Radiation protection and personal dosimetry in a core facility for multimodal small animal imaging

Strahlenschutz und Personendosimetrie in einer Core Facility für multimodale Kleintierbildgebung

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ABSTRACT

Background Clinical imaging techniques such as positron emission tomography (PET) in combination with computed tomography (CT) are increasingly being used in biomedical research involving small animal models. The handling of open radioactive substances (radiopharmaceuticals) necessary for PET imaging requires prior official authorization for handling, the application of radiation protection principles, and regular training. The overriding aim of radiation protection is to protect the personnel directly involved, other persons, and the environment from the harmful effects of ionizing radiation.

Method This paper aims to provide an overview of the regulatory requirements of the Radiation Protection Act (StrlSchG), the Radiation Protection Ordinance (StrlSchV), and the associated standards and guidelines. Furthermore, their implementation in practical work in small animal imaging using PET/CT is shown. We will focus on the individual steps of the imaging process, from delivery of the radiopharmaceuticals to waste disposal. This should provide interested researchers with an initial overview of the safe and successful use of the method. In addition, exposure values from the last six years in the literature were analyzed. While personal dosimetric monitoring in clinical PET/CT imaging has been extensively published, there is no published data known to us for personnel for PET/CT research with small animals. The evaluation of the personal dosimetric monitoring of our small animal imaging facility with 7 employees over 4 years revealed an increased personal and finger dose normalized to the injected activity and compared to human PET/CT imaging. Nevertheless, the annual personal dose or annual finger dose in small animal imaging (Hp(10): 1.7 mSv, Hp(0.07): 64 mSv) is lower than for personnel performing human PET/CT imaging at the local University Department of Nuclear Medicine (Hp(10): 3.8 mSv, Hp(0.07): 156 mSv) or published values, and is well below the legally permissible maximum dose of 20 or 500 mSv per year.

Conclusion The increasing use of PET/CT in small animal research can be safely utilized if the radiation protection principles are implemented and continuously trained.

Key Points

- PET/CT imaging in small animals is increasingly used in biomedical research.
- Radiation protection laws and guidelines have to be known and are relevant in animal experiments.
- Compared to published values from human medicine, activity-specific employee doses are increased in the presented imaging facility.

- The legal personal dose in the studied imaging facility is below legal limits.

Citation Format

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ZUSAMMENFASSUNG

Hintergrund In der biomedizinischen Forschung mit Kleintieren werden zunehmend klinische Bildgebungsverfahren wie die Positronen-Emissions-Tomografie (PET) in Kombination mit der Computertomografie (CT) genutzt. Der für die PET-Bildgebung nötige Umgang mit offenen radioaktiven Stoffen (Radiopharmaka) erfordert sowohl die vorherige behördliche Genehmigung des Umgangs, die Anwendung von Strahlenschutzgrundsätzen als auch regelmäßiges Training. Das übergeordnete Ziel des Strahlenschutzes ist sowohl das direkt tätige Personal als auch sonstige Personen und die Umwelt vor der schädlichen Wirkung ionisierender Strahlung zu schützen.
Methode Diese Arbeit zielt darauf ab, einen Überblick über die regulatorischen Anforderungen aus dem Strahlenschutzgesetz (StrlSchG), der Strahlenschutzverordnung (StrlSchV) und den assoziierten Normen und Richtlinien darzustellen. Weiterhin wird deren Umsetzung beim praktischen Arbeiten in der Kleintierbildgebung mittels PET/CT aufgezeigt. Hierbei konzentrieren wir uns auf die einzelnen Arbeitsschritte der Bildgebung vom Empfang der Radiopharmaka bis zur Entsorgung des Abfalls. Dies soll interessierten Forschenden eine erste Übersicht über die sichere und erfolgreiche Nutzung der Methode bieten. Außerdem wurden Expositionswerte der letzten sechs Jahre mit einer Literaturanalyse erschlossen. Während die personendosimetrische Überwachung bei der klinischen PET/CT-Bildgebung umfangreich publiziert wurde, gibt es keine uns bekannten publizierten Daten für das Personal in der präklinischen PET/CT-Forschung mit Kleintieren. Die Auswertung der personendosimetrischen Überwachung unserer Kleintierbildgebungseinrichtung mit 7 Mitarbeitenden über 4 Jahre ergab eine, im Vergleich zur humanen PET/CT-Bildgebung, erhöhte Personen- und Fingerdosis normiert auf die injizierte Aktivität. Dennoch ist die Jahrespersonen- oder Jahresfingerdosis in der Kleintierbildgebung (Hp(10): 1,7 mSv, Hp(0,07): 64 mSv) geringer als in der humanen PET/CT-Bildgebung der lokalen universitären Klinik für Nuklearmedizin (Hp(10): 3,8 mSv, Hp(0,07): 156 mSv), bzw. publizierten Werten und unterschreitet die gesetzlich zulässige maximale Dosis von 20 bzw. 500 mSv pro Jahr weit.
Schlussfolgerung Die zunehmende Anwendung von PET/CT in der Kleintierforschung bei Umsetzung und kontinuierlichem Training der Strahlenschutzgrundsätze ist somit sicher nutzbar.

Kernaussagen

- Die PET/CT-Bildgebung bei Kleintieren wird in der biomedizinischen Forschung zunehmend eingesetzt.
- Strahlenschutzgesetze und -richtlinien müssen bekannt sein und auch bei Tierversuchen angewendet werden.
- Im Vergleich zu publizierten Werten der Humanmedizin ist die aktivitätsspezifische Mitarbeiterdosis in der betrachteten Kleintierbildgebungseinrichtung erhöht.
- Die gesetzlichen Personendosis-Grenzwerte werden in der vorgestellten Kleintierbildgebung unterschritten.

List of abbreviations

ADR	Agreement concerning the International Carriage of Dangerous Goods by Road (Accord européen relatif au transport international des marchandises dangereuses par route)
CF	Core facility for multimodal small animal imaging
CT	Computed tomography
DIN	German Institute for Standardization
HU	Hounsfield Units
ID	Inner diameter
MRI	Magnetic resonance imaging
OSL	Optically stimulated luminescence dosimeter
PET	Positron emission tomography
RiPhyKo	Guidelines for physical radiation protection control for ascertaining body doses
StrlSchG	Radiation Protection Act
StrlSchV	Radiation Protection Ordinance

Introduction

In the field of biomedical research, the use of imaging methods, e. g., X-ray, single photon emission computed tomography, and positron emission tomography/computed tomography (PET/CT) in animal experiments has increased significantly [1, 2]. These methods provide information about anatomy and morphology as well as physiological and pathophysiological processes. In addition, they can reduce the number of animals needed for experiments due to their noninvasive character and the possibility of using longitudinal study designs [3].

