MECHANICAL INTERACTION BETWEEN SINGLE-SHAFT SILICON MICROELECTRODES AND RAT DURA MATER

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ABSTRACT

Due to the rapid development in micro- and nanofabrication technologies, several types of medical implants have been proposed and applied successfully in neurosurgery. In order to determine the safety margins and design rules of newly emerged realization techniques, in vivo mechanical characterisation is essential to be performed. In this work, experimental investigation is presented focusing on the interaction between rat brain tissue and single-shaft silicon microprobes fabricated by deep reactive ion etching. Physical parameters like penetration force and dimpling were studied in terms of insertion speed (mm/min range) and microprobe cross-section. Insertions were performed through intact dura and pia mater.

KEYWORDS: silicon microelectrodes; tissue penetration; insertion mechanics; dura mater

INTRODUCTION

During medical implantations, microprobes are exposed to great loads as puncturing dura mater. On the other hand, the possible removal of dura is not preferred, since regeneration or local infectious reactions may cause inserted probes to fail. Eventually it is essential to design probes geometries and shapes, which can withstand the mechanical impact and can provide precise drug delivery and/or electrophysiological recording simultaneously. Nevertheless, compromise is necessary to be made due to the dominant implantation phenomenon, dimpling. Dimpling in neurosurgery is generally defined as the distance covered by the microprobe's tip from touching the surface of dura mater until complete puncture happens (maximal force applies). Dimpling can be considered as a significant issue because of traumatic brain injury (TBI) resulting in irreversible tissue damages and poor detection of neuronal activity during electrophysiological measurements [Rennaker, 2005].

Conditions of the surgery, e.g. tissue quality, are also of key importance, since reliable and realistic data are more likely to be recorded during in vivo experiments. During in situ and ex vivo implantation significantly lower force values can be experienced compared to in vivo conditions, providing false impression about the insertion behaviour of microprobes [Gefen, 2004]. Experiments have also proved that removal of dura and pia mater reduces tissue resistance [Sharp, 2009]. Due to the above detailed physiological reasons, these layers are left intact during our measurements.

Our aim was to test long silicon probes in vivo through intact dura mater in order to reveal relationships between insertion parameters and the structural and geometrical design. Effect of insertion speed (in the range of 1-10 mm/min), cross section of the probe and geometry of the robe tip on the penetration parameters (force and dimpling) will be discussed.

EXPERIMENTAL

Seven 3-4 months old Sprague Dawley rats were used for in vivo mechanical experiments. All procedures were conducted according to the Animal Care Regulations of the Institute of Cognitive Neuroscience and Psychology, Research Centre for Natural Sciences, Hungarian Academy of Sciences. A mixture of 37.5 mg/ml ketamine and 5mg/ml xylazine at 0.2 ml/100 g body weight injection volume was applied as initial anesthesia via intraperitoneal injection. Animals were mounted in a stereotaxic frame and a 4 mm diameter craniotomy was performed in order to have access to cortex. Dural surface was cleaned by sterile saline and was left intact, and it served as reference point for calculating the penetration depth, which was 3mm throughout all the experiments. We used Bregma for the determination of the anterioposterior and mediolateral locations of the implantations. Implantation sites were chosen such that ventricles were avoided along the implantation tracks.

The fabrication of silicon microelectrode dummies is detailed in [Fekete, 2013]. Microprobes were fixed in a custom-designed holder, which was attached to an Andilog Centor Easy type force gauge (measuring limit: 10N, resolution: 1mN). Finally this setup was mounted on a stereotaxic frame. The vertical position of the probes was adjusted by a Gamma type stepper motor (1.8° step angle). The measurement setup for in vivo insertion is shown in Fig. 1. Stepping units of the motor was 10μm, while stepping precision was 1μm. Data acquisition was performed by a Labview controlled measurement system through a NI digital I/O card by a sampling rate synchronised to the actual stepping frequency of the linear motor. Insertions were performed at constant speed. Penetration speeds were determined as 1.2, 3, 5.25, 7.5 and 10.5 mm/min.

