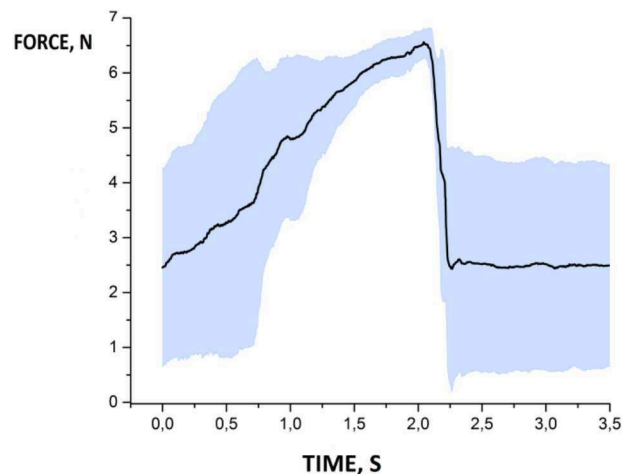


Figure 6: Average signal of chicken eggs breaking

Registration of the fingers opening width

The data were obtained using a Hall sensor that registered the speed of the output shaft of the actuator reducer when passing a magnet attached to the shaft next to the sensor. A passive filter was used to filter the Hall sensor signal. The obtained signal can be used by digital devices for calculating the speed and calculating the width of the prosthesis opening. In the current version of the model with a single Hall sensor, it was possible to achieve the accuracy of determining finger position of 5 mm.

Conclusions

In this paper, we considered aspects of the realization of unit of signal recording for tactile feedback system. We also proposed a location option for the sensors in the structure of prosthesis, which increases the area of the recording surface. A mathematical model for the correct interpretation of the information from the sensors is compiled. The main features of biophysical reception processes, that formulate requirements for the tactile stimulation unit, are considered, and the relationship of the output parameters of the tactile stimulation unit and the input parameters of the sensors of the tactile signal recording unit is described. The developed model of the prosthesis with the blocks of registration of the position of the fingers and of the effort allows for further experiments on the use of various tactile stimulation options.

References

- [1] Biomechanics and the Physiology of Motion / Bershtein NA edited by Zinchenko V.P. Moscow-Voronezh 1997, 43 p.
- [2] Roland S. Johansson, J. Randall Flanagan "Coding and use of tactile signals from the fingertips in object manipulation tasks" Nature on May 2009.
- [3] Gluhanyuk, N.S. General psychology: Course of lectures: / NS. Glukhanyuk S.L. Semenova, A.A. Pecherkina - Mn.: BSU, 2004. -290 p.
- [4] C. Antfolk, M. D'Alonzo, B. Rosén, G. Lundborg, F. Sebelius, C. Cipriani "Sensory feedback in the upper limb prosthetic" Taylor & Francis in Expert Reviews of Medical Devices on January, 2013
- [5] R. Schmidt and D. Dudel, Fundamentals of Sensory Physiology, Moscow, 1984, 287 p.
- [6] Fundamentals of Neuromechanics Francisco J. Valero-Cuevas. - Springer. -2015.- 204p.

Intraoperative Sterile Molding of Patient Specific Templates for Minimally Invasive Cochlear Implant Surgery

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Introduction

Cochlear Implant (CI) surgery is an established treatment to restore severe hearing loss and deafness caused by inner ear dysfunction. To gain access to the cochlea for insertion of the implants electrode carrier mastoidectomy (partial removal of the cranial bone) is performed. This process is sophisticated and time consuming. Minimally invasive CI surgery has the potential to reduce operating time, trauma, hospitalization time, amount of needed anesthetics and costs and additionally improve ergonomics for the surgeon. The concept of this approach is to replace the mastoidectomy by a single drill hole from the surface of the skull to the cochlea. The complexity of this lies in the accuracy requirements resulting from the vicinity of the drill trajectory to the facial nerve. The drill (typical diameter 1.8 mm) has to pass through the approximately 2.5 mm wide facial recess in a depth of about 3 cm. Marker based navigation can not be effectively applied for this intervention. One method to achieve the required accuracy is by using a patient specific template to hold a linear guide for a drill.

