Quantitative Real-Time Imaging for MR-Guided Internal Radiation Therapy

S. Winkelmann[1], J-H. Seppenwoolde[2], P. R. Seevinck[2], E-J. P. Vonken[2], T. Schaeffter[3], C. J. Bakker[2], O. Doessel[1]

[1]Institute of Biomedical Engineering, University of Karlsruhe, Karlsruhe, Germany, [2]ISI, University Medical Center, Utrecht, Netherlands, [3]Division Technical Systems, Philips Research Laboratories, Hamburg, Germany

Introduction

For MR-guided local delivery of drugs or agents, online feedback is required - preferably in a quantitative manner - to make guidance successful and steer the therapy. A clear example is the MR guidance of an internal radiation therapy [1,2] in which microspheres, loaded with the radionuclide Holmium, are administered intra-arterially, aiming at treatment of liver cancer by irradiation. As described in [1], the paramagnetic nature of (non-)activated Holmium-loaded microspheres (HoMS) allows the exploitation of MRI for visualization, as the HoMS act as a T2* contrast agent. During administration, it is important to determine the local biodistribution at the region of interest (for example a tumor). In that way, an interventionalist can first determine the selectivity of tumor targeting and then decide to continue or stop the delivery of HoMS. For example, when a local concentration has reached a sufficient level of radiation dose, no more HoMS should be administered to avoid unnecessary collateral damage to healthy tissue. Since the R2* ideally increases linearly with the concentration of HoMS [2], a suitably fast R2*-mapping technique would consequently offer *online* as well as *quantitative* feedback. In this study, we therefore investigate a fast simultaneous imaging and R2*-mapping technique, based on a radial multi-gradient echo sequence [3] for the online tracking and quantification of the biodistribution in the liver in real-time, during the MR guided administration of HoMS in two living pigs.

Methods and Materials

For fast simultaneous imaging and mapping, a radial multi-gradient echo sequence with 7 echoes was used. As described in [3], the undersampled k-space segments that correspond to different echo times (Fig. 1) are reconstructed separately into single-echo images (SEI) by regridding. This dataset is used for the computation of a high-resolution morphologic image by adding the first three SEIs. At the same time, all seven images are used for pixel-wise mapping of the relaxation rate R2* using a fast numeric approach [4]. The map is further processed, applying a median filter and a noise mask. The morphologic image and the R2*-map are displayed simultaneously in real-time. All imaging was performed on a clinical 1.5T whole-body system (Philips Achieva). First, the mapping approach was calibrated using a phantom, containing samples of HoMS in different concentrations suspended in agar gel. To simulate the treatment of a human patient, a low dose (Ho microspheres of 100mg) and, 38min later, a high dose (350mg HoMS) of Holmium microspheres were administered to the right lateral lobe of the first tumour-free domestic pig after selective fully MR-guided hepatic catheterization [5]. The quantitative biodistribution was dynamically monitored in an angulated sagittal slice during free breathing (7 echoes: TR=14ms, 240x240 Matrix, FOV=360mm, 120 profiles per SEI, slice=16mm, flip angle = 20°, time frame 1.98s). In the second pig, the distribution of two injections of 350mg HoMS was investigated in a transverse view (7 echoes –TR=13.8ms, 240x240 Matrix, FOV = 370x370mm^2, 102 profiles per SEI, slice=12mm, flip angle 25°, duration=1.8s). For reference, the result was compared to that of a (non real-time) fully-sampled cartesian multi-gradient echo sequence applied to the same geometry using 15 echoes (TR=30ms, duration = 7.7s). The reference map was computed using a non-linear least squares fit.

Results

The relaxivity of the HoMS was determined to be $r2^*=(88.5\pm4.4)\,mlmg^{-1}s^{-1}$ in the phantom experiment, which matches well the expected value of $r2^*=(86.8\pm3.5)\,mlmg^{-1}s^{-1}$ [1]. Fig. 2 illustrates the evolution of R2* during administration in 3 selected ROIs of the sagittal view (marked in the morphologic image of the last time frame. Assuming the linear relation $\Delta R2^*=r2^*\cdot C_{HoMS}$, the dynamic R2* pattern was translated into an estimate of the local concentration of the paramagnetic drug dose. The respiratory motion is reflected by the fluctuations of the graph. In the transversal view of the second pig in Fig. 3, the two liver lobes can be distinguished: only the right lateral lobe has been supplied with HoMS. The increase in R2* of $\Delta R2^*=(133-37)s^{-1}=96s^{-1}$ (Fig. 3) implies a mean concentration of $C_{HoMS}=1.1mgml^{-1}$. Quantification by the Cartesian multi-echo reference scan yielded a concentration of $C_{HoMS}=1.2mgml^{-1}$ ($\Delta R2^*=(138-36)s^{-1}=102s^{-1}$).

