Investigation of USPIO-induced field inhomogeneities in a rat stroke model

A-M. Oros-Peusquens[1], M. Irkens[1], M. Schroeter[2], A. Saleh[3], S. Jander[2], N. Shah[1]

[1]Institute of Medicine, Research Centre Juelich, Juelich, Germany, [2]Department of Neurology, Heinrich-Heine University Duesseldorf, Duesseldorf, Germany, [3]Department of Diagnostic Radiology, Heinrich-Heine University Duesseldorf, Duesseldorf, Germany

Introduction

It has recently become possible to label a few cell types, including macrophages, with ultra small superparamagnetic iron oxide particles (USPIO). USPIO-labelled macrophages can be detected by MRI, enabling the visualization of cellular inflammation in subacute stroke [1]. Visualization is based on dramatically enhanced T2* relaxation in cells containing USPIOs [2], with a smaller, but detectable effect on T2. Furthermore, the effect of the nanoparticles on the relaxation rate of water is much stronger when they are inside cells than when suspended in solution [2].

The aim of this study was to investigate the field inhomogeneities created by USPIO accumulation *in vivo*, and their effect on the local R2* relaxation rate. This was performed on the rat brain *in vivo*, in two different stroke models: one of microvascular origin, induced by photothrombosis (PT), and one affecting the macrovasculature, induced by main cerebral arterial occlusion (MCAO). Additionally, a novel method for the display of field-inhomogeneity related information, enabling easier visualization, is presented.

Methods

Experiments were performed at 4T and 9.4T using Varian UnityInova consoles. The 160mm bore, 9.4T magnet, was equipped with 100mm-diameter gradients (270mT/m and 200ms rise time). The whole-body, 4T magnet, had a 120mm animal gradient coil insert (400mT/m and 170us rise time). A home-built animal handling system was used in both cases, including a heating pad and a 4cm diameter surface coil; additional experimental details are given in [3]. For T2* mapping, we employed a multiple gradient echo sequence in a variant termed QUTE [5,6]. The measurement parameters were: TR=2000ms, first echo TE=4.5ms (4T) or 6.5ms (9.4T), echo spacing =3.5ms, flip=90°, FOV=30x30mm, 256x256 pixels, slice thickness 1mm, 8 (4T) or 12 (9.4T) slices. Either 32 or 64 echoes were read out for a given phase encoding step. In a few cases, we interleaved a jittered set of 5 separate acquisitions, to obtain an equivalent echo spacing of 640µs. For each echo, a separate k-space was constructed. Following 2D image reconstruction, the sequence of images corresponding to increasing echo time can be used to plot intensity versus echo time for each voxel, describing the temporal behaviour of an FID from that voxel. Both odd and even echoes were used for mapping. The even echoes were time reversed before Fourier transformation to image space. An additional phase correction was necessary for the even echoes, and performed by interpolating the phase between the adjacent odd echoes. Linear interpolation would require $\varphi_i=(\varphi_{i-1}+\varphi_{i+1})/2$. In order to avoid the effect of phase rolls, requiring 2D phase unwrapping, we interpolated the angle by calculating its trigonometric functions. This is easiest to perform by doubling the value of the all phase angles for all time points. The interpolation reduces to calculating the angle $\varphi_{i-1}+\varphi_{i+1}$ via trigonometric functions, which are continuous (no rolls). For each voxel, a complex-valued FID was reconstructed. For the one-dimensional FID, the phase was unwrapped and corrected for the factor of 2. Following a one-dimensional Fourier transform of the complex FID, a spectrum was obtained.

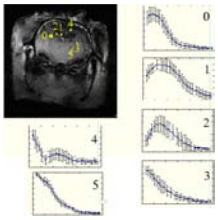

Fig.1 FID shapes at 9.4T. PT model, 2 days after induced stroke, 1day after USPIO injection. In this model, minimal USPIO infiltration is detected at this early time point [4].

