IJISET - International Journal of Innovative Science, Engineering & Technology, Vol. 4 Issue 12, December 2017
ISSN (Online) 2348 – 7968 | Impact Factor (2016) – 5.264
www.ijiset.com

References Of Activities Injected Into Adults In Spect and Pet Imaging in Europe and Particularly in France

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Abstract:

The two main examinations in nuclear medicine are SPECT and PET. They make it possible to study the functioning of the organs. Its principle is based on the administration to a patient of so-called tracers doses of a radiopharmaceutical drug. In order to limit the irradiation of the patient during a diagnostic examination, nuclear medicine determines the activities to be administered according to several criteria.

In this work we describe the references for the activity to be injected in Europe and particularly in France, then we will discuss the possible differences on the proposed activities for radiopharmaceuticals widely used.

In Europe and more particularly in France, the reference structures for the activity to be injected in nuclear medicine examinations are essentially: French Society of Nuclear Medicine (SFMN), European Association of Nuclear Medicine (EANM), Society of Nuclear Medicine and Molecular Imaging (SNMMI), Vidal Hoptimal, National Hospital Center for Information on Medicines (CNHIM).

For the ^{99m}Tc-HMPAO the activity values proposed by the 5 references are practically in the same limits except for the Vidal and CNHIM where they are a little weaker. For the ^{18}F-FDG, the ^{99m}Tc-HMDP, ^{99m}Tc-Tetrafosmin, there are slight variations on the activities proposed by the SFMN, the EANM, Vidal and the CNHIM. On the other hand, the variations are important compared to the values of the SNMMI.
For a better optimization of the activity to be injected (ALARA) and because of the unjustified fear of the nuclear and the carefree patients, it would be better to harmonize the proposed activities for all radiotracers.

Keywords: radiotracers, references of activities injected, adults, France, harmonization

I- Introduction:

The main field of action of nuclear medicine, apart from a minor therapeutic component, concerns the diagnosis, prognosis and therapeutic follow-up of a large number of pathologies thanks to two main types of examinations: scintigraphy or Single Photon Emission Computer Tomography (SPECT) and Positron Emission Tomography (PET). They make it possible to study the functioning of the organs, the metabolism of the constitutive elements of the organism, normal and pathological, and this, at a molecular level. Its principle is based on the administration in a patient at so-called tracer doses of a radiopharmaceutical drug which is the combination of a molecular vector (often physiological product and administered in infinitesimal quantity, thus not causing any allergy or any side effect) with a radionuclide (radioactive isotope emitting radiation which will make it possible to account for the distribution of this vector in the organism, most often in the form of images). The images of nuclear medicine are obtained through imaging devices called cameras which are distinguished by two major types depending on the nature of the radiation they detect, gamma photons for SPECT or positron annihilation photons for PET (8).

In order to limit the irradiation of the patient during a diagnostic examination, nuclear medicine determines the activities to be administered according to several criteria: - the weight of the patient; - the tracer concentration in the target; - the type of examination and the performance of the detector (gamma camera, semiconductor detectors, PET camera, tomographic images ...);- the age of the patient (child or adult) ... The weight of the patient is still the parameter most used in adults. Nevertheless, for some examinations, the activity administered is almost always the same (110MBq of 99mTc for a thyroid scintigraphy in adults) (9).

The objective of this work is first to present the references of activities to inject in SPECT and PET in Europe and particularly in France. Then report the activities proposed by these references for the most used radiopharmaceuticals and discuss any discrepancies between these proposed activities.

II- References of injected activities

In Europe and more particularly in France, the reference structures for the activity to be injected in nuclear medicine examinations are essentially:
- French Society of Nuclear Medicine (SFMN),
- European Association of Nuclear Medicine (EANM),
- Society of Nuclear Medicine and Molecular Imaging (SNMMI),
- Vidal Hoptimal,
- National Hospital Center for Information on Medicines (CNHIM).

II.1. French Society of Nuclear Medicine (SFMN):

The French Society of Nuclear Medicine and Molecular Imaging (SFMN), is a group of French-speaking specialists to promote nuclear medicine, molecular imaging and related techniques. In particular in these areas, the SFMN ensures the national organization of continuous training and the evaluation of professional practices.

