Clinical PET: Study Scheduling and Coordination

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During the last 39 months at Duke University Medical Center, we have performed 1356 clinical positron emission tomography (PET) imaging studies: 68% were fluorine-18 (^{18}F) fluorodeoxyglucose (FDG) brain metabolism scans, 28% were myocardial perfusion (nitrogen-13 [^{13}N] ammonia) and viability (FDG) studies, and 4% were FDG tumor localizations. Three days each week are used for clinical studies. On clinical days, we can perform 2 cardiac perfusion and viability (P & V) and 4-5 FDG brain studies. Cyclotron production of ^{18}F is started at 0730. Automated synthesis of FDG follows with FDG available by 0940. Nitrogen-13 ammonia unit-dose production is scheduled to fit myocardial patient imaging. Image workup and filming are performed on the preceding study during the next study's acquisition. Study archival is accomplished at day's end. With short-lived positron emitters, any deviation from schedule or any loss of coordination will damage the ability of the PET facility to perform requested clinical PET imaging studies.

Positron emission tomography (PET) is being used primarily in large medical centers at this time. The role of PET in clinical studies has received increasing interest since the results of research studies have documented the clinical status of PET (*1-7*). As PET approaches clinical status, some unique technical and scheduling problems are seen to be inherent to the studies.

Organization, communication, and flexibility are vital in the coordination of a clinical PET facility. Coordination of the clinical imaging is complex. The scheduling involves personnel from the cyclotron, radiochemistry, computer, and scanner areas within the PET facility and patient, physician, nursing staff, and ancillary support personnel outside the facility. Time sequencing includes radionuclide production, radiochemical synthesis, radiopharmaceutical quality control, and patient imaging. Any technical or mechanical problems can cause delays or cancellation of the imaging day.

A common problem in a clinical PET facility is the patient who is late for the study. The short half-life of the isotopes and the labor-intensive radiopharmaceutical production make it vital that the patient arrive on time, that the coordination of multiple patients allows for some extra patient-care time, and that decisions concerning the patient imaging procedure are made prior to the procedure. Inpatients and outpatients are scheduled to arrive at least 30 min prior to the imaging procedure to allow discussion of the procedure with the patient and family, acquisition of a short clinical history, insertion of necessary intravenous or intra-arterial lines, arrangements for sedation, and preparation of the patient for monitoring (EEG, Video, and EKG). All female patients of childbearing potential are questioned about pregnancy and breastfeeding prior to the administration of any radioactive material. They are instructed to circle a response (yes or no) to the pregnancy and breast-feeding questions and to initial the patient requisition. If there is any question of pregnancy, the patient's attending physician is contacted and a beta HCG test is performed. Radioactive material is not injected until negative beta HCG results are confirmed.

Once the imaging procedure is completed, the processing and filming are performed while the next patient's study is being acquired. Study archival onto magnetic tape is completed at the end of the day.

The routine clinical studies consist of fluorine-18 (^{18}F) fluorodeoxyglucose (FDG) brain studies (Fig. 1) and myocardial perfusion (nitrogen-13 [^{13}N] ammonia) and viability (FDG) studies (Fig. 2).

PROCEDURES AND METHODS

Cyclotron* production of $^{18}F^-$ for FDG synthesis (*8*) uses the $^{18}O(p,n)^{18}F$ reaction, and requires bombardment of a silver target with oxygen-18 (^{18}O) water with 11 MeV protons for 45–60 min at 15–19 microamps. The $^{18}F^-$ (in water) is transferred to a chemical processing unit, where automated synthesis of FDG is performed over 60 min. Table 1 provides the schedule for [^{18}F]FDG production.

Nitrogen-13 ammonia production involves 16.6 MeV proton bombardment of carbon-13 (^{13}C) in water with reactions of $^{16}O(p,\alpha)^{13}N$ and $^{13}C(p,n)^{13}N$ occurring at 3 microamperes for 7.7 min: delivery to a sterile vial requires another min. Dose preparation and delivery to the scanner room requires 2 to 3 min. A production schedule for ^{13}N-ammonia is shown in Table 2.

