

INVITED ARTICLE

An Overview of Clinical PET/CT

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ABSTRACT

This article is intended to provide an overview of various aspects of clinical PET/CT. These include discussions of:

- (i) Important areas of clinical application;
- (ii) Opportunities in clinical research;
- (iii) Scanner and operating-mode considerations (e.g. BGO vs. LSO, LYSO or GSO scanners, 2D vs. 3D imaging).
- (iv) Study-specific considerations (e.g. patient preparation and positioning issues, injected dose, use of CT contrast agents).

Key Words: Clinical, PET/CT, FDG, Anatomometabolic imaging, Oncology, Brain imaging, Cardiology, 2D vs. 3D, BGO, LSO, LYSO, GSO.

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I. INTRODUCTION

PET and now PET/CT imaging have grown rapidly in the last few years. The concept of fusion of anatomic and metabolic images as “anatomometabolic” images has been present for nearly 15 years, but has been transformed into a valuable clinical practice only quite recently. At present, vast majority of PET scanners manufactured are in the form of PET/CT scanners. The reason for this rapid growth in PET/CT utilization has been the clear demonstration of clinical efficacy for PET/CT in many common cancers and other conditions using PET/CT with FDG as a tracer. While this work had changed the practice of medicine, other tracers coupled with PET/CT also offer great opportunities to expand the use of this method in other diseases. Further, the availability of broadened reimbursement for FDG PET/CT in a variety of countries has facilitated its dissemination.

Sec. II introduces areas of active clinical application. Opportunities in clinical research are mentioned in Sec. III. In Sec IV, scanner and operating-mode considerations are overviewed, with particular attention to comparison of BGO vs. newer scintillators (e.g. LSO) scanners, as well as suitability of 2D vs. 3D imaging in whole body and brain imaging applications. Study-specific considerations including patient preparation,

injected dose, use of oral and intravenous (i.v) CT contrast agents, etc. are explained in Sec. V.

II. AREAS OF CLINICAL APPLICATION

Clinical PET studies covered by Medicare in the United States are summarized in Tables 1 and 2 for FDG and non-FDG PET imaging, respectively. These approved indications are nearly all based on the use of FDG as the tracer. This tracer, 18-F- Fluoro-2-Deoxy-D-glucose is the current cornerstone of PET imaging. It accumulates in viable cancer cells but also in inflammatory tissues. Despite some levels of non-specificity, it is a remarkably valuable tracer. In general, with current PET systems, FDG accumulation in most cancers is sufficiently high that there is visualization of cancers of 6mm and larger in many cases, and typically good detection of untreated cancers of 1cm in size or more. Lesion detectability is affected by a variety of factors related to the scanners including resolution and count-rate performance (see Sec. IV), as well as related to the patient and the tumor: background levels of tracer about the cancer (e.g. liver lesions are harder to detect than lung) and the intrinsic tumor avidity (e.g. lung cancers are more FDG avid than most prostate cancers).

Tables 1 and 2: Clinical PET studies approved for reimbursement by Medicare.

TABLE 1 CLINICAL CONDITION FDG PET	Coverage – (subject to additional guidelines).
Breast Cancer	Staging, restaging, and monitoring response to therapy
<ul style="list-style-type: none"> •Colorectal Cancer •Esophageal Cancer •Head & Neck Cancers (excluding CNS and thyroid) •Lung Cancer (Non-Small Cell) •Lymphoma •Melanoma (excludes evaluation of regional nodes) 	Diagnosis, staging and restaging
Myocardial Viability	Primary or initial diagnosis, or following an inconclusive SPECT prior to revascularization
Refractory Seizures	Covered for pre-surgical evaluation only
Solitary Pulmonary Nodule	Characterization of indeterminate single pulmonary nodule
Thyroid Cancer	Restaging
Cervical Cancer	Staging as an adjunct to conventional imaging
Dementia	Differential diagnosis of fronto-temporal dementia (FTD) and Alzheimer's disease (AD)
<ul style="list-style-type: none"> • Other Cancers • Assessment and Treatment Response • Planning Radiation Therapy 	Coverage with evidence development (Medicare registry)

