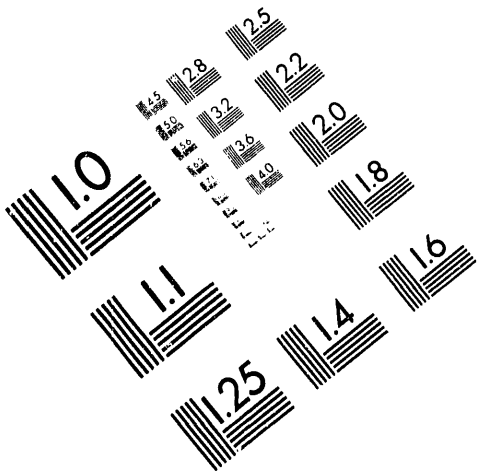
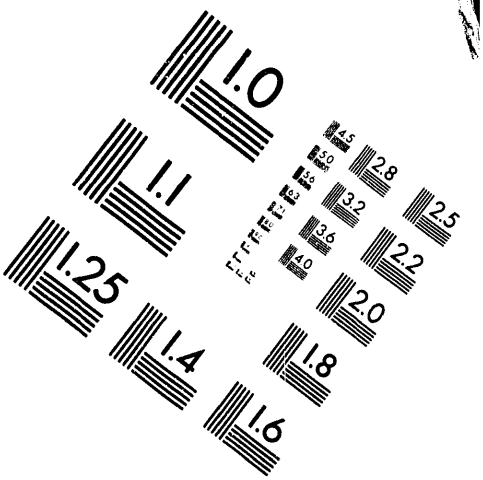


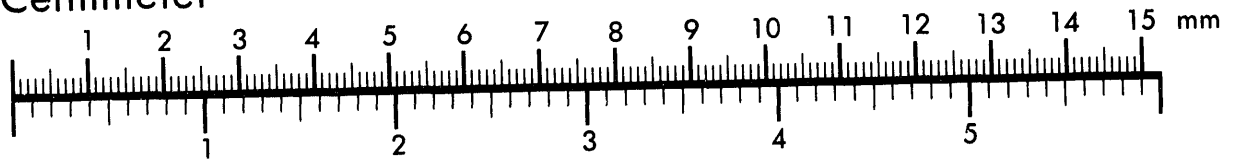
Association for Information and Image Management

1100 Wayne Avenue, Suite 1100
Silver Spring, Maryland 20910

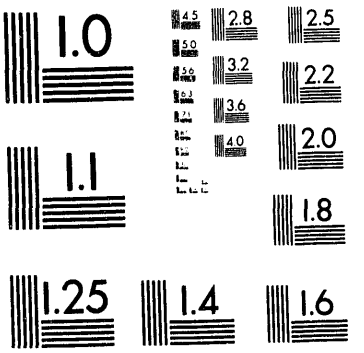
301/587-8202

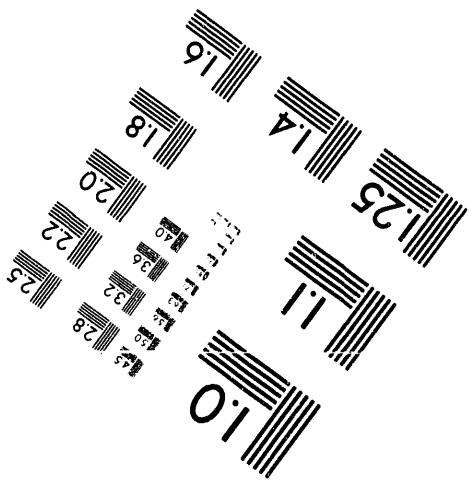


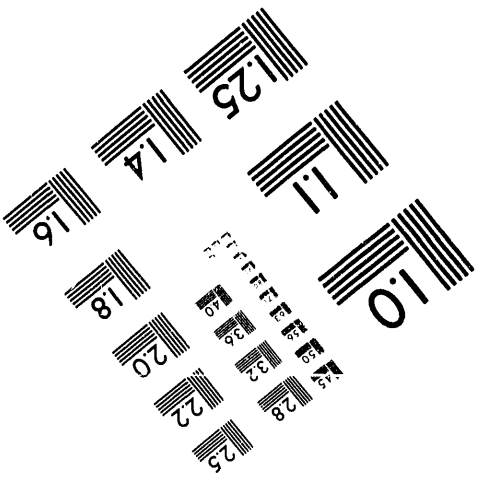
Centimeter



Inches







MANUFACTURED TO AIIM STANDARDS
BY APPLIED IMAGE, INC.

