Planning a Clinical PET Center

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This is the last article in a four-part series on positron emission tomography (PET). Upon completing the article, the reader should be able to: (1) comprehend the various components of the planning process for PET; (2) explain the technical aspects related to radiation protection, radiochemical synthesis, site planning, and acceptance testing; (3) identify staffing requirements for a clinical PET center; (4) identify the numerous pieces of additional equipment necessary for PET radiochemistry and imaging; and (5) prepare PET capital equipment and operating expense budgets.

The process of establishing a clinical positron emission tomography (PET) center requires a basic knowledge of current PET technology, a clear focus on the scope of the proposed program, a broad base of support from the administration and medical staff, great attention to detail, and significant capital outlay.

The 1980s witnessed the emergence of PET into the clinical realm. Dr. Henry Wagner and numerous others have encouraged more widespread clinical applications of PET (*1–5*). Within the past several years, new programs with a strong emphasis on clinical PET, have been successfully launched at a number of institutions (*6–8*).

As the preceding articles in this series have indicated, the technology associated with positron imaging is extremely complex. As an institution ponders its commitment to establishing a PET program, it is vital that its leadership appreciate this tremendous complexity. These decision makers need to understand that PET is far more complex than echocardiography, magnetic resonance imaging (MRI), computed tomography (CT), or even single-photon emission computed tomography (SPECT). Dr. Michael Wilson, of the University of Wisconsin at Madison, has stated that "[PET] is the most complicated imaging technology that there is" (*9*). This sentiment has been echoed by numerous physicians and scientists in the PET field.

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With the possible exception of rubidium-82 (^{82}Rb) myocardial perfusion imaging, the current state of clinical PET is anything but "turn-key." This point was recently emphasized by Dr. John Sunderland, while addressing a "PET Users Meeting" in Washington D.C. (*10*). It is certainly true that great advances have recently been made in the development and implementation of automated radiochemical synthesis techniques and modern cyclotron design has dramatically simplified the operation and reliability of these instruments. However, the fact still remains that a clinical PET program requires a highly skilled team of scientists and technologists working in well equipped, specialized laboratories.

Dr. Michael Kilbourne, of the University of Michigan at Ann Arbor, has stated that, "The people promoting PET—manufacturers and a few individuals—make it seem like it's a very simple operation. It is more difficult than they would like you to believe" (*9*). It is a serious oversimplification to promote the notion that nuclear medicine technologists should be able to effectively perform all aspects of clinical PET radiopharmaceutical production. The current state of the technology, especially in the areas of radiopharmaceutical synthesis and quality control, compartmental modeling, and protocol refinements, requires the significant expertise of highly skilled PET scientists. Dr. Robert Kessler points out that the "cost and complexity are the major barriers to the more widespread use of positron tomography" (*6*).

GETTING STARTED

Initial interest in PET may arise from within nuclear medicine or from any one of a number of different departments within the institution, including cardiology, neurology, psychiatry, or oncology. This initial interest may simmer for a period until the institution finally makes a preliminary commitment to seriously consider a PET program. Generally speaking, the length of this initial period seems to be directly related to the level of interest and breadth of support from the medical staff and various department heads. This period will likely shorten significantly as the clinical applications for PET increase both in number and acceptance, and as reimbursement issues are resolved.

Once the institution makes a preliminary commitment to seriously considering a PET program, an appropriate department such as nuclear medicine should be identified to gather information on specific requirements related to staffing and instrumentation, as well as feasibility. It is at this point that a "PET Startup Team" should be assembled to systematically approach the many issues associated with establishing the program. As a minimum it is suggested that this team consist of the following individuals:

- A senior physician, such as the director of nuclear medicine.
- A medical physicist experienced in nuclear medicine physics and instrumentation.
- A chief technologist or technical director with administrative and fiscal management skills.

If at all possible, it would be most advantageous to also enlist the assistance of a radiopharmacist or radiochemist.

As soon as practical, a final member should be added to this team: a PET consultant. This is an individual who has worked, or is working, in an active PET center and who is very familiar with the numerous details and processes which are required to both establish and maintain a viable PET program. It would be ideal to use this person's expertise from the outset but the institution may be somewhat reluctant to fund consultative fees while a firm commitment is pending on approving a PET program. Such a consultant can be effectively used via telephone and written reports. One or more visits to the consultant's institution might also be useful. In this way, constructive use can be made of the consultant's services without exceeding a reasonable expenditure.

Startup Team Roles and Responsibilities

Some overlap, sharing, or redistribution of the following responsibilities may be appropriate based on individual expertise. The physician member may be specifically responsible for:

- Generating support among medical staff colleagues.
- Conferring with current physician users of various commercial PET systems to determine system suitability.
- Consultation with other interested departments, shaping and defining the scope of the PET program at the institution. The scope may be clinical only, research only, or some mix of both. A clinical program must also be further defined in terms of the types of procedures to be offered and radiopharmaceuticals required.
- Taking a pro-active role in communicating with administration, governing boards, and other appropriate groups, regarding the benefits and complexities of establishing the proposed program.

The physicist member may be specifically responsible for evaluating the technical attributes of the various, currently available tomographic imaging systems and cyclotrons, in order to find the best match between system capabilities and the defined program scope. For example, if it is determined that the program scope is to be limited to the provision of clinically useful, cardiovascular procedures, then those systems optimized for head imaging, in such a way as to preclude thoracic imaging, can be eliminated from consideration.

A valid comparison of performance specifications for various PET scanners is very difficult to achieve. Unlike gamma cameras, NEMA performance tests have not yet been established for measuring resolution, sensitivity, and uniformity. Consequently, it can be very misleading to compare the specifications claimed by the various vendors. Perhaps the only way to obtain such a valid direct comparison is to design and conduct one's own measurements during site visits by:

- Contacting physicist users of currently available systems and making site visits, as necessary. Although vendor representatives are typically anxious to accompany prospective customers on such trips, the most fruitful visits are usually unaccompanied.
- Assessing staffing requirements for PET physicists and computer scientists.
- Addressing radiation safety concerns related to PET.

The technologist member may be responsible for:

- Establishing a projected operating schedule in order to determine the anticipated number of procedures per day.
- Assessing staffing requirements for additional technologists and nurses, in light of the projected daily operating schedule.
- Identifying additional equipment items which will be required for the proposed program. The assistance of a consultant is invaluable in approaching this task, since vendor representatives can provide only limited information. Numerous complex instruments and equipment will be required for a fully functioning, diversified program. Once the desired equipment is identified, vendors must be contacted so that budgetary quotations can be assembled.
- Acting as a liaison with administration in providing program requirements and budget related information.
- Preparing a comprehensive assessment of projected operating expenses associated with each of the proposed PET procedures, especially supply costs related to cyclotron operations, radiochemical synthesis, radiopharmaceutical transport and administration, as well as image acquisition and processing.
- Providing information regarding current and projected reimbursement for clinical PET procedures.
- Preparing projected budgets for capital and operating expenses, as well as participating in the preparation and multiple revision of the Pro-Forma Income Statement.
- Participation in the preparation of a Certificate of Need (CON) application to the state health planning agency (a CON is *not* required in all states).

- Overseeing the preparation of various other administrative documents, including revision of the radioactive materials license and application for a license to operate the cyclotron, if applicable.

The entire team should be responsible for:

- Assessing space requirements to accommodate all aspects of the proposed program. A consultant will play an important role in site planning. Most of the major PET vendors have support staff who specialize in this area. These individuals can create computer-aided design drawings and can provide a wealth of invaluable suggestions to tailor the physical layout to specific program requirements (Fig. 1). It is of tremendous advantage to settle on a well defined program scope prior to commencing site planning. Space requirements increase dramatically as the program becomes more complex and research oriented.
- Assessing staffing requirements for radiochemistry, radiopharmacy, and cyclotron functions, as well as other ancillary support positions which may be required for more complex, research-oriented programs.
- Recommending the key individual, or individuals, who will provide leadership and direction to the program as it matures into an operating PET center. This director or directing committee should have input to and final approval over the selection of major equipment, recruitment of key scientific staff, and site planning.

Defining Program Mission and Scope

Planning will be greatly simplified and accelerated if the mission and scope of the program can be defined early in the process. The mission of the program will very likely be intimately related to the mission of the institution. Research-oriented academic centers will probably have some research component to their PET programs. A program can be defined according to three distinct categories: "clinical only," "research only," or "clinical and research."

