American Society of Nuclear Cardiology Practice Guidelines

PET Myocardial Glucose Metabolism and Perfusion Imaging

Part 1 — Guidelines for Patient Preparation and Data Acquisition

Stephen L. Bacharach, Jeroen J. Bax, James Case, Dominique Delbeke, Karen A. Kurdziel, William H. Martin, Randolph E. Patterson

Part 2 — Guidelines for Interpretation and Reporting

Heinrich R. Schelbert, Robert Beanlands, Frank Bengel, Juhani Knuuti, Marcelo DiCarli, Josef Machac and Randolph Patterson

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Introduction to the Guidelines

Cardiac positron emission tomography (PET) imaging is a well-validated, reimbursable means to assess myocardial perfusion, left ventricular function, and viability. Presently, there is a proliferation of PET instrumentation as well as an increase in educational programs that specifically address PET imaging. Technologists performing PET scans as well as physicians interpreting them should have a sound knowledge of recommended standards for the performance, interpretation, and quality control of cardiac PET in order to provide accurate and clinically relevant information to referring physicians, facilitating optimal patient management.

These guidelines have been developed by the Quality Assurance Committee of the American Society of Nuclear Cardiology (ASNC). The task of the Committee has been to document state-of-the-art PET applications and protocols approved by experts in the field and distribute these protocols to the nuclear cardiology community. The final document was reviewed and approved by the ASNC Board of Directors. ASNC gratefully acknowledges the contributions of Joseph Machac, MD, and Randolph Patterson, MD, and the Cardiovascular Council of the Society of Nuclear Medicine in developing the guidelines and we also wish to thank Helena Balon, MD, and the Practice Guidelines Committee of the Society of Nuclear Medicine for the careful review and endorsement of the guidelines. In addition, these guidelines have been endorsed by the Academy of Molecular Imaging.

Part 1, "Guidelines for Data Acquisition and Patient Preparation," addresses the instrumentation and protocols recommended to yield technically adequate and clinically meaningful cardiac PET scans. This section includes detailed explanations of patient preparation options, recommended quality-control parameters, and scan acquisition and processing techniques. Within this document protocol, items judged to be required are indicated as such. "Standard" means that the parameter value listed represents methodology judged to be standard by the consensus of the committee; its utilization is recommended, but other techniques may also be valid. "Preferred" means that the parameter value listed is expected to provide the best results and its selection is strongly recommended. Techniques termed "optional" indicate that the parameter value listed may be used or another acceptable parameter may be substituted.

Part 2, "Guidelines for Interpretation and Reporting," provides a systematic approach to quality control, display, interpretation, and reporting of cardiac PET scans. Both subjective and objective semiquantitative interpretive methods to evaluate myocardial perfusion and viability are described. The Committee recognizes that all of these options may not be available on computer workstations presently provided commercially. Therefore such recommendations may be considered as general guidelines to direct the nuclear physician's scan interpretation in a detailed and organized fashion. This manual is designed to provide imaging guidelines for those physicians and technologists who are qualified in the practice of nuclear cardiology. Although care has been taken to ensure that information supplied is accurate, representing the consensus of experts, it should not be considered as medical advice or a professional service. The imaging guidelines described in this manual should not be used in clinical studies at any institution until they have been reviewed and approved by qualified physicians and technologists from that institution.

E. Gordon DePuey, MD
Chairman, Quality Assurance Committee

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PET myocardial glucose metabolism and perfusion imaging: Part I – Guidelines for patient preparation and data acquisition

Stephen L. Bacharach, PhD, Jeroen J. Bax, MD, James Case, PhD, Dominique Delbeke, MD, Karen A. Kurdziel, MD, William H. Martin, MD, and Randolph E. Patterson, MD

How This Document is Organized

Part I covers metabolic imaging with FDG (in section A), and perfusion imaging with ^{13}N-ammonia and ^{82}Rb (in section B). The information for each section is in Table format. First there is an introduction to each table, then the Table itself, and finally Notes for the Table. The Table summarizes the acquisition or patient preparation parameters. Each entry in the table refers to a note which discusses the entry in greater detail.

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BACKGROUND

Fluorine 18 fluorodeoxyglucose (FDG) uptake in the myocardium has been well validated as an indicator of myocardial viability.[1-3] In addition, rubidium-82 and nitrogen-13 ammonia are well-accepted myocardial perfusion agents,[4-10] for use in combination with FDG for determination of viability, or alone. The manner in which such data are used clinically and interpreted are described in Part 2. The methods of acquiring the FDG images and the associated perfusion images are given in Part 1. Section A of Part 1 (Tables 1 and 2) describes FDG imaging. Section B of Part 1 describes N-13 ammonia perfusion imaging (B1) and rubidium-82 perfusion imaging (B2). Note that all information below, unless otherwise specified, is applicable only to adult patients.

Oxygen-15 labeled water is often considered the ideal tracer for measurement of myocardial blood flow. Its use is not covered in this document for two reasons. First, it is currently not a Food and Drug Administration–approved drug. Second, it does not usually produce clinically interpretable perfusion images. Instead, a (well-validated) mathematical model must be used to produce numeric values of flow at each region of the myocardium.

