HERCA

Heads of the European Radiological protection Competent Authorities

Metabolic radionuclide therapy: blessing for patient, curse for regulator?

The HERCA workgroup on medical applications experience

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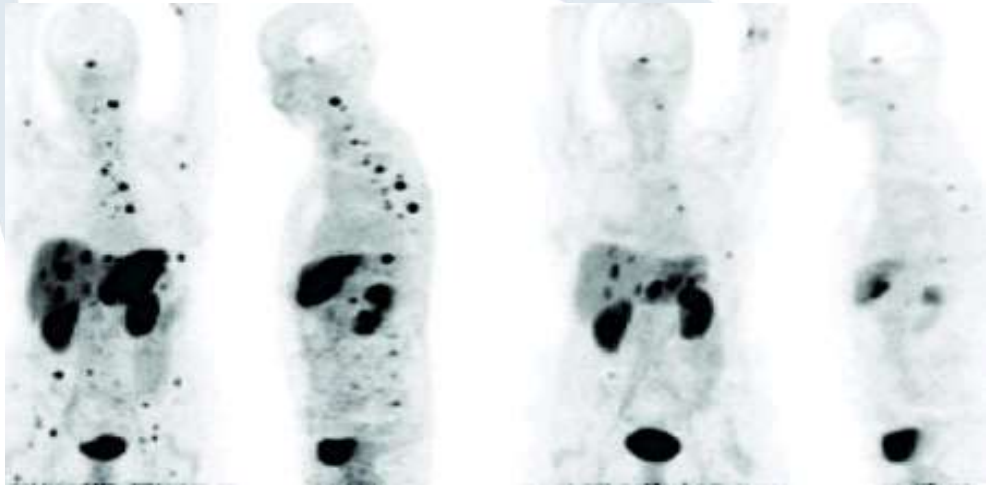
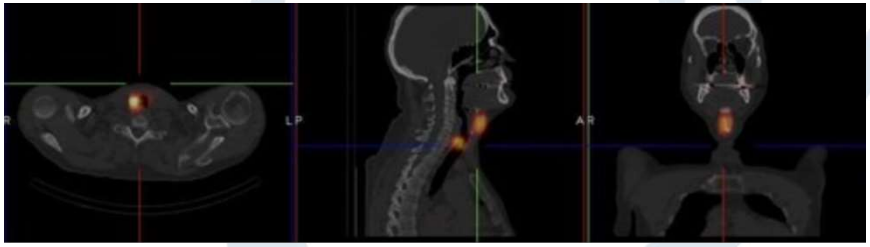
Metabolic radionuclide therapy

- **Nuclear Medicine** is a multi-professional, independent, medical discipline based on the application of probes labelled with radionuclides (radiopharmaceuticals) to both diagnose and treat various diseases. Its scope encompasses molecular imaging, image-guided procedures, and targeted radionuclide therapy- '*EANM'*.



177-Lu-PSMA prostate cancer metastases

131-I thyroid cancer



EU-BSS directive requirements on use of radiopharmaceuticals

17.1.2014 EN Official Journal of the European Union L 13/1

II

(Non-legislative acts)

DIRECTIVES

COUNCIL DIRECTIVE 2013/59/EURATOM

of 5 December 2013

laying down basic safety standards for protection against the dangers arising from exposure to ionising radiation, and repealing Directives 89/618/Euratom, 90/641/Euratom, 96/29/Euratom, 97/43/Euratom and 2003/122/Euratom

EU-BSS directive requirements on use of radiopharmaceuticals

Considerations

(29) A *high level of competence* and a *clear definition of responsibilities and tasks* among all professionals involved in medical exposure is fundamental to ensure adequate protection of patients undergoing medical radiodiagnostic and radiotherapeutic procedures.

Definitions

(80) "radiodiagnostic" means pertaining to in-vivo diagnostic *nuclear medicine*, medical diagnostic radiology using ionising radiation, and dental radiology;

(81) "radiotherapeutic" means pertaining to radiotherapy, *including nuclear medicine* for therapeutic purposes

EU-BSS directive requirements on use of radiopharmaceuticals

Article 19 Justification of practices

1. Member States shall ensure that *new classes or types of practices resulting in exposure to ionising radiation are justified before being adopted*

Article 55 Justification

2. Member States shall ensure that the principle defined in paragraph 1 is applied and in particular that:

(b) all individual medical exposures are justified in advance taking into account the *specific objectives of the exposure and the characteristics of the individual involved*

