Considerations for Laboratory Animal Imaging Center Design and Setup

Brenda A. Klaunberg and Judith A. Davis

Abstract

In vivo animal imaging is an outstanding noninvasive tool to study the pathophysiology of disease or response to therapy; additionally, serial imaging reduces the required number of experimental animals. Because of the tremendous capital investment, we recommend the imaging center be a shared resource to facilitate innovative and productive cross-disciplinary scientific collaborations. A shared center also enables a broader range of imaging, as equipment is often cost prohibitive for smaller facilities. A multitude of factors will determine the architectural design, facility efficiency, and functionality. Important considerations to determine during the planning stages include the types of animals to be imaged, types of imaging studies to be performed, types of imaging equipment and related services to be offered, and the location of the imaging center. Architects must work closely with manufacturers to accommodate equipment-related building specifications; facility planners and veterinarians can provide a practical logistical design that will ensure efficient functionality. Miscellaneous considerations include biosecurity levels, use of radioisotopes, and personnel safety in the imaging environment. The ideal imaging center will include space to house animals and perform necessary preimaging procedures, state-of-the-art in vivo imaging devices and the most up-to-date anesthesia, physiological support, and monitoring equipment. The center staff should include imaging specialists for technical development and data analysis. As it is difficult to provide a comprehensive manual for setting up an in vivo animal imaging center, we offer advice based on our experiences with the National Institutes of Health Mouse Imaging Facility. Because magnetic resonance imaging (MRI) is the most expensive imaging tool, requires specific building design considerations, and poses unique occupational health and safety risks, we focus on MRI as the foundation for an imaging facility design.

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Key Words: animal; computed tomography (CT); design; imaging; in vivo; magnet; magnetic resonance imaging (MRI); positron emission tomography (PET)

Introduction

Congratulations on your decision to build an animal imaging facility. The most advantageous aspect of in vivo imaging is the ability to follow an individual animal over time. This results both in the use of fewer animals per experiment and in a better understanding of the disease process in an individual. In addition, an on-site imaging facility will enhance your institution's capability to conduct basic and translational research relevant to the institute's mission. It is difficult to provide a comprehensive "how-to" guide to build a shared animal imaging center; we offer advice for designing an ideal animal imaging facility based on our experience with the National Institutes of Health (NIH) Mouse Imaging Facility.

Myriad variables may affect the final outcome, but the imaging facility should include the following services: imaging and physiological support equipment, research support (contrast agents, technical expertise, intellectual collaboration), informatics support (data storage, retrieval, analysis, software development, biostatistical support), and animal housing facilities. Careful thought, planning, and consultation with field experts will help prevent expensive errors in facility design.

For several reasons we suggest that your institution's new animal imaging center be a shared resource. Our experience indicates that when designed as a shared resource, an animal imaging center provides more intellectual support than a "core facility." A shared resource center encourages imaging specialists to interact with scientists from other disciplines to ask basic biological questions and then develop, modify, or optimize imaging methods to provide answers. The combined analytical expertise will produce results that magnify and exceed the sum of the individual contributions. Additionally, the capital expenses associated with setting up and maintaining just one magnetic resonance imaging (MRI[1]) suite are significant and usually prohibitive for a smaller institution.

[1]Abbreviations used in this article: BAS, building automation system; CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography

Animal imaging technology is more challenging than that used for human imaging because of the resolution required for diagnostic images, especially for smaller subjects. We highlight particular species-specific issues to consider when designing an imaging facility (general species-specific building design considerations are available in any laboratory animal facility design and planning guide). It is important to determine at the outset the scope of the animals supported (e.g., rodents only, rodents and nonhuman primates, or all laboratory animals) as this information is critical to the design and management of an animal imaging facility—it will influence the purchase of equipment as well as the animal housing facility design. It may also be appropriate to consider the possibility of future expansion or the inclusion of other species. Imaging technologies for small animals are advancing rapidly and an imaging facility should be designed with sufficient flexibility (and space) to expand and adopt new techniques (Budinger et al. 1999).

This article is divided in five major sections:

- Facility design (including general considerations, animal housing and support, MRI-specific considerations, and miscellaneous topics),
- Animal imaging support,
- Personnel,
- Imaging equipment, and
- Data management.

Because MRI has the most restrictive conditions, compared to other in vivo imaging modalities, we use this particular technique as the foundation for the design of an imaging facility. MRI is heavily infrastructure dependent, requiring particular building specifications as well as trained personnel to operate and maintain the equipment. Additionally, MRI poses unique occupational safety hazards.

We give specific advice where we feel it is appropriate, in some cases based on our own experience. We deliberately discuss some topics in general terms because facility planners must tailor plans to their specific imaging needs.

Facility Design

The design of an in vivo animal imaging facility must encompass numerous factors, of which we discuss four major components. The first section concerns general facility considerations and building design, which may be common to any place of employment, but we emphasize aspects that bear on animal research. General considerations include traffic patterns (for personnel and animals), supply storage, administrative and personnel offices, break rooms, restrooms and showers, conference rooms, and environmental criteria.

Next we discuss aspects of animal housing and imaging support—animal housing, procedure rooms, cagewash, husbandry supply storage, and euthanasia. In the third section we address magnet-specific design factors, including magnet location and structural considerations, cryogen gases, magnet room environmental considerations, and work areas and tools in the magnetic environment. In the last section, we discuss miscellaneous facility design considerations such as radiation safety, animal biosafety, laminar flow hoods, ducted biosafety cabinets, and sterilization.

General Facility Considerations

The success of the project depends heavily on frequent and consistent communication among all the parties involved and, especially, on the architect's clear understanding of the design functions and criteria. Common planning errors include lack of communication, faulty assumptions, inaccurate information transfer, and inadequate professional judgment (Ruys 1990). Commissioning the opinions of knowledgeable field experts can help thwart the latter two problems and is well worth the expense. Communication errors—including a failure to ensure the accuracy of all assumptions that inform decisions—are more difficult to guard against. Another frequent problem is the assumption that the architect has more knowledge about the functions of a research animal facility than he or she really does. If design priorities are not clearly established you may learn at a later date that the architect has spent enormous effort on aesthetic details of the design at the expense of functional planning.

