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RESEARCH ARTICLE

Small Animal Imaging Center Design: The Facility at the UCLA Crump Institute for Molecular Imaging

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Abstract

Purpose: The growing number of mouse and rat experiments, coupled with advances in small-animal imaging systems such as microPET®, optical, microCAT™, microMR, ultrasound and microSPECT, has necessitated a common technical center for imaging small animals.

Procedures: At the UCLA Crump Institute for Molecular Imaging, we have designed and built a facility to support the research interests of a wide range of investigators from multiple disciplines. Requirements to satisfy both research and regulatory oversight have been critically examined. Support is provided for investigator training, study scheduling, data acquisition, archiving, image display, and analysis.

Results: The center has been in operation for more than 18 months, supporting more than 13,000 individual imaging procedures.

Conclusions: We have created a facility that maximizes our resource utilization while providing optimal investigator support, as well as the means to continually improve the quality and diversity of the science by integrating physical and biological sciences.

Key words: microPET, microCT, Bioluminescence imaging, Fluorescence imaging, Mouse imaging, Gas anesthesia, Immunocompromised mouse imaging, Imaging facility design

Introduction

Biomedical research utilizing small animals such as mice and rats has expanded dramatically in the past few years as molecular biology and imaging techniques open new opportunities to investigate models of disease. The growing number of mouse and rat experiments, coupled with the increasing number of dedicated small-animal imaging systems such as microPET®, optical, microCAT™, microMR, ultrasound, and microSPECT, has necessitated a common technical center for imaging small animals using these devices and to guide further technology development to meet the scientific needs for which these technologies are employed. These new imaging systems provide investigators unprecedented abilities to examine and measure *in vivo* biological and pharmacologic processes over time in the same animals. Increasingly sophisticated molecular probes and tool sets allow researchers to examine multiple processes at once in the same animal by using different light wavelengths (optical), various molecular imaging probes [positron emission tomography (PET), single photon emission computed tomography (SPECT)] and different contrast agents [magnetic resonance (MR),

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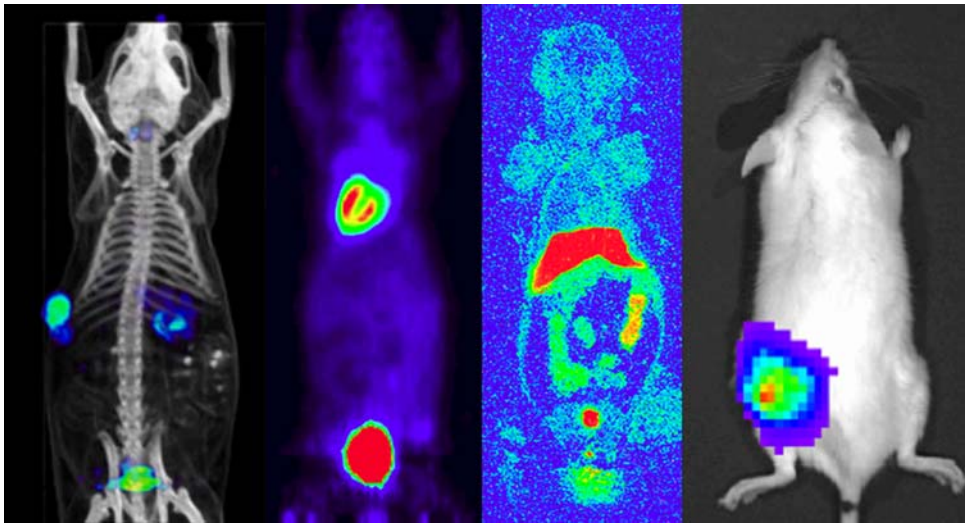

Fig. 1. Example images in mice of microPET-CT, microPET, autoradiography, and optical bioluminescence.

computed tomography (CT)], as well as to define the anatomical structures in which these processes take place. This, in turn, has led to a demand for comprehensive, multimodality imaging facilities that can house animals, support imaging systems, and provide investigators with the tools, methods, and other infrastructure necessary for successful imaging experiments. At the UCLA Crump Institute for Molecular Imaging, we have designed and built such a facility to support the research interests of a wide range of investigators from multiple disciplines. The facility includes support for investigator training, study scheduling, data acquisition, archiving, image display, and analysis. The design requirements to satisfy both research and regulatory oversight were critically examined to create a streamlined process for handling animals and data. Our goal was to maximize our resource utilization while providing optimal investigator support, as well as the means to continually improve the quality and diversity of the science by integrating physical and biological sciences.

