User project report

User project identifier: 1729020993_aniX3

User project title: Manganese-52 for applications on multiple coincidence detection in Positron Emission Tomography

Main contact of the user group: Dr. P. MOSKAL

PRSMAP facility in charge: Hevesy Lab, DK

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008571 (PRISMAP). This document reflects only the view of the author(s). The Agency is not responsible for any use that may be made of the information it contains.

1. Authors

Professor Pawel Moskal, Full Professor Jagiellonian University, Poland

Professor Kuangyu Shi Chief Medical Physicist, Inselspital Bern, University of Bern, Switzerland

Professor Luis Mario Fraile, Full professor Complutense University of Madrid, Spain

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

With the revolution of targeted therapy, theranostics and novel applications in PET, new radionuclides for PET imaging have gained attention as possible candidates for clinical applications. Manganese-52 in its ground state (52Mn) presents interesting characteristics, including a relatively long half-life (5.6 days), suitable for long studies, and the emission of a cascade of multiple prompt γ rays within the β+ decay. Although emission of such gamma rays was regarded as a limitation in PET imaging, introducing a background of spurious coincidences, novel applications such as Positronium Lifetime Imaging and multiplexed PET are based on the detection of the multiple gamma coincidences triggered by the emission of prompt gamma rays with the positron. This project concerned the development of methods to apply 52Mn for Positronium Life-time Imaging (PLI) and multiplexed PET imaging in dedicated systems such as the J-PET in Poland, Biograph Quadra PET in Switzerland and SuperArgus PET in Spain.

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

Two experiments carried out in May and October 2025 in Madrid evaluated 52Mn radiolabelling of therapeutic antibodies (aPDL1 and LEM2/15), in vivo biodistribution in breast cancer mouse models, and the performance of small-animal PET and fast LaBr3-based spectroscopy. Biodistribution at day 6 and longitudinal PET at 7, 14 and 21 days generated datasets to characterise tumour targeting and normal-organ retention. UCM acquired calibration measurements with 52Mn, 44Sc, 68Ga and 22Na in the SuperArgus PET to study system response to 52Mn. Also high-rate LaBr3 waveform data of biological samples were recorded at 5 GSa/s to train neural networks for improved timing and energy reconstruction, linking PRISMAP radionuclides with next-generation detector readout. In the experiments performed in Cracow and Bern the positronium lifetime imaging and double isotope imaging was performed with NEMA IQ phantoms and anthropomorphic phantoms, mouse phantom as well as with two immortalized cancer cell lines: DU145 and MDAMB231. In addition, studies were done also for 20-ml vials, filled with 19mL argon-saturated buffer solutions (pH values 1, 3, 5, 7) + 1 ml ^{52}Mn-MIBI solution to test the possibilities of pH sensing with 52Mn.

4. Conclusions (800 characters max. including spaces)

The Madrid experiments demonstrated the feasibility of using PRISMAP 52Mn for immunoPET and detector R&D under realistic preclinical conditions. CIEMAT has optimised robust 52Mn radiolabelling and imaging workflows for two clinically relevant antibodies in breast cancer models, while UCM has generated calibration and waveform datasets that will enable advanced reconstruction and timing studies. The studies in Cracow and Bern with the J-PET and Biograph Vision Quadra, the multi-photon PET systems, demonstrated applicability of 52Mn for effective positronium imaging and double-isotope imaging. Together, these activities consolidate a multidisciplinary PRISMAP nodes in Madrid, Bern and Cracow and provide a solid basis

for future quantitative dosimetry studies, multi-centre comparisons and translation of 52Mn-based tracers and fast-timing methods towards clinical applications. Exemplary figures and tables from the performed studies are shown below.