A good rule of thumb is to keep all communications clear and concise, and to summarize all discussions, emphasizing the functional goals and reiterating—even at the risk of redundancy—the reasons for the design layout (e.g., purpose, workflow). The old adage "measure twice and cut once" should be rephrased during the building planning stages to "design 20 times and build once"! There is nothing more frustrating—and cost-inefficient—than spending enormous amounts of time and money on a building design only to start remodeling the minute the christening tape is cut because the resulting building design is not practical for its purpose.

The basic components to be determined at the outset for the facility design are traffic patterns, supply storage areas, office space, break rooms, bathrooms, conference rooms, and the various environmental (i.e., heating and cooling) needs.

Traffic Patterns (Circulation)

Although the imaging center will be used for laboratory animals, it is crucial to balance access to the facility and equipment with minimized cross-circulation between animals and personnel. Decisions about circulation must also take into account the potential of one species (including humans) to pose an infectious disease threat to another species. For example, Old World nonhuman primates (NHPs) may be a health threat to New World NHPs (e.g., from herpesviruses), and human diseases (e.g., measles) can be a threat to nonhuman primates in general. It is also desirable to eliminate or minimize contact between animals and humans not associated with the animal research, to prevent potential exposure to allergens.

An equally important consideration is the health status of laboratory rodents that enter the center, especially as many may return to their home housing facilities after imaging. Rodents may arrive from vivariums that have different health restrictions; for example, a strict barrier facility tolerates no murine pathogens, whereas a conventional facility may tolerate some pathogens (e.g., *Helicobacter* spp., Norovirus). In addition, rodents may be immunocompromised and require additional biosafety to protect their health, or they might be infected with a biohazardous organism that requires containment.

All of these factors must be considered during the planning and design process as they inform decisions that affect the following four aspects of workflow: logistics, equipment, people, and corridor width. A "common denominator" in considering decisions about the first three issues is the identification of key travel distances. For example, the entry location for animals coming from other facilities will influence pedestrian and equipment traffic. A dedicated animal entrance central to animal procedure rooms is ideal as it reduces the transit time for the animal, which can be important if the animal is anesthetized. These considerations may also apply to the location of the loading dock if it is used for animals transported to the center for imaging.

Planners should consider the types of equipment that will be moved through the facility (e.g., carts, anesthesia machines, racks, animal transport caging) and common destinations; simple circulation patterns, including short straight distances, increase efficiency.

The size of the imaging rooms and the anticipated activities in those rooms are also important planning factors. In order to assess anesthetized animals during scanning sessions, personnel need sufficient space to move around the imaging equipment. (Manufacturers typically provide environmental requirements for the equipment, but these do not necessarily include the working requirements for staff.) The equipment console areas must be factored into the traffic patterns as well. It is not prudent to locate these desks in areas of high traffic because it is often necessary for the imaging specialist to gather several researchers for discussion during the image acquisition process. The architect should include sufficient room for chairs and bench tops as well as computers.

Another significant circulation pattern involves the movement of technicians and research staff between housing rooms, procedure rooms, and imaging rooms. While reviewing the design drawings, it is important to consider all possibilities for shortcuts. If there is a path that allows for a shorter trip between point A and point B, many people will invariably take that route; the facility design should take this into account.

Corridor width is critical because it determines how well staff can operate, logistically, in the facility; but it is often controversial as wider corridors correspond to less "billable" space. However, corridors less than 8 feet wide can severely hinder functional traffic patterns in a busy animal research center. Carts, racks, and other animal equipment are typically 3 to 4 feet wide, so in smaller corridors passage may be tight or even impossible for carts passing in opposite directions; and standard facility corridors have wall protection rails (high and low) that impinge on the corridor width. For these reasons we recommend a minimum width of 8 feet. We also suggest avoiding single-load corridors and considering the use of alcoves or "nooks" for equipment marshalling or storage space for high-use consumables such as personal protective clothing and equipment (PPE). Columns can create corridor alcoves that can serve as staging areas.

Supply Storage Rooms

The amount of storage space needed in any facility is probably always underestimated. It may be better to think of this type of space as "support space" and then categorize the different types of support space needed. For example, storage space is necessary for consumables (e.g., protective clothing, gloves, drapes, sponges), administrative supplies (e.g., toner cartridges, pens, paper), biologicals and drugs (e.g., anesthetics, physiological support, contrast agents), cages, feed and bedding, hazardous chemicals (including cleaning solutions), medical pathological waste (MPW) containers, and other general supplies.

In addition, because most MRI magnets are superconducting and have specific maintenance requirements, there must be space for the storage of large cylinders of cryogens such as liquid helium and liquid nitrogen. Imaging accessories such as MRI gradients and coils also require storage space.

Once there is agreement on the types and amount of storage space, consider the institution's animal census in order to estimate monthly inventories of animal husbandry items. This drill will provide an idea of the amount of total space necessary to store a month's inventory.

Calculating the amount of space needed makes it possible to determine the best locations for storage rooms and how to distribute the total storage space among room locations. These decisions should also take into account the best location for a loading dock to receive animals and supplies.

Administrative and Personnel Offices

It is essential to consider the needs of the personnel who will operate and maintain the imaging facility. Whether they are researchers, technicians, or husbandry support staff, they will need space to work, place their personal belongings, and eat lunch. The determination of personnel requirements will inform decisions about who might require an office (or a work cubicle) and workspace locations relative to the workflow.

Offices should be close to the occupant's workspace.

