Measurement of the Magnetite Nanoparticles Relaxivity During Encapsulation into PLA Carriers

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Abstract. *PLA are widely used in biomedical applications, where imaging modalities are very demanded. However, there is lack of information about contrast properties of the PLA-magnetite carriers in MRI. We measured the transversal relaxivity of the magnetite nanoparticles during the encapsulation into PLA spheres. The aim was to find a non-invasive method for particles tracking in different loading conditions. MRI measurements were performed on 4.7 T and 0.178 T systems, and the relative contrast, T_2, and r_2 of the PLA with encapsulated (interior) and non-encapsulated (exterior) particles were evaluated and compared. The results showed that these parameters can be used in determination of the magnetic nanoparticles encapsulation into PLA carriers, as well as in quantification of the particles loading rate.*

Keywords: Magnetite nanoparticles, encapsulation, PLA, MRI, relaxivity

1. Introduction

The polymer-based magnetic nanoparticles attract a big interest in biomedical applications, including MRI, hyperthermia, molecules separation, drug targeting, etc [1]. Many types of polymers have been used to synthesise these carriers, however only polylactide (PLA) based polymers are currently widely used in medical applications (tissue engineering). It is mainly because of their excellent biocompatible, biodegradable properties, and low toxicity [1]. Although the magnetic behaviour, as well as general properties of PLA-based magnetic carriers are quite well described [2], there is lack of information about contrast properties of such carriers in MRI applications, in regard to the encapsulation rate of magnetic nanoparticles. We studied the relative contrast, transverse relaxation time (T_2), and transverse relaxivity (r_2) changes induced by different loading factor of magnetite nanoparticles (MGNPs) into PLA carriers.

2. Material and Methods

PLA-magnetite carriers were prepared by a modified nanoprecipitation method as described in [3]. Briefly, 100 mg of PLA was dissolved in 10 ml of acetone to prepare the organic phase. An aqueous colloid was prepared by mixing a solution of Pluronic F68 as a stabilizing agent (25.6 mg in 5 ml) and 0.8 ml magnetic fluid (45 mg Fe_3O_4 / ml). Then, the organic phase was added drop-wise into the aqueous colloid and stirred vigorously for several hours to allow complete evaporation of the organic solvent at room temperature. A turbid nanoparticle suspension was formed. Not-loaded PLA nanospheres were prepared by the same way but without the magnetic nanoparticles. PLA samples were divided into three groups: (i) PLA without MGNPs, (ii) PLA with non-encapsulated MGNPs, and (iii) PLA with encapsulated MGNPs. Moreover, the last were prepared with different MGNPs input concentration (1, 2, 5, 7, 17, 30 mg/ml), resulting in diverse loading factor of MGNPs into

PLA. Relaxivity measurements were performed on 4.7 T system (VARIAN). Images were acquired with T_2-weighted Multi Echo Multi Slice (MEMS) sequence, TR = 81 ms, TE = 8 ms. Transverse relaxation time T_2 was obtained spectroscopically by CPMG-echo pulse sequence. For comparison, relative contrast measurements were performed also on 0.178 T system (ESAOTE), where images were acquired with standard T_2 weighted Gradient Echo protocol (TR = 3500 ms, TE = 22 ms). For all samples, relative contrast, transverse relaxation time T_2, and transverse relaxivity r_2 values were evaluated and compared.

Relative contrast is defined as follows:

$$RC = (I - I_0)/I_0 \tag{1}$$

where I_0 - signal intensity without magnetite nanoparticles (reference), and I - signal intensity with magnetite nanoparticles.

Transverse relaxivity r_2 is calculated as follows:

$$R_2 = r_2C + R_2^0 \tag{2}$$

where R_2^0 - transverse relaxation rate of in the absence of nanoparticles, R_2 - transverse relaxation rate in the presence of nanoparticles, C - nanoparticles concentration

Dynamic Light Scattering (DLS) method (Zetasizer, Malvern Instruments) was used to determine the hydrodynamic diameter (D_{hydro}) of loaded, as well as non-loaded PLA carriers.

3. Results and Discussion

We found that PLA itself have negligible influence to the relaxation properties of medium, as well as to the contrast properties of magnetite nanoparticles (Fig. 1). Relative contrast change for PLA carriers with non-loaded ("out"), and loaded ("in") magnetite nanoparticles with different input concentration is shown in Fig. 2. Although we are able to distinguish among loaded and non-loaded sample, and moreover among different input concentrations, there is no clear gradual pattern enable to determine the rate of nanoparticles encapsulation, based on the different input concentration.

Different situation is in Fig. 3 and Fig. 4, where we can see clearer gradual difference among loaded PLA carriers. Fig. 3 represents T_2 relaxation time decrease for both types of carriers. Different between 5 and 7 mg/ml for input concentration in loaded carriers is not so obvious, as for other concentrations (Fig. 4). For the highest input concentration (30 mg/ml) the encapsulation process probably starts to be saturated, and sample produce T_2 and r_2 values similar to sample with non-loaded particles ("out"). However, transverse relaxivity r_2 provides the best differentiation for the followed encapsulation process.

Hydrodynamic diameters of loaded, as well as non-loaded PLA carriers obtained by DLS method are shown in Table 1.

