RADIOBIOLOGY AND SAFETY

Radiation dose in nuclear medicine: the hybrid imaging

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Abstract

Hybrid imaging procedures such as single-photon emission computed tomography/computed tomography (SPECT/CT) and positron emission tomography/computed tomography (PET/CT) showed a rapid diffusion in recent years because of their high sensitivity, specificity, and accuracy, due to a more accurate localization and definition of scintigraphic findings. However, hybrid systems inevitably lead to an increase in patient radiation exposure because of the added CT component. Effective doses due to the radiopharmaceuticals can be estimated by multiplying the administered activities by the effective dose coefficients, while for the CT component the dose-length product can be multiplied by a conversion coefficient k. However, the effective dose value is subject to a high degree of uncertainty and must be interpreted as a broad, generic estimate of biologic risk. Although the effective dose can be used to estimate and compare the risk of radiation exposure across multiple imaging techniques, clinicians should be aware that it represents a generic evaluation of the risk derived from a given procedure to a generic model of the human body. It cannot be applied to a single individual and should not be used for epidemiologic studies or the estimation of population risks due to the inherent uncertainties and oversimplifications involved. Practical ways to reduce radiation dose to patients eligible for hybrid imaging involve adjustments to both the planning phase and throughout the execution of the study. These methods include individual justification of radiation exposure, radiopharmaceutical choice, adherence to diagnostic reference levels (DLR), patient hydration and bladder voiding, adoption of new technical devices (sensitive detectors or collimators) with new reconstruction algorithms, and implementation of appropriate CT protocols and exposure parameters.

Keywords Hybrid imaging · SPECT/CT · PET/CT · Radiation dose · Dose reduction · Dose optimization

Introduction

According to the National Council on Radiation Protection and Measurements (NCRP) report 160, nuclear medicine procedures have increased from 6.3 million in 1984 to 18 million in 2006. This has led to an increase in per capita annual radiation dose to the US population due to nuclear medicine procedures from 0.14 mSv in 1982 to 0.8 mSV in 2006 [1].

Most of this rapid growth is due to the diffusion of molecular hybrid imaging procedures such as single-photon emission computed tomography/computed tomography (SPECT/CT) and positron emission tomography/computed tomography (PET/CT) that provide relevant functional and anatomical information [2]. These hybrid systems show high sensitivity, specificity, and accuracy and also increase reader confidence and decrease inter-observer variability through more accurate localization and definition of scintigraphic findings [3].

The SPECT and PET have been used for some years to obtain functional and metabolic information in a variety of pathologic conditions. The following introduction of CT determined a significant change, commuting SPECT and PET in hybrid imaging systems (SPECT/CT and PET/CT),

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which are able to provide functional and anatomic images and to overcome the limitations of the separate modalities. Within a few years, hybrid imaging became one of the most powerful diagnostic tools available in a number of nuclear medicine departments across the world, and nowadays it plays a vital role in the clinicians' daily workflow [4].

Hybrid imaging is used in several clinical applications, especially in oncology, since it allows a better localization of disease, its characterization before and after therapy, an accurate delineation for biopsy and therapy planning, as well as the detection of the most clinically relevant lesions [5]. From their initial introduction, the hybrid systems presented a dramatic and rapid diffusion, as shown by the steep rise in pertinent publications (Fig. 1).

A recent advance in the area of hybrid imaging is the combination of PET with magnetic resonance imaging (MRI). PET/MRI hybrid scanners have been introduced into clinical practice both as separate units with a common bed and as a fully integrated unit that allows for simultaneous acquisition of PET and MRI. Although these devices are considerably more expensive than commercial PET/CT units and the clinical indications are still being developed, they have received growing attention (Fig. 2) in regard to the reduction in radiation dose to the patient due to the elimination of the CT component [6].

However, the hybrid systems (Figs. 3, 4) inevitably lead to an increase in medical radiation exposure because the radiation dose to patients is the sum of the dose due to the administered radiopharmaceutical and the dose from the CT component of the study [7]. Therefore, both general and individual justification must be implemented, by adhering to guidelines and evaluating the clinical characteristics of the patient. Furthermore, radiation dose should be optimized so that the patient receives the smallest amount of radiation that will still provide the appropriate diagnostic information [7].

