# Quantification of Extracellular Matrix Components in Arterial Tissue using High-Resolution Micro-Diffusion Tensor Imaging


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## INTRODUCTION

The health of a blood vessel is highly dependent on the composition of various constituents of its extracellular matrix (ECM). Constituents such as elastin, collagen and glycosaminoglycan play a significant role in defining the tissue anisotropic response and in shaping the overall mechanical profile of the tissue. There are a number of techniques to probe the ECM composition and distribution [1], however, these techniques are generally destructive in nature, thus are not clinically feasible. Among various non-invasive imaging techniques, diffusion-weighted magnetic resonance imaging (DW-MRI) can potentially provide clinically relevant biomarkers based on the heterogeneous nature of the arterial ECM [2,3]. The aim of the study is to accurately map the ECM microenvironment of intact arterial tissue using ultra-high resolution diffusion tensor imaging (DTI).

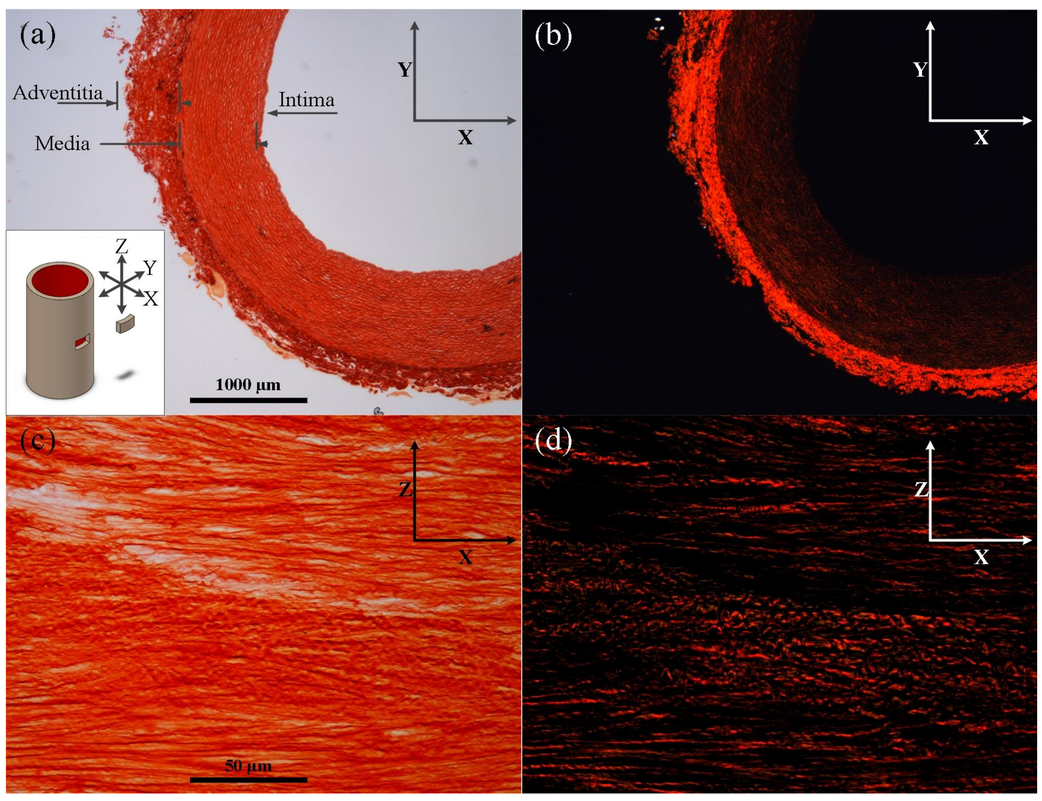


***Figure 1**: Ring section of a common carotid artery stained with picrosirius red (a) under light microscopy (b) under polarised light to isolate collagen from the rest of the constituents (magnification 2X). The layers of the arterial wall: tunica intima, tunica media and tunica adventitia are also marked in (a). Small flat section of the carotid artery under 40X magnification (c) under visible light (d) under polarised light.*

## METHOD

Two samples of intact carotid arteries from pigs aged five months were surgically harvested. Samples were cryo-preserved at -80°C prior to scanning. DT-MRI was performed on a Bruker BioSpin 7T-MR scanner equipped with a cryo-probe. Parameter-selective diffusion encoding scheme, based on SE-EPI sequence was used. Each acquisition was carried out with a b-value of 800 s/mm$^2$, 128 directions and 10 (b=0) reference images. For each dataset the image resolution was set to 0.117 mm$^3$ and each acquisition took approximately 80 minutes. The acquired DWIs were post-processed in FMRIB software library (FSL, Oxford, UK) to obtain local tensor information. The tensor information was then used to calculate fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), radial diffusivity (RD) and three geometric measures ($C_L$, $C_P$ and $C_S$).

