
Quantitative
Imaging
Biomarkers
Alliance



1
2
3
4
5
6
7
8
9

QIBA Profile. FDG-PET/CT as an Imaging Biomarker Measuring Response to Cancer Therapy

Version 1.13

Technically Confirmed Version

November 18, 2016

Copyright © 2016: RSNA

Note to users – when referencing this QIBA Profile document, please use the following format:

FDG-PET/CT Technical Committee. FDG-PET/CT as an Imaging Biomarker Measuring Response to Cancer Therapy, Quantitative Imaging Biomarkers Alliance, Version 1.13, Technically Confirmed Version. QIBA, November 18, 2016. Available from: RSNA.ORG/QIBA.

10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41

Table of Contents

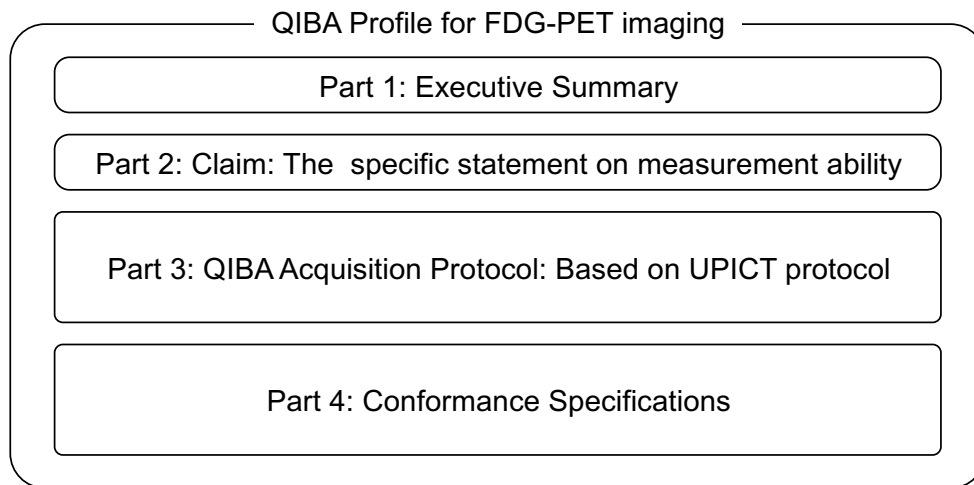
1. Executive Summary	3
Summary for Clinical Trial Use	4
2. Clinical Context and Claims	5
Applications and Endpoints for Clinical Trials	5
Claim: Measure Change in SUV	6
3. Profile Details	7
3.1. Subject Handling	8
3.2. Image Data Acquisition	15
3.3. Imaging Data Reconstruction and Post-Processing	21
3.4. Image Analysis (UPICT Section 9)	24
3.5. Image Interpretation and Reporting (UPICT Section 10).....	24
3.6. Quality Control	25
4. Conformance	35
4.1. Image Acquisition Site	35
4.2. PET/CT Acquisition Device.....	36
4.3. Reconstruction Software.....	42
4.4. Image Analysis Workstation	44
4.5. Software Version Tracking	47
References.....	48
Appendices.....	51
Appendix A: Acknowledgements and Attributions	51
Appendix B: Background Information for Claim	54
Appendix C: Conventions and Definitions.....	57
Appendix D: Model-specific Instructions and Parameters.....	62
Appendix E: Data Fields to be Recorded in the Common Data Format Mechanism.....	66
Appendix F: Testing PET/CT Display and Analysis Systems with the FDG-PET/CT DRO	67
Appendix G: Vendor-neutral Pseudo-codes for SUV Calculation	71
Appendix H: Consensus Formula for Computing Lean-Body-Mass Normalization for SUVs.....	73
Appendix I: QIBA FDG PET/CT Imaging Site and Scanner Checklists.....	76

42

43 1. Executive Summary

44 This QIBA Profile documents specifications and requirements to provide comparability and consistency for
45 quantitative FDG-PET across scanners in oncology. It can be applied to both clinical trial use as well as
46 individual patient management. This document organizes acquisition, reconstruction and post-processing,
47 analysis and interpretation as steps in a pipeline that transforms data to information to knowledge.

48 The document, developed through the efforts of the QIBA FDG-PET Biomarker Committee, has shared
49 content with the FDG-PET UPICT protocol, as well as additional material focused on the devices used to
50 acquire and analyze the FDG-PET data.



51

52

Figure 1: Illustration of the Profile components

53 The Profile Part 3 is largely derived from the FDG-PET UPICT protocol for FDG-PET imaging in clinical trials.
54 In the UPICT protocol, there is a carefully developed hierarchy with tiered levels of protocol compliance.
55 This reflects the recognition that there are valid reasons to perform trials using different levels of rigor,
56 even for the same disease/intervention combination. For example, a high level of image measurement
57 precision may be needed in small, early-phase trials whereas a less rigorous level of precision may be
58 acceptable in large, late-phase trials of the same drug in the same disease setting.

59 The three levels of compliance for UPICT protocols are defined as:

60 ACCEPTABLE: failing to meet this specification will result in data that is likely unacceptable for the intended
61 use of this protocol.

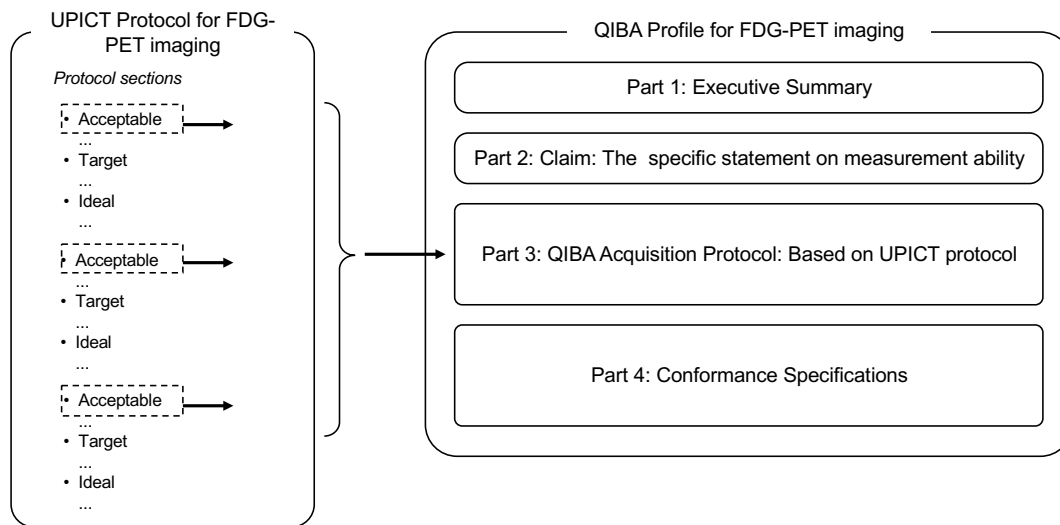
62 TARGET: meeting this specification is considered to be achievable with reasonable effort and equipment
63 and is expected to provide better results than meeting the ACCEPTABLE specification.

64 IDEAL: meeting this specification may require unusual effort or equipment, but is expected to provide
65 better results than meeting the TARGET.

66 ACCEPTABLE values are always provided for each parameter in a UPICT Protocol. When there is no reason
67 to expect better results (e.g. in terms of higher image quality, greater consistency, lower radiation dose,
68 etc.), TARGET and IDEAL values are not provided.

69 This Profile draws on the ACCEPTABLE components of the UPICT Protocol. Later revisions of this Profile are

70 expected to draw on the Target and then Ideal categories of the UPICT Protocol. The Target and Ideal
 71 categories are intended to account for advances in the field and the evolving state-of-the-art of FDG-
 72 PET/CT imaging. These concepts are illustrated in Figure 2 below.



73

74

Figure 2. Relationship between the UPICT Protocol and the Profile.

75 Summary for Clinical Trial Use

76 The QIBA FDG-PET/CT Profile defines the behavioral performance levels and quality control specifications
 77 for whole-body FDG-PET/CT scans used in single- and multi-center clinical trials of oncologic therapies.
 78 While the emphasis is on clinical trials, this process is also intended to apply for clinical practice. The
 79 specific claims for accuracy are detailed below in the Claims.

80 The specifications that must be met to achieve conformance with this Profile correspond to acceptable
 81 levels specified in the FDG-PET UPICT Protocol. The aim of the QIBA Profile specifications is to minimize
 82 intra- and inter-subject, intra- and inter-platform, and inter-institutional variability of quantitative scan data
 83 due to factors other than the intervention under investigation. FDG-PET/CT studies performed according to
 84 the technical specifications of this QIBA Profile in clinical trials can provide qualitative and/or quantitative
 85 data for single time-point assessments (e.g., diagnosis, staging, eligibility assessment, investigation of
 86 predictive and/or prognostic biomarker(s)) and/or for multi-time-point comparative assessments (e.g.,
 87 response assessment, investigation of predictive and/or prognostic biomarkers of treatment efficacy).

88 A motivation for the development of this Profile is that while a typical PET/CT scanner measurement
 89 system (including all supporting devices) may be stable over days or weeks, this stability cannot be
 90 expected over the time that it takes to complete a clinical trial. In addition, there are well known
 91 differences between scanners and or the operation of the same type of scanner at different imaging sites.

92 The intended audiences of this document include:

- 93 • Technical staff of software and device manufacturers who create products for this purpose.
- 94 • Biopharmaceutical companies, oncologists, and clinical trial scientists designing trials with imaging
 95 endpoints.
- 96 • Clinical research professionals.

- 97 • Radiologists, nuclear medicine physicians, technologists, physicists and administrators at healthcare
98 institutions considering specifications for procuring new PET/CT equipment.
- 99 • Radiologists, nuclear medicine physicians, technologists, and physicists designing PET/CT acquisition
100 protocols.
- 101 • Radiologists, nuclear medicine physicians, and other physicians making quantitative measurements
102 from PET/CT images.
- 103 • Regulators, nuclear medicine physicians, oncologists, and others making decisions based on
104 quantitative image measurements.

105 Note that specifications stated as 'requirements' in this document are only requirements to achieve the
106 claim, not 'requirements on standard of care.' Specifically, meeting the goals of this Profile is secondary to
107 properly caring for the patient.

108 A summary of the specifications required to achieve the claim, and formatted as a checklist, are provided in
109 Appendix I. The corresponding specifications are indicated as bold text in the tables of normative
110 statements below as described in Appendix C. This checklist may be used to ascertain a PET imaging site's
111 qualification for quantitative imaging according to the QIBA FDG PET/CT profile.

112 **2. Clinical Context and Claims**

113 FDG is a glucose analogue. The rationale for its use in oncology is based on the typically increased rate of
114 glycolysis in tumors compared to normal tissue. FDG is transported into tumor cells via glucose transport
115 proteins, usually up-regulated in tumor cells. Once internalized FDG is phosphorylated to FDG-6-phosphate;
116 it does not progress any further along the glycolytic pathway and becomes substantially metabolically
117 trapped. FDG uptake is not specific for tumor cells and there are some normal tissues and other processes
118 with increased glucose turnover, e.g. infection and inflammation, that show elevated uptake or
119 accumulation of FDG.

120 **Applications and Endpoints for Clinical Trials**

121 FDG-PET/CT imaging can be used for a wide range of clinical indications and research questions. These are
122 addressed more completely in the FDG-PET/CT UPICT Protocol (UPICT section 1.1). This QIBA Profile
123 specifically addresses the requirements for measurement of tumor FDG uptake with PET/CT as an imaging
124 biomarker for evaluating therapeutic response.

125 Biomarkers useful in clinical research for patient stratification or evaluation of therapeutic response would
126 be useful subsequently in clinical practice for the analogous purposes of initial choice of therapy and then
127 individualization of therapeutic regimen based on the extent and degree of response as quantified by FDG-
128 PET/CT.

129 The technical specifications described in the Profile are appropriate for quantification of tumor FDG uptake
130 and measuring longitudinal changes within subjects. However, many of the Profile details are generally
131 applicable to quantitative FDG-PET/CT imaging in other applications.