TABLE 2 CLINICAL CONDITION NON-FDG PET	Coverage – (subject to additional guidelines).
Perfusion of the heart using: <ul style="list-style-type: none"> • Rubidium 82 tracer • Ammonia N-13 tracer 	Covered for noninvasive imaging of the perfusion of the heart

Additional indications covered by Medicare in the US, which covers about 80 million lives, include essentially “all” cancers under conditions of a registry, in which data are being collected in order to better answer questions of changes in patient management as a result of the PET/CT scans. With this registry, a management decision is made as to how the patient would be treated pre-PET and then how they would be treated after the PET results are available. In this way, it is hoped additional information will become available which will allow patients to be better chosen for PET studies where major changes in management are made based on PET and PET/CT. But, at present, for the Medicare patients, this means that nearly all possible cancers are covered with PET except for initial nodal staging of melanoma and breast cancer, where PET is insensitive for lesion detection.

Thus, in cancer, PET can broadly have the following roles with FDG in the cancer patient:

- 1) lesion detection (finding a new cancer)
- 2) lesion characterization (is a lesion seen on CT or other types of studies malignant or benign?)
- 3) cancer staging (is the tumor localized or disseminated?)
- 4) cancer restaging (has the cancer responded to treatment at the conclusion of treatment or has it progressed/spread?)
- 5) treatment response monitoring assessment (has the tumor responded early in its course of therapy so that it can be predicted as to whether the treatment will work or does it need to be changed?)
- 6) Prognosis (does the PET scan after treatment provide prognostic information?)
- 7) Surveillance (following patients to see if they have recurred and need additional treatment)

At Johns Hopkins, the aforementioned indications represent 90% of the clinical PET practice. However, other areas of PET are growing. In the brain, PET can detect changes of dementia more reliably than the clinical exam. Furthermore, FDG PET can help localize the site of seizure foci in the temporal lobes to help plan surgery. These are growing areas of work, and will become

even more relevant as better treatments of dementia evolve.

In the cardiac area, there is increased use of PET to define myocardial perfusion and viability. PET with Rb-82 (generator produced) or N-13 ammonia (cyclotron produced) are both reported to be more accurate than SPECT imaging in determining if a patient had coronary artery disease. PET/CT can help see if there are calcifications in coronary arteries or if there is, by high performance CT, stenosis of coronary arteries. The assessment of coronary flow reserve and myocardial viability are quite reliable with PET. Thus, there is a large platform of PET scans currently available which are driving the widespread clinical acceptance of PET as an imaging technique.

III. OPPORTUNITIES IN CLINICAL RESEARCH

FDG PET/CT represents the standard to which other PET imaging procedures must be compared. It is clear that many opportunities exist to carefully dissect the precise role for FDG PET/CT in a wide variety of less common cancers. A particularly exciting area is that of "risk adaptive" chemotherapy management using PET/CT. In this approach, PET/CT at baseline in a cancer therapy is performed and then is repeated after 1-2

cycles of treatment. If there is a large decline in glycolysis, the treatment is continued. If there is no decline or a rise in FDG uptake, the treatment will be predicted to ultimately be ineffective or suboptimal and should be changed. This approach is still experimental, but is being tested in a wide range of protocols including lymphoma, where there is emerging data that the PET study is the most robust predictor of response to treatment and prognosis, of the available imaging tests. It is quite possible that this approach, if fully validated, may change the way cancer chemotherapy is given, so that we may more quickly determine whether a treatment is effective or not. An additional area of opportunity with FDG PET is the use of dedicated imaging devices such as those for the breast which may allow for more precise localization of smaller breast lesions (by comparison to use of conventional PET scanners for breast imaging, positron emission mammography (PEM) scanners are less expensive, thus having more potential for systematic screening purposes, are less sensitive to the background emitted from the body and exhibit improved spatial resolution and rate performances).

Another instrumentation opportunity is the use of hand-held FDG detectors which can allow for detection of cancers at the time of surgery by a direct invasive procedure identifying the tumor margins. Thus, FDG is

still a useful tracer in cancer and more opportunities exist. Another role in clinical research is the use of FDG to detect infections, which are also glycolytically active.

