

Society of Nuclear Medicine Procedure Guideline for FDG PET Brain Imaging

Version 1.0, approved February 8, 2009

Authors: Alan D. Waxman, MD; Karl Herholz, MD; David H. Lewis, MD; Peter Herscovitch, MD; Satoshi Minoshima, MD; PhD, Masanori Ichise, MD; Alexander E. Drzezga, MD; Michael D. Devous, Sr., PhD; James M. Mountz, MD, PhD

I. Purpose

The purpose of this guideline is to assist nuclear medicine practitioners in recommending, performing, interpreting, and reporting the results of F-18FDG brain metabolic imaging.

II. Background information and definitions

- A. The document considers the work of previous guideline organizations such as the German Inter Disciplinary Consensus Conference on Clinical Brain PET, The Austrian Guideline for the Use of FDG-PET in Neurology and Psychiatry, The Society of Nuclear Medicine Procedure Guidelines for Tumor Imaging Using F-18 FDG, The Society of Nuclear Medicine Brain Imaging Council and by individual experts throughout the world.
- B. In the brain, glucose metabolism provides approximately 95% of adenosine triphosphate (ATP) required for brain

function. Under physiological conditions glucose metabolism is tightly connected to neuronal activity. [18F]FDG is suitable for imaging regional cerebral glucose consumption with PET since it accumulates in neuronal tissue depending on facilitated transport of glucose and hexokinase mediated phosphorylation. Therefore changes in neuronal activity induced by disease are reflected in an alteration of glucose metabolism. [18F]FDG-PET is currently the most accurate in-vivo method for the investigation of regional human brain metabolism in health and disease states.

- C. The clinical use of [18F]FDG can be regarded as established for a number of diagnostic questions in neurology, neurosurgery and psychiatry. This information is often complementary to the anatomic detail provided by structural imaging techniques such as CT or MRI. However, functional impairment often

The Society of Nuclear Medicine (SNM) has written and approved these guidelines as an educational tool designed to promote the cost-effective use of high-quality nuclear medicine procedures or in the conduct of research and to assist practitioners in providing appropriate care for patients. The guidelines should not be deemed inclusive of all proper procedures nor exclusive of other procedures reasonably directed to obtaining the same results. They are neither inflexible rules nor requirements of practice and are not intended nor should they be used to establish a legal standard of care. For these reasons, SNM cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment about the propriety of any specific procedure or course of action must be made by the physician when considering the circumstances presented. Thus, an approach that differs from the guidelines is not necessarily below the standard of care. A conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in his or her reasonable judgment, such course of action is indicated by the condition of the patient, limitations on available resources, or advances in knowledge or technology subsequent to publication of the guidelines.

All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

Advances in medicine occur at a rapid rate. The date of a guideline should always be considered in determining its current applicability.

precedes structural changes, and may also exist alone. Thus PET imaging provides unique information that is often complementary to anatomic imaging information.

III. Procedure

A. Patient Preparation

1. Pre-arrival (Patient Instruction)
 - a. Patient should be fasting for 4 - 6 hours.
 - b. Oral hydration with water is encouraged.
 - c. Avoid caffeine, alcohol, or drugs that may affect cerebral glucose metabolism.
 - d. Required medications should be taken with water.
 - e. Intravenous fluid containing dextrose or parenteral feeding should be withheld for 4 – 6 hours.
 - f. Pregnancy and breastfeeding – See Society of Nuclear Medicine procedure Guidelines for general imaging.
2. Pre-injection
 - a. Environment – Should be stable for at least 30 minutes prior to FDG injection and in the subsequent uptake phase (at least 30 minutes).
 - (1) The patient should be placed in a quiet, dimly-lit room.
 - (2) Background noise is acceptable with eyes open.
 - (3) Alternatively, studies can be performed with eyes closed if this is being done consistently across comparable scans.
 - (4) The patient should be seated or reclining comfortably.
 - (5) Place intravenous access at least 10 minutes prior to injection to permit accommodation.
 - (6) Instruct the patient to relax, not to speak or read and to avoid major movements.
 - (7) Minimize interaction with the patient prior to, during, and up to at least 30 minutes post injection.
 - b. Blood Glucose - Should be checked prior to FDG administration.
 - (1) If greater than 150 - 200 mg/dL, most institutions reschedule the patient. When hyperglycemia is present, there is increased competition of elevated plasma glucose with FDG at the carrier enzyme and is often usually associated with high intracellular glucose and circulating insulin levels driving FDG into muscle resulting in reduced uptake in the brain.
 - (2) Lowering serum glucose by administration of insulin can be considered, but the administration of FDG should be delayed following insulin administration (with the duration of the delay dependent on the type and route of administration of insulin), probably because the correction of increased intracellular glucose levels lags behind the correction of the plasma glucose level.
 - (3) Best results for clinical FDG imaging of the brain in diabetics can be achieved in a euglycemic situation during stable therapeutic management.
 - c. Bladder
 - (1) Before the scanning procedure is started, the patient should void the bladder for maximum comfort during the study.
 - (2) Advise the patient to void again after the scanning session to minimize radiation exposure.
 - d. EEG
 - (1) For preoperative evaluation of epilepsy, continuous EEG recording is recommended.
 - (2) Monitoring should start ideally 2 hours before injection in order to ensure that FDG is not administered in a post-ictal

