In Vivo Differentiation of Two Vessel Wall Layers in Lower Extremity Peripheral Vein Bypass Grafts: Application of High Resolution Inner-Volume Black Blood 3D FSE

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Introduction: Intermediate-term vein bypass graft (VBG) failure (<24 months) occurs in up to 30-50% of grafts and is typically attributed to neo-intimal hyperplasia causing hemodynamically significant stenosis [1-2]. As VBGs adapt to the high-pressure arterial environment, significant physiologic remodeling of the lumen and some wall thickening occurs, but it remains a challenge to study this remodeling *in vivo* given the small caliber of VBGs (typical 0.5 mm wall thickness). Thus, despite its clinical importance, the pathophysiology of VBG failure, including the balance between physiologic and pathologic thickening, remains uncharacterized [1-2]. The enormous potential of MRI to impact VBG patient management and to understand VBG pathophysiology is hampered by currently achievable resolutions [3]. Using a high-sampling efficiency reduced field-of-view 3D FSE sequence that achieves T1- and T2-weighted (T1W, T2W) black-blood imaging with 0.3x0.3x2 mm uninterpolated resolution at 1.5 T [3], we observe a significant difference in wall area between T1W and T2W images of lower extremity VBGs (LEVBG), and show that it stems from the intrinsic MR signal decay characteristics of the media and adventitia as measured in LEVBG specimens and correlated to histology.

Methods: Six patients and two specimens obtained at surgical revision were scanned with a 1.5 T scanner (General Electric, Milwaukee, WI) 6 months post implantation. A high-sampling efficiency inner volume 3D FSE (IV3DFSE) sequence using non-selective refocusing pulses [3] was used for T1W (17ms TE, 1RR TR) and T2W (60ms TE, 2RR TR) imaging of a 3x3x3.6 cm volume (0.3x0.3x2mm resolution) of the LEVBG. Specimens were imaged in saline at room temperature with a CPMG multi-echo sequence [4] to obtain signal decays and subsequently stained with Masson's trichrome. Lumen and vessel wall areas were measured in *in vivo* images using direct planimetry (Vitrea 4.0, Vital Images, Minnetonka, MN) and compared using the exact Wilcoxon signed rank test. *Ex vivo* signal decays were fitted with mono- and bi-exponential decay models in Matlab (Mathworks, Natick, MA). Fits were compared using the ratio of variances (*F*-test). Inter- and intra-specimen agreement of fitted T_2 times used the unpaired *t*-test.

Results: A significant ($p<0.0001$) difference in wall area was found between T1W and T2W *in vivo* images (mean difference 6.8 ± 2.7 mm^2), with T1W wall area 1.67 ± 0.28 times larger than its T2W counterpart (Fig 1). Adventitial tissue, composed of collagenous material as determined by histology (Fig. 2), had a mean T_2 of 52.6 ± 3.5 ms (Fig. 2). Neo-intimal/medial tissue, composed of cells and proteoglycan matrix (Fig. 2), had a significantly ($p<0.0001$) longer T_2 (174.7 ± 12.1 ms, Figure 2). T_2 was similar between specimens in both tissues ($p>0.18$), indicating little difference in composition. It is noted that adventitial tissue exhibited statistically significant bi-exponential decay ($p<0.001$ vs. mono-exponential). The evident hypothesis that the outer wall boundary in T2W images extends only to the neo-intima/media while in T1W images it includes the adventitia was verified by comparing the mean ratio of signal intensities observed in the *in vivo* images between these layers to their expected values, based on the *ex vivo* fitted T_2 times, by copying the outer vessel boundary in T1W images to T2W images and vice versa to separate the two layers. The intensity ratios were found to be 0.84 ± 0.09 in T1W images (expected value 0.8) and 0.48 ± 0.10 in T2W images (expected 0.45).

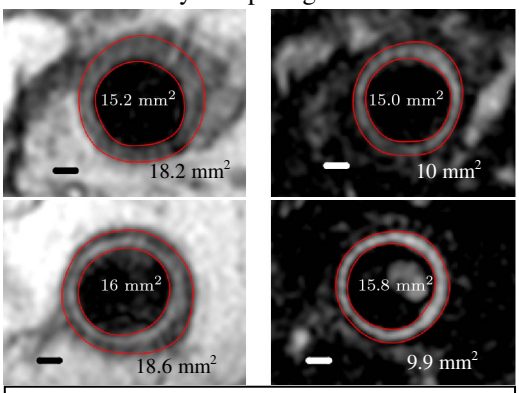

Figure 1 T1W (left) and T2W (right) images obtained in 2 LEVBG patients, demonstrating the larger vessel wall area (number in lower-right hand corner) in T1W compared to T2W images. Lumen measurements are shown inside the lumen. Horizontal lines indicate 1 mm markers.

Conclusion: An efficient IV3DFSE approach for vessel wall imaging enables sufficient spatial resolution to observe and quantify the adventitia vs the neo-intima/media in peripheral vein bypass grafts *in vivo*. Both layers are visible in T1W images, whereas only the media is visible in T2W images. This differential measurement is possible due to a 122.1 ms difference in T_2 between the two tissues. Exploiting differential properties in the T_2 relaxation of the more cellular components of the vein graft wall versus those of the more fibrous portion, one can discern the relative contribution of each of these layers to the complex and multi-factorial pathobiology of vein graft failure *in vivo*.

References: [1] Cox JL *et al*, Prog Cardiovasc Dis 1991;34:45-68. [2] Lau GT *et al*, Semin Vasc Med 2004;4:153-9. [3] Mitsouras *et al*, MRM 2008;59(3):650-4. [4] Poon CS *et al*, JMRI 1992;2:541-53.

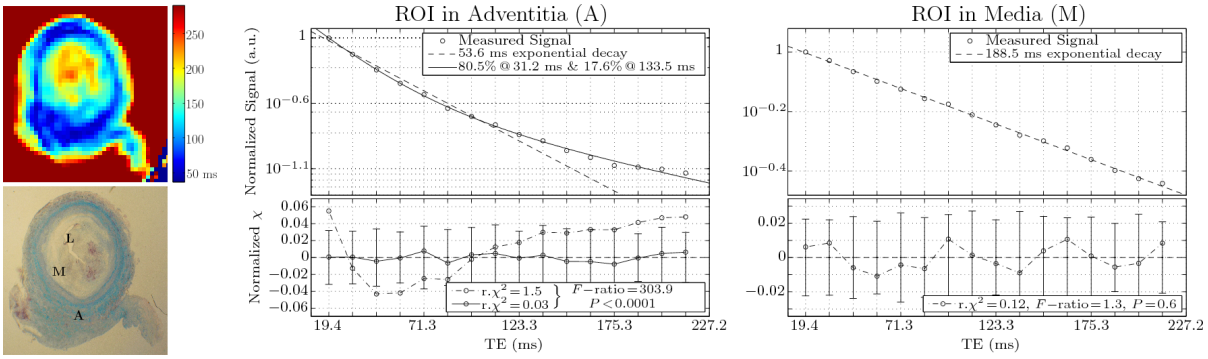

Figure 2 Fitted T_2 map (top left) and corresponding Masson's trichrome histology (bottom left) in one LEVBG specimen, and, example mono- and bi-exponential fits to the signal decay observed in ROIs selected in the adventitia and media. Vertical bars in normalized χ plots indicate mean signal observed in empty space (noise).