혈전분해 응용을 위한 압전형 마이크로 외팔보의 제작 및 실험

백건훈[1], 서영태[1], 방용승[1], 김종만[1], 김성현[2], 김용권[1]
[1]서울대학교 전기 컴퓨터 공학부
[2]분당서울대학교병원 진단방사선과

Fabrication and Experiment of Piezoelectric Micro Cantilever Applicable to Thrombolysis

Kun Hoon Baek[1], Young-Tai Seo[1], Yong-Seung Bang[1], Jong-Man Kim[1], Sung Hyun Kim[2], Yong-Kweon Kim[1]
[1]School of Electrical Engineering and Computer Science, Seoul National University
[2]Diagnostic Radiology, Seoul National University Bundang Hospital

Abstract - This paper describes a resonant driving piezoelectric micro cantilever practicable to ultrasound thrombolysis device for the treatment of ischemic stroke. The proposed piezoelectric cantilever was designed to be a unimorph structure of $Si/SiO_2/Ti/Pt/PZT/Pt$, and fabricated by top-down sequence etching process. The red blood cell (RBC) lysis experiment was carried out to confirm the usability of the proposed cantilever. Total 87.76 % of RBCs were ruptured using the ultrasound generated by up-down actuations of the fabricated cantilever with AC voltage having the frequency of 19.36 kHz and the magnitude of 30 V_{p-p}.

1. Introduction

Ischemic stroke is a kind of brain injury, which is occurred as a blood supply toward the human brain is blocked. In this case, the supply of oxygen and nutrients to the brain is also interrupted resulting in a rapid death of brain tissues. Cerebral thrombosis that produces some blood clots (thrombi) blocking the cerebral vessels is one of the major causes of ischemic stroke. Until now, the medication has been regarded as the most popular treatment method for removing the blood clots in the cerebral vessels, but it has several serious problems such as a long treatment time, hemorrhage risks and complex indication [1]. Another treatment is to deliver directly the clot-disrupting device into the blocked cerebral vessels using catheters. Mechanical thrombolytic device can remove clots rapidly compared to the medication method, and this timesaving merit can dramatically decrease brain damage. Therefore, a number of researches about endovascular mechanical thrombolysis including corkscrew, laser energy, suction-creating saline jets, and so forth has been performed. However, it is still limited to apply them to the cerebral stroke treatments due to vessel-damaging problem [2]. Ultrasound thrombolysis that uses acoustic cavitation, microstreaming, intracellular microcurrents, and so on is prospective treatment, which can reduce direct damage of cerebral vessel [3]. Nevertheless, there are still some challenges in terms of energy efficiency and device size.

Micromachined piezoelectric cantilever is one of the most broadly used transducers in many areas due to their small size, simple structure, and low actuation voltage. Piezoelectric materials convert the electric energy to the mechanical energy by the change of material property without any additional equipments (e.g. permanent magnet for electromagnetic actuator). In addition, resonant driving actuator has several advantage such as the efficient ultrasound energy transduction derived from maximum deflection.

In this paper, ultrasound thrombolysis device using the micromachined piezoelectric cantilever having the resonant driving mechanism for ischemic stroke is designed and fabricated, and the usability of the proposed cantilever was confirmed by the lysis of the RBCs.

2. Design

Fig. 1 shows a schematic view of the proposed piezoelectric micro cantilever for endovascular thrombolysis.

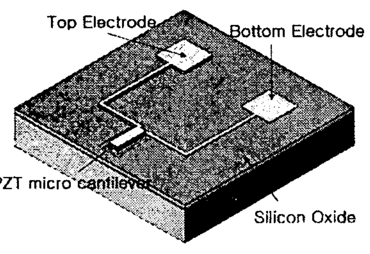


Fig. 1. Schematic view of the piezoelectric micro cantilever

The cantilever was designed to be a unimorph structure with $PbZrTiO_3$ (PZT) active layer and single crystalline silicon unactive layer, respectively. The thickness of the silicon part was determined to be 10 μm. It is relatively thick compared to the PZT layer because the actuator should overcome the fluidic resistance as working in liquids. The piezoelectric cantilever is actuated when the deformation of piezoelectric material is occurred by the electric field. It vibrates maximally by AC voltage which has a same frequency as the resonant frequency of the cantilever, and emits ultrasound for thrombolysis. The resonant frequency of the proposed cantilever was designed to be 40 kHz since the ultrasound at lower frequencies in the range of 20 - 40 kHz is known to show the great effect on thrombolysis [4].