state and should be maintained at least until 20 minutes post-injection. For adequate image interpretation, it is important to be aware if seizures occurred prior to imaging.

B. Information Pertinent to Performing the Procedure

1. History

- a. A focused history should be obtained including any past or current drug use or head trauma, neurological examination, psychiatric exam, mental status exam (e.g. Folstein mini-mental examination or other neuropsychological test), memory impairment, stroke, TIA or epilepsy (type, location). History of brain tumor (type and location), prior brain operations including shunt procedures should also be noted.
- b. Recent morphologic imaging studies (e.g. CT, MRI or prior PET or SPECT brain studies).
- c. Current medications and when last taken. These would include anti-seizure medication, chemotherapy for brain tumors, anticholinesterase drugs for memory impairment in addition to psychotropic pharmaceuticals. These may

influence regional metabolic rate of glucose. If possible, centrally acting pharmaceuticals should be discontinued.

- d. History of diabetes, and knowledge of patient’s fasting state.
- e. Patient’s ability to lie still for the duration of the acquisition (30 minutes to 1 hour). If sedation is required (e.g. patients with Dementia or children), it should be performed after the uptake period prior to imaging.
- f. If sedation is necessary, it should be performed as late as possible following administration of FDG.

C. Precautions

1. Supervision

- a. Continuous supervision of patients during the procedure is important.
 - b. Actual interaction should be kept at a minimum to avoid the effects of functional activation on glucose metabolism.
 - c. Deviation from resting state during the uptake period and scanning needs to be recorded and considered when interpreting scans.
2. Pregnancy is a relative contraindication especially during the first trimester.
3. Refrain from breastfeeding for 24 hours.

D. Radiopharmaceuticals

Radiation Dosimetry in Adults

Radiopharmaceuticals	Administered * Activity MBq (mCi)	Organ Receiving the Largest Radiation Dose ** mGy per MBq (rad per mCi)	Effective Dose ** mSv per MBq (rem per mCi)
[F-18]-2-fluoro-2-deoxy-D-glucose	185 - 740 (5 – 20)	0.16 Urinary Bladder (0.59)	0.019 (0.070)

* Depends on equipment limitations, specific application and patient compliance.

Radiation Dosimetry in Children

Radiopharmaceuticals	Administered Activity	Organ Receiving the Largest Radiation Dose **	Wt adjust
			Effective Dose **
	MBq/ Kg (mCi)/Kg	mGy per MBq (rad per mCi)	mSv per MBq (rem per mCi)
[F-18]-2-fluoro-2-deoxy-D-glucose	5.18 – 7.4 (0.14 – 0.20)	0.32 Urinary Bladder (1.2)	0.050 (0.18)

* International Commission on Radiation Protection; Elsevier; 2000:49, ICRP Publication 80.

