

Expert Information

From the Working Group on Hygiene

**Management of imaging units from a
hygienic point of view**

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1. Significance of non-invasive imaging

In vivo imaging devices are used for non-invasive examination of laboratory animals and patients. This is related to devices as magnetic resonance tomographs (MRT), positron emission tomographs (PET/CT), optical imagers (fluorescence), ultrasound devices, and X-ray machines. The use of these devices in laboratory animals contributes to the reduction of experimental animal numbers because repeated measurements can be conducted in the same live animal during the course of a study (reduction by longitudinal study design). Likewise, the same animal can be used for different research questions. Additionally, invasive techniques can be replaced by different imaging methods. Therefore, these non-invasive imaging methods are important resources for the implementation of the 3Rs (Reduce, Refine, Replace). Because of high initial costs of these optical devices an intensive utilization by many researchers, even from different institutions in a single central imaging unit (core unit), makes sense and is often unavoidable.

However, this involves that the examined animals can originate from different animal facilities or hygienic units; therefore, the hygienic status of the imaging unit cannot be clearly defined. This problem is further emphasised by the fact that imaging is frequently used in infection experiments (BSL2 experiments); as well as, in the study of immunodeficient animals (xenotransplantation, humanized models).

2. Spatial arrangement and requirements of imaging units

Use of patient sites

Imaging of large animals is mostly done in sites (mostly MRT/CT) primarily used for humans and therefore located directly in the hospital area with patient traffic. Because of this, the use of such machines for large animals is only possible outside of working hours (in the evening or during the night) and should only be done after consulting the Officer for Hygiene of the hospital. Animals have to enter the facility through a separate entrance, preparation and anaesthesia have to be conducted in a separate room. Careful cleaning and disinfection of the machines before and after use must have the highest priority in order to avoid any possible exposure of partially immunocompromised patients to transmissible microorganisms.

Use of special sites for small laboratory animals

Imaging units for small laboratory animals can be installed separately from hospital operations, but should be located near to research areas and animal facilities to reduce transportation distance for the animals. The animals which are examined in such imaging units are often from different user groups and from different animal facilities with different or unknown health statuses. Therefore, such an imaging unit should be located in a separate hygienic area to avoid potential exposure to other animal facilities.

3. Constructional requirements for imaging units

Separate animal facility for the imaging unit

Ideally a core facility for preclinical imaging should have its own animal husbandry area available because animals used for measurement in the imaging unit can usually not be returned to the facility of origin due to hygienic restrictions. Experiments requiring repeated or

continuous measurements can span over a long period of time (weeks or months) during which the animals have to be housed in another animal facility. This facility should be located near to the imaging rooms to reduce stress for the animals due to transport. Surgical models are especially affected by the burden due to transportation.

IVC husbandry systems

It is recommended to keep animals in the animal facility of the imaging unit within individually ventilated cages (IVCs) in order to protect animals from other animals of different origin and to avoid potential contamination by unwanted microorganisms. The necessary degree of isolation for animals (IVC, isolator) depends on the hygienic risk (e.g., animals in an infection experiment vs. immunodeficient animals).

Common service rooms of the imaging unit for cage processing and decontamination (cage washer/autoclave etc.) are of advantage because it simplifies the task of cleaning and disinfection. If the cages of the imaging unit have to be processed in another animal facility, they should be autoclaved before transfer to avoid contamination of animals in this facility. The used cages of the imaging unit always have to be considered "contaminated" due to the different hygienic status of their origin. The use of one-way-cages should be considered when there is a high risk of infection via the animals of the imaging unit or their cages.

4. Staff and organisational requirements for imaging units

Since most of the imaging devices are extremely valuable and complex, it is mandatory that they are only operated by specially trained staff. This guarantees the correct technical supervision of the devices and supports the researchers in conducting their studies. Especially in decentralized animal facilities it is important that the operating staff is extensively trained concerning the hygienic management and animal welfare requirements of all stages of the examinations (prior, during and after) and should be in close contact with the local Animal Welfare Officer as well as the responsible veterinarian. Caretaking of animals that stay for a longer period of time in the imaging unit should be covered by the animal staff of this area. If animal staff from a central animal facility entered the imaging rooms a hygienic risk could be posed on the animals in the central facility as animal rooms of the imaging unit should be regarded as potentially contaminated due to the origin of animals from different facilities.