132 FDG-PET scans are sensitive and specific for detection of most malignant tumors [Fletcher 2008]. Coverage
133 for oncology imaging procedures in the US by the Centers for Medicare and Medicaid Services are explicitly
134 listed in the National Coverage Determination (NCD) for Positron Emission Tomography (PET) Scans (220.6).
135 FDG-PET scans reliably reflect glucose metabolic activity of cancers and this metabolic activity can be

136 measured with high reproducibility over time. Longitudinal changes in tumor 18F-FDG accumulation during
137 therapy often can predict clinical outcomes earlier than changes in standard anatomic measurements
138 [Weber 2009]. Therefore, tumor metabolic response or progression as determined by tumor FDG uptake
139 can serve as a pharmacodynamic endpoint in well-controlled Phase I and Phase IIA studies as well as an
140 efficacy endpoint in Phase II and III studies. In tumor/drug settings where the preceding phase II trials have
141 shown a statistically significant relationship between FDG-PET response and an independent measure of
142 outcome, changes in tumor FDG activity may serve as the primary efficacy endpoint for regulatory drug
143 approval in registration trials.

144 **Claim: Measure Change in SUV**

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

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

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

150 The following important considerations are noted:

151 1. This Claim applies only to tumors that are considered evaluable with PET. In practice this means tumors
152 of a minimum size of 2 cm and a baseline SUVmax of 4 g/ml (e.g. [Wahl 2009, de Langen 2012]). More
153 details on what tumors are evaluable are described in section 3.6.5.3.

154 2. Details of the claim were derived from a review of the literature and are summarized in Appendix B.

155 3. The published asymmetric limits of repeatability are based on observations that the test-retest SUVmax
156 differences do not follow a Normal distribution, but that the differences (d) of the logarithms of the test-
157 retest SUVmax values do follow a Normal distribution with a standard deviation of SD(d) [Velasquez 2009,
158 Weber et al. 2015]. The 95% repeatability coefficient (RC) in the log-Normal distribution (i.e. $\pm 1.96SD(d)$)
159 are symmetric about the mean. This suggests that when these limits are converted back to SUV units by
160 exponentiation using $RC = 100(\exp(\pm 1.96SD(d)) - 1)$, the SUV RC limits are necessarily asymmetric. In
161 addition, note that if the standard deviation is not large compared with the level of the measurement, then
162 it can be shown that $100(\exp(SD(d)/\sqrt{2}) - 1)$ is approximately equal to the within-subject coefficient of
163 variation, expressed as a percent [Bland and Altman 1996, Velasquez 2009]. If we assume a wCV of 12% for
164 SUVmax, then the repeatability coefficients are (-28%, +39%), consistent with the findings by Velasquez et
165 al. for advanced gastrointestinal malignancies, and those of Weber et al for non-small cell lung cancer. As a
166 possibly more intuitive motivation that asymmetric limits can be expected, we suppose two measurements
167 $SUV_{max1} = 7.0$ and $SUV_{max2} = 9.75$, then

$$168 \quad (SUV_{max2} - SUV_{max1}) / SUV_{max1} = +39\%$$

$$169 \quad (SUV_{max1} - SUV_{max2}) / SUV_{max2} = -28\%$$

170 In other words, there is net change in SUVmax of 2.75 in either direction representing a physiological
171 difference between two disease states: As an increase it is +39%, or as a decrease it is -28%

172 4. This Claim is applicable for single-center studies using the same scanner. For multi-center studies, if FDG-
173 PET/CT imaging is performed using the same scanner and protocol for each patient at each time point (as
174 described in the Profile), then it is anticipated that this Claim will be met.

175 5. This Claim is based on SUVmax due to the evidence provided in the scientific literature. However, the use
176 of SUV metrics derived from larger regions-of-interest (e.g. SUVpeak) are to be encouraged, as they may

provide improved repeatability. In addition, the use of automated and/or centralized analysis methods will further improve SUV repeatability. Note that while relative limits appear to be appropriate for SUVmax measures, it may be that absolute limits may be more appropriate for SUVs based on mean values for volumetric ROIs [Nahmias and Wahl 2008].

6. While the Claim has been informed by an extensive review of the literature, it is currently a consensus Claim that has not yet been substantiated by studies that strictly conform to the specifications given here. In addition, we note that this Claim should be re-assessed for technology changes, such as PSF (point spread function) based reconstruction or TOF (time of flight) imaging that were not utilized in published test-retest studies. A standard utilized by a sufficient number of studies does not exist to date. The expectation is that from future studies and/or field testing, data will be collected and changes made to this Claim or the Profile specifications accordingly.

3. Profile Details

The following figure provides a graphical depiction that describes the marker at a technical level.

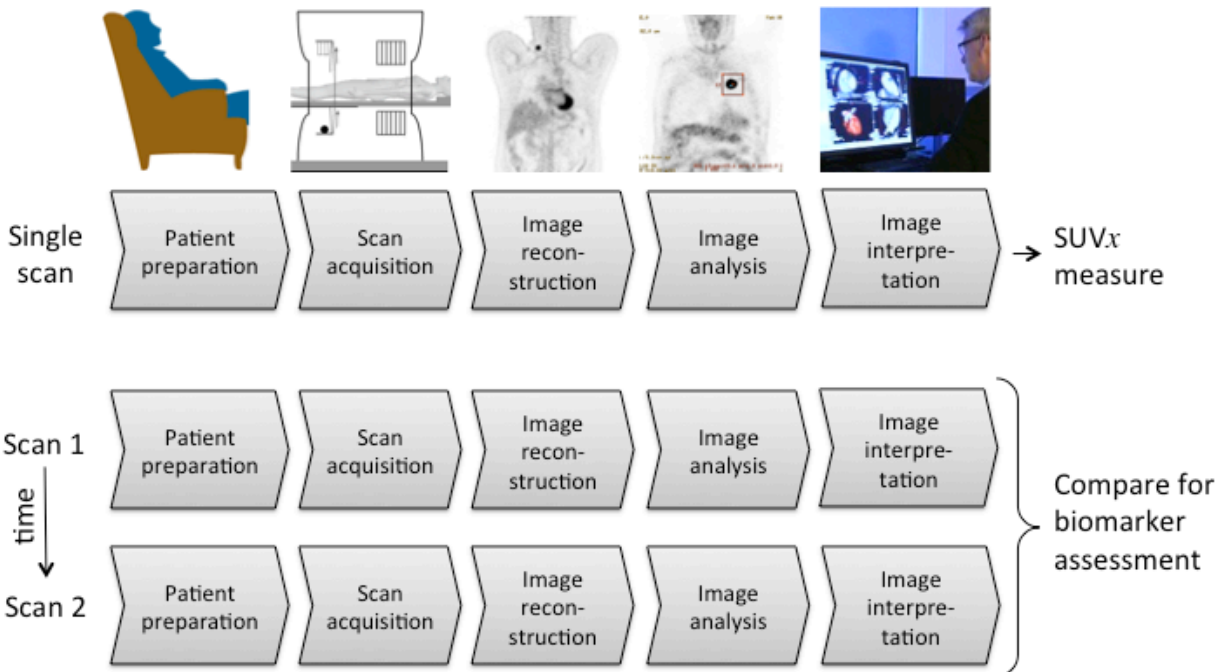


Figure 3: The assay method for computing and interpreting glycolytic metabolic activity using PET/CT may be viewed as a pipeline using either one or two or more scan sequences. The measure SUV_x refers to one of several possible SUV measures, such as SUV_{max}, SUV_{mean} or SUV_{peak}, with normalization by body weight or lean body mass.

Patients may be selected or referred for FDG-PET/CT imaging through a variety of mechanisms. In addition, patients are often required to undergo screening according to pre-scan requirements such as fasting levels and/or serum glucose levels as described below.

The imaging steps corresponding to Figure 1 are:

- 1) Patients or subjects are prepared for scanning (e.g. 6 hr fasting). FDG is administered. Patient waits quietly for bio-distribution and uptake of FDG (typically 60 min)

- 202 2) Scan data from the PET and CT exams is acquired.
- 203 3) Data correction terms are estimated and PET (and CT) images are reconstructed.
- 204 4) Quantitative measurements are performed.
- 205 5) Images are reviewed for qualitative interpretation.

206 Note that steps 4 and 5 may occur in either order or at the same time. More details on the requirements
207 are given below.

208 Images may be obtained at multiple time points over days or weeks, notably at a minimum of two time
209 points before and after therapeutic intervention for a response assessment as is considered by this
210 document. The change in FDG uptake is typically assessed as a percentage according to the formula:

211
$$\frac{[(\text{post-treatment metabolic activity} - \text{pre-treatment metabolic activity}) / \text{pre-treatment metabolic activity}] \times 100\%}{}$$

212 x 100%. Response criteria are then applied to categorize the response assessment. These response criteria
213 are beyond the scope of this document, but are discussed in the PERCIST proposal [Wahl 2009].

214 The following sections describe the major components illustrated in Figure 3:

Section	Title	Performed by
3.1	Subject Handling	Personnel, (including Technologists and Schedulers) at an Image Acquisition Facility
3.2	Image Data Acquisition	Technologist, at an Image Acquisition Facility using an Acquisition Device
3.3	Image Data Reconstruction	Technologist, at an Image Acquisition Facility using Reconstruction Software
3.4	Image Analysis	Imaging Physician or Image Analyst using one or more Analysis Software tools
3.5	Image Interpretation	Imaging Physician before or after information obtained by Image Analysis using a pre-defined Response Assessment Criteria

215 Image data acquisition, reconstruction and post-processing are considered to address the collection and
216 structuring of new data from the subject. Image analysis is primarily considered to be a computational step
217 that transforms the data into information, extracting important values. Interpretation is primarily
218 considered to be judgment that transforms the information into knowledge.

219 **3.1. Subject Handling**

220 This Profile will refer primarily to 'subjects', keeping in mind that the recommendations apply to patients in
221 general, and that subjects are often patients too.

222 **3.1.1 Subject Selection, Timing, and Blood Glucose Levels**

223 The study protocol should include specific directions as to the management of subjects with abnormal
224 fasting blood glucose measurements whether known to be diabetic or not. While it is known that high
225 levels of circulating blood glucose reduce FDG uptake, there is a paucity of scientific data to suggest a
226 specific cutoff for abnormally high blood glucose measurements or if these subjects should be excluded
227 from clinical trials that use FDG-PET/CT scan data. It is important to define how such subjects and the data
228 from their imaging studies will be managed to ensure comparability of imaging data within and among

229 clinical trials. Specifically, consideration should be given to the exclusion of subjects with abnormal fasting
230 blood glucose when quantitative FDG-PET/CT is being used as the study's primary endpoint. Refer to the
231 FDG-PET/CT UPICT Protocol for Diabetic Scheduling and Management discussion (UPICT Section 4.2.2). It is
232 also recommended that the study specifies what level of within subject variability in serum glucose levels is
233 acceptable across time points and how subjects that fall outside that range will be interpreted.

234 **3.1.1.1 Timing of Imaging Test Relative to Intervention Activity (UPICT Section 1.2)**

235 The study protocol should specifically define an acceptable time interval that should separate the
236 performance of the FDG-PET/CT scan from both (1) the index intervention and (2) other interventions (e.g.
237 chemotherapy, radiotherapy or prior treatment). This initial scan (or time point) is referred to as the
238 "baseline" scan (or time point). The time interval between the baseline scan and the initiation of treatment
239 should be specified as well as the time intervals between subsequent FDG-PET studies and cycles of
240 treatment. Additionally, the study protocol should specifically define an acceptable timing variance for
241 performance of FDG-PET/CT around each time point at which imaging is specified (i.e., the acceptable
242 window of time during which the imaging may be obtained "on schedule"). The timing interval and window
243 are dependent upon 1) the utility for the FDG-PET/CT imaging within the clinical trial, 2) the clinical
244 question that is being investigated and 3) the specific intervention under investigation. Suggested
245 parameters for timing of FDG-PET/CT within oncologic trials are more completely addressed in the FDG-
246 PET/CT UPICT Protocol section 1.2.

