In vivo monitoring of bacterial infections using high-field MR microscopy

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Introduction:

The increasing number of antibiotic resistant antibacterial strains requires not only the search for new anti-infective drugs, but also effective preclinical testing methods for potential new drugs and active compounds. Here MRI can deliver information with a high spatial resolution and a good soft tissue contrast in a non-invasive fashion[1, 2]. Therefore we investigate the possibility to monitor the time-course of the infection in a mice model by native (T_2) and marker (^{19}F) based MRI methods. The latter is based on the hypothesis that the ^{19}F-marker are internalized by macrophages [3] migrating to the site of inflammation.

Materials & Methods:

All experiments were performed on a 7 T small animal scanner using a double resonant birdcage coil (^{1}H/ ^{19}F). A mouse muscle abscess model (Balb/C, *Staphylococcus aureus* USA 300) was chosen, since it induces a strong localized infection. The ^{19}F-marker (PFC-emulsion 30% v/v; dose: 100ml) was injected at day 0 and day 2 through the tail vein. For every mouse the time course was monitored by measurements at day 0, 2, 5 and 8, after infection.
At each day a MSME (TE=6ms, TR=6s, NE=40, Resolution: (195 x 195)µm^2, FOV (2.5 x 2.5)cm^2, 10 Slices each 1mm) and a ^{19}F-CSI-SSFP sequence (N-Average=4, TR=13,6ms, Resolution(521x521x2000) µm^3, FOV (2.5 x 2.5 x 1.6)cm^3) were performed. ^{19}F-CSI data were overlaid on a proton image (RARE Rf=4, TR=2.5, TEeff=13.4ms) to get the anatomical context for the ^{19}F data.

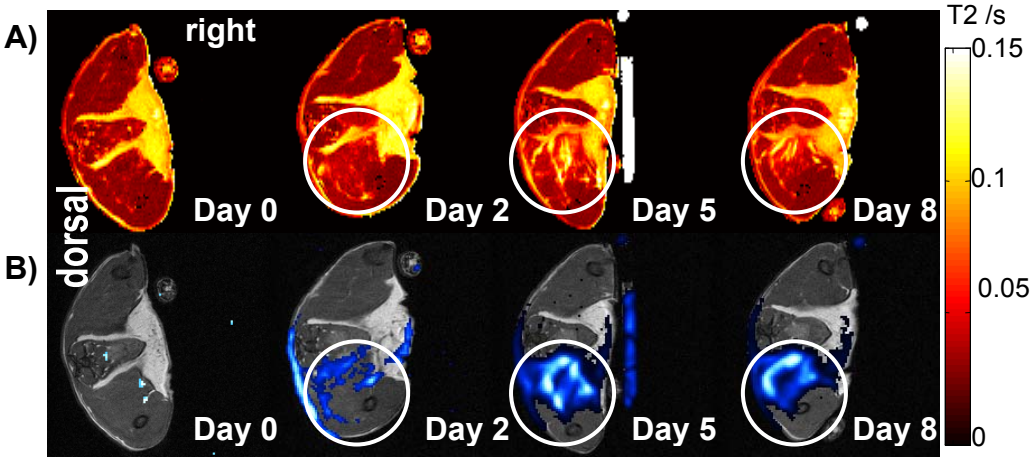

Fig 1.: Transversal slices through mice (Balb/C) thigh, left challenged with *Staphylococcus aureus* USA 300; injection of PFC-emulsion 15min before pathogens and at day 2.
A): T_2 maps **B):** ^{19}F-CSI overlay show marker content

Results:

Fig. 1 A) presents the T_2-maps for a transversal slice through mice thigh. It revealed an area of increased T_2 value (after day 2) in the infected thigh (left leg), which increases further over time. In contrast, no change of the T_2 value is visible in the right thigh, were 0.9% NaCl-solution was injected as reference. Fig. 1 B) presents ^{19}F-CSI data overlaid on an anatomical proton image. The transversal slices are the same as in Fig 1 A). At day 2 an accumulation of ^{19}F can be observed at the rim of the area with increased T_2 values. At day 5 and 8 the ^{19}F signal is also located in the centre of the area with increased T_2 values. No fluorine can be detected in the right thigh.

Discussion & Conclusion:

These results demonstrate the potential of MRI as an infection imaging method. The T_2-maps enable to visualize abscess formation in the mouse muscle abscess model even at early stages (day 2) of infection development. ^{19}F-CSI proved to be capable to visualize the area of infection/ inflammation. For the future a closer look have to be taken at the mode of accumulation of fluorine at the site of infection and to prove the working hypothesis of marker uptake by macrophages. In summary, MRI/ ^{19}F-CSI has the potential to provide new insights into the processes of host-pathogen interaction and to deliver important information for the evaluation of future anti-infective agents.

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References:

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