The "clinical only" program must define its scope in terms of the type of procedures to be offered. A diversified clinical program is one which offers essentially all clinically useful PET procedures, including neurologic, cardiologic, and oncologic. An example of a specialized clinical program would be one which only offers either neurologic or cardiologic procedures, but not both. Specialized clinical programs must also further define their scope in terms of their radiopharmaceutical requirements. This will dictate which method is most appropriate for obtaining PET agents. The alternatives are: (1) a fully equipped and staffed radiochemistry lab and cyclotron; (2) a generator system; and/or (3) unit doses of [^{18}F] fluorodeoxyglucose (FDG) from a regional distribution center. For example, a program which intends to specialize in PET cardiologic procedures may elect to utilize ^{82}Rb generators for myocardial perfusion imaging and purchase FDG, in unit dose form, for metabolic imaging to determine myocardial viability. It should be noted that while the regional distribution concept is the subject of much current discussion and several centers are now being established to provide this function, the FDA has yet to render a decision on whether such arrangements will be acceptable and, if so, under what guidelines.

The "clinical and research" program must define its scope in terms of the types of clinical procedures to be offered and types of research protocols to be undertaken. A diversified clinical and research program is one which offers essentially all clinical PET procedures and some amount of research in one or more areas of investigation (Figure 1 illustrates a site plan for such a program). The research component may be very broad in nature or limited to only one area of investigation, such as PET neurology. An on-site cyclotron and fully equipped radiochemistry lab are usually required. Some special facilities which serve the research aspects of the program may include an animal lab, a binding lab, a fully equipped clinical (blood) lab, and an expanded radiochemistry lab with a designated area for the development of new tracers. Programs which intend to engage in new target development or other cyclotron-related research may opt for a larger cyclotron, in the 16–30 meV range. These cyclotrons usually require a shielded vault.

It might also be appropriate to plan a specialized clinical and research program. An example of such a program would be one which offered clinical PET cardiologic procedures and pursued research interests in the development of new PET cardiac imaging agents.

THE APPROVAL/INSTALLATION PHASE

Private institutions seeking to establish capital programs of this magnitude typically require the approval of their governing boards. Likewise, public institutions require the approval of the appropriate legislative body. Once such approval is obtained, a number of processes can be commenced almost simultaneously.

The Certificate of Need

CON application can be finalized and submitted to the state health planning agency. The agency may require several months to consider the application and may need additional

FIG. 1. Site plan for a clinical and research PET program (CAD drawing provided by Siemens Medical Systems, Inc., published with the consent of Franceschi Architects PA, Charlotte, NC and the North Carolina Baptist Hospital, Winston-Salem, NC).

information or supporting material, therefore it's best to submit the application in as timely a manner as practical. Typical CON application fees are on the order of 0.01% of the total program cost. It is frequently argued that only the PET scanner and not the cyclotron requires CON approval. This argument is based on the fact that the cyclotron is not presently considered a medical device. If the hospital is to be the owner of record for both scanner and cyclotron, however, it seems prudent to submit the CON application for the entire program. A CON is not required in all states.

Acceptance Testing

The best time to negotiate acceptance testing criteria is prior to finalizing a purchase agreement, since this is when the institution commands the most leverage. Numerous, impressive parameters are quoted by sales representatives to demonstrate the superiority of their devices. However, the standard acceptance test values for the same parameters may be significantly less impressive. Discussion with current users can be invaluable in proposing a comprehensive set of on-site acceptance testing criteria which will serve well in assuring a properly functioning device.

For cyclotron testing, Faraday cup irradiations are as important as actual target irradiations. The Faraday cup irradiations test the output of the cyclotron itself. It has been found useful as an acceptance test to require that all of the various cup and target irradiations be performed successfully twice in a row under automatic (computer) control. This regime tests both performance and reliability. Failure of the device to successfully complete the testing program should mean that the entire group of tests be started over, from the beginning. An example of a case where human intervention would not necessarily require a restart of all tests is a foil rupture since this is somewhat of a random and fully anticipated event. Testing for each target should specify beam current, bombardment duration, and nominal product yield activity. If the cyclotron is capable of simultaneous dual or multiple target irradiations, that capability must also be verified. For automated radiochemical synthesis testing, criteria for acceptable yield and radiochemical purity should be established.

For the PET scanner, criteria for acceptable reconstructed axial and transaxial resolution, sensitivity, and uniformity should be established. High count rate performance and randoms fraction should receive special attention, particularly when rapid dynamic acquisitions or high-activity dose administrations (i.e., bolus oxygen-15-water) are anticipated. Also, complete specifications for all software requirements should be defined in advance, to avoid misunderstandings at the time of delivery.

The Purchase Order

Most PET vendors will accept purchase orders with the understanding that the order is contingent upon CON approval. Since both PET scanners and cyclotrons require 9–12 mo to construct and install, most institutions elect to place the order prior to actual CON approval, with the contingency clause stipulation. Issuance of the purchase order allows the establishment of a delivery date upon which construction schedules, ancillary equipment purchases, and personnel recruitment can be based.

Device Registration

Application to register or license the cyclotron, cyclotron products, and long-lived sources associated with the scanner, can now proceed with the appropriate state agency or the Nuclear Regulatory Commission. Certain local jurisdictions, i.e. the City of New York, may also require licensing. Information to be submitted regarding the cyclotron should include the following:

- Location and description.
- Operating and emergency procedures.
- Facility description illustrating the location of radiation monitors, interlock systems, and controlled access points.
- A map of expected radiation fields under various operating conditions.
- A description of the radiation detection devices to be used.
- Instrument calibration procedures.
- A description of the training program, including a provision for the qualification of cyclotron operators.
- A discussion of radiation surveys and inspections to be conducted by radiation safety personnel or a qualified consulting group.

PET Radiopharmaceuticals and the FDA

On behalf of the nuclear medicine community, the Institute for Clinical PET (ICP) has prepared and submitted a Drug Master File (DMF) for the preparation of FDG. The DMF is the required first step in the New Drug Application (NDA) process. DMFs for ^{13}N-ammonia and ^{15}O-water are currently being prepared. Although the ICP is optimistic that FDA approval will be forthcoming in 12–18 mo, this estimate is only a "best guess." In the meantime, PET programs have two options: (1) submit Investigational New Drug (IND) applications to the Food and Drug Administration (FDA) for each proposed PET radiopharmaceutical to be used for administration to patients; or (2) submit a letter to the FDA requesting exemption from the requirement to file an IND application, on the grounds that the in-house compounding of PET radiopharmaceuticals represents the limited practice of pharmacy and medicine.

Radioactive Materials License Amendment

The institution's Radiation Safety Officer is usually responsible for submitting requests for changes in the Radioactive Materials License, however, under certain circumstances a consultant may prepare the amendment. Both limited-use and broad license holders will need to add the four commonly used positron-emitting radionuclides: ^{11}C, ^{13}N, ^{15}O and ^{18}F. Germanium-68 (^{68}Ge) must also be included if that agent is to be used for scanner calibration or as a transmission source. If the use of radionuclide generators (i.e., ^{68}Ga, ^{82}Rb, and ^{62}Cu) is anticipated, these must also be included in the amendment.

Personnel and Recruitment

The number of skilled scientists and technologists possessing PET experience is extremely limited and will likely remain so for some time. As a result, there is intense competition for the relatively few individuals seeking a new position. In light of this competition, planners of new programs need to plan realistic salary levels for the key positions of physicist, radiochemist, and radiopharmacist. The best way to assess current salaries is to contact several existing programs. Since it may take 6–9 mo to attract a suitable individual, it is best to begin recruiting for these positions as soon as possible.

The following positions are suggested as necessary in order to adequately staff a fully functioning, diversified clinical PET program (*6, 7*):

Radiochemistry Lab Director. An individual with an advanced degree (MS, PhD) is needed to implement procedures and develop methods. This person may be a chemist or a radiopharmacist. This person should be competent in a number of areas such as: (1) cyclotron production of radionuclides, including targetry and radiation safety considerations; (2) routine organic and inorganic synthesis; (3) vacuum and gas technology; (4) rudimentary computer programming; (5) simple electrical and electronics diagnosis and repair; (6) instrumentation analysis for high-pressure liquid chromatography (HPLC), gas chromatography (GC), NMR, thin-layer chromatography (TLC), radiometric, etc.; (7) FDA regulations relating to new drug manufacture; and (8) laboratory management. Depending on qualifications, this person may be expensive. Recent starting salaries for individuals with several years experience in PET have ranged from $60,000 to $90,000.

