In-vivo monitoring of therapeutic effects on bacterial infection using high-field ^{19}F-MRI

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Introduction:

In the last few years, several methods have been developed to non-invasively monitor the time course of bacterial infections. In this context, MRI has proven its potential to image edema and infections by utilization of MR-markers [1,2,3]. Perfluorocarbon (PFC) markers internalized by macrophages migrating to the site of inflammation [2] allow background-free inflammation localization. The present study examined PFC markers to evaluate the efficacy of therapeutic measures in time course.

Materials & Methods:

All data were acquired on a 7 T small animal scanner using a double resonant birdcage coil (^{1}H/ ^{19}F). For all measurements, a mouse muscle abscess model (Balb/C, *Staphylococcus aureus* Xen29) was chosen. In this study, the mice were divided into three groups. One group was treated with oxacillin, one with a combination of oxacillin and lysostaphin, and a third group received sodium chloride to serve as a control (injections: 2h p.i, afterwards every 24hrs). With every group, a ^{19}F marker was injected at day 2 through the tail vein. On days 3 and 8, each animal underwent MRI scanning to obtain the time course information. During this, a ^{1}H-Turbo Spin Echo sequence (NA=2; Tf=4; TEeff=13.4ms; TR=2.5s; Resolution=(125 x 125)µm^2; FOV=(2.5 x 2.5)cm^2; 16 1mm slices) and a ^{19}F-chemical shift imaging (CSI) steady-state free precession sequence (NA=4; TR=13,6ms; Resolution=(521 x 521 x 2000) µm^3; FOV=(2.5 x 2.5 x 1.6)cm^3) were performed. The proton data were used to obtain by overlay the anatomical context for the fluorine data.

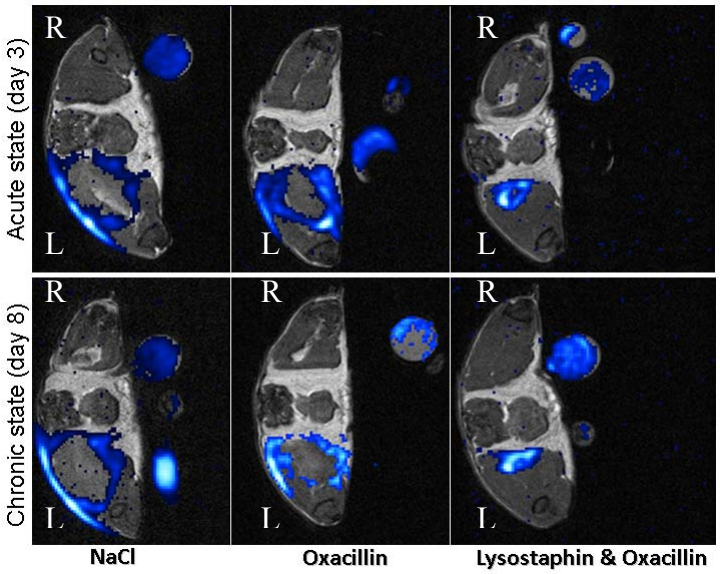

Fig.1: ^{19}F overlay images of transversal slices through mice thighs, showing the different treatments given after injection of *Staphylococcus aureus* in the left thigh. Control tubes containing PFC were placed beside the mice.

Results:

Fig.1 shows transversal slices through the thighs of three mice. In each case, the upper row shows the acute state and the lower row the chronic state of the infection. From left to right, the detected ^{19}F pattern is presented for mice treated with sodium chloride (left), oxacillin (center), and a lysostaphin/ oxacillin combination (right).
In each case, the ^{19}F signal is concentrated at the rim of the edema pattern. No fluorine, however, can be detected in the uninfected thigh. As displayed in the figure, the area surrounded by PFC decreases from left (sodium chloride) to right (*lysostaphin/ oxacillin*).

Discussion & Conclusion:

These results demonstrate the potential of ^{19}F-MRI to monitor therapeutic measures in animal models even at an early state (day 3) of infection. By delivering background-free information the edema pattern size, which condenses in the area surrounded by PFC, can be easily determined. Based on the acquired time course data it can be concluded that oxacilin as well as the lysostaphin/ oxacillin combination show a therapeutic effect on *S. aureus* infection. Furthermore the data also show that the efficacy of the combination is superior to oxacilin alone. Consequently ^{19}F CSI has proven to be useful for evaluating the efficacy of therapeutic measures in time course.

References:

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