The resonant frequency of multi-layered cantilever f_r is defined as

$$f_n = \frac{(\kappa_n l)^2}{2\pi l^2}\left(\frac{\int_h E(z-z_0)^2 dz}{\sum_{i=1}^{N}(h_i \rho_i)}\right)^{1/2} \tag{1}$$

where E, h, and ρ are Young's modulus, density and height of each layer, respectively. $\kappa_n l$ is the modal parameter of the cantilever vibration, and the value is 1.8571. z_0 is the position of the neutral axis, which is calculated by equation (2). The integrated tensile stress over the cross section of the cantilever must be zero at z_0 point [4].

$$\int_h E(z-z_0)dz = 0 \tag{2}$$

Transverse mode is dominant to the vibration of piezoelectric cantilever, because the polling and deformation directions are perpendicular to each other. The length disparity between piezoelectric material and silicon plate makes the cantilever vibrates up and down. Physical characteristics of the cantilever satisfies the followed equation for transverse mode:

$$\left(\frac{l}{h}\right)^2 \text{and} \left(\frac{l}{w}\right)^2 \geq 10 \tag{3}$$

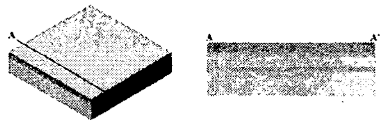
From equation (1), (2) and (3), dimensions of the designed cantilever with the resonant frequency of 40 kHz in the air were determined as described in Table 1.

Table 1. Cantilever design parameter (f_r = 40 kHz)

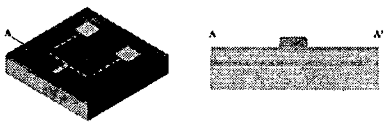
	Si	Oxide	Pt (bottom)	PZT	Pt (top)
Height	9.5 μm	0.5 μm	0.2 μm	2 μm	0.25 μm
Length	535 μm				
Width	90 μm				

3. Fabrication

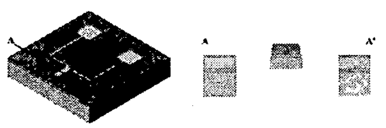
Fabrication process of the proposed piezoelectric micro cantilever is shown in Fig. 2. The first step is an oxidation (5000 Å) of silicon on insulator (SOI) wafer which has 1 μm-thick buried oxide (BOX) layer, and 10 μm-thick device layer. After the oxidation, Ti adhesion layer (300 Å) and Pt bottom electrode (2500 Å) were deposited using DC and RF sputtering process, respectively. Then, PZT sol-gel solution was spun on the Pt bottom electrode to sandwich 2 μm-thick PZT film between top and bottom electrodes. After the formation of PZT film, top Pt electrode (2000 Å) was deposited using RF sputtering process (Fig. 2. (a)). The top and bottom Pt electrode and PZT intermediate layer were then patterned by top-down sequence etching method using inductively coupled plasma reactive ion etching (ICP RIE) process (Fig. 2. (b)). After the etching processes, the oxide and device layers were etched one by one for the definition of cantilever shape. Finally, the cantilever was released using deep RIE process through the backside etching of handle and BOX layers. (Fig. 2. (c)).



(a) Thin film deposition SiO_2/Ti/Pt/PZT/Pt on SOI wafer



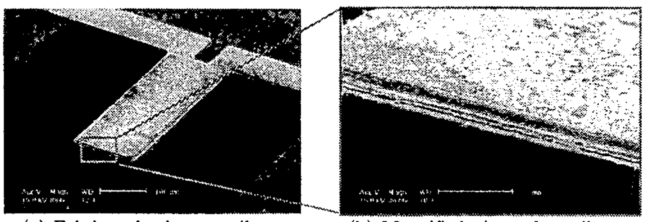
(b) Patterning electrodes and PZT



(c) Cantilever definition and release

Fig. 2. Fabrication process

Fig. 3 is SEM images of the fabricated piezoelectric micro cantilever. The cantilever was fabricated with little structural deformations with aids of robust silicon plate underneath the PZT layer. The magnified view of the cantilever shows the PZT intermediate layer and electrodes deposited on the silicon unactive layer in sequence. (Fig. 3 (b)).



(a) Fabricated micro cantilever (b) Magnified view of cantilever

Fig. 3. Fabrication results

4. Measurement and Discussion

4.1 Resonant frequency of cantilever

We measured the resonant frequency of the fabricated cantilever using dynamic measurement system (DMS) based on the Doppler effect. The measured resonant frequency is 36.19 kHz in the air, which shows little error compared to design value of 40 kHz. This error includes material error due to its physical properties and fabrication error induced from the processes. In this case, the calculated quality factor was 338.2. Otherwise, because of the viscous damping caused in the course of nature, the resonant frequency and quality factor were changed to 19.36 kHz and 13.5, respectively in the water as shown in Fig. 4.

