The Marvel of Advanced Radiolanthanides: Next-Generation Radio-Optical Nanoparticles in Modern Nuclear Medicine

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1. Authors

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2. Context of the project (800 characters max. including spaces)

The aim of this project is to design, synthesize, and characterize innovative nano-radiopharmaceutical tools for theranostics. They are based on a new generation of luminescent upconversion nanoparticles (UCNPs) composed of rare-earth elements, radiolabelled with radionuclides to provide combined diagnostic and therapeutic function. The project focuses on radiosynthesis of UCNPs containing ^{169}Er, followed by preliminary *in vitro* evaluation. These nanoparticles enable photoluminescence imaging under near-infrared (NIR) excitation and, when doped with radioactive isotopes, can be applied in nuclear medicine techniques such as PET or SPECT. This dual-modal imaging offers complementary diagnostic information and highlights UCNPs' potential as multifunctional theranostic agents.

3. Results and discussion (1000 characters max. including spaces)

Five syntheses of ^{169}Er-doped **$NaYF_4$:Yb,Er** UCNPs were done: three core (**$NaYF_4$:Yb,Er-^{169}Er** = C-UCNP-^{169}Er) and two core-shell (**$NaYF_4$:Yb,Er@$NaYF_4$:Yb,Er-^{169}Er** = S-UCNP-^{169}Er), with activities of 5 and 20 MBq and nearly 100% radiolabelling efficiency (Figure 1). All obtained samples exhibited green luminescence under NIR laser excitation, indicating formation of hexagonal-phase nanocrystals. Thin-layer chromatography analysis confirmed high stability of both C-UCNP-^{169}Er and S-UCNP-^{169}Er in reaction mixture (oleic acid/1-octadecene), cyclohexane, water, and serum-containing cell medium, even after 144 h of incubation at 37˚C (Figure 2). Experiment with SK-BR-4 cells revealed that 28.7±0.6% and 47.8±3.9 % of C-UCNP-^{169}Er internalized after 24 h at concentration 1 and 0.1 mg/mL, respectively. Whereas for S-UCNP-^{169}Er at 0.5 and 0.05 mg/mL it was 32.0±4.1% and 57.8±4.0%.

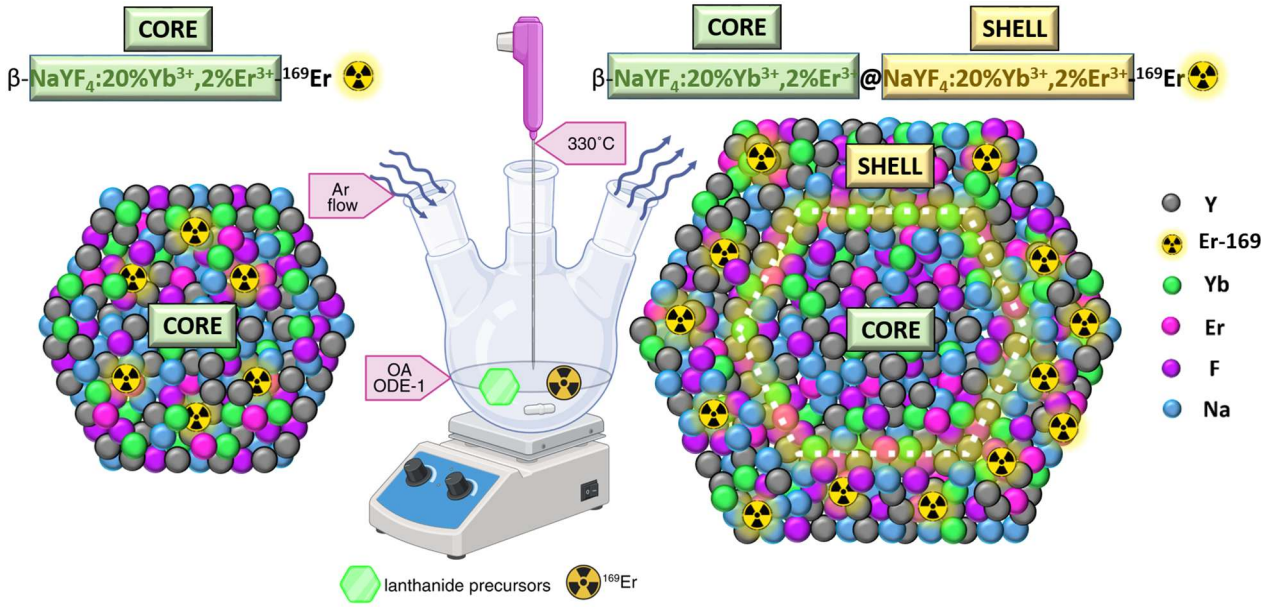

Figure 1. Scheme of core and core–shell synthesis of ^{169}Er-doped upconverting nanoparticles.