Laboratory and section chiefs, principal investigators, and senior scientists should have private offices when possible. Upper-level personnel may need larger offices with enough space for collaborative or private discussions, and if feasible offices should have access to natural light. Postdoctoral fellows may have semiprivate offices, while clerical personnel have open office space. Desk and storage space for laboratory technicians is usually in open areas adjacent to laboratory benches and should include provisions for privacy. Office space for dedicated husbandry personnel is best located in the animal housing facility. It may be appropriate to cluster offices to facilitate the sharing of support staff. Depending on how the facility functions, temporary personnel such as visiting scientists, postdoctoral fellows, and graduate students may also need workspace.

Storage space will also be necessary for records and files, copiers, and mail areas. Additional space should be allocated for frequently used reference manuals, animal study proposals, and standard operating procedures.

Break Rooms

Break rooms should permit the safe consumption of food and beverages away from the imaging and animal holding areas and at the same time should serve as an inviting area for interaction and small informal meetings. These areas may require acoustical separation from surrounding spaces.

All break rooms should have a white board, tack board, table, and chairs. Larger break rooms may also require a bookcase, cabinets, sink and countertops, microwave oven, and refrigerator. Lockable storage in a break room is desirable. There should also be space for waste and recycling containers that are adequately sized to support the occupancy and use of the area.

A library or resource center could be a separate entity or combined with a conference or break room. A multilevel center should have a break area on each floor.

Restrooms and Showers

The number of restrooms and their locations is determined by the size of the facility and the number of employees. Restrooms and other facilities must be accessible to accommodate handicapped employees or visitors.

Personnel may also need showers with changing areas depending on the level of biosecurity at the animal facility. Separate shower and changing areas for both men and women are typically adjacent to or near restrooms. These facilities should include lockers and changing benches, clothes hooks, and an electrical outlet adjacent to a mirror and shelf.

It may also be helpful to provide space for employees to store personal belongings, including food and coats, outside the animal holding area. Lockers may be built-in and located in the corridors, break room, or adjacent to restrooms.

Conference Rooms

Conference rooms serve multiple functions in a research environment. When imaging scientists meet with investigators to discuss a project, the group may consist of only a few people or it may completely fill a conference room, depending on the complexity of the project. Similarly, facility orientation classes (with an emphasis on magnet safety) are recurring events that require a large room. Conference rooms can also be used for facility operations discussions, journal clubs, vendor presentations, and invited speakers.

The number of conference rooms will depend on the facility size, number of investigators supported, and program size. Check with your institution to find out if there are any restrictions on the number of conference rooms allowed.

Each room should be equipped with dry erase boards (or blackboards), electrical outlets to accommodate audiovisual and other projection equipment (laptop, slides, and overhead projectors), light dimmers, and blackout control, as well as telecommunications/local area network (LAN) capabilities.

Conference rooms should be located outside any restrictive areas (such as magnetic fields) and away from sources of noise interference.

Environmental Considerations

Computer rooms, animal rooms, and certain equipment rooms generally have temperature and humidity controls, although the environmental requirements may vary among these different types of areas. When primary control is provided by the building automation system (BAS[1]), the requirements are listed with the systems and components. Whether completely controlled by the BAS or by a combination of BAS and packaged controls (as would be provided for a computer room unit), the ventilation system should be coordinated to prevent simultaneous heating and cooling (unless required for dehumidification). Coordination of humidity control systems can prevent the occurrence of some systems humidifying while others are dehumidifying.

For equipment rooms in which significant heat is generated, the use of standalone, supplemental air conditioning is advisable as a cost-effective alternative to designing the BAS to handle the heaviest heat loads.

Animals and personnel areas require higher humidity levels than equipment or computer rooms, so the temperature and humidity controls for animal rooms, personnel areas, and equipment rooms should be independent of those for the rest of the facility.

Animal Housing and Imaging Support

The ideal imaging center incorporates animal housing space or is located in a large multiuse building with laboratories and the imaging center adjacent to an animal holding facility. Planners should determine the type of animal holding rooms, quarantine space, and husbandry support space early in the design process. In addition, the early development of clear definitions of various types of animal housing space will facilitate the appropriate design, room air pressure differentials, and protocols for animal and personnel movement between different types of space. Elevator redundancy and appropriate size are critical to the success of the facility, and the design should also incorporate staging areas and air locks to help prevent contamination between floors as well as to aid in proper pressurization of rooms and corridors.

Animal Housing

The size and type of housing rooms will depend on the species. The selection of room size (large, small, cubicle, or a mixture) is beyond the scope of this article and should be discussed with the center veterinarian. We highlight general factors to consider.

For rodent housing, it is critical to select the rack type, especially if ventilated, early in the planning process as this decision will influence room size, configuration, heating and air conditioning (HVAC) design, corridor width, and cagewash size (NRC 1996). Other factors to consider include ergonomics, ease of cleaning and decontamination, water system, and ability to contain unwanted pests. It is also important to take into account the room locations in the building as noise (e.g., from a loading dock or cagewash room) can have deleterious effects on mice (Turner et al. 2005, 2007).

Facility planners should incorporate holding room space for the temporary quarantine of animals during verification of their health status before placement in existing center colonies. The location of quarantine space deserves careful consideration. The quarantine rooms should be close to the dedicated animal entrance, allow easy access for personnel, and be separated from the main animal holding rooms. A small procedure room adjacent to the quarantine space, or a biosafety cabinet within the quarantine room, facilitates technical procedures such as phlebotomy for serological screening.

Repetitive design (the use of same-sized blocks of space) can save money and provide flexibility for future renovations. For example, two small animal holding rooms should match the area of one large animal holding room, and two small procedure rooms should match the area of one animal holding room.

Room size, aisle width, and the placement of caging systems will all affect the number of concurrent activities that are possible in the holding room. For example, a large room will permit simultaneous activities such as cage changing, veterinary health checks, and investigative procedures. A smaller room may necessitate scheduling to avoid overlapping space conflicts.