1 of 1

BNL-48964
Conf-930802--2

Laboratory and Cyclotron Requirements for PET Research

David J. Schlyer
Chemistry Department
Brookhaven National Laboratory
Upton, NY 11973

DISCLAIMER

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency thereof, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

RECEIVED
JUN 02 1993
OSTI

MASTER

DISTRIBUTION OF THIS DOCUMENT IS UNLIMITED

Outline

Introduction: Type of facilities

Section 1: Clinical PET with no radionuclide production

Section 2: Clinical PET with a small accelerator

Section 3: Clinical PET with research support

Section 4: Research PET facilities

Section 5: General facility considerations

Summary: Which machine, Which isotopes

Introduction

In a discussion such as this concerning facility configuration, it is desirable to have a common set of references to ensure that everyone is clear about what is being discussed. To this end I have chosen four categories that were formally defined by a task group on PET site and facility planning set up by the American Association of Physicists in Medicine (1). It is obvious that there is really a continuum of facilities and the lines of definition are purely arbitrary. The four categories are:

I. Clinical PET with no radionuclide production facility. This type of center has no cyclotron. All the radiopharmaceuticals are either produced from simple kits using radioisotopes milked from generators or are purchased from a local distribution center. There is no involvement with basic radiotracer development research and there is complete reliance on the equipment vendor for repairs, maintenance and upgrades.

II. Clinical PET with a radionuclide production facility. This type of center has a cyclotron or other small accelerator and some type of automated chemical synthesis apparatus. There is little involvement with basic radiotracer development research and there is nearly complete reliance on the vendor for maintenance, equipment upgrades and new capabilities in the form of new radiotracers.

III. Clinical PET with a research support staff. Along with the accelerator and automated synthesis modules, this center has a scientific support staff of a

chemist(s), physicist(s) or other scientists capable of developing PET procedures and radiopharmaceuticals that have been described in the literature. The major emphasis is to perform routine patient studies, but some independent research is carried out.

IV. Research PET facility. Along with the PET scanner and accelerator, this center will have a team of research scientists performing basic research on developing new radiotracers and procedures. Considerable space is allocated for laboratories and animal facilities. Little or no purely clinical work is done, but there may be an extensive clinical research program.

Usually a type IV operation evolves from a more restricted facility although in several cases such a facility has been set up with no previous history of PET. The transition from a smaller, somewhat focused facility to the more general research facility is usually a gradual one requiring several years. For that reason, this chapter will concentrate mainly on the type I through III facilities with a few words concerning the possibility of expansion.

The most important consideration in facility planning is to be absolutely clear on the intent of the center. Specific goals must be set as to the type of studies which will be done, the radiopharmaceuticals used, the complexity of the scanning protocol, the radioisotopes required, and the amount and complexity of data analysis. This requires input from the scientists and physicians who will be using the center as well as the scientists involved in setting up the center. It is imperative that everyone clearly understand what a particular facility can do and

more importantly, what it cannot do.

Having said that, it is also important to try and envision what type of center this facility could evolve into during the coming years. If there is any possibility of expansion, provisions should be made for this eventuality. With this in mind it may be possible to plan the exact layout of the facilities in a more flexible manner which would allow for rapid changes in the direction and goals of the facility without the expenditure of large amounts of money.

Section 1: Clinical PET with no Radionuclide Production

The simplest type of PET center is one where radionuclide generators or isotopes purchased from a local distribution center are used for PET scans. Typical examples of these isotopes could be Zn-62 → Cu-62 generators, Sr-82 → Rb-82 generators, fluorine-18 delivered from a regional center either as fluorodeoxyglucose (FDG) or as fluoride ion to be processed to the radiopharmaceutical.

This situation does not require any selection of an accelerator, but does require the allocation of some laboratory space. In most cases, the radioisotopes will not be in the form of the desired radiopharmaceutical and must be processed either with a commercial kit, with some more extensive simple chemistry, or in an automated synthesis module. This implies that there must be shielded space somewhere near the tomograph suite to do the processing. The more extensive the chemistry required, the more elaborate the facilities need to be. This will be separate from the space needed to do the blood chemistry which will be in the tomography suite. The bare minimum will be a space to process and a separate space with the facilities to do quality assurance (QA) on the final product before injection. A set of guidelines for the areas needed for these activities is given in Table 1.

Section 2: Clinical PET with a small accelerator

In this type of PET center, a small accelerator is used to generate some or all of the commonly used positron emitting isotopes of oxygen-15, nitrogen-13, carbon-11, and fluorine-18. In addition to these isotopes, some commercially purchased generators may be used.