These high-performance imaging methods are associated with potential radiation exposure, making careful consideration of radiation protection strategies and measures necessary. The goal of the measures is to protect personnel exposed to radiation as well as other uninvolved colleagues and the environment. To reach the protection goals, a number of regulatory requirements must be taken into consideration when handling radioactive substances and radiation [4].

Primarily in the case of experimental animal studies involving PET/CT imaging and the open, high-energy radiopharmaceuticals needed for these studies, radiation protection is a complex endea-

vor including the use of shielding techniques and the careful handling of sources of radiation [5]. PET is an examination method in which the distribution of a radioactively marked radiopharmaceutical in an organism is observed after injection of the radiopharmaceutical into the organism. As a result, conclusions about the underlying physiological or pathophysiological processes can be drawn [6]. Physically, the method is based on the detection of two gamma photons resulting from the annihilation of the positrons emitted by the radionuclide and an electron. A number of different radioactive isotopes, e. g., ^{11}C, ^{68}Ga, ^{18}F or ^{89}Zr, can be used for marking the tracers.

While the basic principles of radiation protection and its use in the clinical setting have been thoroughly examined and work processes have been standardized [4, 7, 8, 9], the basic conditions associated with animal experiments require customized approaches in order to effectively minimize possible risks, e. g., due to unintentional exposure.

The goal of this article is to provide an overview of the legal requirements regarding radiation protection in the field of preclinical PET/CT imaging. The presented practical implementation of these requirements allows researchers to better orient themselves with respect to the complex requirements (▶ **Table 1**) of radiation protection thereby ensuring responsible and effective use of PET/CT imaging.

Moreover, we show, for the first time to our knowledge, personal and finger dose values acquired during operation of a facility for small animal imaging and compare these with values from the clinic for nuclear medicine as well as with values from the literature from the last 6 years.

Regulatory requirements

The primary goal of legal regulations here is to protect people and the environment from the damaging effect of ionizing radiation. According to § 12, Paragraph 1, No. 3 of the Radiation Protection Act (StrlSchG) [15], the handling of radioactive substances with activity exceeding the nuclide-specific exemption limit according to Appendix 4, Table 1, Columns 2 and 3 of the Radiation Protection Ordinance (StrlSchV) [14] requires authorization. The radiation protection supervisor of the facility must apply for the necessary handling permit from the nuclear supervisory authority of the relevant federal state. If the CT component is also a full-protection device, notification must be provided to the supervisory authority in accordance with § 19 of the Radiation Protection Act. The radiation protection supervisor is personally responsible for ensuring compliance with the regulations of the Radiation Protection Act and the Radiation Protection Ordinance and providing the required equipment and personnel. Laws and ordinances form the legal framework whose implementation is defined in standards and guidelines. The latter are extremely important for the planning of laboratories and working areas.

If the radiation protection supervisor can show that safe handling of radioactive substances is ensured, the supervisory authority must issue approval. The requirements are based on the type and severity of the risk resulting from the handling of radioactive substances. The basis of every risk assessment is to define activities and to assign them to handling sites. Exposure, incorporation, and contamination risks can be derived from the type of activity. The ratio of the potential dose for persons in contact with ionizing radiation to the legal dose limits is decisive. While the exposure to external radiation sources is determined by their nuclide-specific exposure rate coefficients, activity, working distance, and duration of stay, the percentage of the activity that can be absorbed must be taken into consideration to determine the dose due to incorporation, Volatile radioactive substances are associated with a higher risk than liquid or solid non-volatile substances. The incorporation risk can be assessed based on the incorporation factor, the nuclide-specific dose coefficient, and the activity in accordance with guidelines for physical radiation protection control for ascertaining body doses [16].

With the risk assessments based on the activities and nuclides being used, categorization into classes is performed. Room categories, safety levels, and radiation protection areas are named here as examples. The classes then result in concrete requirements regarding structure, technology, and radiation protection organization [10, 11, 12] as shown in ▶ **Table 1**.

Training and instructions for handling radioactive substances

Initial handling of radioactive substances must be preceded by training in accordance with § 63 of the Radiation Protection Act [15] and subsequent annual mandatory training. The goal is to raise awareness of all radiation protection matters among every employee and to communicate the most important rules. In addition to the three rules of radiation protection (increase distance, use shielding, minimize duration of stay), location-specific training and practical training regarding work procedures when handling radioactive substances are important factors for minimizing radiation exposure. Important training content includes the portioning and dispensing of small tracer quantities, the effective elimination of contamination, and the proper handling of irradiated animals under consideration of the specific spatial conditions and the conditions of the particular laboratory.

Practical work and implementation of radiation protection

The ALARA principle (“as low as reasonably achievable”) [17], i. e., the ionizing radiation dose must be kept as low as reasonably achievable, is applied to all practical activities regarding small animal PET/CT with respect to radiation protection.

The handling of radiopharmaceuticals in a facility for small animal PET/CT begins, as in human PET/CT, with delivery (▶ **Fig. 1a**, **b**). Depending on site availability, these substances are obtained from special radiochemical or radiopharmaceutical departments of the clinic or from external service providers. In any case, the special requirements according to part 2.2.7 of the ADR must be taken into consideration when transporting radioactive substances [18]. If the limits are exceeded, it is necessary to apply for transport approval according to § 27 of the Radiation Protection Act, to appoint radia-

▶ **Table 1** Overview of the structural, organizational, and personnel requirements for handling radioactive substances above the nuclide-specific exemption limit.