E. Image Acquisition

1. Depending on the clinical question and type of equipment available, FDG imaging may include:
 - a. Static limited field tomographic images.
 - b. Dynamic tomographic images.
 - (1) Multiple sequential images in a field of view, usually covering the whole brain.
 - (2) May be used when absolute quantification of regional metabolic rates of glucose is needed.
 - c. 2D Mode - Coincidence detection only between adjacent detector rings. Septa usually separate small groups of rings.
 - d. 3D-acquisition mode - Coincidence detection using all detector rings. No septa between rings.
 - e. For other dedicated PET-systems (i.e. sector tomographs), not based on full detector rings, equivalent acquisition modes are existent.
2. Scanners
 - a. State-of-the-art dedicated PET scanner
 - (1) A state-of-the art whole-body PET scanner consists of several full rings detectors BGO (Bismuth Germanate Orthosilicate) or LSO (Lutetium Orthosilicate) or GSO (Gadolinium Orthosilicate) or LYSO (Lutetium Yttrium Orthosilicate).
 - (2) Variations on the basic design include the partial ring BGO dedicated PET scanner and the dedicated PET scanner with six position-sensitive sodium iodide detectors.
 - b. Alternatives to dedicated PET scanners
 - (1) Gamma camera with 511 keV collimators imaging single scintillations. (not recommended)
 - (2) Dual-head gamma camera for coincidence imaging (no collimators). Extremely limited performance characteristics.
 - (3) CT-PET scanner: In this system a CT scanner is combined with the PET components of a full ring BGO/LSO/GSO/LYSO scanner. This makes it possible to have PET images corrected by CT attenuation data and concomitant co-registration of functional images from PET and morphological images from CT. This system is becoming the dominant choice due to manufacturing trends.
 - (4) Dedicated brain PET scanners – These specialized machines may have superior performance parameters when compared to full-body scanners and are mainly used for research applications.

Comparison of scanners is beyond the scope of this document. The performance of the coincidence scanner systems has been the subject of debate, especially with regard to their costs and diagnostic accuracy compared to dedicated PET scanners. Limitations include sensitivity, count rate, activity outside the field of view. At present the general opinion is that their clinical reliability is lower than that of full ring BGO/LSO/GSO/LYSO scanners. There is general agreement in the international nuclear medicine community that the standard for PET is the dedicated scanner with a full ring of BGO/LSO/GSO/LYSO detectors on the basis of its excellent physical and clinical performance and the extensive clinical experience in its application in brain studies worldwide. For this reason this procedure guideline will focus on these systems.

3. Limited-field tomographic images.

a. This static scan consists of an emission scan and a transmission scan.

(1) Emission scan

(a) The emission acquisition typically begins 30-60 minutes post injection and lasts between 5 and 60 minutes depending on the injected activity, the type of scanner and acquisition protocol used (2D or 3D).

(b) Adequate scans including attenuation correction can be completed in 5 minutes on a state of art PET/CT with 740 MBq FDG lower dose (185 MBq) slower systems may require additional time to acquire sufficient count density; most systems today use 3D acquisition. IF 2D acquisition is used, longer acquisition times are required to achieve

adequate count density.

(c) Scatter correction can be obtained by removal of non-coincidence events from the emission data.

(2) Transmission scan - Transmission imaging (images acquired with an external source):

(a) Cold transmission - the standard procedure for older generation full ring PET systems is the measurement of attenuation prior to FDG-injection. A Ge-68/68-Ga source is commonly used as an external source of radiation and serves to correct the subsequent emission scan for attenuation.

(b) Hot transmission - transmission imaging following FDG injection is less favorable with Ge-68/68-Ga because of the potential underestimation of attenuation of structures with high uptake, especially in sub-cortical regions.

4. Pre-Emission Attenuation Correction

a. The sequence of the two scans (scanning protocols) and the techniques for performing transmission scans vary according to the tomographic system available and be extremely time consuming.

b. Exact positioning of the patient's head is attempted by external markers, e.g. with the cross-shaped laser marking system available in some scanners.

(1) Patient cooperation is important (ability to lie still for approx. 30 minutes).

(2) If necessary, tools to aid immobilization (e.g. head elastic bands) may be used.