Other clinical research opportunities include the use of PET tracers designed to detect processes in cancer not seen as well or as specifically with FDG. These can include proliferation of tumors (with FLT or FMAU), tumor protein synthesis (with radiolabeled amino acids), tumor hypoxia (with agents like F MISO or FAZA, or EF5). Receptors on tumors can also be imaged using Ga-68 labeled peptides, for example, a very promising approach. Other receptors such as the androgen and estrogen receptors also are exciting targets to allow for more precise individualization of patient therapies. With radiation therapy, it is also possible to potentially better visualize the biological areas of tumors more relevant for therapy through the use of alternative PET tracers, since the biological tumor volume may differ from the anatomic tumor volume. Thus, oncological PET represents an area where unanswered questions abound and there are great opportunities for clinical research with PET.

In the heart, while perfusion is well imaged at present, the optimal integration of perfusion data with anatomic data such as CTA images of the coronary arteries is in no

way resolved. Further, the use of oxidative metabolism to measure cardiac efficacy, the imaging of myocardial innervation to detect arrhythmogenic foci, and the use of agents to directly image plaques represent short and longer term opportunities in the heart.

In the CNS, great opportunities remain to image the over 80 neurotransmitters which have been described, as well as their receptors and the receptor occupancy. These investigations are quite difficult however, and often are limited by low receptor densities and alterations of receptor populations in disease that may be below the resolution or sensitivity of current PET tracers. Nevertheless, high resolution and high sensitivity brain imaging devices can help address these issues. One area of great excitement is the imaging of brain amyloid deposition which can be an early sign of dementia (or a precursor). This can be performed with several agents, most notably the PIB compound, labeled with C-11 which is a prototype of what can be done in the CNS with PET imaging. This area of work represents a great opportunity to look at what may be “pre disease” in the brain, and whether it can be reversed at early stages.

Thus, in oncology, the heart and brain, there are great opportunities for clinical research, some with the popular tracer FDG, and others with more sophisticated and specialized tracers, as noted above. To

perform either clinical or research studies, a properly functioning scanner (with appropriately set operating-mode parameters) must be available. The following section addresses these issues in detail with the aim of providing a framework for the understanding and comparison of different PET scanners in the field.

IV. SCANNER AND OPERATING-MODE CONSIDERATIONS

Unlike the more straightforward concepts of spatial resolution (primarily related to the dimensions of crystals used in different scanners), and sensitivity (determined as the percentage of emitted counts detected by the scanner at very low count-rates), the concept of clinically-relevant count-rate performance is quite complicated and yet very necessary to have a full grasp on (it is very relevant to the task of comparing different scanners and operating modes; e.g. 2D vs. 3D PET imaging). First, it is helpful to explain the concept of ‘*noise-equivalent count-rates*’ (NEC).

A) NEC Plots

Detected photon pairs in PET are not always true coincidences. Instead, they can be (i) scatter coincidences (which arise when one or both of the two coincidence gamma

rays are scattered in the body before being detected), or (ii) random coincidences (which are obtained when two unconnected gamma rays from different disintegrations are detected within the coincidence time window), which become considerably large with increasing activities. Such events add background noise to the detected signal, and therefore degrade the signal-to-noise ratios (SNRs) in the reconstructed images. Additionally, with increasing rates of emitted gamma rays, the scanner will exhibit considerable dead-time effects, thus saturating the detected signal.

A very common method to estimate/compare SNRs for various scanners and different imaging tasks, is to measure the 'noise-equivalent count rate' (NEC) [3-5] which combines the relative amounts of true, scatter, and random coincidences (including dead-time effects) (Figure 1). The NEC rate is often plotted as a function of activity concentration in the field-of-view (FoV). However, we believe that plotting against the total *singles rate* is a better approach since (i) it includes effect of events arriving from outside the FoV, and (ii) it is directly related to the *total* activity in the FoV, as opposed to the activity *concentration*; in fact, typical NEC plots provided by PET companies are obtained from large-phantom studies as functions of activity concentration (and not total activity): this can be *very* misleading

since realistic studies involve smaller effective volumes, and thus smaller total activities for the same concentrations (e.g. cardiac studies involve much smaller active volumes, and therefore can tolerate much larger concentrations).