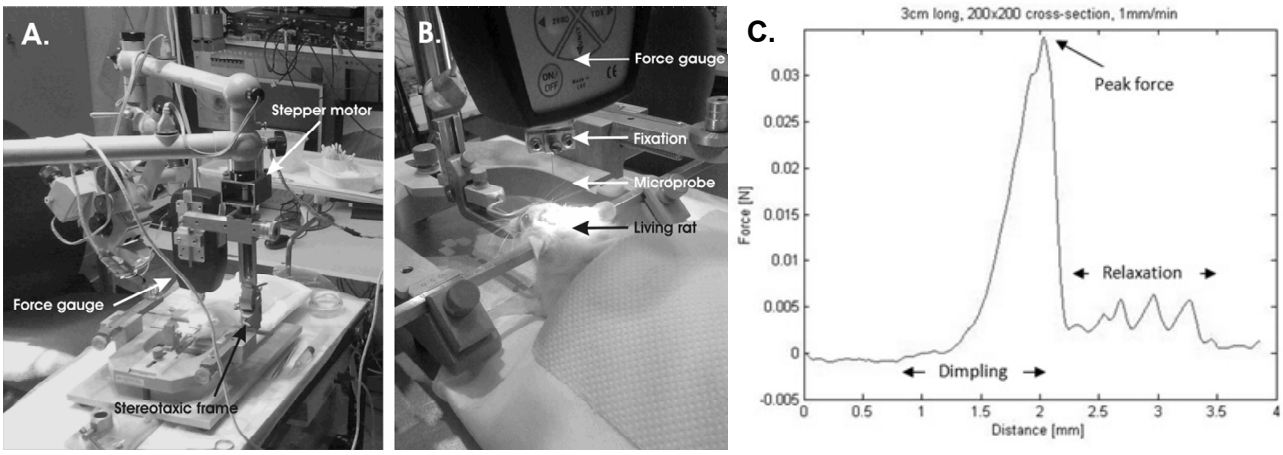

Figure 1: Experimental setup for in vivo testing of penetration mechanics(a. & b.) and a representative force-distance curve (c.)

RESULTS AND DISCUSSION

Penetration force was analysed in the case of several probe cross-sections and at several insertion speeds (see Fig. 2). We concluded that increase in the insertion speed induces a gradual increase in forces acting on the probe tip. Doubling the insertion speed in the analyzed regime, an increase of 10-35% in penetration forces was measured. Speed vs force data suggest that robust probes are more sensitive to the change of insertion speed; however, curve-fitting requires more in vivo experiments to be carried out. On the other hand, a much faster insertion may provide less tissue resistance and easier penetration [Bjornsson, 2006], although in the case of actuation by a linear stepper motor in the analyzed regime this statement still does not apply.

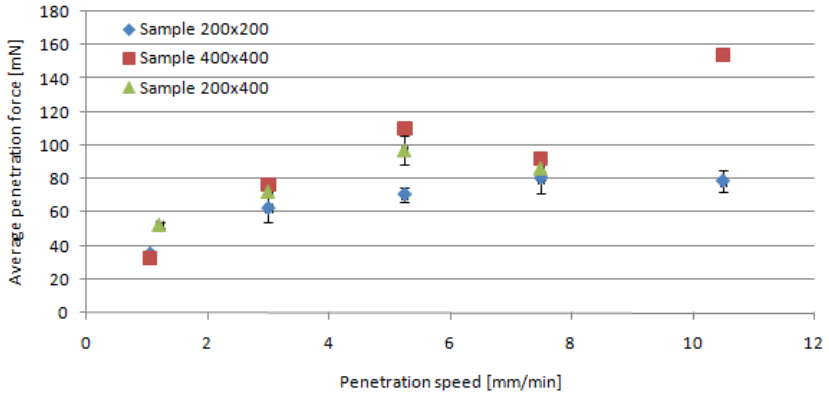

Figure 2: Average value of penetration force plotted against penetration speed

Dimpling was also determined using the measured force-depth curves and was plotted against insertion speed. Data are presented by Fig. 3. Characteristic dependance of dimpling on speed was not observed in the analyzed regime.

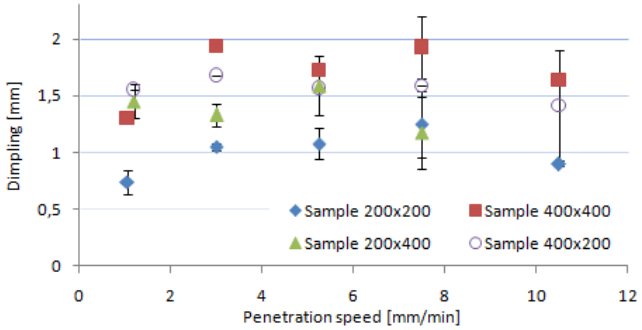

Figure 3: Dimpling of microprobes plotted against insertion speed

The effect of changing the insertion speed followed a trend similar to previously reported results where insertions took place with retracted dura layers. [Welkenhuysen, 2011; Sharp, 2009]. When decreasing the cross-section of the microprobes by a factor of four, penetration forces and dimpling values were reduced by as much as 30-50% at constant insertion speed (see Fig. 2-3).

