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FUNDAMENTAL STUDY ON A NOVEL METHOD FOR DISSOLUTION OF CEREBRAL THROMBUS BY MICRO PIEZO-STIRRER

Zhongwei JIANG*, Zihe LIU,* Shoichi KATO, Michiyasu SUZUKI****

** Department of Mechanical Engineering, Yamaguchi University*
2-16-1,Tokiwadai,Ube 755-8611, JAPAN
e-mail:jiang@yamaguchi-u.ac.jp; liuzihe@yamaguchi-u.ac.jp
*** Department of Neurosurgery, School of Medicine, Yamaguchi University*
1-1-1,Minamikogushii,Ube 755-8505, JAPAN
e-mail: kato-ygc@umin.ac.jp; michi@yamaguchi-u.ac.jp

ABSTRACT

A cerebral thrombus or blood clot might cause cerebral stroke and even decease if the clot could not be dissolved within several hours after it was formed. This paper presents a fundamental study on development of a new type of mechanical micro stirrer for assisting the dissolution of the thrombus with a few amount of thrombolytic agent. The micro stirrer is made of a slight beam embedded with a piezocell. An efficient excitation method for stirring up the thrombus to get a quick dissolution is investigated. Furthermore, to evaluate the dissolution state in vivo, an ideal using the piezo-stirrer as both the stimulator to beat the clot and the probe to evaluate its solubility is proposed. The potential of the piezo-stirrer has been validated experimentally.

1. INTRODUCTION

The mortality or the complication rate due to the cerebral thrombus would be very high if the cerebral blood vessel is not recanalized in time. The complication rate could become lower, if the clot is taken away in the early stage or within the therapeutic time window at which the ischemic organ is still reversible. In the present clinical treatment, the thrombus within in the vessel is dissolved by infusion of the thrombolytic agent directly into the artery. The direct infusion needs a large amount of the agent to dissolve the clot, so it has a high risk of intracerebral hemorrhage, or some kinds of adverse reactions. There are some attempts on this problem, such as using transcranial doppler stimulator[1] to assist the dissolution effect, and using a ultrasonic catheter device to deliver the drugs to the affected area and to stimulate the clot for a quick recanalization[2]. This method is considered efficient to use a few drugs but how to deal with the ultrasonic energy for fast dissolution needs advanced investigation.

In consideration as mentioned above, this paper is concerned with the study on development of a mechanical micro stirrer that can be used in the catheter to assist the clot dissolution speed with a few agents. The proposed stirrer is made of a slight beam embedded with a piezocell. An excitation method for the stirrer, how to beat the clot to get an efficient dissolution of the clot with a few thrombolytic agents, is investigated. Furthermore, evaluation of the solubility of the blood clot in vivo is an unsolved problem, an ideal using the same stirrer to beat the clot and to measure its solubility is proposed. Its possibility is validated experimentally.

2. MICRO STIRRER & EXPERIMENTAL SETUP

Figure 1 shows the schematic of a hand-made stirrer, which is made in a size suitable for fundamental test in the laboratory. The base beam is aluminum cut in size of 60x5x0.5mm and a piezocell of 6x2x0.3mm is bonded on it. The beam is drove in the following way. Input signals, such as sine wave and pulse wave, are formed by a function generator(Yokogawa FG120) and then added to the piezocell through a power amplifier(NF4010). The displacement of the beam is measured by Laser Doppler Velocity Sensor(Sony VL10).

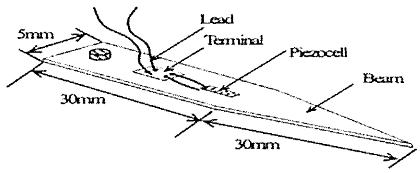

Fig.1. Schematic of piezo-stirrer.

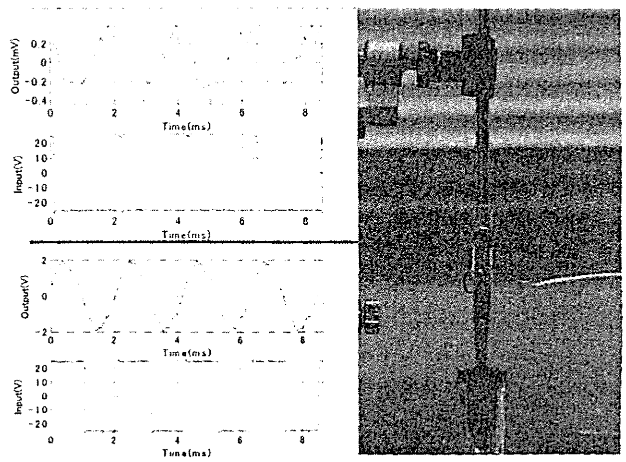

Fig.2. Input pulse with duty ratio of 5% and 50% at 4.7kHz and tip displacement(left), and piezo-stirrer setup(right).