247 **3.1.1.2. Timing Relative to Confounding Activities (UPICT Section 3.2)**

248 Activities, tests and interventions that might increase the chance for false positive and/or false negative
249 FDG-PET/CT studies should be avoided prior to scanning. The allowable interval between the potentially
250 confounding event and the FDG-PET/CT exam will be dependent on the nature of the confounding variable.
251 For example, inflammation may cause focally increased FDG-PET activity (e.g. from a percutaneous or
252 excisional biopsy of a suspicious mass) or might lead to the appearance of a non-malignant mass (e.g.,
253 hematoma) on the CT portion of the study. A percutaneous ablation procedure of a known malignant focus
254 may cause focally increased FDG-PET activity and/or an immediate post-ablation increase in the apparent
255 volume of the ablated target lesion. The time of onset and the duration of the increased FDG-PET activity
256 and/or the change in lesion volume might be different for these two confounding factors.

257 If iodinated contrast is to be used for the CT portion of the PET/CT study, conflict with other tests and
258 treatments should be avoided congruent with community standards of care (e.g., thyroid scan).

259 **3.1.1.3. Timing Relative to Ancillary Testing (UPICT Section 3.3)**

260 Avoid scheduling tests that might confound the qualitative or quantitative results of the FDG-PET/CT study
261 within the time period prior to the scan. For example, a glucose tolerance test should not be scheduled
262 during the 24 hours prior to the performance of FDG-PET/CT. Similarly, other tests that might involve
263 increasing plasma glucose, insulin, or corticosteroid levels should also be avoided. Exercise cardiac stress
264 testing should be avoided during the twenty-four (24) hours prior to the performance of FDG-PET/CT.
265 Similarly, other tests that might involve vigorous exercise and thereby increase muscle metabolic function
266 should also be avoided.

267 **3.1.2 Subject Preparation (UPICT Section 4)**

268 Management of the subject can be considered in terms of three distinct time intervals (1) prior to the
269 imaging session (prior to arrival and upon arrival), (2) during the imaging session and (3) post imaging

270 session completion. The pre-imaging session issues are contained in this section while the intra-imaging
271 issues are contained in section 3.2.1 on image data acquisition.

272 **3.1.2.1. Prior to Arrival (UPICT Section 4.1)**

273 The main purpose of subject preparation is to reduce tracer uptake in normal tissue (kidneys, bladder,
274 skeletal muscle, myocardium, brown fat) while maintaining and optimizing tracer uptake in the target
275 structures (tumor tissue). For more detail, refer to the FDG PET UPICT Protocol (Section 4.1) that addresses
276 (1) Dietary, (2) Fluid Intake, and (3) Other activities that may affect tissue FDG uptake.

277 (1) Dietary

278 a. Diabetic management – Refer to FDG-PET/CT UPICT Protocol sections 1.7.2 and 4.2.2

279 b. Fasting status - Subjects should not eat any food (either oral or parenteral) for at least six
280 hours prior to the anticipated time of FDG administration.

281 (2) Fluid Intake: Adequate hydration (before and after FDG administration) is important both to ensure
282 a sufficiently low FDG concentration in urine (fewer artifacts) and to reduce radiation exposure to
283 the bladder. Adequate hydration is especially important when contrast CT imaging will be used.
284 Whichever hydration strategy is used (how much and when to administer), the protocol should be
285 uniform among sites during a trial. Specific hydration recommendations are presented in the FDG-
286 PET/CT UPICT Protocol (reference Section 4.2.1). The fluid administered should not contain glucose
287 or caffeine.

288 (3) Other Activities: To minimize FDG uptake in muscle, the subject should avoid strenuous or extreme
289 exercise before the PET exam for at least 6 hours (preferably for a time period of 24 hours).

290 The conformance issues around these parameters are dependent upon adequate communication and
291 oversight of the Scheduler or Technologist at the Image Acquisition Facility with the subject.
292 Communication with the subject and confirmation of conformance should be documented.

293 **3.1.2.2. Upon Arrival (UPICT Section 4.2)**

294 Upon arrival 1) confirmation of subject compliance with pre-procedure instructions and 2) the occurrence
295 of potentially confounding events (see listing in Section 4.2.1 of FDG-PET/CT UPICT Protocol) should be
296 documented on the appropriate case report forms.

297 There should be documentation of subject-specific risk factors including, but not limited to, previous
298 contrast reactions (if iodinated contrast is to be used).

299 **3.1.2.3 Preparation for Exam (UPICT Section 4.2.3)**

300 In order to avoid heterogeneous physiological distribution of the FDG, it is critical that subject preparation
301 after arrival and prior to imaging is standardized among all sites and subjects throughout the conduct of the
302 clinical trial.

- 303 • The waiting and preparation rooms should be relaxing and warm (> 75° F or 22° C) during the entire
304 uptake period (and for as long as reasonably practicable prior to injection, at least 15 minutes is
305 suggested as acceptable). Blankets should be provided if necessary.
- 306 • The subject should remain recumbent or may be comfortably seated; activity and conversation
307 should be kept to an absolute minimum. For example, the subject should be asked to refrain from
308 speaking, chewing, or reading during the uptake period. For brain imaging the subject should be in a

309 room that is dimly lit and quiet for FDG administration and subsequent uptake period.

- 310 • After FDG injection, the subject may use the toilet, preferably not for the initial 30 minutes
311 immediately after injection of FDG, primarily to avoid muscular uptake during the biodistribution
312 phase of FDG-uptake. The subject should void immediately (within 5 – 10 minutes) prior to the FDG-
313 PET/CT image acquisition phase of the examination.
- 314 • Bladder catheterization is not routinely necessary; but if deemed necessary (e.g., for the evaluation
315 of a subject with a pelvic tumor such as cervical or prostate cancer), the catheter should be placed
316 prior to injection of FDG. If bladder catheterization is performed, additional strategies to avoid
317 trapping high activity pockets of activity within the bladder should be considered such as retrograde
318 filling of the bladder to dilute the residual activity.
- 319 • Following the administration of FDG, the subject should drink 500 ml of water (or receive by
320 intravenous administration 250 - 500 ml of non-glucose containing fluid). Fluid intake may need to
321 be modified for those subjects on fluid restriction.
- 322 • For specific areas of anatomic interest (e.g., tumors located in the lower abdomen, pelvis or kidney)
323 intravenous diuretic agents may be used (e.g., 20 – 40 mg of furosemide given 15 minutes after the
324 administration of FDG). If bladder catheterization is performed, IV diuretics should be administered
325 as described here so as to ensure that the concentration of activity in the renal collecting systems
326 and bladder is relatively dilute.
- 327 • Sedation is not routinely required, but is not contraindicated provided that the sedative used does
328 not interfere with the uptake of FDG. Sedation may have utility in specific clinical circumstances
329 such as in subjects with brain, head and neck tumors or breast cancer, claustrophobic subjects, or
330 children. The sedative effect should last for the duration of image acquisition; detailed specifications
331 are dependent upon the medication used and the route of administration.
- 332 • The amount of fluid intake and use of all medications (e.g., diuretic, sedative) must be documented
333 on the appropriate case report form.
- 334 • Subjects undergoing a CT scan should empty their pockets and remove any clothing containing
335 metal and any metallic jewelry from the body parts to be scanned, changing into a hospital gown if
336 necessary.

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

Parameter	Entity/Actor	Specification
		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).

- 337 • Diabetic Monitoring and Management (UPICT Section 4.2.2)

338 The subject's blood glucose level should be measured [using CLIA-approved, CLIA cleared, or equivalent
339 (outside US) glucose measurement device or laboratory] within the preceding 2 hours (ideally within 1
340 hour, especially in subjects with diabetes) of FDG administration and documented.

Parameter	Entity/Actor	Specification
Blood glucose level measurement	Imaging Technologist or Lab Technologist	Within 2 hours preceding FDG administration, shall measure and document time of subject blood glucose collection. Glucose measurement should be performed using a CLIA approved, CLIA cleared, or equivalent (outside US) glucose measurement device. If the measurement is always performed at injection time or otherwise according to a protocol relative to injection time, this may be documented in the protocol. Deviations from this process shall be documented.
Blood glucose level documentation	Imaging Technologist or Lab Technologist	Shall enter the results of the blood glucose assay and the time of blood draw on a case report form or similar subject information sheet. Shall enter the results of the blood glucose assay into a common format mechanism used for recording all needed information (Appendix E).
Blood glucose level Threshold	Imaging Technologist	Shall enforce the glucose thresholds for imaging as defined in the Protocol; if not, then reason for non-conformance shall be provided and documented on case report form or similar subject information sheet. Shall document any information on non-conformance with the protocol into a common format mechanism used for recording all needed information (Appendix E).

3.1.3. Imaging-related Substance Preparation and Administration (UPICT Section 5)

3.1.3.1. Radiotracer Preparation and Administration

3.1.3.1.1 Radiotracer Description and Purpose

FDG should be of high quality and purity. For example, the FDG radiopharmaceutical must be produced under Current Good Manufacturing Practice as specified by the FDA, EU, European Pharmacopea or other appropriate national regulatory agency. U.S. regulations such as 21CFR212 or USP<823> Radiopharmaceuticals for Positron Emission Tomography must be followed in the U.S. or for trials submitted to US Regulatory. For example, in the US, for clinical practice, FDG production under NDA or ANDA or under IND for research purposes is mandatory.

3.1.3.1.2 Radiotracer Activity Calculation and/or Schedule (UPICT Section 5.2)

The ¹⁸F-FDG activity administered ranges between about 185 – 740MBq (5 – 20 mCi). The administered activity typically depends upon the local imaging protocol. The local protocol may require fixed activity, or the activity may vary as a function of various parameters including but not limited to subject size or age, scanner model, scanning mode, or percentage of scan bed (slice) overlap. To date there are no data providing evidence of superiority of parameter-dependent administered activity protocols. The exact activity and the time at which activity is calibrated should be recorded. Residual activity remaining in the tubing, syringe or automated administration system or any activity spilled during injection should be recorded. The objective is to record the net amount of FDG radiotracer injected into the subject to provide accurate factors for the calculation of the SUV. The use of automated activity measurement and injection devices is allowed if accuracy is verified.

Parameter	Entity/Actor	Specification
Administered FDG Radiotracer Activity	Imaging Technologist	<p>The Technologist shall</p> <ol style="list-style-type: none">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.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. <p>These values shall be entered into the scanner during the PET/CT acquisition.</p> <p>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.</p> <p>All data described herein on activity administration shall be</p>

Parameter	Entity/Actor	Specification
		documented.
		All data should be entered into the common data format mechanism (Appendix E).

3.1.3.1.3 Radiotracer Administration Route (UPICT Section 5.4)

FDG should be administered intravenously through a large bore (24 gauge or larger) indwelling catheter placed anatomically remote (e.g., contralateral extremity to site of disease if at all possible) to any site(s) of suspected pathology, preferably in an antecubital vein. Intravenous ports should not be used, unless no other venous access is available. If a port is used, an additional flush volume should be used. As reproducible and correct administration of FDG is required for quantification purposes, extravasation or paravenous administration should be avoided. If an infiltration or extraneous leakage is suspected, the event and expected quantity should be recorded and the infiltration site should be imaged. The approximate amount of infiltration should be estimated from the images where possible. If the infiltration is greater than 5% of the administered activity and the quantitative result from the FDG-PET/CT study is a primary or secondary endpoint, the data point might be censored from review or the subject might not be included in the study. The anatomical location of the injection site should be documented on the appropriate case report form or in the Common Data Format Mechanism (Appendix E).

Presuming that the IV access is properly functioning, the same route of administration may be used for iodinated contrast as is used for FDG.

Parameter	Entity/Actor	Specification
FDG Administration	Technologist	<p>Technologist shall administer FDG intravenously through a large bore (24 gauge or larger) indwelling catheter placed anatomically remote to any sites of suspected pathology, preferably in an antecubital vein. Intravenous ports should not be used, unless no other venous access is available.</p> <p>In the case of manual administration, a three-way valve system should be attached to the intravenous cannula so as to allow at least a 10 cc normal (0.9% NaCl) saline flush following FDG injection. For automated injection devices alternate flushing mechanisms are allowed.</p>
Suspected infiltration or extraneous leakage	Technologist and/or Physician or Physicist	Technologist shall document any suspected infiltration, leakage, or external contamination and consider scanning the injection site and/or contaminated materials.
		Record the event and expected amount of FDG into the common data format mechanism (Appendix E).