The means of action of the Society are publications, conferences, courses, exhibitions, study groups, congresses, meetings, awarding of prizes and any means of dissemination, education or training technical in French language.
The journal entitled "Nuclear Medicine Journal" is the mouthpiece of the company that owns the title. This review is the official organ of:

• the French Society of Nuclear Medicine and Molecular Imaging (SFMN),
• the College of Teachers of Biophysics and Nuclear Medicine (CNEBMN),
• French regional associations of nuclear medicine (ACOMEN, AFRINN, APRAMEN, SFMNO),
• the Association of Specialists in Nuclear Medicine of Quebec (AMSMNQ),
• the Luxembourg Society of Nuclear Medicine (SLMN),
• and the Swiss Society of Nuclear Medicine (SSMN).

It brings together the efforts and resources of the various French-speaking nuclear medicine associations, including members of the Belgian Nuclear Medicine Society (BELNUC). As a learned society, the SFMN, like the others created, includes a large number of working groups organized around organ pathologies (cardiology, neurology, oncology, endocrinology, osteo-articular groups) or specific themes (biology). , radiopharmaceutical, image). The missions of these working groups are multiple:

• promote nuclear medicine to the corresponding organ companies
• provide postgraduate education specific to their area of expertise through continuing education workshops
• to issue the procedures guides corresponding to their field of expertise
• organize and develop clinical research protocols related to their group (15)

II.2. European Association of Nuclear Medicine (EANM)

The European Association of Nuclear Medicine (EANM) is a professional nonprofit medical association that facilitates communication worldwide among individuals pursuing clinical and research excellence in nuclear medicine (1).

The European Association of Nuclear Medicine is the largest organization dedicated to nuclear medicine in Europe. In this role, it has become the umbrella organization which represents the whole sector towards the European Institutions and other international institutions. It was founded on September, 1985 in London as the result of a merger between the Society of Nuclear Medicine Europe and the European Nuclear Medicine Society. The first congress of the EANM took place in 1988 in Milan/Italy.

The EANM is incorporated in Vienna/Austria. The EANM membership comprises physicians, scientists, technologists as well as other persons working in nuclear medicine or related fields. Currently, the EANM represents more than 9,000 specialists from 41 different countries within Europe and serves the interests of a community that goes far beyond these numbers and any geographical boundaries.

The EANM's vision is to optimize and advance science and education in nuclear medicine for the benefit of public health and humanity within the concept of personalized healthcare. The EANM acts as umbrella organization for individuals as well as national societies.

The goal of the EANM is to be a platform for the dissemination and discussion of the latest results in the field of nuclear medicine including multimodality imaging and related subjects. It fosters and co-ordinates the mutual exchange of knowledge relating to the diagnosis, treatment and prevention of diseases through the use of unsealed radioactive substances and the properties of stable nuclides in medicine.

As the EANM's cooperation with national societies has expanded beyond Europe, non-European countries have been invited to become affiliated members of the association.

The structure owns a monthly journal entitled "European Journal of Nuclear Medicine and Molecular Imaging" (7).

II.3. Society of Nuclear Medicine and Molecular Imaging (SNMMI)

The Society of Nuclear Medicine and Molecular Imaging (SNMMI), headquartered in Reston, Va., is a nonprofit scientific and professional organization that promotes the science, technology and practical application of nuclear medicine and molecular imaging. SNMMI strives to be a leader in unifying, advancing and optimizing molecular imaging, with an ultimate goal of improving human health. With 18,000 members worldwide, SNMMI represents nuclear and molecular imaging professionals, all of whom are committed to the advancement of the field. In March 1953, sharing an interest in forming a nuclear medicine organization, five radiologists, a cardiologist, two internists, a physicist, an engineer, and a nuclear medicine physician from the Pacific Northwest met in Spokane, Washington. They founded the Society of Nuclear Medicine; all interested in nuclear medicine would be eligible for membership. The first meeting of the society was held in Seattle, Washington, in 1954. The society soon became a national organization, and the original organization became the society's Pacific Northwest Chapter. In 2012, the society changed its name to the Society of Nuclear Medicine and Molecular Imaging to embrace the growing field of developing probes (radioactive or otherwise) for imaging molecular processes both in the clinic and in basic research.