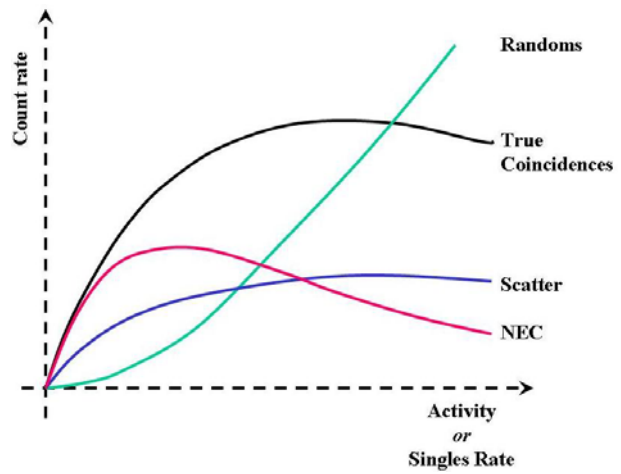


Figure 1: At relatively low activities, NEC increases with increasing activities. However, as activities become large, the dead-time effects (e.g. see true curve at high activities) and fractions of random coincidences begin to dominate, thus degrading the signal-to-noise ratios and therefore decreasing the NEC. The NEC curve therefore provides an estimate of the range of activities within which best image qualities are expected to be obtained.

Furthermore, we emphasize that NEC plots (as well as other performance measures such as spatial resolution and sensitivity) are *only* global and/or approximate measures of image quality, and it is critical that for accurate comparisons of different scanners and use of different operating-modes, actual patient images are analyzed: these images

should be those of typical quality in the application of interest, as opposed to best case studies shown in a sales or marketing demonstration.

B) 2D vs. 3D Imaging

An issue of increasing interest nowadays in clinical PET imaging is that of 2D vs. 3D imaging. Two-dimensional imaging is obtained by the use of septa in between the axial scanner rings in order to only accept dual photon pairs detected within the same ring. Scanners nowadays make use of retractable septa (e.g. GE Discovery ST, STE or RX) or no septa at all (e.g. Philips Gemini, Siemens Biograph family), thus making it possible to perform fully 3D PET imaging in which individual coincidence photons can arrive at detectors in different rings (see Fig. 2). This in effect increases the sensitivity of the scanner. However, aside from computational and mathematical difficulties in the 3D case (which are nowadays properly addressed), the fractions of scatter and random coincidences increase (by a factor of ~3) compared to true coincidences, thus affecting the NEC plots and image qualities.

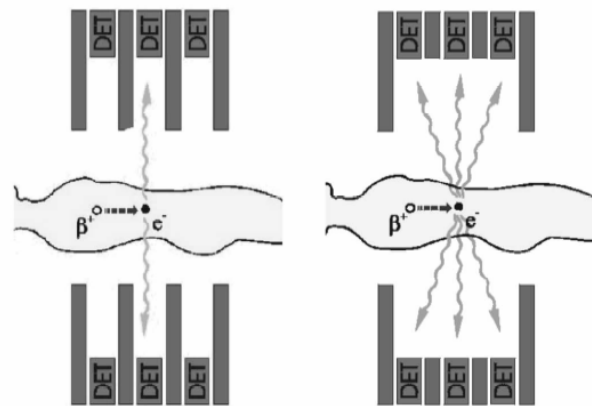


Figure 2: 3D PET imaging is achieved by the use of retractable septa, and results in increases scanner sensitivity compared to 2D imaging. However, it also increases the fractions of scatter and random coincidences (Figure courtesy of C-H. Chen, with modifications).

In brain imaging applications, due to smaller volumes, smaller fractions of scatter and random coincidences are observed; subsequently, it is commonly agreed that 3D imaging is the method of choice in brain imaging. In whole body imaging, however, for conventional BGO scanners, it is commonly agreed that 2D imaging is preferred over 3D imaging. Nevertheless, for scanner making use of newer types of scintillators (e.g. LSO, LYSO, GSO), the issue of 2D vs. 3D in whole body imaging is currently under debate. This is explained next.