In the simplest form, this type of center would have an oxygen-15 source in the form of a small accelerator and receive deliveries of fluorine-18 and perhaps one or two generators. The oxygen-15 only machines are small, compact and require very little shielding. All the current accelerators use the $^{14}N(d,n)^{15}O$ nuclear reaction. The machines available at this time are a compact cyclotron, a small linac, and a tandem cascade accelerator. The choice will depend on the space available, the shielding requirements, and the reliability of the machines.

Since the processing of the oxygen-15 into its final chemical form is done on-line, little space outside of that required for the accelerator is necessary. Quality assurance testing must be done on representative samples to verify that the pH, radiochemical purity, and radionuclidic purity are within QA limits. These samples can then be sent out for pyrogen and sterility testing. The space required for the quality assurance testing will be the same as for a type I facility or about 200 sq ft. The processing space requirements will also be nearly the same as the type I facility and of course they should be separate.

A center which meets the type II criteria might also have a slightly larger

accelerator. This would be a small compact cyclotron or other accelerator which will produce the four most widely used positron emitting isotopes carbon-11, nitrogen-13, oxygen-15 and fluorine-18. Here the spectrum of radiopharmaceuticals which may be administered is much wider. This type of accelerator will require additional shielding as well as space for electronics, water cooling, a heat exchanger, and a control room. The choice of accelerators is much wider in this situation. Nearly all the accelerator manufacturers have an entry into this market. The choice will depend on the exact situation, but some guidelines are given in the summary.

There will almost certainly be some synthesis modules in use which may be supplied by the manufacturer of the accelerator or may be purchased independently. This type of facility has the potential of some expansion in the future. New radiopharmaceuticals may be developed which offer better diagnostic tools of the physician. However, this type of facility will depend on the manufacturer to produce a commercial unit for the production of these radiopharmaceuticals since no manual chemical syntheses or design of automated synthesis modules will be done in-house. The delay between the time a radiopharmaceutical becomes a proven clinical tool and the time a manufacturer releases a module for its synthesis can be significant.

Facilities for the synthesis modules should be made near the cyclotron (to minimize loses due to transfer) and PET tomograph area but well shielded to prevent undue radiation exposure to personnel. The ideal situation would be a

small shielded room with the synthesis modules easily accessible. A consideration in this arrangement is to be sure that a module that must be loaded with fresh reagents for the next synthesis is not in close proximity to another module which still has a substantial amount of radioactivity from the last synthesis. There should also be sufficient space around each module that it is possible to access it and perform maintenance and repairs easily.

Another possibility is to have the synthesis modules in the cyclotron vault or shielded area. This has two disadvantages. If the cyclotron is not completely self shielding, then reagents cannot be added while the accelerator is running. The second disadvantage is that some type of electronics are particularly susceptible to radiation damage (particularly from neutrons) and storage in a high radiation environment will necessitate frequent replacement of these parts. An alternative is to use a substantial amount of shielding around each module, but this again usually restricts access and increases the amount of space occupied by each module.

The amount of space required for this type of facility listed in Table 2.

Section 3: Clinical PET with research support

This type of facility would have an accelerator capable of producing all of the major positron emitters and possibly some other isotopes. It is also possible for this type of facility to employ generators for certain types of studies. There will be significantly more laboratory space required depending on the amount of

effort which is directed towards the development of new radiotracers and the utilization of radiotracers described in the literature. There will also be much more elaborate analytical and quality assurance instrumentation.

By far the most widely used accelerator for this type of facility is the small fixed energy cyclotron. The cyclotron will have an energy of between 10 and 20 MeV protons or 5 to 10 MeV deuterons. The extracted beam current will be on the order of 50 to 100 μA. Most of the accelerator manufacturers have an entry into this market also. In addition to the cyclotron itself, provisions must be made for the associated electronics, water supplies for the electronics and cyclotron, the heat exchanger, and the control console.

The targets associated with the accelerator are usually either attached to the cyclotron as is the case for a negative ion cyclotron, or may be in a target changer as is often the case for a positive ion cyclotron. In both situations, switching between targets may be done remotely. In either case, provisions must be made for maintaining and repairing the target.

Facilities for commercial synthesis modules will be the same as in the type II facility. The ability to carry out synthetic procedures for the production of radiopharmaceuticals however will require a synthesis hood or shielded area where remote operations may be carried out. A typical example would be a shielded synthesis hood (2). These hoods should have shielding capable of reducing the dose rate by at least a factor of 1000 and preferably more. It should contain water in and out, access to nitrogen and vacuum, and a number of

switched electrical outlets for temperature baths, rotary evaporators, HPLC pumps, detectors, etc. In addition there should be penetrations in the hood for liquid and gas transfer lines and electrical cables for the control of solenoids. The hood should also contain a device for measuring radioactivity such as a Capintec ionization chamber. There should be one large opening in the hood so that set up and removal of equipment is not cumbersome.

