Characterization of tumor vascularization in mice using MRE

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1. Introduction

Assessment and follow-up of neo-angiogenesis are major challenges in cancerology for the development of new therapeutical strategies. The micro-vascularisation of tumors is usually characterized via perfusion MRI. Perfusion parameters, however, are subject to several hypotheses on the compartment model. In order to develop new MRI methods for characterizing tumors in mice, we applied Magnetic Resonance Elastography (MRE), a recent technique for assessing the viscoelastic properties of tissues (1, 2). MRE supplies new physical parameters for improving the specificity in breast cancer diagnosis and liver fibrosis staging (3). Our working hypothesis is that alterations of tissue vascularization lead to significant changes in the viscoelastic properties.

2. Subjects and Methods

CT26 tumors were implanted on the flank of Balb-C JRJ mice (n=8). Five (primitive stage), Nine (angiogenic stage) and fourteen (angiogenic + necrotic stage) days after implantation, tumors were imaged *in-vivo* in a horizontal 7T scanner (Bruker, Pharmascan). Each mouse underwent the following imaging protocol: quantitative T1 and T2 relaxation maps, high resolution T2-weighted images for an accurate depiction of the anatomy (RARE sequence, 150µmx150µm in plane resolution) and finally 3D steady-state MRE with a vibration frequency of 1000 Hz. Reconstructed maps of Gd (elasticity) and Gl (viscosity) had an isotropic pixel resolution of $(300\mu m)^3$. Afterwards, tumors were harvested and histopathology (endothelial cells were marked with CD31) was performed to assess the details of their microvascular architecture by optical microscopy.

3. Results

Results show global tissue hardening in the tumors which results from the deposition of extensive extracellular matrix by the myofibroblasts (4). This distinctive appearance could be correlated with the epithelium to stroma ratio (5). From a morphological point of view, a hypersignal in T2-weighted image corresponded to higher viscoelastic parameters in the Gd and Gl maps. We also observed a ring-shape enhancement on the viscoelasticity maps at the angiogenic stage which corresponded to the expected neoangiogenesic area (see Figure 1 top line). Histopathological data were coherent with the MRE images and indicated enhanced neo-vascularization in the peripheral zone.

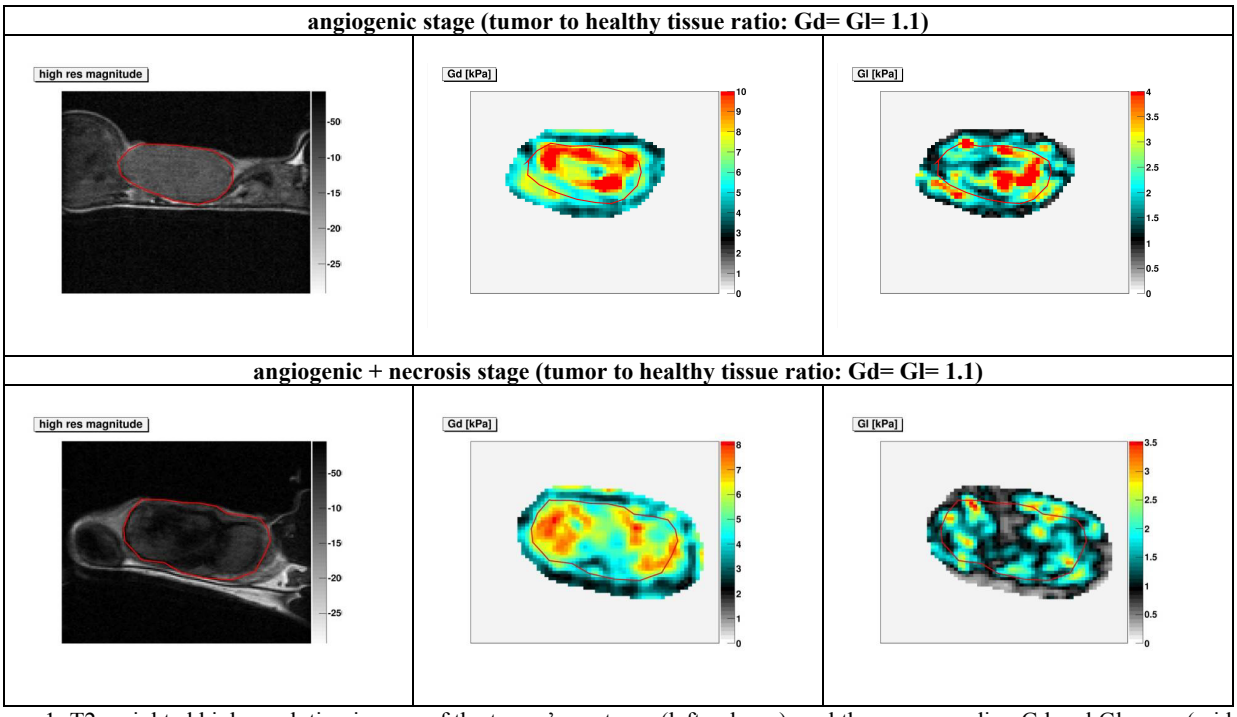

Figure 1: T2-weighted high-resolution images of the tumor's anatomy (left column), and the corresponding Gd and Gl maps (middle and right) for two examples at angiogenic stage (top line) and angiogenic+necrosis stage (bottom line).

4. Discussion/Conclusion

MRE experiments of *in-vivo* mice tumors were performed with high spatial resolution and the first results are very promising. There is a close correlation between alterations in the viscoelastic parameters, the neo-vascularisation and the necrosis state. In order to improve the protocol and add 3D physical parameters, we will record Diffusion Tensor Imaging (DTI) images in the future. Furthermore, we are currently studying the changes in viscoelastic parameters during anti-angiogenic treatment using the combretastatin (CA4P) to validate the use of MRE for the monitoring of new antivascular therapies.

5. References

1 - Sinkus R., Lorenzen J.,Schraders D., Lorenzen M., Dargatz M. and Holz D. High-resolution tensor MR elastography for breast tumour detection **2000**, *Phys. Med. Biol*. 45, 1649-1664.
2- Tanter M., Brecoff J., Sinkus R., Deffieux T., Gennisson JL. Fink M., 2007, Med.
3 – Huwart L, and al. Magnetic resonance elastography for the noninvasive staging of liver fibrosis.. **2008** *Gastroenterology* Jul;135(1):32-40. Epub 2008 Apr 4.
4- Rober A. Weinberg. The biology of cancer. **2007**. Garland Science
5- Keith D. Paulsen, Paul M. Meaney, Larry C. Gilman. Alternative Breast Imagning four model-based approches. **2005**. Springer Science.