C) Scanners based on BGO vs. Newer scintillators

Over the past decade, compared to BGO-based scanners, there has been a considerable increase in the manufacturing of scanners with newer types of scintillators, especially GSO (Philips), LYSO (GE) and LSO (Siemens). These newer scintillators provide three potential advantages:

(i) Faster scintillation rise times, which allow more accurate measurements of photon incidence times, and therefore allow the use of narrower coincidence time windows. This in turn has the advantage of decreasing random rates (see Ref. [1]-Sec. VI) thus improving signal-to-noise ratios, and furthermore introduces the possibility of time-of-flight PET (expected in next-generation PET scanners; see [1]-Sec. VII for detailed discussion).

(ii) Faster scintillation decay times, resulting in smaller dead-time effects (however, in practice dead-time rates are more determined by the electrical components of the scanner and less by the scintillator decay times);

(iii) Improved energy resolution, resulting in a higher ability to reject scatter coincidences, and thus potentially improving signal-to-noise ratios.

In Fig. 3 we plot a qualitative comparison of BGO vs. LSO (or LYSO or GSO) scanners (in whole body applications). We emphasize that the plots are only qualitative, since quantities will vary from scanner-to-scanner

and application-to-application. A number of important observations are made:

(i) NEC plots for LSO-based scanners are improved compared to BGO-based ones. This is due to the aforementioned factors wherein smaller rates of scatter and random coincidences are expected in LSO-based scanners.

(ii) While it is quite clear that in F-18 (most importantly FDG) applications, 2D imaging in BGO-based scanners is preferred over 3D, this distinction is not clear in LSO-based scanners. In fact, there is some experimental evidence [6] that 3D imaging for newer generation scanners in oncologic FDG applications may be preferred over 2D imaging. Therefore, a number of new scanners marketed towards FDG imaging now only allow imaging in 3D (i.e. they do not contain septa).

(iii) However, for radiotracers with shorter half-lives (e.g. Rubidium Rb-82 for cardiac imaging; see [1]-Sec. II-C for more details) the activities will extend further into the high range, and as depicted in Fig. 3, 3D imaging at these count rates could be strongly degraded (very high rate of scatter and random coincidences) compared to 2D imaging. This issue needs to be further investigated using realistic phantoms, simulations and especially by clinical experiments. Currently, we believe that the purchase of scanners with the 3D-only

modality is not justified for centers with an additional interest in imaging with short half-life tracers.

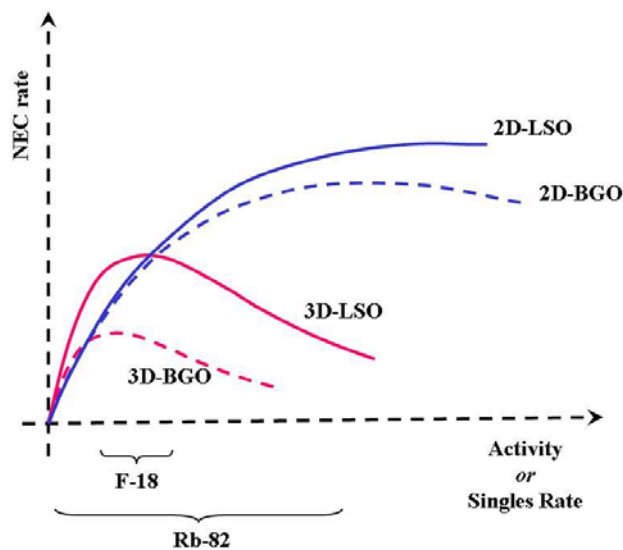


Figure 3: A comparison of NEC plots for BGO- vs. LSO-based scanners (or GSO- or LYSO-based scanners) for 2D and 3D imaging modalities. Clinical activity ranges for F-18 (most notably FDG) studies and Rb-18 (in cardiac imaging) are also shown.

D) Improved Electronics

Aside from the effect of using different scintillators, improved electronics in newer scanners can also make notable improvements in NEC plots and scanner image quality. Such enhancements include improved Time-to-Digital converter (TCD) resolution (resulting in narrower time windows, thus smaller random rates), faster

digital signal processors (resulting in less dead-time) and improved photo-multiplier tubes (PMTs) (with improved resulting energy resolution, thus less scatter coincidences), as for instance introduced in the Pico-3D electronics available in the new commercially available LSO-based PET/CT Biograph scanners from Siemens. Another example is the upgrade of the BGO-based GE ST scanner to GE STE.