Radiopharmaceutical quality control is performed on each batch of [^{18}F]FDG and ^{13}N-ammonia. Quality control tests

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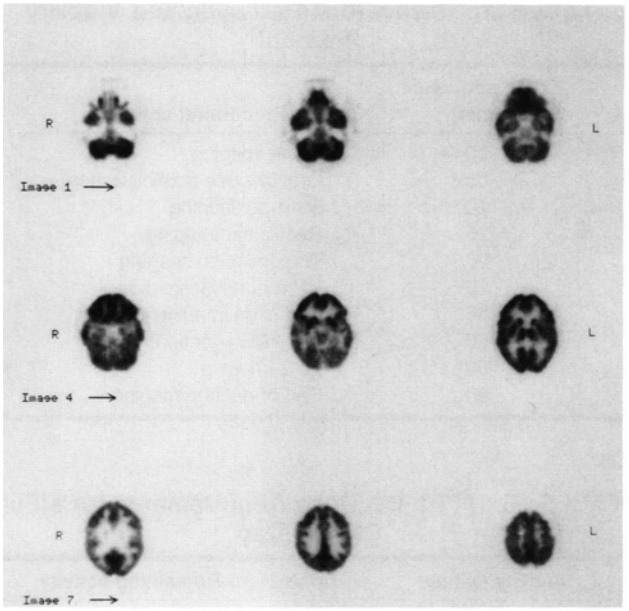

FIG. 1. Normal FDG brain metabolism images.

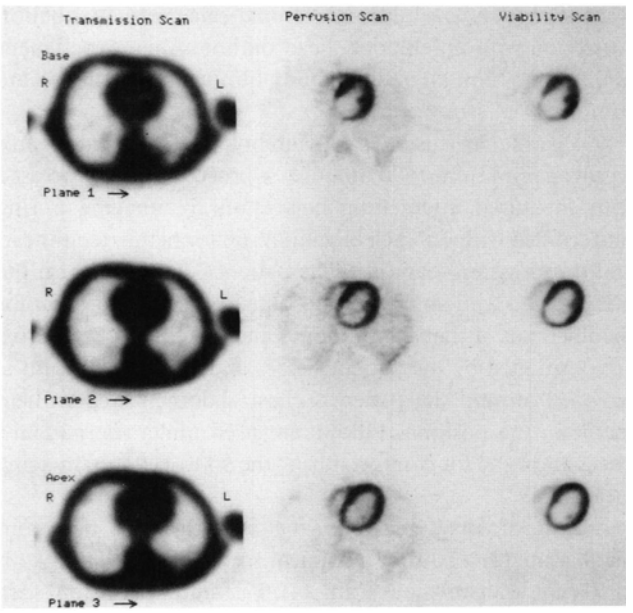

FIG. 2. Normal myocardial perfusion and viability procedure images.

are performed after the administration of these short-lived radiopharmaceuticals. Both radiopharmaceuticals undergo sterility and pyrogen testing and high pressure liquid chromatography (HPLC) analysis. Possible presence of the toxic reagent Kryptofix™ (Sigma Chemical Corp., St. Louis, MO) in FDG is determined by thin layer chromatography (TLC). Sterility testing is done to meet *United States Pharmacopeia* (USP) specifications using soybean-casein digest and fluid thioglycollate media. Pyrogen testing is performed using the bacterial endotoxin (LAL) method.

For a FDG brain study, the patient is NPO for 4 hr prior to the [^{18}F]FDG injection. The patient is injected with 0.143 mCi/kg [^{18}F]FDG in a dimly lit, quiet room. The patient is asked to remain still for 30 min. Then, the patient is positioned in a headholder with straps to help eliminate patient motion during the approximately 40 min imaging procedure. Table 3 demonstrates the timing sequence for a FDG brain scan.

A 3-slice (CTI 911-2) PET scanner, ECAT III (CTI PET Systems, Knoxville, TN), is used to obtain a 12 or 15 slice image study, so it is necessary to scan the patient for 10 min/bed position at 4–5 different bed positions. Current scanners, with multi-slice capability, require only 1 or 2 bed positions, but comparable total imaging times. The number of bed positions and sequencing depends on the requirements of the requested study. Slices are 8.4 mm (FWHM) thick and are centered 12 mm apart (set by adjustment of the scanner's shadow shields). Data collection averages approximately 3 million counts/slice (10 min) in the direct planes and 6 million counts/slice (10 min) in the cross plane.

Reconstructed in-plane resolution is about 8 mm (FWHM).

TABLE 1. [^{18}F]FDG Cyclotron & Radiochemistry Procedures

Time sequence (min)	Procedural activity
00	Start of ^{18}F bombardment (SOB)
60	End of ^{18}F bombardment (EOB)
60	Start of [^{18}F]FDG synthesis (SOS)
125	End of [^{18}F]FDG synthesis (EOS)
125	[^{18}F]FDG activity measurement & radiopharmaceutical preparation
135	[^{18}F]FDG dose available (FDA)
after 135	Product quality assurance & control

TABLE 2. ^{13}N-Ammonia Cyclotron & Radiochemistry Procedures

Time sequence (min)	Procedural activity
0	Start of ^{13}N-ammonia bombardment
7.7	End of ^{13}N-ammonia bombardment
8.7	^{13}N-ammonia activity measurement and product preparation
11	^{13}N-ammonia dose available
after 12	Product quality assurance & control

TABLE 3. FDG Brain Metabolism Protocol

Time sequence (min)	Procedural activity
	NPO for 4 hr prior to injection
00	Patient quiet in dimly lit room
00	[^{18}F]FDG injection
25	Start positioning
30	Bed position 1 imaging
40	Bed position 2 imaging
50	Bed position 3 imaging
60	Bed position 4 imaging
70	End of patient imaging

Reconstruction uses a Hann filter and calculated attenuation correction with an elliptical head outline using a coefficient of 0.088 cm^{-1} on all images. Study filming and archiving are completed later in the day.