We discuss only the use of so-called dedicated, multicrystal, ring positron emission tomography (PET) detector systems. Until the last few years, such systems were available primarily at research institutions. Recently (spurred by their successful use in clinical oncology), a very large number of PET scanners have been (and are continuing to be) installed. This, combined with the rapid increase in availability of FDG without an onsite cyclotron, has made cardiac FDG PET imaging possible at many clinical institutions, with the use of dedicated multicrystal ring PET systems.

We have not included coincidence gamma camera systems or (noncoincidence) collimated single photon emission computed tomography (SPECT) systems. Gamma camera coincidence systems ("hybrid" PET) were not considered, as it was felt that the impact of factors such as linearity of counts with activity, scatter correction, attenuation correction, and so on, had not yet been addressed sufficiently to allow standardized guidelines to be proposed. Noncoincidence collimated SPECT with FDG presented a different problem. Collimated FDG imaging has the advantage of permitting simultaneous, dual-isotope perfusion and metabolism measurements, a valuable feature for viability measurements and a feature that is not possible with coincidence PET. Despite this advantage, relatively few institutions utilize noncoincidence FDG imaging Therefore it is not clear that a "standard" method of acquisition could be determined at this time. Both gamma camera coincidence systems and 511-keV SPECT systems may well play a role in future cardiac FDG viability measurements. When a larger clinical experience has been gained, the development of guidelines for these modalities may prove worthwhile.

SPECT is often used instead of, or in addition to, PET in order to evaluate myocardial perfusion. Guidelines for SPECT perfusion imaging have been published previously.[11] It should be noted that if thallium 201 or technetium 99m SPECT perfusion scanning has been performed, usually no waiting period is necessary (from an instrumentation point of view) before the PET scanning is begun. The photons from Tl-201 and Tc-99m do not interfere with most modern multidetector PET scanner acquisitions. On the other hand, after administration of a PET tracer, it is usually necessary to wait at least 15 or more half-lives (depending on dose) before a low-energy (eg, Tl-201 or Tc-99m) scan is performed. This is because the 511-keV photons from the PET tracers easily penetrate the collimators most commonly used for Tl-201 or Tc-99m imaging.

A. PET FDG "METABOLISM" (UPTAKE) SCANS WITH DEDICATED MULTICRYSTAL PET SCANNERS

Tables 1 and 2 summarize the recommended guidelines for performing FDG scans with dedicated, multicrystal PET cameras, as part of an assessment of myocardial viability. Table 1 summarizes the patient preparation and method of FDG administration. Table 2 discusses the image acquisition.

A1. Patient Preparation

Introduction to Tables 1A and 1B. FDG uptake, combined with a PET or SPECT perfusion measurement, has been well validated as a measure of myocardial viability (see Part 2 of these guidelines). The physiology is complex, but in overview, because FDG metabolism is an adenosine triphosphate–dependent process, uptake of FDG requires viable myocardial cells. One difficulty with this approach is that myocardial cells utilize a variety of substrates to meet their energy needs. Typically about two thirds comes from fatty acid consumption and only about one third from glucose. Therefore, whereas uptake of FDG indicates viability, lack of uptake could either indicate nonviable tissue or indicate viable tissue that was utilizing substrates other than glucose. For this reason, every effort is made to force the myocardium to utilize only, or at least primarily, glucose to meet its energy needs by stimulating a natural insulin response. This is usually accomplished by having the patient fast for at least 6 hours and then administering a standardized glucose load, either orally or intravenously. The approach is outlined in Table 1A.

Table 1A. FDG cardiac PET: Patient preparation guidelines—An overview

Procedure		Technique	For details, see note(s) in text (No.)
Fasting period	Step 1: Fast patient		1
	6-12 h	Preferred	1
	4-<6 h	Suboptimal	1
	Step 2: Check blood glucose and then glucose load (choose one of the following 4 options)		
Oral glucose load	**Option 1:** Oral glucose loading		
	IF: Fasting BG <~110 mg/dL	Standard	1, 2, see Table 1B
	AND: No known diabetes		
	THEN: (1) Oral glucose load: typically 25-100 g orally (see Table 1B)		
	(2) Monitor blood glucose (see Table 1B)		
	IF: Fasting BG>~110-130 mg/dL	Suboptimal	1, 2, 4, 5
	OR: Known diabetes		
	THEN: Oral glucose loading alone may be suboptimal. See Table 1B or either IV protocol for suggestions on proceeding		
	OR		
IV, protocol A	**Option 2:** Hyperinsulinemic/euglycemic IV clamp	Optimal	
	For details, see sample protocol A		4
	OR		
IV, protocol B	**Option 3:** Dextrose IV infusion		5
	For details, see sample protocol B		
	OR		
	Option 4: Acipimox		
Acipimox	Acipimox 250 mg orally (see reference in note 3 for details). Not available in United States		3
	Step 3: Administer FDG		
FDG injection	Time: dependent on which option was selected	Standard	Table 2, item 1
	Administer FDG intravenously. See Table 2, item 1 for details		
	Step 4: Begin imaging		
Begin PET imaging	Time 60-90 min after FDG injection: start imaging		See Table 2
	See Table 2		

Table 1B. Guidelines for BG maintenance (eg, after oral glucose administration) for optimal FDG cardiac uptake BG ~100-140 mg/dL at FDG injection time