As a final note, we emphasize that acquisition considerations such as (i) 2D vs. 3D imaging, and (ii) optimal injected dose (see Sec. V) are very dependent on the particular scanner (types of scintillators, electronics) as well as the application under investigation, and should be optimized not only using phantoms (and possibly realistic computer simulations), but also by reference to actual patient studies.

V. STUDY-SPECIFIC CONSIDERATION

While we note that practice varies from center to center, this section provides our experiences and recommendations with regards to patient preparation and scanning practices in PET/CT imaging.

A) Preparing the Patient

A brief or more detailed review of the patient records by the supervising/interpreting physician is recommended in order to verify the reasons

the PET study is requested. It is critical to pay special attention to recent surgery, infection, chemotherapy, G-CSF treatments and radiation therapy.

Prior to Injection: For FDG PET/CT imaging to detect cancer, optimal images are obtained when the serum glucose levels are low. For a non-diabetic patient, this is the case following several hours of or even overnight fasting. The recommended blood glucose, to be monitored prior to the PET/CT study, is under 200 mg/dl, and ideally under 150 mg/dl. High glucose levels can result in a competitive inhibition of FDG uptake in tumors and an artificially low standard uptake value (SUV), thus potentially decreasing tumor visualization. Furthermore, in order to minimize normal muscle uptake of the radiotracer, extensive exercise should be avoided in the day before the PET scan is performed.

FDG uptake into muscles will undergo an increase for elevated insulin levels. For diabetic patients, therefore, ideally, there should be no insulin given for several hours prior to the injection of the FDG (a patient using a regular insulin sliding scale dose often will take their last injection the evening before the test). As such, it is preferable that they have a morning appointment to have the blood sugar in the appropriate range. For a very brittle diabetic it is sometimes indicated to have them eat some food in the morning,

give a dose of short acting insulin and then inject at three to four hours after insulin dosing. In this way, the blood glucose would be under control, but serum insulin levels would have declined into the normal range.

Another point worth noting is that patients are often scheduled for a number of tests on the same day and these should be checked to avoid any conflicts: e.g. an exercise cardiac stress test is not to be performed the previous day or before the PET scan. Additionally, we note that if 3D or CT angiography of the abdomen is being performed after the PET scan, the images may be degraded due to the use of oral contrast material given as a part of a typical PET/CT preparation: this may make it impossible to segregate out the relevant vessels. In such cases, as an alternative approach to avoid technical issues with subsequent CT angiography studies, water can be given as an alternative to radio-opaque oral contrast for the PET/CT study.

All patients should be weighed when arriving for the study. Oral contrast may be given to improve the overall quality of the CT. This helps differentiate some of the abdominal anatomy and localize sites of disease by separating them from normal bowel activity. One recommended protocol is to use a dilute barium solution (1.3% barium sulfate) as it will sufficiently fill the bowel and at the same time is well tolerated (minimal artifacts caused by “over

attenuation correction” as discussed below). A patient who is 70 kg or less, will receive 525 ml before the injection and 175 ml at about two-thirds of the uptake period. A larger patient will have 700 ml before the injection and 350 ml toward the end of their uptake time. Other protocols can include using water as the oral contrast medium (negative contrast).

Injection Dose: The injection of FDG itself should be weight based. A dose of 0.22 mCi/kg is a standard dose for whole body scanning using a 2D acquisition protocol and a BGO scanner (with the maximum injected dose not exceeding 25 mCi regardless of the patient weight). However, it must be noted that injected dose as well as operating-mode considerations (2D vs. 3D) should be optimized based on the particular scanner and application (see Sec. IV for a more elaborate discussion). As such, for whole-body imaging in 3D imaging, lower doses may likely be more suitable. Typically, acquisition times of about 4 to 5 minutes per bed position (15 cm axial field of view) are typical. A patient that requires a scan ranging from head to toe can receive a 30% larger dose in order to reduce the total field acquisition times (from head to toe). Furthermore, a 30% less dose is given to pediatric patients compared to normal adults in order to limit their exposure. For institutions that use smaller doses (e.g. fixed

10 mCi dose regardless of weight), longer acquisition times are recommended to provide adequate statistical quality in the reconstructed images.

