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Real-Time Cannula Navigation in Biological Tissue with high temporal and spatial resolution based on Impedance Spectroscopy

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Abstract—**In many medical applications a well-directed positioning of a cannula in body tissue is mandatory. Especially the accurate placing of the cannula tip in the tissue is important for efficient drug delivery or for accessing blood vessels and nerves. This paper presents a new approach for a universal cannula navigation system based on tissue classification on the cannula tip by impedance spectroscopy. The cannula serves as coaxial, open ended waveguide which is connected to remote measurement equipment. Objective of the new system is to reach a high spatial and temporal resolution for dynamic cannula guidance. Therefore the proposed coaxial cannula design has been analyzed by Finite Element Simulation to investigate the sensitivity of the cannula tip. For fast tissue impedance spectrum measurement the Time-Domain-Reflectometry method is used in order to achieve a high temporal resolution. Measurement data derived in the laboratory is analyzed and interpreted using the general Cole-Cole model for tissue. Based on the results we propose to use a chirp signal for impedance measurement in order to improve the sensitivity of the system towards specific tissue properties.**

I. INTRODUCTION

NAVIGATION and guidance of a cannula inside body tissue is a common challenge in many medical applications such as blood vessel puncture, nerve stimulus and drug delivery. In particular a correct and precise positioning of the cannula tip in the target tissue is often crucial. Therefore the tissue volume close to the cannula tip has to be continuously analyzed and classified by characteristic tissue properties. In addition to the required precise spatial resolution the measurement equipment must be able to classify the tissue within a short period of time. In many applications the cannula is continuously moving in the tissue until the correct position is reached. For a video-like real-time assistance system for invasive cannula positioning at least 20 measurements per second should be performed.

Today there are many well known methods of cannula and needle guidance such as Magnetic Resonance Imaging (MRI), Computer Tomography (CT) and ultrasound imaging [1,2,3]. Even though MRI and CT systems allow for a high precision positioning due to the high spatial resolution, there are certain major drawbacks. These systems are very expensive, stationary, complicated to handle and in general produce static images only which are not suitable for dynamic cannula guidance. Furthermore CT systems expose the patient to radiation. Ultrasound based cannula guidance systems used to be large as well but recently there was a lot progress in the development of portable devices. However, the spatial resolution of ultrasound systems is inferior to MRI and CT systems and usually gives 2-D images only. A practical disadvantage of ultrasound systems is the need for keeping the position of the ultrasound transmitters stable while inserting the cannula. In general all of the above described systems do not fulfill the requirements set by time-critical situations like acessing the blood vessels for connecting the patient to a heart-lung-machine (HLM).

A promising alternative measurement method for cannula guidance in body tissue is Impedance Spectroscopy (IS). This method is based on the analysis of impedance spectra which are characteristic for every tissue [4,5]. The measurement equipment basically applies multiple frequencies to the tissue via suitable electrodes and measures the response of the tissue. The derived dielectric properties are then analyzed and may be used for classification of certain tissues like fat, muscle and blood. Kalvoy et al. proposed and analyzed an impedance based needle guidance concept [6]. The drawback of the proposed system is the need for an additional neutral reference electrode since the investigated needle is used as monopolar electrode only.

In this paper we present a new bipolar coaxial cannula design optimized for impedance measurements of the tissue on the cannula tip. Inside the hollow cannula we use a coaxial inner wire which serves as a shielded waveguide. The tip of the cannula is an open ended coaxial probe (Fig. 1). After reaching the correct position in the tissue, the inner core of the cannula can be removed and only the hollow needle remains in the tissue.

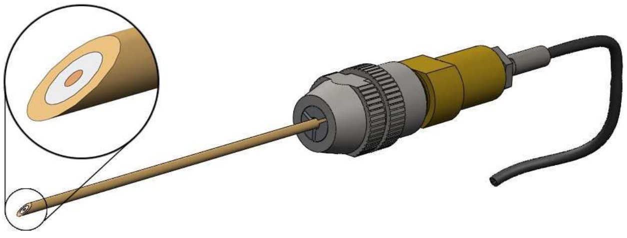

Fig. 1. New coaxial cannula design used during experiments in the laboratory. The hollow cannula contains an inner wire isolated by a dielectric. The new design allows for using the cannula as a wave-guide for Time-Domain-Reflectometry (TDR) measurements.