EU-BSS directive requirements on use of radiopharmaceuticals

Challenges justification[1]

- *Justification* of a procedure in medicine on level 2 (so called "*generic justification*") does not necessarily mean that its application to a particular patient is justified on level 3 (so called "*individual justification*").
- From a regulatory point of view, they need separate consideration from a legal and operational point of view
- Art. 19.4 BSS refers to Art. 55 when medical exposures are involved and underlines that associated *occupational and public exposures* have to be considered, where relevant.
- For regulators, these claims define important constraints to be considered with regard to the *justification of new types of practices*.
- Justification for the medical field requires demonstrated sufficient net benefit for medical exposures based on an adequate level of evidence (biomedical/clinical research).

[1] Multi-stakeholder Workshops on Generic Justification and Accidental and Unintended Exposures : HERCA

EU-BSS directive requirements on use of radiopharmaceuticals

Article 56 Optimisation

1. Member States shall ensure that *all doses* due to medical exposure for radiodiagnostic, interventional radiology, planning, guiding and verification purposes *are kept as low as reasonably achievable* consistent with obtaining the required medical information, taking into account economic and societal factors.

For *all medical exposure* of patients *for radiotherapeutic purposes*, *exposures of target volumes* shall *be individually planned* and their delivery appropriately *verified* taking into account that doses to non-target volumes and tissues shall be as low as reasonably achievable and consistent with the intended radiotherapeutic purpose of the exposure.

6. Member States shall ensure that in the case of a patient undergoing treatment or diagnosis with radionuclides, the practitioner or the undertaking, as specified by Member States, provides the patient or their representative with *information on the risks of ionising radiation and appropriate instructions* with a view to restricting doses to persons in contact with the patient as far as reasonably achievable. For therapeutic procedures these shall be *written instructions*. These instructions shall be handed out before leaving the hospital or clinic or a similar institution.

EU-BSS directive requirements on use of radiopharmaceuticals

Article 58 Procedures

Member States shall ensure that:

(d) in medical radiological practices, *a medical physics expert is appropriately involved*, the level of involvement being commensurate with the radiological risk posed by the practice. In particular:

(i) in radiotherapeutic practices other than standardised therapeutic nuclear medicine practices, *a medical physics expert shall be closely involved*;

(ii) in standardised therapeutical nuclear medicine practices as well as in radiodiagnostic and interventional radiology practices, involving high doses as referred to in point (c) of Article 61(1), a medical physics expert shall be involved;

(iii) for other medical radiological practices not covered by points (a) and (b), a medical physics expert shall be involved, as appropriate, for consultation and advice on matters relating to radiation protection concerning medical exposure.

EU-BSS directive requirements on use of radiopharmaceuticals

Article 61 Special practices

1. Member States shall ensure that appropriate medical radiological equipment, practical techniques and ancillary equipment is used in medical exposure:

(c) involving high doses to the patient, which may be the case in interventional radiology, *nuclear medicine*, computed tomography or radiotherapy. *Special attention* shall be given *to quality assurance programmes* and *the assessment of dose* or *verification of administered activity* for these practices.

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PAPER • OPEN ACCESS

Radiation safety of current European practices of therapeutic nuclear medicine: survey results from 20 HERCA countries

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View the article online for updates and enhancements.

Radiation safety of current European practises of therapeutic nuclear medicine

- Survey results from 20/32 HERCA countries (WP NM)

