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Biopsy Needle Including Bioimpedance Probe with Optimized Sensitivity Distribution

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Abstract. Biopsies are important for diagnosis and prognosis. However, the challenge is to hit the target and obtain representative tissue sample from heterogeneous organs. Bioimpedance can be utilized in needle guidance since many abnormalities change the electrical properties of tissue. Because the biopsy instrument gathers tissue even 1-3 cm forward from the needle tip during sample intake it is important that the measurement is performed in front of the needle, and tissues next to or behind the needle tip do not affect the measurement. We created an enhanced Bioimpedance Probe (BIP) Biopsy needle, which measures impedance in real-time from the very tip of the needle. Our eccentric geometry optimizes the spatial resolution providing 98% of measurement sensitivity on the needle facet and in front of it. Based on simulations, the improvement in spatial resolution from the previously published design is over 90 percentage points. Our enhanced BIP Biopsy needle was tested in different tissues *in vivo* and the results are promising.

Keywords: Bioimpedance, Biopsy, Needle Guidance, Sensitivity Distribution, Tissue Sensing Technology

1. Introduction

Accurate diagnosis and determination of the stage of the disease are enabled by tissue samples, biopsies. They are involved in cancer detection, follow-up of treatment, estimation of disease severity and prognosis. For example, prostate biopsies are utilized for confirming suspected prostate cancer, liver biopsies for determining the progression of fibrosis and cirrhosis and renal biopsies are for different kidney diseases and dysfunctions as well as for transplantation follow-up.

Biopsies have extremely important role since treatment decisions often base on them. Extracted tissue sample is small in order to be minimally invasive and as a result, biopsy covers only a small portion of the total volume of the sampled organ. Because of heterogeneity and variation within the organ, the actual target may get missed. In liver tissue, for example, lesions of hepatitis are unevenly distributed which may lead to sampling error and misdiagnosis [Ratziu et al., 2005]. Standard prostate biopsy procedure includes several biopsies taken systematically from different sites of the organ, but is still insufficient. In fact, risk in prostate cancer for false negative detection is high: In study of Sonn et al., 2013, 38% of Gleason score higher than 7 was not detected with systematic biopsy.

Electrical properties of tissues differ from each other enabling tissue discrimination by bioimpedance spectroscopy. When placing measurement electrode inside the injection needle, bioimpedance can be utilized in needle guidance [Kalvøy et al., 2009]. The first bioimpedance probe needles were thick, but Kari et al., 2015, adapted the bioimpedance measurement in bipolar fashion to standard commercial hypodermic needle and used it with real time classifier for tissue identification.

In addition to different tissue types, cancerous and benign tissues could be differentiated: For example, malign tumors in breast, lung, prostate and kidney have shown to cause significant changes to the electrical properties of tissue [Kimura et al., 1994, Morimoto et al., 1993, Jossinet 1998, Halter et al., 2009a, Halter et al., 2009b, Inagaki et al., 2004]. Therefore the bioimpedance based targeted biopsy is expected to enable more accurate tissue sampling.

Biopsy needle is based on the same idea of bioimpedance sensing injection needle, but it enables the tissue sample intake. A core type biopsy instrument consists of two nested needles, the outer and the inner needle with biopsy cavity for picking a tissue sample. The biopsy needle is in loaded state when set to the target site and then fired forward for sample intake. For example, in prostate cancer the biopsy sample covers a volume 1.5 cm from the needle tip [Patel and Jones 2007].

Mishra et al., 2012, published the real time bioimpedance measuring biopsy instrument. It measured the impedance between the inner needle tip and outer needle tip. Albeit providing insight on the needle location, the electrode configuration generates the sensitivity distribution around the needle, backwards from the needle tip. Because the biopsy instrument fires the needle forward, the actual biopsy is taken much further than where the main portion of the measured impedance originates. Here we introduce an enhanced geometry of a real time bioimpedance probe (BIP) Biopsy needle which measures the impedance from the very tip of the biopsy needle. It enables to take sample from the same volume that is measured with the loaded biopsy needle.

2. Material and Methods

2.1. Bioimpedance probe biopsy needle

The developed bioimpedance probe (BIP) Biopsy needle is 14G core type biopsy needle. It consists of two nested stainless steel needles as the conventional biopsy needle, but the inner needle is a tube, filled with polymer material and stainless steel electrode wire. Polymer insulates the electrode wire from the cannula.

