

A NOVEL FLEXIBLE MICROSENSOR FOR REAL-TIME QUANTIFICATION OF BRAIN EDEMA

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ABSTRACT

A novel flexible brain edema sensor (i.e. sensing for fluid content in brain), that can monitor the evolution of brain edema on a real-time and continuous basis by using thermal conductivity technology, has been designed, fabricated and fully characterized in this work. *In vivo* test shows the measured fluid water contents by the developed edema sensor are well correlated with standard tissue wet-dry method.

KEYWORDS: Brain edema, edema microsensor, thermal conductivity, fluid content in brain

INTRODUCTION

Brain edema is a common clinical problem in which there is excessive accumulation of fluid in the intracellular and/or extracellular compartment of the brain. It is associated with higher mortality and morbidity in many common disease states such as traumatic brain injury (TBI), stroke, and brain tumors [1]. At present, the only available tool for assessing brain edema is neuroimaging with computed tomography (CT) or magnetic resonance imaging (MRI), which is intermittent snapshots and very limited in assessing the real-time effects of any treatment [2,3]. There is currently no technique for continuously monitoring the brain for the development of edema.

In this work, we have developed a novel microsensor that can overcome these limitations and monitor brain edema on a real-time and continuous basis. Based on the fact that the water content in brain tissue is well correlated with the tissue's thermal conductivity, we have developed and characterized the brain edema sensor by measuring the thermal conductivity of the brain tissue.

DEVICE DESIGN

The design and sensing principle of brain edema sensor is shown in Figure 1. As shown in the figure, edema sensor is composed of heating and sensing parts. The two parts are kept at a distance of 100 μm . The central heating part is heated up to a temperature of 2 $^{\circ}\text{C}$ higher than the surrounding tissue. Heat will transfer from heating to the sensing part by thermal conduction and increase the temperature of sensing part, and in turn induce sensing part's resistance change. By monitoring the change of resistance of the sensing part with time, thermal conductivity can be measured, and brain edema can then be deduced with the correlation between thermal conductivity and brain edema.

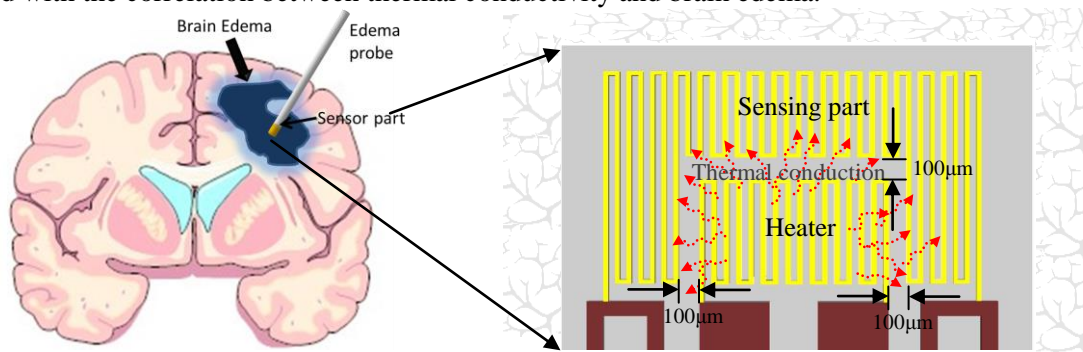


Figure 1: Mechanism of the brain edema sensor: Heat part was kept at a temperature 2 $^{\circ}\text{C}$ higher than surrounding brain tissue, thermal conductivity of the tissue was measured by monitoring the resistance change of sensing part with time.

EXPERIMENTAL

To fabricate the flexible edema sensor, similar to our previous work [4], PI2611 (HD Microsystem) was used as substrate and spun on a silicon wafer. Ti/Gold layer with the thickness of 12 nm/120 nm was evaporated on the substrate and formed the heating and sensing pattern. 1 μm copper was electroplated on gold lead to decrease the resistance thus the effect of lead. Another PI2611 layer was then formed on top as passivation. To further avoid any moisture diffusion from environment, silicon nitride of 100 nm was sputtered as passivation layer. After fabrication, the film was peeled off from silicon wafer and spiral-rolled to form edema probe. Figure 2(a) is the summary of fabrication steps and 2(b) shows the fabricated device.

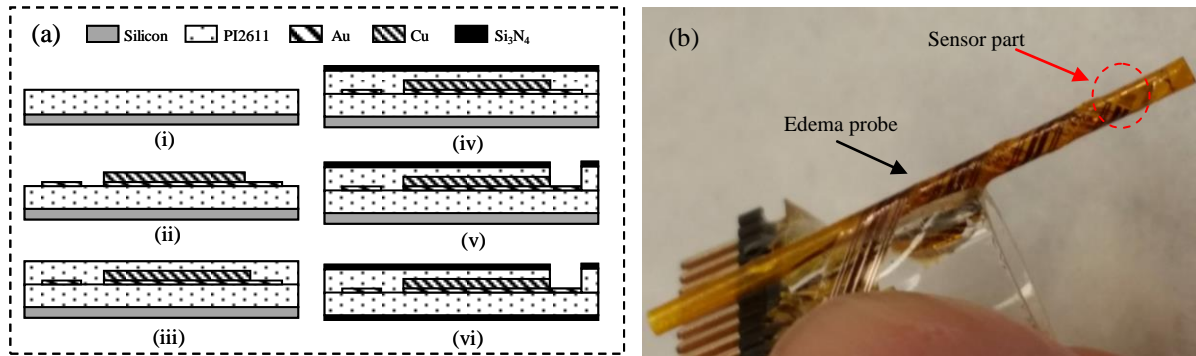


Figure 2: Picture of the fabricated edema probe: (a) Fabrication summary and (b) Fabricated device.