The position statement on dose optimization for nuclear medicine and molecular imaging procedures from The Society of Nuclear Medicine and Molecular Imaging (SNMMI) and the SNMMI Technologist Section (SNMMI-TS) summarized the process of justification and optimization in the following way "the right test with the right dose should be given to the right patient at the right time" [8].

In addition to justification and optimization, to ensure the appropriate use of these procedures, all nuclear medicine facilities should have comprehensive quality control measures in place, their nuclear medicine physicians should have up-to-date training, and their technologists should be appropriately trained and certified [8].

This review focuses on the patient radiation exposure due to both radiopharmaceutical administration and the CT scan modality and emphasizes also the practical ways to reduce the radiation dose to the patients being considered for hybrid imaging.
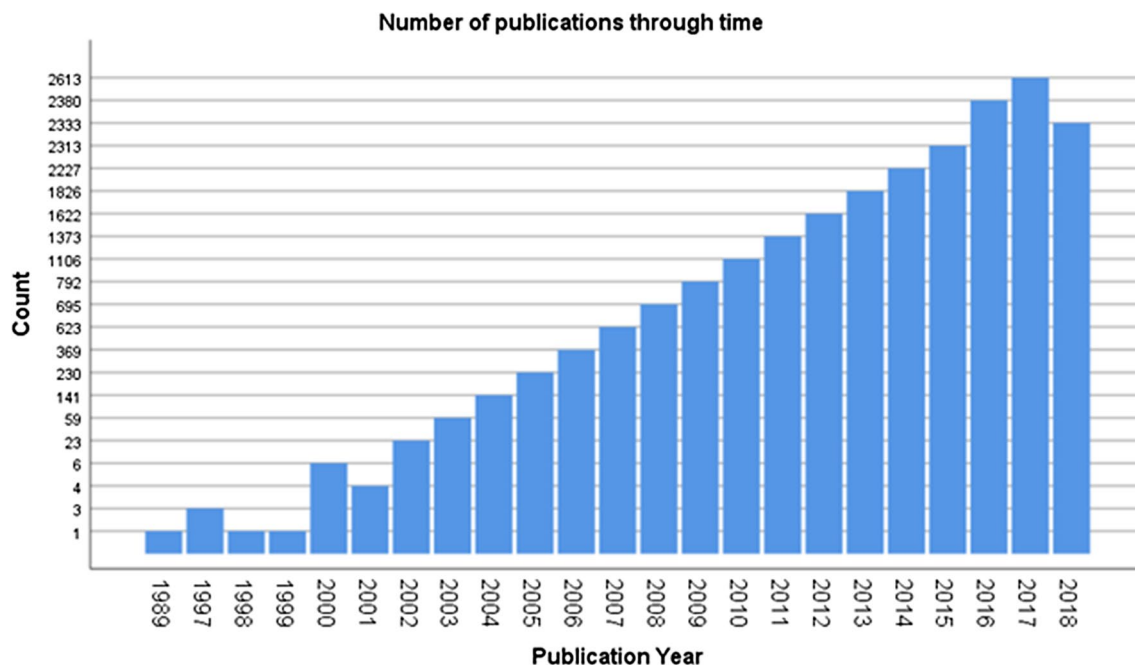