45-60 min after administration BG	Possible restorative measure	Technique	For details, see notes in text (No.)
130-140 mg/dL	1 unit regular insulin	Standard	1, 2
140-160 mg/dL	2 units regular insulin		
160-180 mg/dL	3 units regular insulin		
180-200 mg/dL	5 units regular insulin		
>200 mg/dL	Notify physician		

There are several approaches to administration of glucose. The situation is more complicated should the patient be diabetic, not achieve a sufficiently low fasting blood glucose (BG) level, or have too high a BG level after glucose administration. There are a variety of methods to deal with these situations. Table 1B discusses several options should BG values not reach the desired ranges. In addition, two sample intravenous (IV) protocols (protocol A and protocol B) are given below. These protocols illustrate some of the various possible approaches to IV glucose loading and BG level control. Some of the glucose loading methodologies are easily implemented in standard nuclear medicine facilities, whereas others may be more elaborate than some facilities feel comfortable with performing on a routine basis. The reader is urged to examine Tables 1A and 1B and the two sample protocols and to use them as a guide to developing an approach that will be feasible in his or her own setting.

Notes for Table 1: Patient preparation.

1. Myocardial substrate utilization. FDG is an analog of glucose allowing noninvasive evaluation of glucose metabolism. As mentioned in the introduction to Table 1, the myocardium can use several other substrates for energy production as well, most notably, fatty acids. How much of each substrate is used depends on a variety of factors including hormonal status and availability of the substrates. For these reasons, in the fasting state the distribution of FDG is often quite heterogenous, even in the normal myocardium. For evaluation of myocardial viability with FDG, the substrate and hormone levels in the blood need to be pushed to favor utilization of glucose by the myocardium.[2,12] This is usually accomplished by loading the patient with glucose after a fasting period of at least 6 hours to induce an endogenous insulin response. A shorter fasting time may depress this physiological response. The most common method of glucose loading is with an oral load of 25 to 100 g, but IV loading is also used and has some advantages (as described in detail in the two sample protocols below). Either can be adequate for nondiabetic patients, if the BG level falls sufficiently (see Table 1B for details) before FDG injection. The IV route avoids potential problems due to variable gastrointestinal absorption times or inability to tolerate oral dosage. Note that if the patient is taking medications that may either antagonize or potentiate the effects of insulin, these should be taken into account by the physician.

2. Diabetic patients. Diabetic patients pose a challenge, either because they have limited ability to produce endogenous insulin or because their cells are less able to respond to insulin stimulation. For this reason, the simple fasting/oral glucose-loading paradigm is often not effective in diabetic patients. Unfortunately, coronary artery disease is a complication of diabetes and sometimes patients are evaluated for coronary artery disease before a diagnosis of diabetes has been established. The methods used for loading nondiabetic patients with glucose have been modified to optimize myocardial glucose utilization in diabetic patients with variable success. Oral glucose loading usually results in suboptimal image quality in most diabetic patients, although some image improvement can be seen by waiting 2 to 3 hours after injection before imaging (at the expense of increased decay of the radiopharmaceutical FDG). The reference method is the euglycemic hyperinsulinemic clamp,[13] a rigorous and time-consuming procedure, allowing regulation of metabolic substrates and insulin levels and providing excellent image quality in most patients,[14] especially in those with non–insulin-dependent diabetes mellitus. A shorter IV glucose/insulin loading procedure (30 minutes) has also been used with some success.[18]

3. Acipimox. Acipimox is not currently available in the United States but has been used successfully in Europe. Acipimox is a nicotinic acid derivative inhibiting peripheral lipolysis, reducing plasma free fatty acid levels and indirectly stimulating myocardial glucose utilization.[16,17]

Two sample IV protocols.

4. Protocol A. A sample protocol for IV glucose loading is presented. This protocol is based on one in use at Vanderbilt University Medical Center, Nashville, Tenn, and is adapted from Martin et al.[15]

4.1. IV glucose/insulin loading for nondiabetic patients and fasting BG is less than 110 mg/dL:
- 4.1.1. Prepare dextrose/insulin solution: 15 units of regular insulin in 500 mL of 20% dextrose in a glass bottle. The initial 50 mL is discarded through the plastic IV tubing (no filter) to decrease adsorption of the insulin to the tubing.
- 4.1.2. Prime the patient with 5 units of regular insulin and 50 mL of 20% dextrose (10 g) IV bolus.
- 4.1.3. Infuse dextrose/insulin solution at a rate of 3 $mL \cdot kg^{-1} \cdot h^{-1}$ for 60 minutes (corresponding to an insulin infusion of 1.7 $mU \cdot kg^{-1} \cdot min^{-1}$ and a glucose infusion of 10 $mg \cdot kg^{-1} \cdot min^{-1}$). Monitor BG every 10 minutes (goal BG = 100-200 mg/dL).
- 4.1.4. If BG at 20 minutes is 100 to 200 mg/dL (preferably $<$150 mg/dL), administer FDG intravenously.
- 4.1.5. If BG is greater than 200 mg/dL, administer small IV boluses of 4 to 8 units of regular

insulin until BG decreases to less than 200 mg/dL. Administer FDG intravenously.

