A Multi-pair Electrode Based Impedance Sensing Biopsy Needle for Tissue Discrimination during Biopsy Process

Jaeho Park, Sanghyeok Kim and Inkyu Park

***Abstract*— We demonstrate the biopsy needle integrated with multi-pair electrode based impedance sensing device for biological tissue discrimination. The impedance sensing biopsy needle has several pairs of electrodes which enable the selective tissue analysis during biopsy process. In order to verify the usefulness of the device, we demonstrate the conductance measurement of various saline solutions and the real-time conductance monitoring of soft elastomeric materials during the needle insertion. Finally, the tissue discrimination of porcine meat tissues during the needle insertion was successfully carried out.**

I. Introduction

The electrical properties of biological tissues are determined by the types of cells and the physiological structure of tissues.[1-7] In particular, the plasma membrane in the cell plays a major role to determine the electronic properties because it prevents the ion transport between intracellular and extracellular media, playing a critical role as an electrical capacitor. For these reasons, biological tissues have different responses depending on the AC frequencies and we can discriminate the type of tissues according to their responses.[1] Many researches related to this approach have been done and correlation between diseases and their respective electrical impedance responses have been investigated.[2-7] Especially, cancerous tissues have distinct electrical characteristics as compared to the normal tissues. Therefore, the electrical characteristics of tissues have emerged as critical indicators and alternative diagnostic tools for the cancer.[2-7]

Based on this fact, many medical devices for the diagnosis of cancerous tissues by utilizing their electrical properties have been developed.[7-9] One of them is the biopsy needle which can measure the electrical impedance of tissues in real time to overcome the inaccuracy of conventional transrectal ultrasound guided biopsy. [8] However, this was not capable of selective measurement of small locations within tissue because they used whole inner needle and outer sheath as the electrode rather than the locally patterned electrodes for measuring the electrical impedance of biological tissues.

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In this paper, we demonstrate disposable biopsy needle integrated with electrical impedance sensing elements for the impedance measurement of tissue selectively with the several pairs of microelectrodes. The microelectrodes were patterned on the stainless steel needle with small radius ($\rho < 1$ mm) by screen printing followed by electroplating with gold layer for enhanced biocompatibility. Also, the needle and electrodes were electrically insulated with a heat shrinkable polyethyleneterephthalate (PET) tube. To verify the feasibility of the fabricated sensor for real-time tissue measurement, the impedances of the saline solutions and the polydimethylsiloxane (PDMS) - conductive rubber composite were measured. Finally, we verified that the developed device can discriminate tissues during needle insertion by using the porcine meat containing both muscle and adipose tissues, which are known to have different electrical impedance ranges.

II. Fabrication of Impedance Sensing Needle and Measurement System

A. Needle Preparation

Fig. 1(a) shows the fabrication process of the impedance sensing needle. The stainless steel needle (SUS304) with ρ=0.75 mm was used. Before electrode patterning, the needle was insulated with a heat shrinkable PET tube to prevent the electrical current between the needle and electrodes. Then, a pair of silver (Ag) electrodes (width=100 μm, length= 10 cm, gap=200 μm) were patterned on the surface of needle by

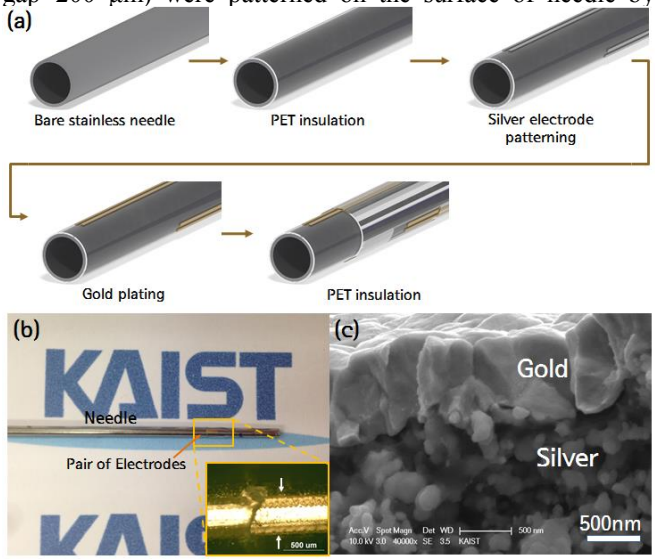

Figure 1. (a) Schematic diagram of fabrication process and (b) photograph of the impedance sensing needle; (c) The cross-sectional image of the gold-plated electrode.

