PhD11

BIOQIC

Magnetic imaging markers for quantification of inflammation beyond macrophage targeting

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Application Area: Cardiovascular **Modality:** MRI, MPI **Related:** PhD 4-8, 14, 15

Background

Detection of inflammation by magnetic nanoparticle (MNP)-based MRI usually exploits the fact that inflammatory processes e.g. in atherosclerosis are associated with an accumulation of phagocytic. However, inflammatory processes also cause major tissue structure alterations including accumulation of sugar-based components (glycosaminoglycans, GAGs) of the extracellular matrix (ECM). These can be targeted with eletrostatically stabilized (ES-) MNPs[1,2].

Hypothesis

ECM activation by inflammatory processes can be quantified based on the accumulation of ES-MNPs using in vivo MRI and other magnetic measurement methods like Magnetic Particle Imaging (MPI). ES-MNP accumulation correlates with immunohistochemical and biophysical tissue markers.

Methods

Animal models for inflammation (e.g. atherosclerosis), injection with ES-MNP, in vivo and ex vivo MRI, in vivo and ex vivo MPI, MPS, TEM, quantitative iron analysis, correlation with BIOQIC-available expertise in biophysical and mechanical tissue characterization, histological processing of tissue samples with focus on ECM components.

Work Packages

WP1: MRI in small animal models

WP2: Kinetics of MNP accumulation

WP3: Tissue mechanics

year 1 → *year 2* → *year 3*

WP1: Quantitative determination of ES-MNP uptake in inflamed tissue at various stages after disease onset and at one time point after injection of ES-MNP. Correlation with histologic assessment and with results of biochemical analyses with respect to ECM-composition. Correlation with other parameters of inflammation used as targets for imaging approaches, e.g. macrophage density, neovascularization.

WP2: Monitoring local kinetics of ES-MNP in unaffected and diseased tissue using MRI. Correlation of the results with histologic assessment of parameters for inflammation. Dependent on the success of particle synthesis, ES-MNP might also be available for detection and quantification by MPI. In this case MPI will also be performed for ES-MNP quantification in vivo and ex vivo.

WP3: The mechanical properties of the inflamed tissue will be assessed and compared with the values of normal reference tissues. Examinations will be performed in vivo by micro-MRE and ex vivo by indentation measurements[3,4].

Clinical Translation

Clinical translation will only be possible on a long time scale (translation category 4). However, this basic research project will lead to better understanding of inflammation imaging in the clinical setting and will shed light on the relationship between structural changes of the ECM and parameters measured by elastography.

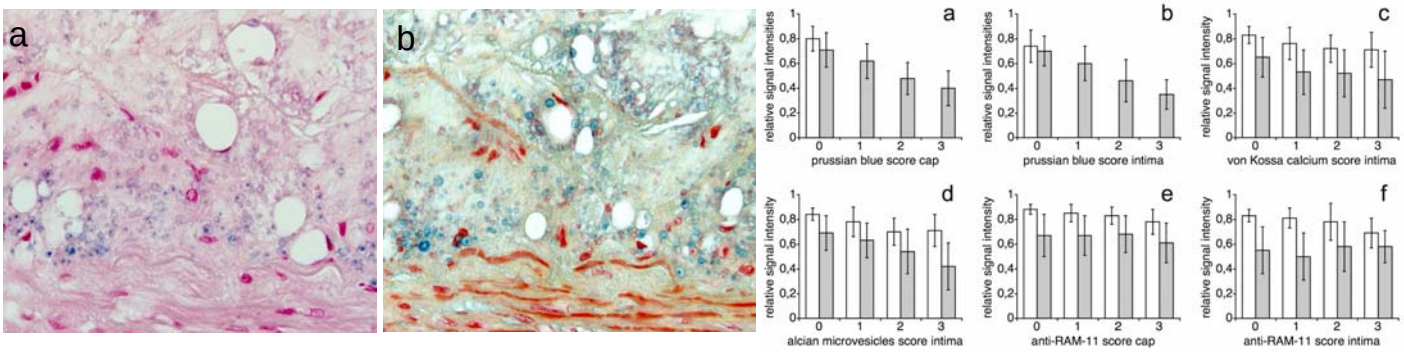

Figure: Blue stained ES-MNP (left a, prussian blue stain) co-localized with blue GAG-containing ECM-structures (left b, Alcian component of Movat pentachrome stain in inflammatory atherosclerotic plaque). MRI signal intensities show good correlation with scorers for iron content (right a, b) and GAG content (right d) but not with the scores for macrophage content (right e, f) of the plaque. There is also correlation with scores for calcifying sites (right c)[1].

Literature

1. Wagner, Schnorr, Ludwig, Stangl, Ebert, Hamm, Taupitz (2013) Int J Nanomedicine. 8: 767-779
2. Ludwig, Poller, Westphal, Minkwitz, Lättig-Tünnemann, Metzkow, Stangl, Baumann, Taupitz, Wagner, Schnorr, Stangl (2013) Bas Res Cardiol. 108: 328
3. Reiter, Freise, Jöhrens, Kamphues, Seehofer, Stockmann, Somasundaram, Asbach, Braun, Samani, Sack (2014). J Biomech 47: 1665-1674
4. Riek, Klatt, Nuzha, Muelle, Neumann, Sack, Braun (2011) J Biomech. 44: 1380-1386