

Scientific report, by Prof. Tal Dvir, research no. 0604512641, “3D Printing of Electronics-Integrated Cardiac Tissue”, granted by the Shlezak Institute

Myocardial infarction (MI; heart attack) is associated with sudden death as well as significant morbidity and mortality. MI results from blockage of one of the coronary arteries that supply the cardiac tissue, leading to ischemia of a segment of the heart. This process eventually leads to the death of contractile cells and the formation of a scar tissue. Since cardiomyocytes cannot proliferate, the cardiac tissue is unable to regenerate, leading to chronic cardiac dysfunction. Cardiac tissue engineering has evolved as an interdisciplinary field of technology combining principles from the material, engineering and life sciences with the goal of developing functional substitutes for the injured myocardium. Rather than simply introducing cells into the diseased area to repopulate the injured heart and restore function, cardiac tissue engineering involves the seeding of contracting cells in or onto 3-dimensional (3D) biomaterials prior to transplantation. Following implantation and full integration in the host, the scaffold degrades, leaving a functional cardiac patch on the defected organ. However, once the 3D cardiac patches have been engineered, *in vitro* assessment of their quality in terms of electrical activity without affecting their performance is limited. This situation might lead to implantation of cardiac patches with limited or no potential to regenerate the infarcted heart. Therefore, engineering an implantable tissue that can provide information on its own function and actively intervene with the tissue function would contribute immensely to the success of this tissue engineering approach. In this research we focused on the development of a method in which recording and stimulating electrodes are simultaneously 3D printed together with extracellular matrix (ECM)-based hydrogel and cardiac cells to generate a microelectronic cardiac patch (microECP). To this end, we developed a unique formulation of autologous, thermoresponsive ECM-based hydrogels, originated from decellularized omental tissue that can be easily and safely extracted from the patient. These hydrogels, which self-assemble under physiological temperature, have been found to support cultivation and tissue organization of cardiac cells. The printing process is executed using a multi-nozzle 3D printer that extrudes a unique formulation of conducting materials for electrode fabrication, alongside cardiomyocyte-containing ECM hydrogel that serves as “bio-ink”. The electrodes in the hybrid patch have been found to be elastic, mechanically durable and electrically conductive. Microscopic analysis and biochemical assays revealed that the cardiomyocytes maintained good viability and functionality while growing in close proximity to the printed electrodes. We have demonstrated the capacity of the electrode-containing constructs to implement real-time recordings of cardiac extracellular potentials and actively control and interfere with the patch function by applying acute electrical stimulation at different frequencies. This resulted in activation and synchronization of the contraction of the cells throughout the patch. Finally, by applying electrical stimulation in the opposite direction of the observed electrical signal propagation, tissue contraction could be manipulated and reversed.