Procedure Rooms

Imaging centers do not have a rule of thumb for determining the number of procedure rooms required. Historically, a typical vivarium provided a 1:4 ratio of procedure rooms to animal holding rooms, but the development of high-intensity rack systems has invalidated this ratio. We suggest adjusting the ratio of procedure rooms to the number of cages rather than the number of animal holding rooms. For imaging support purposes, we suggest considering the complexity of the center (e.g., how many and what types of imaging equipment will be available) and the types of animal preparations likely to occur before imaging. For example, if 20% of imaging support will be for cardiac function, a procedure room may be necessary for the surgical placement of catheters for dye delivery or other procedures.

It is imperative to estimate the amount of time needed for the anticipated procedures in order to plan the rooms accordingly, or the lack of procedural support space may become a bottleneck for imaging procedures. In our experience, every type of imager in the center requires a basic preparation area for anesthesia and setup. For more complex procedures such as venous access or preimaging surgery, it may be possible to share a procedure room between scanners. But again, it is necessary to first determine what the center will be used for and how much preimaging support will be provided.

State-of-the-art laboratory animal anesthesia and monitoring equipment must be standard in all preparation rooms. Such rooms will need gas supply (e.g., oxygen, medical air, nitrogen) for the delivery of inhalant anesthetics and a vacuum exhaust system to remove exhaled anesthetics. External heat sources must be available to maintain the anesthetized animals' basal temperature, and physiological monitoring equipment is important for prolonged anesthesia procedures. Emergency drugs and life support equipment must be available and readily accessible in the event of cardiac or respiratory arrest. Consultation with the laboratory animal veterinary staff during planning will ensure that the rooms are appropriately stocked and functionally designed.

Personnel safety must also be considered, so eye wash stations and NHP bite and scratch kits must be appropriately located.

For teaching purposes we suggest equipping the procedure rooms with double-headed surgical microscopes and/or good video capabilities with projection.

Cagewash

During the planning phase it is important to determine the method and route for bedding delivery and disposal between the loading dock and the cagewash. The cagewash area should be divided into a "dirty" side and a "clean" side with no personnel access between the two. The sides may be separated by a glass partition with a telephone or paging system for communication. Between the "clean" and "dirty" sides, a third area containing the wash equipment may be appropriate in large cagewash operations.

All materials and finishes should be moisture resistant, sealed, and caulked. Finishes in the cagewash area should stand up to frequent high-pressure water cleaning. The type of equipment used in a cagewash will require high-voltage, multiphase electrical sources, high-temperature, high-volume water, and large quantities of clean steam. A careful evaluation of the HVAC requirements of the cagewash area is essential to ensure the safety and comfort of the personnel that work in this environment (NIH 2003).

Access to the "dirty" side should be through impact-resistant double doors (with door sweeps) that open in the direction of traffic via automatic openers. Space is needed for marshalling incoming cages and racks, dumping bedding, breaking down cages, emptying bottles, and loading washers. The "dirty" area should be equipped with a scullery sink, bedding dump station, waste disposal equipment, automatic water manifold flush station, chemical neutralization, prewash stall with a grid floor, a water fountain, and emergency eye wash and shower. A pit may be necessary for the preparation or descaling of the racks and cages.

Depending on the size of the cagewash facility, the "clean" area may be equipped with a large autoclave, bedding dispenser, and water bottle filler. Space for marshalling equipment is also required on the "clean" side of cagewash.

Husbandry Supply Storage

Architects must include adequate space to store clean cage racks, caging, bedding and feed, any special clothing and supplies, cleaning chemicals, husbandry supplies, and procedure room supplies. Storage for chemicals and detergent drums must be located away from heavy traffic zones.

We recommend a separate storage area for bulk storage of feed and bedding. It is important to adequately plan for this space and protect it from being "squeezed out" of the facility as a "value-driven" decision. Storage of feed and bedding should be calculated on the basis of a predetermined reserve supply capacity, anticipated maximum consumption per time period, and maximum holding capacity of the facility.

Euthanasia

The facility must have an area specifically dedicated to euthanasia procedures in order to ensure compliance with international standards. Animals under stress emit pheromones, so it has become standard practice to perform euthanasia away from other live animals (AVMA 2007). The types of species imaged will determine the size of the euthanasia area. A cold room or carcass storage freezer should be included, with careful consideration given to the logistics of removing frozen carcasses (e.g., the difficulty of removing a 70-kg pig from a chest freezer versus a walk-in). It may be necessary to have a controlled-substance storage cabinet in this room, as well as carbon dioxide tanks with euthanasia chambers. A chemical fume hood for in vivo tissue perfusion and a downdraft table area for carcass dissection and tissue harvest are both extremely useful for investigators.

Magnet-Specific Facility Design

MRI magnets have very specialized building and environmental requirements. The designer must therefore work closely with both the end users and the manufacturers to determine the structural details required for the instruments.

Location

Because magnetic forces can inactivate or alter life-supportive devices such as pacemakers and insulin pumps, it is crucial to carefully consider and plan the location of MRI scanners so that the magnetic fields surrounding these instruments (fringe fields) do not interfere with other equipment or present a health hazard to personnel. Fringe fields of neighboring instruments may overlap, but the manufacturing engineers should be consulted before finalizing plans. A magnetic field of 5 Gauss is the FDA-recommended limit for people with pacemakers or other internal devices (Erdogan 2002; Faris and Shein 2006; Shinbane et al. 2007). We recommend that the 5 Gauss fringe field lines be well marked and protected from inadvertent entrance. Areas that personnel or visitors may use (hallways, offices, restrooms) should be either outside all fringe field lines or well below 5 Gauss. In addition to electromagnetic instruments, static MR imaging magnets must be isolated from elevators as well.