The electrode wire is placed eccentrically to the other edge of the needle cannula (see Fig. 1). As a result the electrode can continue from the needle handle straight to the tip of the needle by lying under the biopsy cavity. By these means, the measurement sensitivity is brought to the very tip of the needle.

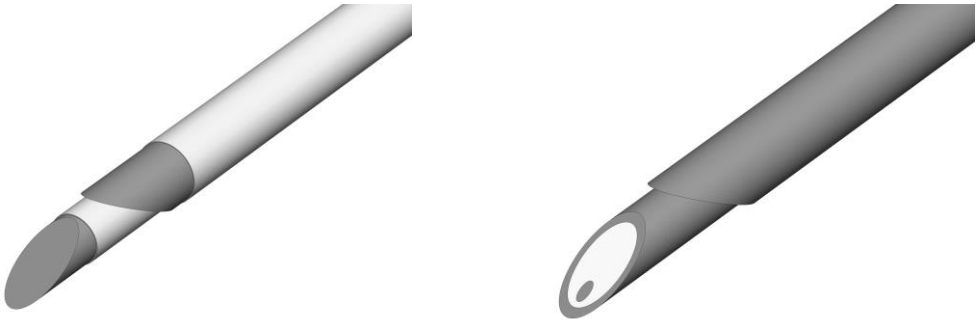

Figure 1. *Bioimpedance sensing biopsy needle geometries: Stainless steel is in grey and insulator in white. The Geometry A on the left, corresponds the solution of Mishra et al., 2012, in which the impedance is measured between the inner needle tip and outer needle tip. The Geometry B on the right, is from our new enhanced BIP Biopsy needle in which the measurement is performed from the very tip of the foremost needle. The biopsy cavity in both solutions is in the inner needle covered with the outer needle.*

BIP Biopsy needle measures bioimpedance spectra in bipolar fashion and the measurement principle is similar as described by Kari et al., 2015. The biopsy instrument is connected to measurement device which is IEC 60601 compatible bioimpedance analyzer developed by Injeq Ltd. The device provides the impedance and phase angle spectra in real-time from multiple measurement frequencies between 1 kHz and 349 kHz. Sampling frequency of the device is 200 Hz.

2.2. Simulation of sensitivity distribution

Sensitivity distribution of two biopsy needles with different geometries A and B are simulated using 3D finite element method. Both needles are simulated in a size of 18G. The other needle, Geometry A, corresponds the solution of Mishra et al., 2012 and measures bioimpedance between the tip of inner needle and the tip of outer needle. The other needle, Geometry B, represents our solution in which the measurement is performed from the tip of the foremost needle. Both of the geometries are shown in Fig. 1.

Both needles are simulated in 50 mm x 50 mm x 50 mm homogeneous medium so that the needle tip is in the middle of the medium. The boundary conditions are such that charge is not allowed to accumulate to the medium nor pass the boundaries of medium.

The measured impedance is defined as

$$Z = \int_V \frac{1}{\sigma} S dV , \tag{1}$$

in which σ is conductivity and *S* sensitivity distribution in the volume *V*. Using reciprocity theorem, sensitivity can be calculated as a vector dot product

$$S = \vec{J}_{reci} \cdot \vec{J}_{current} . \tag{2}$$

In the Eq. 2 $\vec{J}_{reci}$ and $\vec{J}_{current}$ are the current density vectors. Since in bipolar configuration same electrodes act for current feeding and for measurement, the Eq. 2 reduces to

$$S = \left| \vec{J}_{current} \right|^2 . \tag{3}$$

For analysis, sensitivity distribution is normalized to the maximal sensitivity in order to obtain comparable graphs of sensitivity distributions of two biopsy needles.

Since the biopsy is taken in front of the needle tip, we calculated the ratio between measurement sensitivity arising from a cylindrical volume in front of the needle tip to the total sensitivity. The cross section of the cylinder is the same as the one of the inner needle. The cylinder starts from the facet of the inner needle and ends to the length where the front end of the biopsy cavity reaches when fired. Thus, the cylinder represents the volume where the biopsy is expected to be sampled. The total voltage between the feeding and receiving electrodes corresponds to the total measurement sensitivity. The ratio of sensitivity in cylinder to the total sensitivity describes how well the measurement represents the biopsy that will be taken and how much medium next to the needle tip affect the measurement.

