P318 Linking bioreactor technology with optical coherence elastography for characterisation of engineered tissues

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Introduction: The maturation of engineered tissues is promoted through the use of bioreactors mimicking the physical *in vivo* growth environment. Monitoring the maturation of these constructs during culture and characterising them prior to implantation into the patient is important for defining their quality and performance in the clinic. Key properties include scaffold integrity and mechanical properties. Hence, novel non-invasive three-dimensional imaging modalities are required providing rapid results and translational solutions. Optical coherence elastography (OCE) has been coupled with bioreactor technology in order to monitor engineered tissue constructs during manufacture and to overcome drawbacks of tradition elastography approaches.

Method: Agarose hydrogels were prepared to final concentrations of 0.5%, 1.0% and 1.5%. hMSC ($1x10^5$) were incorporated before gelation to prepare cellular gels. Scaffolds were imaged utilizing OCT during mechanical stimulation at 1, 5, 10, 15 and 25 kPa at 1Hz frequency in the hydrostatic force bioreactor[2]. hMSC organoids were cultured over a duration of 12 days. Matrix deposition and changes in displacement were monitored. Displacements maps were generated using elastography algorithms[1].

Results: Improved sensitivity allows phase-resolved OCE to detect small displacements in heterogeneous tissue phantoms caused by either differences in gel concentration or the presence of cells. Clear differences in displacement were detected for hybrid hydrogels prepared from 0.5% and 1.5% agarose compared to 1.0% and 1.0% hydrogels. Interfaces between stiffer and softer gels can be identified. A novel dynamic OCE technique with cyclic compression as the external excitation generated by hydrostatic pressure was established. Phase-resolved OCE algorithms were applied to determine the scaffolds displacement in OCT phase-based images of various tissue phantoms. Our novel approach allows real-time non-invasive monitoring of the displacements tissue phantoms. It enables the investigation of scaffold degradation, material interfaces and heterogeneity as well as changes in scaffold porosity. It further allows the investigation of the effect of mechanical forces on cellular activities during dynamic culture. Future experiments will investigate the maturation of tissue engineered constructs during dynamic culture.

References: [1] Y Reinwald et al. (2016) Online monitoring for mechanical properties of three-dimensional tissue engineered constructs for quality assessment. SPIE. [2] Reinwald, Y., Leonard, K.H.L., Henstock, J.R., Whiteley J.P., Osborne, J.M., Waters, S., Levesque, P., El Haj, A.J. “Evaluation of the growth environment of a hydrostatic force bioreactor for preconditioning of tissue-engineered constructs”, Tissue Engineering: Part C, 21:1-14 (2015).

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