RESULTS AND DISCUSSION

The calibration test of sensing part resistance change with different thermal conductivity was carried out and the result is shown in Figure 3. As shown in the figure, the resistance change increases with thermal conductivity K .

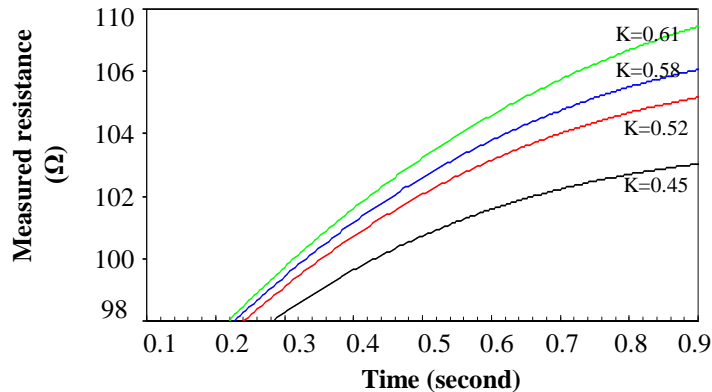


Figure 3: Calibration curve of thermal conductivity versus measured resistance. The slope based on the measured resistance was linearly related to the medium thermal conductivity K

In vitro experiments were performed in agar-glycerol-water mixtures with different water contents (89.78 %, 84.79 %, 79.80 %, 74.81 % and 69.83 %) to create a correlation equation between measured thermal conductivity and water content. As shown in Figure 4, measured thermal conductivity from agar-glycerol-water mixtures with different water contents was well correlated with actual water content (i.e., $R^2 = 0.982$) with standard deviation less than 0.063 % for different mixtures. Controlled cortical impact (CCI) method was used to produce traumatic brain injury in the rat. The probe was further tested *in vivo* in a rat as shown in Figure 5 (a). Brain water content was measured with the wet-dry method to validate the measured data from brain edema microsensor. As shown in Figure 5(b), the measured water contents were well correlated with the water content by tissue wet-dry method.

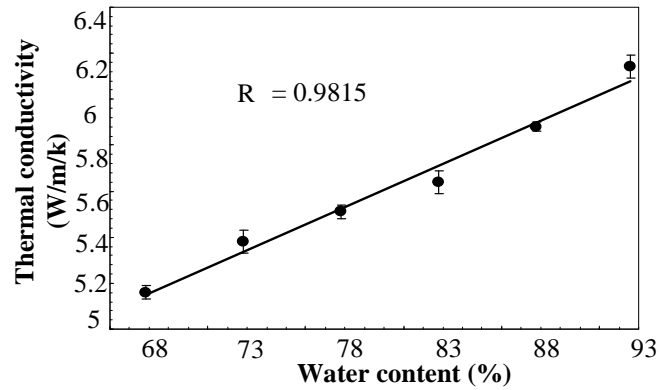


Figure 4: *In vitro* comparison of actual water content and measured thermal conductivity in agar-glycerol-water mixtures. Water content in the agar-water-glycerol mixture was well correlated with measured thermal conductivity.

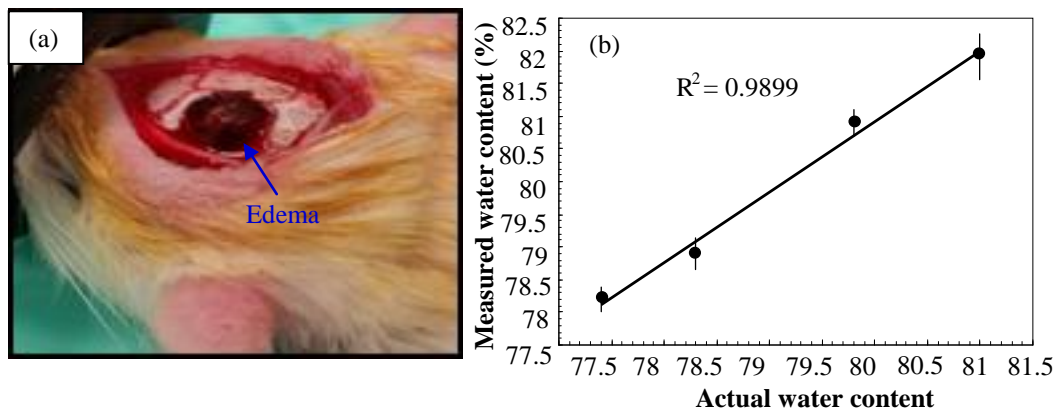


Figure 5: (a) Brain Edema induce in a rat and (b) Measured water content showed good correlation with actual water content measured by wet-dry method.

CONCLUSION

In this work, a flexible brain edema sensor has been fully developed for monitor the evolution of brain edema on a real-time and continuous basis, by measuring thermal conductivity and establish correlation between thermal conductivity and brain edema. *In vivo* test shows the measured water contents by the developed edema sensor are well correlated with standard tissue wet-dry method. The developed edema sensor will be very useful for monitoring traumatic brain injury (TBI), stroke, and brain tumors.

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