Novel chelators for scandium radionuclides for theranostic applications in a prostate cancer model

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

Theranostics in nuclear oncology describes subsequent imaging and treatment of diseased tissue with radionuclides. Diagnostic or therapeutic isotopes are coupled to a vector with high affinity for tumour cells. The use of a single element is beneficial to ensure identical biodistribution, for that, a promising pair is $^{44/47}$Sc for PET imaging and β-therapy. The half-life of ^{44}Sc (3.97 h) makes minibodies or diabodies (5 h) an ideal vector match, the labelling of these molecules with $^{44/47}$Sc is however challenging since the 'gold standard' chelator, DOTA, is only complexing Scandium above 70 °C. To address this mismatch, the design of a novel chelator was aimed in this project.

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

Ligands L_{1-3} were investigated for the labelling behaviour of ^{47}Sc at 37 °C, suitable for minibody/diabody labelling. At physiological pH, L_1 (86.6±13%), L_2 (52.1±4.9%) and L_3 (98.8±1.6%) showed superior labelling over gold standard DOTA (51.9%, Figure 1A). When incubated with FBS (90%), [^{47}Sc]ScL_2 and [^{47}Sc]ScL_3 showed high stability (82.6±1.6% and 100% RCP after 24 h), whereas L_1 was insufficient in maintaining ^{47}Sc, with only free metal being present. As L_3 showed the most favourable complexation behaviour, the *in vivo* compatibility of the [^{47}Sc]ScL_3 system was investigated by SPECT/CT and *ex vivo* biodistribution in healthy mice. Free [^{47}Sc]ScCl_3 was used as a control showing widespread biodistribution with uptake in the liver and spleen, whereas [^{47}Sc]ScL_3 showed rapid clearance with no undesired uptake 2 h p.i (Figure 1B). The full *in vivo* compatibility was confirmed by the analysis of the urine metabolites, revealing only a single species (95.2±1.3% RCP, 2 h p.i.).

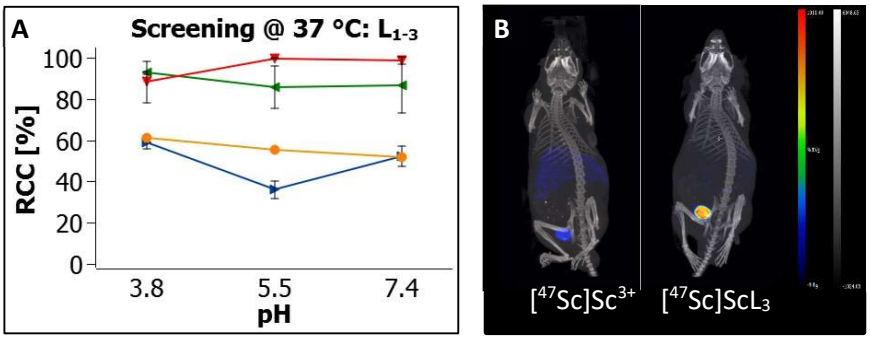

Figure 1. : A) RCC for the reaction of [^{47}Sc]ScCl_3 and L_1 (◀), L_2 (▶), L_3 (▼) and DOTA (●) vs pH at 15 min and B) Static SPECT/CT images of healthy mice 2 h p.i. of [^{47}Sc]Sc-PBS and [^{47}Sc]ScL_3

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

Given the limited production of scandium radionuclides in the UK, Sc-47 made available by PRISMAP was crucial to the project's success. Further, close coordination with the PRISMAP helpdesk facilitated a straightforward project design and promoted networking among the PRISMAP community. The forged relationship will allow us to explore the project further and, as one of the first studies in the UK to use Sc-47, will stimulate additional study throughout the UK's radiochemistry research community. This demonstrates the significant influence PRISMAP had in addition to the data produced.

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

Our experience with PRISMAP was thoroughly positive. The supply of Sc-47 played a key role in the successful completion of the project; further, the advice provided by the PRISMAP helpdesk helped with an optimised project design. The close coordination with the PRISMAP technical manager and the production site NCBJ/POLATOM allowed for flexible deliveries according to the experiment plan and guaranteed a successful project completion.

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

Preliminary results of this project have been presented at the EPSRC-funded CDT Smart Medical Imaging at King's College London. Since final experiments using the Sc-47 provided by PRISMAP are still ongoing, the final data analysis is still pending. Once finished, the results will be presented on multiple occasions, beginning with the final PRIMSAP event on November 19th. The publication of the results is in preparation.

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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