Discussion/Conclusion

The used technique strongly supported the *online* detection and quantification of the distribution of microspheres. The quality of mapping was good for both the high *and* the low dose and showed a convenient representation of the biodistribution. As discussed in [3], the number of echoes has to balance the need for short scan times and the range of R2* values detectable. With the choice of 7 echoes for this application, even the low dose could be detected and tracked with an adequate frame rate of only 2s. In addition to the convenient visualization of the biodistribution, the technique also allowed *online* quantification, assuming the ideal relationship between R2* and the concentration of the HoMS and neglecting nonlinearities coming from diffusion or clustering effects invivo [2]. Applied to a low and non-activated tracer dose of HoMS prior to the irradiation, the method would permit the quantitative analysis of the selectivity of the embolization, while it could provide online therapy control during treatment. The approach is therefore highly recommended for similar applications that demand the dynamic monitoring and quantification of paramagnetic drugs in MR-guided interventions.

References

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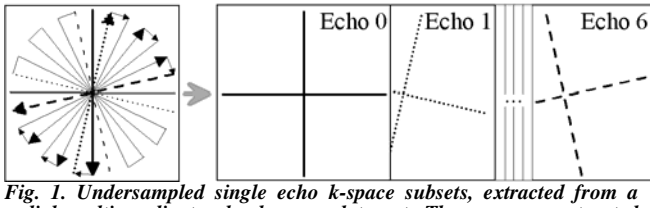

Fig. 1. Undersampled single echo k-space subsets, extracted from a radial multi-gradient echo k-space data set. They are reconstructed separately yielding images at different echo-times.

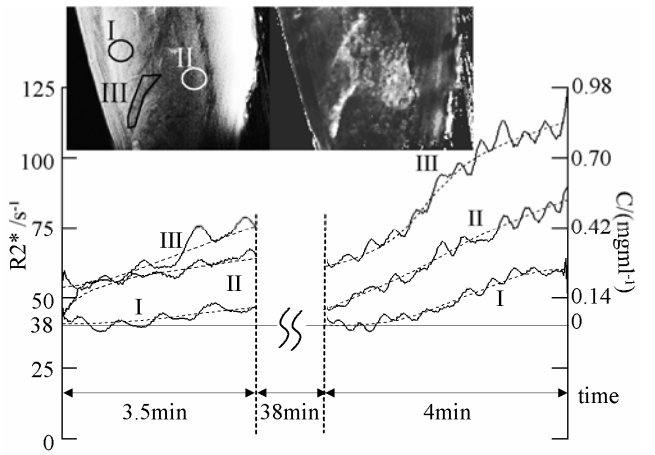

Figure 2: Dymamic study of the R2* evolution after the injection of a low (100mg HoMS) and a high dose (350mg HoMS) in three selected ROIs. The ROIs are marked in the last time frame, showing the morphologic image and the respective map of an angulated sagittal view of the liver. Given the relaxivity of Holmium (ca. 88.5 $mlmg^{-1}s^{-1}$), this offers the dynamic monitoring of local contrast agent concentrations (right vertical axis).

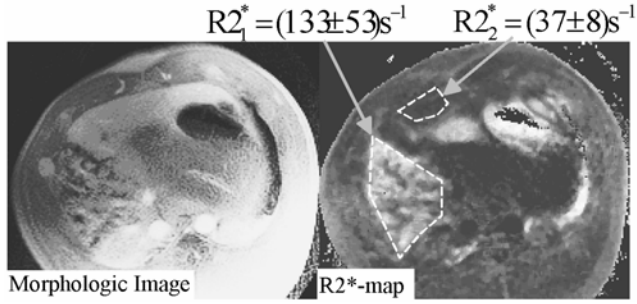

Figure 3: Transversal view of the second pig. The map facilitates to distinguish between regions containing contrast agent and those, which do not. In this case, only the right lateral lobe had been supplied with HoMS. In the other lobe the intrinsic R2* is measured. The R2* values, obtained from the Cartesian 15-echoes reference scan, agreed well ($R2_1^*=(138\pm61)s^{-1}$, $R2_2^*=(36\pm11)s^{-1}$).