Fig. 1 Trend of scientific papers published in medical literature (PubMed) between 1989 and 2018 about SPECT/CT and PET/CT
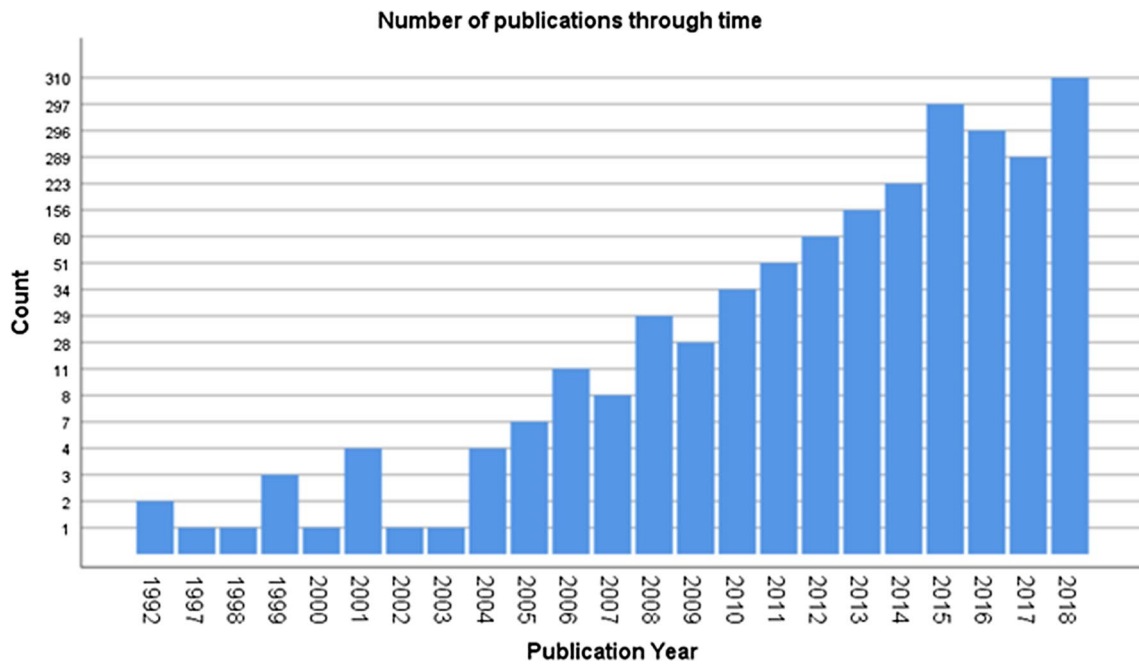
Number of publications through time

Fig. 2 Trend of scientific papers published in medical literature (PubMed) between 1989 and 2018 about PET/MRI

Fig. 3 Example of SPECT/CT system

Fig. 4 Example of PET/CT system

Radiation doses in hybrid imaging

In hybrid imaging, the total radiation dose to patients is the sum of the dose due to the radiopharmaceutical used for SPECT/PET imaging and the dose derived from the CT component of the study. The combined acquisition of functional and anatomical images can substantially increase radiation exposure to patients, particularly in case of a hybrid system with diagnostic CT capabilities.

In nuclear medicine, the effective dose due to the administration of radiopharmaceuticals can be calculated by multiplying the administered activity by the effective dose coefficients per unit of administered activity. Tables 1 and 2 show the dose coefficients reported by Mettler et al. [9], adapted from the ICRP publication 80 [10], and the administered activities in terms of diagnostic reference levels (DRLs) recommended by DLvo 187/00 [11] for SPECT and PET.

The CT component is responsible for a considerable percentage of the patient dose of a hybrid imaging examination [12–14]. The two main dose descriptors in CT are the CTDIvol and the dose-length product (DLP). The CTDIvol represents the estimated mean dose for a single

Table 1 Values of administered activities as reported in DLvo 187/00 [11]. Effective dose coefficients per unit of administered activity (mSv/MBq) for SPECT examinations as reported by Mettler et al. [9]

Organ/Radiopharmaceutical	Effective dose (mSv)	Administered activity (MBq)	Effective dose coefficient (mSv/MBq)
Bone (^{99m}Tc-MDP)	3.4–5.1	600–900	0.0057
White blood cells (^{99m}Tc)	4.0	370	0.011
White blood cells (^{111}In)	7.2	20	0.360
Parathyroid (^{99m}Tc-sestamibi)	6.7	740	0.009
Brain (^{99m}Tc-HMPAO)	6.9	740	0.0093
Cardiac stress rest (^{99m}Tc-sestamibi, 1-day protocol)	12.4	370+1110	0.0085
Cardiac stress rest (^{99m}Tc-sestamibi, 2-day protocol)	12.5	740+740	0.0085
Cardiac stress rest (^{99m}Tc-tetrofosmin)	11.1	370+1110	0.0076

Table 2 Values of administered activities as reported in DLvo 187/00 [11]. Effective dose coefficients per unit of administered activity (mSv/MBq) for PET examinations as reported by Mettler et al. [9]

Radiopharmaceutical	Effective dose (mSv)	Administered activity (MBq)	Effective dose coefficient (mSv/MBq)
^{18}F-FDG (Brain)	4.9	260	0.019
^{18}F-FDG (Cardiac)	4.9	260	0.019
^{18}F-FDG (Tumor)	5.7	300	0.019
^{18}F-DOPA	5.7	300	0.019
^{18}F-CHOLINE	5.1	300	0.017
^{68}Ga-DOTA-peptides	3.7	150	0.025

slice, while the DLP, which is the product of the CTDI-vol and the scan length, estimates the overall radiation dose absorbed by the patient. The DLP can also be used to obtain an approximate estimate of the effective dose to the patient, by multiplying the DLP by a conversion coefficient k specific for the anatomical region under examination ($E = k \times DLP$). K coefficients for adults (standard physique) and pediatric patients of various ages over various body regions are reported in the AAPM Report no. 96 [15].

