Mesostructural changes of heart valve tissue during collagenase degradation

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Introduction and Background

Methods and Results

Discussion and Conclusion

Current Knowledge

- Valvular interstitial cells (VICs) catabolize damaged collagen fibers and help to repair tissues. Severe collagen depletion caused by matrix metalloproteinases (MMPs) induces tissue matrix destruction, altering the viscoelastic property of the heart valve tissues.
- Collagen degradation affects cellular regulations controlled by VICs, and can lead to heart valve diseases.

Current Limitations

- The effects of MMP degradation on the extracellular matrix (ECM) at a local meso-structural level, and the relation with strain state is unknown.

Objectives and Approaches

- An approach to understand and quantify **enzymatic degradation** of collagen fibers is performed
- An application of (0.5 mg/mL) collagenase for collagen degradation is used to simulate effects of MMPs
- Porcine aortic valve specimens are secured at a zero strain state and immersed in PBS or collagenase solution
- Multiphoton Second Harmonic Generation (SHG) imaging of collagen is performed during the degradation process at 30 min intervals for 180 min

Changes in ECM during Degradation

- The image stacks are analyzed in ImageJ and Matlab to determine the changes in layer thickness, fiber organization, and amount of collagen
- Skewness of the pixel intensity histogram is used as a depth independent measure of collagen concentration
- Fast Fourier Transform (FFT) is performed then power spectrum analysis to fit a gaussian model to the angular data to quantify organization
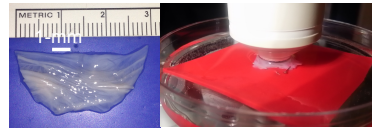

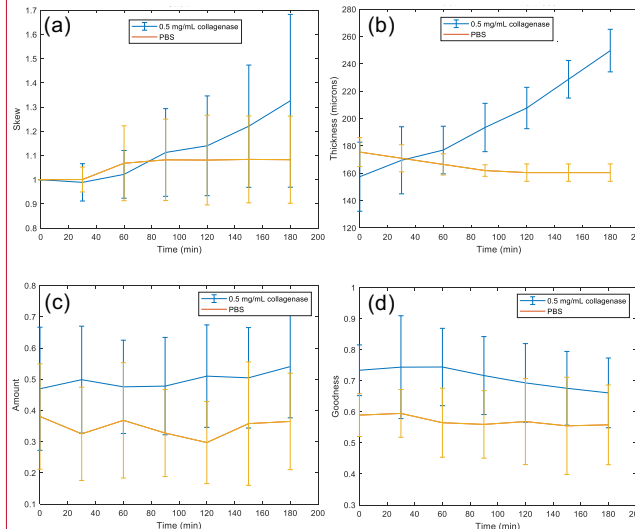**Fig. 1:** Typical AV and experimental setup

Fig. 2: Plots of (a) skewness of the pixel intensity histogram (b) thickness of the local collagen layer (c) amount of fibers contained within 1 deviation and (d) goodness of fit of the gaussian model of fiber organization

Effects of collagenase degradation of structure of Aortic Valve ECM

- Amount of collagen present decreases on overage based on the skewness histogram, but variance remains high and no conclusions can be drawn from this as of now
- The degradation process allows a relaxation of the tissue causing it to swell and expand in overall thickness 59% on average
- Alignment and structure of collagen do not appear to show any significant changes over time based on FFT analysis, although the experimental group seems to have better fits than the control group the variance is high
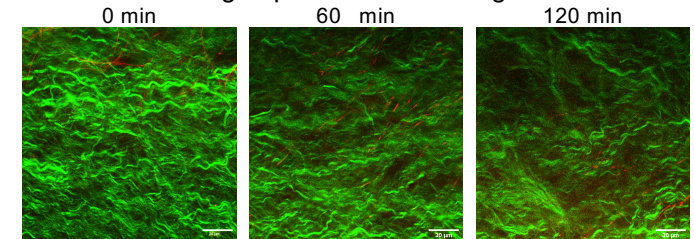

Fig. 3: SHG/TPEF images of collagenase tissue displaying collagen (green) and elastin (red) at time points of 0, 60 and 120 min at the centre of the collagen layer
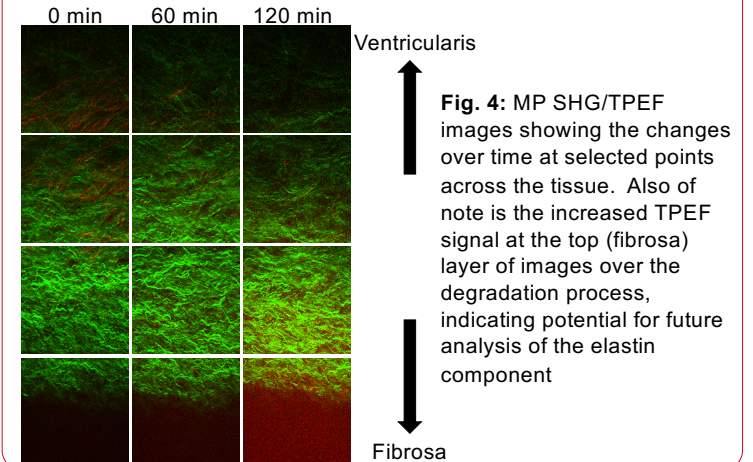

Fig. 4: MP SHG/TPEF images showing the changes over time at selected points across the tissue. Also of note is the increased TPEF signal at the top (fibrosa) layer of images over the degradation process, indicating potential for future analysis of the elastin component