5. Post Emission attenuation correction

a. If a Cesium 133 or CT x-ray source

- is used, the attenuation may be done following FDG injection due to a high photon flux relative to emission data.
- b. Correction factors are obtained by measuring the ratio between a blank scan (performed without patient in scanner) and a transmission scan (performed with an external source when the patient is in position). Positional differences will result in major artifacts.
6. If repositioning of the patient is necessary, great care should be taken to minimize positional differences.
 7. Hybrid attenuation correction (attenuation map calculated from a transmission measurement followed by a segmentation image): These methods calculate an attenuation image based on a short transmission measurement followed by image segmentation.
 8. CT-based attenuation correction of the brain in PET/CT-scanners.
 - a. In CT-PET systems the photon attenuation correction is obtained by means of a measured correction matrix from a simultaneously assessed CT scan in line with PET
 - b. The CT map has to be transformed into a 511keV attenuation map by segmentation and absorption correction and forward projection of the data for use as attenuation correction data.
 9. Mathematical attenuation correction - estimated attenuation correction based on the emission data: Not commonly performed since post emission attenuation systems now commonly available.
 - a. Correction procedures estimating the attenuation based on the estimation of organ density from emission data (i.e. according to Chang).
 - b. Accurate skull attenuation lacking.
 - c. Shape contouring should be used if available.
 - (1) Contours should include scalp and not just grey matter.
 - (2) Contours should be defined for each individual transaxial slice.
 - (3) Correct shape and position of the contours should be reviewed prior to calculation of the corrected slices.
 - d. It is important to note that the different mathematical correction procedures lead to systematic differences in the resulting images, making images obtained with different correction procedures not directly comparable (e.g. with statistical subtraction analyses on a voxelwise basis).
 - e. Differences may appear especially in the occipital and cerebellar regions.
 - f. Measured attenuation correction is preferable to calculated specially if post emission techniques used.
 10. Dynamic studies
 - a. Dynamic studies consist of a sequence of serial images in a limited field, starting at the time of FDG administration and continuing for 60-90 minutes.
 - (1) The acquisition modalities for dynamic studies are only briefly mentioned here because they are not commonly used in clinical routine.
 - (2) This type of acquisition is used to quantitatively assess the regional rates of FDG metabolism by determining appropriate kinetic rate or influx constants.
 - (3) Determination of arterial input function is needed.
 - (4) Measurements of FDG and glucose plasma levels are required.
 - (5) A calibration factor between the scanner events and in vitro activity is needed and can be attained by phantom imaging.
 - (6) Simplified methods for calculation of regional metabolic rates of FDG using

static scanning and arteriolized venous blood sampling provides a compromise between full metabolic quantitation and quantitation of FDG uptake relative to a reference region in the brain.

F. Image Processing

1. Images are reconstructed in the form of transaxial 128 x 128 or 256 x 256 matrix size.
2. Typical pixel size is 2-4 mm.
3. Depending on the resolution of the PET system, a final image resolution may vary between 2.5 -10 mm FWHM. This typically yields adequate image resolution and signal to noise ratios.
4. For reconstruction using filtered back projection, commonly used filters are Hanning or Shepp-Logan.
5. Iterative reconstruction is increasingly being employed.
6. Processing of gamma camera coincidence detection data generally employs iterative reconstruction techniques.
7. Refer to camera manufacturer's recommendations for best choices of iterations, subsets, and smoothness.

G. Data Display

1. Reconstructed transverse images can be displayed for quality control and interpretation.
2. Additional re-sliced images in coronal and sagittal sections should be displayed routinely, which often helps better delineation of lesions.
3. Using volume re-slicing software, transverse slices are most commonly re-sliced to fit the bi-commissural line (the line passing through the anterior and posterior commissures, which can be approximated by the line passing through the anterior and posterior poles of the brain). Re-slicing along the hippocampal axis (parallel to the temporal lobe) is preferred for evaluation of suspected temporal lobe epilepsy. **

4. Re-slicing of reconstructed images helps achieve consistent orientation of the images for interpretation. Sagittal and coronal views along with axial projections are important in characterizing specific anatomic sites.
5. Volume rendering may be helpful for more accurate topographic orientation in some clinical applications. However, such display may also be subject to artifacts and must be used with caution.
6. 3D coregistration with MR structural data can facilitate anatomically accurate reporting.

H. Image Interpretation

1. The extent of normal variability must be appreciated during scan interpretation. Substantial variability may be noted between normal individuals and between scans of a single subject obtained at different times.
2. Individual clinics should obtain or be familiar with an appropriate normal database to best interpret patient studies.
3. Unprocessed projection images should be reviewed in cinematic display prior to viewing of tomographic sections.
4. Projection data should be assessed for the presence and degree of patient motion, target-to-background ratio and other potential artifacts.
5. Inspection of the projection data in sinogram form may also be useful.
6. Images should be viewed on a computer screen rather than from film or paper copy to permit interactive adjustment of contrast, background subtraction and color table.
7. Caution must be used in selecting levels of contrast and background subtraction.
8. Non-continuous color scales may be confusing or misleading if abrupt color changes occur in the range of expected gray matter activity.
9. Thresholding, if used, should be based upon knowledge of a normal database for FDG and instruments used in acquiring the study. Artifacts can be created when inappropriate thresholding

is performed.

