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EDITORIAL

NEW CHALLENGES IN RADIATION PROTECTION WITH EMERGING THERAPIES

Radiation protection issues with novel radionuclide therapies: a real challenge

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In this issue of *The Quarterly Journal of Nuclear Medicine and Molecular Imaging*, ample space is dedicated to recent issues on radiation protection for therapeutic applications of radionuclides. This is an important endeavor since the development of radionuclide therapy cannot come along without several rules and organizational arrangements for patients, staff and the public.

Internal therapy using radionuclides was launched 80 years ago with, as most striking milestone, the use of ^{131}I-sodium iodide (^{131}I) as an effective treatment for differentiated metastatic thyroid carcinoma. Since then, ^{131}I remained worldwide the most used treatment using unsealed sources. Radionuclide therapy has been increasing over the last decade. In 2008, about 400.000 treatments were administered according to the UNSCEAR report,[1] 1.4 million in 2020, and it is expected to rise over 2 million in 2022 due to ongoing developments in radioligand therapy (RLT).[2]

Many treatments were proposed since the early 70s, such as the palliative treatment of metastatic bone pain using strontium chloride (^{89}Sr) or samarium lexidronam (^{153}Sm-EDTMP). Other indications using various radionuclides were haematological malignancies, peritoneal malignancies and radiosynoviorthesis.

During the last two decades, the development of radionuclides and radiopharmaceuticals for the treatment of malignant disorders experienced unprecedented expansion. Nowadays, available treatments for cancer patients fall into three categories: 1) metabolic therapy such as ^{131}I for thyroid cancer by the unique property of differentiated thyroid cancer cells to take up radioiodine by active transport; 2) selective internal radiation therapy (SIRT) to treat liver tumors by direct injection of radiolabeled microspheres into the hepatic artery, and 3) RLT aiming to target specific cells, expressing or overexpressing receptors, for internalization of radioactive elements. Nowadays, in the clinical setting, this concerns somatostatin-receptor bearing tumors and prostate-specific membrane antigen-(PSMA) expressing cells. These therapies come into the concept of *theranostics* where the target is defined by molecular imaging, mainly using ^{18}F- or ^{68}Ga-labeled diagnostic PET tracers, followed by the use of ^{177}Lu, ^{90}Y (or alpha emitters in the coming years), as therapeutic agents.[3] Much more is yet to come and our community must be ready to embrace future challenges!

While established therapies and others in clinical trials have proven effective, the risks for the patients, staff and public that come along with such treatments must be considered.[4] Results from pivotal studies indicate that, when patient selection is well addressed, the benefits clearly outperform the risks, both in the long and short term.[5-7] The justification and optimization principles ensure that the risks for patients are mitigated by the benefits. Most treatments are prescribed on a standard regimen activity and it remains unclear from the Basic Safety Standards set up jointly by the European Commission and the IAEA,[8] to what extent, individual dosimetry is required for patient-tailored therapy. Although such personalized approach

showed valuable, either from the clinical point of view or from radiation protection measures to be enforced, they still need to be widely implemented.[9]

The risks for the staff fully depend on the way the radiopharmaceutical is produced. If in-house production is chosen, all procedures should be fully secured to limit the exposure of the radiopharmacy staff to excessive radiation by using all sorts of protecting methods, such as close cabinets/fume hoods, forceps, lead containers, and (semi-) automated devices. When the radiopharmaceutical is available from an external/commercial source, the radiation risk remains at the level of dispensing and administration. Delivering radionuclide therapies involves non-negligible risks, with transport from the production or dispensing place to the injection room, risk of contamination of spaces and individuals, management of wastes and cleaning up of rooms afterward. This holds true for radiopharmaceuticals that may be spilled or excreted from the patients and for those injected into the liver, with limited excretion. These aspects are treated in the relevant papers on ^{177}Lu and alpha emitters therapies, as well as in the introductory general paper that also covers radioactive microspheres.[10] Specific issues about ^{177}Lu, including the need for in-house labeling for some radiopharmaceuticals, with exposure of the radiopharmacy staff, and the risks related to the potential long-lived contaminant ^{177m}Lu, were addressed elsewhere.[11] Craig *et al.* focused on the specific handling of alpha emitters, that bear together a high intrinsic radiotoxicity and a potential limitation of contamination detection, if appropriate detectors are not available.[12]

Protection of the public is of course of utmost importance and rules need to be enforced to protect the general public, with special attention to pregnant women and young children, but also to give some freedom to comforters or helpers who may agree to receive doses in excess of the dose limits, provided they are properly informed and willing. It is important to keep in mind that the goal of not exceeding the dose limit, as set up by international and national bodies, is driven by the precautionary principle: no measurable harm can be detected and hence expected with such dose levels (*i.e.* 1 mSv per year), when the world population receives an average effective dose of around 2-3 mSv. The release card issued by the Heads of the European Radiological protection Competent Authorities (HERCA) is useful in this regard and its importance outlined.[13]

Finally, when handling high activities of radiopharmaceuticals for therapy involves the risk of exceeding extremity doses. This was recently well studied in a European survey launched by the European Association of Nuclear Medicine (EANM) and the European Dosimetry Group (EURADOS). As outlined by Cunha *et al.*, specific efforts shall be devoted to reducing the dose to extremities.[14] The authors emphasize the importance of training in the manipulation of radioactive sources, preventing contamination, as well as adopting protective measures, such as shielding, and the use of (semi-) automated devices during dispensing and administration of radiopharmaceuticals. All these aspects are dealt with in this issue of QJNMMI and we truly hope that readers will find their way to set up their organization for the rapidly evolving concept of radionuclide therapy.

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