Following injection: It is important that the patient room be kept warm, and blankets are given to patients, to limit the amount of brown fat that is stimulated by the cold environment and thus visualized in the scan.

The time in-between injection to the PET scan varies from center to center. For most whole body oncological studies, an uptake period of about 50 to 60 minutes is used (even longer uptake times are used in some center, in order to increase the tumor-to-background ratios, however this results in the images to have slightly lower statistical qualities). It is important to note that, in order for sequential studies to be quantitatively interpretable and consistent, the *same* duration of uptake time be used in each case (consistency).

Different preparation protocols should be used for patients with head and neck cancer and those undergoing brain-only imaging. If the primary focus is in the face or neck, in order to minimize swallowing and any possible related muscle uptake, oral contrast should not be given. Patients performing brain PET with 3D acquisition should receive only ~10 mCi of FDG and the uptake period can be shortened to 30 minutes (again, this issue is scanner-dependent). Eye

patches and earplugs should be applied to minimize regional brain stimulation.

B) Scanning the Patient

Following the uptake phase, the patient is ready to be scanned, at which time he/she should remove all metal accessories and use the restroom to empty the bladder. In most instances, whole body scans are to be performed in the caudo-cranial direction in order to avoid excessive bladder filling with radioactive FDG during imaging. In patients for whom the major pathology is expected in the region of the head and neck, this protocol can be changed since even involuntary movements can occur over a 15-20 minutes imaging interval and may impair precise fusion of PET and CT data.

One option for performing studies in patients with cancer of the head and neck includes a two- part acquisition: (i) a caudo-to-cranial scan starting at the mid thighs and extending to the supraclavicular region, with the arms placed above the head in order to minimize artifacts (which can occur when an arms-down patient is in the PET field of view but not entirely in the CT field of view [7]) followed by (ii) an arms-down PET/CT acquisition of the region of the head and neck. This latter acquisition can be followed by a diagnostic quality CT contrast study so as to optimize visualization of the head and neck vascular structures and to best separate

those structures from small FDG avid lymph nodes.

The use of i.v contrast is growing in frequency in many PET centers. An issue arising from CT attenuation correction in PET/CT scanners is the fact that with some systems, i.v. and high density oral contrast agents can cause artifacts, appearing as areas of apparently elevated tracer uptake, in PET images (due to “over attenuation correction”). This problem is caused by an over-simplified procedure of converting CT attenuation coefficients to 511 keV attenuation coefficients required for PET, in some systems, and has been addressed to a considerable extent in newer PET/CT systems. Nevertheless, if accurate quantitation is required, the safest approach with such contrast agents remains to additionally perform a lower powered CT scan for more accurate attenuation correction. This is an issue of ongoing debate and remains controversial.

Furthermore, to reduce overall radiation to the patient from CT, it is possible to design protocols so as to increase radiation dose only in the areas which have contrast CT and to use low mA for non-contrast areas.

Before the patient is discharged from the PET center, it must be determined if the PET and CT images are of adequate technical quality and if they have provided the diagnostic information required. Commonly,

we find that re-imaging is not necessary, however in cases when there exists noticeable patient motion, or if there remains, a concern in separating an FDG filled ureter from retroperitoneal lymph nodes, repeat imaging of a small or larger portion of the body can be performed. From our experience, the most common repeat image is in the abdomen/pelvis where there is a question of residual urine vs. FDG-avid tumor.

VI. SUMMARY

In this article, we have outlined important areas of ongoing clinical application as well as clinical research in oncology, brain imaging and cardiology using PET/CT imaging. FDG remains the most widely used radiotracer in clinical PET/CT, with important applications as well as potentials remaining to be explored. Another discussed area of great potential is the development and use of PET tracers designed to detect processes not seen as well or as specifically with FDG. Various scanner-specific (e.g. BGO vs. LSO scanners), operating-mode (e.g. 2D vs. 3D imaging) as well as study-specific considerations were also elaborated.

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