3.1.3.2 CT Contrast Material Preparation and Administration

The use of CT contrast material during FDG-PET/CT imaging is complex and analyzed in detail in the UPICT

378 FDG-PET Protocol (Section 3.2). In summary, the presence of IV and/or oral contrast material improves the
 379 detection of lesions with CT and may improve the anatomic localization, interpretation, and analysis of the
 380 FDG-PET/CT exam. However, the presence of contrast material may affect the attenuation correction of the
 381 PET scan with consequent bias in measured SUVs.

Parameter	Entity/Actor	Specification
CT Contrast Agent	Technologist	Technologist shall record the type and amount of CT Contrast Agent. 1. Was oral contrast used: Type [Positive, Negative], amount (volume in cc). 2. Was IV contrast use: Amount (volume in cc), time of injection.
		Record the event and expected amount of CT Contrast Agent into the common data format mechanism (Appendix E).

382 3.2. Image Data Acquisition

383 This section summarizes the imaging protocols and procedures that shall be performed for an FDG-PET/CT
 384 exam. Detailed descriptions are included in the referenced FDG-PET/CT UPICT protocol sections.

385 The motivation for controlling the image acquisition as tightly as described here is that over the course of a
 386 trial, hardware and software updates will occur. The intent of the Profile is to ensure that the instrument
 387 gives the same results over the duration of the trial.

388 For consistency, clinical trial subjects should be imaged on the same device over the entire course of a
 389 study. If the imaging requirements are qualitative i.e. for relative quantitation, for example the presence or
 390 absence of a lesion or a lesion SUV relative to a reference region, then a replacement scanner may be used
 391 if it is properly qualified. It is imperative, however, that the trial sponsor be notified of scanner substitution
 392 if it occurs.

393 For clinical trials with quantitative imaging requirements, a subject should have all scans performed on only
 394 one scanner unless quantitative equivalence with a replacement scanner can be clearly demonstrated.
 395 However, it should be noted that there are currently no accepted criteria for demonstrating quantitative
 396 equivalence between scanners. It is anticipated that future version of this Profile will provide such criteria.

397 The follow up scans should be performed with identical acquisition parameters as the first (baseline),
 398 inclusive of all the parameters required for both the CT and PET acquisitions.

399 The FDG-PET/CT UPICT Protocol (Section 7.1.1) describes scanning strategies that can be used in a clinical
 400 trial. For strategy 1, there is no intent to obtain a diagnostic CT scan at the FDG-PET imaging session,
 401 however a low-dose CT scan is needed for attenuation correction. For strategy 2, a diagnostic CT scan is
 402 obtained. There are further considerations that must be followed for each of the two strategies. The
 403 workflow chosen for a given protocol should be described in the protocol and should be tailored
 404 commensurate to the level of expectation of the obtained data (e.g. qualitative or quantitative SUV
 405 analysis).

406 Strategy 1: For FDG-PET/CT in which the CT is used for attenuation correction and localization only (not
 407 intended as a clinically diagnostic CT):

- 408 • CT Scout (i.e. topogram or scanogram etc.), followed by
- 409 • CT for anatomic localization and attenuation correction, followed by

410
411
412
413
414
415
416
417
418
419
420

- PET Emission scan acquisition

Strategy 2: For FDG-PET/CT in which a clinically diagnostic CECT is also required, ONE of the following options should be used. Strategy 2a is preferable since it avoids any, all be it possibly minimal, impact of IV contrast enhancement on attenuation correction and therefore SUV determination.

Strategy 2a

- Follow Strategy 1 (above)
- Acquire an additional IV contrast-enhanced diagnostic CT scan

Strategy 2b

- Perform an IV contrast-enhanced diagnostic CT scan
- Follow Strategy 1 (above)

Parameter	Entity/Actor	Specification
Scanning Strategy (Workflow)	Technologist	Technologist shall follow Profile compliant workflow strategy, which will be compatible with Acquisition Device capability. The same workflow used at baseline shall be used at all subsequent time points.

421
422
423
424
425
426
427
428
429
430
431
432
433
434
435
436
437
438
439
440
441
442

For both strategies, there are several common issues specific to the CT exam that may have an impact on quantitative FDG-PET output, which need attention and protocol specification. These include (1) contrast material administration, (2) respiratory motion management instructions and (3) CT scanning technique (kVp, mAs and pitch). Below is a summary of the acceptable level of behavior/procedure for each of these three issues.

At a minimum, all these issues should be addressed in the clinical trial protocol, ideally with consistency across all sites and all subjects (both inter-subject, and intra- and inter-facility) with the target of consistency across all time points for each given subject. The actual details of imaging for each subject at each time point should always be recorded. Any particular clinical trial should NOT allow some sites to implement one strategy and other sites to implement the alternative.

CT Exam Variables and Specifications:

Contrast Agents - The presence of a positive contrast agent (IV or oral), by affecting the CT attenuation map, may affect SUV quantitation [Mawlawi 2006]. If this were the only consideration, then ideal would be to prohibit CT contrast administration. However, in some clinical situations (dependent upon tumor type, tumor behavior or level of anatomic interest), the benefit of CT contrast agents may outweigh the small errors induced in SUV measurement that may include increased SUV variability. Each protocol should specify the desired approach for the given study. Most importantly, for each subject, the same approach should be followed for all imaging time points.

In cases where CT contrast agents are used, there are two main strategies:

Strategy 1: No IV; dilute positive oral contrast allowed

Strategy 2: Use negative or dilute positive oral contrast for the non-attenuation CT scan. Ensure that

the diagnostic CT acquisition (which may be performed with IV contrast) is performed consistently for a given subject across all time points.

Parameter	Entity/Actor	Specification
CT Contrast agent	Technologist	CT contrast agents shall be given commensurate with the workflow strategy as selected from above.

3.2.1 Imaging Procedure

The PET/CT exam consists of two components, the PET emission scan and the CT transmission scan (which may have multiple components). From these data sets, the non-attenuation-corrected PET images may be reconstructed for quality control purposes and attenuation-corrected PET images are reconstructed for qualitative interpretation and quantitative analysis. Instrument specifications relevant to the Acquisition Device are included in Section 4 Conformance – Acquisition Device.

3.2.1.1 Timing of Image Data Acquisition

FDG uptake into both tumors and other body tissues is a dynamic process that may increase at different rates and peak at various time points dependent upon multiple variables. Therefore, it is extremely important that (1) in general, the time interval between FDG administration and the start of emission scan acquisition is consistent and (2) when repeating a scan on the same subject, it is essential to use the same interval between injection and acquisition in scans performed across different time points.

While the “target” tracer uptake time is 60 minutes, the “acceptable” window is from 55 to 75 minutes to ensure that imaging does not begin prematurely so as to allow adequate tumor uptake of FDG and to account for the practicality of work flow that can result in delays in imaging later than 60 minutes after FDG injection. The exact time of injection must be recorded; the time of injection initiation should be used as the time to be recorded as the radiotracer injection time. The injection and flush should be completed within one minute with the rate of injection appropriate to the quality of the vein accessed for FDG administration so as to avoid compromising the integrity of the injection vein

When performing a follow-up scan on the same subject, especially in the context of therapy response assessment, it is essential to apply the same time interval with target window of ± 10 minutes provided that the scan must not begin prior to 55 minutes after the injection of FDG. While there is majority view of the committee that a tighter (narrower) time window, e.g. ± 5 minutes, is better, the current performance specification is written to balance practical and ideal. If a limited anatomy scan is obtained at follow-up after a whole body scan was performed at baseline, one should consider adjusting the timing of the follow up scan to be congruent with the timing for the same anatomic region as achieved during the baseline study.

If, for scientific reasons, an alternate time (between activity administration and scan acquisition) is specified in a specific protocol, then the rationale for this deviation should be stated; inter-time point consistency must still be followed.

Parameter	Entity/Actor	Specification
Tracer Injection Time	Technologist	The time of FDG injection shall be entered into PET/CT scanner console during the acquisition.
Tracer Uptake	Technologist	The Technologist shall ensure that the tracer uptake time for the

Parameter	Entity/Actor	Specification
Time:		<p>baseline scan is 60 minutes, with an acceptable range of 55 to 75 minutes.</p> <p>When repeating a scan on the same subject, especially in the context of therapy response assessment, the Technologist shall apply the same time interval ± 10 minutes provided that the scan must not begin prior to 55 minutes after the injection of FDG.</p>

475 The following sections describe the imaging procedure.

476 **3.2.1.2 Subject Positioning (UPICT Section 7.2.1)**

477 Consistent positioning avoids unnecessary variance in attenuation, changes in gravity-induced shape and
478 fluid distribution, or changes in anatomical shape due to posture, contortion, etc. During PET-CT, subjects
479 should be positioned in the center of the field of view (FOV), preferably with the subjects' arms positioned
480 over head for whole-body imaging (to minimize beam hardening and FOV truncation artifacts). In the case
481 of dedicated brain or head/neck scans, the arms should be positioned down along the body. If the subject is
482 physically unable to maintain arms above head for the entire whole-body examination then the arms can
483 be positioned along the side before the start of the scan, unless the protocol specifically excludes such
484 subjects. Arm positioning in a particular subject should be consistent between the PET emission and CT
485 transmission scans at each time point and should be as consistent as possible across all time points.

486 Respiratory motion causes SUV errors by two mechanisms: motion blurring and errors in attenuation
487 correction due to mismatches between CT-based attenuation map and emission data [Liu 2009]. Various
488 strategies could be used to minimize, document and compensate for respiratory motion. Shallow breathing
489 shall be performed during CT AC acquisition (see UPICT Protocol section 7.1.1). The subject should (a) be
490 monitored and if breathing pattern is not consistent with shallow breathing expectation, coached in the
491 breathing protocol and (b) remain motionless throughout the scan. Alternate CT strategies for achieving
492 PET/CT match may be considered if it can be verified that PET AC artifacts in the vicinity of the diaphragm
493 are routinely minimal. It is of utmost importance that the patient *not* be in end-inspiration phase during CT
494 for PET/CT.

495 The Technologist shall document factors that adversely influence subject positioning or limit the ability to
496 comply with instructions (e.g. breath-hold, shallow breathing, remaining motionless, etc.).

497

Parameter	Entity/Actor	Specification
Subject Positioning	Technologist	The Technologist shall position the subject according to the UPICT specifications and/or specific protocol specifications consistently for all scans.

498

Parameter	Entity/Actor	Specification
Positioning Non-conformance	Technologist	The Technologist shall document issues regarding subject non-conformance with positioning.
		The Technologist shall document issues regarding subject non-

		conformance with breathing and positioning using the common data format mechanism (Appendix E).
--	--	---

499

Parameter	Entity/Actor	Specification
Respiratory motion minimization	Technologist	If the patient is observed to take a deep breath during the CT scan it should be documented and a repeat CT study should be considered.
Respiratory motion minimization	PET/CT Scanner	The PET/CT scanner shall provide methods to minimize the PET image errors introduced by respiratory motion.

500

Parameter	Entity/Actor	Specification
Breathing and motion non-conformance	Technologist	The Technologist shall document issues regarding subject non-conformance with breathing and motion.
		The Technologist shall document issues regarding subject non-conformance with breathing and motion using the common data format mechanism (Appendix E).

501

502

3.2.1.3 Scanning Coverage and Direction (UPICT Section 7.1.1)

503

504

505

506

507

508

509

510

511

For most Oncology indications, anatomic coverage should include from the skull base (external auditory meatus) to the mid-thigh. If other ranges are used, which may be appropriate for specific clinical trials, then the clinical trial protocol should provide specific instructions with justification. Multiple factors affect the decision regarding the scan direction. For example, scanning caudocranial minimizes effects from increasing bladder activity during the scan, important for image quality in the pelvis. For some tumors located in the head, neck, or upper thorax it may be more important to start at the head to minimize head and arm motion between PET and CT. Scanning direction should be specified in the clinical trial protocol. It is critical that for a given subject, scanning direction on baseline scans be duplicated at follow-up time points.