Structural Considerations

MRI uses radiofrequency (RF) to generate images and so is susceptible to interference from the RF of other devices (such as physiological monitoring equipment). Depending on the equipment's specifications, it may be beneficial to locate the magnets in RF-shielded rooms, not only to isolate and protect the magnet and personnel from safety hazards but also to decrease the level of noise in the resulting images. Special acoustical design features may be required to mitigate the transfer of sound and vibration through the structure to adjacent areas.

Many MRI scanners are located on basement or ground levels due to the weight of the instruments, although pits may be appropriate for larger pieces of equipment. The floors of scanner rooms may require reinforcement to support weights from 200 kg to 11,000 kg (24,200 lbs). Access and clearance, both vertical and horizontal, around the equipment must be carefully planned for both equipment requirements and delivery. The weight and size of these instruments may require that they be lowered into their resting places by a crane through a specially designed roof hatch opening. This is another reason that it may be practical to locate the imaging equipment outside the main footprint of the building. Alternatively, the facility design may incorporate wide access doors, with tracks to slide the units into place.

Cryogen Gases

Most MRI magnets are superconducting, and the instrument specifications indicate special cooling requirements (typical cryogens include liquid helium and liquid nitrogen), so the facility design should include both storage capacity for gas cylinders and the clearance needed to add cryogens to the devices.

Inert gases pose a threat of asphyxiation, so each magnet room must include an oxygen sensor that sets off an alarm when oxygen levels fall below normal limits (usually 18%). A method of manually increasing air exchange is desirable to help exhaust gases and increase room oxygen during cryogen filling. Specialized exhaust venting should be installed based on manufacturer recommendations.

Environmental Considerations

MRI suites require stable temperature control for the magnets. The design of the control systems must be closely coordinated with the mechanical systems design and the space layout to minimize environmental fluctuations across magnets. A typical MRI room requires continual monitoring of temperature, humidity, and oxygen levels. Humidity requirements must be coordinated with the equipment manufacturer but are usually around 20-25% with minimal fluctuation. Requirements of the dehumidification system should be listed with the system used.

Work Areas and Tools

Besides the magnet room itself, several operational spaces are needed. Large powerful computer clusters are required to operate the scanner, and these must be located adjacent to the scanner but outside the magnetic field. Furthermore, the operator needs a console area from which to run the scans, and additional workspace adjacent to the console area is very useful for laptops or analytical workstations.

Repairs and maintenance in the magnet room will periodically require the use of nonmagnetic tools (including screwdrivers, wrenches, scissors). It is imperative that facility planners budget for the purchase of nonmagnetic (e.g., beryllium-copper alloy) tools for use in the imaging suite. Nonmagnetic flashlights and cleaning supplies (brooms, mops, and buckets) are another necessity.

Animal preparation must also be considered. An area for basic anesthetic procedures and final preparation (e.g., placement of the imaging coil) is best located close to the magnet; however, simple instruments, such as scissors, scalpels, and needles, can become life-threatening projectiles if taken too close to the magnetic field.

Because of the significant safety hazards associated with working in the MRI environment, we recommend required safety training for all personnel and facility users.

Miscellaneous Facility Design Considerations

Radiation Safety

If your imaging resources will include positron emission tomography (PET[1]), then special consideration must be given to the management of radioactive reagents, animals, and waste. The ideal facility includes a radiochemistry laboratory and cyclotron (as well as a radiochemist) to produce custom radionuclides. Due to the additional space and capital expense requirements of generating custom radionuclides, the reality may be restricted to the use of commercially available reagents such as 2-[18F]fluoro-2-deoxy-D-glucose (FDG). The facility plan must account for the delivery of these radioactive reagents and map the travel paths, keeping in mind minimization of personnel exposure and the implementation of emergency procedures in the event of a spill. The radionuclides needed to generate PET images are gamma emitters, and their half-lives are short (e.g., 109 minutes for FDG) (Vijayakumar et al. 2006).

The design should include space for the housing of radioactive animals and for the management of radioactive waste. Consultation with an institutional radiation safety officer during planning stages will prevent architectural design flaws.

Occasionally, radioactive reagents are used during other types of imaging for later validation of imaging methods (e.g., autoradiography). Design plans should address the need for reagent preparation areas as well as space for a scintillation counter, record keeping, and decontamination chemicals.

Animal Biosafety

The use of biohazardous materials requires appropriate workspaces and storage for such materials. The level of animal biosafety should therefore be determined in the planning stages of the facility design and should take into consideration not only the specific pathogen status of the experimental animals but also the biological reagents used for imaging experiments and the ease of decontamination procedures. Will investigators be using viral vectors, studying the imaging aspects of infectious organisms, or using toxic reagents or other biohazardous materials? If your facility users plan to perform these types of studies, it is beneficial to the animals to perform biohazardous procedures in the imaging facility housing areas and thus eliminate the additional stresses of transportation.

Laminar Flow Hoods

Laminar flow hoods are useful for tasks such as the preparation of toxic experimental drugs or chemicals used for imaging studies (neurotoxins, contrast agents) and for the perfusion fixation of tissue at the end of an imaging session. Fume hoods in procedure rooms should have flow monitors provided by either the control manufacturer or the hood manufacturer (generally applicable to constant volume hoods). These monitors must include an indicator of safe air flow, audible and visual alarms that activate when face velocity (inward air flow from the bottom of hood sash to the work surface) is out of range (<90 or >110 fpm), and an emergency ventilation switch or button.

The building automation system (BAS) should monitor the alarm condition and the emergency ventilation position and should activate an alarm at the operator workstation when either condition exits. The BAS should also initiate any emergency ventilation sequences.

Ducted Biosafety Cabinets

Biosafety cabinets (type B) should be hard-ducted to the BAS-controlled facility exhaust system and the exhaust flow from the cabinet should be constant volume. Where ducted, the cabinet must have an isolating damper on the exhaust to allow for decontamination, and the closed position of this damper should be monitored by the BAS. The system and BAS design should provide an alternate means of exhaust flow to maintain pressurization when the biosafety cabinet is isolated for decontamination.