Radiopharmacist. It is prudent to involve one or more radiopharmacists in the operation of a PET center. The enterprise is presently viewed by the FDA as involving drug manufacture rather than just drug formulation. Several part-time radiopharmacists may be preferable to one full-time person, in order to cover absences due to vacation, meetings and illness. At a number of existing PET centers there are several radiopharmacists who share responsibility for PET. Since radiopharmacists are currently in such short supply, some PET centers have elected to train in-house pharmacists to handle the specifics of PET. Radiopharmacists earn about $50,000 if just out of school; this increases with previous experience.

Two BS Chemists. These individuals will be responsible for the routine synthesis of PET radiopharmaceuticals and for rudimentary repair and maintenance of the cyclotron. Specific duties in the synthesis arena include: (1) ordering, check-in, and stocking of all materials necessary for synthesis; (2) construction and testing of homemade synthesis parts; (3) logging, identity testing, and storage of reagents; (4) synthesis module set-up, cleaning, and calibration; and (5) batch sheet completion and logging. It will be necessary for these chemists to follow FDA/USP Good Manufacturing Practice (GMP) guidelines for the preparation of drugs. It has been found useful for these individuals to have offset schedules since the cyclotron must be initialized at about 6:00 a.m. in order to have FDG available by 9:30 a.m., and the second batch of FDG is often not complete until after 2 p.m. (see Table 1 for sample production schedule). Typical starting salaries range from $25,000 to $33,000.

Physicist. This position may not necessarily be required for a purely clinical program. However, it is important that the various skills possessed by a person with this background be available to the PET center on a few minutes notice. Although the cyclotron and scanner are state-of-the-art technology, both will chronically experience a myriad of minor operational problems. Many of these problems can be solved in a few minutes by someone familiar with their design and operation. For cyclotron problems, this person may be the radiochemistry lab director or one or both of the BS chemists. As with the radiopharmacist's position, it is important to have redundancy in these types of skills. In more research-oriented programs, the physicist may also be involved with testing and calibration of the scanner and compartmental modeling of new agents, as well as radiation safety aspects of the program. Depending on educational background, experience, and level of responsibility, salaries for this position can range from $40,000 to $70,000.

Technologists and Nurses. There are at least two distinct schools of thought regarding technologist staffing for PET. One contends that a dedicated staff of highly skilled technologists should be assigned exclusively to PET on a full-time, non-rotating basis. The other school holds that PET duties should be rotated among either all or a subgroup of the entire technologist staff. There are some obvious advantages and disadvantages to both approaches. Programs with dedicated PET technologists may tend to lack adequate flexibility in accommodating sick time, vacations, and other unplanned staffing emergencies. Many technologists regard PET as a choice opportunity and look forward to the opportunity for growth and challenge which this new technology presents. By rotating staff through the PET center, these opportunities are provided to a larger number, resulting in a positive effect on overall morale and staff retention. A reasonable compromise between the two different approaches is to have a senior level technologist or supervisor who does not rotate and additional technologists who are part of a limited rotation pool.

A clinical program with one scanner that does not desire to

TABLE 1. Sample FDG Synthesis Schedule

Start time	End time	Elapsed time	Event
6:00 am	6:30 am	0:30	Initialize cyclotron and begin setup of FDG module.
6:30 am	8:00 am	2:00	^{18}F production.
8:00 am	9:00 am	3:00	FDG synthesis, Batch #1.
9:00 am	9:30 am	3:30	QC Testing (HPLC, TLC, radioassay, pH, and appearance).
11:30 am	1:00 pm	1:30	^{18}F production. Set up 2nd FDG module.
1:00 pm	2:00 pm	2:30	FDG synthesis, Batch #2.
2:00 pm	2:30 pm	3:00	QC Testing.

strictly quantify tracer uptake by multiple blood sampling, will require at least two technologists for an 8-hr workday. A similar program with two scanners can operate effectively with three technologists, one in each room and a floater. Extending the workday by an additional 4 hr would require an additional 0.5 full-time employee per scanner.

Clinical or research programs that desire to quantify uptake by blood sampling, will require 0.5 to 1 additional technologists per scanner. The additional duties imposed by strict quantitative methods involve sample drawing, counting, and more intensive data processing.

The institution's specific program scope will dictate the need for including the services of registered nurses. A nurse can be particularly useful in assisting in pharmacologic intervention protocols and drawing arterial blood samples. If a full-time nurse cannot be justified, it's helpful to have access to a pool of nurses, such as might exist in the radiology department.

Construction

The construction timetable will be largely dictated by the ability to utilize existing, renovated space or the requirement for an entirely new facility. In 1987, Kessler et al. provided some information on construction costs for a 6000 sq ft PET facility (*6*). At that time, the conclusion reached was that renovation would cost ~$600,000 and new construction would cost nearly $1,500,000.

Installation and Training

Most vendors require at least 8 wk for cyclotron installation and testing. During this time, ancillary radiochemistry equipment should be delivered and installed. The PET scanner will need 1–2 wk for installation and calibration.

Most purchase quotations specify one person-week of on-site training by an applications specialist. This is only marginally adequate, one week each for the scanner and cyclotron is more appropriate. In addition, training visits to at least one other operating PET facility should be strongly considered for technologists, radiochemists, radiopharmacists and cyclotron operators. Such a visit will provide excellent opportunities to learn the intricacies of cyclotron operation and automated synthesis, as well as the details of various clinical imaging protocols. In addition, the staff will establish valuable contacts which they can call upon when future questions or problems arise. Attending professional meetings and continuing education programs, on an ongoing basis, will be vital for the staff to maintain their expertise as the field grows and expands.

ADDITIONAL CONSIDERATIONS

Radiation Protection

Several factors should be considered in the design of the PET facility, in order to minimize the radiation exposure to radiation workers, other hospital staff, and the general public. The use of wall-mounted lead shielding in walls adjacent to uncontrolled areas is an effective way to minimize potential exposure. Table 2 illustrates the effect of increasing lead thickness on the transmission factor for 511 keV photons.

TABLE 2. Effects of Lead Shielding on 511 keV Photons

Lead thickness (inches)	Transmission factor
0	1.0
⅛	0.58
¼	0.33
⅜	0.19
½	0.11
¾	0.04
1	0.01

Three areas of potentially intense radioactivity within the scanner room will require substantial shielding. These are: (1) the pneumatic transfer receiving station; (2) the storage area for phantoms and calibration sources; and (3) the radioactive waste cave. At least two inches of lead shielding is recommended to adequately attenuate these sources. Interlocking lead bricks can serve this purpose but specially fabricated enclosures offer the advantages of greater stability and functionality.

The placement of area monitors in the scanner room, radiochemistry lab, and cyclotron room is highly recommended. Standard personnel monitoring with film badges and hand thermoluminescent dosimetry badges (TLDs) should be augmented by pocket dosimeters.

Minimizing Technologist Exposure. Time, distance, and shielding continue to be the most important principles in minimizing exposure. PET technologists and nurses must be aware of the increased need to limit patient contact time after dose administration. A remote video monitoring system will allow staff to assess the patient from within the control room, without unduly sacrificing patient care.

Standard nuclear medicine syringe shields offer only marginal protection from the highly penetrating 511 keV photons; however, they do serve a useful role in protecting the hands from direct exposure to positrons. Several groups are currently working on various designs for PET syringe shields. Doyal, Dworkin, and Juni have proposed one such design (Fig. 2), which will provide sufficient shielding to attenuate 100 mCi of activity to less than 2 mRem/hr at 10 cm (*11*). Their design also features a portable stand which provides adequate stabil-

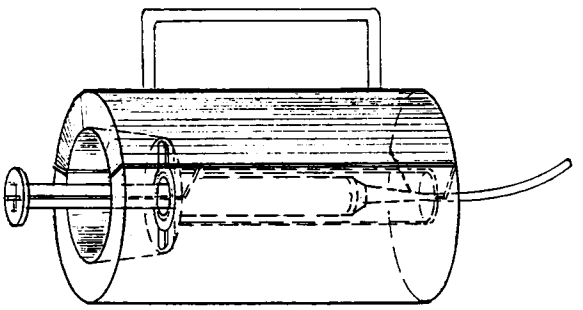

FIG. 2. Proposed design for a PET syringe shield (drawing provided by Laura Doyal, CNMT, William Beaumont Hospital, Royal Oak, MI [U.S. patent pending]).

ity to support the significant weight of the shield, while incorporating a small storage area for injection supplies. Another approach currently in use, involves the automated administration of the dose by a shielded infusion pump. The technologist only receives significant exposure while placing the syringe on the pump. Once shielded, the syringe is then attached to the i.v. line and infusion is begun.