The monthly journal entitled " Journal of Nuclear Medicine" The Journal of Nuclear Medicine (JNM) self-published by the Society of Nuclear Medicine and Molecular Imaging, offers readers around the globe clinical investigations, basic science reports, continuing education articles, book reviews, employment opportunities, and updates on rapidly changing issues in practice and research (14).

The SNMMI is especially the reference to the United States

II.4. Vidal Hoptimal:

VIDAL Hoptimal, the VIDAL application intended for health establishments aims at integrating and harmonizing perfectly within the Hospital Information System of the establishments.
From VIDAL Hoptimal it is possible to directly access the following collections:

• VIDAL Recos
• VIDAL DMI
• British National Formulary (BNF)
• British National Formulary for Children (BNFC)
• Tox'In
• STABILIS
• ANTIBIOGARDE *
• UpToDATE * (* subject to a subscription by the institution)

Accesses are most often contextual, that is to say from the sheet of a specialty with a link that refers to the corresponding data in the database concerned. VIDAL Hoptimal contributes to improving the efficiency of patient care by enabling practitioners to access, for a pharmaceutical specialty, all regulatory information: opinions and summaries of the Transparency Commission, guidelines Good Usage (RBU), Temporary Use Recommendations (RTU), Risk Management Plan (PGR), Therapeutic Information Sheet (FIT) ... or scientific (VIDAL Reco, Tox'In, ANTIBIOGARDE ...). Interfaced with the main software of the Hospital Information System, VIDAL Hoptimal contributes to a better security of the prescription and the dispensation within the health establishments.

VIDAL Hoptimal is available in a stand-alone version, VIDAL Hoptimal Solution Consulting and an interface version with the main software of the Hospital Information System (SIH), VIDAL Hoptimal Integration Solutions. It is directly accessible on the home page of our place of study, Hôpital Bicêtre.

These main features are:
- Ease of use: Simplified search by keyword from a single input area, easy and intuitive navigation.
- Focused on hospital professions: provision of practical, synthetic and structured information on health products, optimization of the treatment booklet, management of equivalences.
- Richness of the documentary database: VIDAL monographs, therapeutic recommendations, reference documents (RBU, PGR, FIT, BUM, and ALD30), Tox'In sheets ...
- Completeness of the drug base: all drugs marketed in France (including all generic drugs and ATUs).
- Customization possible by adding local documents.
- CIO synchro: interoperability guaranteed by synchronization with the CIOsp®.
- LPPR: The complete list of Refundable Products and Services with refund rates and non-GHS registration.

II.5. National Hospital Center for Information on Medicines (CNHIM)

The National Hospital Center for Information on Medicines (CNHIM), an association under the 1901 law, was created in December 1979 by the three unions of Hospital Pharmacists (SYNPREFH, SNPHPU and SNPGH) and at the request of the Direction of Pharmacy and Drug at the Ministry of Health.

The objective of the CNHIM is to disseminate independent, scientific, validated, updated information on all medicines available in France via various computer and telematics media,

adapted to the needs of health practitioners. It has an evaluation review on the drug named Dossier of the CNHIM.

Each CNHIM Dossier article is written by hospital practitioners, pharmacists and physicians, and validated by experts chosen according to their skills and health practitioners gathered on a reading committee (3).

III- Proposed activities for examples of radiotracers and discussion

We will describe the activities proposed by these reference structures for some examples of radiopharmaceuticals:
- 18F-FDG, the most commonly used tracer in PET imaging
- Metastable technetium-99 labeled tracers frequently used for SPECT: 99mTc-HMDP, 99mTc-Tetrafosmin, 99mTc-DMSA, 99mTc-HMPAO

III.1. SFMN

- ✓ ^{18}F-FDG:

The activity injected intravenously in adults depends on the type of PET sensor and the reconstruction algorithms. It ranges from 2 to 4 MBq / kg of body weight. The minimum activity takes into account the recommendation of the camera manufacturer (16).

- ✓ ^{99m}Tc-HMDP:

The activity usually administered is 8 to 10 MBq / kg in adults. In certain special cases (obesity, extreme thinness), the injected activity may go beyond the recommended limits, but it must stay as close as possible to the recommended limits. One can also play on the scanning speed and the delay between the injection and the acquisition to optimize the images (17).