The first clinical results of this approach are presented with the microtable system [1]. Beside the risk of physical damaging the facial nerve or thermal necrosis from heat induced by the drilling process [2] (both not further discussed in this paper) manufacturing of the template is still an issue. Operation planning is done in reference to the frame mounted on the patients skull at the beginning of the surgery. Since this reference can only be determined after fixation, the manufacturing of the template has to be done intraoperative. Manufacturing of the microtable is done none sterile by CNC machining a ULTEM (polyetherimide, PEI) block. In a shortened autoclaving process the finished template is sterilized and then cooled down. The shortened autoclaving of the microtable is neither certified in Europe nor in Russia. The RoboJig system (Figure 1), relying on the same working principle, was developed with a sterile manufacturing system to solve this problem. This paper is centered around the manufacturing unit of the RoboJig.

For sterile manufacturing of the jig different approaches have been developed. The technical requirements include, that the process can be done fast enough to avoid surgical downtime during anesthesia of the patient. This is the reason why 3D printing is currently not an option. Further it has to be guaranteed, that the chain of errors does not lead

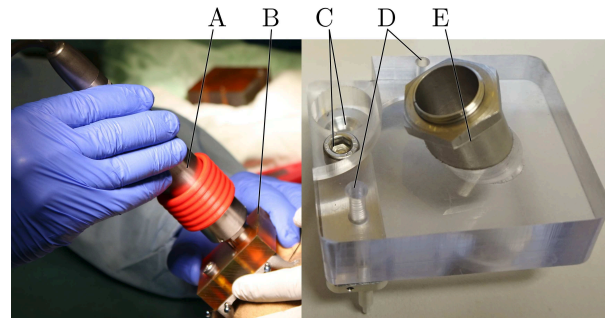


Figure 1: Left: linear guided surgical drill (A) connected to an intraoperativ milled jig (B) during initial cadaver experiment. Right: CNC milled jig prototype with connector holes (C-E).

to deviations larger than 0.5 mm in 30 mm depth during the drilling process. The jig should not hide the view of the situs for the surgeon.

template milling

In the current research setup the template is pre-formed and sterilized ahead of the surgery. The customization is done with a passive hexapod (Schick X1 med 3D, Schick-Dental GmbH, Germany) which positions the template relative to the axis of a drill unit on a linear guide. The struts of the hexapod are based on micrometer screws and adjusted manually. Their length is calculated based on the planned trajectory, which is transformed into the frame coordinates. The adapter on the hexapod platform uses a dowel pin connection dimensional similar to the one on the frame in Figure 1. Based on the planning data a stepped hole is drilled as interface for the surgical drill guide (Figure 1 part A and E). The forces generated during this customization process, as well as the angle of impact of the drill, raise the need for a stiff and highly accurate linear guide. Also a preformed and sterile template is needed for every surgery. Setup of the system and milling took 15 min in an initial cadaver trial. No deviation between drillhole and plan was visible in a postoperative CBCT scan (resolution 0.3 mm). The milling system of the RoboJig was described recently [3].

bone cement fixation

To reduce process forces and complexity an alternative manufacturing approach was developed. Its concept is to adjust a linear guide with the hexapod similar to the template milling approach. After orientation the guide is fixed to a mounting adapter using bone cement [4, 5]. This has

the advantage of low hardware costs and lower effort for certification.

polymer molding

In this paper a novel intraoperative manufacturing approach is presented. Our hypothesis is that a molding process results in lower process forces than in the template milling and therefor leads to a higher manufacturing accuracy and lower manufacturing time at lower costs. Injection molding is well established for processing thermoplastics. The melted material is extruded under high pressure into the mold. This typically leads to sterile parts depending on the environment [6]. For this process a mold has to be created for every new part. This is not feasible for the RoboJig since the part is different for every patient. An adjustable mold is not possible for injection molding because it has to be closed and leakproof. We experimentally investigated two low pressure process with an open mold. Pre sterilized granular material was used in combination with the inductively heated mold as well as a photopolymer cured under UV light.

Materials and Methods

The design of the jig is shown in Figure 1. It contains two holes for the dowel pin connection (Figure 1 part D) on the titanium frame of the system, two holes for the connection screws (Figure 1 part C) and one guiding hole for attaching a surgical drill unit (Figure 1 part A) through a locking ring (Figure 1 part E). Critical structures regarding accuracy, are the dowel pin connectors, the guiding hole and the lower surface of the jig attaching to the frame. The shown manufacturing concept is based on the adjustment of the guiding hole by a sterile hexapod. The endeffector of this hexapod is a 14 mm pin that is held in place in the fluid polymer during curing to create the guiding surface (not applied in initial tests). The shape of the jig is defined by the open mold shown in Figure 3.

