IN-VITRO AND IN-SILICO MODELING OF THE EFFECT OF GAG ON THE OPENING ANGLE OF THE ASCENDING PORCINE AORTA

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Introduction

Residual stresses (RS) play a vital role in vascular mechanics. RS contribute to the magnitude and intramural distribution of mechanical stresses in-vivo, which in turn play an important role in dictating lethal ruptures. Circumferential RS, which can be assessed ex-vivo using the opening angle method, remain poorly understood, and the proper implementation of RS in computational models remains an active area of research. Our previous efforts show that the opening angle is highest in the ascending region compared to other regions of the thoracic porcine aorta [1]. This suggests that circumferential RS exist in higher magnitudes in the ascending aorta, which is the focus of this work. Previous reports have also shown that circumferential RS are associated with the intramural extracellular matrix (ECM) constituents, such as collagen, elastin, and glycosaminoglycans (GAG) [1,2]. The purpose of this study was to decipher the extent of contribution of GAG to circumferential RS in the ascending aorta, and to gauge their effect in a computer model.

Methods

In-vitro experimentation involved excising sets of two adjacent aortic rings from the ascending region in 5 porcine aortas. One ring served as a control, while the second ring underwent enzymatic GAG depletion using 15U/mL hyaluronidase, 0.075U/mL chondroitinase ABC, 0.75U/mL heparinase for 48 hours at 37ºC. The opening angle was then measured and the sulfated GAG content was quantified.

The in-silico study involved creating a finite element ascending aortic ring computer model using FEBio (https://febio.org/). The model combined an elastic porous solid matrix with the Donnan swelling induced by the presence of fixed charge densities (FCDs), simulating the presence of GAG [3]. The mechanical behavior of the solid matrix was modelled using a Holmes-Mow constitutive relationship, for which material parameters were estimated by curve fitting stress-strain curves obtained from experimental biaxial tests. The dimensions of the rings were acquired experimentally in a previous study [1], from 15 rings of 5 porcine aortas, from which the intramural FCDs distributions were also estimated using the quantified GAG content. The simulated opening angle was finally compared against experimental results.

Results

In-vitro investigations demonstrated that removal of GAG significantly reduced the opening angle in the ascending region by approximately 25.5% (paired sample t-test, p=0.009). In addition, the simulated aortic ring model with embedded FCDs in the solid matrix yielded an opening angle of 37 deg, accounting for 32.5% of the experimental opening angle of control rings in the ascending region, which was about 113.6±16.8 deg.

Discussion

Computer simulations have been found valuable in understanding the mechanics and the physiology of cardiovascular tissue and has the ability to predict ruptures, making it a promising technology for clinical applications. In this work, both in-vitro and in-silico studies demonstrated that GAG contribute to the opening angle of the ascending porcine aorta. The discrepancy between experimental and computational results was minor, as the contribution of GAG to the opening angle was 28.9±12.3 deg experimentally, vs. 37 deg computationally. These results suggest that a significant portion of RS is modulated by the amount of GAG present in the aortic wall, and that their effect on RS should not be ignored in future computer models. While eliciting new inquiries, these findings answer questions which not only contribute to basic science, but may also play an important role, in the longer run, in personalized medicine through computational modeling of vascular diseases.

References

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Acknowledgements