- ✓ ^{99m}Tc-Tétrafosmin:

To obtain quality imaging from a scintillation camera, the injected activities must be adapted to the weight of the patients.

- Protocol on 1 day: rest and stress: 3.7 and 11 MBq / kg
  stress and rest: 3.7 and 11 MBq / kg
- Protocol over 2 days: stress: 11 MBq / kg
  rest: 11 MBq / kg.

For a middle-aged adult, the activities administered are therefore between 600 and 900 MBq for each of the 2 exam times (effort / rest). The 2-day protocol may be preferred for overweight patients to achieve sufficient image quality (19).

- ✓ ^{99m}Tc-DMSA:

A maximum activity of 100 MBq can be injected in adults (18).

- ✓ ^{99m}Tc-HMPAO:

The recommendation for the activity administered in adults is 750-900 MBq (20).

III.2. EANM:

- ✓ ^{18}F-FDG:

The minimum recommended administered FDG activity and PET acquisition duration for each bed position must be adjusted so that the product of the FDG activity and PET acquisition duration is equal to or greater than the specifications set out below. Therefore, one may decide to apply a higher activity and reduce the duration of the study or, preferably, to use a reduced activity and increase the study duration, thereby keeping ALARA principles in mind as well. In these guidelines two recommendations are provided for determining the minimum FDG administered dose in adults, which assume a linear and a quadratic relationship, respectively, between PET acquisition time per bed position, patient weight and recommended FDG activity. Compared with linear activity prescription, the quadratic scheme results in a slightly higher administered activity for patients >75 kg; this compensates for the lower signal to noise ratio (and hence degraded image quality) due to excessive attenuation, which occurs when linear activity prescription is applied.
The following specifications are given when imaging sites prefer the use of a linear relationship for pragmatic reasons (minimum acceptable administered activity recommendation):
1. For systems that apply a PET bed overlap of ≤30 %, the minimum recommended administered activity is calculated as follows:
FDG (MBq)=14 (MBq·min·bed−1·kg−1) × patient weight (kg)/emission acquisition duration per bed position (min·bed−1).
2. For systems that apply a PET bed overlap of >30 %, the minimum FDG administered activity is calculated as follows:
FDG (MBq)=7 (MBq·min·bed−1·kg−1) × patient weight (kg)/emission acquisition duration per bed position (min·bed−1).
Alternative: This alternative includes using a quadratic relationship between recommended administered FDG activity, weight and duration of emission acquisition. In this case use the above equations to determine the administered activity for a 75 kg patient. Next, multiply this activity by the square of the patient weight/75. This will provide the minimum administered activity.

1. For systems that apply a PET bed overlap of ≤30 %, the minimum administered FDG activity is calculated as follows:
FDG (MBq)=1,050 (MBq·min·bed−1·kg−2) × (patient weight (kg)/75)2/emission acquisition duration per bed position (min·bed−1).
2. For systems that apply a PET bed overlap of >30 %, the minimum FDG activity is calculated as follows: FDG (MBq)=525 (MBq·min·bed−1·kg−2) × (patient
weight (kg)/75)2/emission acquisition duration per bed position (min·bed−1) (1).

- ✓ ^{99m}Tc-HMDP :

For bone scintigraphy in adults, the average activity administered by a single intravenous injection should be 500 MBq (300 – 740 MBq, 8 – 20 mCi. The administered activity usually ranges between 8 and 10 MBq/kg for adults. Lower activities may be used when equipment with higher detector sensitivity or resolution recovery resulting in similar image quality is available. For markedly obese adult patients, the administered activity may be increased to 11 – 13MBq/kg. If the injected activity falls outside these recommended limits for clinical reasons, the deviation should be kept as small as possible. Practitioners could be required to justify administration of activities greater than local national DRLs (22).