In addition to this major synthesis hood, it is desirable to have one or more hoods with less shielding but the same amenities so that synthetic procedures may be worked out with low levels of radioactivity without interfering with routine synthesis for PET studies. Ideally these hoods would be in a separate room so that one does not interfere with the other. They should both have direct access to precursor radioactivity so that it is not necessary to transport the radioactivity in the laboratory.

Section 4: Research PET facilities

The final category is a complete research operation. This type of facility can take many different forms. The accelerator will be one which is capable of producing all of the positron emitting isotopes and may be capable of producing a much wider variety of isotopes. The cyclotron energy can be up to 40 MeV for protons and may have the ability to run other particles. As was mentioned earlier, it is uncommon for this type of facility to be built from the ground up. It is much more usual that this type of facility will develop over the course of several

years. To this end, it is necessary to plan expansion of a facility even at the smallest level since a little foresight at that juncture can save grief and hundreds of thousands of dollars in added expense when the time comes to expand the facility. This is especially true in the choice of an accelerator since this piece of equipment should be expected to have a useful lifetime of 15-20 years.

A common situation in developing a PET center is that it must be established in a pre-existing structure. This will put limits on the ability to expand at a later date. Even here however, it is possible to have power, air conditioning and other utilities with sufficient reserve to allow some additional equipment and space to be added.

If the space is being constructed specifically for a PET facility, every effort should be made to allow for expansion in some direction. The expansion can be up or down or on any side. If the expansion is to be to the side, then provision should be made to have the central pieces of equipment (cyclotron, tomograph) as near as possible to this wall. Utilities should be run in a way which is consistent with any envisioned expansion.

Section 5: General facility considerations

The following is a checklist of considerations for the design of a PET facility. Each item should be considered on how best to fulfill the requirements. Of course not all the items will apply to all levels of PET facility, but thought should be given to how these needs could be meet if the facility should expand in the future.

Although this chapter deals with the laboratory and accelerator space, the checklist for the tomograph area is given since functional areas may and should overlap.

Checklist

A. Functional Areas - Tomograph

1. Tomograph room - size, floor loading, cable trenches
2. Control Room - view of patient area, cable trays, computer floor
3. Computer equipment room - access to drives and electronics
4. Archival storage room - type of archive (optical, tape)
5. Data analysis room - workstation access, ease of data retrieval
6. Patient preparation - supplies at hand, crash cart, sink
7. Waiting room - comfort, entertainment of patients and family
8. Janitorial closet - ease of access, floor drain
9. Lavatories - unisex, employees and patients
10. Blood Laboratory - test equipment, analytical equipment
11. Office space - quiet space for work during lulls
12. Automated blood sampling - provisions for sampler or people
13. Automated metabolite analysis - provisions for robot or people
14. Tour facilities - a space for show and tell
15. Storage of biohazard waste
16. Communication equipment to cyclotron and laboratory

B. Functional Areas - Cyclotron

1. Cyclotron Vault - size, wall thickness, trenches, room for expansion

   208, 440 V, expanded 110 V, addition of beam lines

2. Power Supplies and Electronics - access, water and air conditioning

3. Heat exchanger - access, testing for radioactivity

4. Cryogen storage - separate area if possible, gas bottle storage

5. Control room - cable trenches, computer floor, adequate metering

   extra 110V outlets

6. Spare parts storage - 1 spare of major components

7. Shop space, electronic and mechanical - size and equipment

8. Radioactive parts storage - radioactive decay before disposal

9. RF shielding

10. Magnetic field shielding

11. Use "tie-point" wiring, well documented, many extra cables and conduits

12. Target repair and maintenance area with radioactive waste disposal

13. Extensive communication equipment to PET and laboratory

14. Overhead electric cranes for equipment moving

C. Functional Areas - Laboratory

1. Chemistry laboratory - size, number of sinks, utilities

2. Reagent storage, refrigerators - number and type

3. Synthesis module room - separate if possible, shielded

4. Quality assurance - space for test equipment, low background
5. Radionuclide generator storage - separate if possible
6. Office space - sufficient for employees, outside laboratory
7. Lavatories - easily accessible
8. Janitorial storage - sufficient size, floor drain
9. Gas Cylinder storage - near laboratory and loading dock
10. Conference area - sufficient for the entire PET group
11. Eating areas - amenities (microwave, toaster oven, hot water)
12. Hazardous waste storage - outside laboratory
13. Supply storage (gloves, lab coats)
14. Record storage - fire resistant room if possible, computer records
15. Instrument to computer links
16. Communication to PET and cyclotron
17. Emergency/Safety exits
18. Safety Shower - decontamination area and supplies
19. Area for sterile set up of radiopharmaceuticals