In 2017, the UK Institute of Physics and Engineering in Medicine conducted a nationwide survey of CT doses for a wide range of SPECT/CT–PET/CT imaging procedures [16]. Table 3 presents a summary of the doses and scan lengths used for different types of examinations and clinical purposes. In these data, each clinical purpose was associated with a wide range of doses and there was a significant overlap in doses for different clinical purposes, thus highlighting the need for optimization in hybrid imaging. For most studies, the CT effective doses were less than 30% of the ones due to radiopharmaceuticals and they only exceeded the 50% mark in case of the radiopharmaceuticals administered for half-body PET/CT and meta-iodobenzylguanidine (mIBG) SPECT/CT examinations.

In hybrid imaging, the effective dose due to the CT component depends on the different clinical purposes such as attenuation correction (AC), anatomical localization, and sometimes even diagnosis. Buck et al. [17], with reference to diagnostic SPECT/CT, reported an additional 6–14 mSv to the radiation dose of the radiopharmaceutical, depending on the field of view in z-axis. While Buck et al. indicate a dose range of 2 to 4 mSv for low-dose SPECT/CT, Roach et al. showed that CT scans used for chest/abdomen anatomical localization amount up to 1–2 mSv [18]. Sawyer et al. [19] reported typical values of around 1.1 mSv for

Table 3 CTDI vol (mGy) and DLP (mGy/cm) suggested values [16]

Examinations		Clinical purpose[a]	CTDIvol (mGy)	DLP (mGy/cm)	Scan length (cm)
PET-CT	Half-body	AC	2.4	232	92
		AC&L	3.2	307	94
		AC&D	4.2	336	91
	Cardiac	AC	1.5	33	21
	Brain	AC	1.2	23	22
		AC&L	6.8	126	19
		AC&D	20.6	429	22
SPECT-CT	Bone scan	AC	6.0	168	28
		AC&L	3.4	114	33
		AC&D	11.2	476	30
	Cardiac	AC	1.6	34	17
	mIBG	AC&L	4.0	183	42
	Octreotide	AC	5.4	217	40
		AC&L	3.3	152	43
		AC&D	5.6	216	38
	Parathyroid	AC	6.0	98	16
		AC&L	4.9	122	26
		AC&D	12.1	285	21
	Post-thyroid ablation	AC&L	4.6	128	35
	Sentinel node	AC&L	4.3	153	33

[a]AC, attenuation correction; AC&D, attenuation correction and diagnosis; AC&L, attenuation correction and localization of the nuclear medicine signal; CTDI$_{vol}$ volume computed tomography dose index; DLP, dose-length product; mIBG, meta-iodobenzylguanidine

the chest, around 1.3 mSv for abdomen–pelvis and around 0.2 mSv for the head. Montes et al. [13] reported similar values (≈ 1.2 mSv) for chest and abdomen–pelvis and 0.6 mSv for the head–neck region. Miller [20] showed an even lower radiation exposure for the CT component of the SPECT/CT examination, such as 0.47 mSv for an abdominal non-diagnostic localization and attenuation-correction scan. These data were also confirmed by Kneifel who assessed an effective dose of 0.5 mSv [21].

The strength of effective dose resides in its capability both to compare radiation exposure due to different imaging techniques and to estimate the biological risk derived from said exposure. However, the estimated value of effective dose is subject to a high degree of uncertainty, related to the tissue-weighting coefficients that are used and their estimation of relative biologic risk [22]. Thus, effective dose must be interpreted as a broad, generic estimate of biologic risk, and differences of several mSv do not imply a true discrepancy in biologic risk [23, 24].

