Does the presence of micro-vasculature alter the dispersion properties of shear waves? A rat aortic ring model at multiple frequencies using Magnetic Resonance Elastography.

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PURPOSE:

The presence of micro-obstacles can influence the propagation of the shear waves[1] and hence alter the apparent mechanical properties[2] as assessed via Magnetic Resonance Elastography (MRE). Disease or therapies can change the mechanical integrity and organization of vascular structures. If blood vessels represent a source for wave scattering (i.e represent micro-obstacles), MRE should be able to sense these changes. We follow the hypothesis that the presence of an underlying fractal-like stiff structure is capable of generating on the macroscopic scale apparent power law behavior in an otherwise non-dispersive material. To verify this hypothesis, multi-frequency MRE was performed to quantify alteration of the shear wave speed (C_s) due to the presence of vascular outgrowth using a rat aortic ring model. The model is based on the capacity of fragments of aorta to generate vascular outgrowth once cultivated in Matrigel[3].

METHODS:

Eighteen fragments of rat aortas were immersed in Matrigel and cultivated. At 1 day (D1, n=6), 5 days (D5, n=6) and 8 days (D8, n=6) after their inclusion, the fragments were imaged at 7T (Bruker, Pharmascan). T_2-weighted images (113µm in plane resolution) and 3D steady-state MRE at different 5 frequencies (ω=100, 115, 125, 135 and 150Hz; 300µm in plane resolution) were recorded[4]. The average wave speed C_s was calculated within a ring of ~900µm thickness around each aorta and normalized to C_{s0} of the corresponding Matrigel. Finally, the frequency evolution was fit to the power law model[5] $C_s \sim |\omega|^y$. After scanning, optical microscopy was performed on each fragment at D1, D5 and D8 to visualize the spatial organization of the outgrowths.

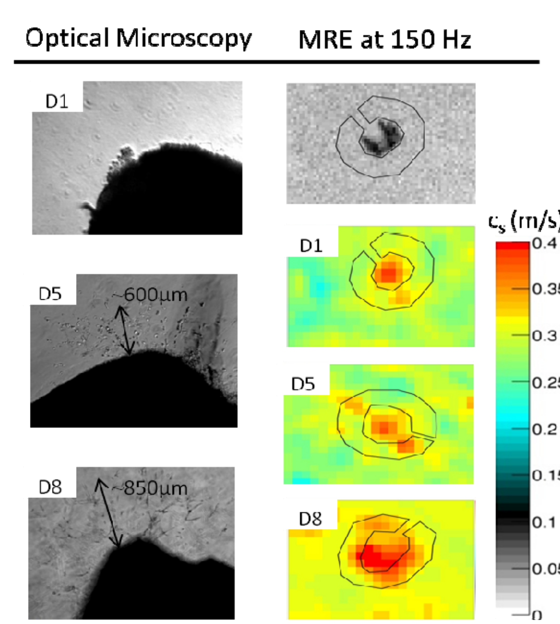

Fig.1: Left: Optical microscopy of one fragment of aorta at D1, D5 and D8. Right: Zoom of typical anatomical image and C_s maps at 150Hz obtained at different time points.

RESULTS:

At D1, no vascular outgrowth was visible while at D5 and D8 a rim of outgrowth was observed on the six fragments achieving an approximate thickness of 600µm and 850µm, respectively (Fig.1). Over the 5 frequencies, a general trend, showed an increase of the normalized C_s in the presence of the vascular outgrowth at D5 and D8 compared to D1 (without outgrowth). This increase is significant at 150 Hz (P=0.0008, Kruskal-Wallis test) (Fig.2). The study of the normalized frequency dependence from 100-150Hz revealed a power law behavior in the presence of vascular outgrowth at D5 and D8 (**y=0.06**±0.07, **y=0.10**±0.04, respectively) significantly different than that observed in the empty gel (**y=-0.02**±0.07, which is compatible with y=0; P=0.013, ANOVA test) (Fig.3).

CONCLUSIONS:

➔The vascular outgrowth acted as micro-obstacles that MRE was able to sense by measuring the shear wave speed C_s on the macroscopic scale. ➔ MRE could provide valuable information about changes in the micro-structure of biological tissue and especially blood vessels.

➔ Frequency dependence compatible with power law behavior is observed at D5 and D8. ➔ The dispersion properties of shear wave could represent a novel structural imaging biomarker of vasculature.

CLINICAL IMPACT:

As shown recently, anti-vascular therapies are influencing the shear stiffness of tumors and the change is correlated to changes in vessel density[6]. Apparently, the slope of the shear wave speed is influenced by the presence/absence of vessels and has thereby the potential to provide additional information about the spatial organization of the vascular bed.

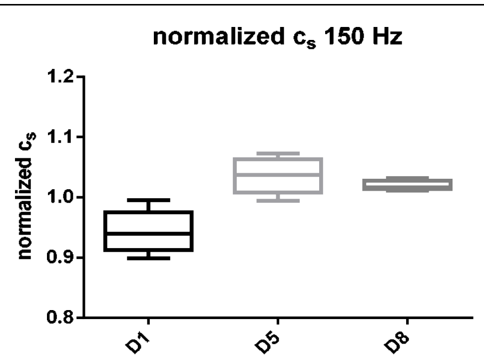

Fig.2: The vascular outgrowth generated by the aortic ring model at D5 and D8 altered the shear wave propagation by increasing the shear wave speed c_s compared to D1 (without vascular outgrowth) (P=0.0008, Kruskal-Wallis test).

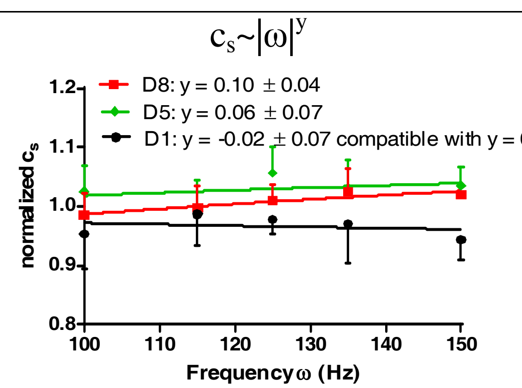

Fig.3: The study of frequency dependence revealed a power law behavior in the presence of vascular outgrowth at D5 and D8 significantly different than the one observed at D1 (P=0.013, ANOVA test).

REFERENCES: (**1**) O'Doherty, R.F. & Anstey, N.A. (1971) *Geophysical Prospecting*, 19, 430-458. (**2**) Lambert, S.A and al.. (2012) *ESMRMB*, Lisbon. (**3**) Nicosia, R.F. (2009) *J Cell Mol Med*, 13, 4113-4 (**4**) Sinkus, R and al. (2005). *Magn Reson Imaging*, 23, 159-165. (**5**)Bagley R. L. & Torvik P. J. (1983) *J. Rheol.*, 27, 201. (**6**) Juge, L and al. (2012) *Radiology* 264, 436-444**.**