material choice

In the current template milling approach ULTEM 1000 (PEI) is used as material. Its benefits lie in its high young's modulus and medical certification. Due to its high transition temperature it is not suitable for the molding approach. For an alternative material a low transition temperature is favorable to reduce risk and cooling time. Still the material should withstand the autoclaving process without losing form stability. A high melt flow rate (low viscosity) ensures that small structures in the mold get modeled. This is important for building the dowel pin connection. The chosen material should not inhibit medical certification of the system. Table 1 summarizes the properties of alternative materials. For an initial selection material probes were heated and cured in a miniature mold. The resulting probes are shown in Figure 2. From this initial experiment CALIBRE and TOPAS were chosen for further work because

of their material properties, melting behavior (little to no blistering) and transparency (enables view on the situs).

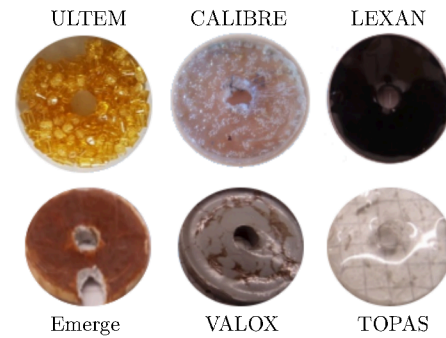


Figure 2: Materials after initial mold test in which the granulate was heated to its transition temperature

Table 1: comparison of material properties of suitable polymers from corresponding material data-sheets

	ULTEM 1000	CALIBRE 2081	LEXAN HP1REU
Material type	poly-etherimid	poly-carbonate	poly-carbonate
Young's modulus [MPa]	3500	2400	2400
Density [$\frac{kg}{m^3}$]	1270	1200	1200
Transition temperature [$^{\circ}C$]	195	142	126
Mold shrinkage [%]	0.5 - 0.7	-	0.7
Melt flow rate [$\frac{^{\circ}C}{kg}$]	9 [$\frac{337^{\circ}C}{6.6kg}$]	22 [$\frac{330^{\circ}C}{1.2kg}$]	35 [$\frac{300^{\circ}C}{1.2kg}$]
Melt volume flow rate [$\frac{^{\circ}C}{kg}$]	13 [$\frac{360^{\circ}C}{5kg}$]	-	33 [$\frac{300^{\circ}C}{1.2kg}$]
ISO 10993-1	yes	yes	yes

	Emerge 9500CR	VALOX HX312C	TOPAS 8007
Material type	poly-carbonate	polybutylene terephthalate	cycloolefin-copolymere
Young's modulus [MPa]	2270	2500	2600
Density [$\frac{kg}{m^3}$]	1290	1310	1020
Transition temperature [$^{\circ}C$]	109	54	75
Mold shrinkage [%]	-	1.6	0.1 - 0.5
Melt flow rate [$\frac{^{\circ}C}{kg}$]	10 [$\frac{260^{\circ}C}{5kg}$]	35 [$\frac{250^{\circ}C}{1.2kg}$]	-
Melt volume flow rate [$\frac{^{\circ}C}{kg}$]	-	31 [$\frac{250^{\circ}C}{1.2kg}$]	32 [$\frac{360^{\circ}C}{2.16kg}$]
ISO 10993-1	yes	yes	yes

mold design

Main task of the mold is providing an accurate negative volume for the jig. Figure 3 shows the design concept. The mold is build from three detachable parts for releasing the final jig. All structures relevant for the system accuracy (pins for the connection interface of the later part) are on a single part to avoid inaccuracy resulting from assembly.

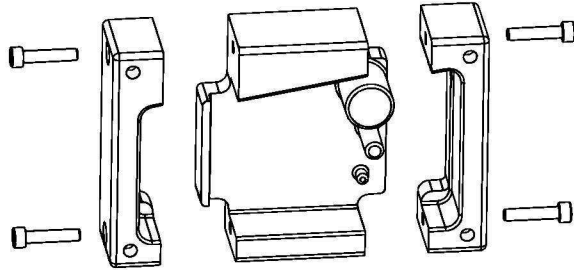


Figure 3: Design of the mold

system setup

The sterile hexapod uses magnetic ball joints to attach on a grid of base points on both connecting platforms. Since the micrometer screws allow for an adjustment in six degrees of freedom this coupling options leads to redundancy for most endeffector positions. This redundancy enables optimization regarding the systems accuracy. More information about the used hexapod can be found in [7, 8]. For a clinical implementation of either the granular melting or the photopolymer approach a lid has to be added to shield the system from its environment.