Myocardial perfusion and viability (P & V) procedures require a minimum of 90 min. P & V procedures are processed with measured attenuation correction by imaging a ring source filled with 1.8 mCi of gallium-68 for blank, rectilinear, and transmission scanning. The patient is positioned on the imaging bed with an intravenous line in the right forearm for the injection of the ^{13}N-ammonia and [^{18}F]FDG. Both arms are positioned by the patient's sides and a gentle restraint is wrapped around the patient's chest/abdomen area to help maintain the position. Pillows are used under the patient's knees and head for comfort during the 90 to 120 min imaging procedure.

Imaging involves the following five scans: (1) a 10-min blank scan, (2) a 10-min rectilinear scan (for positioning), (3) a 10-min transmission scan, (4) a 10-min perfusion scan following a 3-min delay after ^{13}N-ammonia injection, and (5) a 10-min viability scan following a 30-min delay after FDG injection.

Viability studies are done in a glucose-loaded state. Glucose (100 g) is administered orally approximately 27 min prior to the ^{13}N-ammonia injection and 45 min prior to the [^{18}F]FDG injection. Patient doses for the procedure are 0.214 mCi/kg for ^{13}N-ammonia (15.0 mCi average adult dose) and 0.143 mCi/kg for [^{18}F]FDG (10.0 mCi average adult dose). Time sequencing for the myocardial P & V study is shown in Table 4.

Imaging requires only one bed position for a 3-slice image study. The scanner's shadow shields are set to provide a slice thickness of 16.0 mm (FWHM) centered 20 mm apart. Typical ^{13}N-ammonia 10-min images contain 6 million counts in the direct planes while the cross plane has 12 million counts. The [^{18}F]FDG images contain 3 million counts in the direct planes and 6 million counts in the cross plane. Reconstruction uses measured attenuation correction on all images.

TABLE 4. Myocardial Perfusion and Viability Protocol

Time sequence (min)	Procedural activity
00	Blank imaging
05	Oral glucose administration
10	Start positioning
15	Rectilinear imaging
20	Transmission imaging
32	^{13}N-ammonia injection
35	Perfusion imaging
50	[^{18}F]FDG injection
80	FDG imaging
90	End of patient imaging

TABLE 5. [^{18}F]FDG Dose Requirements for a Full Clinical Day

Activity @ time		Dose	Remaining activity
280.0 mCi	0930		
271.3 mCi	0935	10.0 mCi	261.3 mCi
122.4 mCi	1135	10.0 mCi	112.4 mCi
98.5 mCi	1156	10.0 mCi	88.5 mCi
66.6 mCi	1241	10.0 mCi	56.6 mCi
42.6 mCi	1326	10.0 mCi	32.6 mCi
24.5 mCi	1411	10.0 mCi	14.5 mCi
10.9 mCi	1456	10.0 mCi	0.9 mCi

RESULTS AND DISCUSSION

On a typical clinical imaging day, 2 myocardial P & V studies and 4–5 FDG brain metabolism procedures are scheduled. Initial 60-min ^{18}F cyclotron bombardment begins at 0730 with a 60-min synthesis following. Table 5 shows that a starting FDG activity of 280 mCi is the absolute minimum required for a full day's schedule and is sufficient only if all events occur on time. A starting activity of 300 to 340 mCi is a more appropriate amount with which to attempt a maximum schedule. The amount of FDG produced from a 60-min bombardment is usually 220–280 mCi. Second batches of FDG are necessary on maximum-schedule days and production schedules are determined by using the first batch activity and the patient schedule.

A second FDG production run creates many problems, such as the difficulty of scheduling a second ^{18}F production among ^{13}N-ammonia runs, and increased radiation dose to radiochemistry personnel who have to disassemble the FDG synthesis unit so soon after termination of the first synthesis.

A limitation on our production of $^{18}F^-$ results from the necessity of degrading the energy of protons from 27 MeV to the 11 MeV design energy of our fluoride target. The energy degrader itself has presented problems above 18 μA of beam current, which together with some target problems, is limiting our $^{18}F^-$ production. With sufficient ^{18}F activity, we have made as much as 400 mCi of FDG.