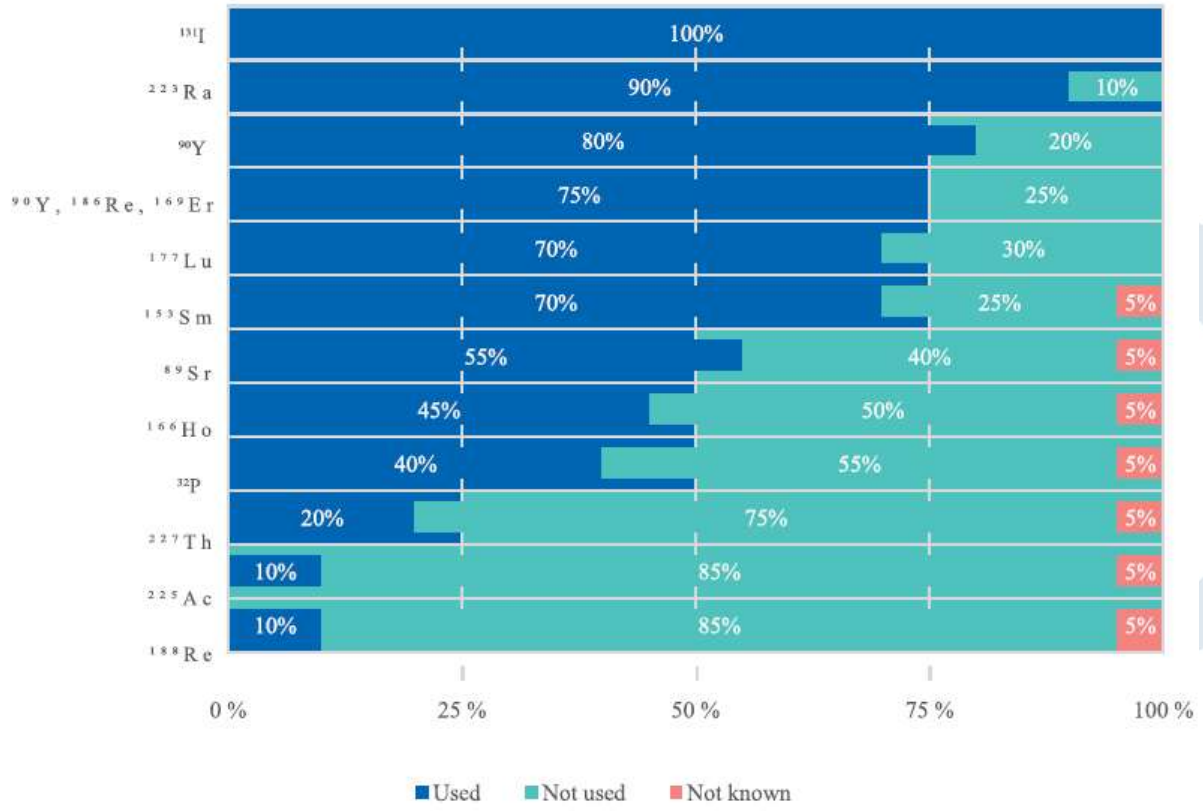
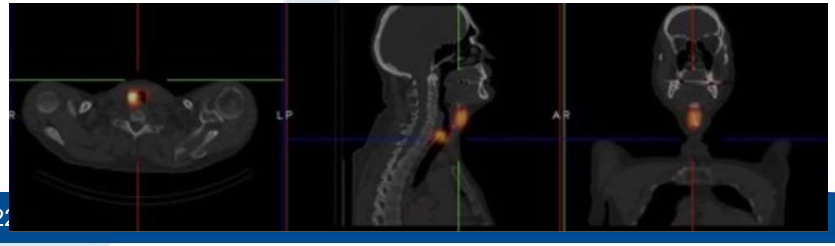


Figure 1. Therapeutic use of radionuclides in 20 European countries per radionuclide licensed by a radiation protection authority.



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Radiation safety of current European practises of therapeutic nuclear medicine

- Patient hospitalisation and waste water management
  - 65% of responders regulatory requirements for hospitalisation if reference criterium (1 mSv for members of the public; dose rate limitation 5-30 µSv at 1m) is exceeded
  - Treatment specific radioactive waste management only in few responders (depending on the radiopharmaceutical)