melt on and curing

To melt on the granular polymer it has to be heated to its transition temperature. The heating process should be fast and uniform while avoiding overheating and thus carbonisation of the melt. The system should be reasonably small to fit in the OR environment and pose a minimal risk to the clinicians. Inductive heating of the mold was chosen as compromise of those requirements.

experimental evaluation

To evaluate the feasibility of the manufacturing process two experiments were conducted. Aim was the production of an accurate jig comparable to a milled version. The pin for the guiding hole was not used in both initial experiments. In the first experiment the mold was filled with granular CALIBRE or TOPAS and then inductively heated until uniformly melted (Figure 5). After curing the jig was removed and measured with a coordinate measuring arm (FARO GAGE, Faro Technologies Inc., Lake Mary, FL, USA). Four specimen were produced for CALIBRE and ten from TOPAS (showed better initial results regarding accuracy). In a second experiment the medical photopolymer Med610 (Stratasys, Minnesota, USA) was used and cured

under UV light exposure. Typically this polymer is used for printing of patient specific templates for dental surgery.

Results

The described melt on process was successfully applied. Figure 4 shows two finished templates. The standard deviation of the measured distances of the dowel pin holes was 0,058 mm (n=10) for the TOPAS and 0,149 (n=4) for the CALIBRE specimen. The photopolymer approach was discarded due to blistering of the material (Figure 6C).



Figure 4: Cured jig made from TOPAS granulate (left) and CALIBRE granulate (right)

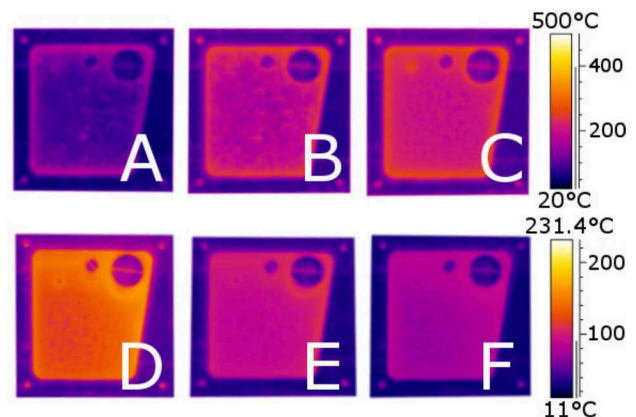


Figure 5: Exemplary heating and curing process taken from an infrared camera. A - C show the temperature distribution of the melt after 5 min, 25 min and 45 min respectively. D - F show the cooling process after 5 min, 15 min and 25 min. Please note the different color scale for A - C and D - F.

Discussion

The complete process currently takes 70 min plus the time for the system setup (5 - 10 min). Increasing the power output of the induction heater is not an option because it leads to carbonization of the edges of the jig while the inner parts are still granular (Figure 6A). The heating process can be started before surgery to avoid a bottleneck during the intervention. Curing can be speed up by emerging the mold in sterile water, however this has not been tested yet. An overview over the planned workflow is shown in Figure 7. The top surface of the jig might become uneven due to

shrinkage in the curing process (Figure 6B). This is not relevant for the system accuracy. Only the guiding holes (Figure 1 parts D and E) and the bottom surface (Figure 4) are relevant reference structures. UV curing did not meet the requirements. During the process gas development leads to hollow volumes. Blistering is avoidable by successively adding layers of < 1 mm thickness but this increases the process time and therefor eliminates its advantages over conventional 3D printing.

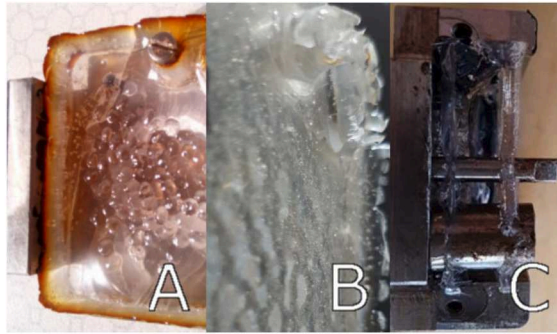


Figure 6: Three failure modes during molding. Uneven and fast heating (A), uneven surface from uneven heating and melt shrinkage during curing (B) and gas formation when UV curing thick layers of Med610 (C).