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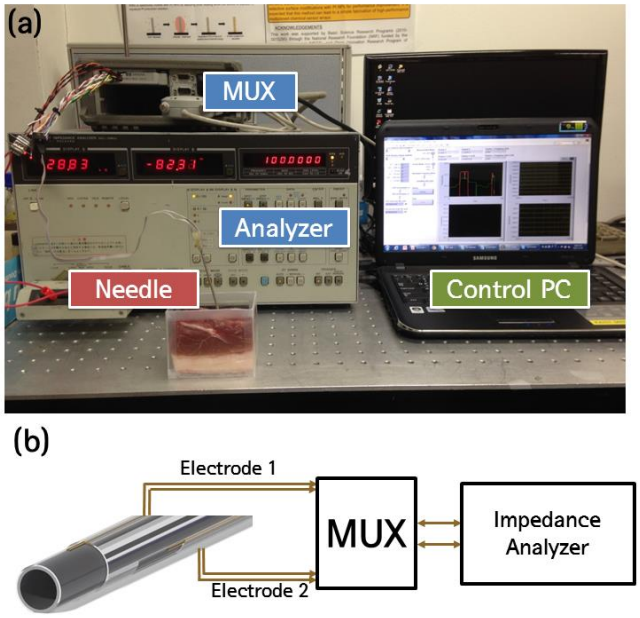

Figure 2. (a) System setup and (b) schematic for the multi-electrode impedance measurement by needle

screen printing of silver paste. Here, we used microscale line patterns in order to acquire local electrical impedance of tissues around electrodes and fabrication of multi-pairs of electrode patterns on the single needle. After patterning one pair of electrodes, another pair of electrodes with a length of 1cm shorter than the first pair was printed on the opposite side of the needle for longitudinal mapping of electrical impedance. The needle with printed electrode patterns was sintered in a convection oven at 120°C for 20 min. After the sintering, the electrodes were electroplated with gold (Au) for biocompatibility and the needle was insulated with PET layer again to passivate areas other than the sensing locations. Fig. 1(b) shows the photograph image of fabricated impedance sensing needle.

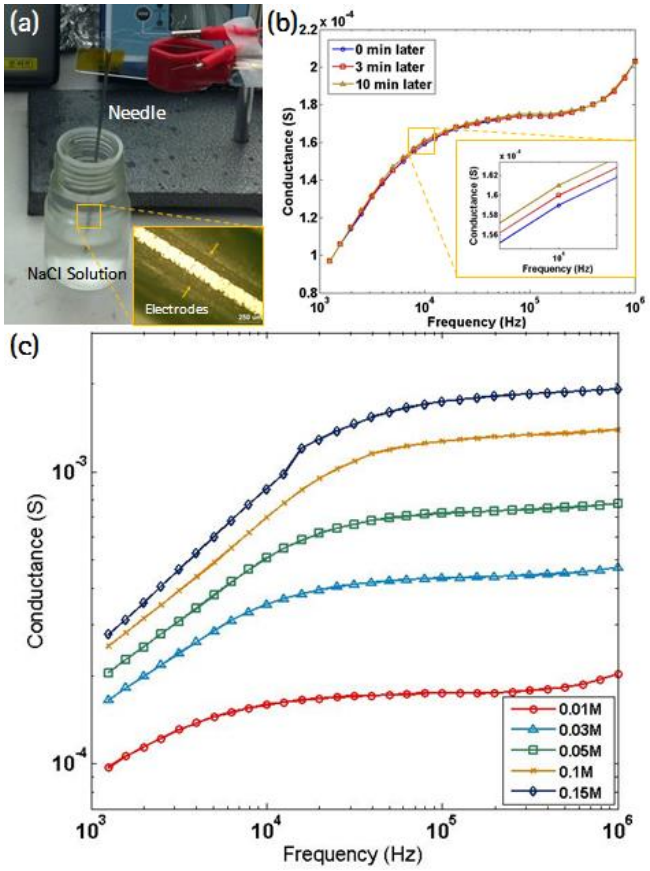

Figure 3. (a) System setup for saline solution measurement, (b) repeatedly measured conductance of 0.01M NaCl solution and (c) measured conductance data of 0.01M, 0.03M, 0.05M, 0.1M, 0.15M NaCl solution.