Structural requirements [10, 11, 12]	
1.	Delimitation and access restrictions ▪ Structural delimitation of the radiation protection areas ▪ Labeling of the radiation protection areas (▶ **Fig. 2**). ▪ Access and mandatory routes ▪ Air lock useful; mandatory starting with room category 2 ▪ Access only for authorized personnel; security with suitable lock system ▪ Exiting of the radiation protection areas after clearance measurement of personnel and objects
2.	Shielding ▪ Delimitation of the general premises ▪ Shielding of radiation protection areas (limit: 1 mSv/year) ▪ Shielding of walls is usually sufficient for small animal experiments
3.	Protection against theft ▪ Security level determines the barrier requirements for facades, rooms, and storage containers ▪ Identification of all possible means of theft ▪ Provision of sufficient lighting, possible installation of a security alarm system ▪ Emergency plans in the event of theft or unauthorized access
4.	Fire safety ▪ The risk level determines the necessary fire resistance of the materials used to build walls and ceilings, doors and airlocks, cable guides, pipes, and air ducts. ▪ Setting up fire and smoke compartments ▪ Removal of potential fire hazards
5.	Airflow and ventilation ▪ The room category determines measures for preventing contamination of supply and exhaust air systems ▪ Prevention of the spread of radioactive substances into unauthorized areas ▪ Prevention of the inhalation of radioactive substances with efficient air circulation and air removal ▪ Use of airlocks and flues without affecting air circulation ▪ Ruling out of reversal of the flow direction ▪ Removal of exhaust air always via the roof with the possibility of taking samples starting at room category 2
6.	Wastewater ▪ Analogous to ventilation, the room category determines the scope of measures ▪ Prevention of contamination of the general water supply by designing suitable drains or local filtration or by storing contaminated wastewater ▪ It must be possible to take samples from the wastewater ▪ Almost no contaminated wastewater in the case of small animal experiments
Organizational requirements	
1.	Definition of responsibilities ▪ If the radiation protection supervisor is not an expert or there are no resources to independently fulfill responsibilities: Appoint a radiation protection officer with expert group S4.2 for handling open radioactive substances 10 times the exemption limit [13] ▪ The radiation protection officer is responsible for maintaining radiation protection on-site, e. g., defining radiation protection measures, checking their effectiveness, and optimizing measures ▪ An expert physician is not needed when using radiation on animals
2.	Radiation protection instructions ▪ Instructions regarding daily handling of radioactive substances ▪ Instructions for a disaster (emergency plans) ▪ Provision of means for decontamination and limiting radiation exposure ▪ Contact data for fast communication with experts ▪ Use of work instructions for standardizing processes
3.	Applied radiation protection ▪ Provision of suitable shielding by means of syringe shields, grabber tools, lead castles, etc. ▪ Introduction of dose reference values for optimizing/reducing exposure
4.	Documentation ▪ Documentation and reporting of activity in the radiation protection area ▪ Listing of all radioactive sources (test sources) ▪ Annual leak test of contained sources by experts ▪ Documentation of issued instructions

▶ **Table 1** (Continuation)

Personnel requirements	
1.	Dosimetric monitoring ▪ Monitoring of radiation exposure for employees using official personal dosimeters (whole-body and hand dose, possibly eye lens dose, ▶ **Fig. 4**) ▪ Checking and classification of dosimetry results ▪ Grouping of persons with professional exposure to radiation based on the dose to be expected and the incorporation risk, usually in category A [14] ▪ **Regular examination of people with professional exposure to radiation by a company physician**
2.	Training and technical qualifications ▪ Training of new personnel working in radiation protection areas ▪ Annual training requirement for any personnel entering the radiation protection area, e.g. also for people taking care of the animals, technicians, cleaning staff ▪ Proof of technical qualifications of the radiation protection officer

tion protection officers for transport, to train drivers, to properly equip the vehicles, and to provide adequate transport documentation. Depending on the activity, the radiotracers are delivered to the facility according to regulations [19] as an excepted package (UN2910) or as a radioactive substance (UN2915) in packaging in accordance with a type A package. The delivery is documented and countersigned by the transporter and an employee of the facility. After arrival, the radiotracer is transferred in the transport container to the hot laboratory (control area, see ▶ **Fig. 2**) and removed from the transport container. The total radioactivity is checked with a dose calibrator and is also documented. The container with the radiotracer is then equipped with a suitable lead shield and also stored behind a further lead shield. Since this step usually involves maximum activity according to the handling permit, radiation exposure is potentially highest. Gripping aids and container shields should be used whenever possible (▶ **Fig. 1c**) to reduce exposure [20].

Quality control of scanners and other devices

For exact quantitative PET/CT imaging, all devices for determining radioactivity, like dose calibrators, well counters, and especially PET scanners, must regularly undergo quality checks. Manufacturer-specific radiation sources are used for these checks. Long-lived radionuclides like ^{22}Na, ^{137}Cs, and ^{152}Eu with activities in the range of 18 kBq to 20 MBq are typically used for this. The type and frequency of quality checks (every workday to annually) and the necessary nuclides are based on the specifications of the manufacturer of the device.

The radioactive sources of radiation needed for quality checks are only removed from their secure shielding when they are ready to be used and are handled as briefly as possible. When not in use, these substances are shielded and stored in a safe where they cannot be accessed.

The user only briefly comes into contact with the radioactive sources during all of these tasks so that the exposure time is typically very short (max. 10 s) and there is maximum activity usually of 20 MBq.

Preparing the PET/CT scan

In addition to daily quality control, employees prepare the workplace and the animals for upcoming experiments. For short-lived nuclides like ^{11}C or ^{15}O, it is typical to anesthetize the animal for the first PET/CT scan and to place the injection catheter prior to arrival of the radiotracer at the facility in order to allow quick injection of the radiotracer soon after delivery. In the case of nuclides with a medium half-life like ^{18}F or ^{68}Ga, the animal is prepared for the PET/CT scan either after or at the same time as the arrival of the radiotracer at the facility (▶ **Fig. 1e**, **f**).