Parameter	Entity/Actor	Specification
Scanning Direction	Technologist	The Technologist shall scan the subject caudocranial for whole body examination unless otherwise specified by the protocol. Each patient should be scanned consistently (in the same direction) over all time points.
		The scanning direction shall be entered into the PET/CT console during the acquisition and will be recorded by the scanner into the appropriate DICOM field.

Parameter	Entity/Actor	Specification
Anatomic Coverage	Technologist	The Technologist shall perform the scan such that the anatomic coverage is acquired according to the protocol specifications and the same for all time points.

512

513 **3.2.1.4 Scanner Acquisition Mode Parameters**

514 We define acquisition mode parameters as those that are specified by the Technologist at the start of the
515 actual PET/CT scan. These include the acquisition time per bed position, the bed overlap, the acquisition
516 mode (2D or 3D), with or without cardiac and/or respiratory gating and CT technique. These parameters do
517 not include aspects of the acquisition that occur earlier (e.g. injected amount of 18F-FDG or uptake
518 duration, CT contrast agent injection) or later (e.g. reconstruction parameters) in the overall scan process.

519 *PET Acquisition*

520

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 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.
PET acquisition mode	Technologist	The key PET acquisition mode parameters (e.g., time per bed position, acquisition mode, with or without gating) <u>shall be set as specified</u> by study protocol and used consistently for all patient scans.

521

522 *CT Acquisition*

523 For the CT acquisition component of the PET/CT scan, this Profile only addresses the aspects related to the
524 quantitative accuracy of the PET image. In other words aspects of CT diagnostic accuracy are not addressed
525 in this Profile. In principle any CT technique (parameters include kVp, mAs, pitch, and collimation) will
526 suffice for accurate corrections for attenuation and scatter. However, it has been shown that for estimating
527 PET tracer uptake in bone, lower kVp CT acquisitions can be more biased. Thus higher kVp CT acquisitions
528 are recommended in general. In addition if there is the potential for artifacts in the CT image due to the
529 choice of acquisition parameters (e.g. truncation of the CT field of view), then these parameters should be
530 selected appropriately to minimize propagation of artifacts into the PET image through CT-based
531 attenuation and scatter correction. Finally, extremely low x-ray flux can lead to a bias in CT images.
532 Protocols should allow high enough mAs to avoid this artifact.

533

Parameter	Entity/Actor	Specification
-----------	--------------	---------------

Parameter	Entity/Actor	Specification
CT acquisition mode	Study Sponsor	The key CT acquisition mode parameters (kVp, mAs, pitch, and collimation) shall be specified in a manner that is expected to produce comparable results regardless of the scanner make and model and with appropriate radiation doses consistent for the role of the CT scan: diagnostic CT scan, anatomical localization, or accurate corrections for attenuation and scatter.
		CT dose reduction techniques may be used if demonstrated to retain quantitative accuracy.
CT acquisition mode	Technologist	The key CT acquisition mode parameters (kVp, mAs, pitch, and collimation) shall be set as specified by study protocol and used consistently for all subject scans.

534

535

536

Parameter	Entity/Actor	Specification
-----------	--------------	---------------

537

538 Regarding CT radiation exposure, the lowest radiation dose necessary to achieve the diagnostic objective
539 should be used. For a given protocol, the purpose of performing the CT scan (with the intent of attenuation
540 correction only or attenuation correction and anatomic localization versus one intended for diagnostic CT
541 purposes with contrast and breath-hold) should be determined. The CT technique (tube current, rotation
542 speed, pitch, collimation, kVp, and slice thickness) used should result in as low as reasonably achievable
543 exposure needed to achieve the necessary PET image quality. The technique used for an imaging session
544 should be repeated for that subject for all subsequent time points assuming it was properly performed on
545 the first study.

546 3.3. Imaging Data Reconstruction and Post-Processing

547 3.3.1 Imaging Data Reconstruction (UPICT Section 7.3)

548 Reconstructed image data is the PET image exactly as produced by the reconstruction process on the
549 PET/CT scanner, i.e. a PET image volume with no processing other than that occurring during image
550 reconstruction. This is always a stack of DICOM slices/files constituting a PET image volume that can be
551 analyzed on one or more of the following: PET scanner console, PET image display workstation, PACS
552 system, etc. See Section 4 Conformance – Image Reconstruction Software for specifications.

553 The PET reconstruction parameters include the choice of reconstruction algorithm, number of iterations
554 and subsets (for iterative algorithms), the type and amount of smoothing, the field of view and voxel size.
555 The quantitative accuracy of the PET image should be independent of the choice of CT reconstruction
556 parameters, although this has not been uniformly validated. In addition, if there is the potential for artifacts
557 in the CT image due to the choice of processing parameters (e.g. compensation for truncation of the CT
558 field of view), then these parameters should be selected appropriately to minimize propagation of artifacts
559 into the PET image through CT-based attenuation and scatter correction.

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	Technologist	The key PET reconstruction parameters (algorithm, iterations, smoothing, field of view, voxel size) shall be followed and set as specified.
Correction factors	Technologist	All quantitative corrections shall be applied during the image reconstruction process. These include attenuation, scatter, randoms, dead-time, and efficiency normalizations.
Calibration factors	Scanner	All necessary calibration factors needed to output PET images in units of Bq/ml shall be automatically applied during the image reconstruction process.

561

562

563 As part of the image reconstruction and analysis, correction factors for known deviations from the
564 acquisition protocol can potentially be applied. These corrections can include, for example, compensation
565 for mistakes in data entry [Kinahan 2010], variations in FDG uptake period [Beaulieu 2003], and errors in
566 scanner calibration factors [Lockhart 2011]. Corrections for known data entry errors and errors in scanner
567 calibration factors should be corrected prior to the generation of the reconstructed images, or immediately
568 afterwards. Corrections that are more ad-hoc in nature, e.g. corrections for variations in FDG uptake period
569 or plasma glucose levels or partial volume correction, should only be applied as part of the image analysis
570 step. That is, not used to modify the reconstructed PET image.

571 **3.3.2 Image Data Post-processing (UPICT Section 8)**

572 Processed image data are images that have been transformed in some manner, including but not limited to:
573 smoothing, image zoom, rotation/translation, resampling, interpolation, slice averaging, MIP, etc. This is
574 typically a stack of DICOM slices/files constituting a PET image volume. If image registration or
575 interpolation is required, then where applicable, perform the ROI analysis on the original PET image set
576 using appropriately modified ROIs. The intent is to preserve the numerical accuracy of the true PET image
577 values.

578 Standard whole-body FDG-PET oncology studies typically include all necessary data corrections and
579 processing within the reconstruction process and do not require additional processing other than (e.g.) data

580 de-identification. More advanced studies such as those including dynamic imaging may require additional
581 processing as specified in the individual protocol.

582 Briefly described here are concepts presented in UPICT Section 8.2.3 regarding difference between
583 'visualized data' and 'data used for quantification'. At the acceptable level, for visual
584 inspection/interpretation of PET/CT data using the display workstation, bi-linear or tri-linear interpolation
585 and zooming may be used to display the images in a different matrix size than the original data. In addition,
586 so-called maximum intensity projections (MIP) may be generated as they may facilitate localization and
587 detection of lesions. Additional processing, such as zooming, re-binning, reorientation and filtering may be
588 applied upon user request only. User should be able to manipulate color scale settings (window/level and
589 color table). It should always be possible to revert to the default orientation, zoom and bin size (preferably
590 a 'revert to default' button is available).

591

592 **3.3.3 Imaging Data Storage and Transfer**

593 Discussions of archiving PET data often mention 'raw data'. This is an ambiguous term as it can refer to:
594 **scanner raw data** (i.e., sinograms or list-mode) or image raw data. To avoid confusion, the term raw data
595 should not be used without making it clear which form is under discussion.

596 **Image raw data** is the image data exactly as produced by the reconstruction process on the PET or PET/CT
597 scanner, i.e., a stack of DICOM slices/files constituting a PET image volume with no processing other than
598 that occurring during image reconstruction. This is always a stack of DICOM slices/files constituting a PET
599 image volume that can be analyzed on one or more of the following: PET scanner console, PET image
600 display workstation, PACS system, etc.

601 **Post-processed image data** are images that have been transformed after reconstruction in some manner,
602 including but not limited to: smoothing, image zoom, rotation/translation, resampling, interpolation, slice
603 averaging, MIP, etc. Such images may be only produced for temporary analysis and display, or they may be
604 saved as DICOM slices/files, and can still be analyzed on one or more of the following: PET scanner console,
605 PET image display workstation, PACS system, etc.

606 For archiving at the local site or imaging core lab (if relevant), the most important data are the original
607 images, i.e., the image raw data. In the unlikely event that the scanner raw data (which should be archived
608 by the local site) is required for later reprocessing; this should be made clear in the protocol.

609

610

Parameter	Entity/Actor	Specification
Data archiving	Technologist	The originally reconstructed PET images (image raw data), with and without attenuation correction, and CT images shall always be archived at the local site. If processed PET images are required, they shall be archived as separate secondary datasets. If scanner raw data need to be archived for future reprocessing, this should be defined prospectively in the Protocol.

611

612 **3.4. Image Analysis (UPICT Section 9)**

613 The Image Analyst, through interaction with the Workstation Analysis tools, shall be able to perform
614 specified measurements. Image Analysis has qualitative and quantitative tasks. Both require consistency
615 and images of sufficient quality. Quantitative imaging requires additional system characteristics described
616 further in this Profile.

617 **3.4.1 Input Data**

618 The output images of Reconstruction, but not Post processing, are considered the input for Image Analysis.
619 If the Image Analyst alters input data (e.g. zoom), the original input data will be maintained as a separate
620 file, both to be stored. (See Section 3.2)

621 **3.4.2 Methods to Be Used**

622 Each tissue/organ to be investigated quantitatively (either tumor lesion or normal tissue) is characterized
623 by defining a region-of-interest (ROI) and calculating a parameter such as the maximum SUV within the ROI.
624 The image analyst will use tools (as defined in Section 4.4 Conformance – Image Analysis Workstation) to
625 define ROIs and measure SUVs.

626 **3.4.3 Required Characteristics of Resulting Data (UPICT Section 9.3)**

627 The specific trial protocol shall prospectively define the SUV parameter that is required for each lesion, or
628 normal tissue, which will be used for the imaging endpoint. Some studies may also compare different
629 metrics and will require recording multiple parameters. SUV measures (and the analysis tools used to
630 obtain them, including software version) shall be specified for each protocol and shall be used consistently
631 across all subjects and across all sequential lesion measurements.

632 SUV's are intended as a measure of relative uptake and in that sense, can be regarded as dimensionless
633 (unitless); however, using strict interpretation of the units for the common calculation of body weight
634 normalization, this yields units of g/ml. Under the assumption that on average 1 ml of tissue weighs 1 gm
635 (e.g., water), a dimensionless SUV would be obtained. Display system manufactures typically, but not
636 always, indicate units of g/ml if images are scaled to SUVs with a body weight normalization. This is
637 presumably to differentiate between body weight (or lean-body-mass) and body-surface-area
638 normalizations, which would show different units (and values). Based on the lack of consensus and that
639 many display systems already use units, the recommendation below is to use units of g/ml.

640
641 It should be clear which values belong to which lesion. This can be done by capturing DICOM coordinates
642 along with the SUV or secondary screen captures of the ROI for identification. It should be reported which
643 SUV measure is used, i.e. statistic and type of normalization.

644 If a reference tissue (e.g. liver) SUV is measured, then, that SUV should be reported along with lesion SUV
645 data.

646 The analysis software should generate a report.

647 **3.5. Image Interpretation and Reporting (UPICT Section 10)**

648 No QIBA Profile specification can be provided for image interpretation at this time. Image Interpretation is
649 considered to be beyond the scope of this document. Refer to FDG-PET/CT UPICT Protocol (Section 10). In
650 addition, further interpretation of the quantitative results (e.g. PERCIST [Wahl 2009]) and/or normalizing

651 SUV to reference tissue values (e.g. liver or blood pool) can also be specified as part of a specific trial
652 protocol.