2.3. Animal study

The BIP Biopsy needle was tested *in vivo* with anesthetized piglet. Muscle, adipose, liver and kidney tissue were measured with multiple punctures. During the puncture, data was collected from moving BIP Biopsy needle which was loaded. Thus, it represents the authentic biopsy procedure. The study was authorized by ethical committee (ESAVI-6377) and controlled by experienced veterinarian.

The punctures were performed in visual control in order to ensure that the correct tissue type was reached. The tissue sample was taken only after the data collection in order to prevent unnecessary tissue damage. One puncture last about 5 s – 10 s and the total amount of data from muscle and liver tissue resulted in 1 min and from adipose and kidney about in 30 s. The mean and standard deviation was calculated over the time containing all different punctures.

Due to electrode polarization phenomena and measurement error the absolute impedance and phase angle results are not relevant and are comparable only with the results measured with the same measurement set up. More important than the actual values are, however, the differences between tissues. That provides an insight whether the tissue discrimination is possible to perform by using our BIP Biopsy needle and the utilized measurement device.

3. Results and discussion

3.1. Sensitivity distribution

The sensitivity distribution with Geometry A is spherical and located around the needle (Fig. 2). It measures in front of the needle tip, but also next to it and behind the foremost tip. With Geometry B, representing our solution, the distribution is focused on the needle facet to smaller volume than with the other solution (Fig. 2). In practice, it does not measure anything next to the needle or behind it.

Advantage of Geometry A is that it is more robust and it can provide more steady signal. If the whole volume is homogeneous, it provides representative results. However, heterogeneities next to the

needle tip affect the measurement result and the device is not so sensitive to small targets. Even if needle would detect the target, the desired sample may get missed since the measurement is performed from much larger volume than the tissue sample is taken.

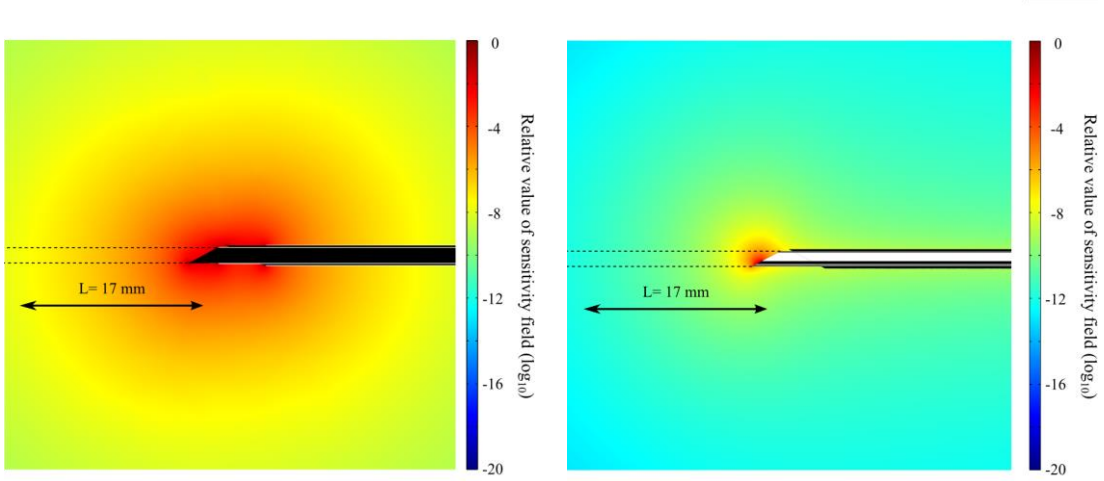

Figure 2. *Cross section of the 3D simulated sensitivity distribution for Geometry A on the left and for Geometry B on the right. Dashed lines in front of the needle show the cylindrical volume where the biopsy will be gathered (end of the cylinder out of the figure)*

Biopsy needle fires the needle parts about 2 cm in front of the loaded needle. Thus, the biopsy is taken only in front of the needle tip. The measurement result behind or next to the needle tip is irrelevant.