Martin [23] evaluated the inherent uncertainties in estimating effective dose to be about ± 40%. As a consequence, biologic risk should be described using broad categories: negligible, < 0.1 mSv; minimal, 0.1–1 mSv; very low, 1–10 mSv; and low, 10–100 mSv [23]. He also suggested that because effective dose was defined by the ICRP [ICRP 103] to represent an overall risk averaged over all ages and both sexes for a reference patient, neither the Monte Carlo-based organ-dose coefficients nor the DLP-based k values [15] should be used to calculate effective dose estimates for individual patients or to predict population risks.

Moreover, the k coefficient is based on data averaged over many scanner makes and models and therefore cannot accurately represent a specific scanner. Finally, since the dose coefficients are calculated using a simplified anthropomorphic patient model, all estimates of effective dose are applicable only to scans of a standard adult patient. Considering the recent increase in the number of overweight and obese patients, the calculated values of effective dose should therefore be used with caution.

In conclusion, although the effective dose can be used to estimate and compare the risk of radiation exposure across multiple imaging techniques, clinicians should be aware that it represents a generic evaluation of the risk derived from a given procedure to a generic model of the human body. It cannot be applied to a single individual and should not be used for epidemiologic studies or the estimation of population risks due to the inherent uncertainties and oversimplifications involved.

Dose reduction and optimization in hybrid imaging

Practical ways to reduce radiation dose to patients eligible for hybrid imaging include adjustments to both the planning phase and throughout the execution of the study (Table 4).

Planning phase

Prior to the execution, SPECT/CT and PET/CT must be subject to the principle of individual justification of radiation exposure, which is stated as a sufficient net benefit when balanced against possible detriment that the examination might cause. Both the prescriber and the nuclear medicine physician must take into account the specific objectives of the examination and the clinical data of the patient involved, in order to avoid unnecessary radiation exposure [11].

In addition to the radiation exposure justification, the choice of the radiopharmaceutical which has shorter physical and biological half-life also permits to reduce the patient radiation dose. Usually, 99mTc-labeled radiopharmaceuticals should be preferred due to the favorable physical properties of the radionuclide.

DRLs are a useful tool to optimize the radiation dose to patients undergoing SPECT/CT or PET/CT examinations. The DRLs can be defined at a national level or at an institutional or local level. The DRLs related to the radiopharmaceutical component of a hybrid imaging procedure are established in terms of administered activity, while the CTDI$_{vol}$ and the DLP are used for the CT component. Currently in Italy, the DRLs for planar and SPECT radiopharmaceuticals are set at a national level in DL 187/00, while for the PET radiopharmaceuticals they are defined only at a local level. As to the CT component, the adoption of the standard

Table 4 Radiation dose reduction methods in hybrid imaging

Planning phase	General and individual justification of the examination
	Choice of the radiopharmaceuticals, promoting the ones with shorter physical and biological half-lives
	Adherence to national and/or institutional DLRs
	Patient hydration and bladder voiding
Execution phase	Detectors with higher energy resolution (CdZnTe in SPECT/CT)
	Special collimators, which allow a higher sensitivity (variable focus collimators)
	Iterative algorithms able to reconstruct the image with less counts without affecting spatial resolution

diagnostic DRLs is not appropriate because of differences in the clinical purpose, scan range, and image quality requirements of hybrid imaging CT scan. Two surveys have been recently conducted in Switzerland and UK in order to evaluate CT doses for a wide range of PET/CT and SPECT/CT procedures aiming to propose national DRLs [16, 25].

Hydration and bladder voiding are also important ways for dose reduction in hybrid imaging since they limit the radiation dose to the bladder, which is the critical organ subject to the higher exposure. As a reference, for an adult patient the bladder radiation dose during a FDG PET/CT study is 0.16 mGy MBq^{-1} [10].

Execution phase

During the execution of a SPECT/CT or PET/CT examination, several approaches can be used to reduce the radiation dose to the patient, including new technical devices (sensitive detectors or collimators), appropriate reconstruction algorithms, and proper work practices (CT protocols, appropriate selection of exposure parameters).

New multiple solid-state high-efficiency detectors (cadmium zinc telluride—CdZnTe) and optimized acquisition geometry allow to reduce the patient exposure to ionizing radiations. Thanks to an excellent energy resolution, CdZnTe detectors provide an improved count rate. These devices, mainly used in nuclear cardiology, provide a fourfold to sevenfold improvement in sensitivity thanks to higher resolution and contrast-to-noise ratio, if compared with a conventional dual-detector SPECT. Duvall et al. [26] demonstrated that these detectors still provide a high-quality image even while significantly reducing the administered radiopharmaceutical activities [27]. These data were also confirmed in bone scintigraphy by Koulikov et al. [28] who reported a significant reduction of the radiation dose without compromising lesion detection or image quality.