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II. SYSTEM CONCEPT

Objective of the developed measurement system is to gain precise information about the tissue close to the tip of the cannula. As measurement method we use impedance spectroscopy for determining characteristic dielectric properties of the tissue. Because of the thin cannula design there is almost no space for placing electrodes or other sensing equipment on the cannula tip. Therefore the proposed cannula design (Fig. 1) forms a coaxial probe which serves as a waveguide. Remote measurement equipment is connected to the waveguide probe via a coaxial cable. The complete measurement setup is shown in Fig. 2. An arbitrary signal generator feeds a measurement signal into the cable. The signal travels along the cable and the cannula until it reaches the cannula tip. From the electrical point of view the tip forms an open ended coaxial cable and therefore the signal is reflected. The reflected signal travels back along the cable and superposes to the input signal. The resulting waveform is continuously sampled by a high-speed sampling unit. If the cannula tip is in contact with biological tissue not all measurement signal components are fully reflected since the tissue acts as a complex load impedance at the end of the waveguide (Fig. 3). According to the Cole-Cole model for tissue the load impedance is frequency dependent and characteristic for each tissue [7]. The resulting shape of the partially reflected and phase shifted measurement signal superposed to the input signal carries tissue specific information which is analyzed and used for tissue classification.

For measuring an impedance spectrum of a sample many impedance spectroscopy based systems use sine wave sweeps. The drawback of a sweep is the duration required for capturing the complete impedance spectrum within the relevant frequency range. Since the developed system is intended to be used for dynamic cannula guidance, Time-Domain-Reflectometry is used as an alternative method. Therefore the signal generator in Fig. 2 generates a periodic rectangular signal. According to Fourier such a signal is composed of the fundamental superposed by harmonics. The required frequency sweep is replaced by applying all relevant frequencies at the same time by a rectangular pulse.

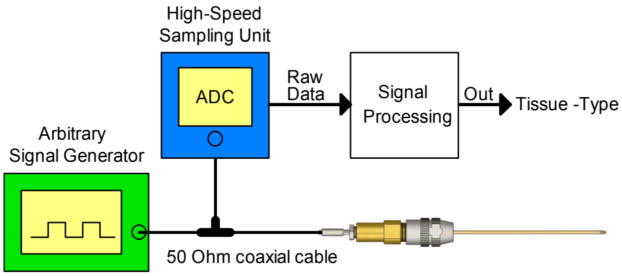

Fig. 2. Measurement setup for the tissue impedance measurement on the cannula tip. An arbitrary waveform generator feeds a signal into the coaxial waveguide cannula. The reflected signal superposes to the input signal and the resulting waveform is sampled by a fast sampling unit.

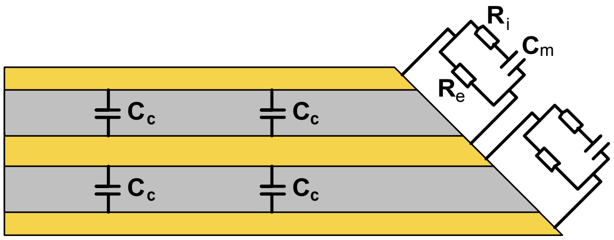

Fig. 3. Equivalent electrical circuit of the frequency dependent load impedance formed by the tissue on the cannula tip. The Cole-Cole model is used for the equivalent circuit.

III. FINITE ELEMENT SIMULATION

Since a high spatial resolution is required, the sensitivity of a typically shaped cannula tip towards the tissue volume close to the tip is simulated. The investigated cannula has an outer diameter of 1.25 mm, an inner diameter of 0.8 mm and a coaxial inner wire of 0.3 mm. The tip has an angle of 30 degrees. A low frequency Finite Element Simulation shows the resulting current density distribution in a homogeneous tissue when a voltage signal is applied to the inner coaxial wire and the cannula itself is at ground potential as well as the boundaries of the simulated tissue volume (10 x 10 x 10 cm^3). Fig. 4 (A) shows the voltage pattern and Fig. 4 (B) the current density pattern. The absolute values are dependent on the applied signal level and the tissue parameters and are not relevant for a sensitivity analysis. Fig. 4 (C) illustrates the investigated volume in longitudinal direction in front of the tip. The volume is subdivided into thin slices with a thickness of 0.1 mm. The losses generated by the tissue within the slices is compared to the total tissue losses. The result is presented in Fig. 5. The graph shows the relative losses as a function of the distance to the cannula tip. According to the simulation results approximately 81 % percent of all losses are generated within a distance of 1.0 mm and 85 % within a distance of 1.5 mm.