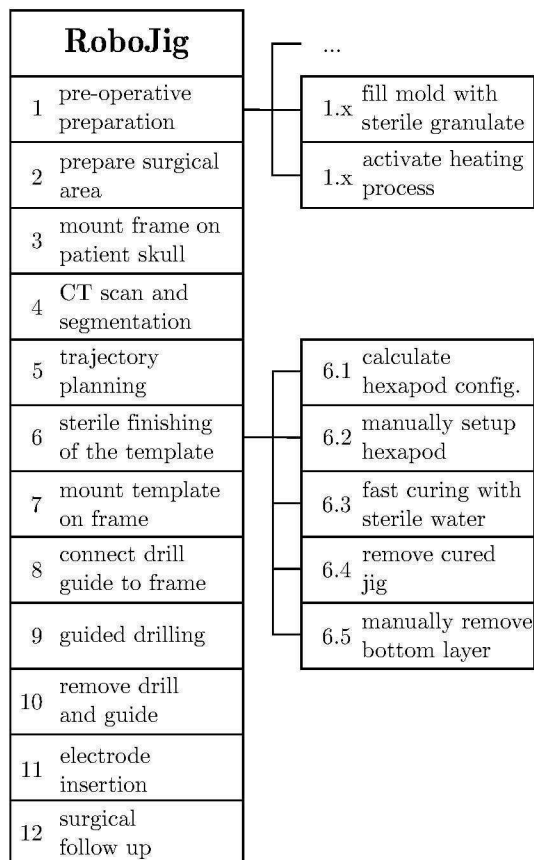


Figure 7: Proposed surgical workflow for the RoboJig system.

Conclusions

The concept of low pressure molding granular thermoplastics was successfully proven. Relevant structures were reproduced sufficiently accurate in the initial experiments. Still the surface quality can be improved by parameter optimization. For a clinical implementation further work is needed. Accuracy has to be evaluated in a next step by using multiple molded jigs to drill into artificial bone. Also the system needs to be optimized regarding usability, safety and process time. Currently the milling approach is beneficial due to shorter processing time. Implementing the workflow shown in Figure 7 could change this.

References

- [1] R. F. Labadie, R. Balachandran, J. H. Noble, G. S. Blachon, J. E. Mitchell, F.A. Reda, B. M. Dawant, and J. M. Fitzpatrick. Minimally invasive image-guided cochlear implantation surgery: First report of clinical implementation. *The Laryngoscope*, 124 (8):1915–19, 2014.
- [2] A. Feldmann, J. Anso, B. Bell, T. Williamson, K. Gavaghan, N. Gerber, H. Rohrbach, S. Weber, and P. Zysset. Temperature prediction model for bone drilling based on density distribution and in vivo experiments for minimally invasive robotic cochlear implantation. *Annals of Biomedical Engineering*, 44(5):1576–1586, 2016.
- [3] M. Kluge, G. J. Lexow, T. Lenarz, O. Majdani, and T. S. Rau. Untersuchungen zur Genauigkeit des intraoperativen Fertigungssystems für den RoboJig. *Tagungsband der 16. Jahrestagung der Deutschen Gesellschaft für Computer- und Roboterassistierte Chirurgie, CURAC 2017*, pages 262–265, 2017.
- [4] B. Vollmann, S. Müller, D. Kundrat, T. Ortmaier, and L. A. Kahrs. Methods for intraoperative, sterile pose-setting of patient-specific microstereotactic frames. *Proc. of SPIE*, 9415M:9415, 2015.
- [5] T. S. Rau, G. J. Lexow, D. Blume, M. Kluge, T. Lenarz, and O. Majdani. Micro-stereotactic frame utilizing bone cement for individual fabrication: an initial investigation of its accuracy. *Proc. SPIE*, 10135:101350, 2017.
- [6] M. Schönberger. *Autosterilität: Grundlagen und experimentelle Betrachtung der Kunststoff-Prozesstechnik*. dissertation, Technische Universität München, 2014.
- [7] J. P. Kobler, J. Kotlarski G. J. Lexow, T. S. Rau, O. Majdani, and Tobias Ortmaier. Design optimization of a bone-attached, redundant and reconfigurable parallel kinematic device for skull surgery. *IEEE International Conference on Robotics and Automation (ICRA)*, page 2364–2371, 2014.
- [8] J. P. Kobler, K. Nülle, G. J. Lexow, T. S. Rau, O. Majdani, L. A. Kahrs, J. Kotlarski, and Tobias Ortmaier. Configuration optimization and experimental accuracy evaluation of a bone-attached, parallel robot for skull surgery. *Int J CARS*, 11(3):421–436, 2016.

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