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Gadolinium-labeled PLGA Nanoparticles for Magnetic Resonance Imaging

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To date, the main two classes of clinically used contrast agents for magnetic resonance imaging (MRI) are soluble paramagnetic gadolinium chelates and superparamagnetic iron oxide particles. While iron oxides predominantly increase T2-relaxivity and thus provide negative contrast, gadolinium chelates are often requested as they increase T1-relaxivity and enhance positive contrast. As particulate contrast agents are preferable due to a more favorable signal-to-noise ratio, the goal of our present work was the development of poly(D,L-lactide-co-glycolide) (PLGA) nanoparticles labeled with chelated gadolinium.

Briefly, biocompatible and biodegradable PLGA nanoparticles were prepared by solvent evaporation technique. 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) was covalently coupled to their surface using polyethylene imine (PEI) as a spacer. As free gadolinium ions are toxic, DOTA was chosen for complexation, which gives a highly stable gadolinium chelate. The resulting nanoparticles were characterized in terms of size, gadolinium content and relaxivity. Their mean diameter as determined by DLS was 103.1 ± 0.6 nm at a PDI of 0.102 ± 0.016. They had a gadolinium load of 183 µg/mg PLGA as quantified by ICP-OES. NMR relaxation studies at 1.5 T showed a T1-relaxivity (r1) of 12.5 mM⁻¹S⁻¹ and a T2-relaxivity (r2) of 15 mM⁻¹S⁻¹ at 37°C, which compares favourably with low-molecular weight agents and suggests suitability for in vivo use.

To conclude, PLGA nanoparticles have been successfully prepared and labeled with gadolinium chelates to enhance contrast in MRI. On this basis, future work is dedicated to site-specific targeted MRI, to the development of multilabeled particles for simultaneous use in different imaging techniques and to theranostics combining imaging and drug delivery.

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