GENERATION OF MECHANICALLY FUNCTIONAL CARTILAGE CONSTRUCTS USING COMPRESSIVE LOADING IN-VITRO
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Introduction
To date, success in the repair of articular cartilage has been inconsistent and can result in formation of mechanically inferior fibro-cartilage, thereby increasing the chances of damage recurrence. One possible repair strategy is the implantation of mechanically functional tissue produced \textit{in-vitro} using tissue engineering. In this study, compressive loading was applied to immature, pre-cultured, cartilage-like constructs with the aim of increasing the constructs’ compressive moduli to reach those of native cartilage.

Methods
Bovine synoviocytes were seeded on to non-woven polyethylene terephthalate fibre scaffolds and pre-cultured in chondrogenic medium for 4 weeks. From dynamic compressive mechanical testing of these constructs, it was found that the application of strains in the range of 13 to 23 \% would be suitable to induce stress within the constructs’ matrices. Using an in-house built compressive bioreactor in a quasi-strain controlled mode, the constructs were consequently subjected to a cyclic compressive loading regime resulting in strains ranging from 13 to 23 \% at 1 Hz for 1 hour per day for 28, 56 or 84 days. At each time point, the dynamic compressive moduli at 18 \% strain were measured at 1 Hz, and histology carried out for each construct using Alcian blue/Sirius red and type I and type II collagen staining.

Results
After 56 days of compressive loading, the dynamic compressive moduli of the constructs were comparable to the higher values for native cartilage (Figure 1). Construct matrices stained homogenously with Alcian blue and collagen type II, with relatively low amounts of collagen type I staining. No statistically significant changes were observed at 84 days.

Discussion
The moduli values achieved in this study surpass those previously attained for tissue-engineered cartilage [Lima \textit{et al.}, 2007]. We hypothesised that the high moduli values were attained due to the bioreactor mechanism causing the loading regime to change as the constructs developed; the stress and strain applied increased with construct stiffness and thickness respectively, thereby achieving a suitable and consistent level of cellular stimulation to promote further elaboration of cartilage-like matrix and increasing moduli values. Given these constructs contain cartilage-like matrix and similar moduli as native cartilage, they could potentially favour long-term cartilage repair when implanted.

References