When extensive use of a certain type of device leads to the use of more than one device, these should be located in areas with different hygienic status. Only animals with a specified hygienic status should be examined in the dedicated device and area. This precaution minimizes the risk of infection with a new pathogen during examination.

If there is only one imaging device available, the supervisor of the imaging unit has to schedule the daily order of examinations with the device according to the hygienic status of the animals to be examined.

5. Hygienic measures for users of imaging equipment

Within the imaging unit everyone should use dedicated protective clothing which is only allowed in this area. Disinfection of hands and use of gloves in case of contact with animals is mandatory.

Quarantine times for those users who have been in the imaging unit and also work in other animal facilities have to be clearly defined and controlled.

All working protocols should be described in detail in SOPs. All users have to agree and absolutely follow the rules of hygienic and disinfection procedures. Dedicated staff is responsible to control the following of these hygienic rules.

6. Hygienic requirements for the animal facility in imaging units

For import of animals into an imaging unit, reliable health reports must be presented. The animal facility has to define in advance which hygienic status of animals (e.g. absence of certain pathogens) or which biological safety level is pivotal for the use of the devices. The hygienic status of the imported animals should be checked on site according to fixed health monitoring programmes in order to continuously monitor the presence of pathogens within the imaging unit.

The usual working routine with IVC cages (e.g. change cages exclusively under a laminar flow hood) has to be complied (see GV-SOLAS recommendations: "Information about handling techniques of individually ventilated cages (IVCs)").

Animals treated with radioactive isotopes should be housed separately in a dedicated shielded room until radioactivity has cooled down. Also incoming material (bedding, food, corpses, excrements) must be stored in this room until cooling down of the radioactivity.

The animal facility of the imaging unit must supply sufficient cage capacity to ensure enough time for acclimatization for all animals scheduled for examination prior to measurements.

For radioactive animals, sufficient space has to be calculated for the cool-down times of isotopes after measurements.

7. Hygienic measures for examination of animals in imaging equipment

Hygienic order of measurement groups

In single devices only animals of the same origin should be measured at one time to avoid cross contamination. Subsequently all surfaces and devices (anaesthesia masks, restrainer, sliding carriages, probes, coils) have to be cleaned and disinfected. Gloves and if necessary, lab coats must be changed before further animals are examined. After handling of animals with a high infection risk, cleaning and disinfection of the whole room should be considered before continuing working with the next animal group.

Reduction of germs by laminar flow technique

Animals transferred to the imaging room in an IVC cage, or a closed cage should be handled only in a laminar flow hood. Preparation of animals for imaging and post-processing procedures should be conducted completely under laminar flow conditions, i.e., taking weight, induction of anaesthesia (for inhalation anaesthesia a fume hood is required), depilation if required, injection, warming etc. Animals should be returned to their IVC cages under laminar flow conditions for recovery after imaging. The fact that for the duration of the measurement

protection of the laminar flow is interrupted, should not detain staff from using this technique whenever possible.

Use of closed restrainers for measurements

Animals should, if possible, be examined in closed containments when examined in optical devices and should be put into these containments under laminar flow conditions. For such purpose single use cages, in which animals can be examined in X-ray devices, or commercially available disinfectable and closed sliding carriages of different manufacturers, which are suitable for examinations in MRT, CT, PET-CT and others (with respective adapters) can be suitable options. The latter should be thermoregulated and should allow for a controlled monitored inhalation anaesthesia. By using closed containments unwanted contamination of the device (through urine, faeces, blood, hair, or dust) during measurement taking can be avoided. Cleaning of soiled, hardly accessible parts of the devices can be avoided.

If it is not possible to use closed containments during imaging a sterile mat should be used to place the animals on it while lying in the imager. These can prevent the seepage of e.g. urine into the device. Details of the optical devices which are difficult to clean (they are often not built for easy cleaning) can be covered to reduce contamination risk during work with animals.

Between examinations of every animal all surfaces which had been in contact with the animals must be treated with an immediately effective disinfectant according to the manufacturer's recommendations.

