Diffusion tensor imaging identifies atrial regional changes associated with atrial fibrillation remodelling

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Background: Structural remodeling in the context of persistent atrial fibrillation (PAF) has been mainly characterized by imaging techniques focused on fibrosis detection. Diffusion tensor imaging (DTI) has demonstrated its direct relationship with histological properties and myocyte organization, which may provide a more complete structural information. However, the potential of DTI in the characterization of the AF-related structural substrate remains unknown.

Purposes: To evaluate the performance of DTI-derived parameters to characterise the structural remodelling derived from persistent AF and its relationship with specific atrial regions associated with AF maintenance (i.e., driver regions).

Methods: Two experimental groups of pigs were studied: control (n=7) and PAF (n=10). The PAF swine model was developed using rapid atrial pacing until the animals reached a stage of self-sustained PAF. The AV node was ablated to prevent heart failure due to fast ventricular activation rates. A second lead in the right ventricular was used for ventricular pacing at 60-110 bpm. Animals with PAF were studied after ≥ 6 months in self-sustained persistent AF. AF animals underwent invasive electroanatomical to identify driver regions based on instantaneous frequency modulation maps. After euthanasia, explanted hearts from AF animals and controls underwent DTI including 15 diffusion weighted images with a b-value of 600 s/mm² plus a non-DWI volume (isotropic resolution, 0.6 mm³). DTI images were segmented and divided into 13 atrial anatomical regions. Driver regions in AF animals were also segmented and classified as functional regions of interest (ROIs) (Figure 2B). Afterwards, diffusion tensors were estimated and scalar features were analyzed (Figures 1A and 2A) according to both anatomical and functional ROIs.

Results: DTI analysis in AF animals revealed region-specific structural remodelling (Figure 1B). Compared to controls, PAF animals showed an increased fractional anisotropy (FA) in both right and left atrial free walls (Figure 1C). Other anatomical regions, such as the superior vena cava (SVC), the coronary sinus (CS) or the left atrium roof developed higher axial diffusivities in AF compared to controls (Figure 1D), without significant alterations in FA (Figure 1C). AF driver regions were frequently located in the CS, the SVC and the LAA (Figure 2C). AF driver ROIs into the CS and the SVC showed intracase increased diffusivities and decreased linear indexes compared to non-driver regions. However, AF driver ROIs in the LAA showed increased intervoxel main eigenvector dispersion in contrast to non-driver ROIs (Figure 2C).

Conclusion: DTI sequences provide atrial structural information associated with functional tissue properties relevant for AF maintenance.
**A** Radial diffusivity or mean between eigenvalues 2 and 3. Non-axial directions.

Axial diffusivity or main eigenvalue, fibers' main direction.

**C** Fractional anisotropy: Relationship between diffusivities at different directions.

Low values indicate loss of structure. High values indicate a high organised tissue.

**B**

RAA indicates right atrium appendage; RAFW indicates right atrium free wall; PRA indicates posterior right atrium; LAFW indicates left atrium free wall; ARA indicates anterior right atrium; ALA indicates anterior right atrium; LAR indicates left atrium roof; PMA indicates posterior mitral annulus; CS indicates coronary sinus; SVC indicates superior vena cava; LAA indicates left atrium appendage; PVs indicates pulmonary veins; IVC indicates inferior vena cava.

**E** Radial diffusivity (1000 mm^2/s).

**D** Axial diffusivity (1000 mm^2/s).

**No changes**

**Increased anisotropy**

**Decreased diffusivity in axial direction**

**Increased diffusivity in radial directions**

**Increased diffusivity**
A
Cl or morphological linear index
Intervoxel main eigenvector (main direction of diffusion) dispersion
High values indicate a cigarette diffusion morphology
Low values indicate a coherent fiber direction neighbourhood
High values indicate angle changes or fiber crosslinking

B
Atrial endocardium (electroanatomical anatomy)
Atrial endocardium (magnetic resonance anatomy)
LAR as a driver region
LAA as a driver region
Functional regions of interest segmentation

C

D

RALA indicates right atrium appendage; RAFW indicates right atrium free wall; PRA indicates posterior right atrium; LAFW indicates left atrium free wall; ARA indicates anterior right atrium; ALA indicates anterior right atrium; LAR indicates left atrium roof; PMA indicates posterior mitral annulus; CS indicates coronary sinus; SVC indicates superior vena cava; LAA indicates left atrium appendage; PVs indicates pulmonary veins; IVC indicates inferior vena cava.