The expanding use of animal models in biological research, new *in vivo* imaging devices, growing use of multiple imaging systems, and diversity of biomarkers has created a need for dedicated small-animal imaging facilities with more comprehensive means to accomplish a diverse array of experimental paradigms. At our institution, the facility must be capable of handling large numbers of animals from multiple investigators who utilize a wide range of imaging modalities, including MicroPET® (Siemens Preclinical Solutions, Knoxville, TN), bioluminescent/fluorescent optical imaging systems (Xenogen, Alameda, CA, USA), microCAT™ (Siemens Preclinical Solutions, Knoxville, TN, USA), and digital autoradiography (Fig. 1). Each of these systems has various support requirements, which include dose drawing equipment, well counter, anesthesia, isolated imaging specifications, maintenance and monitoring of biological functions, biosafety cabinets, computer infrastructure, data archiving, and image analysis tools.

The complexity of imaging systems and animal models requires that the imaging center provide specialized training and support, even for investigators who have a wide range of familiarity with imaging processes. The goal of the facility must be to provide a known, stable, consistent, and accurate imaging procedure, with easy access to the final images and the software tools required to analyze and interpret the results. For some imaging methods, such as optical imaging [1], this only requires appropriate training and occasional support for supplies, service, and software upgrades. Other imaging methods, such as PET [2, 3], require dedicated staff, cyclotron time, and radiochemistry support for experiments. In particular, the use of ionizing radiation (radioisotopes), instruments that produce radiation (microCT) or require radiation for use and calibration (microPET®) require oversight by staff trained in radiation safety. These individuals perform regular equipment calibration and provide assistance with experiments and complex data processing.

To meet the demands of investigators, we designed, built, and put into routine use a comprehensive small-animal imaging technical center. A large number of design criteria were considered to ensure the best workflow of animals, personnel, and data through the facility.

Design Objective

Facility Requirements

Perhaps, the single most important factor when designing an imaging facility is to decide what its role will be; specifically, the instruments to be included and the level of technical and financial support that will be required to create and maintain the devices and services, as well as to advance the technology of the center. Inclusion of short-term vivarium space is another key consideration, because space and personnel support are major factors in the design.

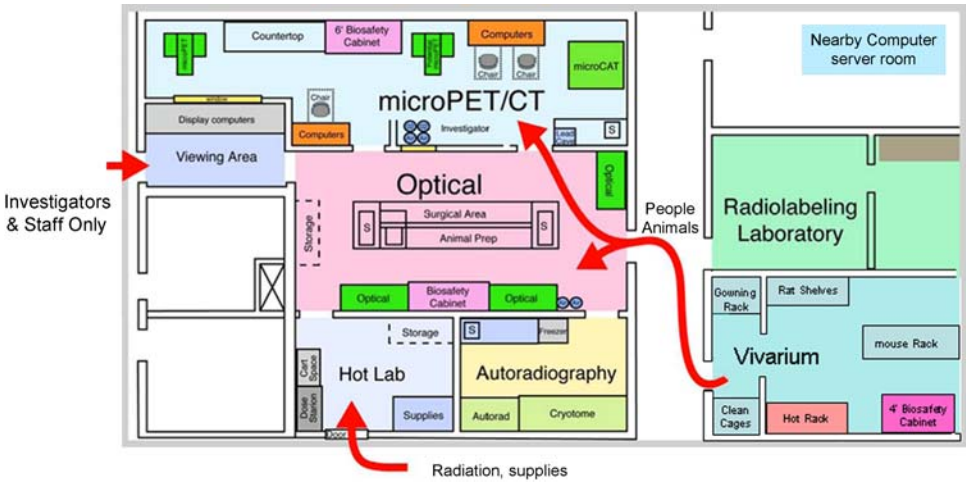

Fig. 2. Crump Imaging Facility layout.

As soon as the role of the facility is defined, key personnel need to be identified who will enable the facility to pursue these goals. A flexible design supporting upgrades and replacements is essential, especially with ongoing development of new, improved imaging devices and computational and analysis systems, to improve the technical capability of the center. A facility designed to only meet current requirements may not be compatible with the upgrades or future expansion required for the changing needs of the biomedical research community.

As soon as an imaging device equipment list has been chosen, the support required in terms of staff, space, and computer requirements can be determined. These parameters vary considerably, depending on the imaging device. In our facility, the supported devices are microPET® [4], microCAT™ [5], optical imaging [1, 6], and digital autoradiography with a cryosectioning and imaging system. The proper and best use of these systems, including the rules and regulations stipulated by the Biohazardous Materials, Radiation Safety and Animal Research committees, were all considered in the design plan. In particular, we were required to meet specifications necessary to pass Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) standards. Solicitation of advice and inclusion of the various committees in the design process ensured that the facility met the local, state, and federal requirements for handling the radiation, animals, and hazardous materials used in the imaging research.