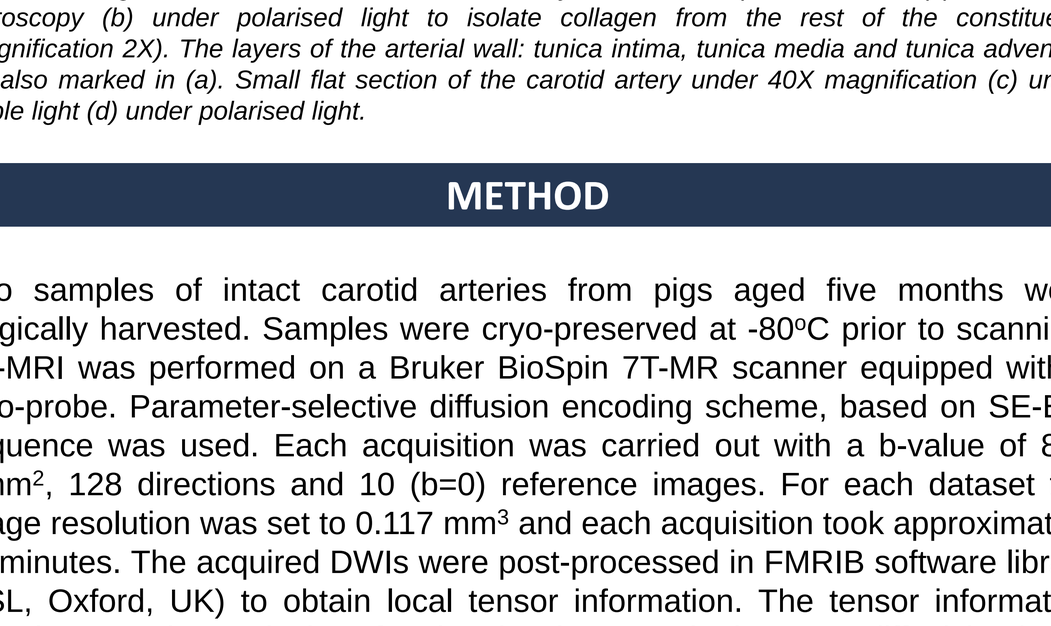


***Figure 2**: Diffusion MRI of an intact common carotid artery using a parameter-selective diffusion encoding scheme based on Spin Echo – Echo Planar Imaging*

## RESULTS

The heterogeneous nature of the ECM microenvironment is depicted in Figure 3. Directionally invariant indices (FA and MD) and geometric measures indicate high ECM density in the outer regions of the media. The 3 phase (3P) plots show that the tensor profile of the ECM in media is highly heterogeneous and is location dependent.

The projection of calculated helical angles onto individual fibres and the distribution of fibre angles evident from linear and circular distributions indicate a predominantly circumferential fibre alignment. For both samples, the helical angles are in the range of ± 20°. Super-resolution Track Density imaging at 0.0117 mm$^3$ resolution (reconstructed) shows the histology like depiction of the arterial tissue (Figure 4).

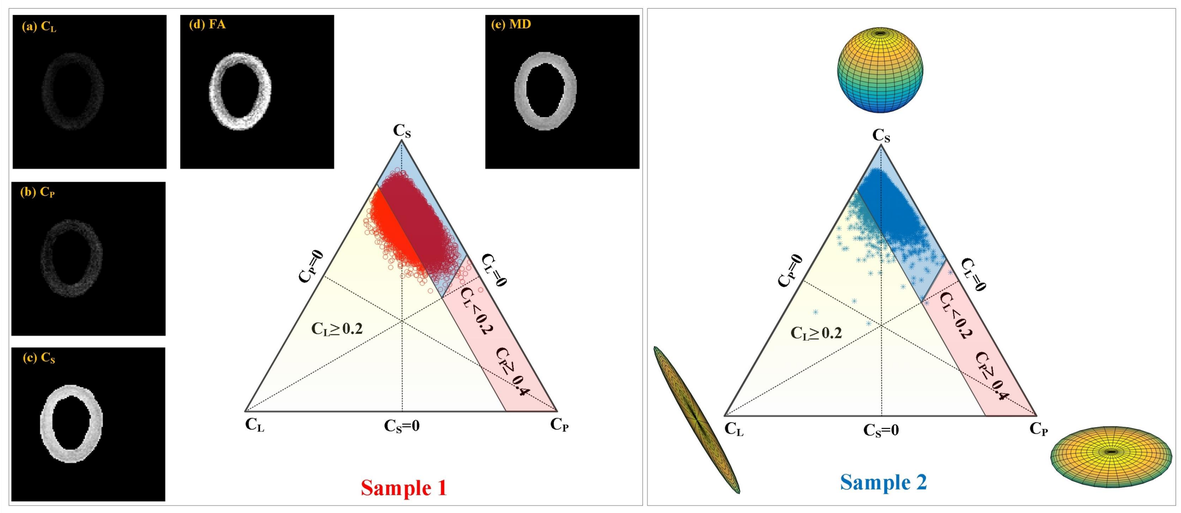


***Figure 3**: Geometric measures and directionally invariant indices (FA and MD) to highlight the regions of anisotropic and isotropic diffusion (sample 1). The 3 phase diagrams illustrate the heterogeneous nature of the arterial ultrastructure using the calculated diffusion tensor profile (sample 1 and sample 2).*