Nitrogen-13 ammonia production occurs at much lower beam currents and higher proton energy than ^{18}F production. No problems have developed in production of sufficient unit-dose activity of $^{13}NH_3$.

Post-use testing for sterility and pyrogens has been justified by the results. Out of 537 batches of FDG and 328 batches of ammonia, 5 have shown growth in USP sterility testing (4 FDG, 1 NH_3). All have been isolated events, showing no patterns characteristic of a systematic sterility problem, with no events in the last 8 mo. There have been no batches of either product that were uninjectable due to excessive endotoxins.

In developing PET centers, study scheduling should be scaled to radiopharmaceutical production capability. Since FDG is likely to be the most frequently used radiopharmaceutical, its availability will dictate the level of clinical imaging attainable. Additional FDG synthesis units ameliorate the effects of limited FDG production capability but at this time represent an expensive solution in terms of money and personnel support.

The timetables and production schedules shown are accomplished only if every element occurs at the proper time. Disruptions of the schedule commonly occur. Late or no-show patients, equipment problems, and handling of very ill patients cause scheduling problems. Therefore, coordination of every activity in the clinical PET center is extremely important.

A daily clinical imaging schedule of the proposed patient procedure sequencing times is posted by 0730. The schedule is finalized after a preliminary check of the scanner quality control (which is run overnight), cyclotron initial startup, and first-patient availability. PET personnel and instrumentation schedules revolve around this clinical schedule. Table 6 shows a daily clinical schedule. At this time, communication begins among physicians, nursing staff, and ancillary support personnel (patient transporters, EEG monitoring personnel, ward secretaries, etc.), in an attempt to ensure a smooth, efficient flow of patients and procedures through the day's schedule.

Occasionally the schedule must be changed to accommodate the patient's availability and/or ability to tolerate the procedure. With scheduling changes, personnel in PET and persons involved in the study from outside the PET laboratory need to cooperate in order to shift schedules to efficiently accommodate the patient's needs. When instrumentation failure in the PET facility causes delay and/or cancellation of the clinical day, every effort is made to reschedule the patient's procedure at a time convenient to the patient and referring clinician. The difficulty of daily scheduling necessitates that the personnel in the PET facility give maximum effort to coordination, communication, and organization and still have a flexible attitude.

Current clinical procedure protocols at our institution are subject to change with growing experience and as new information becomes available. New procedure protocols are anticipated in the future with the advent of our facility's growth and the growth of the field of clinical PET imaging.

With our staffing, we have found it necessary to familiarize all personnel with a wide range of tasks to maintain the operation of the facility when someone is on vacation or ill. Furthermore, task-sharing helps distribute personnel radiation exposure since some areas of operation involve longer exposure times and higher radiation levels such as drawing and injecting doses and holding patients for imaging procedures.

Personnel who are willing to communicate and work together will produce a final high quality study, enabling the clinical PET imaging center to reach its highest potential.

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TABLE 6. Daily PET Facility Clinical Schedule

Cyclotron	Ring source	Synthesis	Notes
SOB = 0730			^{18}F for 60 min
EOB = 0830		SOS = 0830	[^{18}F]FDG
	Load at 0835		Use ^{68}Ga
SOP = 0855			Myocardial P&V
SOB = 0915			^{13}N-ammonia
EOB = 0923			Dose preparation
^{13}N Ammonia injection #1 at 0926, imaging at 0929			
		EOS = 0935	Dose preparation
[^{18}F]FDG injection #1 at 0946, imaging at 1016			
	Load at 1025		Use ^{68}Ga/[^{18}F]FDG
SOP = 1045			Myocardial P&V
SOB = 1105			^{13}N-ammonia
EOB = 1113			Dose preparation
^{13}N-Ammonia injection #2 at 1126 with imaging at 1129			
[^{18}F]FDG injection #2 at 1136 with imaging at 1206			
SOP = 1156 [^{18}F]FDG injection #3 at 1156, brain imaging at 1226			
SOP = 1241 [^{18}F]FDG injection #4 at 1241, brain imaging at 1311			
SOP = 1326 [^{18}F]FDG injection #5 at 1326, brain imaging at 1356			
SOP = 1411 [^{18}F]FDG injection #6 at 1411, brain imaging at 1441			
SOP = 1456 [^{18}F]FDG injection #7 at 1456, brain imaging at 1526			
End of imaging at 1606			
Procedure filming and archiving until approximately 1700			

SOB = start of bombardment; EOB = end of bombardment; SOS = start of synthesis; EOS = end of synthesis; SOP = start of the imaging procedure

NOTE

* CS-30, The Cyclotron Corporation/Computer Technology & Imaging, Berkeley, CA/Knoxville, TN. Protons—27 MeV, deuterons—14 MeV, alpha particles—26 MeV.

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