Design Considerations

Facility Layout

The equipment layout should be designed to optimize the workflow of people, animals, and radiation pathways and exposure. The detailed specifications for each device are available from the equipment vendors, and attention must be given to provide proper power, heating, cooling, and access to the various systems. Consideration must also be given to allowing space for oxygen tank replacement, investigator cart storage, ability to open instrument access panels, and sufficient space for multiple people to work in the same room together.

It is essential to be all-inclusive in the layout design stage. Miscellaneous items to consider include dose transport carts, lead "cave" enclosures, bulk supply storage, gas tanks, refrigerators, freezers, large biohazardous waste containers, supply cabinets, portable anesthesia systems, and various often-overlooked items needed to keep the facility clean. Overlooking such details as where to locate lead enclosures for radiation sources can greatly reduce the usable space.

Equipment layout configurations can be readily examined using various software programs, such as PowerPoint (Microsoft, Redmond, WA, USA; Fig. 2). Different layout arrangements can be easily examined by using a floor plan and scaled representations of the various facility components. In the plans, allowing sufficient space for passage behind occupied chairs is essential, because this can impede access of multiple investigators to other parts of the facility in a busy center. An examination of the space required for occupied chairs can often make the difference between a usable versus cramped design layout and can be easily overlooked during the planning stage.

Animal Housing, Handling, and Preparation

An essential part of the imaging facility is an adjacent location for animal housing and preparation. Without an adjacent vivarium, investigators would need to bring animals from remote locations to the imaging devices, and then remove them immediately to clear the room for the following investigator. In the past, this created a host of problems, because animal housing areas are not typically set up to handle radioactive animals and have many restrictions

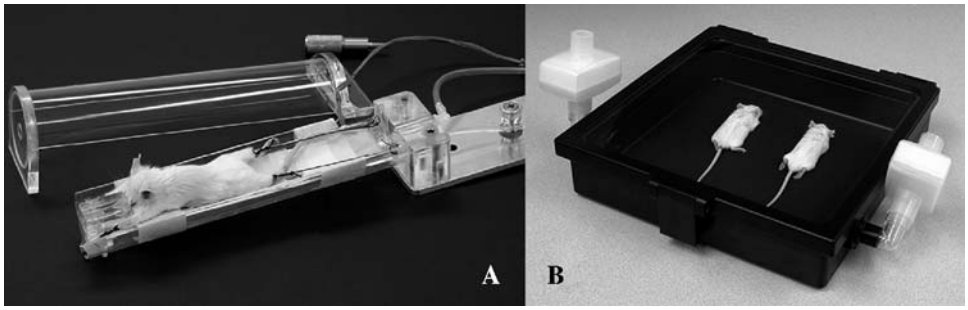

Fig. 3. Imaging chambers for mice in microPET/CT **(A)** and optical system **(B)**.

due to the diversity of animals in the general vivarium. In most cases, investigators were required to store animals overnight in their own labs, creating oversight and housing problems. Care and cleaning of animals can be a problem for investigators who cannot dedicate an appropriate portion of their space for animal storage, as well as wasted space versus a single central facility for imaging. In addition, if viral outbreaks occur in an animal room, animals stored in the same room, even if they are not infected, must nonetheless be placed in quarantine, consequently disrupting imaging experiments. This is particularly a problem for longitudinal imaging experiments, because the loss of measurements at certain time points may render the experiment useless. Another potential problem occurs when animals require surgery or other preparatory steps prior to imaging, such as injection with a viral delivery agent. These procedures may require a biosafety cabinet and an authorized location, which not all investigators have access to in their laboratories or departments.

To accommodate these considerations, we created a dedicated animal housing and preparation space located adjacent to the imaging facility. This room has a dedicated "hot" rack for cage storage of radioactive animals, a ventilated cage rack for mice, shelves for rat cage storage, and a biosafety cabinet. The biosafety cabinet is used for cage changing and animal preparations, including viral injections. When investigators bring their animals in for imaging experiments, they can store the animals for the duration of the study in this vivarium space. This saves considerable time and regulatory oversight for all involved parties as well as standardization of research approvals. The inclusion of this space in our facility is the single most appreciated support feature by both users and oversight agencies.

