SUPERTOROID-BASED FUSION OF CARDIAC DT-MRI WITH MOLECULAR AND PHYSIOLOGICAL INFORMATION

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INTRODUCTION

The supertoroid-based representation is an evolution of the toroidal model that enhances the three-dimensional perception of myocardial tissue structure and organization using DT-MRI **[1]**. The supertoroidal model, as a superset of genus-0 and genus-1 shapes, improves the effectiveness of the diffusion tensor characterization of myocardial architecture post myocardial infarction (MI) **[1]**. However, successful characterization of tissue properties relies on relating structural information with physiological or molecular information obtained from different sources. Because the supertoroidal model offers the ability to incorporate two additional parameters, γ_1 and γ_2, we are able to fuse standard structural DT-MRI information with parameters from other modalities. Changes in myocardial structure and function are dependent on alterations in the extracellular matrix (ECM), which is modulated by activation of matrix metalloproteinases (MMPs). The purpose of this work is to employ the supertoroids to combine the regional structural information derived from cardiac DT-MRI, with regional activation of MMPs, and associated changes in myocardial perfusion and cellular viability in porcine heart at 2 weeks post-MI.

METHODOLOGY

The supertoroid is a geometric primitive that incorporates the visual features conveyed by the increase in genus and a continuum that fully encodes the local eigensystem. The supertoroidal parametric equation is a function of the geometric shape metrics $C_L = (\lambda_1 - \lambda_2)/\lambda_1 + \lambda_2 + \lambda_3$, $C_P = 2(\lambda_2 - \lambda_3)/\lambda_1 + \lambda_2 + \lambda_3$, and $C_S = 3\lambda_3/\lambda_1 + \lambda_2 + \lambda_3$ **[2]** and is parameterized as follows:

$$C_S \geq C_P \Rightarrow \Im(\theta,\phi) = \left(\cos^{(1-C_P)^{\gamma_1}}\theta \left\{ (C_L + C_P) + C_S \cos^{(1-C_S)^{\gamma_2}}\phi \right\} \sin^{(1-C_P)^{\gamma_1}}\theta \left\{ (C_L + C_P) + C_S \cos^{(1-C_S)^{\gamma_2}}\phi \right\} \sin^{(1-C_S)^{\gamma_2}}\phi \right),$$

$$C_S < C_P \Rightarrow \Im(\theta,\phi) = \left(\cos^{(1-C_P)^{\gamma_1}}\theta \left\{ C_S + (C_L + C_P)\cos^{(1-C_S)^{\gamma_2}}\phi \right\} \sin^{(1-C_P)^{\gamma_1}}\theta \left\{ C_S + (C_L + C_P)\cos^{(1-C_S)^{\gamma_2}}\phi \right\} \sin^{(1-C_S)^{\gamma_2}}\phi \right),$$

where $\Im$, the parameterized glyph surface, is a function of both azimuthal $\theta \in [0,2\pi]$ and polar $\phi \in [0,2\pi]$ coordinates. The role of γ_1 is to control the sharpness of the shape in the medium and minor diffusion directions. The parameter γ_2 controls the shape along the perpendicular axis, which is aligned with the major direction of diffusion. ***Experimental Protocol:*** Myocardial infarction was created in a pig by surgical occlusion of the marginal branches of left circumflex. 2 weeks post-MI pig was injected with a ^{99m}Tc-labeled radiotracer (RP805), which identifies MMP activation, followed by injection of ^{201}Tl for evaluation of myocardial perfusion and viability. ***DT-MRI Acquisition*:** Pigs were euthanized ~30 min after ^{201}Tl injection, hearts were excised and perfused with saline. Each heart was then placed and positioned in a container and filled with Fomblin (Ausimont, Thorofare, NJ). DT-MRI data were collected with a 3.0T scanner (Siemens, Erlangen, Germany) using a segmented EPI sequence. An icosahedral diffusion encoding gradient scheme containing 6 directions was applied with a constant b-value=600s/mm^2. A single image with a b-value=0s/mm^2 (T2-weighted) was also obtained. Fifty short-axis image slices with resolution 2×2×2mm^3 were acquired with TR=5400ms and TE=84ms. In order to increase SNR, a total of 32 averages were performed over 6 hours and the EPI factor was set to 7. ***RP805 and ^{201}Tl Tissue Analysis*:** Following MR imaging hearts were sliced (5mm), cut in 8 radial pies and divided into endocardial and epicardial segments for gamma-well-counting for determination of RP805 and ^{201}Tl activity, expressed as percent of injected dose/gram of tissue (%ID/g) and percent of non-ischemic region (%NI), respectively. Results from gamma-well-counting were coregistered to the T2-weighted image and RP805 and ^{201}Tl values were associated to each voxel belonging to the relative segment.