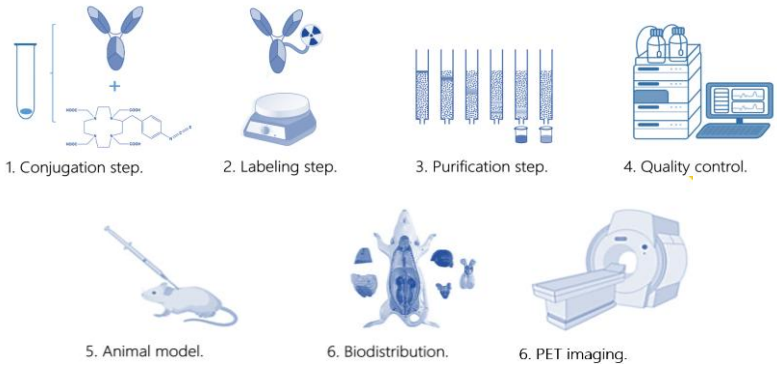

Figure 1. Overall workflow for the biomedical experiments performed at CIEMAT

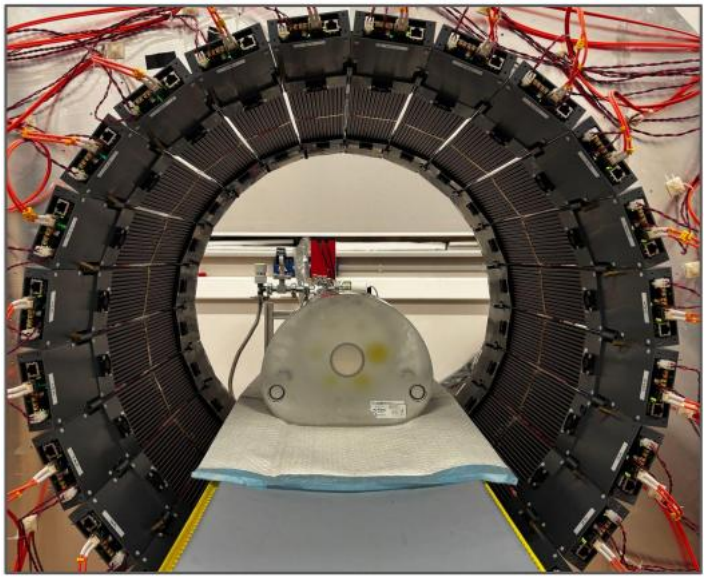

Figure 2. Photograph of the J-PET scanner from the positronium imaging of the NEMA phantom filled with 52Mn.

Table 1. Summary of 52Mn experiments performed at CIEMAT in Madrid

Experiments	Institution	Main Objective	Key Methods	Status
1A – 22/05/2025	CIEMAT	52Mn-DOTA-aPDL1 radiolabelling and biodistribution in EMT6 mammary tumour model	Conjugation, 52Mn labelling, PD-10 + SEC-150 purification, HPLC QC, ex vivo biodistribution at day 6	Radiolabelling and biodistribution completed; data available for analysis
1B – 22/05/2025	UCM	PET response to 52Mn and other isotopes	SuperArgus PET measurements of tubes with 52Mn, 44Sc, 68Ga, 22Na in coincidence with external detector	Data acquired; detailed analysis pending due to detector issues and extra calibrations

2A – 13/10/2025	CIEMAT	52Mn-DOTA-LEM2/15 immunoPET in triple-negative breast cancer model	Radiolabelling, purification, HPLC QC; static PET at 7, 14, 21 days on Compact PET/CT and SuperArgus	Imaging and animal studies completed; quantitative analysis ongoing
2B – 13/10/2025	UCM	Fast spectroscopy and ML-ready waveforms from 52Mn-labelled samples	LaBr3 detectors, 5 GSa/s waveform acquisition, singles analysis for timing/energy optimisation	Waveform dataset acquired; neural-network development and training in progress

Table 2. Summary of major ^{52}Mn measurements

Measurement Type	Date	Activity (MBq)	Duration (hours)
NEMA IQ (cold background)	May 2025	7.998	19.2
NEMA IQ (hot background)	May 2025	5.22	42.5
Cell line experiment	May 2025	3.979	3.7
CRM + tissue samples	May 2025	7.52	19.3
Mouse phantom	Oct 2025	2.3	3.8
Anthropomorphic phantom	Oct 2025	5.22	41.5
pH experiments (Ar/O_2)	Oct 2025	4.03	60.5

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

52Mn was produced, purified and delivered through PRISMAP, ensuring access to a long-lived, high-purity positron-emitting radionuclide that is not routinely available neither in Poland nor in Spain or Switzerland. PRISMAP coordinated the supply for both series of experiments conducted in Mai and October in Cracow, Bern and Madrid. Delivery of 52Mn by PRISMAT enabled to perform radiolabelling and preclinical imaging and UCM to acquire PET and fast-timing measurements from the same batches, original tests of positronium imaging and multi-isotope imaging with J-PET and Biograph Vision Quadra. Access to PRISMAP documentation and contacts also facilitated regulatory, safety and transport procedures, enabling the scientists form Cracow, Bern and Madrid to participate in the wider European 52Mn research programme.

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

PRISMAP support was essential to realise these experiments. The reliability of 52Mn delivery and the radionuclidic purity met the needs of both radiochemistry and detector studies. For future calls, longer-term

planning of shipment dates and activity levels, together with more flexible batch splitting, would further optimise the synchronisation between radiolabelling, animal work and detector measurements. Additional technical workshops focused on 52Mn data analysis and cross-calibration between centres would enhance the impact and comparability of PRISMAP-supported studies.

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

Data analysis from Experiments performed in Mai and October 2025 is ongoing; at the time of this report, no dedicated publications arising specifically from these 52Mn experiments have yet been submitted. The consortium plans at least six manuscripts, focusing on (i) 52Mn immunoPET radiochemistry and preclinical evaluation of aPDL1 and LEM2/15 and (ii) detector and machine-learning aspects based on PET and LaBr3 waveform data, (iii) positronium imaging using J-PET, (iv) double-isotope imaging using J-PET, (v) positronium imaging using Biograph Vision Quadra and (vi) double isotope imaging using Biograph Vision Quadra. Results are intended to be disseminated at major nuclear medicine and instrumentation conferences (e.g. EMIM, EANM, IEEE NSS/MIC) and through seminars within the PRISMAP community. So far one conference talk entitled “First experimental demonstration of positronium lifetime imaging with the novel radionuclide 52Mn using J-PET scanner” was given at the 2nd Symposium on new trends in nuclear and medical physics held in Poland in September 24-26, 2025.

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."

Funding acknowledgement

"This work was supported by the European Union's Horizon 2020 research and innovation programme as a user project of PRISMAP – The European medical radionuclides programme (GA 101008571)".