Improved T2* based quantification of holmium-loaded microspheres in gels and liver tissue using multiple gradient echo sampling of FID rather than SE signals

P. R. Seevinck[1], J-H. Seppenwoolde[1], J. Zwanenburg[1], and C. J. Bakker[1]

[1]Image Sciences Institute, University Medical Center, Utrecht, Netherlands

Introduction- In transcatheter hepatic arterial embolization (THAE) with radioactive holmium-166 microspheres (HoMS) quantitative assessment of the radionuclide biodistribution is of major importance. Since holmium is strongly paramagnetic it can be used as a T_2^* contrast agent[1]. Previous studies have shown successful qualitative depiction of HoMS in vivo, however, initial attempts to use the T_2^* effect to quantify the highly inhomogeneous biodistribution of HoMS yielded a severe underestimation for higher HoMS doses[1]. In those studies, T_2^* relaxometry was done with multiple gradient echo (MGE) sampling of SE (MGESE) which was then considered the method of choice for low T_2^* quantification since it allows sampling of the SE peak at $TE_{gradient\ echo}$=0ms, which implies no dephasing due to static field inhomogeneities[1,2]. In the work reported here, we demonstrate by in vitro and ex vivo experiments that the observed underestimation can be attributed to the diffusion sensitivity of the T_2^* signal decay following a SE peak. This can be demonstrated with MGESE, and can be eliminated by using multiple gradient echo sampling of FIDs (MGEFID) rather than SEs, as this study demonstrates by a detailed analysis of the T_2^* signal decay behavior, conducted using an interleaved sampling scheme.

Materials & methods- ***Phantom experiments:*** An agarose gel HoMS dilution series with HoMS concentrations ranging from 4 to 15 mg/ml was created to provide a wide range of R_2* values. $MnCl_2.4H_2O$ was added to the native gel to increase the baseline R_2* value ($R_2{*}_{gel}$=29.7 s^{-1}) to mimic liver tissue. ***Ex vivo rabbit experiment:*** Known amounts of HoMS (20-120 mg) were administered successively to the hepatic artery of four excised rabbit livers. Quantitative MR imaging was applied after successive administrations. ***MRI*** Signal decay characterization of HoMS gel phantom: Ultradense sampling of FID and SE signals was applied using interleaved MGE sampling of FID and SE (iMGE(SE)) as presented before[3]. Quantitative imaging: MGEFID and MGESE were applied for quantitative imaging. For MGESE the echo time (TE_{SE}) was varied to study the influence of diffusion. The minimal echo time (TE_{min}) and echo spacing (ES) for MGEFID were kept as short as possible. Acquisition parameters are shown in Table 1. ***Post-processing:*** Odd echoes were used for weighted least squares (WLS) mono-exponential fitting to determine R_2* maps. Data with an SNR<3 were excluded from analysis to prevent the influence of Rician distributed noise. For MGEFID, the value of S_0 (S at t=0ms) was included in the fitting procedure to allow R_2^* determination of voxels displaying fast signal decay presenting less than 3 echoes with SNR<3. S_0 was determined in a ROI in the phantom/liver containing no HoMS.

Table 1. MR imaging parameters

Experiment	*HoMS gel phantom*		*Ex vivo rabbit liver*	
Parameters	**iMGEFID**	**iMGESE**	**MGEFID**	**MGESE**
Interleaves	10	10	1	1
Echoes	15	7 (15)	15	15
ES (ms)	1.42	1.44 (1.52)	1.55	1.55
ES_{eff} (ms)	0.14	0.14 (0.15)	1.55	1.55
TE_{min} (ms)	2.54	-	2.11	-
TE_{SE}(ms)	-	8.2;13.9;26	-	30.8
TR (ms)	500	500	500	500
Matrix	160	160	256	256
FOV (mm)	160	160	256	256
Slice (mm)	10	10	4	4
Flip (°)	90 °	90 °	90°	90 °

Results- Ultradensely sampled FID and SE signals of the HoMS phantom are presented in Figure 1. Only the MGEFID data showed a clear mono-exponential behavior, where SE data deviates from mono-exponential signal behavior with increasing TE_{SE}. At t=0ms the value of S_0 is displayed, which is used for WLS fitting of MGEFID data. The calibration curves presented in Figure 2 display a decreasing HoMS relaxivity with increasing TE_{SE} for MGESE. The relaxivities equal r_2^*=89 $s^{-1}mg^{-1}ml$, r_2^*=80 $s^{-1}mg^{-1}ml$, r_2^*=70 $s^{-1}mg^{-1}ml$, r_2^*=47 $s^{-1}m^{-1}ml$, for FID, $SE_{TE=8.2}$, $SE_{TE=13.8}$, $SE_{TE=26}$, respectively. R_2^* maps of ex vivo rabbit livers with HoMS administered are displayed in Figure 3. An underestimation is observed for MGESE data, specifically at higher R_2^* values which decreases for lower TE_{SE} (Fig. 3a-c). The highest values are determined in the R_2^* map of MGEFID data (Fig. 3d). In Figure 4 the integral HoMS dose administered to the ex vivo rabbit livers is plotted versus the injected amount of HoMS. The underestimation observed for the MGESE data was strongly reduced when using MGEFID.