The hazard of Ag has been reported that the Ag has the cytotoxicity and genotoxicity for human cells.[10] Therefore, Ag electrodes cannot be directly used for the insertion into biopsy process of biological tissues. Instead, the Ag electrodes were electroplated with gold (Au) layer. In order to achieve a uniform layer of Au, the needle with Ag electrodes was immersed in the Au electroplating solution and the electroplating was carried out at a current density of 1mA/cm^2 for 1000 seconds. Fig. 1(c) shows the cross-sectional image of the electrode after the electroplating process. A smooth, uniform and dense gold layer was deposited onto the top surface of porous and rough Ag electrode.

B. Measurement System Configuration

Fig. 2 shows the system for the real-time measurement of electrical impedance from multiple pairs of electrodes. The electrical impedance at the electrodes was measured by the impedance analyzer (Agilent 4192A) with sinusoidal signals of multiple frequencies from 5 Hz to 13 MHz. A multiplexer (Agilent 34904A) was added between the needle and the impedance analyzer for the multiplexed measurement. When the measurement was completed at one pair of electrodes, the circuit was switched to other pair of electrodes by the multiplexer. This sequence was carried out every 0.5 second, which enabled real-time measurement at multiple locations along the axis of the needle.

III. Experiments and Results

A. Conductance Measurements of Saline Solutions

In order to verify the feasibility of the impedance sensing biopsy needle, the conductance of various saline solutions was measured. Fig. 3 shows the setup for measurement and measured conductance of saline solutions between the frequencies of 1 kHz and 1 MHz. Only one pair of electrodes was used for the measurement and the NaCl concentrations of saline solutions were varied as 0.01 M, 0.03 M, 0.05 M, 0.1 M and 0.15 M. Also, the conductance of NaCl solution of 0.01 M was repeatedly measured with intervals of 3 and 10 minutes, respectively, to verify the repeatability of the sensing biopsy needle. As shown in Fig. 3(b), the conductance of the sample solution was hardly changed during repetitive measurement cycles. The average difference between the initial conductance and the conductance after 10 minutes was only 0.64 %. Furthermore, the higher the concentration of NaCl was, the higher the conductance of saline solution was measured. Generally, if the ionic concentration of solution

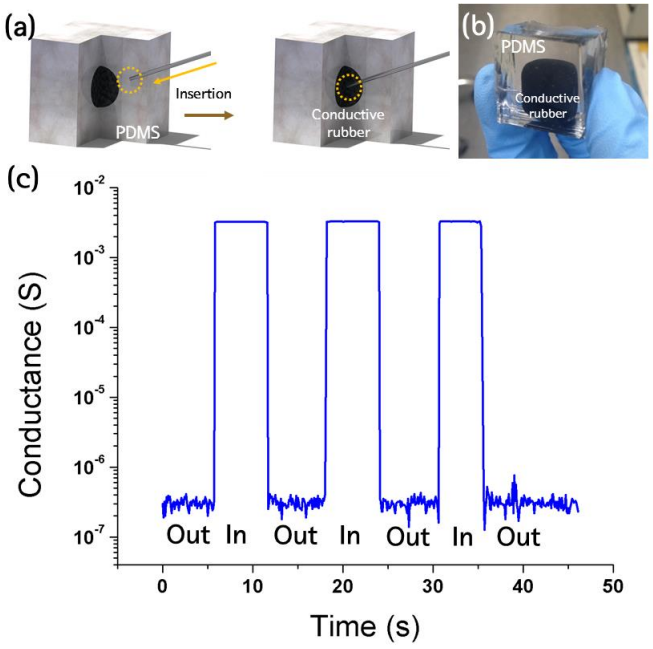

Figure 4. (a) Schematic image of the dynamic needle insertion experiment, (b) image of PDMS-conductive rubber composite and (c) results of measured conductance during the needle insertion.

becomes higher, the number of current carrier becomes larger. Therefore, we could verify that measured conductance shows proper trends and the impedance sensing with the needle operated properly.

