http://www.presm.org
ISSN 2005-8446

PRESM

International Symposium on
PRecision Engineering and Sustainable Manufacturing

PRESM 2020

PROCEEDINGS

November 15 Sun - 18 Wed, 2020
Online Symposium

Organizer

Korean Society for Precision Engineering (KSPE, Korea)

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Monitoring Real time Contractility of 3D Engineered Heart Tissues by Printing a Strain Gauge-Embedded Microphysiological System

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KEYWORDS : 3D printing, Microphysiological system, Strain gauge, Two-post platform, Engineered heart tissue

There are the growing interests in microphysiological systems (MPS), also known as organs-on-chips, recapitulating human-like physiology. Mechanical contraction is important factor affecting the development of engineered heart tissue (EHT). In addition, each cardiomyocyte (CM) in EHT should contract synergistically with consistency to conduct its own function. Currently, there are several methods to monitor the contractile force of CMs. The force transducer is to measure the contractile force directly by connecting the 3D EHT with transducer in real-time. However, this method is inevitable to damage to the 3D EHT for measuring the contractility because the tissue should be connected to the force transducer by using a clamp or hook. Next, optical readout system utilizes the principle of Hooke's law and the displacement is measured by optical camera. Although this system can invasively measure the contractile force of tissue constructs without damaging them, this analysis requires huge amount of data for real-time analysis. Also, Piezoresistive cantilever is used to measure the change of resistance induced by the deflection due to the mechanical contraction of monolayer of cardiomyocytes on the cantilever. This method is eligible to monitor the contractility in real-time, however, artificial forces, such as the stiffness of the cantilever, are applied to monolayer cells, inhibiting tissue generation from native cell-cell contact. In this research, we propose the strain gauge-embedded MPS integrated with the two-post platform, which is optimized to quantify or monitor beating rate, rhythm, and contractility of 3D EHT. To fabricate suggested system that is composed of strain gauge embedded multiple layers and two posts, three materials are sequentially extruded by multi-head 3D printing technique: biocompatible thermoplastic polymer, sacrificial polymer, and conductive polymer that is a mixture of carbon black and silicone elastomer. Biocompatible thermoplastic polymer is used to print a base layer and two-post structure that will be exposed to contractile stress and cells. Next, sacrificial polymer is used to print a sacrificial layer, and conductive polymer is utilized to make the strain gauge sensor and electrodes. To show the feasibility of developed system, the change of electrical resistance was measured by a multimeter. In addition, the deformation, induced by the well-known contractile force of CMs, was analyzed using commercial finite element analysis program (ANSYS). Ultimately, we are expecting that suggested system can be used for studying drug responses or the contractile development of human stem cell-derived cardiac tissues later.

ACKNOWLEDGEMENT

This research was supported by the MSIT (Ministry of Science and ICT), Korea, under the ICT Creative Consilience program (IITP-2020-2011-1-00783) and the High-Potential Individuals Global Training Program) (2020-0-01517) both supervised by the IITP (Institute for Information & communications Technology Planning & Evaluation).

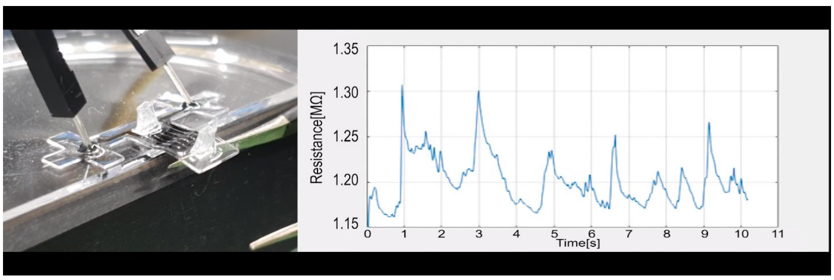

Fig. 1 Measurement of resistance change according to the deformation of strain gauge embedded MPS fabricated by 3D printing