DESIGN AND SETTING UP OF THE UNIT OF MOLECULAR IMAGING OF LARGE ANIMALS AT THE NATIONAL CENTRE FOR CARDIOVASCULAR RESEARCH

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INTRODUTION

Biomedical research addresses increasingly complex problems related to the biochemical processes that occur in living organisms. As in clinical research, medical imaging techniques are excellent tools to study these processes. A molecular image can be defined as a visual representation, characterization, and quantification of biological processes at the cellular and subcellular levels within living organisms without disturbing the system under study. Lately, considerable effort has been directed towards the development of these non-invasive high-resolution imaging techniques for their use in large animals.The aim of this work is to describe the differents aspects to be take in account while designing and setting up a molecular imaging unit others than the image process itself, like the special size animal models, dealing with such models implies higher dose injection, larger volume waste, and hardest handling specimens.

MOLECULAR IMAGING TECHNIQUES

Molecular imaging techniques have become important tools for the clinical diagnosis of several diseases. These techniques are today in a highly mature state in the clinical field and are now being rapidly developed for use in biomedical (preclinical) research.
Among currently available techniques are those allowing acquisition of high resolution anatomical images (CT, MRI), while others offer high sensitivity physiological/molecular
imaging (PET, SPECT, optical). However, used separately each technique offers limited information, and therefore the emphasis of imaging applications for research is on
multimodal imaging, wherein images from different techniques are combined to yield an image of high resolution and sensitivity.

MOLECULAR IMAGING UNIT OF LARGE ANIMALS

DESIGN IMAGING UNIT

ORGANIZATION

The development of the imaging techniques mentioned above (PET, CT) implies the handling of non-sealed radioactive isotopes and the use of equipment emitting ionizing radiation (RX), which is why, according to the Spanish legislation, it is necessary to have a radioactive facility (RF) authorized by the competent authorities.

Central Laboratory of Radioisotopes PET. Designed for the manipulation of high activities or high-risk isotopes (volatile iodine, high-energy gamma). It is also used for the management and control of the RF and contains the central radioactive waste depots.

Molecular Imaging Unit (MIU). Specialized Unit in molecular imaging. This unit will be in charge of the preparation of the doses, atdministration to the animals, and their obtaining the images analysis. This unit is part of the Animal Facility.

HANDLING OF LARGE ANIMALS

The animal model that is going to be used principally in the MIU is the pig. Due to the fact that the CNIC has vocation translational, It has been elected the porcine model by his anatomic-physiological similarity to the human being. The animal will be kept in independent cages inside the animal zone before the procedure. The operator will realize an anaesthesia with intramuscular injection to be able to realize the manipulation of the animal under safety conditions. A vesical sounding will be realized for continuous withdrawal of urine, in order that this way, once incorporated the radioisotope, the potentially contaminated urines will remain contained in a shielded container avoiding the risk of contaminated fluids. Once prepared, the pig will be transported in a stretcher adapted up to the zone of injection of isotopes next to imaging room. Finished the image acquisition, the pig still marked with the isotope, but after incorporation and imaging acquisition time, will be transported to cells different from the original ones. These cells will be located in an independent lairage room conveniently shielded. Once passed the period of decay of the radioisotope, the animal will be transported to his conventional cage and there will be realized the radiological

SETUP CRITERIA

WORK NORMS AND TRAINING

For working with PET/SPECT isotopes and the radiation emitting equipment, the general norms for working with radioactive isotopes apply. These include norms regarding the operator: personal protection (gloves, lab coat, etc.), abiding by the norms of hygiene, use of appropriate shields, correct use of the dosimeter, etc.; norms regarding the work area: signposting, order and cleanliness, containment, monitoring, access control, etc.; and norms regarding the surroundings: contamination and radiation monitoring and correct waste management.
The personnel should be trained in specific aspects as handling of PET/SPECT isotopes, handling of animals, and emergency response.

WASTE MANAGEMENT

The radioactive waste of PET isotopes generated due to the accomplishment of planned works carried out, to incidents (accidental spillages, waste from marked animals, etc) and the cleanliness of material and areas of work.

- The solid residues and liquids produced will be stored in the own containers of withdrawal (bottles of polypropylene in shielded container, shielded bin, etc) and stored in a location prearranged of the laboratory up to its decay (normally between 24 and 48 hours).
- The cutting material and the hypodermic needles used for the injection of radiotracers, they will settle in approved standard containers. These containers will be shielded by another container up to his decay.
- In the lairage rooms destined to marked animals, there is a system adapted for the containment of urines and contaminated excrements. Effluent will remain confined up to his total decay; later to be evacuated to the network of sewer by means of a remote operator controlled electrical valve system.

