Selective positive contrast of subvoxel field-disturbers using off-resonance excitation

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Introduction: Positive contrast by means of selective excitation is a helpful way of visualizing objects of clinical interest, like iron-labeled cells, paramagnetic agents or labeled therapeutics. In regular gradient echo imaging, these entities cause negative contrast due to intra voxel dephasing effects which cannot be distinguished from signal voids caused by other effects, and is subjected to partial volume effects. Positive contrast can be generated by selectively exciting the off-resonance protons surrounding the paramagnetic material while suppressing the on-resonance background. This mechanism has been shown to be effective for e.g. iron-labeled cells [1] and gadolinium containing structures [2,3]. However, in these cases, contrast was based on macroscopic effects from relatively large clusters of paramagnetic particles occupying several voxels. In this work we will show that the same mechanism is also effective on a microscopic scale, i.e. we will show that it is feasible to selectively obtain signal from protons that reside in the vicinity of Holmium-166 loaded microspheres, used for internal radiation therapy [4].

Theory: The presence of HoMS gives rise to a distribution of dipole fields inside a homogeneous object. For an individual sphere, the field is given by $B_{r} = \frac{\gamma M_{HoMS}}{4\pi}$, with $M_{HoMS}$ being the magnetization of the HoMS material. The field strength at a location $r$ from the center of the sphere is given by $B_{r} = \frac{\gamma M_{HoMS}}{4\pi r^{3}}$. This results in a voxel intensity that is related to the concentration of HoMS. The resulting positive contrast can be manipulated by the user since the number of excited protons will depend on the excitation bandwidth and profile and on the frequency shift $\Delta f = f_{0} - f_{r}$.

Materials and methods: Phantoms: An agarose gel series (1% by weight) containing HoMS concentrations ranging from 0 to 7.0mg/ml was made in plastic spheres (38mm diameter). MnCl2·4H2O was added to the native gel to decrease the baseline T1. The Holmium content of the microspheres was 18.6% by weight resulting in a volume susceptibility of 0.880m (SI units) [5]. Experiments: 2D spin echo projection measurements were performed on a clinical 1.5-T MR scanner (Siemens, Healthcare, Best, The Netherlands) using an rf-excitation bandwidth of 1050Hz without slice selection gradients and various values of center frequency $f_{c}$ (TR=1.5s, TE=10ms, FOV=192x192mm², matrix=96x96, pixel size=2x2mm²). The center frequency of the phantom, $f_{phantom}$, was determined by the full width at half maximum (FWHM) of spectrum. Taking the frequency $f_{phantom}$ as a starting point for $f_{c}$, the excitation pulse was manually shifted with respect to $f_{phantom}$ in steps of 100Hz covering a total range of -700Hz to +700Hz. From the images, signal intensities were measured for the various concentrations of HoMS using an ROI the size of the samples. Simulations: Simulations were carried out using Matlab 7 (The Mathworks, Natick, Massachusetts). Spherical objects with radius R=15µm were placed at equidistant locations in a homogeneous 3 T B0-field. The inter particle distance was chosen in such a way that a certain concentration of objects was homogeneously distributed over the total volume. For a box with a lattice size equal to the distance between objects and a grid resolution of 2 µm, the frequency was determined for each grid element by calculating the total B-field induced by the objects plus the main field $B_{0}$.

Results: 2D coronal spin echo projection images of the phantoms are shown in figure 1 for three different center frequency offsets a) $f_{c} = f_{phantom}$ b) $f_{c} = +700Hz$, c) $f_{c} = -700Hz$. Concentrations of HoMS are indicated by the numbers near the samples. In the left image, the sample without HoMS shows the maximum signal intensity, followed by respectively 2.0, 3.9, 5.8 and 7.6 mg/ml. In the middle image, where the center frequency $f_{c}$ was shifted by +700Hz, the samples with the relatively high concentrations 5.8 and 7.6 mg/ml show high signal intensities and the sphere with 2mg/ml shows a bright area. This bright spot is likely caused by clustering of microspheres resulting in a locally high concentration. In the right image where $f_{c}$ was shifted by -700Hz, the samples containing concentrations of 2.0 and 3.9 mg/ml show high signal intensities whereas the other spheres display a very low signal. In figure 2, the measured intensities for $f_{c}$ between -700Hz and +700Hz are plotted for each concentration HoMS. Figure 3 shows a close-up of the large $f_{c}$-shifts to show that the signal intensities for the various concentrations intersect each other, reversing the contrast between concentrations. In figure 4, results of the simulations are shown. Excited proton fractions $S_{0}$ calculated for the various concentrations are plotted as a function of frequency offset. The resultant signal intensity profiles are similar to the experimental results, including asymmetric signal behavior around $f_{c} = f_{phantom}$. A difference is visible between simulation and experiments for the intersection point of the profiles. For the simulations, the profiles intersect one another at the same $f_{c}$-shift, while this is not the case for the experimental results.

Discussion and Conclusions: It was shown that it is feasible to excite protons that reside in the vicinity of HoMS inside a voxel by shifting the center frequency $f_{c}$ of the rf-excitation pulse. Due to this frequency shift, on-resonance protons having a Larmor frequency close to $\gamma B_{0}/2\pi$ are not excited and signal is only generated by protons strongly influenced by the dipole fields invoked by the microspheres. The total signal intensity of a voxel is related to the concentration HoMS in that voxel. The asymmetric behavior for positive and negative shift can be explained by the asymmetric frequency distribution in the vicinity of a magnetic dipole [7]. The resulting positive contrast can be manipulated by the user since the number of excited protons will depend on the excitation bandwidth and profile and on the $f_{c}$ frequency shift. In addition, the measured signal will be weighted by concentration a dependent T2 decay. These aspects lead to image contrast that is not straightforward to predict as illustrated by the images in figure 1 where a $f_{c}$-shift of +700 and -700Hz do not provide the same contrast. We therefore believe that the method is sufficient for qualitative purposes like depiction of the distribution of HoMS but more research needs to be done to elucidate the observations and investigate the potential of quantitative analysis.