D. Construction and Access Considerations

1. Equipment transportation, unloading and installation area
2. Floor loading (including access routes)
3. Ensure that the floor is level
4. Ceiling heights - sufficient for all equipment and cranes

5. Access for cryogens

6. Controlled access to areas of possible radioactivity

E. Radiation Protection Considerations

1. Air turnover in vault areas and laboratories

2. Pressure gradients in the facility

3. Shielding in the accelerator vault

4. Shielding around the synthesis modules

5. Monitoring equipment in the facility (portal)

6. Stack monitoring

7. Electronics in high radiation areas should be radiation insensitive

8. Robotics for synthesis, target manipulation

9. Decontamination facilities and supplies

F. Facility Environment

1. Electrical supplies - voltages, currents and phases

2. Air Conditioning - general area, computer areas, humidity, filtration

3. Water supply and floor drains, sinks with holding tanks

4. Chilled water supply

5. Establish controlled areas

6. Fire detection and safety

7. Telephone, FAX service

8. Housekeeping

Summary: Which machine, Which isotopes

The final question is what type of facility should be planned. This comes back to the first question "What are the specific goals of this center ?". This must be agreed upon by all parties before the first phone call to the manufacturers are made. Clearly the PET field has changed during the past ten years a great deal. It will probably change even more over the next ten. For this reason, as much flexibility as possible should be incorporated into the final design.

An extensive evaluation of the types of accelerators is beyond the scope of this chapter. Information on types of accelerators and their characteristics can be found in a recent review (3). However, some general questions to be asked when choosing an accelerator are in order. It is assumed that the goals and the planned capabilities of the facility are clearly in mind when these questions are asked and it is merely a choice between several type of accelerators. It has already been decided that the accelerator will produce only oxygen-15 or it will produce all the common positron emitting isotopes.

The key questions to be asked when choosing an accelerator is given below (3).

1. Will this machine produce the amount of radioisotope necessary for the type of facility being planned?
2. Is the machine and the targetry reliable?

3. What are the initial costs and how do these compare to the operational costs?

4. What personnel will be required to maintain the machine and associated hardware?

5. What will be required to shield this accelerator?

6. What are the power and water requirements and are connections available?

7. Is help from the manufacturer available and how much does it cost?

8. How will the radiation safety aspects be implemented and documented?

9. How will radioisotope emissions to the environment be monitored and controlled?

10. Are the target materials required for routine isotope production readily available?

Acknowledgement: This work was carried out at Brookhaven National Laboratory under contract DE-AC02-76CH00016 with the U.S. Department of Energy and supported by its office of Health and Environmental Research.

Acknowledgement: This work was carried out at Brookhaven National Laboratory under contract DE-AC02-76CH00016 with the U.S. Department of Energy and supported by its office of Health and Environmental Research.

Table 1
Space requirements for the type I facility

Activities	minimum space	utilities
Commercial kits	100 sq ft	sink, eye wash
Simple chemistry	150 sq ft	sink, eye wash, emergency shower reagent storage
Synthesis modules	200 sq ft	sink, eye wash, emergency shower reagent storage replacement parts
Quality Assurance	200 sq ft	HPLC, pH tests TLC, gamma counter Clean area

Table 2
Space requirements for the type II facility

Activities	minimum space	utilities
Oxygen-15 accelerator	200 sq ft	see list
Synthesis modules	200 sq ft	sink, eye wash, emergency shower reagent storage replacement parts
Simple chemistry	150 sq ft	sink, eye wash, emergency shower reagent storage
Quality Assurance	200 sq ft	HPLC, pH tests TLC, gamma counter Clean area

Table 3
Space requirements for the type III facility

Activities	minimum space	utilities
Cyclotron	500 sq ft	cyclotron dependent
Shielded Hood	300 sq ft	see list
Hood	200 sq ft	see list
Synthesis modules	200 sq ft	sink, eye wash, emergency shower reagent storage replacement parts
Quality Assurance	200 sq ft	HPLC, pH tests TLC, gamma counter
Office space	4 x 150	electrical, computer
Electronics shop	200 sq ft	electrical, water
Parts storage	200 sq ft	none
Lavatory	50 sq ft	

DATE
FILMED
9/8/93

END