

Mechanical loading determines collagen fibril diameter independent of cell activity

U.Cheema¹, CB Chuo¹, Padmini Sarathchandra¹, Showan N. Nazhat² R.A. Brown¹,

¹University College London, UCL, Tissue Repair and Engineering Centre, Stanmore Campus, London HA7 4LP, ² Division of Biomaterials & Tissue Engineering, Eastman Dental Institute, London, WC1X 8LD, United Kingdom

Introduction

The mechanical properties of most vertebrate tissues are dominated by the fibrous protein collagen. It is important that the material properties of connective tissues fulfil a variety of tensile, compressive, shear and torsional load bearing functions. These are achieved by standard adaptations of the fibrous, anisotropic form of their collagen component. A key determinant of that is the distribution of fibril diameters. Collagen fibril diameter in native tissues varies considerably from tissue to tissue, and between age, repair and growth stages

We have tested the idea that fibril diameter can be regulated directly, using mechanical loading to promote fibril fusion in plastically compressed collagen materials (Brown *et al.* 2005).

Materials and Methods

Acellular collagen gels were made, as previously described, and routinely compacted by a combination of compression and blotting. The rate of compaction was controlled by the force applied and the extent of fluid removal to a porous 'sink'. The compacted gel was cut into three strips of 7 mm x 33mm. Each of these strips were then loaded, and treated as N=1.

Load was applied parallel to the tethered axis of the collagen gels. A single pattern of cyclical load was applied, with each cycle lasting 20 minutes. The control regimen was application of one cycle and test regimens applied between 12 and 144 cycles. Collagen gels were analysed for fibril diameter (electron microscopy) or quasi-static tensile mechanical properties directly after the treatment

Results and Discussion

Collagen fibril diameter clearly increased with increasing load cycle number as frequency analysis and as median diameter. The median baseline fibril diameter (1 cycle) was 29 ± 4.6 nm and this increased > 2 fold to 70 ± 10 nm after 144 cycles ($P < 0.001$) (figure 1).

The break stress, break strain and elastic modulus of the collagen material increased with increasing cycle number, particularly between 48 and 144 cycles. Break stress and modulus increased by 4.5 and 2 fold respectively.

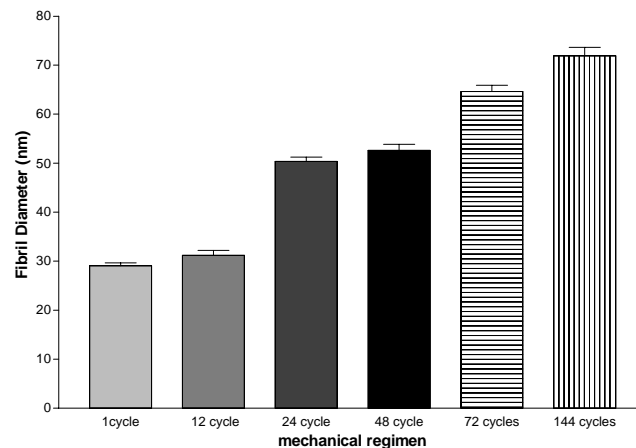


Figure 1. A histogram showing increasing fibril diameter as collagen is cyclically loaded.

Conclusions

This study represents the first demonstration, to our knowledge, that both fibril diameter and overall material properties can be directly controlled, without cells, through mechanical loading. This would suggest that material properties of the natural collagen polymers *in vivo* may also be controlled by a combination of local, cell generated strains and external loading. It also redirects how we can engineer biomimetic collagen materials for implants by providing previously impossible cell-independent control of mechanical properties.

References

Brown, R.A. Wiseman, M. Chuo, C.B. Cheema, U. Nazhat, S.N. 'Ultraprapid Engineering of Biomimetic Materials and Tissues: Fabrication of Nano- and Microstructures by Plastic Compression.' 2005. *Adv. Funct. Mater.* 15 (11): 1762-1770

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