Table 1: Hydrodynamic diameters of MGNPs and PLA carriers.

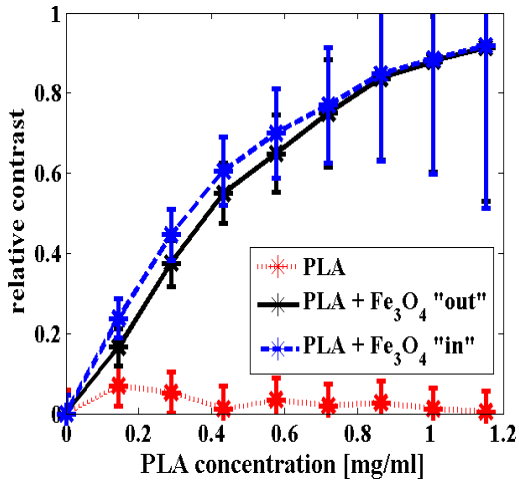|	MGNPs	out	in (1 mg/ml)	in (2 mg/ml)	in (5 mg/ml)	in (7 mg/ml)	in (17 mg/ml)	in (30 mg/ml)
D_{hydro} (nm)	71.5	146.1	167.1	139.85	138.85	122.6	205.35	173.35
PDI	0.137	0.11	0.062	0.18	0.17	0.1	0.1	0.1

Fig. 1. Comparison of relative contrast values of blank PLA carriers and PLA carriers with loaded ("in") and non-loaded ("out") MGNPs in concentration range of 0.01 – 0.08 mg/ml.
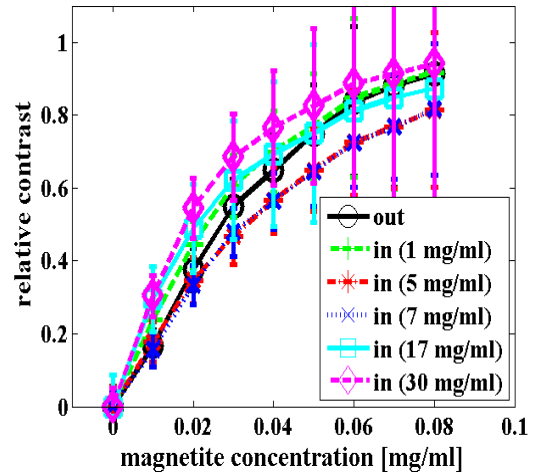

Fig. 2. Relative contrast values of PLA carriers with loaded ("in") and non-loaded ("out") MGNPs in concentration range of 0.01 – 0.08 mg/ml. Loaded samples are with different MGNPs input concentration (1, 5, 7, 17, 30 mg/ml).
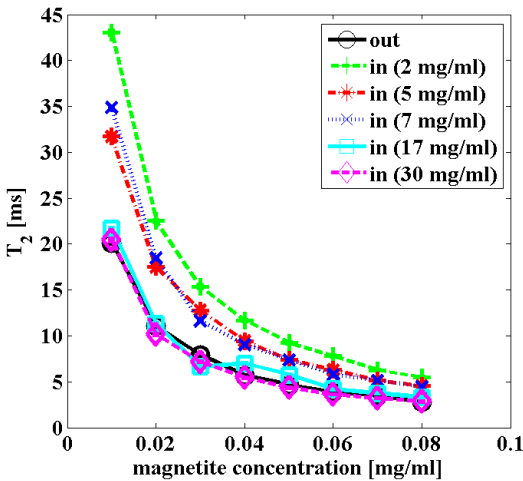

Fig. 3. T2 relaxation time values of MGNPs outside PLA ("out"), and encapsulated into PLA ("in") with different MGNPs input concentration (2, 5, 7, 17, 30 mg/ml).
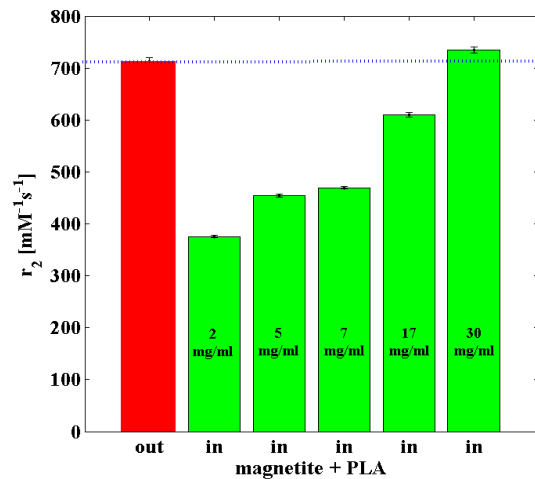

Fig. 4. Transverse relaxivity r2 values of MGNPs outside PLA (out), and encapsulated into PLA (in) with different MGNPs input concentration (2, 5, 7, 17, 30 mg/ml).

4. Conclusions

The studied MRI parameters (relative contrast, T2, r2) of the MGNPs encapsulated into PLA showed that we are able to distinguish between loaded and non-loaded particles, as well as to determine the rate of encapsulation from the relaxivity value. It can be used in biomedical applications to determine the rate of drugs encapsulation into carrier system, as well as for drug delivery, and drug release tracking.

Acknowledgements

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