Functional and Structural Differences in Fibrosis Determine Atrial Fibrillation Inducibility

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Introduction: Atrial fibrosis has been associated with increased incidence of atrial fibrillation (AF); however, how fibrosis may allow AF to sustain and develop has not been well characterized. Utilizing a transgenic goat model, we aim to evaluate how atrial fibrosis may affect conduction and if there are differences in fibrotic characteristics between inducible and non-inducible animals.

Method: Using a transgenic goat model with cardiac-specific overexpression of TGF-β1, a short period of rapid atrial pacing was performed in the right atrium to test if the animal sustained AF. An electrophysiology study was conducted to measure conduction characteristics in normal sinus rhythm. Conduction speed, direction, and anisotropy within the fibrotic regions of the inducible and non-inducible animals were compared. Structural analysis using DTI-MRI further characterized structural differences within the fibrotic regions of the two groups. Histological samples were compared to evaluate the underlying fibrotic architecture.

Results: The overall conduction speeds between the fibrotic regions of the inducible and non-inducible groups were identical; however, further analysis revealed underlying functional differences between the fibrotic regions. The conduction anisotropy and conduction direction heterogeneity are lower in the fibrotic region of the inducible animals, $p<0.01$. Structural analysis indicated that there is increased structural isotropy and higher diffusion within the fibrotic region of the inducible group, $p<0.01$. The underlying fibrotic architecture showed differences between the two groups, with an increase in obstructive fibrotic strands and a greater angle difference between the fibrotic and tissue strands in the inducible animals, $p<0.01$.

Conclusion: There are functional, structural, and architectural differences within the fibrotic region between the inducible and non-inducible groups of transgenic goats. The underlying fibrotic characteristics may have a role in determining how AF may develop and sustain. It is important to include heterogeneity within the fibrotic zones of computational models to realistically simulate arrhythmias.

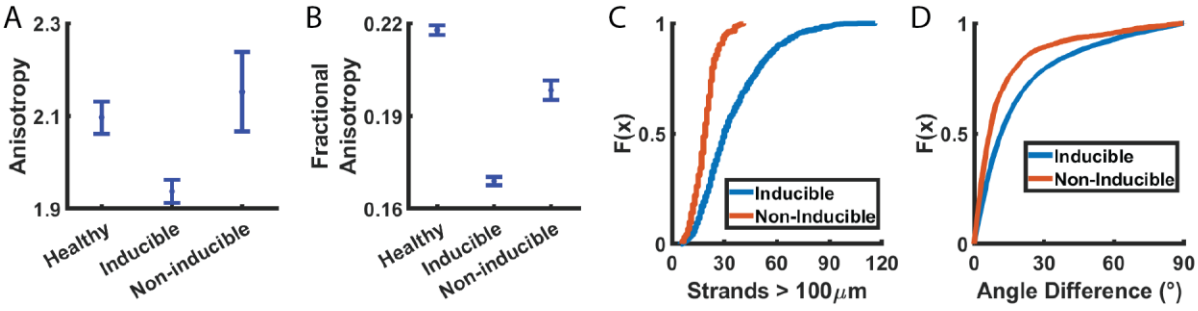

Figure 1: Functional and structural differences within the fibrotic regions. A) Conduction anisotropy is lower in inducible animals. B) Inducible animals had increased structural isotropy. C) There was an increase in obstructive fibrotic strands in inducible animals. D) The fibrotic strands have a larger angle deviation from the tissue fibers in the inducible animal group interrupting the tissue fibers.