3D Real-Time Magnetic Particle Imaging of Cerebral Blood Flow in Living Mice

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Introduction

Magnetic particle imaging (MPI) is a new tomographic imaging modality that directly and quantitatively images the concentration of iron oxide nanoparticles without anatomical background signal [1]. It combines high sensitivity [2,3] with the ability of fast volumetric imaging. Recently, 3D real-time MPI of the blood flow through the heart and lung of mice has been demonstrated [4] using a clinically approved MRI contrast agent. In this contribution, the cerebral blood flow in living mice is imaged, revealing dynamic information at a rate of 46 volumes per second.

Methods

The basic principle of MPI is described in [1]. In brief, the non-linear response of iron-oxide nanoparticles to an applied oscillating field generates higher harmonics of the excitation frequency, which can be detected over a broad frequency range. Spatial encoding is achieved using a *selection field* that confines the signal response to a small region, called the *field-free point* (FFP). The FFP is moved over the object of interest using *drive fields* in all spatial directions, thus allowing rapid 3D spatial encoding.
Brain MPI of three anesthetized mice was performed on an experimental scanner [4] shown in Fig. 1. The field of view of 16.8 x 20.4 x 16.8 mm³ was imaged at a repetition rate of 46 Hz. Total scan duration was 40 seconds. The iron particles (Resovist®, Bayer Schering Pharma AG, Germany) were bolus-injected into the tail vein at the beginning of the scans. Dosages were 56, 27, and 103 µmol(Fe)/l for the three mice, respectively. For human applications, a dosage of 40 µmol (Fe)/l is reported to be well tolerated [5]. The selection field gradient in AP direction was $dH_z/dz = 5.5\ T/m/\mu_0$. The drive field with frequencies (f_x, f_y, f_z) = (25.3, 26.0, 24.5) kHz and amplitudes $H_{Dx} = H_{Dy} = H_{Dz} = 18\ mT/\mu_0$ moves the FFP in a 3D box-shaped Lissajous pattern. The particle signal picked up by the receive coils (cf. Fig. 1) is amplified and detected in the frequency range between 50 kHz and 1 MHz. The voxel resolution was chosen to be 0.6 x 0.6 x 0.6 mm³. Reference MRI scans of the sacrificed mice were acquired with a mouse coil insert to a whole-body medical MRI scanner (Achieva 3.0T, Philips Healthcare, The Netherlands) using a turbo-spin-echo sequence. MRI resolution was 0.25 x 0.25 x 0.5 mm³.

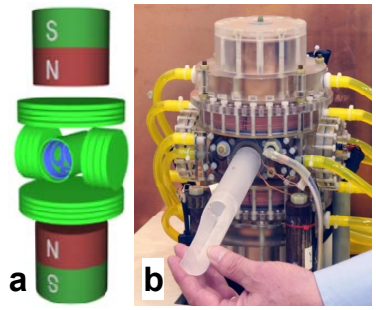

Figure 1: MPI scanner setup. (a) Two permanent magnets (red/green) generate the selection field that has a field-free point (FFP). The drive coils (green) move the FFP over the imaging volume. Dedicated receive coils (blue) pick up the particle signal. (b) Scanner and mouse support.

Results and Discussion

Figure 1a shows a sagittal slice through the 3D MPI data of mouse #1 at about 3 s after bolus injection, when the bolus is passing the brain. In the lower part of the image, an arterial signal is visible, while veins appear in the upper part. Figure 1b shows a manual fusion with the MRI data. Figure 1c shows a surface rendering of the MPI signal at the same point in time as in Fig. 1a and 1b. Colored arrows indicate five signal regions, which show different temporal signal evolution. The intensity of single voxels from each of these regions is plotted in Fig. 1d. While the arterial signal (red) is modulated with the heart beat, signal from the veins (green, blue) is rather smooth. From the modulated signal, a heart rate of 254 bpm is extracted by Fourier analysis. In the veins, the peak signal indicating the bolus passage occurs more than a second later than in the arteries, i.e., after perfusing the brain. In two lateral regions (magenta and cyan colored arrows), signal builds up during the bolus passage and persists until the mouse is removed from the scanner (Fig. 2d at 29 s). We speculate that this signal either corresponds to gray matter perfusion or perfusion of the masseters.
In the reconstructed images, regularization used to mitigate effects of limited SNR restricts spatial resolution to about 1.5 mm in AP direction. Higher SNR, e.g. achievable with dedicated MPI nanoparticles, would allow reconstructing a resolution on the order of ~ 0.5 mm, as expected for particles with a 30 nm magnetite core [6]. However, SNR can also be increased by averaging time frames and thus sacrificing temporal resolution. For dynamic evaluations like in Fig. 2d, the signal level could be increased by averaging over a region of interest instead of using single voxels.

Conclusion

MPI is capable of volumetric 3D real-time imaging of iron oxide nanoparticles at concentrations which are on the order of tolerable doses in human applications. The high temporal resolution allows discrimination between anatomical regions by differences in the dynamics of the particle signal. In combination with the ability to quantify particle concentrations, this adds valuable information, which is hard to obtain by contrast-enhanced MRI.

Acknowledgement

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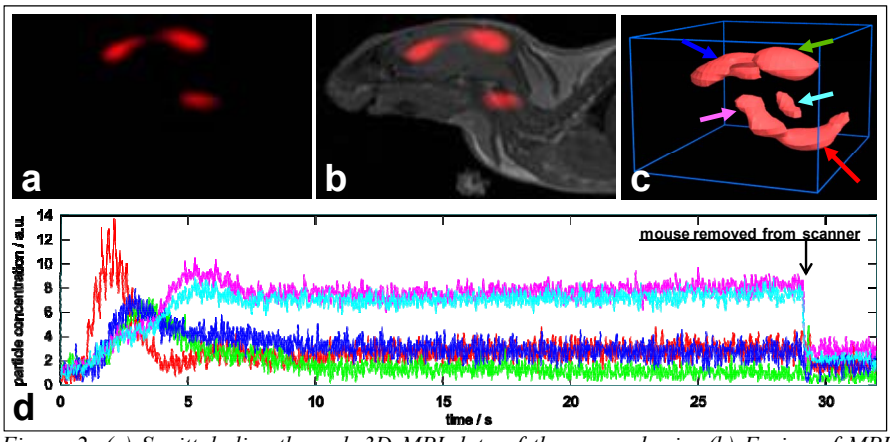

Figure 2: (a) Sagittal slice through 3D MPI data of the mouse brain. (b) Fusion of MPI data with MRI reference. (c) Surface rendering of 3D MPI data at the same point in time as shown in (a,b). (d) Signal evolution after bolus injection for single voxels located in the regions indicated by colored arrows in (c).

References

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