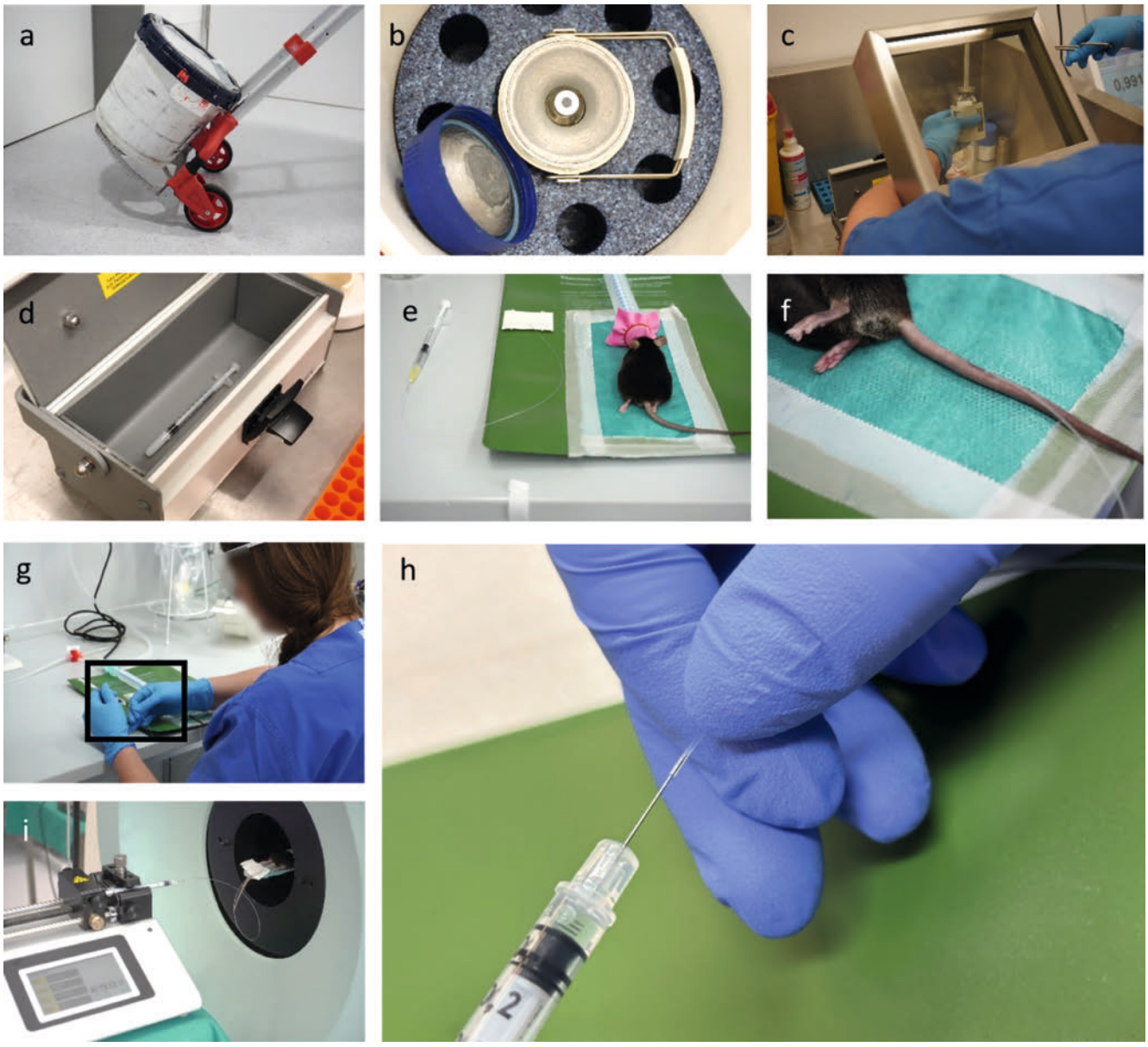
Injection and distribution of the radiotracer

Just prior to the planned injection of the radiotracer, the necessary activity of 10 to 20 MBq in a species-specific volume (e.g., 5 ml/kg body weight mouse: 20 g – max. 100 µl) [21] is drawn into the syringe and the radioactivity in the syringe is determined with a dose calibrator. Preparation of the syringe is typically associated with the highest exposure for employees. Therefore, this procedure is performed behind a lead shield with additional shielding of the head region by leaded glass (▶ **Fig. 1c**). The exposure time can be minimized by routine execution of this procedure. The syringe with the radiotracer is transported from the hot laboratory to the animal in a portable lead bag (▶ **Fig. 1d**).

In the case of static PET scans, the radiotracer is injected at the preparation site as a manual bolus over a period of 2–10 seconds (▶ **Fig. 1 g, h**). In the case of manual applications in humans, syringe shields are used. When working with small animals, handling is significantly more difficult than in humans due to the smaller application volumes. Due to their weight, syringe shields make it difficult to connect the cannula to the catheter, resulting in application errors and contamination. Therefore, these are often not used [5].

The contamination risk is highest during injection. Leaks in the syringe-catheter system, an excessively high application pressure, backflow, or residual drops of liquid can cause contamination.

The residual activity in the syringe is then determined at the activity measurement station and the syringe is then disposed of in a drop container behind a lead shield (▶ **Fig. 3c**). After injection



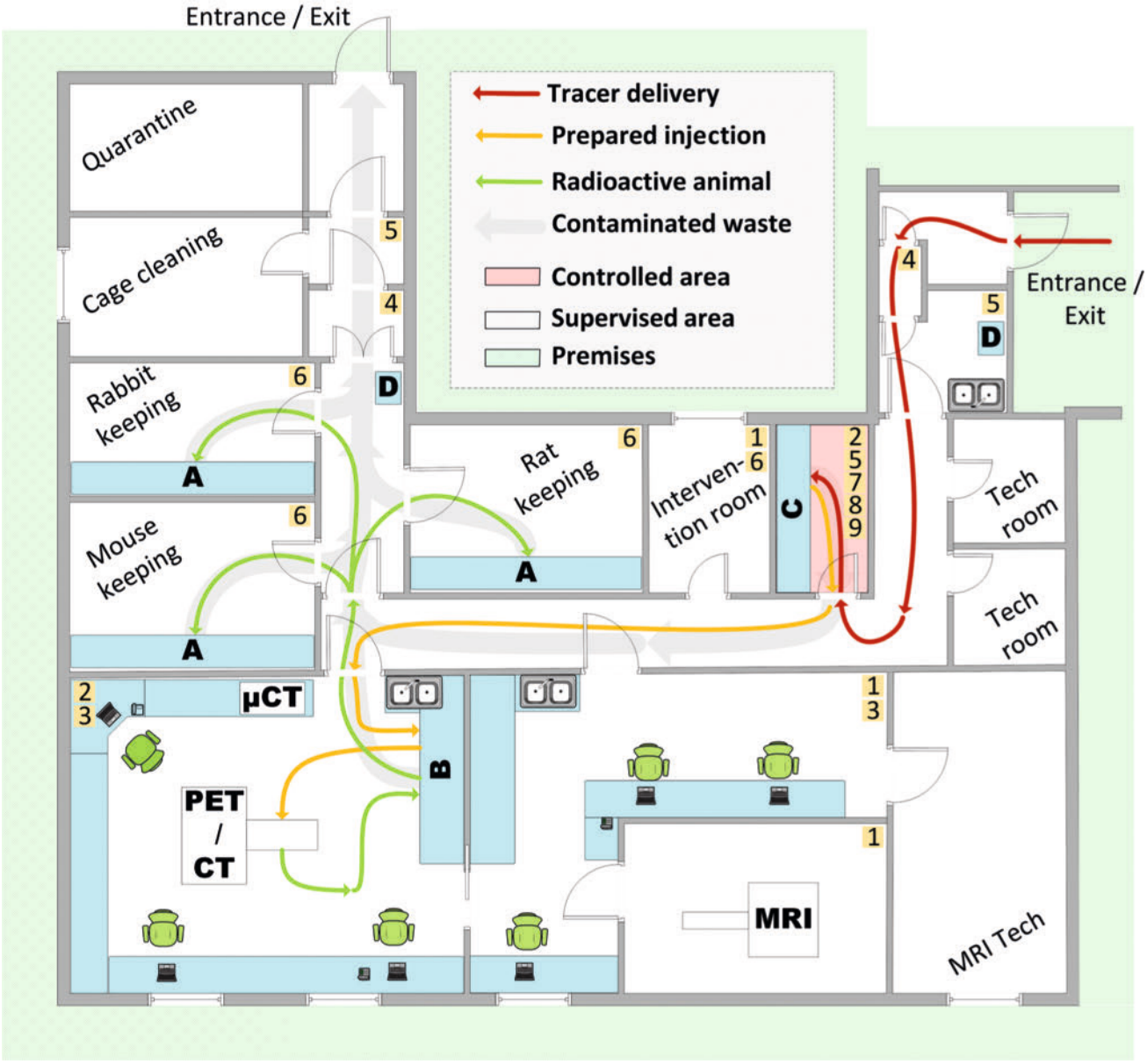
▶ **Fig. 1** **a** Delivery of the radiopharmaceutical in shielded transport container; **b** Opened transport container with shielding container inside and vail in the middle; **c** Handling of the radiopharmaceutical vail with the aid of gripping forceps, working inside a lead shield with viewing window; **d** Transport shield with filled radiopharmaceutical in fine-dose syringe for injection into the animal; **e** Mouse under anesthesia – preparation for injection of the tracer into the tail vein; **f** Microcatheter in the tail vein of a mouse; **g, h** Connecting the radiopharmaceutical syringe to the microcatheter; **i** Injection of the radiopharmaceutical using a syringe pump in a mouse undergoing dynamic PET/CT acquisition.