4.1.6. Stop dextrose/insulin infusion at 60 minutes and start 20% dextrose at 2 to 3 mL · kg^{-1} · h^{-1}.

4.1.7. During image acquisition, continue infusion of 20% dextrose at 2 to 3 mL · kg^{-1} · h^{-1}.

4.1.8. At completion of the acquisition of the images, discontinue infusion and feed a snack to the patient and advise re: risk of late hypoglycemia.

4.1.9. ALERT: (1) If BG is greater than 400 mg/dL, call the nuclear physician immediately. (2) If BG is less than 55 mg/dL or if the patient develops symptoms of hypoglycemia with BG less than 75 mg/dL, discontinue dextrose/insulin infusion and administer one amp of 50% dextrose intravenously and call the nuclear physician.

4.2. IV glucose/insulin loading for diabetic patients or fasting BG greater than 110 mg/dL:

4.2.1. Prepare insulin solution: 100 units of regular insulin in 500 mL of normal saline solution in a glass bottle. The initial 50 mL is discarded through the plastic IV tubing (no filter) to decrease adsorption of the insulin to the tubing.

4.2.2. Prime patient with regular insulin:

4.2.2.1. If fasting BG is greater than 140 mg/dL, prime the patient with 10 units of regular insulin IV bolus.

4.2.2.2. If fasting BG is less than 140 mg/dL, prime the patient with 6 units of regular insulin IV bolus.

4.2.3. Infuse insulin solution at a rate of 1.2 mL · kg^{-1} · h^{-1} for 60 minutes (corresponding to an insulin infusion of 4 mU · kg^{-1} · min^{-1}).

4.2.4. After 8 to 10 minutes or when BG is less than 140 mg/dL, start 20% dextrose infusion at 1.8 mL · kg^{-1} · h^{-1} (corresponding to a dextrose infusion of 6 mg · kg^{-1} · min^{-1}).

4.2.5. Monitor BG every 5 to 10 minutes and adjust dextrose infusion rate to maintain BG at 80 to 140 mg/dL.

4.2.6. After 20 to 30 minutes of stable BG, administer FDG.

4.2.7. Maintain the IV insulin + 20% dextrose infusion for 30 minutes after FDG injection.

4.2.8. At completion of the acquisition of the images, discontinue infusion and feed a snack to the patient and advise re: risk of late hypoglycemia.

4.3. For lean patients with Type I juvenile-onset diabetes mellitus, alter protocol 4.2 as follows:

4.3.1. If fasting BG is less than 140 mg/dL, inject 4 units of regular insulin and infuse insulin solution (prepared as in 4.2.1 above) at 0.3 mL · kg^{-1} · h^{-1} (1 mU · kg^{-1} · min^{-1}).

4.3.2. After 8 to 10 minutes of infusion or when BG is less than 140 mg/dL, start 20% dextrose at 2.4 mL · kg^{-1} · h^{-1} (8 mg · kg^{-1} · min^{-1}).

5. Protocol B. A sample protocol for IV glucose loading is presented. Protocol B is based on the protocol in use at the Emory University–Crawford Long Memorial Hospital (Atlanta, Ga). An abstract describing this protocol has been published.[18] This protocol has been used in over 600 subjects (over one third of whom were diabetic), resulting in good-quality images in over 98% of studies.

5.1. If fasting BG is less than 125 mg/dL, give 50% dextrose in water (D-50-W), 25 g, intravenously. SoluCortef (hydrocortisone), 20 mg, should be added to the D-50-W to minimize the rather severe pain that can occur at the injection site with D-50-W. This is compatible and avoids the pain that limits patient cooperation. There is no negative effect on the quality of the FDG studies.

5.2. If fasting BG is between 125 and 225 mg/dL, give D-50-W, 13 g, intravenously.

5.3. If fasting BG is greater than 225 mg/dL, administer regular aqueous insulin as per the following formula:

Regular aqueous insulin Dose units = (BG − 50)/25.

5.4. After 30 to 60 minutes, if BG is less than 150 mg/dL, give FDG intravenously; but if BG is greater than 150 mg/dL, give more regular insulin, using the formula in 5.3 above, until BG is less than 150 mg/dL, before giving FDG. Giving FDG when BG is 150 to 200 mg/dL resulted in many poor-quality studies.

A2. FDG Cardiac PET Acquisition Parameters

Acquisition parameters for PET cardiac FDG imaging are itemized in Table 2 and its attached notes.

PET scanner instrumentation and design are continually evolving. New crystal materials LSO and GSO (lutetium oxyorthosilicate and gadolinium oxyorthosilicate, respectively) are now available. These crystals have higher light output and shorter dead time than the conventional BGO (bismuth geimanate) crystals but have reduced stopping power for 511-keV photons. Some manufacturers have included LSO- and GSO-based systems alongside their conventional BGO systems. In certain applications (eg, 3-dimensional [3D],

Table 2. FDG cardiac PET: Acquisition guidelines (for dedicated, multicrystal PET scanner)