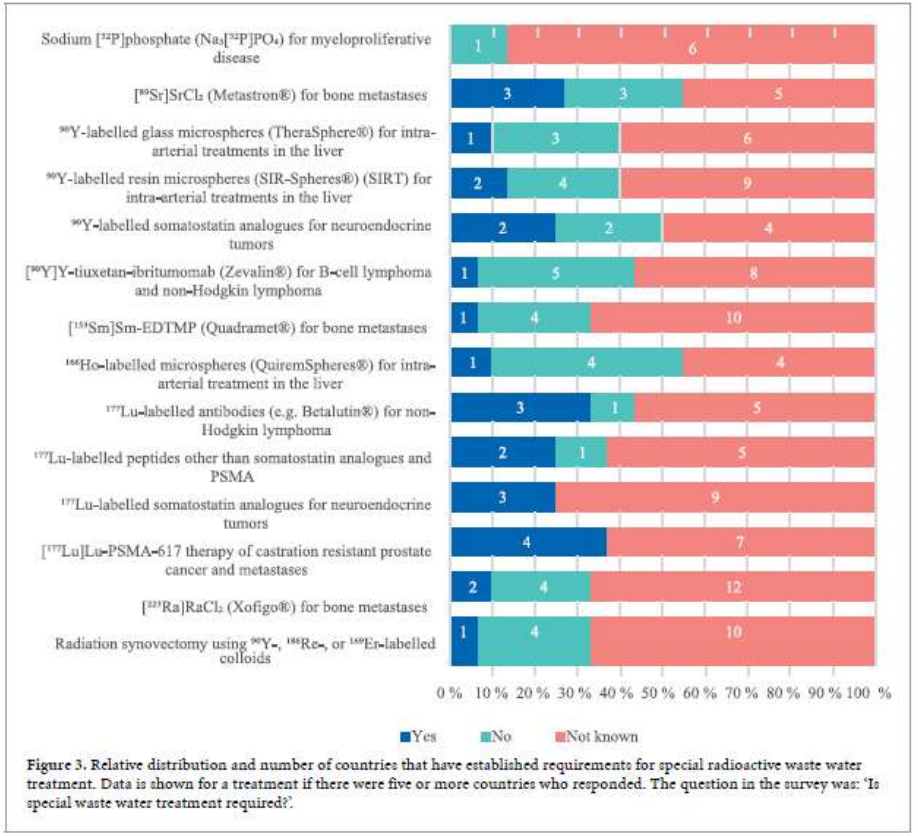


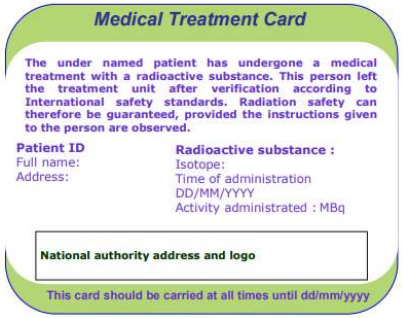
Figure 3. Relative distribution and number of countries that have established requirements for special radioactive waste water treatment. Data is shown for a treatment if there were five or more countries who responded. The question in the survey was: 'Is special waste water treatment required?'.

Radiation safety of current European practises of therapeutic nuclear medicine

- **Justification of new radiopharmaceuticals**
  - Regulatory requirements for justification in 85% of responders; involvement other ministeries
- **Individual treatment planning and –verification**
  - For all radionuclide therapies in 55%, some therapies in 30%, not required in 15 % of responders
  - Dosimetry in 85% of the responders (^{90}Y-labelled microspheres, ^{131}I, ^{166}Ho-labelled microspheres, ^{177}Lu-labelled PSMA)
  - Verification required in 45 % of the responders

Radiation safety of current European practises of therapeutic nuclear medicine

- Involvement MPE
  - The requirement for the MPE to be closely involved in non-standardized radionucliude therapies is implemented differently in the responding countries (including: 'available without delay', 'being present during treatment', 'involved in different steps, but not required during the dose delivery')
  - EANM position paper on art 56 BSSD for nuclear medicine therapy (European Journal of Nuclear Medicine and Molecular Imaging (2021) 48:67–72)
- Radiation protection instructions
  - Deceased recently treated patients in 70 %, cremation in 65 % MS
  - Release criteria in all MS
  - Patient release card (HERCA)



2011

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EU-BSS directive implementation: Identified challenges.

Metabolic radionuclide therapy: Challenges for regulatory bodies rather than a curse

- **Article 19 and 55 Justification**
  - For justification of new types of practices involving use of radiopharmaceuticals associated occupational and public exposures have to be considered
  - Justification on generic level precedes new practices in medical exposure

- **Article 56.1 Individually planned target volumes**
  - Large differences identified in the practices among hospitals in Europe: a few perform dosimetry, software is more in test use/under development or there is a lack of evidence regarding the use of them
  - Overlap with pharma legislation (DG Health)
  - Co-operation with HERCA and EANM might increase awareness of HERCA inspectors on possibilities of dosimetry tools and EANM might support hospitals to implement new regulations based on the Article 56.1

EU-BSS directive implementation: Identified challenges.

- **Metabolic radionuclide therapy continued**
  - **Article 58 d i) Involvement MPE**
    - Large differences were identified in interpretation of the Article
    - HERCA statement on implementation of the article might support national practices
    - EANM position paper
  - **Article 61.1 quality assurance programmes, assessment of dose, verification of administered activity**
    - Finding partners to be able implement EU-BSS directive properly and optimize radiation protection
      - Field of radiology: fruitful collaboration with COCIR
      - Comparable collaboration in field of Metabolic radionuclide therapy (NMEU)

Questions