of the radiotracer, the animal is transferred to a heated anesthesia chamber. The animal remains there during the tracer distribution time and is then transferred to the scanner just prior to the PET/CT scan.

In special cases like dynamic PET imaging, the animal is transferred to the PET/CT scanner directly after anesthetization and placement of the injection catheter. After positioning of the animal in the scanner, the radiotracer is injected continuously over a period of 30 seconds (mice) to one minute (rats) while PET imaging is initiated (▶ **Fig. 1i**). The longer injection time can result in a higher body and finger dose. A dose reduction for employees can be achieved here by using a syringe pump or injection pump.

PET/CT scan

During PET/CT imaging, the radiation exposure for employees is to be considered low due to the shielding effect of the device. Full-protection devices are typically used for CT imaging in the preclinical area. Therefore, the radiation exposure is negligible. The animal is monitored mainly by monitoring its breathing and cardiac rhythm by means of a vital signs monitoring system suitable for small animals (e. g. Biovet, m2 m Imaging Corp, Newark, USA or model 1030 Monitoring & Gating System, SA Instruments Inc. Stony Brook, USA). A visual/manual check of the animal is only needed in the case of deviations from spontaneous breathing or



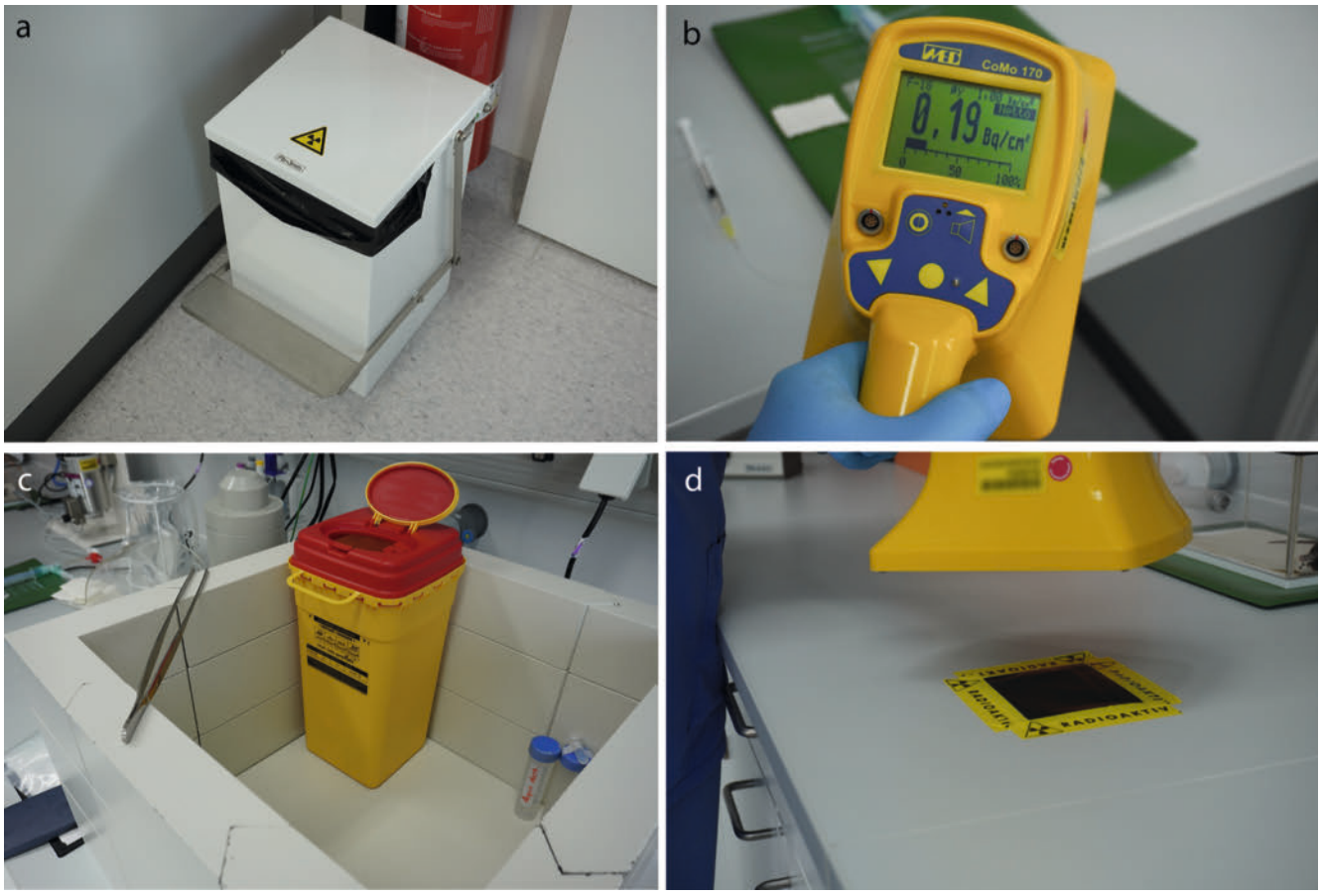
▶ **Fig. 2** Floor plan of the core facility for multimodal small animal imaging of the Rostock University Medical Center with PET/CT imaging system (Inveon Multimodality PET/CT, Siemens Healthineers), µCT (Skyscan 1076, Bruker) and 7 Tesla Biospec MRT (Bruker). Transport routes for the nuclides in the building are indicated by arrows. Room types: 1 – laboratory rooms, 2 – measurement rooms, 3 – writing and evaluation rooms, 4 – airlocks, 5 – decontamination rooms or rooms for cleaning protective clothing, 6 – animal husbandry and experimentation rooms, 7 – rooms for collection and, if necessary, decay storage and preparation of decay storage, decay storage and preparation for removal of residual materials, 8 – storage rooms for radioactive materials, 9 – storage rooms for residual materials, 10 – rooms for waste water systems, 11 – rooms for exhaust air/exhaust air system (not shown), 12 – social rooms (not shown). A – individually ventilated cages, B – animal preparation/injection and recovery area, C – tracer preparation, D – contamination monitor.