Sterilization

An autoclave is necessary if investigators perform surgical procedures in the imaging facility. Its location must be considered during the building design because it will need a steam or water source and exhaust vent, and it should be convenient to the surgical suites. In addition to sterilizing surgical instruments, the autoclave can be used for decontamination: it is often acceptable to treat biohazardous agents in the autoclave and then dispose of them as normal harmless waste.

Animal Imaging Support

Most laboratory animal imaging entails putting the animals under general anesthesia. The animals must be immobilized in order to produce optimal diagnostic images, otherwise the artifacts that result from movement may invalidate the imaging session. Anesthesia also eliminates the stress associated with restraint. It is possible to train some animals to tolerate restraint with certain imaging devices; however, it is imperative that the investigator work with the center laboratory animal veterinarian to determine the best methods to achieve the imaging goals.

In this section, we discuss anesthesia equipment in the imaging environment, the importance of physiological monitoring, and surgical support of imaging studies.

Anesthesia Equipment

There are numerous animal anesthesia protocols; the center veterinarian can help determine the most appropriate method for the particular imaging experiment. In our experience, inhalant anesthesia is most desirable for both short and long procedures—the animals undergo a short induction period and, more importantly, a short recovery time.

The ability to remotely and rapidly adjust the animal's level of anesthesia is vital during a lengthy MRI procedure. Therefore, we recommend the installation of inhalant anesthesia devices in all imaging areas. Such installations will include a source of anesthetic delivery gases (oxygen, medical air, nitrogen, nitrous oxide), a precision vaporizer, a ventilator, and variably sized endotracheal tubes and facemasks. Depending on the species to be imaged, the facility may need several different ventilators and associated equipment, some of which may need to be compatible with the MRI environment, or capable of working at a distance from the magnet.

Physiological Monitoring

Physiological monitoring of the animal is necessary in order to maintain safe anesthetic levels. The availability of reliable equipment (and feasibility of use) is species dependent, but at a minimum should include a method to measure core body temperature, respiratory rate, and heart rate. Other physiological parameters that may be measured include electrocardiogram (ECG), blood pressure, electroencephalogram (EEG), end-tidal carbon dioxide levels, anesthetic gas levels, blood gases or pulse oximetry, and respiratory wave patterns. Anesthetized animals cannot maintain optimal core body temperatures, so an external heat supply is essential. Circulating warm water blankets and warmed air are two common methods used with MRI; in these cases, it is important to consider the route of the wires and tubes from the animal to the monitoring device, and the possibility of noise introduction to either the image or physiologic data. Electronic or paper anesthetic records should be maintained for every animal regardless of species.

Surgical Support

A dedicated surgical suite must be included in the plans if your facility will provide surgical support. Sterile surgical instruments and proper sterile surgical attire (sterile drapes, caps, gowns, gloves, and masks) must be available, along with a method of instrument cleaning (sonicator) and resterilization (autoclave). A presurgical preparation area should be isolated from the operating room to prevent the possibility of aerosolized hair and dust contamination of surgical wounds.

Personnel

The management of a successful laboratory animal imaging center requires a variety of personnel with an assortment of skill levels. The ideal imaging facility employs enough personnel to be "self-contained" and to address any problem in a timely fashion and thus minimize downtime. We suggest that the ideal imaging facility employ imaging specialists, animal support personnel, computer information technologists, and housekeeping and building maintenance staff. We also discuss occupational safety issues unique to the magnetic environment.

Imaging Specialists

Doctorate-level researchers are necessary to facilitate scientific collaborations and nurture the advancement of animal imaging technologies. Those who use MRI should be skilled in the physics of the imaging process in order to develop new methods as needed.

Specially trained personnel are also necessary to maintain the imaging magnets and operating software. Such expertise may be available through service and maintenance contracts with the vendor; however, the lack of on-site personnel may result in imaging time delays and disruption to imaging studies. If funding will allow, operating specialists for each of the imaging modalities is ideal, but intelligent, ambitious, and technically skilled personnel may also perform satisfactorily.

Animal Support

Animal support personnel are critical to the success of the imaging center. Technicians are needed to perform imaging anesthesia, catheterization, and other assorted surgical procedures. Technicians can also learn to run routine scans in order to free up intellectual time for the imaging physicists. Husbandry personnel and support staff are required to maintain the animal housing facility. A small facility may require some technical and husbandry overlap, but a larger facility should have dedicated teams to handle the workload. Veterinarians and veterinary technicians are vital to maintaining the health of the animal colonies and imaging subjects. Again, the number and variety of animals housed in the center will determine the number and type of personnel needed.

Computer Information Technology

All of the aforementioned imaging equipment and physiological monitoring devices create digital data, and so a number of computers are necessary to support the facility's programs. In addition to running the operational software for imaging devices, computers handle data management and staff needs (e.g., email, supply orders, record keeping). Our experience suggests that a local network facilitates data storage and manipulation, so it is necessary to retain on-site personnel capable of maintaining the network computer equipment. Although computer downtime will inevitably occur, it should be kept to a minimum. Data processing and management personnel are discussed in the data management section below.

Housekeeping and Facility Maintenance

Housekeeping and building maintenance services are needed for a busy facility that employs numerous personnel. In addition to removing waste and tidying up break rooms, housekeeping is integral to facility decontamination. High-traffic areas of animal movement require routine disinfection to control the spread of disease and allergens. As discussed earlier, room temperature and humidity must be carefully controlled for scanner rooms, computer rooms, and animal housing rooms. Fluctuations from normal ranges should be corrected as quickly as possible, so building maintenance personnel should be available at any time of day or night.