Dose Transport. Dose syringes in pneumatic carriers travel through the pneumatic system at ~15 ft/sec. At this speed the incidental exposure to personnel is generally considered insignificant; however, it is important to plan for the occurrence of a jammed carrier. A system which has a feedback mechanism to assist in identifying the location of a jam will be very useful. The route of the pneumatic system should be designed to avoid sharp bends in the tubing, as well as areas of potentially prolonged exposure of non-radiation personnel. For example, it would be preferable to route the tube beneath a hallway rather than offices or a cafeteria.

Microbore teflon lines with an internal diameter (i.d.) of 32 mm, routed through metal conduits, are effective in minimizing personnel exposure during the transit of PET gases. Multiple lines should be initially installed to provide some flexibility for the future and redundancy in the event of problems. Difficulties associated with a line rupture can be minimized if the lines are maintained under a slight negative pressure from the cyclotron room. Ventilation equipment serving the cyclotron room, radiochemistry lab, and scanner room should provide at least 30% fresh air at 10 equivalent air changes per hr. Exhaust from the cyclotron room should be handled through a separate system.

The manual transport of PET doses can be safely accomplished using a shielded transport cart. This is the same device commonly used to transport therapeutic quantities of radioiodine.

Radiochemistry

Effectively planning and equipping the PET radiochemistry lab is virtually impossible without the assistance of an individual experienced in PET radiochemistry. It requires a clear focus on the program's scope and objectives, an intimate, detailed knowledge of synthesis requirements, operation of the many pieces of sophisticated equipment, and a clear understanding of the process flow from reagents to radiopharmaceuticals. The most appropriate individual to make the final decisions affecting this lab would be the senior PET radiochemist. Several key items of laboratory equipment require additional comment.

Automated Synthesis Modules and Robotic Systems. Generally speaking, these modules or systems are worth buying (*12*). To date, the synthesis modules seem to be somewhat more reliable but the robotic systems offer greater flexibility. This flexibility can be a disadvantage in the event of a major malfunction, since not only is the capability lost for automated synthesis of one agent, but all others as well. As with the targets, it is important to develop performance and reliability acceptance specifications, to be proven twice in a row. Radiochemical purity should also be tested by the appropriate quality control method. Generally, radiochemical purity of at least 95% should be achievable by properly functioning FDG synthesis modules.

For busy clinical programs, it may be wise to consider the purchase of two FDG modules (Fig. 3), since lengthy clinical days will require two FDG production runs. In any case, a second fluorinated product will mandate a second unit. It is advisable to specify that the second synthesis module include a separate controlling computer. This will facilitate the simultaneous use of both modules, should that need ever arise.

There must be an emphasis on minimizing the radiologic dose to the staff. Dismantling a synthesis module within 1–2 hr after the completion of a full-scale FDG synthesis, i.e. 150–300 mCi, will result in a 20–30 mRem whole-body dose. Presuming 250 workdays per year, a daily 20 mRem dose results in a yearly dose of 5 rads. This is the current NRC 10 CFR 20 limit. This limit may be reduced once the results of the BEIR-V Committee have been widely disseminated. This exposure problem can be avoided if a second FDG module is utilized or if a single unit is shielded and dismantled within a hot cell.

Automated synthesis modules for the production of a number of ^{11}C compounds are currently under development. These include hydrogen cyanide (HCN), labeled fatty acids and acetate, and methyl iodide. Methyl iodide is a precursor for such agents as methyl spiperone, carfentanil, and methionine. List prices for these modules range from $30,000–$50,000.

Some cyclotron manufacturers provide shielded utility space to accommodate a limited number of synthesis modules. These modules have also been mounted within hot cells; this greatly aids opening and reconfiguring of the unit when another synthesis is required soon after the first since it can be performed without radiation exposure to the chemist. Synthesis modules have also been mounted within shielded fume hoods. Such a configuration is especially appropriate for modules which produce potentially dangerous gases, such

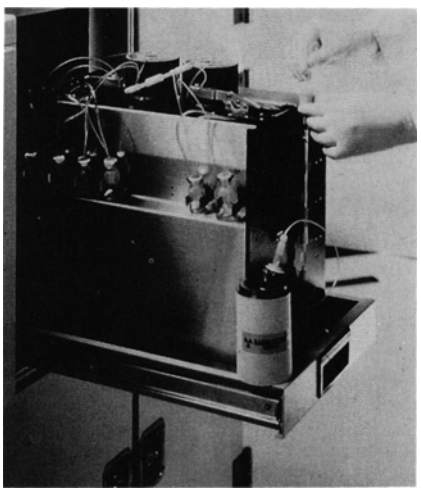

FIG. 3. The Chemical Process Control Unit (CPCU) from CTI, Inc., an automated synthesis module for the production of F-18-labeled compounds such as fluorodeoxyglucose (FDG).

as ^{11}C-HCN. Another, relatively recent approach is the use of specifically designed "hot boxes." These provide shielding and utilities for one or more synthesis modules and can include exhaust capability if required. They offer an attractive alternative when both funding and space are scarce.

Hot Cells. It has been argued that hot cells are not a strict requirement for a purely clinical program which will only be using automated synthesis modules (*7*) (Fig. 4). Hot cells are appropriate for any program which anticipates the need for manually synthesized radiochemicals. There are some tradeoffs between hot cells and radiochemical fume hoods equipped with lead bricks. Hot cells are considerably more expensive than fume hoods. Current list pricing for a double cell with manipulators is between $100,000–$130,000. One encouraging sign is the entry of several additional vendors to this market; competition may help to reduce pricing.

Hot cells provide superior shielding in all six directions with good accessibility. A lead thickness of 60 mm is commonly used in PET. A pass-through feature between cells effectively doubles the size available for a given radiochemical procedure. If a considerable volume of manually synthesized radiochemicals is anticipated, a hot cell will serve well in minimizing the chemist's exposure.

It is a good idea to equip at least one cell with a pair of remote manipulators. The advantages of two manipulators have been: (1) coverage of the entire enclosure and (2) the ability to perform two operations simultaneously, such as holding and pouring. Manipulators can range in price from $35,000–$50,000 for a pair. One popular vendor of manipulators is Sargent Industries (Red Wing, MN). Their CRL Model-G mounts on the front of the cell above the leaded glass door. If the lab can accommodate a 10-ft ceiling, the CRL Model-7 is a less expensive option which mounts on the top of the cell. The difference in price between these models is ~$20,000 per pair.

Fume Hoods. In contrast to a hot cell, a 5-ft wide radiochemical fume hood with a reinforced base sells for less than $10,000. Shielding in a hood can be provided by about 100 interlocking lead bricks and two leaded glass bricks at an additional cost of $10,000. Therefore, several hoods can be purchased for the price of one hot cell. Each hood could be dedicated to one or more radiochemical synthesis module. A fume hood is more expensive to install and maintain because of the added utility and ventilation requirements. A shielded fume hood can be used for non-radioactive organic chemistry procedures, e.g., HPLC solvent degassing, but affords poor accessibility with the lead shielding in place. If the budget is tight and space is not a severe limitation, three to six fume hoods could be substituted for two hot cells.

At least one chemical hood is needed for the safe handling of organic solvents or noxious compounds. It is recommended that a stainless steel radiochemical fume hood be bought since it can serve both purposes. The fume hood should be equipped with a reinforced base capable of supporting at least 200 lbs/sq ft. Additional hoods would be useful to house some of the ^{11}C chemistry boxes. As previously mentioned, this is especially important if the radiochemical is a gas, such as HCN.

Laminar Flow Hoods. Two laminar flow hoods are recommended. The first, shown in Figure 5A, will be used by the radiopharmacist for dose dispensing. This hood should be equipped with a recessed ion chamber for radioassay of the radiopharmaceuticals. It is important that care be taken in the design of the base so that the ion chamber itself can be

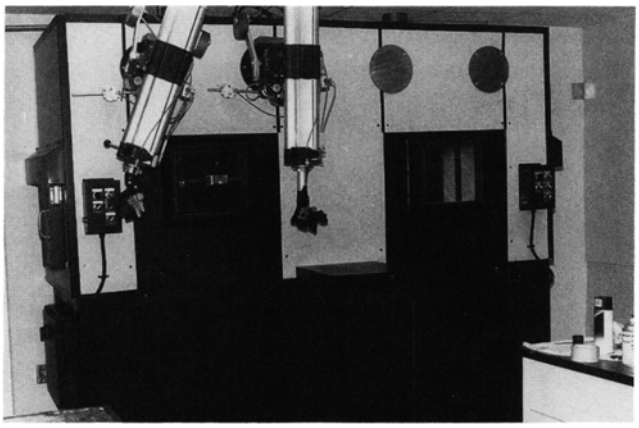

FIG. 4. A double hot cell provides optimal protection during manual synthesis of PET radiochemicals. Note the pair of manipulators mounted on the left-hand cell (photo provided by Von Gahlen Intl., Inc., other hot cell vendors include Capintec and Atomic Products).

