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Bio-MEMS Sensors for Real-Time Shear Stress on Endothelial Cell Dynamics

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Abstract- **Precise characterization of shear stress in the arterial trees is critical to elucidate the effects of spatial versus temporal shear stress gradients on the biological activities of endothelial cells (EC). We developed micro electrical mechanical systems (MEMS) sensors, comparable to the size of EC (2 x 80 μm), to deliver the spatial and temporal resolution necessary at a frequency response > 100 Hz. We provided the first *in vitro* evidence of real-time wall shear stress on EC couple with real-time gene expression of monocyte chemoattractant protein (MCP-1).**

Key words- micro electro mechanical systems (MEMS), shear stress, endothelial cells, monocytes

I. INTRODUCTION

Shear stress regulates endothelial cells (EC) morphology and their complex biological activities. *In vivo*, velocity profiles are asymmetric in shape due to geometry, and both time-varying and spatial-varying components of pulsatile flow. The emerging MEMS (Micro Electro Mechanical Systems) technology offers an entry point to overcome the temporal and spatial resolution necessary to characterize shear stress on EC dynamics at the arterial bifurcation.

II. METHODS

Both bulk and surface micromaching techniques were utilized to fabricate the MEMS shear stress sensors. MEMS shear stress sensors were operated based on the heat transfer principle [1]. The heat convection from a resistively heated element to the flowing fluid was measured, from which a value for shear stress was inferred. A linear relation between V^2 and $\tau_w^{1/3}$ can be obtained as $V^2/R \propto \tau^{1/3}$ [2]. The sensing element of the shear stress sensor, a polysilicon strip, 2 x 80 μm^2, was deposited on the silicon nitride film (Fig. 1).

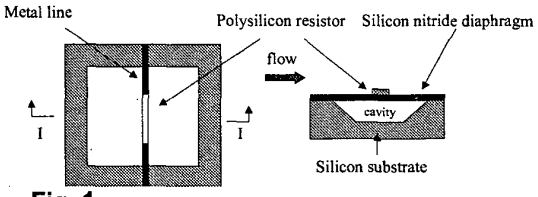

Fig. 1

To enhance the sensitivity, we created a vacuum chamber to minimize the heat conduction to the substrate (as evidenced by the "Newton ring")(Fig. 2).

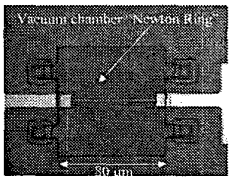

Fig. 2

The polysilicon strip, or the sensing element (80 μm long, 2 μm wide, and 0.5 μm thick), was located at the center of a vacuum chamber diaphragm, above the bottom of the cavity. Doping or ion implantation of the polysilicon strip was achieved with Boron to a low sheet-resistance value of 50 Ω/cm^2 with a typical resistance between 1.25 ~ 10 kΩ at the room temperature.

A flow system was designed to deliver well-defined flow profiles simulating pulsatile

and oscillating flow conditions in arterial circulation (Fig.3). This unique configuration ensured velocity uniformity and absence of flow separation across the width of the channel during flow reversal. The theoretical formulation for the pulsatile flow generated by this flow channel can be accessed on line at http://atvb.ahajournals.org[3].

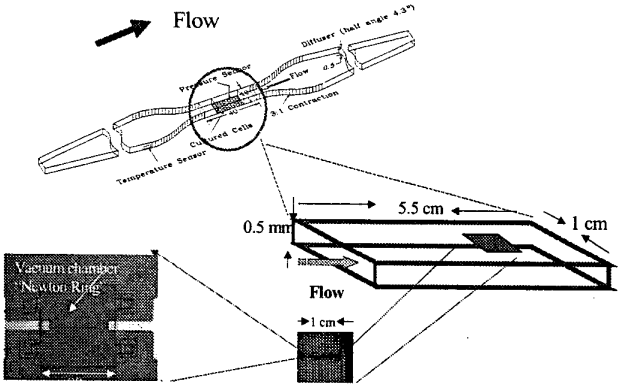

Fig. 3 The MEMS sensor chip was embedded in the upper wasll while the EC monolayers were seeded on the bottom wall.

III. RESULTS

The MEMS sensors feature three novel aspects: (1) The diaphragm is on the vacuum cavity, which minimizes the heat conduction from the diaphragm to the substrate. (2) The resistors are uniformly doped to a low sheat-resistance value of 50 Ω/cm2, resulting in a typical resistance between 1025Ω~5Ω at room temperature compared to that of the traditional sensors (5~50Ω), a unique property of MEMS sensors for achieving high frequency responses. (3) The small size of the sensor (2 μm x 80 μm) provides a high spatial resolution.

We demonstrated the *in vitro* real-time shear stress on EC known to occur at the arterial bifurcations. Figure 4 illustrates the distinct shear stress provides at the reattachment point where oscillatory flow occurs. Pulsatile flow, circled in dark blue, occurs in the medial wall.

IV. DISCUSSION

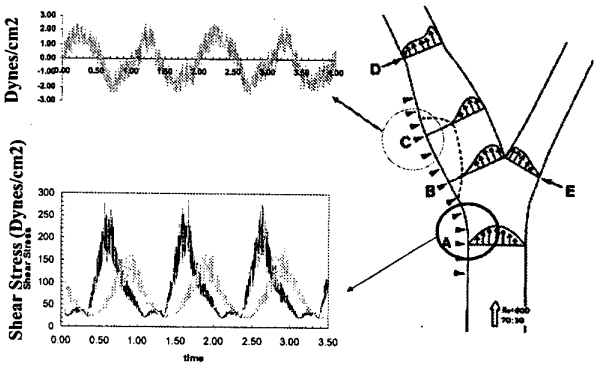

Fig. 4 Real-time shear stress measurement at the arterial bifurcations.

The central theme in this paper was to understand endothelial cell sensing and signaling in response to shear stress by embracing the MEMS technology. By understanding the forces that lead to local endothelial dysfunction, the pathophysiological mechanisms of cardiac disease might be further uncovered. The MEMS sensors offer an entry point to reveal the significant time-dependent variations in the hemodynamics of the arterial circulation under differing physiologic conditions.

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