Using Immunocompromised Animals

The majority of imaging experiments make use of immunocompromised animals, primarily SCID and nude mice. To maintain the health of the animals over the course of imaging experiments, which can last several weeks, a pathogen barrier must be maintained around the animals at all times. We addressed this challenge by constructing imaging chambers to house the animals during the imaging process (Fig. 3). Mice are positioned and placed within the chamber using sterile techniques inside a biosafety cabinet, which provides a sterile laminar flow of air over the workspace. Chambers have been designed for both microPET® and microCAT™ imaging (Fig. 3A) [7], as well as for optical imaging (Fig. 3B).

Anesthesia and Standard Operating Procedures

Imaging experiments are typically designed to noninvasively monitor biologic processes over time, either in the same animals on different days or in short-term individual experiments using a group of animals undergoing the same procedure. A common procedure is to look at a baseline condition and compare image data acquired at various time points after an intervention, which might be viral vectors, gene activation/deactivation in transgenics, cell transplants, drug therapies, or radiotherapy. Using the same methods to acquire data, image comparisons over time takes advantage of any systemic biases, because it is presumed that conditions are similar in both measurements. It is therefore advantageous to create standard operating procedures (SOPs) for all imaging work. These procedures are also useful for obtaining approval from review committees and regulatory agencies, because nearly all the imaging work in the facility follows the same methods and protocols.

All microPET® and microCAT™ imaging in rodents is performed using the imaging chamber (Fig. 3A). The chamber is designed to provide gas anesthesia, which maintains a constant level of sedation and avoids movement artifacts that can occur when injected anesthetics begin to wear off. A constant level of anesthesia is essential for all imaging systems, particularly those sensitive to any movement during acquisition such as microCT and microMR. By providing gas anesthesia, the investigators' need to purchase and track usage of controlled substances such as ketamine or pentobarbital is reduced or eliminated. Animals can become hypothermic in as little as 5 minutes at standard room temperature, in part due to the large airflow in the facility to cool the imaging systems. For this reason, we also heat all of the boxes used to induce anesthesia and keep animals sedated during tracer uptake. Recent work has

Fig. 4. Wall-mounted gas anesthesia vaporizer and manifold system, adjacent biosafety cabinet with heated induction boxes. Note the lead enclosure for radioactive sharps container.

shown that the relative uptake for radiolabeled compounds, particularly in peripheral tumors, is highly dependent on animal temperature [8]. The imaging chamber is also calibrated to maintain a constant normal physiological temperature during the imaging process, a vital step if the imaging procedure lasts more than a few minutes.

Similar to the microPET/CT anesthetic system, gas anesthesia is provided as an option for optical imaging experiments, because many investigators use immunocompromised mice and need to maintain barrier conditions during the imaging process. For some investigators, injected anesthetics are still a suitable option for optical imaging, because they find it simple and efficient to inject multiple mice and stage groups to go through the imaging process. This approach is more difficult to perform using the gas system. In general, gas anesthesia should be preferred because of its ease of use, ability to maintain a constant depth of anesthesia, and the short induction and recovery time resulting in less stress to the animals [9]. The isolated optical imaging chamber (Fig. 3B) is not heated; instead, it is kept on a recirculating water bath pad in the biosafety cabinet to keep it warm inside the biosafety cabinet. The Xenogen IVIS imaging box provides a heated stage, so heating of the isolation chamber during imaging is not necessary. Using either water baths, heated boxes, or heated imaging stages, rodents are kept warm at all times while under anesthesia.

In collaboration with Summit Medical (Bend, OR, USA), we designed a gas anesthesia system capable of handling all imaging requirements in an easy-to-use manner (Fig. 4). For the microPET®/CT area, a wall-mounted dual vaporizer arrangement with a manifold system is used to feed anes-

