Degradation of arterial collagen with applied strain: critical influence of matrix content and collagen crimp

Robert Gaul[1,2], David Nolan[1,2], Tomasso Ristori[3], Sandra Loerakker[3], Carlijn Bouten[3], Caitríona Lally[1,2]
[1]Trinity Centre for Bioengineering, Trinity College Dublin, Dublin, Ireland. [2]School of Engineering, Trinity College Dublin, Dublin, Ireland. [3]Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands

Abstract

Introduction

Collagen fibre turnover is a key feature of the mechano-biologically driven remodelling of arterial tissue, stimulated by the degradation of existing collagen. Despite this, literature has focused on strain-induced collagen reorientation rather than degradation [1]. It has previously been shown that pure collagen exhibits a V-shaped degradation profile as a function of strain (Figure 1a) [2].

This study aims to identify, for the first time, the strain mediated degradation behaviour of arterial tissue using a combination of experimental and theoretical methods.

Methods

Stress relaxation tests were carried out on porcine arterial dogbone specimens in the presence of purified collagenase to mimic *in vivo* enzymatic degradation (Figure 1b). Degradation rate constants, $1/\tau$, were calculated for each strain level (Figure 1b) and small angle light scattering analysis (SALS) was used in parallel to identify changes in fibre alignment (eccentricity).

To help explore the influence of the complex arterial structure on its degradation profile, a 1D numerical model was developed. The model consists of two spring elements in parallel, representing collagen fibres and non-collagenous ground matrix. The collagen element degrades according to the V-shaped profile and, importantly, can incorporate a transmural gradient of collagen fibre crimp.

Results

Degradation results showed an initial increase in degradation rate with strain followed by a plateau, before a final sharp increase (Figure 1c). Structural analysis using SALS found an inverse trend, with initial fibre alignment increasing at low strain levels followed by reduced alignment as strain increased (Figure 1d).

The 1D model predicted a similar degradation response, but only once fibre crimp and non-collagenous ground matrix were incorporated into the model (Figure 1c).

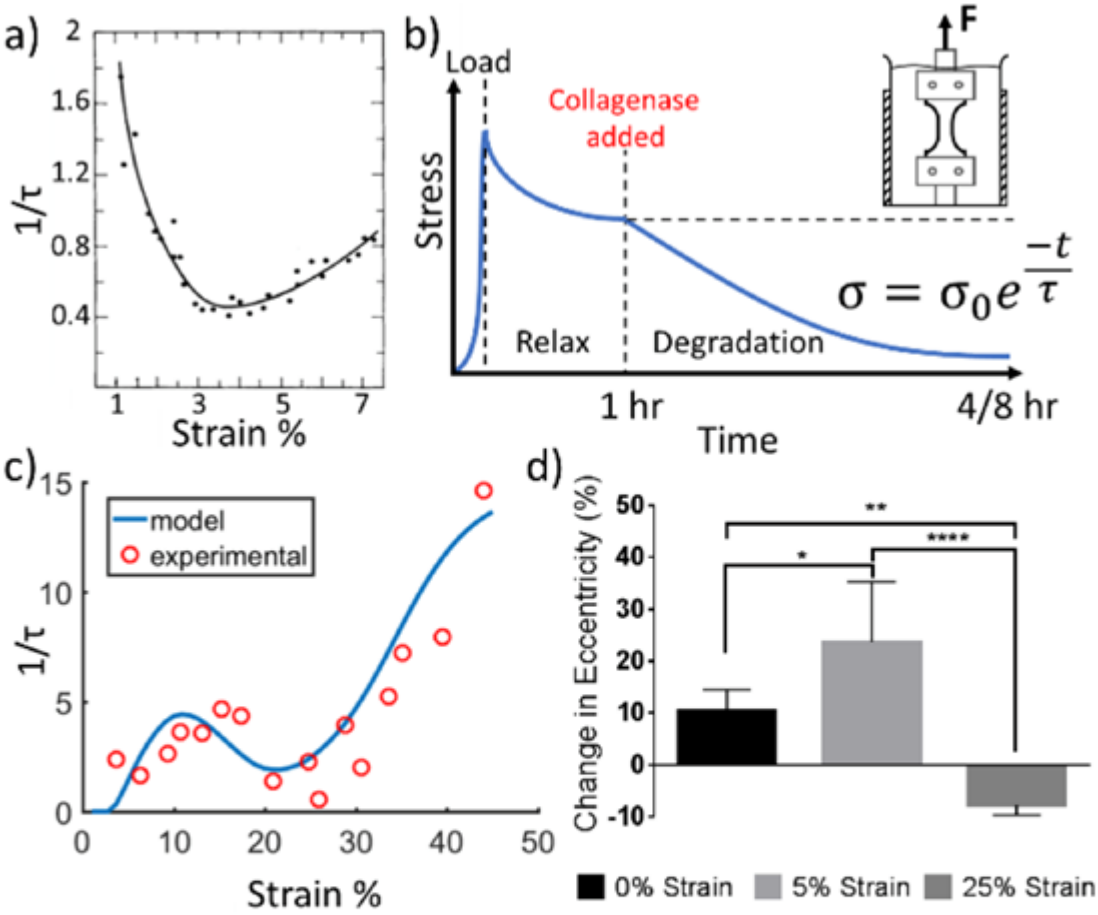

Figure 1 a) V-shaped degradation response for pure collagen used for the 1D numerical artery model (adapted from [2]), b) schematic of experimental protocol, c) experimental results (circles) overlaid on the numerically predicted response (solid line), d) relative degradation induced changes in fibre eccentricity under different strain regimes observed using SALS, n=7, *p<0.05, **p<0.01, ****p<0.0001.

Discussion

Using a combined experimental and numerical approach, this study has identified, for the first time, the complex strain-mediated degradation mechanism of arterial tissue. The complementary numerical model helps unravel the mechanisms at play. No degradation occurs initially; as collagen fibres are crimped they bear no load and hence do not undergo degradation. Next, degradation increases as fibres begin to un-crimp and take up the load. When all fibres are fully stretched, the V-shaped behaviour resumes. SALS results further support this finding, identifying a similar trend in relative fibre alignment post degradation.

These findings offer substantial new insights into arterial degradation and may be used to aid the design of novel intravascular devices to induce controlled remodelling or repair in potentially vulnerable, rupture prone arteries.

References

1. Gaul *et al.,* JMBBM, 75:359-368,2017.

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