Discussion & conclusions- T_2^* MGEFID data of homogeneously distributed HoMS in gel showed mono-exponential behavior, in contrast to the T_2^* MGESE data, which deviated from mono-exponential signal behavior with increasing TE_{SE}. The TE dependence of the MGESE signal, originating from diffusion, manifests itself as a damping effect on the T_2^* signal decay (motional broadening) and as a consequence decreases r_2^* relaxivity of HoMS (Fig. 2). Since HoMS is supposed to acts in the static dephasing regime according to the criterion $\delta\omega << \omega_D$ (ω_D=dyn. freq. scale ;$\delta\omega$=magn. freq. scale)[4], the damping phenomenon was not predicted by the relaxation regime[2]. However, a specific criterion for SE to be in static dephasing was defined in literature[5], which might help to explain the damping behavior that was observed for MGESE. This is currently being investigated. For the MGEFID data there was no dependence of diffusion observed. Although MGEFID strongly reduced the underestimation of HoMS present in the ex vivo rabbit livers compared to MGESE (Fig. 4), a small underestimation persists at higher HoMS doses, which might be attributed to clustering of HoMS in arterioles. We conclude that quantification of high R_2^* relaxation rates induced by HoMS can be done best using MGEFID, despite the supposed advantage of the inclusion of the SE peak for quantification[1,2]. The longer echo times of the SE allow diffusional motion to influence the R_2^* relaxation rate negatively, although the system was thought to act in the static dephasing regime. In quantification practice, this results in an underestimation of the true R_2^* relaxation rate and as a consequence of the determined amount of T_2^* contrast agent present. The findings in this study apply to HoMS, but could be relevant to other T_2^* agents such as (U/M)SPIO's as well.

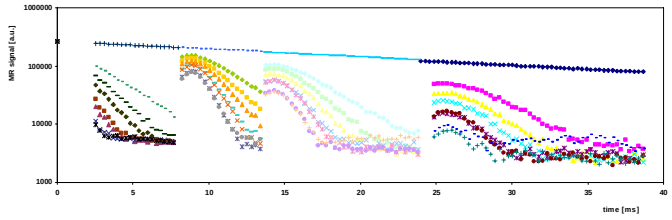

Fig. 1. Ultradensely sampled FID and SE (TE=8.2; 13.9; 26ms) signals on a logarithmic scale.

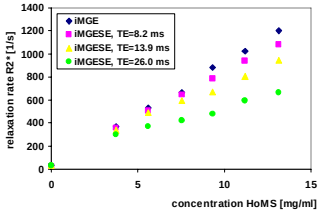

Fig. 2. R_2^* calibration curves of HoMS determined with MGESE and MGEFID

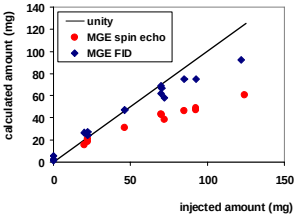

Fig. 4. Integral HoMS dose in rabbit liver determined with MGESE and MGEFID

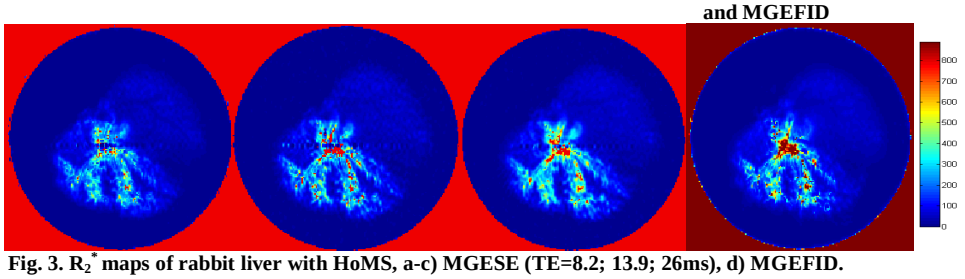

Fig. 3. R_2^* maps of rabbit liver with HoMS, a-c) MGESE (TE=8.2; 13.9; 26ms), d) MGEFID.

References

[1] Seppenwoolde JH, MRM 2005, 53: 767-84
[2] Liu W, 14th ISMRM 2006: 927
[3] Seevinck PR, 15th ISMRM 2007: 1786
[4] Yung KT, MRI 2003, 21: 451-463
[5] Yablonskiy DA, MRM 1998, 39:417-428