7. **Long-term stability of PLGA-PFCE nanoparticles**

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Introduction: Perfluoro-15-crown-5-ether (PFCE) encapsulated poly(lactic-co-glycolic acid) (PLGA) nanoparticles (NPs) are used for unambiguous identification and quantification of labelled cells through ^{19}F Magnetic Resonance Imaging (MRI)[1]. ^{19}F MRI has high specificity due to the natural lack of fluorine in biological tissues[2].

PLGA-PFCE nanoparticles have been developed in our group for about 10 years[3], and can be produced at GMP grade[4] for clinical cell tracking. We aim to study stability of PLGA–PFCE NPs in terms of PFCE content, diameter and polydispersity index (PDI) over time.

Methods: PLGA-PFCE NPs were prepared by a mini-emulsion method[3]. Briefly, PLGA and PFCE together constitute the organic phase which was added to the water phase (polyvinyl alcohol) and emulsified by probe sonicator. Following overnight solvent evaporation, NPs were washed several times by ultracentrifuge and freeze dried. Post-preparation, diameter and PDI were determined by Dynamic Light Scattering (DLS) and PFCE content was established using ^{19}F Nuclear Magnetic Resonance (NMR). NPs formulated 2016 onwards were re-characterized recently using the same methods to study stability in terms of PFCE content, diameter and PDI. Fluorescence in ICG-encapsulated NPs were determined using a microplate-reader.

Results: Typically, PLGA-PFCE NPs have values of 191±31 nm diameter, 0.12 PDI and 30±8% PFCE content. Average change in diameter, PDI and PFCE content of re-characterized NPs were around 17 nm, 0.044 and 5% respectively. 4-year old NPs still exhibited fluorescence.

Conclusion: PLGA-PFCE NPs stored at -20˚C are stable for a minimum of 6 years in terms of diameter, PDI and PFCE content making them reliable imaging agents for cell tracking.

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References:

1. Swider E, Staal AHJ, van Riessen NK, Jacobs L, White PB, Fokkink R, Janssen GJ, van Dinther E, Figdor CG, de Vries IJM *et al*: **Design of triphasic poly(lactic-co-glycolic acid) nanoparticles containing a perfluorocarbon phase for biomedical applications**. *Rsc Adv* 2018, **8**(12):6460-6470.

2. Staal X, Koshkina O, Srinivas M: **In vivo 19-fluorine magnetic resonance imaging**. *Fluorine in Life Sciences: Pharmaceuticals, Medicinal Diagnostics, and Agrochemicals* 2019:397-424.

3. Srinivas M, Cruz LJ, Bonetto F, Heerschap A, Figdor CG, de Vries IJ: **Customizable, multi-functional fluorocarbon nanoparticles for quantitative in vivo imaging using 19F MRI and optical imaging**. *Biomaterials* 2010, **31**(27):7070-7077.

4. Swider E, Daoudi K, Staal AHJ, Koshkina O, van Riessen NK, van Dinther E, de Vries IJM, de Korte CL, Srinivas M: **Clinically-Applicable Perfluorocarbon-Loaded Nanoparticles For In vivo Photoacoustic, (19)F Magnetic Resonance And Fluorescent Imaging**. *Nanotheranostics* 2018, **2**(3):258-268.

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