PET in clinical trials

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How might a clinical trial differ from routine clinical PET/CT imaging?

- IRB
- Patient Preparation
- Radiotracer
- Scan Protocol
- Image reconstruction
- Analysis (quantitative?)
- Sending the data somewhere.

Oncologic FDG Applications vs ...

- Other radiotracers and applications (new opportunities)
- FDG Oncology

Other radionuclides?

- O-15 (2 min), N-13 (10 min), C-11 (20 min) from cyclotron
- Ga-68 (68 min) from Ge-68 generator
- Cu-64 (13 hr)
- I-124 (4.2 days)
- ...

⁶⁸Ga DOTA-TATE



gallium-68





Synthesis Unit

Eckert and Zieglar, from radiopharma.com

ITG, from radiomedix.com

¹³NH₃ Dynamic Rest Study



¹³NH₃ Dynamic Stress Study



Jobs for physicist when imaging new radionuclide.

- Oversee *pathway* for dose to injection site.
- Do a phantom and tell everyone, "We're good to go."
 - Make sure it's a meaningful phantom.
 - Measure SUV in uniform phantom?
 - Dose calibrator?
 - Where does your activity come from?

¹⁸F Florbetapir



Newberg, et al, J Nucl Med June 1, 2012, vol. 53 no. 6, 902-907

¹⁸F fluoride bone scan



From a site qualification document for a complicated Cardiac PET Clinical Trial:

• Reminder that we will need to collect the following documents at PSV:

- Site Personnel Worksheet
- Copy of American College of Radiology PET accreditation
- CTAIS (completed as a Word document);

- We;
 Form FDA 1572 (unsigned; with BOX 1, 3, 4 & 6 completed at minimum);
 Current signed and dated CV (w/in past 2yrs) & medical license for PI;
 Current Transcelerate-approved GCP Certification for PI (w/in past 2 yrs.) If Sub-Investigators identified at time of PSV, nice to have their CVs/m and GCP certificates
- Reminder that PI and all site staff noted on Form FDA 1572 and Delegation of Duties Log must have current Transcelerate-approved GCP training documentation. ##### can provide site with free access to the training.

Oncologic FDG-PET

- The vast majority of current clinical PET studies
- A lot of clinical trials

(By the way, what is FDG?)



Typical Protocol for FDG PET

- Patient fasts for >4 hrs
- Patient is injected with FDG
- Uptake for 45 120 minutes, quiet, inactive
- Scan (CT + PET) ~30 min

Pre Therapy (12/01/2006)





Images courtesy R.E. Coleman, MD

PET Quantitation - SUV

 $SUV = \frac{radioactivity\ concentration^*}{injected\ activity^*/patient\ size}$

- Radioactivity concentration is what the scanner delivers in image pixel values, assuming all calibrations are done and all corrections are performed.
- 2. Injected activity must be adjusted for any residual dose.
- 3. Patient size can be:

Patient mass (weight) Patient lean body mass (approximated from height and weight) Patient lean body mass (as determined from CT)

*Corrected appropriately for radioactive decay

SUV





QIBA

"RSNA organized the Quantitative Imaging Biomarkers Alliance (QIBA) in 2007 to unite researchers, healthcare professionals, and the industry to advance quantitative imaging and the use of imaging biomarkers in clinical trials and clinical practice. The Society is committed to transforming patient care by making radiology a more quantitative science."

The initiative includes:

- Collaboration to identify needs, barriers and solutions to create consistent, reliable, valid and achievable quantitative imaging results across imaging platforms, clinical sites, and time.
- Accelerating development and adoption of hardware and software standards to achieve accurate and reproducible quantitative results from imaging methods.

QIBA FDG-PET/CT Profile

A detailed guide for obtaining accurate, repeatable SUV measurements with PET.

Scanner performance, imaging site practices, and image analysis are all covered.



Page 1

FDG PET Profile Claim

Claim: Measure Change in SUV

Conformance to this Profile by all relevant staff and equipment supports the following claims:

Claim 1: Tumor glycolytic activity as reflected by the maximum standardized uptake value (SUVmax) is measurable from FDG-PET/CT with a within-subject coefficient of variation of 10-12%.

Claim 2: A measured increase in SUVmax of 39% or more, or a decrease of -28% or more, indicates that a true change has occurred with 95% confidence.

Patient height and weight

Parameter	Entity/Actor	Specification
Height and Weight	Imaging Technologist	The Technologist shall measure and document subject height and weight and enter this information into the scanner during the PET/CT acquisition.
		Subject body weight shall be measured at the time of each PET/CT scan with standardized measurement devices and with the subject in an examination gown or light clothing. Subject height shall be measured and documented at the time of baseline FDG-PET scan with standardized measurement device. Measurement of subject height is not required at each subsequent time point unless other subject-centric factors (e.g. growth in pediatric population or shrinkage in elderly population) are relevant in combination with a prolonged interval between imaging time points such that a change in height might be significant.
		If subject cannot be moved from the bed, the date and source of information should be documented.
		The Technologist shall measure subject height and weight and enter this information into a common data format mechanism used for recording all needed information (Appendix E).