- ✓ ^{99m}Tc-Tétrafosmin :

When a 1-day ^{99m}Tc protocol is used (i.e. two administrations of activity on one day), the activity for the second examination has to be three times higher than the first administered activity. It should be noted that if the stress examination is performed first, irrespective of a 1- or 2-day protocol, and reported as normal, the rest examination can be omitted.
There is limited evidence in the literature demonstrating activity amounts to be injected for optimal images in the different settings of patients and instrumentation. Coming down to a classical SPECT acquisition the following activities to administer are recommended, according to the ALARA principle, for a normal weight adult patient (e.g. BMI <25) for a gated study on a multiple-head scintillation camera, using filtered back-projection, an acquisition duration of 15 min and a pixel size of around 6 mm:
Two-day protocol: 350 – 700 MBq/study

One-day protocol: 250 – 400 MBq for the first injection, three times more for the second injection (10).

- ✓ ^{99m}Tc-HMPAO :

The activity administered in adults ranges from 555-1110 MBq (typically 740 MBq) (13).

III.3. SNMMI:

- ✓ ^{18}F-FDG:

In adults, the activity to be injected intravenously is 370 to 740 MBq (10-20 mCi) (5).

- ✓ ^{99m}Tc-HMDP :

The usual activity in adult patients is 740-1 110 MBq (20-30 mCi) injected intravenously. For grossly obese adult patients, the administered activity can be increased to 11-13 MBq / kg (300-350 µCi / kg) (6).

- ✓ ^{99m}Tc-Tétrafosmin:

The Food and Drug Administration's (FDA) recommendations for the maximum dose administered for a combined rest and stress study (conducted on the same day) are a total of 1480 MBq (40 mCi) radiopharmaceuticals labeled with 99mTc. When rest and stress studies are performed on different days, the dose may be 1110 MBq (30 mCi) for each injection. Doses can be adjusted at the discretion of the prescribing physician (21).

- ✓ ^{99m}Tc-HMPAO:

In adults, from 555 MBq to 1110 MBq (15-30 mCi) of administered activity can be used (12).

III.4. Vidal Hoptimal :

- ✓ ^{18}F-FDG:

The recommended adult activity of 70 kg is 100 to 400 MBq. This activity must be adapted according to the body mass of the patient and the type of camera used (23).

- ✓ ^{99m}Tc-HMDP:

In a patient of about 70 kg, the recommended average activity is 500 MBq (300 to 700 MBq). Different activities may be justified. In patients with reduced renal function, the radioactivity to be administered should be carefully determined because increased exposure to radiation is possible.
In patients with high bone absorption and / or severe renal impairment, dose adjustment may be necessary (27).

- ✓ ^{99m}Tc-Tétrafosmin:

When the rest / stress injections are performed on the same day, the activity of the second injection must be at least three times the residual activity of the first injection. The activity of the first injection is between 250 and 400 MBq and the activity of the second injection, administered at least 1 hour later, between 600 to 800 MBq. For TEMP studies with ECG synchronization, the recommended activities are in the high values of these intervals. For resting injections and stimulation tests performed on two different days, the recommended activity for each injection of tetrofosmin (99mTc) is between 400 and 600 MBq. For studies in large individuals (eg, abdominal obesity, large mammary mass) and ECG-synchronized TEMP, the recommended activities are within the high values of these intervals. For resting myocardial scintigraphy and stimulation tests performed on the same or two days, the total activity administered should not exceed 1200 MBq. Clinical studies have shown that a minimum activity of 550 MBq is required for ECG-synchronized TEMP. Activities administered in ECG-synchronized TEMP should follow the recommendations above.
As a complementary examination for the diagnosis and localization of myocardial infarction, a single injection of tetrofosmin (99mTc) (250-400 MBq) administered at rest is sufficient (24).

- ✓ ^{99m}Tc-HMPAO:

The recommended activity for adults and the elderly varies from 350 to 500 MBq (26).

- ✓ ^{99m}Tc-DMSA:

The recommended activity in adults is 30 to 120 MBq (25).

III.5. CNHIM:

- ✓ ^{18}F-FDG

The recommended adult activity of 70 kg is 100 to 500 MBq. This activity must be adapted according to the body mass of the patient and the type of camera used (2).

- ✓ ^{99m}Tc-HMDP:

In adults, the recommended average activity is 500 MBq (300 to 700 MBq). Other activities may be necessary (2).