10. Comparison of serial images to assess worsening or improvement requires appropriate normalization techniques to avoid artificially created differences. Differences in threshold settings, color or Grey scale windowing, SUVs of reference areas need to be minimized.
11. Three-dimensional renderings may be useful in appreciating overall patterns of disease.
12. Images should be evaluated with reference to recent anatomic brain images (CT or MRI). Specific attention should be paid to the extent of metabolic abnormalities relative to underlying morphologic defects as well as to the possible effects of atrophy and partial volume effect. Interpreters should be familiar with the document “Ethical Clinical Practice of Functional Brain Imaging” issued by the Ethical Subcommittee for Functional Brain Imaging, a subcommittee of the SNM Brain Imaging Council.

I. Quantitative Interpretation

1. Absolute Glucose Metabolism
 - a. A quantitative analysis can be performed when it is possible to calculate the curve of the arterial FDG concentration against time (arterial input function). It requires direct sampling of arterial blood (serial measurements). It is often combined with dynamic data acquisition, but can also be combined with static scanning.
 - b. Some non-invasive alternatives to arterial blood sampling have been studied:
 - (1) Arterialized venous blood sampling
 - (2) The input function can be retrieved from the PET images using the aorta, or left ventricle.
 - c. Rate constants can then be estimated

by compartmental modeling, or influx constants by graphical analytic approaches.

- d. Correction factors, including the so called “lumped constant” ($LC = 0.42 - 0.82$), can be used to convert the FDG values to values reflecting glucose metabolism. In this way glucose metabolic rate can be measured in absolute units (e.g. in $\text{mol min}^{-1} \text{g}^{-1}$).
 - e. For clinical purposes absolute quantification approaches are typically not necessary, particularly when considering the high inter-individual fluctuation of absolute cerebral glucose metabolism. In addition, most diagnostic applications depend on patterns of relative regional abnormalities, not on quantitative metabolic rate of glucose.
1. Observer Independent Analysis
 - a. Owing to advancements in image processing technology developed in brain mapping research, automated or semi-automated brain mapping techniques can be applied to routine clinical studies.
 - b. In conjunction with pixel-wise comparison to normal control data or database, individual statistical maps (such as Z score maps) may be used to provide additional information to conventional image interpretation.
 - (1) The techniques are usually based on slice display (customarily axial) or stereotactic surface projection displays.
 - (2) These methods commonly involve automated image realignment in the bi-commissural stereotactic system and anatomic standardization.
 - (3) When employing this type of analyses for image interpretation, it is critical to use methods validated and

- published in scientific literature.
- (4) The diagnostic accuracy may also be affected by differences in image characteristics between individual cases and cases included in the normal database.
- (5) The quality of the normal database may affect diagnostic accuracy. Morphing artifacts due to faulty alignment between individual subjects and a composite normal database may occur.
- (6) Quality control of such analyses is essential for proper diagnosis given that these complex analyses are prone to errors and artifacts.
- (7) Fully automated diagnostic systems are under development. These methods should be used with caution until they are scientifically validated and approved for clinical use and pitfalls and artifacts are fully understood by potential users.
- (3) Instrumentation used i.e. PET with measured attenuation correction, PET with transmission correction, attenuation correction with CT
- h. Assessment of the technical quality of the study (good, adequate, poor).
- i. Potential artifacts such as
 - (1) Patient movement
 - (2) Medications which affect cerebral metabolism
 - (a) These medications are listed explicitly under Point L.1
 - (3) Observed seizure activity
- j. Describe abnormalities including:
 - (1) Location
 - (2) Extent
 - (3) Symmetry or asymmetry
 - (4) Reference to a normal database if quantitation is employed. Normalization to a specific reference site in brain i.e. cerebellum, total brain, pons, basal ganglia, or thalamus.