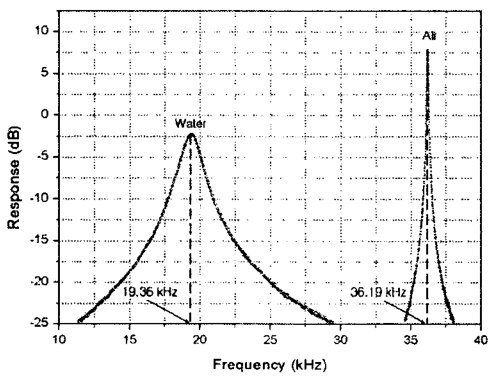


Fig. 4. The Measured resonant frequency of cantilever

Table 2. Resonant frequency of the micro cantilever

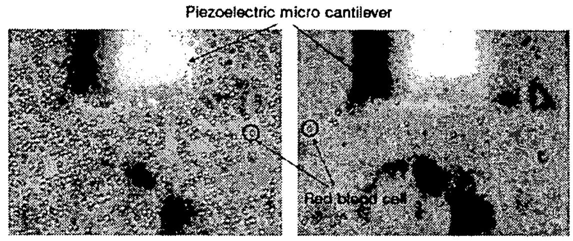
	Design	Measurement	
		Air	Water
Resonant frequency (error)	40 kHz	36.19 kHz (9.53 %)	19.36 kHz (51.6 %)

4.2 Cell lysis experiment

In vitro cell lysis experiment was performed inside the chamber to make similar to *in vivo* circumstance. The cavity under the cantilever was utilized as a chamber by attaching polydimethylsiloxane (PDMS) block to underneath the device.

We dropped 5 % diluted blood on the cantilever and applied the AC voltage with frequency of 19.36 kHz and magnitude of 30 V_{p-p} to the piezoelectric micro cantilever during 8 minutes. Here, we assumed that 5 % diluted blood has similar damping property to water.

Fig. 5 shows the initial state of the RBCs, and the ruptured RBCs by ultrasound after 8 minutes. Quite a number of RBCs were disappeared after ultrasound cell lysis experiment compared to the initial state.



(a) Before lysis (b) After lysis

Fig. 5. The Lysis experiments of RBCs using the fabricated cantilever

Fig. 6 shows the remained number of the RBCs according to the increment of the lysis time. The number of RBCs are barely changed until 6 minutes, however begins to decrease drastically after 6 minutes. The ruptured RBCs were 395 (54.33 %) and 638 (87.76 %) after 7 and 8 minutes, respectively. Most RBCs were ruptured in a few minutes, and this clearly shows that the proposed piezoelectric cantilever has a possibility to be applied to the cerebral thrombolysis.

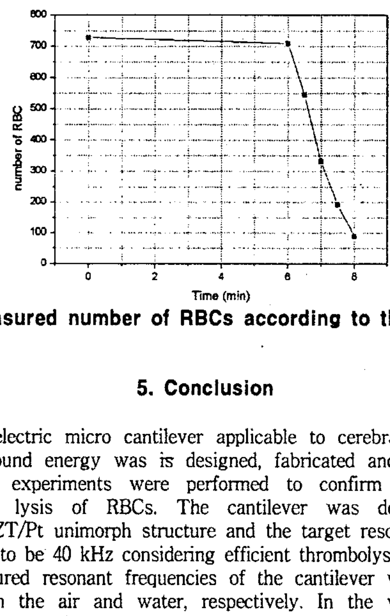


Fig. 6. Measured number of RBCs according to the lysis time changes

5. Conclusion

The piezoelectric micro cantilever applicable to cerebral thrombolysis using ultrasound energy was is designed, fabricated and characterized. Fundamental experiments were performed to confirm the feasibility through the lysis of RBCs. The cantilever was designed to be SiO_2/Ti/Pt/PZT/Pt unimorph structure and the target resonant frequency was decided to be 40 kHz considering efficient thrombolysis.

The measured resonant frequencies of the cantilever were 36.19 and 19.36 kHz in the air and water, respectively. In the water, resonant frequency and quality factor were decreased to 53.5 % and 4 %, respectively compared to the case of the air.

Lysis experiment of RBCs was performed using ultrasound induced from the resonant driving of the proposed cantilever. The result showed that 86.76 % of RBCs were effectively dissolved within 8 minutes.

From this result, the proposed piezoelectric micro cantilever shows a possibility to be applied to the cerebral thrombolysis.

References

[1] D. Brown, et al., "Survey of emergency physicians about recombinant tissue plasminogen activator for acute ischemic stroke," *Annals of emergency medicine*, vol. 46, no. 1, pp. 56-60, 2005.

[2] H. L. Lutsep, "Mechanical thrombolysis in acute stroke," *eMedicine*, 2006.

[3] S. Atar, et al., "Perspectives on the role of ultrasonic devices in thrombolysis," *J. Thrombosis and Thrombolysis*, vol. 17, pp. 107-114, 2004.

[4] C. W. Francis, "Ultrasound-enhanced thrombolysis," *Echocardiogrhphy*, vol. 18, no. 3, 2001.

[5]] R. Sandberg, et al., "Temperature and pressure dependence of resonance in multi-layer micro cantilever," *J. Micromech. Microeng.*, vol. 15, pp. 1454-1458, 2005..