FIG. 5. (A) A laminar flow hood set up for dispensing PET radiopharmaceuticals. Note the reinforced base and lead bricks. (B) A small laminar flow hood provides a clean environment for the preparation of radiopharmaceutical synthesis apparatus.

shielded. Additionally, the manifold between the work surface and the bottom of the superstructure presents a radiation gap which will require shielding. This may entail some detailed design work since disruption to the manifold may interfere with the vertical airflow dynamics. Capintec (Ramsay, NJ) recently announced a shielded laminar flow hood which meets these criteria.

A second laminar flow hood can be used for the preparation of the radiopharmaceutical synthesis apparatus (Fig. 5B). In the case of FDG, the preparation of the various columns, reagents and vials is best carried out in the relatively clean environment of a laminar flow hood. Use of this second laminar flow hood may avoid future regulatory difficulties. The FDA views the PET facilities as drug manufacturers rather than simply drug formulators. This means that PET centers are subject to GMP regulations. The FDA is in the process of developing modified GMP guidelines by which PET centers will be evaluated. These guidelines are expected to be in place by early 1991. The guidelines will almost certainly require adherence to some basic level of sterile technique such as that afforded by a vertical laminar flow hood.

Dose Calibrator. Several ion chambers are needed in a PET facility. The two hot cells require at least one chamber between them. Since they are connected, one is sufficient although provision for a second unit would be prudent. The laminar flow hood used for dispensing will also require an ion chamber. A third ion chamber near the FDG synthesis module would allow for local measurement of radioactive parts. As an example, this unit would be convenient when radioassaying parts of the module while troubleshooting a chemical process that is not working correctly. At one PET center, all radioactive parts of the FDG module are routinely assayed as a preventative diagnostic measure. An ion chamber in the scanner room is important for the assay of certain agents that are delivered directly from the cyclotron. These agents include ^{13}N and gases such as ^{11}C or ^{15}O-carbon monoxide, ^{11}C or ^{15}O-carbon dioxide, and ^{15}O oxygen (as O_2). Victoreen (Cleveland, OH) has recently developed a semiautomated gas-dispensing apparatus similar to that used for radioactive xenon (Figs. 6A–B). This system will include an ion chamber for measurement of radiogas activity just prior to patient administration.

Dose calibrators specifically designed for PET are now available from several vendors. A common feature of these units is their ability to accommodate multiple ion chambers, and remote displays, tied to a central electronics unit. Experience has shown that buying one control unit can be somewhat limiting; the redundancy of a second control unit is extremely helpful in the event of occasional instrument malfunction.

Pneumatic Transfer System (PTS). A PTS is especially useful when the scanner is located on a different floor than the radiochemistry lab. After the unit dose is dispensed at the radiopharmacy hood, the PTS will deliver it to the patient injection area. For certain procedures, injections will be made in the scanner room. Doses for procedures which require time

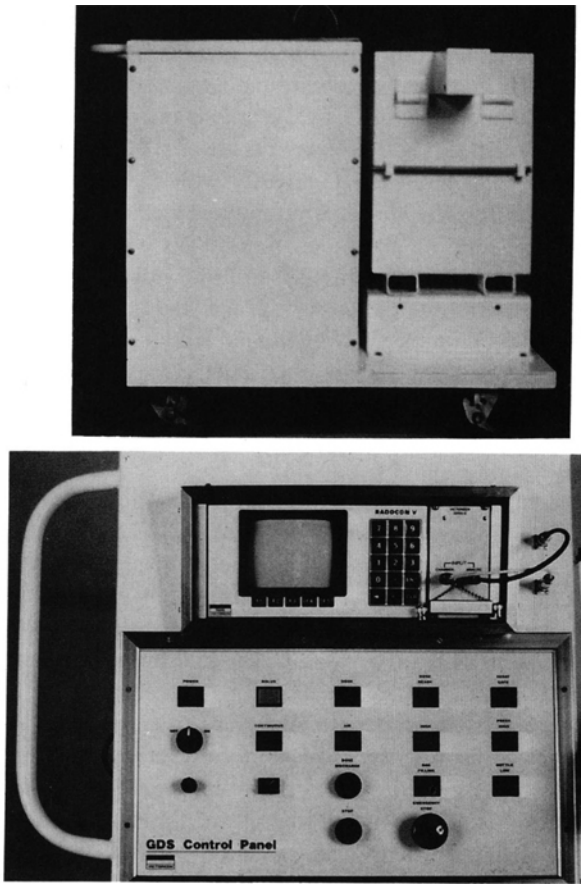

FIG. 6. (A) The Victoreen Gas Delivery System (GDS) includes a shielded cart, gas mixing chamber, and ion chamber. The patient's exhalations are routed to a discharge line for roof level exhaust. (B). The GDS is capable of administering metered doses of PET gases under microprocessor control.

for tracer localization in target tissues and blood clearance should be delivered to a separate patient prep room. Since scanner room time is generally the limiting factor in PET, it is much more efficient in terms of patient throughput to utilize such a prep room. The pneumatic system will need to be capable of delivering to both areas. Short-lived radiopharmaceuticals are best delivered directly from the cyclotron to the scanner room. For example, in the case of ^{13}N ammonia only ~20 mCi may be produced by the cyclotron and this amount constitutes a unit dose.

Dose Delivery Via Microbore Tubing. At one PET center, 4-in. i.d. conduits connect the cyclotron to both the scanner room and the radiochemistry lab. In the conduits, numerous lengths of 1/16-in. OD stainless steel tubing have been strung. The tubing leading to the scanner room is used to deliver short-lived radioactive gases as well as ammonia, for redundancy several tubes are dedicated to each type of product. The gas tubes are connected directly to the gas-dispensing apparatus, mentioned above. The ammonia tube is connected directly to a syringe housed in a remotely controllable syringe pump. This allows the injection to be performed with a minimum of staff intervention. One note of caution when utilizing such a design, it is vital to purge the lines which handle solutions on a frequent basis with water for injection

(WFI) in order to maintain sterility. In addition, periodic sterility and pyrogen testing is strongly advised.

HPLC. High-pressure liquid chromatography (HPLC) is a cornerstone of modern biochemical synthesis and pharmaceutical quality control (Fig. 7). Successful use of HPLC requires a significant skill level and familiarity with these devices. HPLC functions by flowing a liquid through a column under very high pressure, on the order of 5000–6000 psi. HPLC columns vary based on the specific substrate with which they are loaded. As the sample passes through the column it is separated based on molecular weight and structure. The separated components then pass through a detector. A radiometric detector will count the emitted 511 keV photons. A plotted distribution of the resulting count peaks represents the radiochemical composition of the sample.

At least one HPLC is recommended for each product to be made on a routine basis which requires HPLC for quality control. In addition, a backup unit is recommended because HPLCs traditionally exhibit a fair amount of downtime. This is not to say that HPLCs don't work well, but typically they have not been used in a patient-care environment where things must work almost all the time.

It may seem somewhat wasteful to buy so many HPLCs. There are various methods available to more efficiently use HPLCs such as connecting several columns to one pump via a switching valve. Drawing from several different solvent reservoirs often has a detrimental effect on pump lifetime, so this solution may decrease initial equipment costs but then later result in lower operational reliability. An even bigger problem may be keeping track of pump and column histories so that solvents and analyses do not conflict. Examples of such problems would include failure to establish a flat baseline, occasional appearance of ghost peaks, and chronic microbial growth in a column. Without a dedicated chromatography specialist it is difficult to succeed at continually switching HPLCs between different analyses.