Feature		Technique	For details, see note in text (No.)
Dose	5-15 mCi (185-555 MBq)	Standard	1
Image start time	45-60 min after injection (keep constant for repeat studies)		2
Image duration	10-30 min (depending on count rate and dose)		3
Acquisition modes	2D	Standard	4
	3D	Optional	4
	Static	Standard	4
	Dynamic	Optional	4
Total counts	Knowledge of machine performance characteristics (eg, noise equivalent counts) is essential.		5
Pixel size (reconstructed)	2-3 mm	Preferred	6
	4-5 mm	Optional	6
Attenuation correction	Measured attenuation correction: Simultaneous or immediately after scan	Preferred	7
	Segmented attenuation correction	Optional	7
Reconstruction method	FBP or iterative expectation maximization (eg, OSEM)	Standard	8
Gating	Electrocardiographic gating of myocardium	Optional	9
Patient positioning	Arms out	Preferred	10
	Arms in	Optional	10

septa-out imaging) systems with these new crystals may offer improved performance over conventional 2-dimensional (2D) (or 3D) BGO systems. In addition, changes in electronics, crystal/photo multiplier (PM) tube arrangements, and scatter and randoms corrections recently have been used to improve the performance of BGO-based machines in 3D mode. Designing a machine always involves making choices and tradeoffs between various machine characteristics (eg, sensitivity and scatter). As a result, there are variations in scanner characteristics between various models of machine from the same manufacturer, as well as between manufacturers.

Therefore Tables 2, 3, and 4 should only be taken as guides to appropriate image acquisition, not as representing hard-and-fast rules. This is especially true when assessing 3D versus 2D acquisitions, as well as when determining the appropriate number of total true events necessary to create a "good" quality image. It is critical for the user to have a good understanding of the characteristics of his or her PET scanner (eg, plots of noise equivalent counts vs activity concentration, dead-time and randoms measurements, scatter fraction) in order to know how the machine will behave under the circumstances of cardiac imaging. See, for example, "Performance Measurements of Positron Emission Tomographs," NEMA Standards Publication NU2-2001 (National Electrical Manufacturers Association, 2101 L Street, NW, Washington, DC 20037).

Notes for Table 2. I. Image Acquisition

1. Dose: Typically, 5 to 15 mCi is injected in a peripheral vein (see counts requirements below). Injection speed is not critical (bolus to 2 minutes). To reduce patient dose to the bladder, patients should be encouraged to void frequently for 3 to 4 hours after the study.
2. Wait a minimum of 45 minutes before starting the static scan. Uptake may continue to increase and blood pool to decrease as time progresses, even after 45 minutes. Longer than 90 minutes may give better blood pool clearance and uptake, when necessary (eg, diabetic or high BG subjects), but could result in reduced count rate. If a follow-up FDG PET study is envisioned, it is important to duplicate the timing of the scan. Note that because FDG uptake is time-dependent (ie, it is possible that uptake may continue beyond 60 minutes), comparing two scans acquired at different postinjection acquisition times can be misleading.
3. Duration is typically 10 to 30 minutes. If acquired in 3D (ie, septa-out), compared with 2D with the same machine, a smaller dose is typically required to

achieve the same total count rate, but imaging time may or may not be reduced, as a result of count rate limitations and increased scatter (see 4 below). In some machines, beyond a certain dose, septa-out mode (3D) will actually produce poorer-quality images for the same dose and imaging time than septa-in (2D) mode. For this reason, it is critical to have fully characterized the performance of the system (see 4 below).

4. Two-dimensional versus three-dimensional acquisition: Three-dimensional acquisition (ie, septa-out) is, in principle, many times more sensitive than 2D (septa-in). However, this often is only true at low doses. Randoms, dead time, and scatter can greatly reduce the effective sensitivity of 3D acquisitions, and at the usual 2D doses (typically 10 mCi), 3D acquisitions can (depending on the scanner characteristics) actually produce poorer-quality images than 2D for the same imaging time. Therefore in the past 3D has often only been used when the dose must be minimized (eg, in normal volunteers, in children, or when multiple studies are planned). The 3D acquisition is an option that should be considered only by those institutions that are able to carefully monitor and assess randoms, dead time, and scattered events. Note that 3D imaging may be more practical with the advent of LSO- and GSO-based PET scanners and even with BGO scanners with new-generation optimized PM/crystal coupling schemes and high-speed electronics. Still, the use of 3D cardiac imaging with these new-generation machines remains to be fully characterized. Use of 3D is highly dependent on the ability to minimize and accurately correct for dead time, randoms, and scatter. Typically, there is much greater scatter with 3D (ie, septa-out) operation than with 2D (septa-in) operation, for all crystal types. The newer crystals (LSO or GSO) and newer-generation electronics (with BGO) may in principle permit reduction of randoms and dead time and therefore may permit shorter imaging time to be achieved. The degree to which any of these improvements can be achieved in practice for cardiac imaging remains unknown at this writing. Scatter remains much higher in 3D than in 2D mode even for new-generation 3D machines. The user must carefully evaluate plots of noise equivalent counts and other system parameters to determine the optimum dose of FDG in 3D mode. Note that some new scanners only permit septa-out operation.

   Static versus dynamic acquisition: Static acquisition produces images that allow relative quantification of FDG uptake on a regional basis. Such images (along with perfusion images) are the standard basis for making viability determinations.[1-3] However, there is one form of dynamic imaging that has a significant practical advantage. Consider what is normally the 10- to 30-minute duration static scan, begun around 60 minutes after injection. It is clinically desirable to acquire these data as a 3- or more frame dynamic data set. If the patient should move during the end of the study, one can then utilize only those dynamic frames with no motion (summing them together to make one static image). This is easily implemented and takes almost no additional operator time. A more elaborate dynamic acquisition may optionally be used when FDG kinetic analysis over the entire uptake period is to be performed (eg, compartmental analysis or Patlak analysis). Kinetic analysis permits absolute quantification of the rate of FDG utilization. Performing and interpreting such kinetic analyses[19] can be complex and requires experience with kinetic modeling.