Activity (Dose) Measurement

Parameter	Entity/Actor	Specification
Administered	Imaging	The Technologist shall
FDG Radiotracer Activity	tracer Technologist	 Assay the pre-injection FDG activity (i.e. radioactivity) and time of measurement,
		Inject the FDG as prescribed in the protocol, within the range defined in the protocol.
		3. Record the time that FDG was injected into the subject,
		 Assay the residual activity in the syringe (and readily available tubing and components) after injection and record the time of measurement.
		These values shall be entered into the scanner during the PET/CT acquisition.
		For scanners that do not provide for entry of residual activity information, the net injected radioactivity should be manually calculated by decay correcting all measurements to the time of injection and then subtracting the residual radioactivity from the pre-injection radioactivity. The net injected radioactivity is then entered into the scanner during the PET/CT acquisition. All data described herein on activity administration shall be

Scan Parameters

Parameter	Entity/Actor	Specification
PET acquisition mode	Study Sponsor	The key PET acquisition mode parameters (e.g., time per bed position, acquisition mode, with or without gating) <u>shall be</u> <u>specified</u> in a manner that is expected to produce acceptably low image noise regardless of the scanner make and model.
		The key acquisition mode parameters shall be specified according to pre-determined harmonization parameters.

Reconstruction Parameters

Parameter	Entity/Actor	Specification
PET image reconstruction	Study Sponsor	The key PET reconstruction parameters (algorithm, iterations, smoothing, field of view, voxel size) shall be specified. The image voxel size should be <5 mm (strongly prefer 3 – 4 mm), with <3 mm voxels for head and neck imaging.
		The key PET image reconstruction parameters shall be specified according to pre-determined harmonization parameters.
PET image reconstruction	The key PET reconstruction parameters (algorithm, iterations, smoothing, field of view, voxel size) shall be followed and set as specified.	

Accreditation or Qualification

Parameter	Entity/Actor	Specification
Accreditation / Qualification	Imaging Site & Image Acquisition Device	Shall maintain and document Accredited status for clinical practice (ACR, IAC, TJC, etc.) or Qualified status for clinical trials (e.g. ACRIN, SNM-CTN, CALGB, CROs, etc.).

Physicist's Qualifications

naging Facility oordinator	Medical physicists shall be certified in Medical Nuclear Physics or Radiological Physics by the American Board of Radiology (ABR); in Nuclear Medicine Physics by the American Board of Science in Nuclear Medicine (ABSNM); in Nuclear Medicine Physics by the Canadian College of Physicists in Medicine; or equivalent certification in other countries; or have 3 years of PET experience. Regardless of certification, the physicist should have specific experience in PET and its quantitative use.
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Dose Calibrator

Parameter	Entity/Actor	Specification
Constancy	Technologist	Shall be evaluated daily (or after any dose calibrator event) using a NIST-traceable (or equivalent) simulated F-18, Cs-137, or Co-57 dose calibrator standard and confirmed that net measured activity on the F-18 setting differs by no greater than ±2.5 % from day to day.
Accuracy	Technologist	Shall be evaluated monthly (or after any dose calibrator event) with a NIST-traceable (or equivalent) Cs-137, Co-57, or simulated -138 dose calibrator standard. Shall confirm that net measured activities differ no greater than ±2.5% from expected value.

Quantitative Scanner/DoseCal QC

Phantom tests: SUV measurements	Imaging Site	Using ACR or uniform cylinder phantom or equivalent shall obtain an SUV for a large central ROI of 1.0 with an acceptable range of 0.9 to 1.1.
		Using ACR or uniform cylinder phantom or equivalent shall obtain an SUV for a large central ROI of 1.0 with an acceptable range of

Parameter	Entity/Actor	Specification
		0.95 to 1.05.

Image Noise

Parameter	Entity/Actor	Specification
Noise	Medical Physicist	Shall perform qualitative or quantitative assessment of image noise in phantom images to be of consistent and acceptable quality.

Imaging Device Quantitative Capabilities

PET Scanner calibration	Acquisition Device	Shall be able to be calibrated according to the following specifications: Using a uniform cylinder containing F-18 in water (ideally the same used for dose calibrator cross-calibration)
		Slice-to-slice variability shall be no more than \pm 5% (not including end slices, as per ACR PET Core Lab).
		In-plane uniformity for above phantom shall be less than 5%.
		Immediately after calibration, using the same filled phantom and scanned sufficiently long to minimize statistical noise, and an ACR- type ROI analysis
		The average measured SUV shall be in the range of 0.98 to 1.02. (Note this is not the performance expected during clinical imaging operation as discussed in preamble to this Section). This technique removes the variability due to radionclide measurement.

Imaging Device Quantitative Capabilities (2)

Weight	Acquisition Device	Shall be able to record patient weight in lbs or kg as supplied from the modality worklist or operator entry into scanner interface. Shall be stored in Patient Weight field (0010,1030) in the DICOM image header, as per DICOM standard.
		Patient weight shall be specifiable with 4 significant digits. Patient weight shall be transferrable directly from measurement device into scanner by electronic, HIS/RIS, or other means, bypassing all operator entry, but still permitting operator correction.

QIBA FDG PET Profile Comments

- If you are not familiar with the issues of quantitative PET, read this document.
- Even if you are familiar, it is a good way to spend a couple of hours.
- You (the physicist) are probably the only one in your institution who will.