653 Typically the trial protocol will state how quantitative response is measured. For example, response can be
654 based on the hottest lesion, but sometimes the change of the sum of SUVs is used. In other words, how
655 quantitative response is measure should be specified *a priori* by the trial itself. This also applies to target
656 lesion selection.

657

Parameter	Entity/Actor	Specification
Image Reporting	Imaging Facility	Imaging reports shall be populated from DICOM header information using structured reporting.

658

659 **3.6. Quality Control**

660 The following section deals with multiple aspects of quality control in FDG-PET/CT studies. (See FDG-PET/CT
661 UPICT Protocol Section 12 for additional information). This includes selecting and qualifying a PET/CT
662 imaging facility, imaging personnel and PET/CT scanners and ancillary equipment. In addition, the use of
663 phantom imaging (prior to study initiation and ongoing) is discussed as well as identifying subjects whose
664 data may need to be censored due to lack of data integrity. Finally, post-image-acquisition quality
665 assessment is detailed.

666 **3.6.1 Imaging Facility**

667 It is essential to implement quality processes that ensure reliable performance of the scanner and
668 consistent image acquisition methodology. These processes must be in place prior to subject imaging and
669 be followed for the duration of the trial. A facility “imaging capability assessment” is a prerequisite to
670 facility selection for participation in any clinical trial involving the use of FDG-PET/CT as an imaging
671 biomarker. This imaging capability assessment will include:

- 672 • Identification of appropriate imaging equipment intended for use in the trial
- 673 • Documented performance of required quality control procedures of the scanner and ancillary
674 equipment (e.g. dose calibrator, glucose meter, etc.)
- 675 • Radiotracer quality control procedures
- 676 • Experience of key personnel (technologists, radiologists, physicists and/or other imaging experts)
- 677 • Procedures to ensure imaging protocol conformance during the trial

678 **3.6.1.1 Site Accreditation/Qualification Maintenance**

679 Whilst imaging facility accreditation is generally considered to be adequate for routine clinical practice
680 purposes (e.g., ACR, IAC, and TJC), facility qualification (e.g., SNM-CTN, ACRIN, and imaging core labs) is
681 required for clinical research/clinical trial participation. In order to be considered to be compliant with this
682 Profile, an imaging scanner/facility must provide documentation of current qualified status. Appropriate
683 forms, checklists or other process documents should be maintained and presented upon request to verify

684 that ongoing quality control procedures are being performed in a timely manner as dictated by specific
 685 clinical study requirements. If exceptions to any of the performance standards stated below occur and
 686 cannot be remediated on site, the site should promptly communicate the issue to the appropriate internal
 687 overseer for advice as to how the irregularity should be managed. In addition to documenting the level of
 688 performance required for this Profile (and the level of performance achieved), the frequency of facility
 689 accreditation/qualification also needs to be described.

690 It is important to note that that imaging facility Accreditation and/or Qualification, as defined in this Profile,
 691 are considered necessary, but are not sufficient for conformance with this Profile. For conformance with
 692 the Profile, and thus to support the claims of the Profile, all normative requirements must be met.

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.).

693 **3.6.2 Imaging Facility Personnel**

694 For each of the personnel categories described below, there should be training, credentialing, continuing
 695 education and peer review standards defined. Guidelines for training/credentialing for each resource
 696 category are summarized below (UPICT Protocol Section 2.1).

Parameter	Entity/Actor	Specification
Personnel Roster	Imaging Facility Coordinator	Each site shall, at the time of trial activation and prior to subject accrual, have the support of certified technologists, physicists, and physicians (as defined below), experienced in the use of FDG-PET/CT in the conduct of oncological clinical trials.
Technologist	Imaging Facility Coordinator	Technologist certification shall be equivalent to the recommendations published by the representatives from the Society of Nuclear Medicine Technologists Section (SNMTS) and the American Society of Radiologic Technologists (ASRT) and should also meet all local, regional, and national regulatory requirements for the administration of ionizing radiation to patients.
Medical Physicist	Imaging Facility Coordinator	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.

Parameter	Entity/Actor	Specification
Physician	Imaging Facility Coordinator	Physicians overseeing and interpreting PET/CT scans shall be qualified by the ABR (Diagnostic and/or Nuclear Radiology) or American Board of Nuclear Medicine (ABNM) or equivalent within the United States or an equivalent entity appropriate for the geographic location in which the imaging study(ies) will be performed and/or interpreted.

697

698 **3.6.3 FDG-PET/CT Acquisition Scanner**

699 FDG-PET/CT studies as described in this Profile require a dedicated PET/CT scanner. PET/CT scanners should
700 be identified based on manufacturer, name and model. Hardware specifications should be documented.
701 Scanner software name and version should be documented at the time of trial initiation and at the time of
702 any and all updates or upgrades.

703 The PET/CT scanner must undergo routine quality assurance and quality control processes (including
704 preventive maintenance schedules) appropriate for clinical PET/CT applications, as defined by professional
705 and/or regulatory agencies. In order to assure adequate quantitative accuracy and precision of PET/CT
706 imaging results, additional quality assurance measures are required, as discussed below.

Parameter	Entity/Actor	Specification
Physical Inspection	Technologist	Shall, on a daily basis, check gantry covers in tunnel and subject handling system.
QA/QC Checks	Technologist	All QA/QC procedures recommended by the manufacturer shall be performed at the frequency recommended by the manufacturer and documented. A table of QA/QC procedures for a subset of specific PET/CT scanners from each vendor is included in Appendix G.2. Daily QA procedures shall be performed prior to any subject scan.

707 **3.6.3.1 Ancillary Equipment**

708 3.6.3.1.1 Dose Calibrator

709 The following guidelines are collected from ANSI standard N42.13, 2004 and IAEA Technical Report Series
710 TRS-454. All requirements assume measurements on unit doses of FDG and that calibration sources are in
711 the 'syringe' geometry (i.e., no bulk doses).

712 The Constancy test ensures reproducibility of an activity measurement over a long period of time by
713 measuring a long-lived source of known activity.

714 The Accuracy test ensures that the activity values determined by the dose calibrator are correct and
715 traceable to national or international standards within reported uncertainties.

716 The Linearity test confirms that, for an individual radionuclide, the same calibration setting can be applied
717 to obtain the correct activity readout over the range of use for that 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 $\pm 2.5\%$ 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 F-18 dose calibrator standard. Shall confirm that net measured activities differ no greater than $\pm 2.5\%$ from expected value.
		The scanner calibration shall be tested using a NIST-traceable (or equivalent) simulated F-18 source object, e.g. a uniform cylinder, large enough to avoid partial volume effects or other resolution losses.
		Shall be evaluated monthly (or after any dose calibrator event) with a NIST-traceable (or equivalent) simulated F-18 dose calibrator standard. Shall confirm that net measured activities differ no greater than $\pm 2.5\%$ from expected value.
Linearity	Technologist or Radiation safety officer or Qualified Medical Physicist	Shall be evaluated at least annually (or after any dose calibrator event) and should be within $\pm 2.5\%$ of the true value over an operating range of 37-1110 MBq (1 to 30 mCi).
PET Radiation Dose	Dose Calibrator	Shall record the radiation dose from the administered activity and accompanying information in a DICOM Radiopharmaceutical Administration Radiation Dose Structured Report.

719

720 3.6.3.1.2 Scales and stadiometers

721 Scales and stadiometers should be inspected and calibrated at installation and annually.

722

Parameter	Entity/Actor	Specification
Scales and stadiometers	Approved personnel	Shall be evaluated annually or after any repair by qualified personnel. Shall be confirmed that error is less than $\pm 2.5\%$ from expected values using NIST-traceable or equivalent standards.

723 3.6.3.1.3 Blood glucose level measurement device

724 Glucose measurements should be made using a CLIA-approved, CLIA-cleared, or equivalent (outside the US)
 725 glucose measurement technique.

Parameter	Entity/Actor	Specification
Blood glucose level measurement device	Approved personnel	Shall have QA/QC testing and calibration performed using a CLIA-approved, CLIA-cleared, or equivalent (outside US) procedure.

726

727 3.6.3.1.4 Clocks and timing devices

728 PET/CT scanner computer and all clocks in an imaging facility used to record activity/injection
 729 measurements should be synchronized to standard time reference within +/-1 minute. These include any
 730 clocks or timekeeping systems that are connected with a subject’s FDG-PET/CT study, in particular those
 731 associated with the dose calibrator, the injection room, the scanner, and the acquisition computer(s). The
 732 synchronization of all clocks (to date, time of day and to time zone) should be monitored periodically as
 733 part of ongoing QA program. In particular, clocks should be inspected immediately after power outages or
 734 civil changes for Daylight Savings (NA) or Summer Time (Eur). Correct synchronization could be achieved
 735 using the Consistent Time Integration Profile as defined in the IHE IT Infrastructure Technical Framework.
 736 The Consistent Time Profile requires the use of the Network Time Protocol (NTP) (www.NTP.org).

Parameter	Entity/Actor	Specification
Scanner and site clocks	Approved personnel	PET/CT scanner computer and all clocks in an Imaging facility used to record activity/injection measurements shall be synchronized to standard time reference within +/-1 minute. Synchronization of all clocks used in the conduct of the FDG-PET/CT study shall be checked weekly and after power outages or civil changes for Daylight Savings (NA) or Summer Time (Eur)
Scanner and site clocks	Specific Device	Provide time synchronization as per the IHE Consistent Time Integration Profile.
Dose calibrator clock	Dose Calibrator	Electronic record of output from a dose calibrator shall be synchronized with other time keeping devices.

737

738 **3.6.4 Phantom Imaging**

739 To qualify the PET/CT scanner for clinical practice or for a clinical trial, a phantom imaging procedure is
 740 required. In addition to certain generally available, commonly used phantoms, purpose-specific phantoms
 741 may be provided to simulate certain types of cancers or anatomic locations and therefore might vary from
 742 trial to trial based on the need to evaluate particular diagnostic, staging and/or treatment response
 743 performance and/or anatomic location. Options that might be considered on a per-protocol basis include,
 744 but are not limited to:

- 745 1. each site uses a single phantom for the duration of the trial but not necessarily the same model of
 746 phantom used at other sites
- 747 2. all sites use phantoms of the same model for the duration of the trial
- 748 3. all sites use phantoms built to precise specifications for the duration of the trial
- 749 4. all sites share a single phantom for the duration of the trial.

750 The phantom scans and performance evaluation should be performed prior to the start of a trial and
 751 repeated during the course of the trial as specified by the individual protocol. Any changes to scanner
 752 equipment, either hardware or software, should be immediately reported to the trial sponsor and/or
 753 imaging CRO and may result in the need for re-qualification prior to imaging additional trial subjects. In
 754 particular, it is strongly recommended that subjects in a longitudinal study be scanned on the same PET/CT
 755 system with the same software version whenever possible.

756 Image noise levels are measured using an anthropomorphic phantom (e.g. NEMA, ACR, SNM, EANM) with a
 757 uniform area to assess image 'noise' by means of the coefficient of variation (COV), also known as the
 758 relative standard deviation (%RSD), which is expressed as a percentage and is defined as $COV = (SD / Mean)$
 759 $\times 100$, for the voxel values within a specified volume of interest (VOI). The phantom should be filled such
 760 that the activity concentration in the uniform area is approximately 3.7 – 7.4 kBq/ml (0.1 to 0.2 uCi/ml),
 761 similar to the expected average normal tissue concentration at the time of imaging in an average weight
 762 (70-80 kg) subject in combination with the intended FDG dosage. The phantom should be scanned using the
 763 minimal time per bed specified in the trial protocol or using the routinely applied time per bed in the local
 764 clinical setting. Moreover, image reconstruction methods and settings should equal those specified in the
 765 trial protocol or equal those routinely applied in the local clinical setting. A region of interest (ROI) should
 766 be positioned entirely within the phantom's uniform area and as much as possible centrally located within
 767 the phantom. The ROI should be a cubical or rectangular volume, with the length of each side as close as
 768 possible to, but no less than, 3 cm. A sphere measuring no less than 3 cm. in diameter may also be used as
 769 the ROI on systems that have the capability to accommodate this strategy. The COV of the voxel values thus
 770 determined should be recorded and should be below 15%. If the COV of the voxel values thus determined is
 771 above 15%, the acquisition time should be increased accordingly.