5. The counts per slice necessary to yield adequate-quality images will vary from institution to institution depending on, among other things, scatter and randoms corrections, as well as the amount of smoothing that is done. If one tries to achieve on the order of 7 mm full width at half maximum (FWHM) in-plane resolution and has 10% to 15% scatter (National Electrical Manufacturers Association), then a typical good-quality study in 2D might have on the order of 50,000 true counts per millimeter of transaxial distance over the region of the heart (eg, for a 4.25-mm slice separation, the counts would be $50{,}000 \times 4.25 = 250{,}000$ counts per slice). These numbers are very approximate and may differ from one scanner type to the next. With a 10-mCi injected dose, these total counts could be achieved in 20 to 30 minutes depending on system sensitivity. If one is willing to accept a lower resolution (eg, more smoothing) or more noise, imaging time can be reduced. For a description of 2D versus 3D acquisition mode to reduce scanning time, see note 4 above. Low uptake and high blood pool activity situations (eg, diabetes or high glucose levels) may require longer imaging time and/or (preferably) later imaging times.
6. It is recommended that 2 to 3 mm per pixel be used. A “rule of thumb” in nuclear medicine physics is that one needs at least 3 pixels for every FWHM of resolution in the image. For example, if the data are reconstructed to 8 mm FWHM, then one needs roughly 8 mm/3 = 2.7 mm/pixel. Many institutions achieve a 3-mm or better sampling rate with a 256×256 array over the entire field of view of the camera. Other institutions choose to use a 128×128 array over a limited field of view (eg, 25 to 35 cm

diameter) centered over the heart, in which case, 2 to 3 mm/pixel is easy to achieve (cutting out extraneous structures in the field of view) even with a 128 × 128 array. Either method is acceptable to achieve the desired 2 to 3 mm/pixel. Greater than 3 mm/pixel may be acceptable for older PET cameras with resolution worse than 1 cm.

7. Attenuation correction is a far more severe problem in coincidence imaging than in SPECT imaging[20]; it is therefore essential that accurate attenuation correction be performed. Note that segmented attenuation correction schemes may give errors for those slices that contain a mixture of lung and liver tissue adjacent to the heart. Similarly, the ability of computed tomography–based attenuation correction to be used to image the heart (especially at the free wall/lung interface) will depend on the results of future research. An as-yet-unsolved problem with computed tomography attenuation correction for the heart is the effect of respiration, which can severely influence apparent free wall uptake.
8. Filtered backprojection versus iterative reconstruction method: Filtered backprojection (FBP) is the standard method used for reconstruction. FBP images are subject to streak artifacts, especially when too short a transmission scan is used for attenuation correction (or when the subject is obese or large). This can affect visual analysis but usually does not adversely affect quantitative analysis with regions of interest (the streaks tend to average out properly over typical volumes of interest). Iterative methods (eg, the method of ordered-subset expectation maximization [OSEM]) have been adopted in other FDG imaging situations (eg, oncology), yielding images with better noise properties. Although high uptake structures, such as the heart, may not improve their noise characteristics with OSEM, the surrounding lower uptake structures do improve, and streak artifacts are nearly eliminated, thus greatly improving the visual appearance of the image. However, low uptake areas (such as myocardial defects and the left ventricular cavity at late times) may have slightly (artificially) elevated activity levels unless sufficient iterations are performed. It is recommended that one thoroughly characterize the PET machine and its reconstruction algorithm's behavior with a realistic cardiac phantom.
9. Usually, FDG PET counts are sufficiently large to yield a high-quality ventricular motion study (typically 8-16 time points), in a manner similar to SPECT gated perfusion studies (but at higher spatial resolution). Given that ventricular contraction and thickening are often clinically useful for assessing viability, gating should be performed when possible. It is important that the gating software does not adversely affect the ungated images (eg, by loss of counts as a result of beat length rejection). Monitoring the length and number of the accepted beats is highly desirable.
10. Ideally, the patient should be positioned supine, with arms out of the camera field of view. This can be tolerated by nearly all patients, provided some care is given to support of the arms or by use of an overhead bar to hold onto. There are, however, cases in which "arms-out" imaging is not possible (eg, in patients with severe arthritis), and imaging must be performed with the arms at the side. In this case the transmission scan time may have to be increased, and it is of critical importance that the arms not move between transmission and emission or artifacts will result.

B. PET PERFUSION SCANS: N-13 AMMONIA AND Rb-82

Most of the literature about viability and prediction of recovery after revascularization with PET is based on mismatch perfusion/metabolism (see Part 2 of these guidelines). N-13 ammonia and Rb-82 are PET tracers of perfusion and provide optimal perfusion images for comparison because the images are acquired with the same PET system and can be displayed with similar parameters as the FDG images. However, if these PET perfusion agents are not available, the FDG images can be interpreted in conjunction with SPECT perfusion images (see Part 2 below). In addition, these tracers, especially Rb-82, can be used alone to assess perfusion.

