Imaging of inflammation in the peripheral nervous system by ^{19}F MRI

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Introduction

Inflammatory cells play an important role in the pathophysiology disorders of the nervous system (1,2). Iron oxide-based contrast agents are commonly used to visualize neuroinflammation by magnetic resonance imaging (MRI). Unfortunately, local hemorrhages, blood pool effects and passive diffusion of iron oxide particles through a defective blood-nerve barrier can hamper the information gained (3).

In contrast to iron oxide contrast agents, ^{19}F markers have shown their potential in unambiguous imaging of labeled cells (4 5 6). In the present study, 3D ^{19}F chemical shift imaging (CSI) was applied *in-* and *ex vivo* to visualize macrophage infiltration in focal peripheral nerve demyelination using a lysolecithin model.

Materials and Methods

Lysolecithin in saline (2%, 10µl) was injected into the proximal left sciatic nerve of 7 male Lewis rats. When injected intraneurally, lysolecithin dissolves myelin sheaths followed by macrophage infiltration. At days 0 and 3 after surgery, a perfluoro-crown-ether (PF15C) emulsion (30% v/v, 500µl each injection) was administered intravenously.

MRI was performed on a 7T small animal scanner using a home-built surface coil adjustable to both frequencies. A home-built solenoid coil was used for *ex vivo* imaging and spectroscopy of the isolated sciatic nerves. *In vivo* ^{1}H 3D gradient echo (TE/TR: 2.9ms/60ms; FOV: 50x50x50mm; MTX: 100x100x100; NA: 1) and ^{19}F 3D steady-state free precession chemical shift imaging (ssfp-CSI) (7) (TAQ/TR: 10.1ms/13.5ms; spectral points: 64; MTX: 40x40x40; NA: 2) was performed five days after the surgery. Two ^{19}F SSFP-CSI scans, one with excitation pulse phase alternation and one without 180° phase shift alternation, were performed with otherwise identical parameters to minimize banding artifacts.

Following *in vivo* MRI, the rats were sacrificed and both sciatic nerves were excised. *Ex vivo* ^{1}H 3D Turbo Spin Echo (TSE) (TEeff/TR: 49.12ms/500ms; FOV: 40x15x15mm; MTX: 256x96x96; NA: 1) and ^{19}F 3D ssfp-CSI (TAQ/TR: 10.1ms/13.5ms; spectral points: 64; FOV: 40x15x15mm; MTX: 128x48x48; NA: 15) scans of both isolated nerves were acquired. For quantification, *ex vivo* ^{19}F NMR (TAQ/TR: 204.8ms/10000 ms; spectral points: 4096; NA: 60) of both nerves was acquired with a reference containing trifluoroacetic acid (TFA).

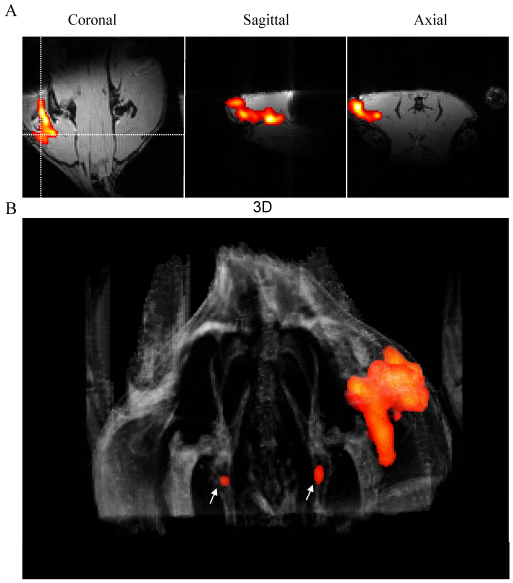

Fig.1) Results from in vivo scanning. A)From left to right: ^{19}F/^{1}H overlay images in the coronal, sagittal and axial directions. B) ^{19}F/^{1}H 3D overlay reconstruction. The arrows point to signal located in the lymph nodes. All images show that the ^{19}F signal is restricted to the left injured nerve and to the site of the skin incision.

Results

Fig.1 shows the *in vivo* results from one exemplary animal. Fig.1A/B show that the ^{19}F signal is restricted to the area of the left nerve as well as to the operation wound. Furthermore, in the 3D reconstruction, two signal areas can be seen that represent lymph nodes (arrows, Fig1.B). Fig2. shows the *ex vivo* results from the same animal as in Fig.1. The upper spectrum in Fig2.A shows that no signal could be detected in the untreated right nerve using ^{19}F NMR. However, a strong ^{19}F NMR signal could be observed in the left nerve (lower spectrum). The segmented 3D ^{1}H image in Fig2.B (left) shows the location of a reference tube (red), the right nerve (green), and the left nerve (blue). In the overlay, other than the reference tube, signal could only be observed in the treated left nerve (right image, Fig2.B).

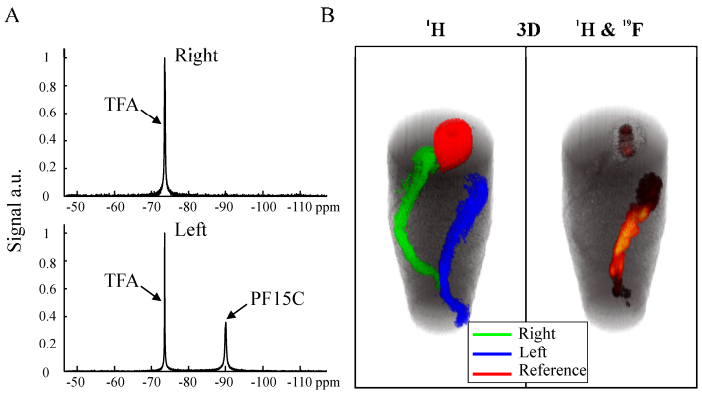

Fig.2) Results of ex vivo ^{19}F spectroscopy and ^{1}H/^{19}F imaging for the same animal as in Fig.1. A) Spectrums of the PF15C signal of the right/left nerve with a TFA reference. B) Left: 3D reconstruction of the ^{1}H data showing the location of the right (green)/ left (blue) nerves and the reference capillary (red). Right: ^{19}F/^{1}H 3D overlay reconstruction. All data show that PF15C signal could only be located in the left nerve.

Discussion and Conclusion

Using *in-* and *ex vivo* ^{19}F CSI, a strong signal was observed in the injured left sciatic nerves after systemic application of a PF15C emulsion on days 0 and 3 after surgery. Furthermore, no signal was detected on the right nerve, indicating lack of inflammation. These results were confirmed by histological findings in which macrophage infiltration into the left nerve was visualized while the right nerve was unaffected (data not shown). Thus, using 3D ^{19}F CSI, information about macrophage infiltration could be gained within acceptable measurement times. Besides spatial information, this technique allows simultaneous acquisition of spectral information that might be used for *in vivo* quantification in the future.

References

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