heartbeat. Moreover, the distance from the irradiated animal and the radiation source is simple to maximize in this work step.

Aftercare and wakeup phase of the animal

After conclusion of the PET/CT scan, the animal is transferred to a cage behind a shield. The cage is labeled as radioactive by a card indicating the nuclide that was used and the clearance date. The animals remain in the facility or in an area with a handling permit until decay of the radiotracer. After decay of the radiotracer, the animals can be transferred to other housing.

When an experiment requires the killing of the animal and removal of its organs directly after the PET/CT scan, special care is taken to avoid contamination. The cadaver or the removed organs are then stored in the hot laboratory until decay of the radiotracer. If transcardial perfusion is performed, the solutions used for perfusion like saline, PBS, or paraformaldehyde are collected in suita-



▶ **Fig. 3** **a** Shielded waste container for contaminated consumables; **b** Surface contamination monitor for contamination search at the workplace; **c** Drop container for contaminated syringes and needles behind a lead shield; **d** Clearance measurement of a contamination site after decay time, decontamination could not be achieved initially (e. g., due to liquid penetration into a damaged table surface).

ble containers and also stored in the hot laboratory until the radioactivity reaches the exemption limit for the particular nuclide.

The workplace is then checked for radioactive contamination with a surface contamination monitor (▶ **Fig. 3b**). If the surface is contaminated, it is cleaned and tested again. A surface is considered not contaminated when the clearance values are below the values specified in Table 1 Appendix 4 of the Radiation Protection Ordinance [14]. If decontamination is not possible, the corresponding area is blocked off and labeled with information about the nuclide and the clearance time. Temporary closure of the entire room is possible but is usually not necessary for the nuclides and activities used in preclinical imaging. However, the radiation protection officers must be informed of the incident and unintentional spreading of the contamination must be effectively prevented with containment and proper labeling. To determine a sufficient decay time, 10x the half-life of the radionuclide is used in practice. The contaminated surface can only be released after another clearance measurement (▶ **Fig. 3d**).

Disposal of waste

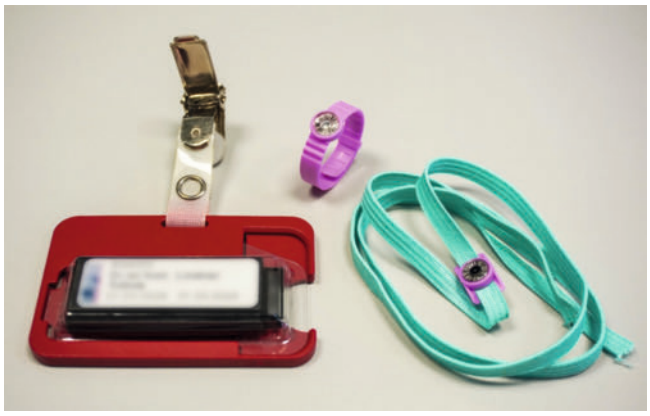
Radioactive waste from the facility is stored in various shielded containers based on the specific isotope (▶ **Fig. 3a**) until the nuclide-specific exemption limit according to Table 1 of Appendix 4 of the Radiation Protection Ordinance [14] has been reached and is disposed then of in the facility's municipal waste after an active clearance measurement. The amount of waste is documented for the annual report to the responsible authorities.

Exiting radiation protection areas

When personnel leave the radiation protection area, a clearance measurement using a hand-foot-clothing contamination monitor must be performed in order to prevent contamination with radioactive substances outside the control and monitoring area. Especially subsequent unintentional absorption of radioactive substances into the body via the skin or hand-mouth ingestion or inhalation is to be prevented at this point.

Personal dosimetry sample data

For radiology technicians and medical personnel working in PET/CT areas of nuclear medicine, values for radiation dose per employee are documented in the literature [4, 8, 9, 22], e. g., in the form of the absorbed dose normalized to the injected activity



▶ **Fig. 4** Personal dosimeter – left: optically stimulated luminescence dosimeter (OSL dosimeter) for measuring the deep personal dose Hp(10); center: thermoluminescence detector (TLD) – ring dosimeter for measuring the surface personal dose Hp(0.07) for estimating a local skin dose or organ dose of the hands; right: TLD for measuring the eye lens dose Hp(3).

[23]. Corresponding values are not yet available for those performing research involving animal experiments. Therefore, we conducted a retrospective study of the official personal dosimetry analysis of our core facility (CF) for multimodal small animal imaging. The CF has one 7 Tesla BioSpec MRI scanner (Bruker Biospin Gmbh, Ettlingen, Germany), one Skyscan 1076 µCT scanner (Bruker), and one Inveon Multimodality PET/CT scanner (Siemens Healthineers AG, Zürich, Switzerland, ▶ **Fig. 2**). The CT scanners are full-protection devices. Therefore, radiation exposure during operation is negligible.