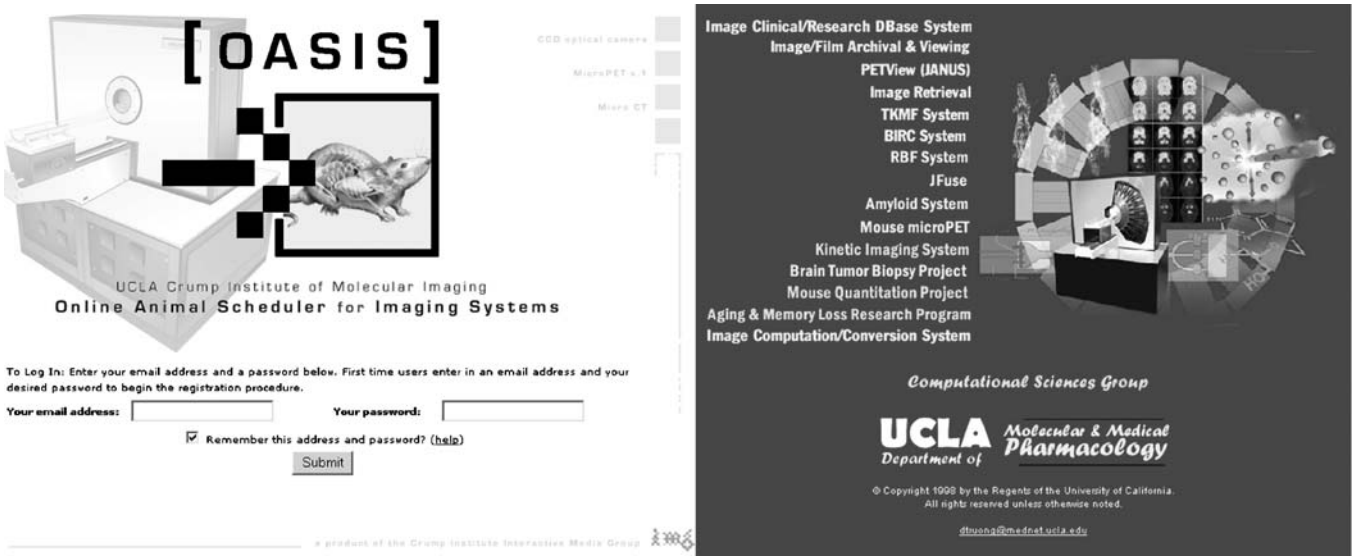

Fig. 5. Websites for scheduling optical usage (left) and archiving (right).

Fig. 6. Radiation dose transportation cart, with a raised floor (shaded inset) to improve weight balance.

thetic gas to two microPET® systems, the microCAT™ system, four induction boxes, and two nose cone stations for positioning the animals in the imaging chamber. The space-saving wall-mounted system frees up valuable countertop space and creates less clutter. The manifold system has orifices that provide constant specific flow rates to various locations, eliminating the need for flow valves that require constant adjustments as demand for anesthesia varies. Anesthetic gas is turned on or off by using a simple cutoff switch located at each point-of-use location. A similar system is in place for use with the optical imaging systems. The imaging facility also maintains a cart-mounted gas anesthesia system operating off a small oxygen tank for use when animals need to be transported between various locations, or for times when two different concentrations of anesthetic gas are needed, because the wall-mounted system can only supply anesthesia to all the imaging locations at a single concentration. All anesthetic waste gases are captured using a separate manifold system and vented out of the facility, eliminating the expense and need for constant changing of charcoal filters. Typically, animal-use areas also include an air filtration system for keeping the air free of odors.

Scheduling

At UCLA, we typically support 100–150 microPET®/CT experiments and 100–150 optical imaging experiments per week. Optical imaging is handled separately from microPET®/CT, because the optical systems are user-operated and do not require scheduling of cyclotron staff. A website (Fig. 5A) is used to schedule time online on a first-come, first-served basis for approved projects. With three optical systems, access has not been a problem.

Scheduling for microPET® and microCAT™ experiments require scheduling of cyclotron-based production of radiolabeled imaging probes. Details and priorities of the multiple demands for various radiolabeled imaging probes are scheduled by a Research Allocation Committee (RAC), which meets weekly to determine the following week's schedule. Requests are sent via email to the Imaging Technology Center manager, who meets with the head of the Tech Center for producing radiolabeled imaging probes. The needs of the following week's imaging studies are discussed and decided in the RAC committee meeting and emailed to all the investigators. Typically, this gives the investigators 4–7 days' notice for their imaging experiments. As most experiments involve using the same animals imaged at various time points, a research plan covering several weeks can be submitted to ensure the requested times are provided as closely as possible to the ideal imaging times. The RAC committee also provides oversight of all the imaging, radioprobe production and communication centers, and functions to assure that commitments to faculty, students, staff, and funding sources are fulfilled.