8. Establishment of SOPs for hygienic management in imaging units

SOPs should define the following:

- Specification of access requirements for animals and potential hygienic risks (including exclusion of animals due to their hygienic status)
- Specification of access requirements for researchers and animal technicians
- Description of working procedures at the devices including corresponding hygienic precautions (maintenance schedule and a backup plan for complete decontamination after unexpected infections)
- User manual for management of the animal rooms in imaging units: Maintenance and husbandry of animals after imaging examinations and associated hygienic and safety precautions
- Realistic evaluation of achievable decontamination of imaging devices with permitted substances including any remaining risk after use of procedures
- Definition of individual competence, responsibility and authorization
- Appointment of the technical staff for the handling of devices with the necessary authority to control, decide and instruct
- Instruction and control of all users about the rules for use and hygiene
- Commitment of all users for unrestricted compliance with hygienic and disinfection measurements

9. Cleaning and disinfection measures of equipment and test chambers

Recommendations of manufacturers for decontamination, the spectrum of activity of the applied disinfectant, and the hygienic status of the animals should all be taken into consideration. Manufacturers understand the sensitivity of the materials used in the devices such as non-autoclavable plastics which may become cloudy after disinfection with certain chemicals: E.g., polyoxymethylene (POM) and Teflon can be damaged by ethanol or electronics and cameras by H₂O₂. In general, they advise that with the recommended chemicals a complete decontamination of the measurement chamber cannot be guaranteed, i.e., not all pathogens which are relevant for the user may be destroyed. Decontamination of imaging chambers or boxes and devices by fumigating or nebulizing hydrogen-peroxide is considered critical by the manufacturers because they cannot exclude an impairment of functions. The risk of using hydrogen-peroxide for decontamination is completely on the operator and voids all warranty. However, there are commercial contractors who offer sterilization of rooms including imaging devices by using hydrogen-peroxide. Their knowledge on this topic ensures the operational reliability of the devices and should be used in any case.

Examples of chemical disinfectants: Ethanol 70%, quaternary ammonia compounds, mixtures from ethanol + aldehydes + quaternary ammonia compounds, oxygen active peroxide compounds.

10. Summary

The hygienic status of different animal groups examined in imaging units can vary. With the exception of surface disinfection there is no official recommended method for decontamination of imaging units. Therefore, there is a significant danger of spreading unwanted pathogens between animals. This problem can only be minimized by clear procedures for every working step within an imaging unit.

11. References

- Brenda A, Klaunberg J, Davis A. 2008. Considerations for laboratory animal imaging center design and setup. ILAR J 49(1):4–16. <https://doi.org/10.1093/ilar.49.1.4>
- Desinfektionsmittelliste des RKI: Bundesgesundheitsblatt 2017;60:1274-129.
<https://doi.org/10.1007/s00103-017-2634-6>
- Desinfektionsmittel-Liste des VAH, Stand 2017.
<https://vah-online.de/de/vah-liste>
- DVG-geprüfte Desinfektionsmittel für den Einsatz in der Tierhaltung, Stand 2018.
<http://www.desinfektion-dvg.de/index.php?id=1800>
- Gutzeit A, Steffen F, Gutzeit J, Gutzeit J, Kos S, Pfister S, Berlinger L, Anderegg M, Reischauer C, Funke I, Froehlich JM, Koh DM, Orasch C. 2018. Would it be safe to have a dog in the MRI scanner before your own examination? A multicenter study to establish hygienic fact related to dogs and men. Eur Radiol 29(2):527-534. <https://doi.org/10.1007/s00330-018-5648-z>
- GV-SOLAS: Hinweise zum Umgang mit einzelbelüfteten Käfigen/IVCs.
http://www.gv-solas.de/fileadmin/user_upload/pdf_publikation/Hygiene/20151023hyg_ivc.pdf
- Lauber DT, Fülöp A, Kovács T, Szigeti K, Máthé D, Szijártó A. 2017. State of the art in vivo imaging techniques for laboratory animals. Lab Anim 51(5):465-478.
- Stout D. 2011. How to Set Up a Small Animal Imaging Unit. In: Kiessling F, Pichler BJ, Hrsg. Small Animal Imaging. Berlin, Heidelberg: Springer, 29-46.
- Tolba RH. 2011. Institutional Preconditions for Small Animal Imaging. In: Kiessling F, Pichler BJ (eds) Small Animal Imaging. Berlin, Heidelberg: Springer, 61-68.
- Voipio H-M, Bronstad A, Forslid A, Karhi T, Ostergaard G. Animal Handling and Management in Imaging Units. Recommendations by the Working Package 4 in the Nordic infrastructure for mouse models (NorIMM). submitted

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