- ✓ ^{99m}Tc-Tetrafosmin:

Two-day protocol: 400 – 600 MBq/study

One-day protocol: 250 – 400 MBq for the first injection, 600- 800 for the second injection.

In both cases, the maximum total activity administered should not exceed 1200MBq (2).

- ✓ ^{99m}Tc-HMPAO:

The recommended activity for adults and the elderly varies from 350 to 500 MBq (2).

- ✓ ^{99m}Tc-DMSA:

The recommended activity in adults is 30 to 120 MBq (2).

The activity values proposed by these references are summarized in table 1. Table 2 compares these values of activities with DRLs in France.

Tableau 1: Activities proposed by the references for the 5 radiotracers

References / Radiotracers	SFMN	EANM	SNMMI	VIDAL	CNHIM
^{18}F-FDG	2-4 MBq/Kg (140-280MBq)	Calculated by weight and duration of acquisition	370-740MBq	100-400MBq	100-500MBq
^{99m}Tc-HMDP	8-10MBq/Kg (560-700MBq)	4,3-10,5MBq/Kg (300-740MBq)	11-13MBq/Kg (740-1110MBq)	300-700MBq	300-700MBq
^{99m}Tc-Tétrafosmin One day protocol	First injection:3,7MBq/ Kg (259MBq) Second injection: 11MBq/Kg (770MBq)	First injection:250-400MBq Second injection: 750-1200MBq	Maximum total activity for both exams:1480MBq	First injection:250-400MBq Second injection: 600-800MBq	First injection:250-400MBq Second injection: 600-800MBq
^{99m}Tc-Tétrafosmin Two days protocol	11MBq/Kg / Study	350-700MBq/ Study	1110MBq/ Study	400-600MBq/ Study	400-600MBq/ Study
^{99m}Tc-DMSA	100MBq	Not proposed for adults	Not proposed for adults	30-120MBq	30-120MBq
^{99m}Tc-HMPAO	750-900MBq	555-1110MBq	555-1110 MBq	350-500MBq	350-500MBq

Tableau 2: Activities proposed by references for 5 radiotracers compared to DLR in France (10)

References / Radiotracers	SFMN	EANM	SNMMI	VIDAL	CNHIM	Currents DRL (10)	Proposed DLR (10)
^{18}F-FDG	2-4 MBq/Kg (140-280MBq)	Calculated by weight and duration	370-740MBq	100-400MBq	100-500MBq	350MBq	260MBq (3,6MBq/Kg
^{99m}Tc-HMDP	8-10MBq/Kg (560-700MBq)	4,3-10,5MBq/Kg (300-740MBq)	11-13MBq/Kg (740-1110MBq)	300-700MBq	300-700MBq	700MBq	670MBq (9,5MBq/kg
^{99m}Tc-Tétrafosmin One day protocol	First :3,7MBq/Kg (259MBq) Second: 11MBq/Kg (770MBq)	First :250-400MBq Second: 750-1200MBq	Maximum total activity for both exams:1480 MBq	First:250-400MBq Second: 600-800MBq	First:250-400MBq Second: 600-800MBq	First :300MBq Second: 800MBq	First :300MBq Second: 800MBq (3,7 et 10,5MBq/Kg)
^{99m}Tc-Tétrafosmin Two days protocol	11MBq/Kg / Study	350-700MBq/ Study	1110MBq/ Study	400-600MBq/ Study	400-600MBq/ Study	850/ Study	650MBq /Study (8MBq/Kg)
^{99m}Tc-DMSA	100MBq	Not proposed for adults	Not proposed for adults	30-120MBq	30-120MBq	Not proposed	Not proposed
^{99m}Tc-HMPAO	750-900MBq	555-1110MBq	555-1110 MBq	350-500MBq	350-500MBq	500-800MBq	650-800MBq

For the ^{18}F-FDG, the ^{99m}Tc-HMDP, ^{99m}Tc-Tetrafosmin, there are slight variations on the activities proposed by the SFMN, the EANM, Vidal and the CNHIM. On the other hand, the variations are important compared to the values of the SNMMI. In fact, the SNMMI values are much higher with activity differences that can exceed 300MBq.
For the DMSA we have just noted the proposed activities in the child at the level of the guidelines of the EANM and the SNMMI. Indeed DMSA is mainly used in pediatrics. The values proposed for DMSA by the SFMN, Vidal and CNHIM are almost the same and comply with NRD in France.

