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EDITORIAL

Dose optimization in nuclear medicine

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Nuclear medicine contributes significantly to the health, healthcare and quality of life of European citizens, particularly in major clinical areas such as cancer and cardiovascular disease. Every year in Europe over 6 million patients benefit from a nuclear medicine procedure, 95 % of which are diagnostic and 5 % therapeutic. The number of procedures will increase in the coming years, in particular with the increasing number of installed PET/CT systems, the increasing use of dedicated systems for cardiology using new detector technologies, and the introduction of new molecules and radiopharmaceuticals for diagnostics and therapy through rapid developments in molecular biology and medicine.

Diagnostic procedures imply the administration of activity levels that do not lead to the appearance of radiation deterministic effects and keep the stochastic risk associated to the exposure to ionizing radiation at the minimum level compatible with the diagnostic purpose.

The stochastic risk is considered to depend linearly on dose (linear no-threshold—LNT—model) although there is not complete agreement in the scientific community because of possible other effects (e.g. bystander effect and hormesis). In any case, at present, as recommended by the International Commission on Radiological Protection (ICRP), the risk assessment should be carried out based on the LNT model taking into account the absorbed doses in all irradiated tissues or organs of interest.

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In a diagnostic context, the determination of the absorbed doses (i.e. a dosimetric study) is required before the introduction of a new radiopharmaceutical to the market (to obtain a marketing authorization by the corresponding agencies such as EMA or FDA) providing the indication of the range of activity to inject for the procedure.

However, commonly, absorbed dose calculations can be easily done using published dose coefficients, calculated for phantoms of different gender and age by the ICRP for frequently used radiopharmaceuticals. Current dose coefficients as provided by the ICRP will be soon updated taking into consideration the new ICRP/ICRU adult and pediatric reference phantoms, and as regards the effective dose, the new organ/tissue weighting factors of ICRP Publication 103 [1].

Currently, the optimization process is implemented in Europe by applying so-called diagnostic reference levels (DRLs), which are, unfortunately, a tool with major limitations, including the fact that it does not take into account the quality of the diagnostic procedures. Actually, the application of DRLs in nuclear medicine tends to lead to the use of standardized activities administered to the patient, but not to a real optimization.

Most of these nuclear medicine procedures, however, are done on an ad-hoc basis; the administered activities still vary from country to country. This fact is reflected in many of the European Association of Nuclear Medicine (EANM) guidelines for diagnostic procedures, in which most of the administered activities vary within a certain range.

Moreover, while the attention to the activity administered to the patient has certainly reached high levels, it seems that not the same attention is paid to the quality of diagnostic procedures. In fact, there are very few studies on the optimization of image quality versus patient dose and the introduction of technological innovations has led in

almost all cases to a reformulation of the patient activity (i.e. reduction) but not to a general reevaluation of the optimization of the diagnostic procedures.

In pediatric nuclear medicine, optimization is of upmost importance due to the higher radiosensitivity of the young patients and the possibility of further radiation exposures in the future life. In this case, particular efforts have been undertaken in recent years to harmonize the activities administered worldwide [2].

These issues highlight the need to improve the process of optimization of the administered activity in diagnostic nuclear medicine. The importance of optimization should be emphasized especially in planning for patient future repetitions of radiological examinations for disease follow-up to keep the cumulated dose to a minimum. From the same point of view, also tracking the history of individual exposures must be considered. Of course, exposure must be minimized (applying the ALARA principle) in any examination, and the justification process should evaluate risks and benefits at the moment of the decision independently of the cumulated patient's radiation dose. In fact, performing a radiological procedure, excluding angiography and interventional radiology, involves adding a low additional stochastic risk to the patient, in any case, however, lower than the risk due to the omission of the medical benefit of the procedure itself. If the history of individual patient exposures is known, the practitioner can establish better the real need for a radiological examination, and in particular, he/she can better plan future exposures. It is therefore useful to have a tool that makes the history of exposures to ionizing radiation to a patient easily available, such as the IAEA smart card project.

Optimization of *therapeutic* procedures in nuclear medicine requires knowledge of the patient-individual absorbed doses and all the modern aspects of radiobiology (e.g. BED, EUBED, etc.). In the past, nuclear medicine therapies were substantially restricted to the treatment of benign and malignant thyroid diseases with ^{131}I and only recently there was a major development of new radiopharmaceuticals that have been introduced or are about to be introduced into clinical use.

Radioiodine, due to its very high selective uptake by the thyroid tissue, has a very wide therapeutic window and is used in almost all cases as a normal drug, albeit with radioactive characteristics, by administering fixed standard activities without dosimetry. On the contrary, the use of new radiopharmaceuticals, whose uptake by the tumor tissue is not so selective, requires individualized treatments involving the calculation of absorbed doses to the tumor and healthy tissues and the application of the specific concepts of radiation therapy and radiobiology.

In recent years, new developments in methodology comprising quantitative imaging with SPECT/CT systems, improved integration methods for obtaining the time-integrated activity coefficients and Monte-Carlo-based individualized radiation transport calculations allow for a more accurate estimate of the absorbed doses delivered to healthy tissue and tumors. As has been stated in a recent review article on the evidence base for the use of internal dosimetry in the clinical practice of molecular radiotherapy by Strigari et al. [3], this evidence implies a correlation between the absorbed doses delivered and the response and toxicity, indicating that dosimetry-based personalized treatments would improve outcome and increase survival.

Even in the case of nuclear medicine therapy with ^{131}I itself, there is increasing evidence that some selected patients with advanced disease would benefit of an optimized treatment enhancing the absorbed dose to the tumor while avoiding serious adverse effects to healthy tissues.

In summary, it can be stated that a lot of work toward optimization has already been done; further efforts, however, are needed in the future for optimizing diagnostic and therapeutic nuclear medicine procedures with respect to safety and efficacy for patient benefit.

Compliance with ethical standards

Conflict of interest Michael Lassmann and Guido Pedroli declare that they have no conflict of interest.

Human and animal studies This article does not contain any studies with human or animal subjects performed by any of the authors.

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