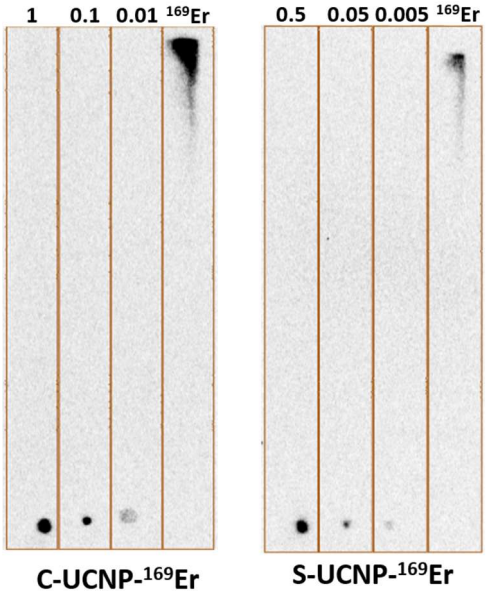

Figure 2. Stability of ^{169}Er-labelled C-UCNP (1, 0.1, 0.01 mg/mL) and S-UCNP (0.5, 0.05, 0.005 mg/mL) at various concentrations in a serum-containing cell culture medium after 144 h.

4. Conclusions (800 characters max. including spaces)

Synthesis of ^{169}Er-UCNPs by thermal decomposition method was successfully carried out to establish a radiosynthesis protocol. Proper physicochemical characterization, including morphological analysis using electron microscopy and photoluminescence measurements, will be performed once the isotope has decayed. Excellent stability of ^{169}Er-UCNPs was observed in various media. Initial *in vitro* studies demonstrated high internalization of UCNPs, however, surprisingly better internalization was observed for lower concentration This might be due to aggregation of UCNPs with time at higher concentration. Collectively, these initial results demonstrate that ^{169}Er-UCNPs can be synthesized with high yield and stability, however, more studies are required.

5. Involvement of the PRISMAP services (600 characters max. including spaces)

The project has greatly benefited from PRISMAP, which produced and supplied the rare radioisotope ^{169}Er, highly relevant and interesting for our experiments. This isotope, not readily available in Poland, was used for radiolabelling rare-earth–based upconversion nanoparticles (UCNPs)—to the best of our knowledge, for the very first time in Poland and, globally, as one of the first attempts to radiolabel this type of UCNPs for theranostic applications.

6. Feedback to PRISMAP (600 characters max. including spaces)

PRISMAP is a great initiative providing unique opportunities for researchers in radiochemistry and radiopharmacy. All PRISMAP team members I have corresponded with were very kind, responsive, and supportive throughout the entire process. Moreover, the rare isotope was provided free of charge, which is highly appreciated, although the transport costs were relatively high, making access difficult without additional funding. I understand that it is a very specific and restricted type of transport, especially by air, but delivery costs could be challenging to manage for another batch or isotope.

7. Publications and other dissemination activities (conferences etc.)

At this stage, no results have been published yet, as obtained data are still insufficient. However, we expect that in the future with more studies on ^{169}Er-UCNPs, we would obtain more results and prepare a presentation for a scientific conference. Moreover, if similar radiolabelling and *in vitro* studies can be achieved with other similar radioisotopes, we may prepare material publication. We are still waiting for the physicochemical characterization of the ^{169}Er–radiolabelled nanoparticles after radioisotope decay.

Appendix 1. Dissemination guidelines for user projects as agreed in the signed User Agreement

Dissemination rules

Only user groups that are allowed to disseminate the results which they have generated under the project may benefit from the access, unless they are working for SMEs.

For each user group project, a publishable project summary and a publishable summary of the results will be published on the European Union Horizon 2020 PRISMAP project website www.prismap.eu. The publication of results in journals or at conferences is strongly encouraged.

To ensure the long-term sustainability of the PRISMAP initiative, proper recognition of the contributing facilities, their services and the involved persons is necessary. All participating PRISMAP facilities shall be acknowledged in the publication. Acknowledgement and co-authorship of PRISMAP staff members who participated in the experiment shall be considered according to the research field best practices and verified with the PRISMAP Technical Manager before any publication.

The user group shall contact the PRISMAP Technical Manager 30 days prior to submission of publications or other communications of results that were obtained by making use of services provided by PRISMAP (radionuclides delivered or medical services provided). The Technical Manager will communicate to the user group the list of PRISMAP facilities and persons that have contributed to each specific project and the way this contribution must be acknowledged in the publication/communication or where co-authorship is required to reflect specific scientific contributions.

Users must comply with Horizon 2020 dissemination rules (i.e. acknowledge that their work was financially supported by the European Union's Horizon 2020 Research and Innovation Programme by including the following acknowledgement: "This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008571 (PRISMAP)"), and grant open access to resulting publications and related data.

Dissemination shall take place only once legitimate interests regarding intellectual property have been safeguarded. A maximum publication delay of 90 days may be granted for this purpose.

Acknowledgements

The list of name(s) to be mentioned in the acknowledgment section is sent to the technical manager by the main contact of the involved facilities.

A general sentence will be added by the corresponding author of the article (user side):

"The authors would like to thank the members of the PRISMAP consortium and of the PRISMAP user selection panel, coordination and management team for their advice and support."

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