EQUIPMENT

Imaging Area:
- Imaging equipment PET/CT and PET/RM.
- Anaesthesia table.
- Shielded screen .
- System for the manipulation of the sedated animal.

Central PET lab area:
- Manipulation cell.
- Dose dispensing system
- Activimeter.
- Shielded carrying box for internal dose transport
- Tungsten syringe shielding.
- Trolley for internal dose transport
- Radiation and contamnation Monitor.
- Wastebaskets or furnishings for temporary waste storage.

Lairage Area for injected animals:
- individual systems for controlling the liquid wastes of the animals.
- Shielded screen for the protection of the personnel
- Radiation and contamnation Monitor.

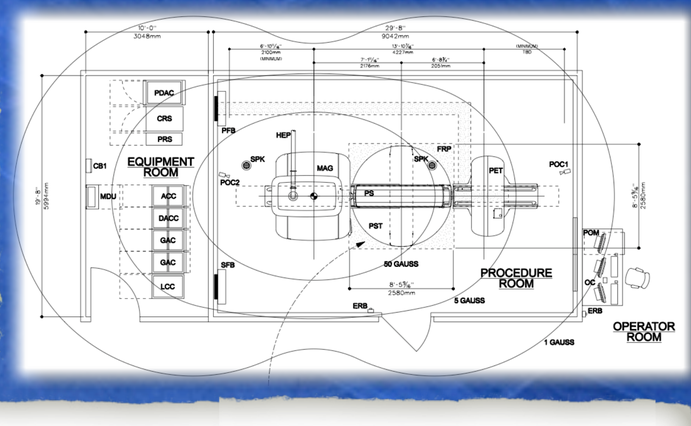
BIOSAFETY

In the MIU, it is necessary to contemplate the tests that combine with the inoculation of microorganisms of the Risk Group 2, or it is possible the situation where an animal is infected by some microorganism and this of natural form could suppose some risk of transmission to the scientific staff and to the personnel in charge of the animal care area. Biosafety´s procedures that are destined to reduce these risks:
- Sanitation of surfaces and materials with germicides.
- The remains of corpse of the animal and his effluent ones are gathered in approved, closed containers. The generated containers are processed by autoclave in the own installation and later they are withdrawn by a managing authorized company, which will incinerate.
- In case of big animals marked with radioisotopes and inoculated with micro-organisms of from risk group 2, who die during a study or are sacrificed, follows a specific procedure of waste management and decontamination.

PERSONNEL AND DOSIMETRY

The personnel implied in the manipulation of PET isotopes and radiation emitting equipment is as follows:
- Personnel in charge of Radiation Protection management: Made up of the Responsible of the RF and a team of assigned technicians. These personnel will be in charge of the reception and registration of the commercial radioactive material and the operations of monitoring and control of the RF.
- Molecular Imaging Unit: Made up of a Person in charge holding a Supervisor license and a team of technicians with operator licenses. These personnel will be in charge of the development of the different imaging techniques.
- Research Personnel: They will carry out the techniques of labelling experimental tracers with PET isotopes.

Dosimetry of occupationally exposed personnel of Category A and B must be done by means of individual dosimeters. In our case, we use thermoluminescence dosimeters. The whole body dose must be controlled during the entire working day by means of lapel dosimeters. For the personnel who directly handle the radioactive isotopes, the hand dose must also be controlled by means of ring dosimeters. After an accident an additional control by means of internal dosimetry must be done.



CONCLUSIONS

- ☑ The research in cardiovascular image in big animals joins in an alone imaging device two promising technologies of image that even had not been achieved to join still. It is the fusion of PET and MR. It is a question of the merger of the PET and of the RM. The RM does not issue radiations since there do the devices that use X-rays. It is logical, therefore, that the combination of both methods finishes not only giving good results but it is very profitable to level of the Radiological Protection.
- ☑ In the work with large animals one tries to obtain levels of doses lower than the personnel that realizes these technologies in the clinical area, since the doses used for large animals are in the order of the doses applied to human beings.
- ☑ The previous cold training, as well as the selection of personnel are vital actions to reach the target of the safe use of these isotopes and to support the low doses.

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