Adhesive and Soft Cardiac Strain Sensor Using Catechol-bearing Hydrogels

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Statement of Purpose: Cardiothoracic open-heart surgery has significantly improved the treatment of cardiovascular disease. Patient health following open-heart surgery are monitored by measuring changes in cardiac output, which can indicate common complications such as systemic inflammatory response syndrome (SIRS) and vasoplegia. Current methods for monitoring cardiac output involve either thoracic echocardiography (TTE), which provides limited discontinuous data, or pulmonary artery catheter, which is highly invasive. Alternatively, cardiac output can be measured by monitoring strain and flow velocity changes through the aorta. However, mismatch of mechanical moduli between current implantable devices and human organs impedes accurate recording of strain response data and limits chronic implantation due to inflammation and scarring. In addition, lack of adhesion between implants and organs necessitates the use of external adhesives, increasing deployment time and leading to increased invasiveness and inaccurate data. Hydrogel-based electronics typically exhibit moduli in the range of 1-100 kPa and are suitable for direct interfacing with human organs (E = 1-30 kPa). Further, adhesion can be promoted through the inclusion of catechol motifs in four-arm (polyethyleneglycol)-dopamine precursors (PEG-Dopa, Huang W. Adv Funct Mater. 2018;28:29:1801059). Here, we propose the use of a conductive hydrogel-based strain sensor for cardiac strain sensing applications. PEG-Dopa is crosslinked and made conductive in the presence of metal cations (e.g. Fe^{3+}, V^{5+}, Ag^{+}, Au^{3+}). The storage modulus and gelation kinetics have been found to be tunable between 0.1-10 kPa by varying the metal cation, and the device exhibits an electromechanical response suitable for measuring relative changes in cardiac output.

Methods: PEG-Dopa + M^{z+} hydrogels were prepared using previously reported methods (Mou C. J Mater Chem B. 2019;7:16090-1696). Briefly, under an N_2 (g) blanket, four-arm poly(ethylene glycol) succinimidyl carboxymethyl ester (M_w ~ 10,000 g /mol; Jenkem Technology Ltd, Plano, TX) was combined with dopamine hydrochloride (2:3 mol ratio, neutralized with N-methylmorpholine) in anhydrous N,N-dimethylformamide (DMF) for 18 h. The product was dialyzed against doubly-distilled H_2O (dd-H_2O) with pH ~ 3.5 (titrated with 1 M HCl) for 24 h and then against dd-H_2O for 2 h. The final product of PEG-Dopa was lyophilized and stored at −15 °C until further use. PEG-Dopa was then dissolved in 50 mM tris base solution and combined with metal precursor (Fe^{3+}, V^{5+}, Ag^{+}, or Au^{3+}) in 50 mM tris base solution, maintaining a molar ratio (M^{z+}:catechol) of 0.42. The product was then drop casted into Teflon molds and connected with a custom polyimide flexible printed circuit board (PCB). Device performance was measured *ex vivo* using a porcine aorta attached to a Harvard Apparatus Pulsatile Blood Pump. Mechanical characterization was performed using a TA Instruments DHR-2 stress-controlled rheometer and Instron 5943, and electromechanical changes were characterized using a Tektronix Keithley 2400.

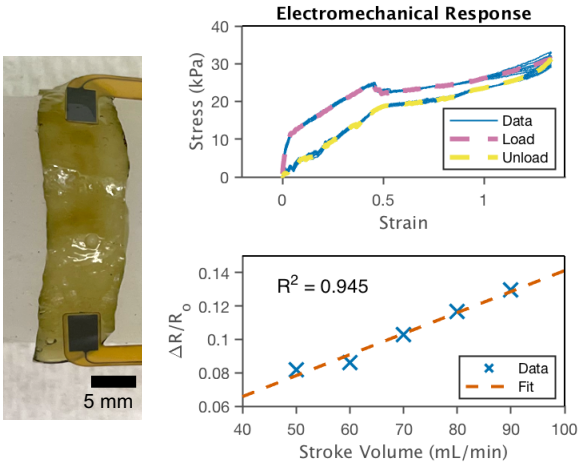

Figure 1. Image of the device on an Ecoflex pulsatile flow model, stress-strain response of [Fe^{3+}]-PEG-Dopa, and the resistance change upon applying different stroke volumes through a pulsatile pump.

Results: Storage moduli of PEG-Dopa + M^{z+} hydrogels were found to be 4730±210, 1530±46, 603±15, and 57±8 Pa for Fe^{3+}, V^{5+}, Ag^{+}, and Au^{3+} respectively. The device exhibited a modest conductivity of 0.05 S/m and a gauge factor of 0.03. Resistance change was found to be linearly related to stroke volume (R^2 = 0.945, Figure 1). Future work will include an *in vivo* demonstration in a pig. In conclusion, adhesive and strain-sensitive catechol-bearing hydrogels are a promising approach to minimally invasive and continuous monitoring of cardiac output.

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References:
1. Huang W. Adv Funct Mater. 2018;28(29):1801059.
2. Mou C. J Mater Chem B. 2019;7:16090-1696.