Hot Lab

When the number of scheduled experiments is large, a high-level radiation area or "hot lab" for receiving, storing, measuring, and dispensing the individual radiation doses is essential. The holding-and-dispensing operations require a dose calibrator and dose drawing apparatus with appropriate amount of shielding. Tungsten dose carriers are used for routine transportation of the injection doses to the imaging devices, and specially modified dollies are used for the dose transportation boxes and lead pigs containing the high activity level deliveries from the cyclotron. Use of special dollies or handcarts is preferred over use of standard laboratory carts, because they are less likely to overturn during transport (Fig. 6). Given the weigh of the transportation box, usually 25 kg or more, sufficiently strong dollies with large wheels (similar to those typically used by delivery companies) are recommended. For ease of use, it is also worthwhile to raise the base a few inches to improve handling and balance the weight over the wheels to reduce back and arm strain on the transport personnel. The box must also be securely attached to the dolly so that it cannot fall out or unbalance when moving. Storage space for dollies, mop, and bucket, and other occasionally used support equipment is necessary, something that is often overlooked during the design stage.

MicroPET® and MicroCAT™

Of all the equipment in the facility, the microPET® imaging system requires the highest level of planning and support. Use of the system requires either purchasing radioisotopes or obtaining them from a dedicated cyclotron

with automated, semiautomated, or traditional chemical synthesis support. In either case, scheduling of experiments, delivery and use of radiolabeled probes, imaging study, tomographic image reconstruction, and archiving of large image data require a high degree of personnel support, instrumentation, and coordination. In our case, we support two microPET® systems that frequently require coordination with use of the microCAT™ system. These systems require ancillary equipment such as gas anesthesia, biosafety hoods, counter space, and storage space for supplies and incidental equipment, and additional computers for database and image display. Space must also be provided for lead brick shielding to house sources, radioactive needle containers, hot animals, and for unspecified shielding needs.

Due to the high level of expertise required, we opted to use dedicated staffing of the microPET® and microCAT™ systems to ensure that the result of each imaging experiment is consistent and accurate. At our location, radiation safety regulations require that personnel who operate equipment that uses or produces radiation be trained in radiation safety. Rather than train everyone using the facility how to safely operate the equipment, using dedicated staff is preferred for safety and efficiency. In our case, this requires 2.5 full time staff to provide support on a 12-hour daily basis. In addition to microPET®/CT support, the staff conduct quality control measurements for all the imaging systems and maintain usage records for the various oversight committees. As our imaging center is also a technology center where the technologies are not only used but also technical advances occur, we have a full-time imaging physicist who directs the center.

Optical Imaging

Our facility houses three Xenogen IVIS bioluminescent optical imaging systems [1], two of which are capable of imaging fluorescence [6]. Investigators attend a two-hour training seminar that covers scheduling, use, and archiving of data, followed by a hands-on training session. Most people do not need further training or help beyond this initial session. All supplies, including Luciferin, Coelenterazine, solutions, gloves, filters, etc., are provided as part of a recharge fee. Bioluminescence substrates are kept in a −20°C freezer within the imaging facility. As the optical systems are easy for investigators to learn and operate, and are used in a more qualitative fashion, these instruments are located in a central core area that is available for use around the clock. Access to imaging any day or time is particularly useful for imaging biological processes, which progress on their own timeframe and may not be well suited to a typical workday/weekly schedule.

Autoradiography

Although the cryomicrotome and Fuji BAS digital imaging system (Fuji, Stamford, CT, USA) are less frequently used, they are a critical part of the validation of new imaging compounds labeled with ^{14}C, ^{3}H, and positron emitting radionuclides [10]. The infrequent use of these devices by investigators makes it more efficient to use the facility staff to run the equipment. The cryomicrotome is potentially dangerous because of the presence of a sharp blade, and the Fuji BAS system is fairly delicate. Thus staff operation is preferred, although not required. A sink, counter space, and a −20°C freezer are needed for creation of the cutting blocks and cleaning of the plates and blocks.

Data Tracking, Archiving, and Retrieval

For microPET® and microCAT™, the staff assigns each new animal a unique ID number using a simple Excel spreadsheet. Each imaging session is assigned a specific ID number, which is generated from our internal archiving website (Fig. 5B), after entering information related to the investigator, radiolabeled probe, and animal ID [11]. The session ID is used to retrieve images and is the primary identification of the imaging experiment. Adjacent to each imaging system acquisition computer, we have a database computer used for generating session IDs, animal IDs, and web access, and for entering session-specific information into our database. All information related to the specific imaging session is entered into the database, including the injected probe, injection time, reconstruction parameters, and any information that the investigator may specify. Because information is essential to the investigator during later data analysis steps, we store this file on a department network site that is archived nightly. This database also enables nearly instant access for the center manager to create usage and billing reports, because we operate as a cost center.

All of the imaging devices are connected to a private Ethernet network backbone. Using a specifically designed archiving website, session ID numbers can be created and data sent to archive by either the user or the imaging facility staff. Optical and autoradiography data are sent to the archive by the investigators following collection of the data. Optical images may also be copied to USB flash cards, Zip disks, or CDs for immediate use. Both microPET® and microCAT™ images are sent to the archive following image reconstruction by the facility staff.