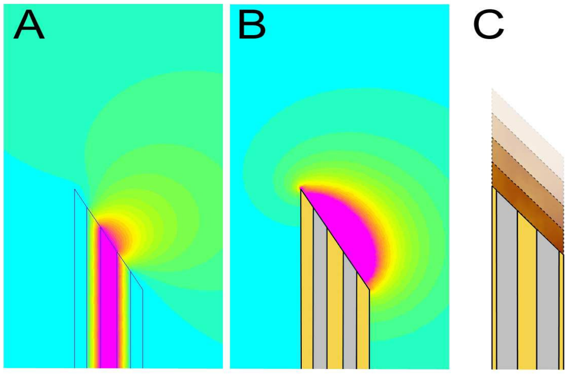

Fig. 4. Finite Element Simulation results for a cannula tip inserted in homogeneous conductive media. (A) shows the distribution of the voltage pattern, (B) shows the resulting current density in the tissue close to the cannula tip. (C) illustrates the investigated volume for spatial sensitivity analysis in front of the cannula tip.

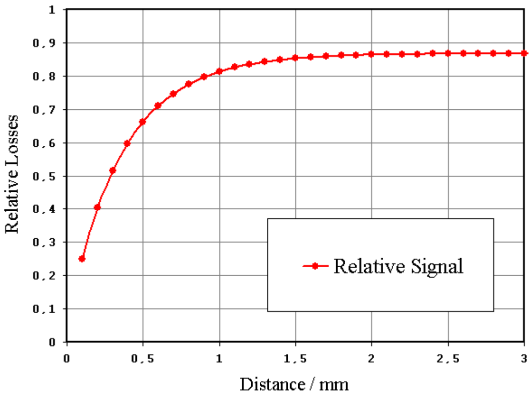

Fig. 5. Finite Element Simulation result of the spatial sensitivity study. The graph shows the relative losses of a small tissue volume in front of the cannula as a function of the distance to the cannula tip.

IV. MEASUREMENT RESULTS

The above described coaxial cannula is tested in the laboratory during in-vitro experiments. A Tektronix AFG 3252 is used as stable signal generator and feeds rectangular pulses with sharp rising edges into the coaxial cable and the cannula at a frequency of 5 kHz. The resulting waveform is captured using a fast digital oscilloscope (LeCroy WaveRunner 104 Xi). The laboratory setup is prepared as shown in Fig. 2. The cannula tip is inserted into three different pork tissues: fat, muscle and blood. Fig. 6 shows the measured waveforms of the resulting signal. The first rising edge arises out of the voltage divider created by the inner generator impedance and the characteristic cable wave impedance. Then the signal level remains constant while the rising edge travels to the cannula tip and back to the signal generator. The partially reflected signal superposes to the input signal and forms the second rising edge. Only the shape of the second rising edge contains information about the complex tissue impedance on the cannula tip. This signal is analyzed in time domain. Fig. 7 compares the signal level of all tissues after t = 14.0 ns.

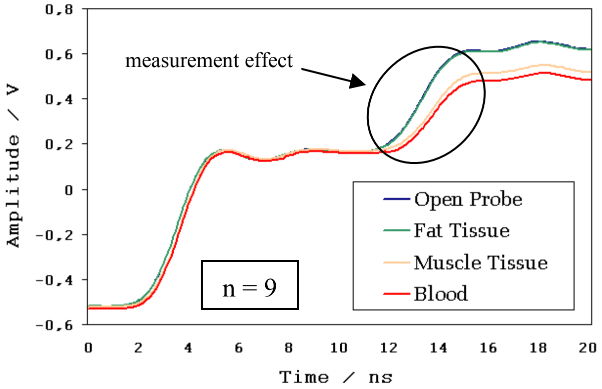

Fig. 6. Measurement result of laboratory experiments. The graph shows the acquired waveform of the measurement signal. The second rising edge is the reflected rectangular signal superposed to the input signal and carries all relevant measurement information.