Unique MRI Personnel Safety Considerations

Because of the hazards associated with working near a high magnetic field, employees should be carefully screened for contraindications to the MR environment. People with cardiac pacemakers, cochlear implants, drug pumps, or other metallic implants such as shrapnel should not work in close proximity to the magnets. The magnetic fields may cause metallic implants to shift within tissue or they may inactivate working devices, which could result in a fatal accident (Erdogan 2002; Faris and Shein 2006; Shinbane et al. 2007). Signs should be posted in highly visible areas all around the facility to warn people of the magnetic environment. As stated earlier, magnets are best located in isolated areas where people may not inadvertently wander into the magnetic fields.

Imaging Equipment

An introductory overview of several in vivo imaging methods follows; details about each technique are beyond the scope of this paper. The methods briefly described here are magnetic resonance imaging (MRI), x-ray computed tomography (CT[1]), positron emission tomography (PET), ultrasound, and optical imaging. We advise facility planners to further educate themselves on each of the techniques or to consult with a field expert before making final decisions.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is a versatile, 3-dimensional imaging modality that uses the nuclear property of spin in certain isotopes of elements to form anatomical images (Driehuys et al. 2008; Haake et al. 2000). The expense of MRI instrumentation (usually on the order of $1 million) and the specific structural and environmental design requirements make this a likely device for a shared imaging facility.

MR images can be made sensitive to a variety of physiological conditions such as blood flow, perfusion, functional brain activity, or white matter orientation in the central nervous system or musculature (Kwong et al. 1992; Mori and Zhang 2006; Tseng et al. 1999). MRI can distinguish grey matter from white matter in the CNS of embryonic mice with resolutions below 100 μm (Jacobs et al. 1999). An exciting recent development in MRI is the ability to track individually labeled cell populations in vivo, which is of great utility in tracking stem cells in a living animal over time (Epstein et al. 2002; Frank et al. 2003; Shapiro et al. 2004).

MRI is prone to image artifacts and blurring due to animal motion. "Gating" is a process that enables the capture of images at timepoints triggered by specific events, thus eliminating motion artifacts; for example, cardiac gating captures images during defined phases of the cardiac cycle (Johnson 2008). Use of cardiac gating can eliminate artifacts due to periodic motion such that cine loops (movie) of images can be acquired to image different phases of the cardiac cycle, providing direct measurement of cardiac wall movement, ejection fraction, and cardiac muscle perfusion (de Crespigny et al. 1991; Rose et al. 1994). Respiratory gating is similar to cardiac gating but is triggered by a defined timepoint of the respiratory cycle.

X-ray Computed Tomography

X-ray computed tomography (CT) uses a series of radiographic images, acquired at different angles around the animal, to mathematically construct a 3-dimensional image of the subject (Paulus et al. 2000). For most in vivo small animal imaging the x-ray source and detector rotate around the animal in synchrony. High-resolution small CT systems are called "microCT" to describe both the high resolution of the available images (~10 microns isotropic) and the smaller size compared to human clinical CT scanners (Jiang et al. 2000).

This image modality excels in visualizing bone structures, fat tissue, and air spaces due to the intrinsic high contrast between these tissues. CT can be effective at imaging lean soft tissue when combined with a contrast medium suitable for the application. Contrast media have been developed (or adapted from human practice) for many applications in small animals; studies include localization of tumors, vascular tree imaging, renal clearance, and hepatic structure (Bakan et al. 2002; Vera and Mattrey 2002; Weber et al. 2004).

Positron Emission Tomography

Positron emission tomography (PET) constructs an image based on radioisotope decay of a tracer agent given to the animal before the imaging session (Cherry 2004; Hutchins et al. 2008). PET is the most specific imaging modality of the main volumetric imaging methods (MRI, CT, and PET) because the image is constructed solely from the gamma rays formed by the positron-electron annihilation in the PET agent (Cherry 2006). The most commonly used PET agent is 2-[^{18}F]fluoro-2-deoxy-glucose (FDG) to monitor glucose uptake in areas of high metabolic activity such as the brain and tumors. Because glucose is ubiquitously metabolized throughout the body, an anatomically familiar image is created. Newer, specific PET agents can target cell surface binding sites or gene expression, but these need to be used with combination techniques such as PET/CT or PET/MRI to provide an anatomically meaningful reference (Beyer et al. 2000; Yaghoubi and Gambhir 2006).

The current generation of microPET scanners has an image resolution of less than 1 mm, which is much larger than CT or MRI but a substantial improvement over human clinical PET scanners (Catana et al. 2006; Shao et al. 1997). Only a small selection of common PET agents are commercially available. The development of vendor-available highly specific PET agents will make PET/CT and PET/MRI powerful tools for future biomedical research.

Ultrasound Imaging

Ultrasound imaging uses sound waves and their echoes from tissue interfaces to produce 2-dimensional images in real time. Ultrasound imaging is immediate, total scan times tend to be short, and the equipment requires no special facility support other than a dark and quiet room.

Clinical ultrasound (up to ~14 MHz) is an excellent imaging tool to watch moving tissue such as cardiac wall motion, blood flow through tissues, and some anatomical structures such as fetuses. Ultrasound technology has advanced to use higher-frequency ultrasound (up to ~55 MHz) to produce high-resolution images of mice noninvasively (Foster et al. 2000, 2002; Zhou et al. 2004). Novel experimental uses of ultrasound include image-guided injections of mouse embryos (Slevin et al. 2006). It is now possible to use a series of 2-dimensional images to construct a 3D image or to actually image in 4D (Yagel et al. 2007). Clinical applications of 3D ultrasound include cardiac evaluation and cancer diagnosis (Badea et al. 2007; Correale et al. 2007; Mitterberger et al. 2007; van den Bosch et al. 2006).

Optical Imaging

Optical imaging capitalizes on the physical properties of light (generated by various mechanisms) to generate 2-dimensional images. A variety of optical imaging devices are available for laboratory animals.