Since dimpling was not apparently sensitive to insertion speed, statistics in the case of individual probe geometries was derived and compared (see Fig. 4). It is clearly shown that increase in interfacial area of the microprobes has a disadvantageous effect on the expectable tissue resistance.

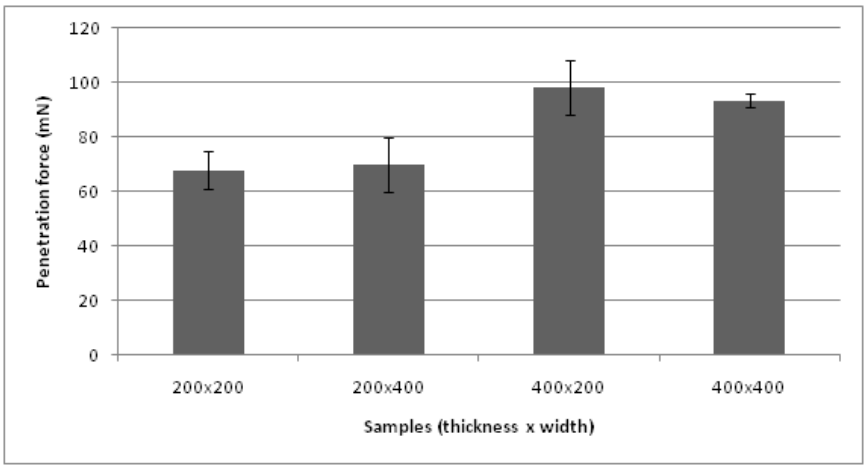

Figure 4: Mean value of dimpling plotted against insertion speed -

CONCLUSION

In this work, the mechanical interaction of rat brain tissue and long silicon microprobes fabricated by deep reactive ion etching was characterised during in vivo insertion tests assisted by a linear stepper motor. Penetration force and dimpling were measured through intact dura mater and evaluated in the case of probe samples featured by various cross-sections. In the investigated speed regime, the increase in insertion speed between 1-10mm/min induced a monoton increase in the average penetration force. By doubling the insertion speed in the analyzed regime, an increase of 10-35% in penetration forces was measured. When decreasing the cross-section of the microprobes by a factor of four, penetration forces and dimpling values are reduced by as much as 30-50% at constant insertion speed. Comparing penetration forces to fracture forces we found that decreasing the interfacial area of probes contributes to a moderately decreasing trend in the values of penetration force, however, fracture forces are reduced more drastically by decreasing the cross-sections.

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REFERENCES

[1] Rennaker, R.L., Street, S., Ruyle, A.M., Sloan, A.M., 2005. A comparison of chronic multi-channel cortical implantation techniques: manual versus mechanical insertion. J. of Neurosci. Meth. 142, 169–176.

[2] Gefen, A., Margulies, S. S., 2004. Are in vivo and in situ brain tissues mechanically similar? J. of Biomechanics 37, 1339–1352.

[3] Sharp, A. A., Ortega, A. M., Restrepo, D., Curran-Everett, D., Gall, K., 2009. In Vivo Penetration Mechanics and Mechanical Properties of Mouse Brain Tissue at Micrometer Scales. Trans. on Biomed. Eng. 56, 45-53.

[4] Fekete, Z., Hajnal, Z., Márton, G., Fürjes, P., Pongrácz, A., 2012. Fracture analysis of silicon microprobes designed for deep-brain stimulation, Microelectronic Engineering 103 (2013) 160-166.

[5] Bjornsson, C. S., Oh, S. J., Al-Kofahi et al., 2006. Effects of insertion conditions on tissue strain and vascular damage during neuroprosthetic device insertion. J. of Neural Eng. 3, 196-207.

[6] Welkenhuysen, M., Andrei, A. A., Ameye, L., Eberle W. and Nuttin B., 2011. Effect of Insertion Speed on Tissue Response and insertion mechanics of a chronically implanted silicon-based neural probe. IEEE Tr. on Biomed. Eng. 58, 3250-3259.

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