Note that this document does not address methods for performing stress studies (eg, protocols for administration of pharmacologic stress agents). These protocols are, for the most part, generic for all perfusion agents (see, for example, the guidelines for myocardial perfusion stress protocols, published by the American Society of Nuclear Cardiology[21]). The specific differences for N-13 ammonia or Rb-82 imaging are related to the duration of uptake and clearance by these radiopharmaceuticals, and both these factors are mentioned below.

B1. N-13 Ammonia Acquisition Protocol

Introduction to Table 3. Table 3 summarizes the recommended guidelines for performing N-13 ammonia perfusion scans with dedicated, multicrystal PET cameras, as part of an assessment of myocardial viability or in its own right. N-13 ammonia is a valuable agent for measuring either absolute or relative myocardial blood flow.[4,5,7,9,10] For measurements of absolute flow, dynamic acquisition from the time of injection is required,

Table 3. N = 13 ammonia cardiac perfusion studies

Feature		Technique	For details, see note in text (No.)
Patient preparation	Overnight fast (>6 h)	Preferred	
	No caffeine or caffeinated beverages for 24 h	Preferred	
	No theophylline-containing medications for 48 hours	Preferred	
Dose	10-20 mCi (typical) (370-740 MBq)	Standard	1
	Bolus or <30-s infusion	Preferred	1
Imaging acquisition	Static	Standard	
	Start time: 1.5-3 min after end of infusion	Standard	2
	Duration: 5-15 min	Standard	3
Pixel size (reconstructed)	2-3 mm	Preferred	4
	4 mm	Optional	
Attenuation correction	Measured attenuation correction: immediately before scan	Standard	5
	Measured attenuation correction: immediately after scan	Optional	5
Reconstruction method	FBP or iterative expectation maximization (eg, OSEM)	Standard	4
Gating	Electrocardiographic gating of myocardium	Optional	6
Patient positioning	Arms out	Preferred	7
	Arms in	Optional	7

followed by fitting to one of several possible physiologic models. Absolute flow measurements will not be discussed here, because they are performed primarily in a research setting. Relative perfusion measurements, described below, are often used clinically (with FDG) in the determination of viability. See also the introduction to Table 2 above. Methods for normalizing and interpreting these scans are discussed in Part 2 below.

Notes for Table 3.

1. Uptake is relatively rapid (typically complete in 90 seconds), and radioactive decay (10-minute half-life) is fast. Typically uptake images are acquired no sooner than about 90 seconds after the end of infusion. Therefore a very slow infusion will require static imaging to be delayed, potentially resulting in count loss because of the 10-minute half-life. Large patients may benefit from higher (25-30 mCi) doses.
2. The static image should not include the initial rapidly changing uptake portion of the study. Therefore a minimum of 90 seconds should typically elapse between the end of infusion and the beginning of the static scan. In fact, the arterial blood concentration of ammonia is often still quite significant even at 90 seconds after a rapid bolus injection. Nonetheless, many published data are based on only a 90-second delay before the start of imaging.
3. After an initial period of rapidly changing activity levels during the uptake period, the decay-corrected ammonia concentration subsequently usually changes only very slowly. However, the 10-minute N-13 half-life makes acquisition durations longer than 20 minutes of limited value unless total counts are very low.
4. It is desirable to keep reconstruction parameters similar to those used for the FDG portion of the viability study (see notes for Table 2) in order that perfusion and metabolism are affected by reconstruction parameters in the same way. This permits more accurate comparison between the two image sets.
5. Measured attenuation is preferred. Either prescan or postscan is satisfactory, providing it has been verified that the user's attenuation correction software can adequately correct for residual emission activity. Attenuation correction simultaneous with emission scan is not recommended unless data become available to indicate the high count rate, rapidly changing distribution of the isotope will not adversely affect the transmission scan. See notes on attenuation correction in Table 2.
6. If myocardial contraction information is desired, the FDG portion of the study is likely to give a higher-quality gated image. If stress ammonia scans are anticipated, it is indeed possible to achieve sufficiently high-quality gated ammonia scans to evaluate wall motion (and probably ejection fraction, although the latter remains to be validated).
7. Ideally, the patient should be positioned supine, with the arms out of the camera field of view. This can be tolerated by nearly all patients, provided some care is

given to a method to support the arms. Alternatively, an overhead bar has often been used as a hand-hold for arm support. In those very few cases in which arms-out positioning is not possible (eg, patients with very severe arthritis), the arms can be in the field of view. In this case the transmission scan time may have to be increased, and it is of critical importance that the arms not move between transmission and emission, or artifacts will result. Note that when performing ammonia/FDG perfusion/metabolism studies, it is best to keep patient positioning similar for both studies.

B2. Rb-82 Perfusion Acquisition Protocol

Introduction to Table 4. Table 4 summarizes the acquisition parameters necessary to acquire an Rb-82 perfusion study with a dedicated PET camera.[5,10] See the introduction to Table 2 for further comments about machine performance requirements.

Notes for Table 4.