For FDG, a refractive index detector is required to detect non-radioactive FDG mass peaks. An RP-18 column (Alltech Associates, Deerfield, IL) can be used for elution. For ^{13}N ammonia, a conductivity detector is used to detect cold mass peaks with the Hamilton (Reno, NV) PRP X-200 column, or equivalent, employed for the separations. For other products different detectors will be necessary. Several groups have used electrochemical detectors for the fluorodopas and UV-VIS detectors are deservedly ubiquitous. It is hard to anticipate one's needs since new methods are continually being developed. Bear in mind that a quality detector can cost $4,000–$10,000.

When buying an HPLC it is advantageous to purchase the complementary data system also. Such a data system will allow the development of routine analytical recipes and customization of printouts. HPLCs and GCs take up a lot of bench space, 4 to 6 ft each, so plan accordingly.

Gas Chromatography (GC). The GC (Fig. 8) is used to analyze both gases and liquids. It is commonly used in quality control of PET gases for both clinical and research applications. The GC will require a supply of helium gas as the flow-through medium, at an expense of $300 per yr. A complete GC system, such as the HP-5890 is offered by Hewlett-Packard (Palo Alto, CA), can be purchased for ~$20,000, not including the radiometric detector.

Radiometric Detectors for HPLC and GC. There are several choices for radiometric detectors. Beckman Instruments (Fullerton, CA) model 170, at a price ~$5000, is a microprocessor-controlled device that is relatively easy to install and use; similar units are available from Berthold (Nashua, NH) and others. Some centers use 2-in. × 2-in. sodium iodide detectors and the appropriate nuclear instrumentation module (NIM) electronics, fashioned into homemade detectors. This latter type of equipment is available from several companies such as Ortec (Lenoir City, TN), Canberra (Meriden, CT), Nuclear Data (Schaumburg, IL) and Tracor (Austin, TX). The cost of the home-built system is less but the device requires more effort to get working. In choosing detectors, the main consideration should be compatibility with the HPLC data system. Ideally, there should be one radiometric detector per HPLC and GC.

Thin-Layer Chromatography (TLC). TLC is recommended for use in quality control procedures for PET radiopharmaceuticals. The sample in a liquid medium is allowed to travel

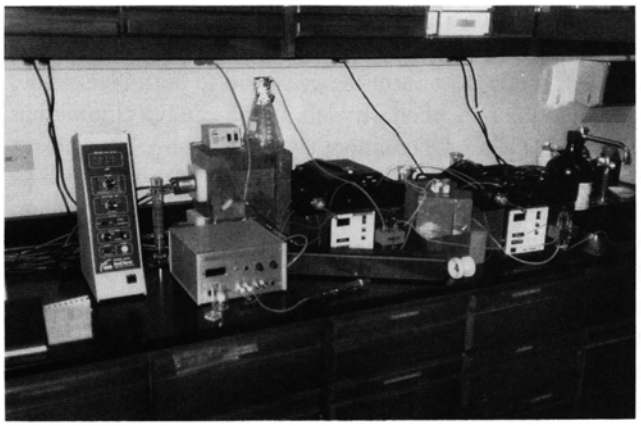

FIG. 7. HPLC apparatus for PET, note the lead shielding and amount of bench space required.

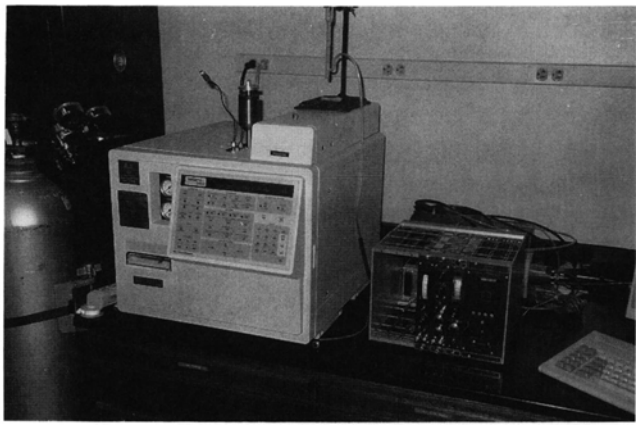

FIG. 8. A gas chromatography unit (GC) from Hewlett-Packard, Inc., Note the helium gas tank secured to the lab bench.

up a thin silica plate. Its rate of travel is proportional to the size of the molecule. This plate is then developed and the composition of the sample is determined, based on the distribution of the various components. This technique is generally much less sensitive than HPLC.

Plate readers have been used at many institutions and have been found to be reliable instruments. The imaging scanner takes up several feet of bench space and a large cylinder of counting gas is required. It will be important to indicate to the vendor that the instrument will be used with positron-emitting radionuclides so that it is configured with the appropriate collimator. Vendors offering similar TLC products include Berthold (Nashua, NH), Bioscan (Washington, DC), and Packard (Radiomatic) (Downers Grove, IL).

Gamma Spectrometer. A sophisticated solid-state detector, such as a hyperpure germanium, and a high-level multichannel analyzer are not strictly necessary in a PET facility. Since the typical 10- or 11- meV cyclotron can, at worst, only produce low levels of detectable radionuclide impurities, these radionuclides don't need to be assayed on a routine basis. This analysis can usually be performed on borrowed equipment, when necessary. Most academic institutions have suitably equipped physics, chemistry and engineering departments at which initial assays can be made. These assays are important for methods validation and for regulatory submissions (IRB, RDRC, IND, NDA). Subsequent assays are necessary only when a new type of target is used. The cyclotron manufacturer may be induced to provide a certificate of analysis for each target. Such a certificate would list the amount and identity of each radionuclidic impurity produced by that target. For non-academic institutions, it is very likely that these certificates will provide sufficient evidence of target-related impurities.

Interlocking Lead Bricks and Radioactive Waste Storage. Bricks can be used to shield hoods, to construct radioactive waste storage containers and to shield radiometric detectors, such as HPLC and GC. Many other ad hoc uses occur also. A fairly representative PET center purchased 1200 2-in × 4-in × 8-in lead bricks. Lead bricks cost $30–$40 each. For a strictly clinical operation, fewer will be needed. As an alternative to individual lead bricks, preformed shields can be purchased. However, such shields are less transportable and reconfigurable.

Radioactive waste caves will be needed near the cyclotron targets, the hot cells, the radiopharmacy hood, and in the scanner room. More than one cave is recommended because of the dose and potential for contamination associated with carrying radioactive waste more than few feet. One option is to construct a metal frame into which the lead bricks are placed. The other option is to purchase precast lead enclosures. Each cave should have a movable top which can be closed after use. Although short-lived, this waste must be shielded until the following day.

Lab Benches and Casework. Standard lab furniture is acceptable. Stainless steel bench tops are not necessary but will certainly not be detrimental. It is recommended that utilities on the work counters include vacuum and water (with cup sinks). Two large sinks are also useful. Solvent cabinets for the storage of flammable solvents and acids are necessary unless centralized storage facilities are close by. Generally, possession of more than a few pints of each of several types of solvents mandates an approved storage cabinet.

Water Purification System. This is a very useful piece of equipment. There will be many cases where a local supply of high quality water will be needed. Examples include preparation of HPLC and TLC solvents, general solution make-up and rinsing of reusable clinical labware. The initial cost will be $3000 – $5000 depending on the system purchased.

Laboratory. A dishwasher is helpful unless there is a local service which handles dirty labware. A dishwasher relieves the tedium of hand washing and is also more reliable. The dishwasher can be plumbed into the water purification system so that the final rinse is made with high quality water. Clean equipment can subsequently be autoclaved if it is to be used as part of a radiopharmaceutical synthesis.

Autoclave. A provision for both steam and ethylene oxide sterilization will be important. Generally these services are available through the sterile supply department of most hospitals. Testing and validation of such a system are very involved so this should be contracted out if at all possible.

Helium Leak Detector. A small helium leak detector is suggested. This instrument can be very helpful in troubleshooting certain cyclotron and target problems, which might otherwise involve significant downtime. Gow-Mac (Bridgewater, NJ) and Varian (Lexington, MA) are among the vendors offering this product.

Synchronous Clock. Because of the large number of interrelated activities required for PET, it is vital that those activities be synchronized effectively. One means to accomplish this is through the use of a computer-controlled digital clock system. Such clocks should be located in the scanner room, in the scanner control room, the patient prep room(s), the cyclotron room, the radiochemistry lab, and the clinical chemistry lab. The clock network can alternatively be controlled by the cyclotron control computer (typically a PC), a VAX/microVAX, or even a SUN workstation. Talus Engineering (Melbourne, FL) has designed such synchronous clock systems for PET applications.

