MICROINSTRUMENT FOR TRANSDERMAL, WOUNDPOTENTIAL MEASUREMENTS

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1. ABSTRACT

In vivo animal studies have shown that electrical fields radiate laterally from skin wound sites [1]. In addition, in vitro testing of keratinocytes (the first cellular response to wound healing) has shown cathodally-directed migration in physiological DC electrical fields (100-200 mV/mm) [2]. Results from human wound studies are less forthcoming due to mechanical fragility inherent with standard drawn glass electrode probes. An MEMS alternative was therefore pursued as a reliable, repeatable, wound potential measuring device.

This paper presents the design, fabrication and preliminary testing of an individually addressable, micro-needle array for the measurement of endemic electric fields in wounded tissue. Recording sites are defined by photolithographically patterning thin film Pt electrodes onto a glass substrate, which end in an array of electrical contacts [5]. Aligned anodic bonding of silicon to glass and subsequent dicing with a diamond embedded saw blade create silicon columns attached as an array to both the glass substrate, and the thin film electrodes. The outcome is an array of silicon micro-needles bonded to an electrically insulating glass substrate with Pt electrodes addressing individual needles. Wet chemical etching (HNA) [3,4] sharpens the columns into needles that are sharp enough to pierce skin yet robust enough to withstand multiple penetrations with minimal tip damage (Figure 1). Using a 38.7mV sinusoidal input, an input/output separation distance of 6 inches and a 1 M Ω resistor in parallel, an output signal of 18-20mV was measured by the micro-needle array.

2. METHODS

2.1 Silicon substrate

The needles were fabricated in 4 inch diameter, (100) oriented, p+, silicon wafers. Aluminum was used as a dry etch mask and was deposited onto the polished silicon surface using a CHA Industries electron beam evaporator. Standard photolithography and aluminum etching opened patterns for silicon etching by Reactive Ion Etching (RIE). The patterned aluminum wafer was subsequently etched in a Technics Micro-RIE using sulfur hexafluoride (SF₆) and oxygen (15 and 1.4 sccm, respectively) at 400 watts to a final depth of 18.5 μ m. An orthogonal set of trenches, 150 μ m deep, on 300 μ m centers, was made into the etched surface with a wafer dicing saw (MicroAutomation I006), creating an array of silicon pillars. The aluminum was then removed using a wet etchant (PAN) followed

by a BOE dip to remove any silicon dioxide from the silicon chip surface.

Figure 1. Wound Potential Device

2.2 Glass substrate

Pyrex 7740 glass wafer was used as a platform for the electrodes. Normal photolithographic procedures were used to pattern photoresist on the glass surface as a lift-off mask for the thin film electrode array. The wafer was dipped in a 50:1 HF solution prior to being placed in the CHA Electron beam evaporator (E-beam) for tantalum (Ta) and platinum (Pt) deposition (100 $\text{\AA}$ and 500 $\text{\AA}$, respectively). The Pt was then patterned by lift-off of the photoresist in organic solvent.

2.3 Anodic Bonding

The silicon and glass wafers were aligned so as to position the Pt electrodes between the glass and silicon and the contact pads directly beneath the appropriate silicon pillars. Once manually aligned, the bonding cathode was brought down onto the glass surface, adding enough pressure to ensure contact throughout the bonding process. Bonding was performed at 425°C, and 1000V for 1 minute.

2.4 Needle fabrication

The silicon top surface of the bonded pair was coated with photoresist and hard baked for > 1 hour. With the glass side down on the dicing saw, cuts were made in the silicon surface, to a depth of about 350 μ m. This resulted in an array of silicon 3D structures

with a 200 μm square base, and 150 μm tall, on top of which sits a 350 μm tall, silicon, rectangular column with a 100 μm square cross-section. The silicon structures were then etched in "HNA" (1:8:1 hydrofluoric: acetic: nitric acids) until the desired needle shape was obtained. The over baked photoresist on the tops of the columns protected the surface long enough to sharpen them (at which point they fall off) and helped produce needles of uniform height. The chip was then rinsed and oven dried. The needles were then punctured through aluminum foil (~100 μm thick) until the tips of the needles were exposed. The assembly was placed in the E-beam (tips towards the source) for deposition of 100 $\text{\AA}$ Ta and 500 $\text{\AA}$ Pt. The foil acted as a shadow mask, protecting all underlying structures from metal deposition. The aluminum foil was removed leaving metal only at the tips of the needles. The entire chip was then coated with 1000 $\text{\AA}$ of PECVD silicon nitride (Technics) and subsequently etched by an RIE using CF_4/O_2 (15 sccm) and 200 W until the silicon nitride was removed from the tips of the needles [6] (Figure 2).

Figure 2. Completed array showing etched silicon micro-needles and electrodes attached to a glass substrate.

3. EXPERIMENTATION AND RESULTS

3.1 Resistance measurements

After the initial bonding and before the second set of dicing cuts were made, contact resistance was measured. A Fluke 8060A Digital Multimeter was used. Three resistance measurements were made: 1) the surface of the silicon --45 Ω 2) the electrical contact pad and the silicon --280 Ω 3) electrical contact pad to another electrical contact pad (using the silicon as the connection between them) --735 Ω .

3.2 In vitro resistance measurements

A saline solution at physiological concentrations was used to test individual addressing and isolation of contacted needles. A stainless steel reference electrode and the tips of the micro-needle array, connected by a Fluke 8060A Digital Multimeter, were placed into the solution and resistance measurements were taken between individual electrodes when their tips were in versus out of the saline solution. Out of solution, the needles were an open circuit (isolation). In the saline, a resistance of 430k Ω was measured.

3.3 In vivo ECG measurements

Using a Medi-Trace 1 S'Offset ECG AgCl as a source electrode, a 38.7 mV sinusoidal signal was introduced into the system. Measurements of the signal were taken by the micro-needle array placed 6 inches from the ECG electrode along the subject's forearm. A 1 M Ω resistor was placed from the micro-needles to ground to decrease the current through the subject's tissue. 18-20mV was measured by a single micro-needle. Using the same arrangement, a sub-dermal DC resistance value of 613k Ω was calculated.

4. SUMMARY

Utilizing MEMS technology, a transdermal micro-needle array, with individually addressable needles, was fabricated and bench tested. It was shown that the device has the mechanical strength to puncture the skin and the electrical conductivity to measure both resistance and potential differences both in vitro and in vivo. These measurements lay the groundwork for further testing, specifically the recording of biopotentials related to wound generation and healing.

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6. REFERENCES

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