1. Scout scanning: Scout scanning is recommended before each injection to ensure that the patient is correctly positioned and is not unnecessarily exposed to radiation. This can be done with a fast transmission image or with a low-dose Rb-82 injection (10-20 mCi). Note that the scout scan can also be used to estimate circulation and cardiac blood pool clearance times, which assist in selection of the optimum injection to imaging delay time (see 3 below).
2. General dose considerations: In determining appropriate patient dosages,[6] the following issues should be considered: (1) Patient exposure is typically low relative to SPECT because of the short half-life of the isotope. (2) Staff exposure is typically high because of the limited effectiveness of shielding and the higher dosages used in Rb-82 PET. (3) Three-dimensional imaging requires less dosage than 2D imaging because of the improved sensitivity of the system; however, the dead time of the camera may not allow one to utilize improved sensitivity. (4) Newer imaging crystals (LSO and GSO) allow imaging at higher count rates, as does new generation of electronics coupled with BGO systems. Count rate issues are especially critical to Rb-82 imaging. Important note: See 2D versus 3D notes to Table 2. For Rb-82 imaging, 3D imaging, even with new-generation scanners, must be used with care.
3. Rest imaging time: Rest imaging should be performed before stress imaging to reduce the impact of residual stress effects (eg, stunning, steal). About 80% of the useful counts are acquired in the first 3 minutes; 95% of the useful counts are obtained in the first 5 minutes, and 97% are obtained in the first 6 minutes. The patient should be infused with Rb-82 for a maximum of 30 seconds. After the dose is delivered, patients with normal ventricular function (left ventricular ejection fraction [LVEF] $>50\%$) are typically imaged starting 70 to 90 seconds after the injection. For those with reduced ventricular function (LVEF 30%-50%), imaging usually is begun 90 to 110 seconds after termination of the infusion, and those with poor function (LVEF $<30\%$) are typically imaged at 110 to 130 seconds. These times can be estimated from observations of the scout scan. Ideally, patients should be imaged by a dynamic acquisition to allow for retrospective removal of phases that have Rb-82 in the blood pool. Electrocardiographic gating can also be used with Rb-82. Images can be acquired by 2D or 3D imaging modes (but see 2D vs 3D notes to Table 2 above).
4. Rest transmission imaging: Rb-82 myocardial perfusion should only be performed with attenuation correction.[20] Two techniques are typically used for creating the transmission maps: direct measurement of patient attenuation and segmentation of patient-specific attenuation maps. The latter are relatively insensitive to noise but are very dependent on the quality of the program used for performing the transmission scan segmentation and are influenced by lung attenuation inhomogeneities (eg, partial volume effects from liver). Transmission data are typically performed sequentially, so it is essential that the patient remain still between transmission and emission images.
5. Stress testing: The long infusion time for Rb-82 and slow uptake require some modifications to conventional stress testing. On average, the patient must remain at peak stress for somewhat longer than conventional SPECT-based radionuclide stress testing. The radionuclide should be injected in a manner such that all of the Rb-82 is taken up in the stress state. See previously published guidelines for further information on pharmacologic agents for stress testing.[21]
6. Stress transmission imaging: These images should be acquired while the patient is at the peak of stress. If the patient cannot tolerate this or if the stress testing protocol will not allow this, the technologist and physician must carefully inspect the transmission and emission data sets to ensure that they are properly registered in the transaxial, sagittal, and coronal planes.
7. Processing protocol: Several corrections are required for creating data sets that can be used for reconstruction. Rb-82 data must be corrected for randoms,

Table 4. Rb-82 rest/stress myocardial perfusion imaging guideline

Feature			For details, see note in text (No.)
3D dose: BGO systems	10-20 mCi (370-740 MBq)	Optional	1
2D dose: BGO systems	30-50 mCi (1110-1850 MBq)	Standard	1
3D dose: LSO/GSO systems	30-40 mCi (1110-1480 MBq)	Optional	1
2D dose: LSO/GSO systems	40-60 mCi (1480-2220 MBq)	Standard	1
Patient positioning	Use scout scan: 10-20 mCi Rb-82 (370-740 MBq)	Preferred	2
	Use transmission scan	Optional	2
Injection rate	Bolus of ≤30 s	Standard	
Imaging time	3-6 min		3
Imaging delay after injection	LVEF >50% = 70-90 s LVEF <50% = 90-130 s	Standard	3
Imaging mode	Phased/dynamic	Standard	3
Rest attenuation correction	Measured attenuation correction, before or after	Standard	4
Stress testing	Pharmacologic agents	Optional	5
Stress attenuation correction	Measured attenuation correction, must be performed during stress to ensure image registration	Standard	6
Reconstruction method	FBP or iterative expectation maximization (eg, OSEM)	Standard	7
Reconstruction filter	Butterworth or low-pass filter (band-pass filters not recommended) 10-15 mm kernel	Standard	7
Pixel size (reconstructed)	2-3 mm	Preferred	7

scatter, dead time, attenuation, and decay before reconstruction can begin. Once these corrections are applied, the data can be reconstructed with either FBP or iterative algorithms. For viability studies, it is often desirable to match the resolution of the FDG and the perfusion (Rb) agent, although this is less critical when the data are divided into 8 or fewer sectors per short-axis slice and comparisons made on a sector-by-sector basis. For rest/stress comparisons, the rest/stress must have matched resolution. Filtering with FBP, or additional filtering of the OSEM (eg, Butterworth, Hanning, Gaussian), is usually necessary to achieve adequate noise properties. Again, care must be taken to match reconstructed resolution when making pixel-by-pixel comparisons of perfusion and metabolism.

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