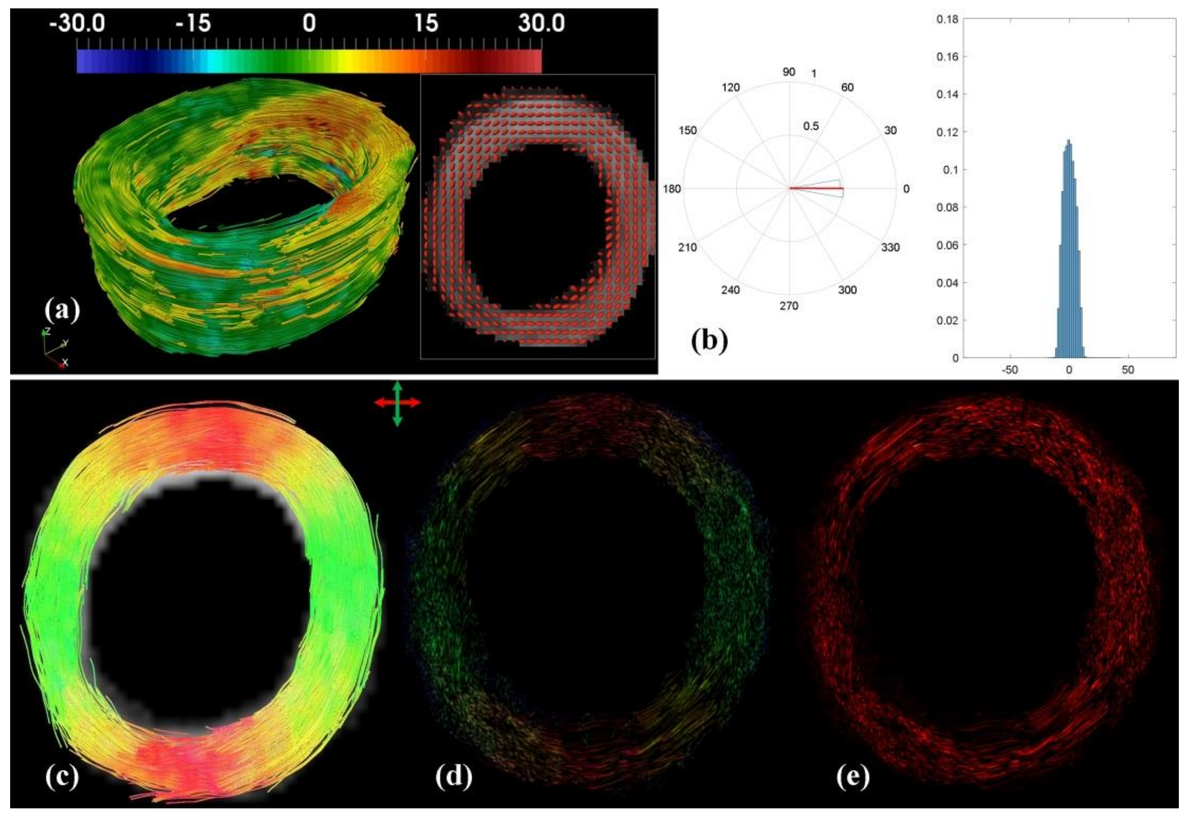


***Figure 4**: Reconstructed fibre tracts depicting the underlying microstructure of intact arterial tissue. (a) Projection of Helical angle on reconstructed fibre tracts, inset in (a) highlights the principal direction of the fibrous structure in terms of ellipsoids. (b), The circular and linear distribution of the helical angle. (c), Fibre orientation using directionally encoded colour. (d), Super-resolution Track Density imaging with directionally encoded colour. (e), Super-resolution Track Density Imaging at 0.0117 mm$^3$ resolution (reconstructed).*

## CONCLUSION

This study demonstrates the fidelity of DTI technique in mapping the microenvironment of the arterial ECM. The proposed acquisition and post-processing scheme may have the potential to provide further insights into the role of ECM in arterial disease progression in-vivo.

## REFERENCES


[1] Flamini et al., EURASIP J Adv Sig PR, (2010).
[2] Ghazanfari et al., *Biochem Biophys Res Co* 426, 54-58 (2012)
[3] Pierce et al., *Ann Biomed Eng* 38, 2447-2463 (2010)


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