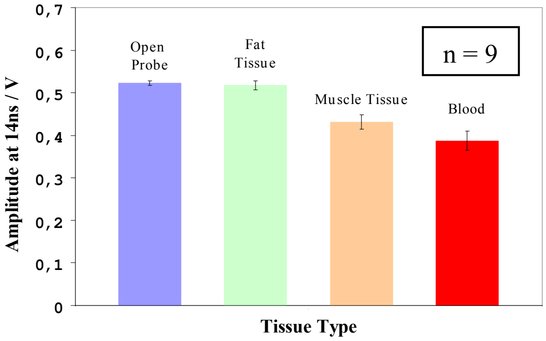

Fig. 7. Comparison of the measurement signal level at t = 14 ns for all tested tissue impedances and an unterminated open probe with no load on the cannula tip.

V. DISCUSSION

The measurement results presented in Fig. 6 and Fig. 7 show that the developed system works in principle. All tested tissues show a different and characteristic signal distortion which is analyzed and compared to each other in time domain. The classification between fat and muscle as well as between fat and blood can easily be done by the signal level analysis. Due to the high difference in electrical conductivity of the tissues this method gives stable results. However, the classification between muscle and blood is based on a small difference in the time domain measurement signal only. Especially the conductivity of blood varies from sample to sample and therefore causes high tolerances which makes it difficult to classify between muscle and blood.

It is important to have a more detailed look at the applied rectangular measurement signal characteristics and the resulting effects in combination with the complex tissue load impedance presented in Fig. 3. The spectrum of a rectangular pulse signal contains the fundamental as well as harmonics. The amplitude of the harmonics dramatically decreases according to the sinc(x) - function while the frequency increases [8]. Due to the equivalent circuit schematic of the tissue presented in Fig. 3 the resulting AC-current in the tissue is divided into two paths. At low frequencies the bigger part flows through the resistor R_e which represents the *frequency independent electrical conductivity* of the tissue. The cell membrane capacitance C_m is high impedant and blocks the current flow through the interior of the cells. At higher frequencies the cell membrane capacitance C_m becomes more and more low impedant and therefore a higher current will now flow through the cells and the inner cell plasma which is represented by R_i. *At higher frequencies it is possible to use this frequency dependent effect for further classification* of the tissues since the frequency dependent behaviour of the tissues is in general not identical. However, in this case the spectrum analysis of the applied rectangular pulse shows that the shape of the reflected measurement signal is dominated by the large amplitude level of the low frequency fundamental (Fig. 8). Only a small part of the resulting characteristic waveform distortion is caused by a frequency dependent effect because of the low initial amplitudes of the higher frequency harmonics. In order to enhance the sensitivity of the cannula guidance system towards tissue characteristic frequency dependent effects it is proposed to use a measurement signal with certain spectral properties. It would be benefitial if the amplitude of higher frequency components in the applied signal is in the same range like the fundamental. This will lead to an optimized frequency dependent relative signal change caused by the current divider effect in the tissue. However, the waveform of the applied measurement signal must be suitable for measuring all relevant frequency components within a short period of time in order to fullfill the requirements of a real-time system for dynamic cannula guidance. A promising type of measurement signal is a chirp signal as investigated in [9]. Fig. 9 shows such a linear chirp signal in time domain and Fig. 10 shows the resulting amplitude spectrum of this chirp. The amplitude of all relevant harmonics is almost identical up to a defined cutoff-frequency which makes this signal attractive for future use.

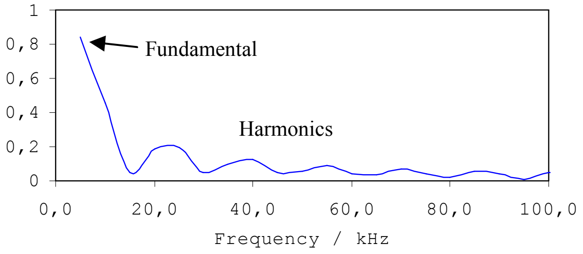

Fig. 8. Normalized amplitude spectrum of the used rectangular signal. The fundamental is at 5 kHz, the harmonics decay according to the sinc function.

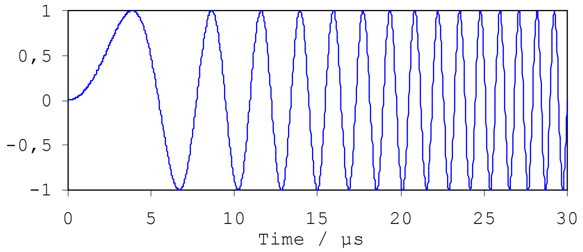

Fig. 9. Linar chirp signal with da duration of 30µs. The shown signal covers a bandwidth from 10 kHz to 1 MHz.