Special collimators provide higher acquisition sensitivity for specific organ examinations. A variable focus collimator was developed by Siemens retaining the magnifying properties of a cone-beam collimator near the center of the field of view and eliminating the truncation artifacts at the edges of the field that are common to pinhole and focusing collimators. Imbert et al. [29] assert that these collimators provide a great improvement in count sensitivity compared to conventional parallel-hole collimators. Their use, assisted by a cardiocentric acquisition and the IQ SPECT reconstruction method, allowed the collection of up to four times as many counts from the heart during a myocardial perfusion SPECT study. Furthermore, Morgan et al. [30] showed that Tc-99 m sestamibi myocardial perfusion images, which are quantitatively equivalent to those acquired with the standard injected activity using LEHR collimation, can be obtained with IQ SPECT technology

in half the time and with half the injected dose. Therefore, the injected dose of radiotracer could be reduced by a factor of four if the IQ SPECT acquisition time were doubled to arrive at the same standard acquisition time used with LEHR collimation.

The introduction of iterative reconstruction methods (e.g., ordered-subset expectation maximization, OSEM) allowed the reduction of the SPECT radiopharmaceutical dose without affecting spatial resolution. These iterative reconstruction methods loop through the data, comparing the reconstructed image to the ''best estimate'' of the image made by the software [27]. Several studies conducted in different fields proved that it is possible to achieve the same image quality with a smaller number of collected counts [31–34].

Similarly, also in CT imaging the introduction of iterative methods allowed significant radiation dose reduction without sacrificing image quality. It is now recognized iterative methods, compared with FBP method, increases detectability at a given radiation dose and allows radiation dose reduction while maintaining low-contrast detectability.

In hybrid imaging, the structural information provided by CT serves different purposes such as AC, anatomical localization, and sometimes even diagnosis. The radiation dose due to CT can be reduced by an accurate choice of CT protocols (i.e., low- or high-dose CT) and scan parameters, such as tube potential, tube load, rotation time, beam width, pitch, and reconstructed image thickness. With regard to the acquisition protocol, clinicians should adjust the CT imaging procedure, taking into account the patient's clinical data [27]. As a general rule, low-dose acquisition is suggested when a recent diagnostic CT is available, in case of evaluation of treatment response, and to better study lesions showed in planar or SPECT images.

A large number of studies covering the previously mentioned parameters have been published [35]. The introduction of simulation tools allows to optimize the CT scanning parameter by adding an artificial level of noise to the CT raw data in order to simulate a lower-dose examination, without affecting the image quality. As mAs is directly related to dose, a lower mAs examination will definitively produce a lower radiation dose scan [14]. A useful method to reduce the dose to radiosensitive organs close to the body surface (i.e., mammary glands, thyroid glands, and eye lenses) in SPECT/CT is the organ-based tube current modulation. This system works by reducing the tube current (kVp) when the tube comes close to these organs. To compensate for this reduction, the tube current in the X-ray projection from the opposite side is increased thus leaving mean image noise constant [27]. Proper scan length can be estimated easily from the internationally published dose reference levels, usually expressed using the CT dose index and dose-length product. Automatic exposure control techniques are now integrated in all new CT scanners, and a large number

of studies have shown their usefulness in patient dose reduction.

Conclusions

Hybrid imaging techniques, such as SPECT/CT and PET/CT, can improve nuclear medicine physicians' daily practice, allowing a more accurate localization and definition of scintigraphic findings thanks to their high sensitivity, specificity and accuracy.

Since the combined acquisition of functional and anatomical images can increase radiation exposure due to the addition of the CT component, clinicians should make adjustments to both the planning phase and the execution phase of the study in order to reduce the radiation dose to patients eligible for hybrid imaging.

With the growing diffusion of PET/MR and the use of new reconstruction algorithms coupled with multiple solid-state high-efficiency detectors (CdZnTe), hybrid imaging is expected to play a greater role in the near future.

Compliance with ethical standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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