772 The normative list below is based on the NEMA Image Quality, ACR, and uniform cylinder phantoms as
 773 appropriate.

Parameter	Entity/Actor	Specification
Phantom tests: Frequency	Imaging Site	Shall perform and document results of the following tests no less than quarterly.
Phantom tests: cross calibration with dose calibrator	Imaging Site	Shall perform quarterly and after scanner upgrades, maintenance or repairs, new setups and modifications to the dose calibrator.
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.
Phantom tests: axial uniformity measurements	Imaging Site	Using uniform cylinder phantom or equivalent shall obtain a slice-to-slice variability of less than 10% for the slices within the central 80% of the axial FOV
		Using uniform cylinder phantom or equivalent shall obtain a slice-to-slice variability of less than 5% for the slices within the central 80% of the axial FOV
Phantom tests: resolution measurements	Imaging Site	Shall perform and successfully obtain phantom imaging results for cold and hot object imaging as described. For cold object imaging, the test phantom will be the ACR PET phantom or the Deluxe Jaszczak phantom (or equivalent) with six sets of acrylic rods arranged in a pie-shaped pattern with the following diameters: 4.8, 6.4, 7.9, 9.5, 11.1, and 12.7 mm. The 9.5, 11.1, and 12.7 mm diameter rods must be visible; if necessary up to 1 cm slice averaging can be used. For hot object resolution, the fillable 12 mm diameter 'hot' cylinder for the ACR phantom must be visible; for CTN phantom, all hot objects greater than 10 mm must be visible and for NEMA phantom, 13 mm sphere must be visible. Also see Section 3.6.4.2."
		Harmonized image reconstruction protocols are available. (i.e., known recovery coefficients versus size for a given test object such as the modified NEMA NU-2 Image Quality phantom)
Phantom tests: noise measurements	Imaging Site	The phantom shall be filled with an FDG concentration of activity concentration in the uniform area is (approximately 0.1 to 0.2 $\mu\text{C}/\text{ml}$) and scanned using the intended acquisition protocol. Using a rectangular or spherical region as close as possible to, but no smaller than, 3cm to a side, the COV of the voxel values within the region should be below 15%, for the slices within the central 80% of the axial FOV.

774

775 3.6.4.1 Uniformity and Calibration

776 Verification of scanner normalization with a uniform phantom is a minimum requirement for all scanners
777 used in clinical trials including those that only have qualitative endpoints. For trials with quantitative PET
778 measurements, this assessment should also include a comparison against a dose calibrator to ensure
779 quantitative accuracy; that is, a comparison of the absolute activity measured versus the measured amount
780 injected should be performed. This comparison is particularly important after software or hardware
781 upgrades. If the trial requires absolute quantification in baseline images or absolute changes in longitudinal
782 studies, it should be considered to include an image quality and/or contrast recovery QC assessment as part

783 of the routine QC procedures and/or scanner validation process, see Appendix E of the UPICT Protocol.
 784 Clinical trials using only relative changes in longitudinal studies may not require contrast recovery
 785 assessments provided there is appropriate consideration for the minimum size of target lesions based on
 786 the partial volume effect.

787 An essential requirement for extracting quantitative data from images is that there be known calibration
 788 accuracy and precision and/or cross calibration of the PET/CT system against the (locally) used dose
 789 calibrator (within 10%). The QC procedures should utilize the same acquisition/reconstruction protocol,
 790 software and settings that are used for the subject scans.

Parameter	Entity/Actor	Specification
Uniformity QC	Technologist or Physicist	<p>At least quarterly and following software upgrades, shall assess transverse and axial uniformity across the central 80% of image planes by imaging a uniform cylinder phantom.</p> <ol style="list-style-type: none"> 1. The standard deviation of a large central 2D ROI shall be compared with similar previous scans to check for measurable differences. 2. The mean values of a large central 2D ROI for these image slices shall be compared with similar previous scans to check for measurable differences.
Cross Calibration	Technologist or physicist	At least quarterly and following software upgrades or changes to the dose calibrator, shall perform checks to monitor and identify discrepancies between the PET scanner and dose calibrator.

791

792 **3.6.4.2 Resolution (UPICT Section 12.1.1.11)**

793 The assessment of adequate resolution should include both a qualitative evaluation (using clinical images)
 794 and quantitative assessment (using phantom-defined criteria). The phantom-defined requirements are
 795 more completely described in UPICT protocol Section 12.1.1.11.

Parameter	Entity/Actor	Specification
Resolution	Nuclear Medicine Physician	Shall perform, on at least an annual basis, and document a qualitative resolution QC test by using the routine image processing protocols and demonstrating resolution of normal gross anatomic features within clinical images of the brain, heart and abdomen.
Resolution	Medical Physicist	Shall perform (on at least an annual basis) and document performance of a quantitative assessment (using a phantom with differing size defined targets such as the ACR or NEMA IQ phantoms processed with routine image reconstruction protocols) for lesion resolution.

796 **3.6.4.3 Noise (UPICT Section 12.1.1.12)**

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.

797
798 **3.6.4.4 Phantom imaging data analysis**

799 For PET image analysis, there are many combinations of hardware and software that are used. The software
800 alone comprises multiple layers including the operating system, several base modules for input and display,
801 and the components that draw/calculate ROIs and calculate SUVs. It has been demonstrated that even
802 changes in the underlying operating system can produce changes in the quantitative output produced by
803 the display and analysis system [Gronenschild 2012]. Surprisingly little effort (outside manufacturer's
804 internal processes) has been applied to testing or validating the quantitative accuracy of SUV
805 measurements produced by display and analysis methods.

806 To provide a method for testing and validating quantitative accuracy of SUV measurements produced by
807 the display and analysis methods, the QIBA FDG-PET/CT Biomarker Committee has developed an FDG-
808 PET/CT digital reference object (DRO), which is a synthetic test object comprised of stacked DICOM images
809 representing an FDG-PET image volume and an aligned CT image volume. The PET and CT images are based
810 on the NEMA/MITA NU-2 Image Quality phantom. The DRO has pre-determined test objects to evaluate
811 ROI functionality and pre-determined DICOM header information to test SUV calculations. Since the DRO is
812 created synthetically, any image display software is expected to reproduce the known values exactly,
813 except for the insignificant machine precision errors. Further details are given in Appendix F.
814 Recommended versions of vendor-neutral pseudo-codes for SUV calculation are given in Appendix G. All
815 software used for image analysis should be verified by the procedures in 4.4.3.

Parameter	Entity/Actor	Specification
Image Analysis Software	Imaging site.	All software used for image analysis shall be verified by the procedures in 4.4.3.

816 **3.6.5 Quality Control of FDG-PET/CT studies**

817 **3.6.5.1 Data Integrity**

818 The integrity of DICOM image headers should be reviewed and confirmed for DICOM standard
819 conformance, regulatory conformance (including privacy protection, such as may be required by such rules
820 as the HIPAA Privacy Rule if applicable), protocol conformance, sufficiency for the intended analysis (e.g., to
821 compute SUV) and consistency with source data such as CRFs. In some cases, internal references such as
822 the liver can be used for quality control to confirm acceptable ranges of SUVs.

823 **3.6.5.2 Determination of Image Quality**

824 CT images should be reviewed by the Image Analyst for assessment of image quality and for potential
825 artifacts such as beam hardening, metal objects, and motion. PET images should be compared to the CT
826 images for proper image registration and potential attenuation correction artifacts. Both uncorrected and
827 attenuation corrected images may need to be assessed to identify any artifacts caused by contrast agents,

828 metal implants and/or subject motion. For example, movement or mis-registration can lead to poor quality
829 quantitative data and invalid numbers. Some images may be too poor in quality to quantify. Statistical
830 quality of images is important to report, but not a full substitute for quality. Liver noise assessment as
831 defined per PERCIST [Wahl 2009] is considered a reasonable start.

832 **3.6.5.3 Determination of Evaluable Tumor Lesions**

833 The definition of specific tumors that are evaluable should be addressed prospectively in the clinical trial
834 protocol. Protocol-specific guidelines should document whether or not minimum size criteria and/or
835 minimum baseline SUV criteria for target lesion qualifications are used, and if so, how such criteria will be
836 used.

837 The criteria below represent the best known practices based on published data, and can provide a guideline
838 for determining evaluability.

839 Selection of Target Lesions (UPICT Section 10.2.1.1)

840 The lesion to be measured should be free of artifacts, for example, from nearby intense FDG containing
841 structures (like the bladder) or due to motion or attenuation correction artifacts.

842 Minimum Baseline SUV (UPICT Section 10.2.1.1.1)

843 From the SNM Global Harmonization Summit (2010) and in the meta-analysis by de Langen et al (2012),
844 there was consensus that to reliably measure a change in the FDG uptake of a lesion, a high baseline FDG
845 uptake is necessary. For illustration, a 30% decrease in lesion uptake may be more reliably measured, and
846 potentially more meaningful, if the initial lesion uptake had an SUV of 5 g/ml as opposed to an SUV of 2
847 g/ml.

848 UPICT Acceptable level: A minimum FDG-avidity is required and should be specified in the clinical trial
849 protocol. This can be determined by either a subject-specific threshold as proposed with PERCIST [Wahl
850 2009] or as a general cutoff. For a general cutoff, a SUV_{max} of 4 is suggested for all target lesions, although
851 in some settings a lower minimum SUV_{max} may be acceptable, such as in the lung or breast. Alternative
852 methods have been proposed [Lodge and Wahl 2013].

853 The measurement for mean liver SUV is made using a 3-cm diameter spherical ROI placed in the right lobe
854 of the liver at the level of main portal vein and equidistant between the porta hepatis and lateral liver
855 margin. Care should be taken to avoid placing the ROI close to the edge of the liver [Subramaniam 2012].
856 Further details are given in UPICT Section 10.2.1.1.1. If the liver is not in the field of view or is abnormal to a
857 degree that normal liver cannot be assessed, then the alternate comparator is to use a minimum threshold
858 level of 2.0 x mean SUV of blood pool in a 3D ROI defined as a 1 cm diameter cylinder in the descending
859 thoracic aorta extending over 2 cm, tracking the long axis of the aortic lumen, avoiding the wall of the aorta
860 or areas of plaque or calcification. If the descending aorta is not evaluable a VOI of the same volume should
861 be measured from elsewhere in the thoracic aorta.

862 Minimum Lesion Size

863 The SNM Global Harmonization Summit suggests that tumors should typically be over 2 cm in diameter for
864 target lesion inclusion at baseline. Lesions smaller than 2 cm (or otherwise not easily measurable) with a
865 high enough FDG uptake, may still be evaluable.

866 Evaluation of lesion size (e.g., longest diameter) may be difficult. This may be due to intrinsic lesion
867 characteristics (e.g., infiltrative or CT lesion isodensity to surrounding tissue) or due to the anatomic
868 location of tumor (e.g., bone marrow site). Lesions subject to partial volume effect of SUV measurement,

869 notably due to anatomic location and attenuation correction errors (e.g., peri-diaphragmatic lesions at
870 either lung base or hepatic dome) potentially should be excluded.

871 **3.6.5.4 Determination of subjects unsuitable for FDG-PET/CT analysis**

872 Reference Section 3.1.1 "Subject Selection, Timing, and Blood Glucose Levels"

873 ***3.6.6 Quality Control of Interpretation***

874 To promote quantifiable performance standards for the quality control of interpretation there is a need for
875 intra-reader variability studies. In a 2-Reader paradigm, then inter-reader variability is needed as well. It is
876 currently unclear what statistics to evaluate and how these performance metrics should be used in the
877 analysis.