J. Reporting

1. Clinical reports for brain PET or PET-CT imaging should include the following clinical information including:
 - a. Indications for the study.
 - b. Brief history emphasizing the main reason for the study e.g. memory loss.
 - c. Duration of the problem.
 - d. Other essential clinical information including medications.
 - e. Recent findings on prior nuclear medicine studies.
 - f. Findings on other imaging modalities such as MRI
 - g. Study technique
 - (1) Dose and route of radiopharmaceutical and uptake period
 - (2) Blood glucose level
1. Interpretation and Conclusions
 - a. Provide a reasonable differential diagnosis of the findings based on peer reviewed and generally accepted disease specific patterns.
 - b. Integrate all other pertinent facts including historical information, laboratory information, co-morbid conditions, medications, any recent therapy including surgery or radiation therapy, additional diagnostic studies such as CT, MRI or EEG.

- c. Consider the impact of atrophy or structural lesions as well as partial volume effects.
 - d. If relevant clinical or additional testing results are not available for review, state the limitation of the conclusions and recommend additional test as indicated.
 - e. When studies are difficult to interpret due to a pattern not commonly described using well-accepted criteria, the report should contain statements, which would aid the referring physician to better understand why a specific diagnostic entity could not be ascribed to the pattern noted.
 - f. Caution should be mentioned in the reporting of quantitative information as limitations of the quantitative technique need to be clearly understood by the interpreting physician before issuing a report as normal or abnormal based on quantitative findings.
- (1) The blank scan also serves for attenuation correction.
 - (2) This test takes a short time (30 minutes) and can be performed daily.
 - d. Since many studies are performed using CT for morphologic comparison and fusion as well as attenuation correction CT quality control should be performed by a trained CT technologist and physicist.

K. PET scanner quality control

1. Clinical scanning should be accompanied by a strict quality control program consisting of specific performance tests including:
 - a. Normalization procedure: to ensure the existence of an adequate correction of the changes in efficiency among the crystals of the detectors. This procedure takes several hours and can be performed every month, providing that there are no detector failures.
 - b. Setup scan: to ensure that all detectors are working properly.
 - (1) The setup scan changes the detect gains to modify any possible drifts.
 - (2) This takes about two hours and can be done weekly
 - c. Blank scan: to ensure that the detectors have not drifted since the last normalization.

2. Performance tests can be usually carried out according to the international recommendations according to:
 - a. American guidelines are published by NEMA (National Electrical Manufacturer Association).
 - b. European guidelines are published by IEC (International Electrotechnical Committee).

L. Pitfalls, Artifacts, Sources of Error

1. Medications altering cerebral metabolism including
 - a. Sedatives
 - b. Drugs such as amphetamines, cocaine
 - c. Narcotics
 - d. Anti-psychotic medications
 - e. Corticosteroids

Most medications predominantly alter global metabolism with modest effects on regional distribution.

2. Hyperglycemia
3. Patient motion during the data acquisition may result in image artifacts and render the study non-interpretable.
4. Misregistration between the emission and transmission scans.
5. Calculated attenuation using a per file calculation may result in falsely increased activity in the superior aspect of the brain.
6. Calculated attenuation does not correct

for variations of skull thickness. Subjects with hyperostosis frontalis may have falsely reduced frontal activity.

7. Without absolute metabolic quantitation, only relative information is available. The most active area on a study may be hypo or hyper metabolic which may influence the final interpretation.

M. Issues Requiring Further Clarification

1. What constitutes a “normal” database
 - a. How many subjects
 - b. Is age matching important?
 - c. Is gender matching important?
 - d. Is neuropsychological testing important?
 - e. Is a neurologist assessment needed
 - f. Can quantification be done using normals derived from a different PET/attenuation system than a subject done on a different device.
 - g. Is structural imaging required?
2. Adequate exclusion criteria for “normal” volunteer subjects
3. Quantification Techniques
 - a. Limitations of methods for clinical use versus research use
 - b. Are corrections for multiple comparisons necessary?
 - c. Do these techniques produce morphing errors?
 - d. Validation concerns
 - e. What constitutes an abnormal study
 - f. Sensitivity, specificity, accuracy issues for individual techniques need clarification and objective methods to establish diagnostic thresholds.
4. Co-Registration Techniques
5. Hardware versus Software fusion
6. Image Reconstruction Techniques

IV. Concise Bibliography

1. Asenbaum S. Guideline for the use of FDG-PET in Neurology and Psychiatry. Austrian Society of Nuclear Medicine 2001; www.ogn.at

