

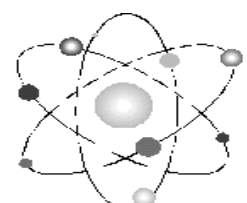
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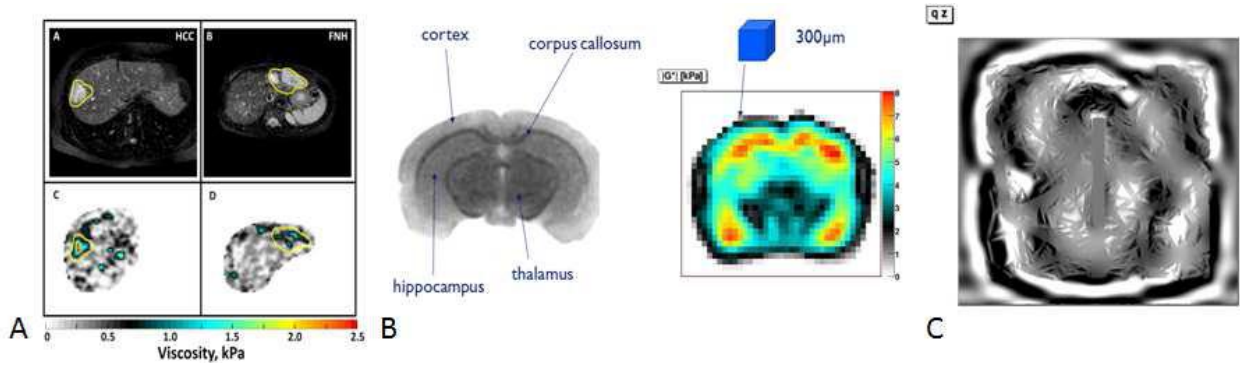
Viscoelastic Properties of Biological Tissue: Can Viscosity and Dispersion Properties be used for Characterizing Tumors?

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Great effort is currently undertaken to develop novel non-invasive imaging biomarkers for the characterization of malignant lesions as well as early prediction of response to therapy. Potential candidates in the field of MRI are methods sensitive to the structural integrity of tissue. For instance, diffusion weighted MRI has been identified by the European "Innovative Medicines Initiative" (IMI, <http://www.imi.europa.eu/>) as an important candidate for sensing cell death in the context of cancer drug therapies. Here, subcellular and cellular characteristics are indirectly assessed via the Brownian motion of water molecules.

More directly, viscoelastic properties can be measured non-invasively via MR-elastography. Here, low-frequency mechanical waves are sent into the body and visualized via motion sensitized MR sequences. This allows studying biomechanical properties (i.e. the complex shear modulus) preclinically but also clinically in humans. Recent results for liver tumors in humans (A) and multiple sclerosis in a mouse model (B) will be presented. Most interestingly, it seems for both cases that the shear viscosity is the more pertinent marker for demonstrating subtle architectural changes. Malignancy is typically accompanied by strong angiogenesis. The architecture of these newly created vessels differs markedly from normal vasculature. We therefore developed the hypothesis that the presence of a fractal-like hindering structure embedded in tissue (i.e. the vascular tree) could give rise to those observations. Therefore, architectural changes of the vasculature should lead to changes in viscoelasticity. First data from a colon-cancer model in mice under anti-vascular treatment do support this assumption. Furthermore it is shown, that the dispersion properties of shear waves are linked to the underlying micro architecture of the medium (similar to anomalous diffusion effects). Results from FEM simulations as well as real experiments with hard spheres embedded in soft gels following power-law grain-size distributions are presented. These observations would qualify MR-elastography far beyond a tool to perform in-vivo rheometry: it would give access to micro-architectural properties of tumor angiogenesis at the macroscopic imaging scale.





A: Shear viscosity of a malignant (HCC) and a benign (FNH) focal liver lesion. **B:** Shear viscoelasticity in the mouse brain as measured at 1000Hz. **C:** The presence of the vascular tree alters shear wave propagation at the microscopic level.