Local Area Computer Network. A system whereby all the computers in the PET center could communicate would facilitate operations. For example, synthesis, quality control and dispensing records could be appended to each patient's scan data. In addition, a sophisticated logging program would allow easy retrieval of patient files for display and analysis. Such a network would also facilitate tracking of patient populations. Most current generation PET systems utilize thin-wire ethernet to link remote workstations, file servers, and other processors. This same network can be extended to include all the computers in the radiochemistry and clinical chemistry labs; thereby, allowing a means to integrate all the information related to any given patient's procedure.

Small Equipment. Several small equipment items would be worth buying. An oscilloscope can be very useful in troubleshooting a variety of electronic problems. An instrument such

as a Tektronix (Beaverton, OR) model 2235 (about $2,000) is recommended. Two ultrasonic cleaners, one small and one large, will be useful. A small (undercounter) freezer for the storage of temperature sensitive reagents will be needed. Administration of doses can be handled by infusion and withdrawal pumps. These pumps are available from a number of manufacturers (such as Harvard Apparatus (S. Natick, MA) and Orion Research, (Boston, MA)) for about $1,500. An ice machine (or a local supply of shaved ice) has been shown to be very useful. An additional cyclotron control system located in the scanner room has been found to facilitate cyclotron control by the camera technologists. This is especially useful in the production of PET gases.

Glassware and Reagents. This general heading can be subdivided into several categories. The enriched stable nuclides required as targetry material, constitute a continuing high level expense for a PET center. Although they are considered consumables, a large initial procurement will be necessary. For the ^{18}F target, the ^{18}O-water precursor costs about $90/g for 95%–97% enriched material. Two production runs per day will use ~0.8 g. Over a year this amounts to 200 g or $18,000. Since delivery from the two main suppliers (Isotec (Dayton, OH) and Cambridge Isotope Labs (Woburn, MA)) is currently running 6–9 wk from receipt of order it is important to maintain a 50 g–100 g stock, stored in more than one container. For the ^{15}O target, the ^{15}N (N_2) gas precursor is similarly expensive. A 450 ml cylinder containing 26 STP liters costs $6000–$7000. An ^{15}O (O_2) flow study uses 1 cc/min for 30 min. One cylinder is thus good for about 800 studies. For the ^{13}N target, the ^{13}C powder precursor is cheap by comparison: one gram costs ~$250. A target loading takes 0.1 g and is good for at least 50 irradiations. Therefore one gram is sufficient for 500 studies. To the number of anticipated clinical studies must be added the requisite testing and quality control irradiations. Especially during start-up, these additional runs can result in a significantly higher rate of usage.

General laboratory equipment, chemicals, and glassware not specifically dedicated to any particular product will certainly cost upwards of $10,000. One research/clinical center has spent more than $40,000 supplying the hundreds of small items that are part of a working laboratory.

Initial stocking for parts for radiopharmaceutical syntheses must be budgeted, too. During each FDG production about $100 of disposable items are used. Reusable supplies for FDG include reaction vessels (40 or 50 needed at about $20 each) and stopper assemblies. The stopper assemblies are generally made and tested in-house.

Miscellaneous Items. Tools can be an unexpectedly large expense. Even with a warranty or a service contract, many repairs can best be made by PET personnel because of the time saved. A similar situation exists in the radiochemistry laboratory with its many high technology instruments. Such in-house repairs are predicated on a well stocked tool chest. Initial tool costs can be $5000–$10,000.

There are many replacement parts for the cyclotron and targets that are well worth stocking. These include cathodes, anodes, target foils, and stripping foils. It is useful to have many of the commonly used fittings on hand also. These may include Swagelock fittings, Legris fittings, CPC fittings, etc. The manufacturer should be able to supply a comprehensive listing of recommended spare parts. It is not uncommon to routinely stock items such as indicator-light bulbs, O-ring seals, various cables and wires, electrical connectors, and heating bath oil. All of these supplies may cost as much as $10,000.

Clinical Chemistry

In a purely clinical program where strict quantitative analysis is not routinely considered necessary, this lab will probably not be required. Clinical and research/clinical programs which rely on blood sampling to quantify compartmental tracer uptake will require this lab. Key components of the lab would include a centrifuge, well counter, glucose analyzer, and possibly a blood gas analyzer (for ^{15}O studies). The automated well counter is extremely sensitive to background activity, so its location relative to potential radioactive sources must be carefully considered in the site planning process. The well counter should be interfaced to a computer that has software to decay correct sample counts. It has also been found very useful to link this computer to the PET computer workstation via a network.

Ancillary Imaging Equipment

Among the proposed equipment for the scanner suite, several items require additional comment.

ECG Monitor. This is necessary if pharmacologic intervention studies are planned, especially in association with cardiac PET procedures.

Stretchers. These are not intended for patient transport but to accommodate patients waiting for FDG brain imaging. Since the agent requires 45–60 min for optimal localization and blood clearance, these patients need a means to rest comfortably and quietly. Specify a 4–5 in mattress thickness.

Remote Video Camera System. See remarks in the section dealing with radiation protection.

Immobilization Device for Patient's Head. Various schemes and designs are in use or development which attempt to manage the problems associated with minimizing patients' voluntary or involuntary motions during brain imaging. One of the most successful solutions is offered by Tru-Scan, Inc., of Annapolis, MD. They offer a moldable thermoplastic mask which is contoured to the individual patient's face and fastens to the imaging table. Some modification of the PET imaging table may be required. This system is priced at ~$3000, including table modification. The disposable face masks are priced at $33 each, but these are only reusable for the same patient.

Additional Computer Workstation. An additional workstation can be placed in the reading room to facilitate access to processed studies during interpretation sessions. This station can access patient study files via the network link to the main file server system. This allows the workstation in the control room to continue current acquisition and processing tasks without interruption. Research programs will likely require

several additional workstations for data analysis and software development.

Site Planning

As previously mentioned, Figure 1 illustrates a design for a diversified clinical and research PET facility at the North Carolina Baptist Hospital-Bowman Gray School of Medicine, Winston-Salem, N.C. A purely clinical facility would not require the animal or binding labs and the size of the radiochemistry lab could be reduced. The PET centers at Vanderbilt University and the University of Tennessee (Knoxville) have been fully described elsewhere (*6,7*).

Cyclotron Room. Despite their relatively small size, modern cyclotrons and their associated shielding typically weigh ~120,000 lbs. For this reason, ground floor installation is recommended. The concrete slab, upon which the cyclotron rests, is specific to the cyclotron selected. Existing flooring must be completely removed down to the ground. Most manufacturers specify the minimum interior size of the cyclotron room as 20 ft × 25 ft, with a 10-ft ceiling. Wall-mounted lead shielding is optional, but should be considered, even for self-shielded units, if the cyclotron will be adjacent to areas occupied by non-radiation personnel. Lead thickness on the order of ¼-⅜ in should be considered in this situation. Each cyclotron has specific exhaust, air conditioning, and chilled water requirements. Refer to the manufacturer's site planning guide for these details.

It has been found useful to have the cyclotron control console close to the cyclotron. However, because of the noise, magnetic fields, and radiation fields associated with the cyclotron, it is convenient to have the console situated either in a separate room, or within the radiochemistry lab. For ease of troubleshooting, one center has placed a console on a cart which can be rolled into the cyclotron room as needed.

Radiochemistry Lab. At least 600 sq ft of space devoted to clinical radiochemistry is recommended. This is considered a minimum for a diversified, purely clinical program. Significantly more space is required to support research. For greatest efficiency, the radiochemistry lab should be adjacent to the cyclotron room.

As a minimum, bench space in the radiochemistry lab should be at least 75 linear ft. The instrumentation required in the radiochemistry lab will occupy an immense amount of bench space. One active research/clinical center utilizes the following bench space configuration:

Cyclotron Room: 8 linear ft (for target and ion source repair, etc., one radioactive waste storage cave).

Cyclotron Control: 12 ft (two monitors, printer, logbooks, writing area).

Radiochemistry Lab: 55 ft plus 20 ft of wall space (three HPLCs, GC, dose calibrator, pyrogen testing station, two carrels, two refrigerators, one freezer, two hot cells, two laminar flow hoods, three radiochemical hoods, three sinks, two radioactive waste storage caves).

Instrument Lab: 15 ft plus 15 ft wall space (TLC plate scanner, electronics shop oscilloscope, multi-channel analyzer, one sink).

Clinical Lab: 30 ft plus 30 ft wall space (two HPLCs, glucose analyzer, blood gas analyzer, two microfuges, one freezer, one refrigerator, one automated gamma well counter, one sink, one incubator, one oven).