As soon as data are placed in the proper archiving network folder, the archiving process is completely automated. Image data is copied to a large disk array for online storage and immediate access, which—for security reasons—does not allow public access. Image data and sinograms are also burned onto DVDs. As soon as data are archived, the folder location is automatically deleted to free up disk space.

Image data is retrieved by users accessing the archiving website and requesting the unique session ID given to each experiment. The request is handled automatically, with a copy of the image data retrieved from the archive placed on

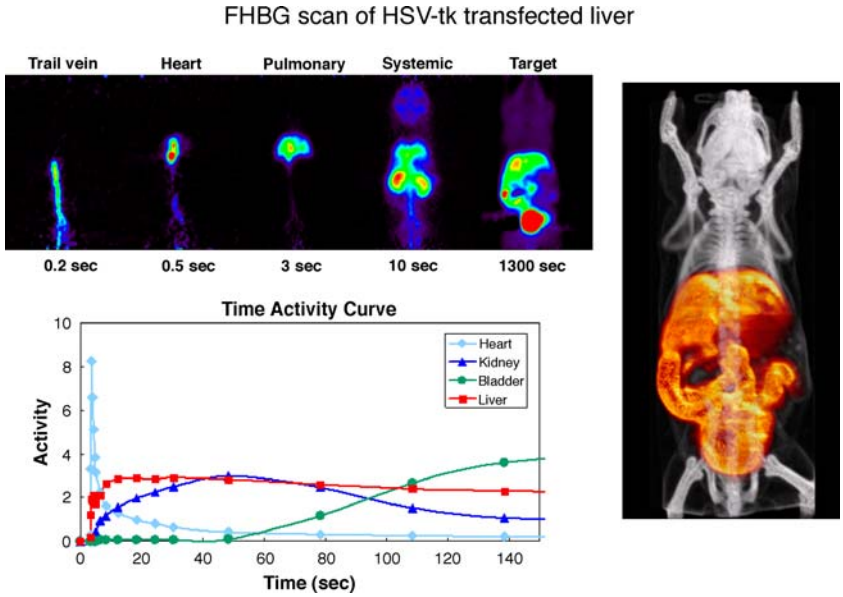

Fig. 7. Dynamic microPET images of 18F-HBG in a mouse infected with HSV-tk demonstrating the biodistribution of the compound over time. Right image shows the PET probe distribution after 1 hour in color over a coregistered microCT image.

a public network folder. The folder is automatically cleared of image data at midnight to maintain space for copying new data. Investigators are provided with software and training so that the image analysis work can be carried out wherever desired.

Computer Support

To handle the large amounts of data generated on a daily basis, an isolated private gigabit network and switch are necessary. The archiving and retrieval systems discussed above are essential for quick and easy access to the images by the investigators. A computer cluster is essential for creating microCT images and for microPET® images using iterative reconstruction techniques [12]. A properly designed and supported network is required to ensure quick and easy flow of data for viewing and processing. With the large amounts of data generated daily, it is also essential that the network and computers function continuously with little or no interruption. Otherwise, the individual imaging computers would quickly fill up and prevent further imaging experiments.

As soon as the system is configured, IT personnel support is reduced, but it is vital that there be on-call support to fix problems or equipment failures. Ongoing routine support is required for burning the archived data to DVD, which is typically initiated one or more times per day, depending on the data load. Support for the computer cluster can be variable, depending on the type and configuration of the computers and the user demands. At our institution, the cluster is a shared resource, and time is available for other users. With proper priority settings and process queuing, sharing of the cluster is feasible.

Image Display and Analysis Support

Images can be displayed with a variety of software packages. Optical images are viewed using the Living Image software from Xenogen. Images from microPET® and microCAT™ are viewed using ASIPro (Siemens Preclinical Solutions, Knoxville, TN), AMIDE [13], or JANUS [14]. Software is available to all investigators either online or from the facility manager. For dual PET-CT imaging experiments, investigators are currently provided with coregistered images in a single file containing both PET and CT data. This simplifies the data display and analysis.

General data analysis and image interpretation support are provided by the imaging staff and imaging physicist. More complex analysis support, such as tracer kinetic and pharmacokinetic modeling, is available through a UCLA software package called Kinetic Imaging System (KIS) [15], a commercial version from Siemens Preclinical Solutions, called Miraview Research, or for more extensive modeling, through an affiliated Data Analysis Technical Center at UCLA.