2. Chugani HA, Functional brain imaging in pediatrics. *Pediatr Clin North AM* 1992; 39: 777-799.
3. Cook GJ, Maisey MN, Fogelman I. Normal variants, artifacts and interpretative pitfalls in PET imaging with 18-flouro-2-deoxyglucose and carbon-11 methionine. *Eur J Nucl Med* 1999; 26: 1363-78
4. Cranston I, Marsden P, Matyka K et al. regional differences in cerebral blood flow and glucose utilization in diabetic man: the effect of insulin. *J Cereb Blood Flow Metab* 1998; 18: 130-40
5. Devous MD. Functional brain imaging in the dementias: Role in early detection, differential diagnosis and longitudinal studies. *Eur J Nucl Med Mol Imaging* 2002; 29: 1685-96
6. Devous JS. Imaging and epilepsy. *Brain* 1997; 120: 339-377.
7. Drzezga A, Arnoald S, Minoshima S et al. F-18 FDG-PET studies in patients with extra-temporal and temporal epilepsy: evaluation of an observer-independent analysis. *J Nucl Med* 1999; 40: 737-746
8. Hasselbalch SG, Knudsen GM, Videbaek C et al. No effect of insulin on glucose blood-brain barrier transport and cerebral metabolism in humans. *Diabetes* 1999; 48: 1915 – 1921.
9. Herholz K, FDG PET and differential diagnosis of dementia. *Alzheim Dis Assoc Disord* 1995; 9: 6-16.
10. Kuwert T, Bartenstein P, Grunwald F et al. Clinical value of positron emission tomography in neuromedicine. Position paper on results of an interdisciplinary consensus conference. *Nervenrzt* 1989; 69: 1045-160.
11. Lucignani G, Schmidt KC, Moresco RM et al. Measurement of regional cerebral glucose utilization with fluorine-18-FDG and PET in heterogenous tissues: Theoretical considerations and practical procedure. *J Nucl Med* 1993; 34: 369-9

12. Messa C, Fazio F, Costa DC, Ell PJ. Clinical brain radionuclide imaging. *Sem Nucl Med* 1995; 25: 111-143.
13. Minoshima S, Frey KA, Koeppe RA et al. A diagnostic approach in Alzheimer's disease using three-dimensional stereotactic surface projections of Fluorine-18-FDG-PET. *J Nucl med* 1995; 36: 1238-1248
14. Minoshima S, Koeppe RA, Mintun MA et al. Automated detection of the intercommissural line for stereotactic localization of functional brain images. *J Nucl Me* 1993; 34: 322-329
15. Phelps ME, Huang SC, Hoffman EJ et al. Tomographic measurement of local cerebral glucose metabolic rate in humans with F-18 2-fluoro-2-deoxy-d-glucose; validateion of method. *Ann Neurol* 1979; 6: 371-388
16. Ruotsalainen U, Suhonen-Polvi H, Eronen E et al. Estimated radiation dose to the newborn in FDG-PET studies. *J Nucl Med* 1996; 37: 387-93
17. Schelbert HR, Hoh CK, Royal HD et al. Procedure guideline for tumor imaging using fluorine-18-FDG. *Society of Nuclear Medicine. J Nucl Med* 1998; 39: 1302-5.
18. Schreckenberger M, Spetzger U, sabri O et al. Localisation of motor areas in brain tumour patients: a comparison of preoperative 18-FDG-PET and intraoperative cortical electro-stimulation. *Eur J Nucl Med* 2001; 28: 1394-1403.
19. Setani K, Schreckenberger M, Sabri O et al. Comparison of different methods for attenuation correction in brain PET: effect on the calculation of the metabolic rate of glucose. *Nuklearmedizin* 2000; 39: 50-55
20. Signorini M, Paulesu E, Friston K et al. Rapid Assessment of regional cerebral metabolic abnormalities in single subjects with quantitative and nonquantitative (18F) FDG PET: A clinical validation of statistical parametric mapping. *Neuroimage* 1999; 9:63-80
21. Silverman DHS. Brain 18-F-FDG PET in the diagnosis of neurodegenerative Dementias: Comparison with perfusion of SPECT and with clinical evaluations Lacking Nuclear imaging. *J Nucl Med* 45 (4): 594 - 607
22. Society of Nuclear Medicine Brain Imaging Council. Ethical clinical practice of functional brain imaging. *J Nucl Med* 1996; 37: 1256-1259