Laser Doppler imaging (LDI) is a useful clinical tool for assessing blood flow in patients and animals (Bohling et al. 2006; Humeau et al. 2007). It can be used to evaluate perfusion during healing, surgery, and other circumstances. Devices are relatively inexpensive, have short scan times, and have no special environmental requirements.

Fluorescence imaging requires a fluorescent marker (fluorophore), an excitation light source, and a sensitive detector. This technique has been used microscopically for many years, and has recently been adapted to in vivo imaging of small animals (Graves et al. 2004; Hassan and Klaunberg 2004; Montet et al. 2007). Fluorescence imaging is useful for cell trafficking, tumor diagnosis, and staging; however, many natural fluorophores in the animal body can interfere with accurate signal localization (Hoffman and Yang 2006; Zacharakis et al. 2006). Several in vivo fluorescence imaging devices that are commercially available do not generally require special facility housing and are typically easy to operate. The recent incorporation of fluorescence imaging in fiber-optic technology enables the imager to observe fluorescent signal in vivo at a cellular resolution with minimal invasiveness (Al-Gubory and Houdebine 2006; Pelled et al. 2006; Snedeker et al. 2006).

Bioluminescence imaging (BLI) takes advantage of a biochemical reaction to produce light (Sato et al. 2004; Shinde et al. 2006; Zhao et al. 2005; Zinn et al. 2008). This technique is useful for any reporter gene study—for example, on tumor growth and metastasis, cell trafficking, or intracellular functions. The imaging device is similar to the in vivo fluorescence imager (black box with camera) and is typically easy to operate.

Data Management

One cannot overestimate the importance of data management when planning an imaging facility. The collection of data is often only a fraction of the time needed to process and analyze the data. Data storage is another important factor to consider.

Data Processing

It is essential to discuss data processing and management during the initial facility planning stages. In vivo imaging can produce enormous volumes of digital data in a brief amount of time—a single 3-dimensional dataset can be as large as several gigabytes. Most of the imaging data are collected in a proprietary raw format that requires reconstruction into a usable form. Depending on the complexity of the data, simple personal computers may be adequate to acquire, reconstruct, and analyze some data. Other datasets require much more sophisticated software and hardware to perform the tasks, so access to powerful computer clusters may be necessary. Data movement over local network connections will eliminate the need to produce hard copies for transport to other computers and will facilitate more rapid data reconstruction and analysis. Networking also makes it much easier to bank data for storage before archiving.

Data Analysis

Data analysis can require much more time to evaluate than it took to collect, so the ideal imaging center employs data management specialists to assist investigators with data processing and analysis. In a busy facility, it is often difficult for imaging specialists to find the extra time to help with analysis. A dedicated specialist (or team) to assist with data analysis may prove invaluable. It may be prudent to include a veterinary radiologist on the analytical team to help interpret image data, and a biostatistician to help with statistical analysis. In our experience, many facility users have no experience in interpreting anatomical images or manipulating 3-dimensional datasets, and some analysis software can be difficult to learn. Some investigators have no interest in learning the analysis, preferring instead just to be given the results. Whether the imaging specialists teach investigators to perform their own analysis, or the data management team performs the evaluation, the level of scientific collaboration should be clearly defined before the analysis begins.

If the facility offers analysis as part of the imaging services, coauthorship may not be necessary; however, all parties involved should be clear on this topic. For those who prefer to analyze their own datasets, computer workstations with appropriate software packages should be accessible. Not only are such stations useful for data processing, but the analytical team can use them to discuss results with investigators, and investigators can use the areas to produce images for publications and presentations.

Data Storage

The tremendous amount of data generated with imaging requires a decision about who will store the information. One option is for a dedicated team of data managers to archive the raw and reconstructed data and give the investigators a hard copy (e.g., on a CD, DVD, or portable storage device) to store. Alternatively, the building design must allocate space for archival data storage. Data will have to be periodically removed from computer storage areas to allow space for the constant production of new data.

Summary

Designing a laboratory animal in vivo imaging facility is clearly no small task. The planners and designers must educate themselves about all aspects of a functional facility and convey this knowledge to the architects and builders. It is absolutely imperative that experienced advisors be included in the planning to avoid costly mistakes. A well-designed imaging center will facilitate a smooth and efficient operational workflow.

The large capital expense of equipment, personnel, and overhead costs suggest that a shared imaging facility may be the most efficient use of resources. A shared resource will foster cross-disciplinary collaborative scientific efforts and result in conservation of resources, reduced duplication of effort and equipment, and the production of outstanding data.

The ideal imaging facility will offer state-of-the-art in vivo imaging equipment and incorporate animal housing and preparation areas to minimize transportation requirements. The overall facility design will encompass the following main general considerations:

- personnel workspaces and comfort,
- animal housing and imaging support areas,
- specific building requirements for particular types of imaging such as MRI, and
- miscellaneous considerations that include biological and radiation safety.

The imaging devices should reflect the needs of the users and help to satisfy the goals of their experimental studies. If the budget is strictly limited, facility planners must choose the most essential imaging modalities for facility operation based on anticipated studies. A large or unlimited budget naturally yields the most versatility for state-of-the-art in vivo imaging devices. In addition, modern anesthesia and physiological monitoring equipment are necessary to maximize animal safety. Specialized personnel are required for imaging technical development, and additional support staff (from housekeeping services to veterinary care) are essential for successful facility operation. Effective data management is crucial to the completion of imaging projects.

Most importantly, the engagement of innovative facility designers and skilled imaging experts in careful planning that takes into account the present and future needs of users, along with good resource management, will result in a highly utilized and successful in vivo animal imaging facility.

Acknowledgments

The authors thank H. Doug Morris for his editorial comments and contributions to the imaging sections of this article, especially those about MRI. We also thank Daryl DesPres for reading the manuscript for completeness. The views, opinions, and findings are those of the authors and do not reflect official policy or positions of the Department of Health and Human Services, the National Institutes of Health, or the United States government.

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