Relaxometry of new nanoparticles at 3 Tesla: Effect of core size and coating on r1, r2, r2*

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Introduction

Molecular imaging is one of the major interests in modern diagnostic medicine. New contrast agents with shaped functionality and strong relaxivities are desired. In this study new nanoparticles with different core sizes and coatings were examined and tested.

Material & Methods

Ironoxide nanoparticles doped with manganese were synthesized with different core sizes ranging from 5 nm to 7.5 nm. They were coated with Poly(maleic anhydride-alt-1-tetradecene) (PC) and chain end amino modified poly(ethylene glycol) (PEG). Additionally, a fraction of the as prepared hydrophobic nanoparticles was placed into lipid micelles. The core sizes of particles were measured by transmission electron microscope (TEM) (CM 300 UT, Philips). The concentration of the nanoparticle dilutions were estimated by atomar absorption spectroscopy (Perkin Elmer 2100). Dilution series were prepared. Five dilution levels were placed in a row in a water bath for each sample. In a second row a Resovist® dilution was placed serving as a control standard.

T1, T2 and T2* at 3 Tesla were measured with a clinical whole-body scanner (3T Intera, Philips Medical Systems, Best, Netherlands). For the estimation of T1 a Look-Locker sequence [1] (2D shot gradient echo: TR/TE=9.4/4.6ms, α=6°, TFE-factor 8 (3dummies), TI-prepulse delay 67ms, 60 phases with delay 5000ms, bandwidth 143Hz/pixel, FOV=200x200mm^2, matrix 208x208, slice thickness 5mm, scan time 4:52min) was used. T2 was measured by a multi-echo spin-echo sequence (TR/TE=2000/4.6ms, α=90°(180° refocusing), TSE-Factor 30, 30 echoes, bandwidth 546Hz/pixel, FOV=200x200mm^2, matrix 208x208, slice thickness 5mm, scan time 7min). T2* was estimated with a multi-echo gradient-echo sequence (TR/TE=500/85ms, α=30°, EPI=111 with no blips, EPI bandwidth 796Hz/pixel, FOV=200x200mm^2, matrix 224x224, slice thickness 5mm, NSA 3, scan time 5:35min). Localized volumetric shimming was applied for all sequences. T1, T2 und T2*-maps were calculated with an experimental software (relaxfitv1.7 [1] and T1fit, Philips Research Laboratories Hamburg). For the T2*-maps only odd echoes were considered meaning 56 echoes with an echo spacing of 3ms were taken into account. ROIs were drawn manually containing the center of the test tubes to minimize contamination by ringing effects. From the collected values the concentration independent relaxivities r_x (x= 1, 2 and 2*) were calculated using the equation

$$R_x = 1/T_x = 1/T_{x,dissolver} + r_x \bullet \text{concentration(nanoparticle dilution)}.$$

Results

The TEM-images show mono disperse nanoparticles (Fig. 1). An example of a calculated T2* map is shown in Fig.2. An overview of the numerical result is given in table 1. For both coatings the r2 and r2* are increasing with the core size. Interestingly, the opposite behaviour is found in the micelles doped with the PC-coated nanoparticles.

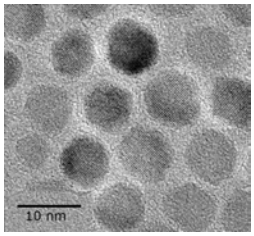

Fig.1: TEM of 7.5 nm sized mono disperse nanoparticles.

Coating	core / nm	r2* / [1/mMs]	r2 / [1/mMs]	r1 / [1/mMs]
PC	7.5	102	86	2,2
PC	6.5	73	63	2,8
PC	5	47	42	3,2
PEG	7.5	704	430	8,3
PEG	6.5	404	369	2,7
PEG	5	282	241	0,7
Micelles	7.5	693	219	0,3
Micelles	6.5	974	144	0,2
Micelles	5	1056	124	0,2
Resovist®	-	274	261	6,7

Table1: Relaxivites at 3T related to iron content of nanoparticles coated with PC and PEG. Micelles were doped with a hydrophobic pre-stage of the nanoparticles.

Discussion

It has to be taken in account that the analyzed relaxivities are related to the molarity of the iron content and not to the number of particles. Assuming the particles as ideal spheres it can be found that relaxivities related to the particle would increase with smaller core size since the surface area increases. Nevertheless, it can be assumed that the smaller r2, r2* of the PC coated particle related to the thicker coating that is used. The PEG coated particle allows the water to come closer to the core. A stronger interaction follows with a stronger dephasing. To understand the results of the doped micelles the amount of loading has to be clarified, so further examinations are necessary. Nevertheless high relaxivities were reached.

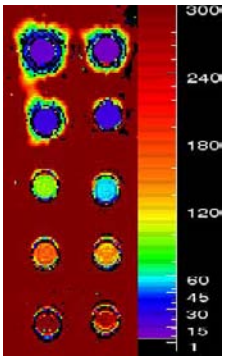

Fig.2: T2*-map in ms of a dilution series of resovist (left) and a 7.5nm PC-particle sample (right). Decreasing iron concentration direction buttom.

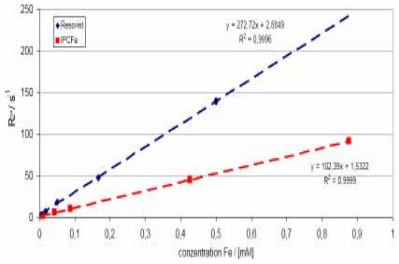

Fig.3: Concentration dependent R2* relaxivities curve with gradient and correlation coefficient corresponding to Fig.2.

Conclusion

The applied sequences together with the analyzing tools have shown to be an effective package to determine in-vitro relaxivities of new nanoparticles on a clinical 3T scanner. The influence of the core size and the coating on the relaxivities has been shown.

References

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[2] Dahnke H. et. al., Molecular Imaging 2005. Vol4, No3;261