

20. Internal structure of Gd-doped polymer entrapped-perfluorocarbon nanoparticles affects ^{19}F relaxation

Alvja Mali^{1,2}, Margot Verbeelen³, Paul B. White⁴, Alexander H.J. Staal³, N. Koen van Riessen^{1,3}, Cyril Cadiou⁵, Françoise Chuburu⁵, Olga Koshkina^{3,7}, Mangala Srinivas^{1,6,*}.

¹ Department of Cell Biology and Immunology, Wageningen University and Research, Wageningen, The Netherlands.

² Leiden University Medical Center, Leiden, The Netherlands.

³ Department of Tumor Immunology, Radboud Institute for Molecular Life Sciences, Radboud University Medical Center, Nijmegen, The Netherlands.

⁴ Institute for Molecules and Materials, Radboud University, Nijmegen, The Netherlands.

⁵ ICMR Equipe Chimie de Coordination, Universite de Reims.

⁶ Cenya Imaging B.V., Amsterdam, The Netherlands.

⁷ University of Twente, Sustainable Polymer Chemistry Lab, Enschede, The Netherlands.

* Corresponding author. E-mail: managala.srinivas@wur.nl

Introduction: fluorine-19 (^{19}F) magnetic resonance imaging (MRI) features one of the most investigated and innovative techniques for quantitative and unambiguous cell tracking. An important category of ^{19}F MRI contrast agent is based on paramagnetic resonance enhancement (PRE). A modification of perfluorocarbon (PFC)-loaded nanoparticles with paramagnetic chelates can enhance agent's functionality or create "smart" agents. **Method:** we explored if the formation of multi-core structure and the resulting nanoconfinement of perfluorocarbon affects the PRE of both ^{19}F -nucleus and proton. For this purpose, we compared the behavior of fractal multicore PFCE-PLGA nanoparticles with core-shell nanocapsules. As gadolinium-agents we used two different hydrophobic gadolinium chelates that differ only in the length of a hydrophobic linker and a hydrophilic chelator (Prohance). **Results:** our results show that the structural properties play an important role for ^{19}F MR relaxation. Indeed, paramagnetic chelates affected both longitudinal and transverse ^{19}F relaxation in fractal multi-core nanoparticles, but not in core-shell nanocapsules, where only an increase of the transverse relaxation rate could be detected. Moreover, different from conventional emulsions, since the polymeric matrix remained water-permeable, proton enhancement additionally was observed in MRI. Additionally, multicore nanoparticles showed sensitivity to various pH environments in terms of transverse relaxation time while preserving their physiochemical stability. This effect was not observed with the core-shell nanoparticles. **Conclusion:** Co-encapsulation of PFC with paramagnetic chelates in nanoparticles for ^{19}F MRI can lead to multifunctional imaging probes. The importance of the internal structure of the nanoparticles in terms of ^{19}F relaxation properties was also demonstrated by dependence on the pH conditions.