Table 1 Displacement and performance of piezo-stirrer

Frequency (kHz)	Duty ratio (%)	Displacement (μm)	Stirring Performance
0.93	5.0	2.980	×
	10.0	**5.480**	O
	50.0	**16.300**	O
4.7	5.0	0.812	×
	10.0	1.250	×
	50.0	**3.920**	O
43.04	10.0	0.334	×
	50.0	1.210	×
52.38	→	0.432	×

The frequency characteristics of the stirrer were first measured by the laser displacement implement, and the maximum tip displacements at the resonant frequencies are selected and listed up in Table 1. The stirrer gives the largest motion about 16μm in amplitude at 930Hz. Also the duty ratio of 50% has larger displacement than the other duty ratio. To validate the stirring performance, the beam tip is inserted into a small vessel which is filled with liquid(Fig.2), and then one adjusts the input waveform or parameters, for pulse input the period and the duty ratio, and eyes the turbulence on the liquid. The observed results for pulse input at several frequencies are described in Table 1, where mark '**O**' means the case that the turbulence has been observed and mark '×' means the whirlpool can not be eyed. In the experiment, several types of input waveforms, such as sine and triangle waveforms were also tested but the pulse input is found the most efficient. Some sample results of the pulse inputs at 4.7kHz with duty ratio of 5% and 50%, associated with the displacement obtained from the Laser Doppler Sensor, are plotted in Fig.2. It was evident that the turbulence on the liquid that can be easily eyed is in the case that the tip displacement of the stirrer is larger than 3μm, and the whirlpool can be also observed carefully at very small stirring motion if a suitable duty ratio and frequency of the input pulse is applied.

3. THROMBUS SOLUBILITY MEASUREMENT

As mentioned above, the thrombus solubility might be estimated according to the stirring performance observed by eyes in the laboratory. It is firmly difficult to evaluate the dissolution effect in vivo when a catheter type stirrer is used. Also no efficient method has been established in present literature to measure or evaluate the thrombus solubility in vivo. In this section, an ideal for measuring and evaluating the in vivo solubility is proposed and the validation is made by fundamental experiments.

It is well known that the piezoelectric material has both actuator function and sensor function. It comes an ideal that use the same stirrer in the vessel for beating the blood clot and evaluating its dissolution state. In common sense, as the clot is dissolving the counteraction to the motion of the stirrer goes weakly, which leads a change in

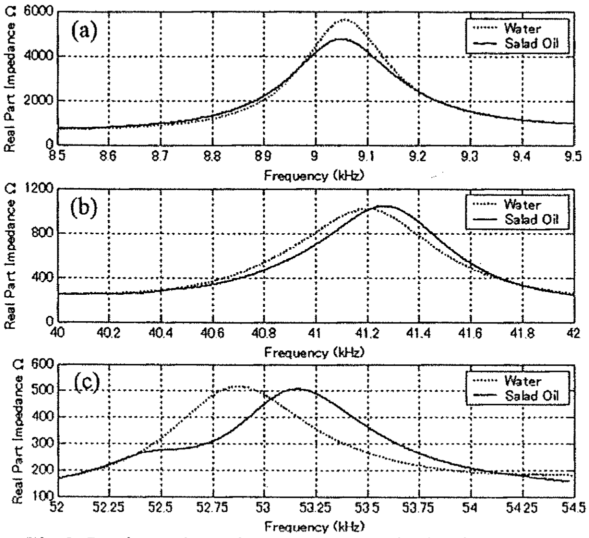

Fig.3. Real part impedance response obtained at ranges (a) 8.5-9.5kHz, (b) 40-42kHz, (c) 52-54.5kHz.

the stirrer mechanical impedance. So the problem to be solved comes to that how to measure the mechanical impedance change easily and precisely. The piezoelectric impedance based technique is therefore introduced for this study and its potential is validated experimentally.

In the fundamental test, the stirrer is inserted in the vessels filled with water and salad oil and so on, the piezocell is connected to an impedance analyzer(HP 4192), so that a sweep sine voltage generated by the analyzer is added to piezocell. The piezoelectric impedance change due to different kinds of liquid is measured and transmitted to a computer for data processing. Figure 3 shows the real part responses of the impedance measured at three seleted frequency ranges [(a)8.5-9.5, (b)40-42, (c)52-54.5] kHz. It is found that the waveform variations on water and salad oil is obvious and the difference of the peak frequencies are about (a) 7Hz, (b) 73Hz and (c) 283Hz respectively. This means the impedance measurement is an efficient way to estimate the dissolution state in vivo and the accuracy will be depend on the selected frequency range.

4. CONCLUSIONS

A novel method using a mechanical excitation to dissolve the cerebral thrombus is proposed and the fundamental experiments shows that the piezo-stirrer has high potential to be used both for dissolving the blood clot and for evaluating the thrombus solubility in vivo.

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