PhD5

BIOQIC

Quantitative tissue characterization by multimodal imaging of tumor perfusion and effective-medium mechanical parameters in a preclinical model of lymphoma.

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Application Area: Perfusion, Flow, Cancer **Modality:** MRI, US, PAT **Related:** PhD 1-4, 9, 12

Background

The mismatch between perfusion and metabolism has been shown to provide a metric for the classification of tumors[1]. Perfusion changes the viscoelastic properties of tissues and can thus be quantified in vivo by mechanical parameter imaging such as MR elastography (MRE). This project is aimed at the development and experimental validation of methods for quantitative, noninvasive 3D imaging of perfusion and viscoelastic properties in lymphoma mouse models preclinical MR imaging and MRE. These methods will be complemented by state-of-the art Ultrasound (US) and Photoacoustic tomography (PAT).

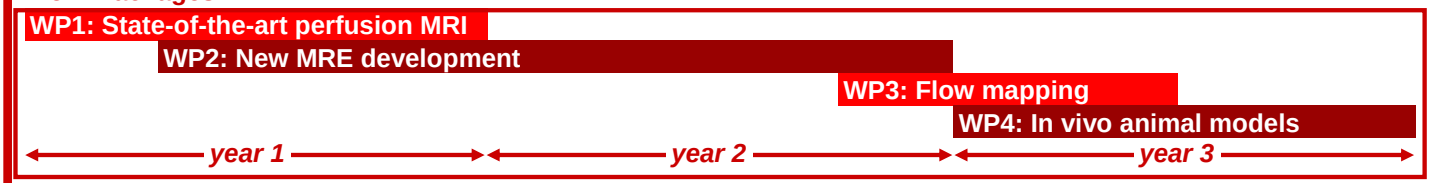
Hypothesis

Multimodal and noninvasive measurement of viscoelasticity and perfusion in tumors using MRI, MRE, PAT and US Doppler imaging will provide robust metrics for tumor characterization.

Methods

Methods for high-resolution preclinical MRE in small-animal high-field systems will be developed and validated in phantoms[2]. Therefore, actuators for efficient multifrequency shear-wave excitation in the mouse will be combined with ultrafast image acquisition based on echo-planar imaging sequences. MRE in a lymphoma mouse model will be compared to PAT and US Doppler measurements. PAT measures flow based on hemoglobin contrast[3] or the signal amplitude change due to the inflow of exogenous contrast agents[4]. The challenges are high-resolution mapping of viscoelastic constants, alignment of MRI and MRE with US imaging and demonstration of PAT flow measurements in deep tissue in vivo. The development and validation of comparative methods (healthy vs. tumor) are also of interest due to the potential for clinical translation.

Work Packages



WP1: Validation of existing perfusion MRI methods, to identify those best suited to measuring perfusion in lymphoma mouse models. This will involve a quantitative comparison with 3D US Doppler imaging.

WP2: New MRE methods for preclinical applications in the mouse will be developed and validated by US Doppler. This involves actuator development (based on piezo electrical devices), sequence development (single shot wave field acquisition) and inversion algorithms (multifrequency inversion).

WP3: The temporal and spatial distribution of systemically administered exogenous contrast agents and their effect on the PAT signal amplitude will be tested to quantify flow rates by PAT.

WP4: Following experimental validation in phantoms, promising methods will be evaluated *in vivo* in animal models.

Clinical Translation

While it is difficult to make predictions about clinical translation of preclinical methods within the duration of this project, we nevertheless believe that knowledge on the biophysical parameters in tumors help to improve imaging markers in future clinical examinations of cancer.

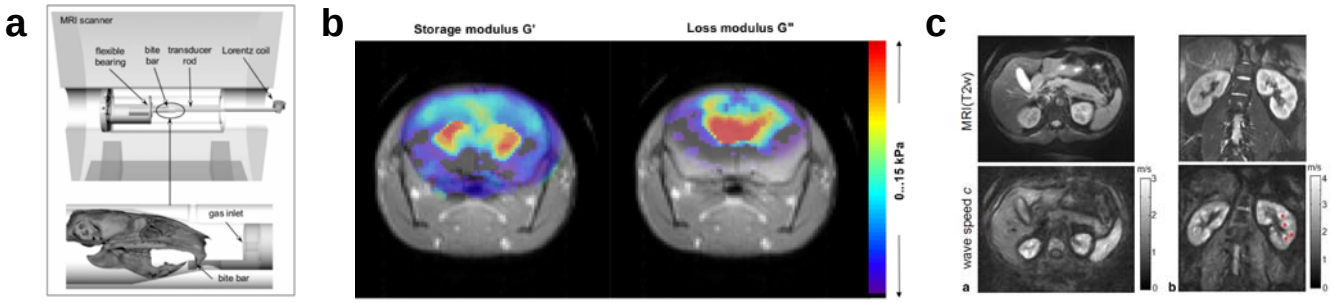


Figure: MR elastography of mouse and patients. a) Setup of the actuator based on Lorentz coils in a preclinical MRI scanner. Within the project, a piezo-driven actuator will be developed. b) Current resolution of MRE in the mouse brain. Details of viscoelastic constants are not resolvable due to the mono-frequency setup (from 5). c) High-resolution MRE of abdominal organs in healthy volunteers. Wave speed maps of the liver and kidney are shown demonstrating details in stiffness corresponding to anatomical structures (from 2)

Literature 1. Apostolova, et al (2014) Strahlentherapie und Onkologie. 190: 575-58, 2. Dittmann et al. Magnetic resonance in medicine 2016; 3. van den Berg et al. (2015) Photoacoustics. 3(3):89-99; 4. Lutzweiler et al. (2014) Optics Letters 39(14):4061-4064; 5. Hain et al. PloS one 2016;11(8):e0161179.