A time period of 4 years (2019–2023) and in total 7 employees (radiology technicians and research fellows) were included in the analysis. During the analysis period, a maximum of 5 employees was present at the same time and worked at the CF for between 4 and 48 months. A total of 1295 injections with ^{68}Ga and ^{18}F radiotracers were administered to mice and rats during this time period. In total, 20.3 GBq of activity with 15 ± 5 MBq per injection were administered. The monthly dose values measured by official body and finger dosimeters (National Institute for Personal Dosimetry and Radiation Protection Training, ▶ **Fig. 4**) were normalized to the activity injected by employees in the particular month and are shown in ▶ **Table 2**. Current literature values are compared to the values from the CF in ▶ **Table 2**. For this purpose, a PubMed search for the key works “occupational”, “dose”, “PET”, “occupational exposure”, “PET”, “PET/CT” was performed (search period 03/04–03/15/2024). The inclusion criteria for the analysis were scientific studies in English and German addressing radiation protection and personal dosimetry in small animal imaging or in clinical facilities.

▶ **Table 2** shows that an increased normalized dose per activity is reached in small animal imaging compared to human PET/CT imaging. It must be taken into consideration that the values differ greatly in the indicated studies. For example, Yin et al. showed a lower finger dose per activity of 14.3–37.57 µSv/GBq for radiology technicians, while Eakins et al. calculated a normalized average finger dose of 581 ± 779 µSv/GBq for radiology technicians [26, 35]. These differences are probably due to the fact that tasks like the dispensing of the activity, injection, and patient positioning in the scanner are performed by different groups of people in the clinical routine so that dose values are difficult to compare. All work steps are primarily performed by one person in small animal imaging. Moreover, the degree of automation, e. g., injection systems [24], is greater in clinical use and the higher volumes make it easier to use syringe shields compared to small animal imaging. However, as a result of the low injected activity per animal, the calculated total doses are below the limit values in spite of the very high dose normalized to the activity. Maximum capacity utilization of the CF results in a maximum annual finger dose of 323 mSv for one employee when the absorbed dose per GBq of activity is multiplied by the total injected activity. (Assumptions: 24 GBq of total injection activity per year for 200 workdays, 8 animals per day, and 15 MBq of injected activity/animal; 13440 µSv/GBq). Analogously, the maximum achievable annual personal dose would be 4.7 mSv (24 GBq of total injection activity x 195 µSv/GBq). The calculated dose values are much higher than the actual personal doses measured by official dosimeters since the maximum capacity utilization of the CF is not reached in reality and personnel rotate through the different workplaces of the CF.

▶ **Fig. 5** shows the actually measured monthly dose values from the CF and the clinic for nuclear medicine. A significant difference between the monthly body dose values of employees in small animal imaging with at least one injection compared to the monthly body dose values for radiology technicians in the clinical setting (mean: 0.07 mSv vs. 0.17 mSv, $p < 0.00001$) and no significant difference between the finger dose values (4.06 mSv vs. 5.51 mSv, $p = 0.43$) were seen. The absolute values for annual personal dose (0.5 ± 0.5 mSv/a, min-max 0–1.13 mSv/a) and finger dose (20 ± 25 mSv/a, min-max 0–63 mSv/a) of all CF employees is less than the values for human PET/CT imaging (personal dose: 2.1 ± 1.1 mSv/a, min.-max. 0.6–3.8 mSv/a; finger dose: 62 ± 57 mSv/a, min.-max. 10–156 mSv/a). However, statistical verification of this statement regarding annual personal and finger doses is not useful at this point due to the small sample size and the lack of continuity regarding the persons working in small animal imaging throughout the year. In total, the examined dose values for employees at the core facility are significantly less than the legal limits for persons with professional exposure to radiation in category A (20 mSv/a and 500 mSv/a). The normalized dose values indicate that training regarding the handling of radioactive substances is essential among new as well as experienced employees to keep exposure as low as possible.

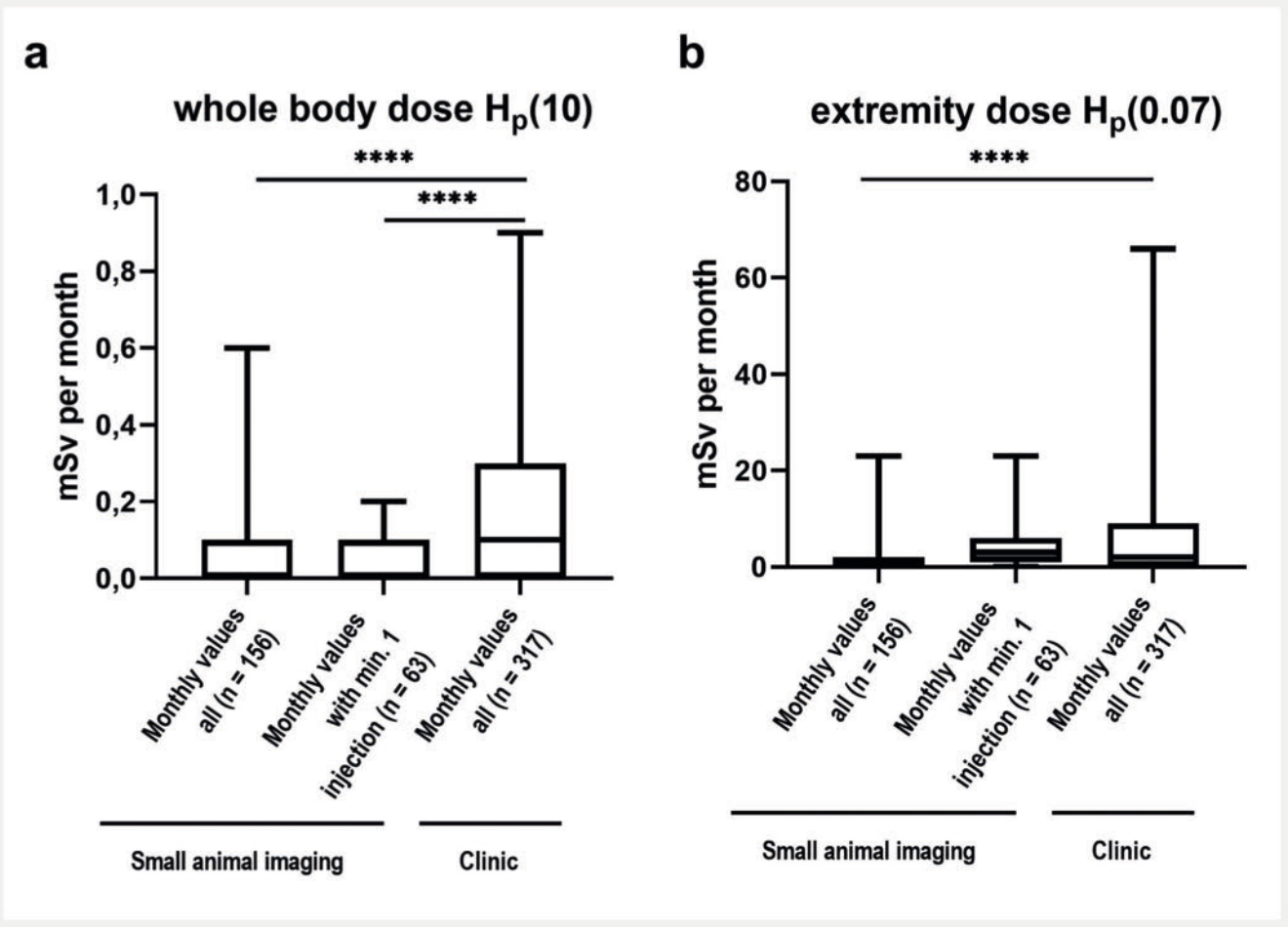
In animal experiments, analysis of the eye lens dose is also of interest since the eyes come in much closer contact with the syringe and thus the activity due to the small size of the syringes and catheters (ID 0.28 mm) compared to clinical use. These values are currently recorded on a continuous basis, but a useful analysis is not yet possible.