Results and Discussion

The creation of a comprehensive Imaging Technology Center specifically dedicated to multimodality imaging of small animals is a relatively new topic. In the past, incremental slow growth in the number of imaging systems has often led to new devices being added to existing facilities or investigators laboratories, with little or no planning to address usage patterns or layout: the available space was simply converted and used as best possible. The dramatic rise in high-throughput mouse imaging over the past several

years, made possible by new or improved imaging systems such as microPET®, microCT, and optical systems with software management, archival, and analysis systems, has created a need for consolidated imaging facilities that are optimized for these imaging experiments. To keep pace with the growing number of PET experiments, the cyclotron and radiolabeling facilities have also had to undergo innovation and automation to meet the applications growth, often in support of both human and animal research [16].

In the 18-month period since the creation of the imaging facility, over 13,000 imaging experiments have been conducted. These include dual- and trimodality imaging sessions and longitudinal studies using the same animals, sometimes lasting up to several months [17, 18]. Another area of interest has been following the biodistribution of new compounds over time using the dynamic capabilities of microPET (Fig. 7). Investigators have benefited from the consolidation of the imaging devices, associated technologies, and the support of centralized staff. Bringing together the investigators into one facility has also increased the interaction between different research groups and enhanced the collaboration and shared learning of techniques. Students, staff, and postdocs have the opportunity to learn from each other, particularly the small tricks and details of animal imaging that can save time and resources, as well as from their diverse science backgrounds and interests.

The gas anesthesia system, combined with integrated heating to prevent hypothermia, has nearly eliminated loss of animals during the imaging procedures and stabilized body functions during experimental protocols. By providing gas anesthesia to all investigators, we have also reduced the amount of time due to complications associated with each investigator individually purchasing, storing, and handling paperwork for the use of injectable anesthetics (controlled substances) such as ketamine, xylazine, and pentobarbital. With the imaging systems located within the same or adjoining rooms, wall-mounted gas anesthesia systems running to several locations are now feasible for multimodality imaging experiments.

The centralized vivarium space located adjacent to the imaging facility has also saved considerable time for researchers by eliminating the need to locate and transport animals to and from remote animal storage locations. The separation of radioactive animals to a dedicated rack for isotope decay enables the veterinary staff to service the nonradioactive cages; thus, investigators do not need to worry about animal husbandry, except for the short time during radioactive decay. Inclusion of a biosafety cabinet allows for cage changing of immunocompromised animals and also a location for procedures such as viral injections. Access to the vivarium is simplified by having the same badge-activated locks as the adjacent imaging facility; there are no special codes or keys required.

The inclusion of an animal surgical area has also encouraged some investigators to consider new experiments where imaging experiments must be conducted during or immediately following any surgical interventions [19, 20]. By including an area suitable for animal surgeries, we have opened up the possibility to do interventions and experiments that were previously not possible. The surgical area is also useful for investigators who have infrequent surgical procedures and have limited space or equipment in their own labs. The surgical area is also useful for training new personnel in procedures such as tail vein injections, because using this space does not interfere with imaging experiments in adjacent areas.

The colocalization of equipment has also facilitated the training of new researchers. The facility was designed to have sufficient space to hold small workshops and is located adjacent to a conference room with suitable space for holding training seminars for up to 30 people. Part of the ongoing support for the facility includes routine training, research seminars, and workshops, so the ability to hold seminars nearby and sufficient space to hold workshops within the facility are a useful feature.

Investigators have benefited from the central facility and the use of standard operating procedures through faster authorizations from animal use, radiation, and biosafety committees. The oversight committees also benefit from the reduced time and questions when reviewing authorization requests, having a centralized location for inspections and the knowledge that the imaging experiments are conducted using SOPs, usually under the supervision of the facility manager. With the fast pace of research, the ability to obtain quick authorizations and fast access to the imaging systems and the analysis of data resulting from them improves the overall quality of research and satisfaction of the users, and accelerates their science.

Conclusions

We have designed, built, and put into routine use a small-animal imaging facility to handle the needs of a wide range of imaging experiments using microPET®, microCAT™, bioluminescence and fluorescence optical imaging systems, and autoradiography. The facility has excellent accessibility to the imaging devices and can maintain a high level of experimental throughput for multiple users. The overall design also facilitates the increasingly common use and comparisons of multiple imaging modalities applied to a wide range of biological and pharmacological problems. Consolidation of the imaging devices centralizes staffing and increases communication and collaboration between investigators, creating a more productive environment that better utilizes our resources to support a large number of investigators from many different disciplines.

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