B. *Real-time Response to Dynamic Needle Insertion*

In order to investigate whether the tissues near the biopsy needle are cancerous or normal tissues during the biopsy, the impedance sensor on the needle should be capable of in-situ impedance measurement during the needle insertion process. To verify this, we demonstrated dynamic needle insertion test in which the conductance change is detected in real-time during the needle insertion. As shown in Fig. 4(a-b), a phantom for the test was made by using PDMS and conductive rubber. Fig. 4(c) shows the measured conductance graph for repeated insertion and pull-out with an interval of 5 seconds. When the needle tip was situated within PDMS, the measured conductance was very low ~3.74 X 10^{-7} S. However, as the needle tip penetrated into the conductive rubber, the conductance was immediately increased to ~ 3.25 x 10^{-3} S immediately. From this result, we could confirm that the impedance sensing needle can capture the impedance change rapidly and thus can be utilized for the real-time tissue measurement.

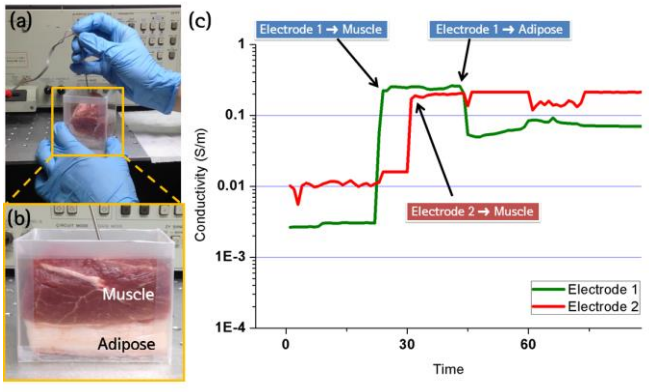

Figure 5. (a) Photograph image of real-time measurement and tissue discrimination of porcine meat and (b) sample of porcine meat which had both the muscle and adipose tissue. (c) measured conductivity data during the needle insertion; Electrode pair 1 is the pair of electrodes near the tip of needle and Electrode pair 2 is 1cm shorter one than electrode 1.

C. *Real-time Tissue Discrimination during Needle Insertion*

Using the fabricated impedance sensing biopsy needle, we demonstrated the real-time tissue discrimination of porcine meat during the needle insertion process. Two pairs of electrodes were used for the measurement so we could simultaneously measure the tissue impedance not only at the tip of needle but also at 1 cm behind the tip. Fig. 5(a) and (b) shows the experiment result with the porcine meat. The used porcine meat contained both muscle and adipose tissues whose layers were clearly distinguishable in their electrical impedance values. The conductance data from the impedance analyzer were automatically converted into the conductivity data by using the pre-calculated cell constant of electrode. The reference conductivities of tissues could be found from previous work by C. Gabriel et al.[11], in which the conductivities of muscle and adipose tissues range from 10^{-1} to 10^{0} S/m and from 10^{-3} to 10^{-1} S/m, respectively, at the frequency of 1 kHz.

Fig. 5(c) is the graph of measured conductivities at the frequency of 1kHz during the needle insertion process. First, when the needle penetrated into the surface of meat, the conductivity at the electrode pair 1 was instantly increased to 0.25 S/m, which was compatible with those of muscle tissues from the reference. With the further insertion, the conductivity at the electrode pair 2 was measured around 0.2 S/m. After further insertion, the measured conductivity from the electrode pair 1 was suddenly dropped to 0.05 S/m, which was in the range of adipose tissues from the reference. On the other hand, the conductivity from the electrode pair 2 still remained unchanged since it was still in the muscle tissue. From this result, we can confirm that the impedance sensing needle could not only measure the impedance of tissues selectively in real time but also discriminate different regions by simultaneous measurement at multiple spots along the length of needle.

IV. Conclusion

In this paper, we demonstrated the novel biopsy needle integrated with impedance sensing electrode array for the real-time measurement of tissue properties. With the impedance sensing needle with multiple pairs of printed microelectrodes, we could achieve local measurement of the electrical impedance of tissues. Furthermore, we could discriminate between muscle and adipose tissues by using the conductivity data. Based on the significant difference in the impedance between cancerous and normal tissues, the impedance sensing needle can be potentially used as an assistive tool to conventional imaging techniques during the biopsy process.

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