▶ **Table 2** Literature overview of published dose values from clinical PET/CT operation normalized to the injected activity in µSv/GBq with dose values from our small animal imaging. Original values from the respective literature with additional conversion to µSv/GBq are given for better comparability. Converted values are marked with *.

Study	Employees	$H_p(10)/A$	$H_p(0.07)/A$
CF small animal imaging	Radiology technician, scientist (with at least one injection)	194.70 ± 274.80 µSv/GBq (min.-max.: 0–1230 µSv/GBq)	13440 ± 15640 µSv/GBq (min.-max.: 0–74020 µSv/GBq)
Adliene et al. [24]	Radiology technician (IRIDE injection system)	4.85 ± 0.18 nSv/MBq *(4.85 ± 0.18 µSv/GBq)	/
	Radiology technician (ALTHEA injection system)	6.17 ± 0.23 nSv/MBq *(6.17 ± 0.23 µSv/GBq)	/
Costa et al. [25]	Radiology technician	Min.-max.: 11.5 nSv/MBq–23.8 nSv/MBq *(min.-max.: 11.5 µSv/GBq–23.8 µSv/GBq)	/
Eakins et al. [26]	Radiology technician	/	581 ± 779 µSv/GBq
	Medical physicist	/	163 ± 67 µSv/GBq
Farkas et al. [27]	Radiology technician	/	0.0011665 µSv/MBq/technician/d *(1.12 µSv/GBq/technician/d)
Kollaard et al. [28]	Nuclear medicine personnel	/	Min.-max.: 100–4430 µSv/GBq (Median 830 µSv/GBq)
McCann et al. [29]	Radiology technician, radiochemist	/	0.25 mSv/GBq (min.-max.: 0.01–3.34 mSv/GBq) *250 µSv/GBq (min.-max. 10–3340 µSv/GBq)
Mosima et al. [30]	Radiology technician (radiographers)	Min.-max.: 0.25–1.43 µSv/mCi *(min.-max.: 6.76–38.65 µSv/GBq)	Min.-max.: 2.44–38.3 µSv/mCi *(min.-max.: 65.95–1035.1 µSv/GBq)
	Radiochemist (Radiopharmacists)	Min.-max.: 0–0.32 µSv/mCi *(Min.-max.: 0–8.65 µSv/GBq)	
Pavičar et al. [31]	Radiology technician, nursing staff (technicians, nurses)	Min.-max.: 15.61–18.55 µSv/GBq	Min.-max.:16.99–25.44 µSv/GBq
Riveira-Martin et al. [32]	Nursing staff (nurse)	6.5 ± 2.3 µSv/GBq	318 ± 136 µSv/GBq (min.-max.: 228–474 µSv/GBq)
Soret et al. 2020 [33]	Radiology technician (PET/MRI)	10.3 ± 4 nSv/MBq *(10.3 ± 4 µSv/GBq)	/
Soret et al. 2022 [34]	Radiology technician (PET/CT)	4.7 ± 1.2 nSv/MBq *(4.7 ± 1.2 µSv/GBq)	/
	Radiology technician (PET/MRI)	10.3 ± 3.5 nSv/ MBq *(10.3 ± 3.5 µSv/GBq)	/
Yin et al. [35]	Radiology technician (injecting nurse)	/	0.84 ± 0.47 mSv/Ci (min.-max.: 0.53–1.39 mSv/Ci) *(22.7 ± 12.70 µSv/GBq, min-max: 14.3–37.57 µSv/GBq)
	Radiology technician (dispensing technician)	/	0.75 ± 0.72 mSv/Ci (min.-max.: 0.19–1.94 mSv/Ci) *(20.27 ± 19.46 µSv/GBq, min-max: 5.14–52.43 µSv/GBq)

Conclusion

Measurement of the radiation dose for employees working in small animal PET/CT imaging is required by law and is performed by the corresponding facilities. However, specific values for this area are currently lacking in the scientific literature. In this article, we present for the first time retrospectively analyzed personal and finger dose values of scientific and technical personnel working with open radioactive substances in animal experiments. Although these dose values are very high compared to published values normalized to the activity from clinical PET/CT imaging,



▶ **Fig. 5** Monthly dose values of employees in a small animal imaging facility (n = 7, medical technologist for radiology (MTR) and scientific employees) and employees of the Clinic for Nuclear Medicine (n = 7, MTR only) for PET/CT examinations over a period of 4 years (2020–2023) divided into a) body dose determined with optically stimulated luminescence dosimeter and b) finger dose determined with ring dosimeter. Monthly dose values of employees absent for longer periods (e. g., due to illness or parental leave) were not considered. Statistics: Kruskal-Wallis test with post-hoc analysis by Dunn's multiple comparisons test and $p < 0.05$ considered as significant, **** for $p < 0.0001$, Whisker show maximum value).

the absolute dose values per year show that the radiation exposure is lower than that of radiology technicians in a university hospital for nuclear medicine.

Empirical data was able to be acquired by analyzing official personal dosimeter data, particularly the eye lens dose, from various PET/CT facilities performing animal experiments. Prospective data collection is to be given preference over retrospective analysis in order to identify targeted exposure pathways. In spite of the small database that makes it difficult to make statistically verified statements, the dose values presented here indicate very low exposure for employees working in small animal PET/CT imaging. This is advantageous since the use of PET/CT imaging in biomedical research has become increasingly important due to the fact that it is noninvasive, the number of test animals can be reduced, and a wide range of physiological and pathophysiological processes can be visualized.

Conflict of Interest

The authors declare that they have no conflict of interest.

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