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THIN FILM SILICON BIOSENSOR FOR THE DETECTION OF SPINAL CORD INJURY (SCI)

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INTRODUCTION

Globally, an estimated 500 thousand people suffer a trauma induced or disease rooted spinal cord injury (SCI), leading to a higher rate or morality in those injured, and large reaching social and economic impacts [1]. SCIs lead to a decreased quality of life for the patient, as well as extra care and time from family and health care professionals during treatment. It is estimated that the annual strain a SCI causes globally is US$4 billion, with a single SCI patient costing between $1 and $5 million a lifetime depending on the severity of injury and age of the patient at the time of injury [2,3]. Current diagnosis of a SCI is normally done via a doctor's inspection of the injury and the patient's motor and sensory functions. In less apparent cases CT scans, MRI, or x-rays can be done to identify any injuries or complications from the injury [4]. However, a doctor's diagnosis does not accurately describe the severity of the SCI and various imaging techniques are recurring, costly and time-consuming. This defines a need for a simple, cost-effective, and safe test for the diagnosis and characterization of SCI so a patient can get the care they need quickly and effectively. Many studies have shown that the protein S100B can be used as a diagnostic biomarker shortly after an injury is sustained when it comes to SCI [5,6]. Therefore, we proposed a novel, cost-effective, and simple to use thin film silicon microfluidic biosensing device for the diagnosis of SCI. A distinct advantage of thin film biosensor is easy reproducibility and fabrication technique. Moreover, these can be used as a standalone or independent biosensor detecting proteins or could be integrated with other detection systems. Deflection observed due to the collection of the injury protein will be quantified and will be directly proportional to the concentration of the proteins. Therefore, the proposed biosensor would provide an accurate diagnosis as well as characterize the severity of the SCI. Such a device will bridge the innovation gap, improve prognosis and management, and reduce the number of confirmatory tests. Thereby, helping cut the cost of diagnosis.

METHODS

Design of the microfluidic mould was created using CAD software licensed by Autodesk, San Francisco. Using standard lithography process, the microfluidic design was transferred on a glass mask. This mask was used to transfer the print on a silicon wafer. Microfluidic chips were fabricated using soft lithography technique and replica molding from polydimethylsiloxane (PDMS). PDMS was mixed 10:1 with curing agent then poured over silicon negatives to form a microfluidic channel in the top layer of the chip. Our chips are designed with one inlet and one outlet connected to a

central detection chamber (figure 1). Once degassed, the PDMS covered negatives are baked for 10 minutes at 80°C.

Thin Silicon membranes were created for sensing the SCI proteins present in the samples injected into the microfluidic chip. Thin film was fabricated using the same PDMS ratio poured over a glass slide and placed in a spin coated for the desired thickness of the thin membrane.

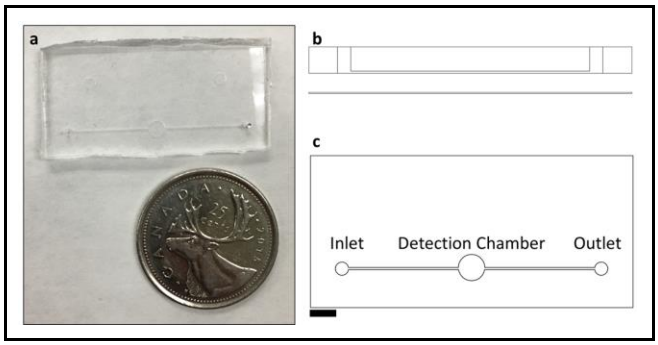

Figure 1: a) Fabricated microfluidic device. b) Exploded side view of device. c) Top view of device with labeled inlets and outlest.

Multiple slides were spin coated at 3 different RPM's (1200, 1800, and 2400) which were then characterized for thickness and roughness using a Profilometer (figure 2). Once spin coated, the slides were placed in the oven in the same manner as the top layers. The top layer and thin membrane were bonded together via plasma treatment for 45 seconds which activates the surface of the PDMS for adhering. Once the surface has bonded together the chip is placed back into the oven for an hour to finish bonding. To create a silicone biosensor, the device was functionalization using a three step process. The first step is Oxygen (O_2) plasma treatment of the microfluidic devices. This created O_2 functionalities on the silicon surface making it hydrophilic. Once completed, the channel is filled with diluted polyethylenimine (PEI) incubated for an hour, and flushed with ethanol. As PEI contains amine groups, creation of the surface which allows binding of detection proteins becomes an easy and one step process. Finally, the channel was filled with glutaraldehyde (GA), incubated for another hour, and then flushed again with deionized water and ethanol. This helps in the formation of imine group in the chip. 10ug/ml of S100B antibodies were then introduced into the channel.

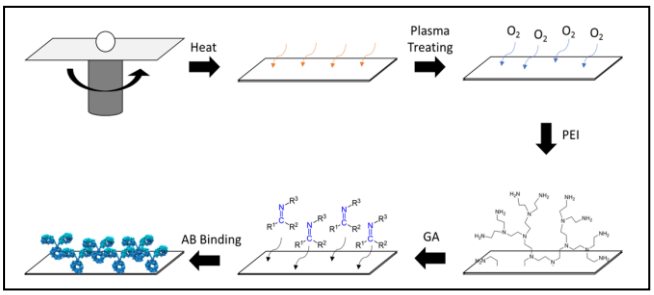

Figure 2: Process of fabrication and functionalization of thin membrane. Spin coated formed PDMS thin membrane undergoing functionalization steps via oxygen plasma treating, PEI, and GA, then binding of antibodies.