For the ^{99m}Tc-HMPAO the activity values proposed by the 5 references are practically in the same limits except for the Vidal and CNHIM where they are a little weaker. The activity values proposed by the SFMN, the EANM, Vidal and the CNHIM are generally in agreement with the DRL_S (Diagnostic Reference Level) or NRDs unlike those of the SNMMI.

In general, the principle of maintaining radiation exposure "as little as reasonably possible" (ALARA) must be respected. In addition, the activity of a radiopharmaceutical to be administered must be determined in accordance with national legislation and the Euratom Council Directive 2013/59. This directive describes the basic safety standards for protection against the dangers arising from exposure to ionizing radiation. According to this directive, the Member States are required to bring into force the necessary regulations to comply with the Directive. One of the criteria is the designation of diagnostic reference levels (DRL or NRD) for radiopharmaceuticals; these are defined as activity levels for standard sized patient groups and for widely defined equipment types. It is stated that levels will not be exceeded for standard procedures. In France, the Institute for Radioprotection and Nuclear Safety (INRS) is the body in charge of NRDs.
Nuclear medicine physicians in each country should adhere to the NRDs and the rules set out in local laws (11).

The nuclear medicine departments and, in general, the aforementioned reference structures take into account the publications of the International Commission on Radiological Protection (ICRP) on the biological effects of radiation, NRDs, as well as dosimetric problems for patients and medical personnel. .
The activity to be administered is, in general terms, a compromise between the quality of the image and the radiation exposure of the patient and the staff. The higher the activity administered, the better the quality of the image and the higher the radiation exposure of the patient and staff. The activity to be administered depends on the type of equipment (single or multiple head scintillation camera, or camera based on a CZT detector), patient characteristics (body weight), acquisition protocol (protocols of one or two days, imaging time, pixel size, controlled acquisition) and the radiopharmaceutical. The reconstruction method may also be important, that is to say a filtered backprojection compared to an iterative reconstruction.

The three key principles of radiation protection are justification, optimization and dose limitation. The dose limits and dose constraints of the ICRP are not recommended individually for a patient, as they can reduce the effectiveness of the diagnosis or treatment of the patient, thus doing more harm than good.

The focus is therefore on the justification of medical procedures and the optimization of protection and, for diagnostic procedures, on the use of diagnostic reference levels.

In the case of exposure due to diagnostic and interventional medical procedures, the purpose of the diagnostic reference level is to optimize protection, but it is not implemented through constraints on the individual doses of the patient. This is a mechanism to manage the patient's dose so that it is proportionate to the medical goals. It is thus a comparison process between the practice (readings for groups of patients) and the reference value, and then the implementation of actions in case of exceeding (4).

For a better optimization of the activity to be injected (ALARA) and because of the unjustified fear of the nuclear and the carefree patients, it would be better to harmonize the proposed activities for all radiotracers. The example was given with the pediatric dosing card harmonized by the EANM and the SNMMI. In 2008 the EANM published the first version of the pediatric dosage card. In 2011 the North American consensus guidelines recommended a set of administered activities for pediatric nuclear medicine. During the EANM congress in 2012 a working group of the EANM and the SNMMI met to study the possibilities to harmonize these guidelines. The purpose of this publication was to identify differences between these guidelines and suggest changes in both, in order to achieve a level of harmonizing. In August 2016 the last update of the EANM Pediatric Dosage Card was issued (6).

IV. Conclusion

The radiopharmaceutical activities to be injected into nuclear medicine should be "as low as reasonably possible". They are determined according to several criteria, the most used of which is the weight of the patient. In France the references for the activity to be injected are essentially the French Society of Nuclear Medicine (SFMN), the European Association of Nuclear Medicine (EANM), the Society of Nuclear Medicine and Molecular Imaging (SNMMI), the Vidal Hoptimal and the National Hospital Center for Information on Medicines (CNHIM). Sometimes significant variations on the activities proposed by the references are noted.
Although NRDS may be country or region specific, it is best to work towards harmonizing different proposals to have the same activity values.

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