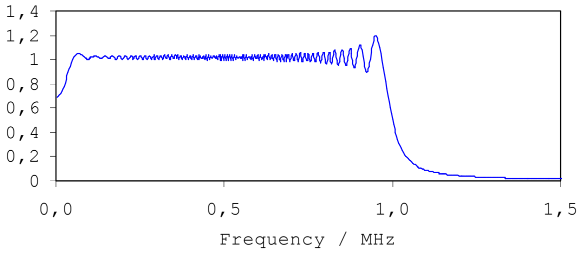

Fig. 10. Normalized amplitude spectrum of the chirp signal shown in Fig. 9. The amplitude of all harmonics remains almost constant up to a specified cutoff frequency. In this particular case the cutoff frequency is 1 MHz.

VI. CONCLUSIONS

This paper presents a novel approach for a cannula guidance system based on impedance analysis of the tissue. The system is primarily intended to be used in time critical emergency situations and allows for a fast access to blood vessels for connecting a heart-lung machine. Main objective of the development was to build a system which gives both high spatial and high temporal resolution. The FEM-Simulation results of the new coaxial design show a very good spatial resolution. More than 80 % of the measurement signal of the prototype cannula with an outer diameter of 1.25 mm are generated in a distance smaller than 1.0 mm to the cannula tip. Advantage of the coaxial cannula tip is the small distance between the inner wire and the outer cannula wall which leads to a small and well defined sensitivity zone. The open end of the coaxial waveguide simply forms two electrodes and allows for measuring the tissue impedance without the need for an additional reference electrode.

In order to optimize the temporal resolution of the system we employ Time-Domain-Reflectometry as fast measurement method. For determination of characteristic tissue impedance within a short period of time we apply rectangular pulses to the tissue and analyze the response. Measurement results prove the system concept and a detailed view at the signal and tissue properties leads to a proposal for using chirp signals in future experiments to further enhance the system accuracy. The broadband chirp signals spread the measurement signal enery with an almost constant amplitude up to a defined cutoff frequency. This allows for measuring the tissue impedance spectrum with higher accuracy over the whole interesting frequency range.

REFERENCES

[1] S. P. DiMaio et al, “A System for MRI-guided Prostate Interventions,” Proceedings of IEEE BioRob, pp. 68-73, Pisa, 2006

[2] E. Hagmann et al, “A haptic guidance tool for CT-Directed percutaneous interventions,” Proccedings of IEEE IEMBS’04 conference, vol.1, pp.2746-2749, 1-5 Sept. 2004

[3] A. Kluge et al, ”Puncture of the popliteal artery using a Doppler-equipped (SMART) needle in transpopliteal interventions,” Eur Radiol 2003, vol.13, pp.1972-1978

[4] O.G. Martinsen, S. Grimnes, *Bioimpedance and Bioelectricity Basics*, Academic Press, 2008, ISBN: 0123740045

[5] R. Pethig, ”Dielectric properties of biological materials: biophysical and medical applications”, IEEE trans. Electr. Insul. vol. 19,pp.453-474, 1984

[6] H. Kalvoy, L. Frich, S, Grimnes, O.G. Martinsen, P.K. Hol, A. Stubhaug, “Impedance-based tissue discrimination for needle guidance,”Physiological Measurement, vol. 30, pp. 129-140, 2009

[7] S. Grimnes, O.G. Martinsen, “Cole electrical impedance model – a critique and an alternative,”IEEE Transactions on Biomedical Engineering, vol.52,no.1,pp.132-135, Jan. 2005

[8] M. Min, U. Pliquett, T. Nacke, A. Barthel, P. Annus, R. Land, ”Signals in bioimpedance measurement: different waveforms for different tasks,” IFMBE Proceedings 17Proc.13th Int.Conf. on Electrical Bioimpedance (ICEBI 2007), pp. 181-184, Graz, 2007

[9] M. Min, R. Land, T. Paavle, T. Parve, P. Annus, ”Broadband spectroscopy of a dynamic impedance”, Proceedings of ICEBI 2010, Gainesville, Florida, USA, April 2010