RESULTS

As these thin silicon film will acts as biosensor based on it deflection, sensitivity of the system relies on the thickness of the film. Thin films created were characterized for the minimum acceptable thickness and roughness using the Profilometer. It was found the different RPMs for spin coating created distinctly uniform and repeatable thickness (figure 3).

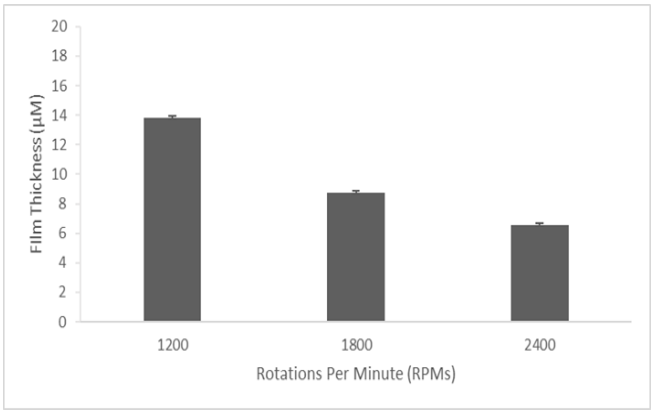

Figure 3: Comparison of thin membrane thicknesses and rotations fabricated by spin coating PDMS for 10 minutes.

Additionally, we found the surface roughness to be minimal in the samples, with

the smallest roughness in the 1200 RPM samples. The largest differences in the profile of the membrane was at the end of the PDMS layer on the glass slide and where the clean glass slide begin due to the surface tension of the PDMS (figure 4). RPMs above 2400 generated thin films which were difficult to transfer, bond and test in the microfluidic device.

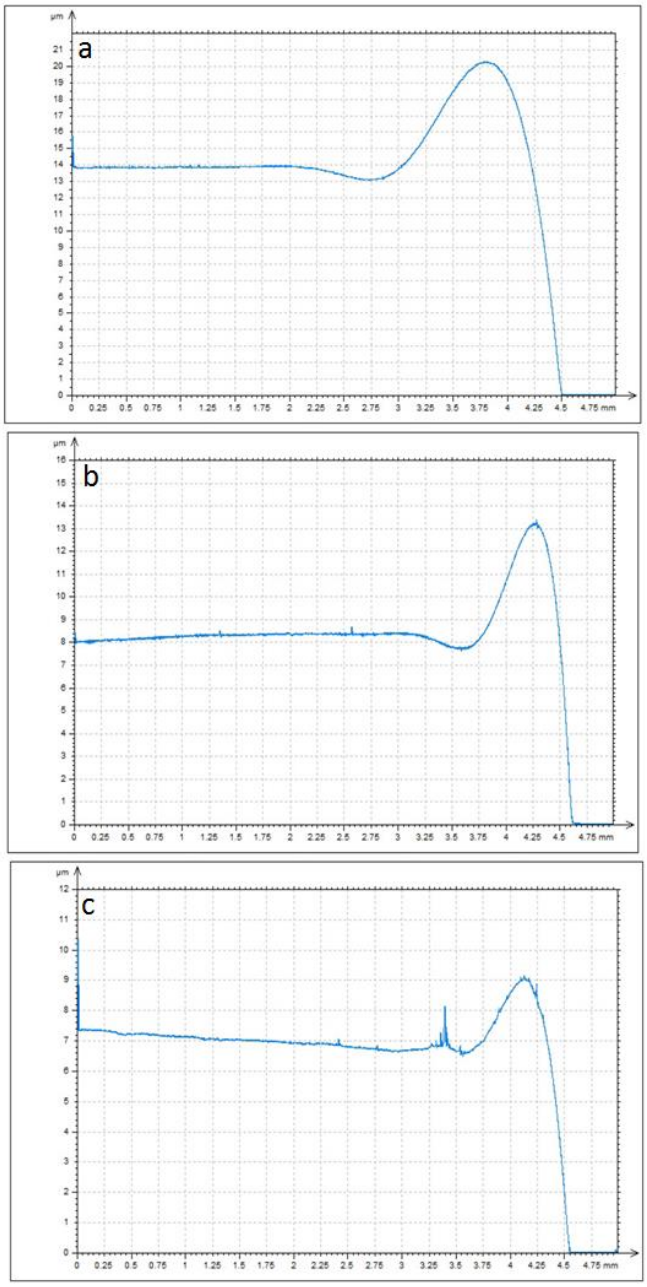

Figure 4: Sample of Profilometer data for different spin coatings, right hand side is blank slide a) 1200 RPM. b) 1800 RPM. c) 2400 RPM.

Antibody introduced into microfluidic devices with thin films showed equal and reliable binding on the surface. This was an affirmation for the success of the creation of silicon thin film based microfluidic device.

CONCLUSIONS

We have developed an inexpensive, rapidly fabricated and easy to functionalize thin film based microfluidic chip for the detection of SCI from the bodily fluid. We have shown that the thickness plays a critical role in creating thin film biosensor and the thickness of the affects the performance and sensitivity of the biosensor.

ACKNOWLEDGEMENTS

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