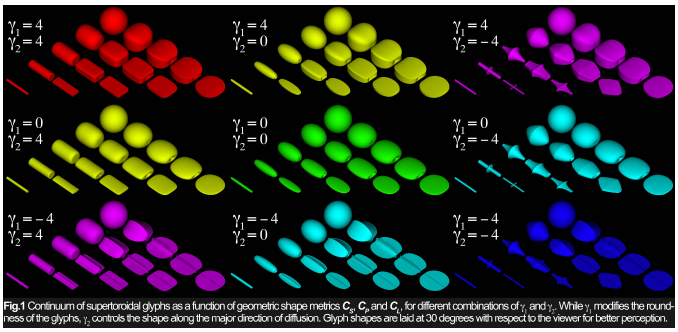

Fig.1 Continuum of supertoroidal glyphs as a function of geometric shape metrics C_L, C_P and C_S for different combinations of γ_1 and γ_2. While γ_1 modifies the roundness of the glyphs, γ_2 controls the shape along the major direction of diffusion. Glyph shapes are laid at 30 degrees with respect to the viewer for better perception.

RESULTS

Synthetic Data: Supertoroidal fields were computed in a representative continuum of possible shapes for different values of γ_1 and γ_2 (**Fig.1**). The vertices of the triangular continuum represent the extreme values for linear anisotropy (high C_L), planar anisotropy (high C_P) and isotropy (large C_S). Varying the values of γ_1 and γ_2 influence the shape of the supertoroidal glyphs and allows highlighting structural properties such as isotropic or anisotropic regions within the tensor field. Alternatively, γ_1 and γ_2 can vary as a function of regional information obtained from other modalities.

Experimental Data: To demonstrate the fusion of DT-MRI and molecular and physiological data, we varied γ_1 as a function of RP805 uptake and γ_2 as a function of ^{201}Tl activity in a porcine heart 2 weeks post-MI, as displayed in **Fig.2**. Compared to the case of γ_1 and γ_2 constant (**Fig.2B**), varying γ_1 as a function of RP805 uptake (**Fig.2C**) creates glyphs whose shape roundness vary across the myocardium, i.e. the roundness increases in the infarcted regions. Varying γ_2 as a function of ^{201}Tl activity (**Fig.2D**) controls regionally the glyph along the principal direction of diffusion and conveys the myocardial perfusion information through the supertoroidal shapes. Finally, we combine the structural, molecular and pathophysiological information by varying γ_1 and γ_2 as a function of RP805 and ^{201}Tl, respectively (**Fig.2E**).

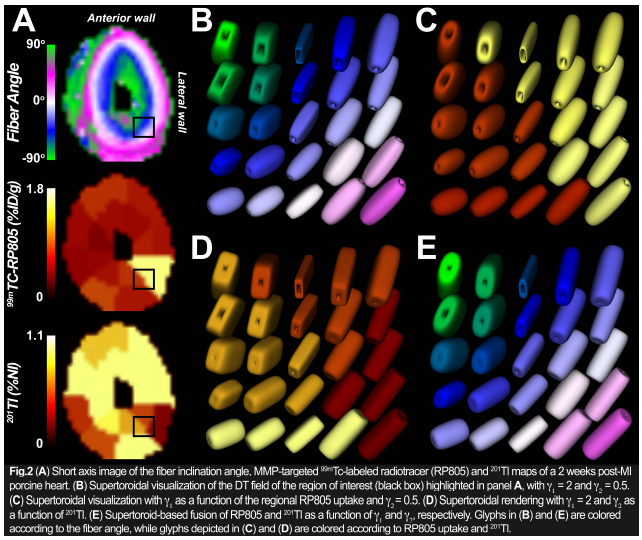

Fig.2 (**A**) Short axis image of the fiber inclination angle, MMP-targeted ^{99m}Tc-labeled radiotracer (RP805) and ^{201}Tl maps of a 2 weeks post-MI porcine heart. (**B**) Supertoroidal visualization of the DT field of the region of interest (black box) highlighted in panel **A**, with γ_1 = 2 and γ_2 = 0.5. (**C**) Supertoroidal visualization with γ_1 as a function of the regional RP805 uptake and γ_2 = 0.5. (**D**) Supertoroidal rendering with γ_1 = 2 and γ_2 as a function of ^{201}Tl. (**E**) Supertoroid-based fusion of RP805 and ^{201}Tl as a function of γ_1 and γ_2, respectively. Glyphs in (**B**) and (**E**) are colored according to the fiber angle, while glyphs depicted in (**C**) and (**D**) are colored according to RP805 uptake and ^{201}Tl.

DISCUSSION

The supertoroid-based representation enhances the three-dimensional perception of biological tissue structure and organization using DT-MRI. The incorporation of two additional free parameters in the supertoroidal function allows the tuning of the glyph surface in order to highlight different structural properties **[1]**. Alternatively, these free parameters can be used to fuse the visualization of structural DT-MRI information with molecular or pathophysiological information provided by other modalities. In conclusion, the availability of additional free visualization parameters provides flexibility to the supertoroidal model that can be used to improve the discrimination among different structures or to incorporate information arising from different modalities into a unique integrated visualization scheme.

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References: **[1]** Mekkaoui C *et al*. ISMRM 2009; **[2]** Westin C-F *et al*. ISMRM 1997.