The total amounts to 119 linear ft plus 65 ft of wall space. The labs are crowded but not excessively. The space described above is designated for clinical use. The bulk of the research is generally done in other labs in the facility (small animal, large animal, organic chemistry).

Lab bench utilities should include cup sinks as supplements to the one or two large sinks. Standard utilities such as water, air and vacuum should be provided. Generous use of electrical strips is necessary since instruments will occupy much of the bench space.

Provision should be made for the storage of at least seven full-size gas cylinders. The cylinders are the backups for those used by the cyclotron and need to be on-hand. In addition, gases will be used by the GC and the TLC plate reader so wall mounts must be installed in the lab. It is often useful to have a supply of pure compressed gas available in the lab for miscellaneous procedures such as bubbling in organic reactions. External tanks will be needed since house compressed gas is generally not pure enough.

Scanner Suite. The minimum size of the PET imaging room is considered to be 15 ft × 20 ft. It is preferable, though not required, to locate the imaging area in close proximity to the radiochemistry lab. When this is not practical, a PTS should be considered for the delivery of unit doses and microbore tubing for delivery of PET gases. The scanner and associated computers require rigid environmental control. A monitoring system to alert facilities management personnel to problems in temperature or humidity control is strongly recommended. Several manufacturers recommend the use of a surge protection device for the scanner. As discussed previously, wall-mounted lead shielding should be considered if the imaging suite will be adjacent to non-radiation areas. Such wall-mounted shielding will require reinforced metal studs to support the additional weight; this reinforcement will markedly increase construction costs.

The scanner suite should include an adjacent control room to accommodate the computer workstation for acquisition and processing. A leaded glass window and lead shielding for this room will help reduce technologist exposure. A computer room with raised flooring must also be planned to house the hardware for the PET computer system. Space requirements will vary by vendor.

Patient Preparation Room. One or two prep rooms may be appropriate depending on the anticipated volume of FDG procedures. This room should be provided with a comfortable stretcher, medical gases and suction. An intercom station and/or a nurse call system would also be useful. If the budget allows, it would also be useful to install a remote video camera. This space may require additional wall shielding, if exposure to non-radiation workers in adjacent rooms is a potential concern. An 8 ft × 10 ft room should be adequate for this function.

Intercom Stations. It is extremely useful to install a dedi-

cated intercom system to facilitate communication between key parts of the PET center. Stations have been found useful in the cyclotron room, radiochemistry lab (by the dispensing radiopharmacy hood or PTS), the patient prep rooms, the scanner room and control room, and the reading room. It might also be advisable to install stations in the lab director's and physicist's offices.

Support Space. Significant economy can be realized if the PET center is physically integrated into an existing nuclear medicine facility. Space for reception and scheduling, patient waiting, rest rooms, staff lounge, storage, reading room, and transcription can all be shared.

Budgeting for PET

Capital Equipment. The projected capital equipment expenses described in Table 3 are based on current list pricing as of May 1990. Be advised that discounts may be available on certain items. For the purposes of this example, it is assumed that the defined program will be configured to accomplish both head and body clinical imaging with a single scanner and to utilize a full range of PET radiopharmaceuticals, to be synthesized in-house. Construction costs will vary greatly depending upon the amount of new construction required; therefore, no construction estimate has been included with this example. The bottom line, $5.27 million, represents a significant portion of a typical, large hospital's annual capital budget (*6,7*).

Operating Expenses. The projected annual direct expenses described in Table 4 are based on the same program configuration described above. As illustrated in Tables 4 and 5, radiopharmaceutical production costs, maintenance costs, and salaries represent the major components of the operating budget. For maintenance costs, some economy might be realized if an in-house service engineer could be identified and suitably trained. Such an arrangement would still require a "parts only" service contract. The bottom line, $1.13 million, before depreciation, represents a significant annual expense for the institution, with only poor prospects for short-term revenue (*6,7,13,14*).

A typical depreciation schedule for PET capital assets specifies a 15-yr life for the cyclotron, hot cells, and construction, a 10-yr life for the radiochemistry equipment, and an 8-yr life for the scanner and all other equipment (*6*).

Revenue Allowances and Reimbursement. Due to the uncertainty currently surrounding the reimbursement issue, projecting anticipated revenue is much more uncertain than simply multiplying procedure charges by the number of anticipated procedures (*15*). A very conservative approach would be to assume 10% reimbursement in the first year, increasing by 10% each additional year up to 50%. Of the nonreimbursable charges, which are assigned as "patient responsibility," assume that 20% will actually be paid. The remaining balance would be written off as bad debt.

TABLE 3. Sample Capital Expenses for a Diversified Clinical Program with One Scanner

Equipment	Cost
Scanner Room	
Whole-Body scanner	$2,440,000
Gas administration system	42,500
Additional workstation	30,000
Surge protector	20,000
Defib/Crash cart	9,000
ECG monitor	8,500
Stretchers (2)	6,000
Infusion pumps (2)	3,000
Remote video camera and monitor	3,500
Cyclotron Room	
Self-shielded cyclotron and targets	1,950,000
Helium leak detector	15,250
Radiochemistry Lab	
Automated synthesis modules (3)	140,000
Hot cells (2)	115,000
Remote manipulators (1 Pr)	30,000
Fume hoods (2) and Casework	50,000
Laminar flow hoods (2)	13,000
Interlocking lead bricks (1000)	30,000
Shielded transport cart	2,000
Pneumatic transfer system (60 ft distance)	8,000
PTS station shielding (send and receive)	12,000
Lead enclosures for synthesis modules (2)	15,000
Dose calibrators	39,000
HPLC systems (3)	60,000
HPLC/GC radioactivity detectors (4)	21,000
HPLC, other detectors (4)	27,000
HPLC columns	4,000
Gas chromatography	14,200
Thin-Layer chromatography scanner	16,600
Gravimetric Balance	2,300
pH Meter	1,100
Refrigerator	1,400
Freezer	750
Incubator	4,200
Water purifier	4,600
Lab dishwasher	3,200
Personal computers (2)	4,000
Target precursors	25,400*
Reagents and glassware	10,000*
Miscellaneous items	10,000*
Clinical Lab	
Auto wellcounter	35,000
Centrifuge	1,600
Glucose analyzer	4,200
Common Use Items	
Lead waste caves (3)	16,500
Area radiation monitors (3)	4,050
Survey meters (2)	2,700
Pocket dosimeters (8)	1,960
Intercom stations (6)	4,500
Synchronous clock (8 units)	1,200
Oscilloscope	2,000
Tools	5,000
Total	$5,270,210

* Consumable items may be included in operating budget.

TABLE 4. Sample Operating Expenses

Expenses	Cost
Salaries	
Salaries*	$303,100
Benefits (23%)	69,713
Subtotal	$372,813
Variable Expenses	
Radiopharmaceuticals†	$280,800
Other supplies	78,000
Subtotal	$358,800
Fixed Expenses	
Maintenance‡	$360,000
Utilities	30,000
Radiation safety	4,700
Training and travel	4,000
Subtotal	$398,700
Total direct expenses before depreciation:	$1,130,313

* Assumes a radiochemist as lab director, a radiopharmacist, a physicist, a chemistry/cyclotron technologist, two nuclear medicine technologists, and a radiology nurse.

† Assumes six patients per day, each patient receives a transmission scan, an NH_3 perfusion and FDG metabolism study. These are interleaved to optimize scanner time during FDG localization (7). Two FDG production runs are assumed. A realistic expectation for the first three months of operation is one to two patients per day, increasing to five to six per day in six months. Table 5 lists some typical per dose expenses for radiopharmaceutical production.

‡ Assumes initial warranty period (first year) has expired.

TABLE 5. Sample Direct Per Dose Costs for PET Radiopharmaceutical Production

Agent	Cyclotron supplies	Radiochemical supplies	Total
NH_3	$10	$50	$60
FDG	$30	$90	$120

CONCLUSION

Planning a PET center is by no means a trivial task. It requires a great deal of time and painstaking detail. A designated "start-up team" can effectively utilize different skills and talents in approaching the various aspects. The importance of establishing the program's mission and scope as early as possible cannot be overstated. A great deal of emphasis must also be placed on attracting individuals with sufficient scientific and technical expertise—even the finest equipment cannot perform properly without a competent staff. The directors of the institution must fully realize the magnitude of the financial commitment required and the risks associated with the uncertainty of clinical reimbursement.

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