In our solution, 98.3 % of the total measurement sensitivity is from the volume in front of the needle tip. With Geometry A, the corresponding value is only 4.85 %. According to the simulation results, only the new geometry, Geometry B, enables spatially accurate measurement that represents better the same volume as the tissue sample will be taken.

3.2. Spectra of *in vivo* tissues

Impedance and phase angle spectra of *in vivo* tissues are shown in Fig. 3. In addition to tissue properties, the measured values are dependent on the measurement setup. Boundary conditions and noise affect them. The deviation of the absolute results from the true impedance can be safely ignored, as long as the errors are mostly systematic, i.e. measurement results are well repeatable and the results differ substantially for different tissue types.

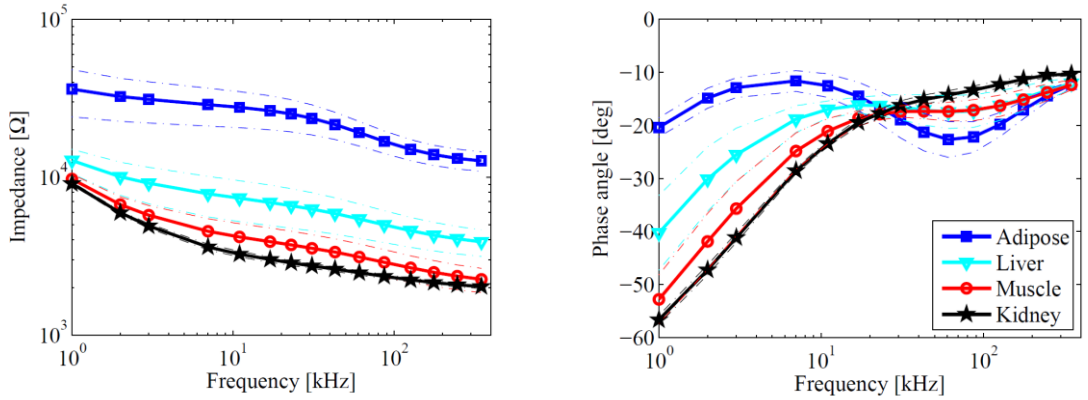

Figure 3. *Mean impedance and phase angle spectra of in vivo tissues. Standard deviation shown in dashed lines.*

Adipose tissue is less conductive than the other tissues, as expected. Kidney is the most conductive material and it has the smallest standard deviation. In phase angle spectra, different tissues show different kind of frequency behaviour. Kidney tissue has the strongest frequency dependence and its phase angle changes from -60° to -10° when measurement frequency increases from 1 kHz to 349 kHz.

Phase angle values overlap each other in frequencies 10 kHz – 50 kHz and 200 kHz – 349 kHz, but in other frequencies, the values are at least one standard deviation away from the others. Over all, the tissues differentiate from each other when using multiple measurement frequencies and the information of impedance and phase angle spectra.

Since the spectra of different tissues differ from each other, it is possible to create classifier for tissue discrimination. Similar mathematical classifier could be used as in Injeq's BIP Needles [Kari et al., 2015]. Results are promising, and the study should be continued with deeper analysis about differences between benign and cancerous tissues, damaged or healthy tissue in specified medical application. If their electrical properties differ significantly as expected, our developed BIP Biopsy could provide tool for targeting the tissue sample more accurately than is possible without the measurement.

4. Conclusions

Representative biopsy is important for diagnosis but challenging to achieve without targeting methods. Bioimpedance can be utilized for identification of the location of the needle tip. Previous design measured impedance around the biopsy needle. With that design heterogeneities next to the needle affect the measurement result and therefore there is a risk of missing the target. We created bioimpedance probe (BIP) Biopsy instrument that improves the spatial resolution and measures the impedance only on the very tip of the needle.

According to the simulation results with the previous geometry, only 5 % of the measurement sensitivity distribution was in front of the needle tip. With our enhanced geometry, 98 % of the total sensitivity lies in front of the needle facet.

Animal studies with our BIP Biopsy needle provided promising results: Adipose, muscle, liver and kidney tissues had different kinds of frequency spectra. According to the preliminary results, the developed BIP Biopsy instrument has potential to be developed for biopsy targeting tool. Further study will be performed with cancerous tissues for specific applications.

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