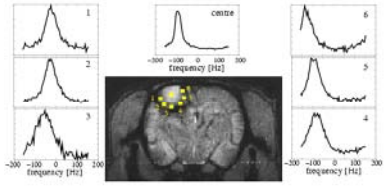

Fig.2 Shapes of the FT of the FID at 4T. PT model, 7 days after stroke, 1 day after USPIO injection. Large accumulation of macrophages at the edges of the lesion is identified by histology for the PT model at this time point following stroke [4]. Similar information is provided by the peak width: homogeneous region in the center of the lesion, large field inhomogeneity at the edges..

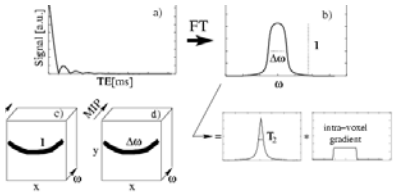

Fig.3 Schematic representation of different quantities reflecting the effect of internal field gradients.a)perturbed FID;b)its Fourier transform: convolution between Lorentzian shape and hat function (profile);c) peak intensity of the FT of the FID as a function of its frequency; d) same for peak width.

Results and discussion

A non-exponential decay of the intensity with echo time was observed in a large number of voxels, different from predictions for FID decay in a strong field regime [6]. As seen in Fig. 1, for a rat measured at 9.4T, the decay pattern ranges from nearly exponential to far from exponential, and resembles a sinc function in many cases. Intra-voxel field gradients are most probably the cause for the observed behaviour of the FID. Indeed, assuming a field inhomogeneity which can be described by zero- and first-order terms only, it is easy to show that its effect on the signal is to produce a shift in frequency and convolute the FID decay with a product of sinc functions, one in each voxel dimension. From the Fourier transformed FID, we can extract important information: centroid (field value), width (T2*) and shape (the field is strong enough to produce "profile" shapes in some cases). For a case where the accumulation of USPIO-labelled macrophages is known to be well localized, Fig. 2, we show examples of the shapes of the Fourier transform of the FID in the region. Two maps were produced, as shown schematically in Fig. 3: one of the peak intensity for each voxel (point c), one of the peak width (point d). The main field can be mapped as well, and the information is consistent with field maps produced from phase evolution with echo time (not shown). The maximum intensity projection (MIP) of the peak intensity maps shows a strong susceptibility weighting. This is due to the fact that, for voxels with equal magnetization, the intensity displayed in this maps has an additional weighting introduced by the width of the peak, which is influenced by field inhomogeneities.. Examples of peak intensity maps, and peak width maps are presented in Fig. 4-6, for different stroke cases.

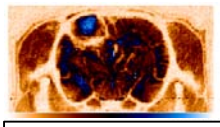

Fig.4 Peak intensity (left) and width (right). PT model, 7d post stroke, 1d USPIO. 4T.

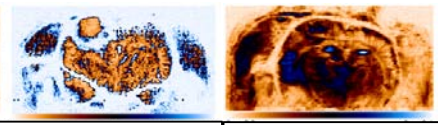

Fig.5 Peak intensity (left) and width (right). PT model, 2d post stroke, 1d USPIO. 9.4T.

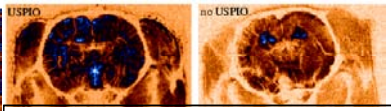

Fig.6 Peak intensities for MCAO stroke models, 7 days post stroke: left, with USPIO; right, without. Measurements at 4T.

Conclusions

A multiple gradient echo sequence has been used to study field inhomogeneities in the rat brain, following stroke and in some cases injection of USPIO. Besides providing quantitative information about the field, using the Fourier transform of the FID provides a very good way to visualise regions of enhanced field inhomogeneity. A careful study of the variety of the lineshapes is required and should allow one to extract quantitative information about intra-voxel field gradients.

References: [1]A.Saleh et al.,NMR Biomed 2004; 17: 163-169.; :[2] C.Bowen et al., Magn.Reson.Med.48:52-61(2002); [3] M.Schroeter et al., abstract submitted to ISMRM 2006;. [4] Shah et al., http://eenc.uni-leipzig.de/Shah.pdf; [5] Dierkes et al., Intern. Congr. Series 2004;1265:181-5; [6]J.H. Jensen and R. Chandra, Magn.Reson.Med.43,226-236(2000);.

.