878 **4. Conformance**

879 **Relation of this Profile to Expectations for QIBA Profile Compliance**

880 Definitions (from Appendix C):

881 Qualified: The imaging site is formally approved by an appropriate body (i.e. ACRIN, CQIE, SNMMI-CTN,
882 EANM-EARL, NCRI, an imaging laboratory or CRO) for a specific clinical research study.

883 Accredited: Approval by an independent body or group for broad clinical usage (requires ongoing QA/QC)
884 e.g. ACR, IAC, TJC.

885 Compliant: The imaging site and equipment meet all the requirements described herein, which are
886 necessary to meet the QIBA Profile claim.

887 The requirements included here are intended to establish a baseline level of capabilities. Providing higher
888 levels of performance or advanced capabilities is both allowed and encouraged. Furthermore the QIBA
889 Profile is not intended to limit equipment suppliers in any way with respect to how they meet these
890 requirements. Institutions meeting the stated criteria are considered to be QIBA Compliant.

891 **4.1. Image Acquisition Site**

892 Typically clinical sites are selected due to their competence in oncology and access to a sufficiently large
893 subject population under consideration. For imaging it is important to have availability of:

- 894 • Appropriate imaging equipment and quality control processes,
- 895 • Appropriate ancillary equipment and access to radiotracer and contrast material,
- 896 • Experienced Technologists (CT and PET trained) for the subject handling and imaging procedure,
- 897 • Appropriately trained Radiologists/Nuclear Medicine Physicians for image analysis and diagnostic
898 interpretation,
- 899 • Appropriately trained image analysts, with oversight by a Radiologist or Nuclear Medicine Physician,
- 900 • Medical Physics support to ensure appropriate scanner and equipment calibration,
- 901 • Processes that assure imaging QIBA Profile-compliant image generation in appropriate time window

902 A QA/QC program for PET/CT scanners and ancillary devices must be in place to achieve the goals of the
903 clinical trial. The minimum requirements are specified above. This program shall include (a) elements to

904 verify that imaging facilities are performing imaging studies correctly and (b) elements to verify that
 905 facility's PET/CT scanners are performing within specified calibration values. These may involve
 906 additional PET and CT phantom testing that address issues relating to both radiation dose and image
 907 quality (which may include issues relating to water calibration, uniformity, noise, spatial resolution – in
 908 the axial plane-, reconstructed slice thickness z-axis resolution, contrast scale, and others) and
 909 constancy. There is agreement that some performance testing (e.g., constancy phantom) adds value;
 910 however, acceptable performance levels, frequency of performance, triggers for action and mitigation
 911 strategies need further definition before these can be required. This phantom testing may be done in
 912 addition to the QA program defined by the device manufacturer as it evaluates performance that is
 913 specific to the goals of the clinical trial.

Parameter	Entity/Actor	Specification
PET/CT Scanner	Acquisition Facility	This Profile shall only address full ring PET/CT scanners.
CT Scanner Calibration	Technologist	Shall perform daily water equivalent phantom analysis; ensure that output is acceptable and manually enter on form /electronic database.
PET Scanner Calibration	Technologist	Shall perform daily/weekly/monthly scanner QA as recommended by manufacturer; ensure that output values are acceptable and manually enter on form/electronic database
PET Scanner Calibration Constancy Check	Technologist	Shall perform constancy phantom (e.g., Ge-68 cylinder) scan (preferably NIST traceable or equivalent to gather information regarding uniformity as well) at least weekly and after each calibration.
Dose calibrator	Imaging site or Manufacturer	Calibrated to F-18 using NIST traceable source or equivalent either by site or calibrator manufacturer.

916 4.2. PET/CT Acquisition Device

917 Distinct from the performance specifications and frequency of testing described in Section 4.1 which apply
 918 to quality control of the Acquisition Device at the imaging facility, this Section defines performance
 919 specifications of the Acquisition Device to be met upon leaving the manufacturing facility. In order to be
 920 compliant with this Profile, the Acquisition Device should be held to the same standard whether a mobile
 921 utility or a fixed installation; a mobile scanner may require additional calibration to achieve this
 922 performance.

923 The PET/CT scanner should use DICOM attributes to follow version numbers of software for: 1 Acquisition,
 924 2 Reconstruction, 3 Post-processing, 4 Display and ROI analysis, 5 Dynamic Analysis. Note that this Profile
 925 does not specify dynamic imaging performance requirements. Performance requirements regarding
 926 software version identification, documentation and tracking across time are described in Section 4.5.

927 The PET scan acquisition start time should be used for the decay reference time and the integral model
 928 should be used for decay correction. The scanner should perform all decay corrections (i.e. not the

929 operator). Image data are to be given in units Bq/ml. “Derived” images (distinct from “Original”) should be
930 flagged following the DICOM standard and should retain the scan acquisition date and time fields.

931 All needed information for fully corrected administered activity (e.g. residual activity, injection time,
932 calibration time) is required. Note that use of the term administered activity below refers to fully corrected
933 net radioactivity.

934 Baseline level (i.e. equivalent to the UPICT protocol level of 'Acceptable') compliance requires that the
935 DICOM image set from the subject’s PET/CT scan and necessary metadata (that is not currently captured by
936 all PET scanner acquisition processes) is captured in trial documentation, e.g. case report forms. The
937 metadata is required to perform the quantitative analysis and perform quality control on SUV covariates.
938 This includes for example, post-injection residual activity and subject height. This data should be captured
939 in the 'Common Data Format Mechanism' as described in Appendix E.

940 The DICOM format used by the PET/CT scanner should meet the Conformance Statement written by
941 manufacturer of the PET/CT system. PET data shall be encoded in the DICOM PET or Enhanced PET Image
942 Storage SOP Class, and in activity-concentration units (Bq/ml) with additional parameters in public DICOM
943 fields to calculate SUVs (e.g. height, weight, scale factors). CT data should be encoded in CT or Enhanced CT
944 Image Storage SOP Class. DICOM data shall be transferred using the DICOM Part 8 network protocol or as
945 offline DICOM Part 10 files for media storage including CDs and DVDs. They shall be transferred without any
946 form of lossy compression.

947 The meta-information is the information that is separate, or in addition to, the image values (in units of
948 Bq/ml) that is deemed necessary for quantitatively accurate representation of PET SUVs. The meta-
949 information may also include other information beyond that need for calculation of SUVs, i.e. the type and
950 or sequencing of therapy, the blood glucose levels, the scanner SUV stability history, etc. The actual
951 mechanism of capturing the information is not specified in this Profile. The intent here is to list what
952 information should be captured rather than the mechanism itself. The mechanism can range from paper
953 notes, to scanned forms or electronic data records, to direct entry from the measurement equipment into
954 pre-specified DICOM fields (i.e. from the PET/CT scanner or auxiliary measurement devices such as the dose
955 calibrator). Ideally all of the specified meta-data will be captured by direct electronic entry to DICOM fields,
956 after suitable modification of the DICOM format for PET imaging.

957 In some facility workflows, the Acquisition Device may also provide workstation/analysis tool functionality.
958 For example, the display of an SUV statistic (considered in Section 4.4.1) or display of Tracer Uptake Time
959 (considered in Section 4.4), may also apply to the Acquisition Device, if used in this manner.

960 The concept endorsed here is that the needed meta-data is identified. Through revisions of this Profile, the
961 DICOM standard, and technology the meta-data is inserted into the analysis stream (Figure 3) in a more
962 direct manner and technology and accepted standards evolve.

963

Parameter	Entity/Actor	Specification
CT calibration tracking	Acquisition Device	Daily water equivalent phantom values shall be tracked in the DICOM header.
PET calibration factor	Acquisition Device	The current SUV calibration factor shall be included in the DICOM header.
PET QA status	Acquisition	Date/time and status of system-wide QA checks should be

Parameter	Entity/Actor	Specification
	Device	captured separately.
Dose calibrator calibration	Acquisition Device	Calibration factor for an F-18 NIST -traceable (or equivalent) source with identifying information shall be tracked in the DICOM header with Date/Time.
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 radionuclide measurement.
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.
Height	Acquisition Device	Shall be able to record patient height in feet/inches or cm/m as supplied from the modality worklist or operator entry into scanner interface. Shall be stored in Patient Size field (0010,1020) in the DICOM image header, as per DICOM standard.
		Patient height shall be specifiable with 3 significant digits. Patient height 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.

Parameter	Entity/Actor	Specification
Blood glucose level	Acquisition Device	<p>Shall be able to Record patient blood glucose level, in units of mg/dl, or mMol/l, time of measurement, as supplied by operator entry into the scanner interface. Shall be recorded in the DICOM image header in the Acquisition Context Sequence using DICOM PS 3.16 TID 3471 PET Covariates Acquisition Context.</p> <p>Patient blood glucose level shall be transferrable directly from measurement device into the scanner using the Modality Worklist NM/PET Protocol Context TID 15101, bypassing all operator entry, but displaying it to the operator and still permitting operator correction.</p>
Administered Radionuclide	Acquisition Device	<p>Shall be able to enter the radionuclide type (i.e. F-18) by operator entry into the scanner interface and through predefined protocol Shall be recorded in Radionuclide Code Sequence (0054,0300) in the DICOM image header [e.g. (C-111A1, SRT, “¹⁸Fluorine”)].</p>
		<p>Shall be able to accept the radionuclide type (i.e. F-18) directly from the measurement device (dose calibrator) or management system, using the Sup 159 Radiopharmaceutical Administration Radiation Dose Report bypassing all operator entry, but still permitting operator correction.</p>
		<p>Shall be able to accept the radionuclide type (i.e. F-18) from the DICOM Modality Worklist either from the NM/PET Protocol Context, if present, or by deriving if from the Requested Procedure Code via a locally configurable table of values.</p>
Administered Radiotracer	Acquisition Device	<p>Shall be able to record the radiotracer (i.e. FDG), as supplied by operator entry into the scanner interface. Shall be recorded in Radionuclide Code Sequence field (0054,0300) in the DICOM image header, e.g. (C-B1031, SRT, “Fluorodeoxyglucose F¹⁸”).</p>
Administered Radiotracer radioactivity	Acquisition Device	<p>Shall be able to enter the administered radioactivity, in both MBq and mCi, as supplied by operator entry into the scanner interface. Shall be recorded in Radionuclide Total Dose field (0018,1074) in the DICOM image header in Bq.</p>
		<p>Shall be able to record with separate entry fields on scanner interface:</p> <ol style="list-style-type: none"> (1) the pre-injection FDG radioactivity (2) time of measurement of pre-injection FDG radioactivity (3) the residual activity after injection (4) time of measurement the residual radioactivity after injection <p>Shall automatically calculate the administered radioactivity and</p>

Parameter	Entity/Actor	Specification
		<p>store in the Radionuclide Total Dose field (0018,1074) in the DICOM image header.</p> <p>Alternatively, shall be able to receive this information as per DICOM Supplement 159.</p> <p>Patient Administered Radiotracer radioactivity information shall be transferred directly from measurement device into scanner by electronic, HIS/RIS, or other means, bypassing all operator entry, but still permitting operator correction.</p>
Administered Radiotracer Time	Acquisition Device	<p>Shall be able to record the time of the start of activity injection as supplied by operator entry into the scanner interface. Shall be recorded in Radiopharmaceutical Start Date Time field (0018,1078) (preferred) or Radiopharmaceutical Start Time field (0018,1072).</p>
		<p>Shall be able to record the time of the start of activity injection as supplied by operator entry into the scanner interface. Shall be recorded in Radiopharmaceutical Start Date Time field (0018,1078). I.e., not Radiopharmaceutical Start Time field (0018,1072).</p>
		<p>Shall be able to record the time of the stop of activity injection as supplied by operator entry into the scanner interface. Shall be recorded in Radiopharmaceutical Stop Date Time field (0018,1079).</p>
Decay Correction Methodology	Acquisition Device	<p>Encoded voxel values with Rescale Slope field (0028,1053) applied shall be decay corrected by the scanner software (not the operator) to a single reference time (regardless of bed position), which is the start time of the first acquisition, which shall be encoded in the Series Time field (0008,0031) for original images.</p> <p>Corrected Image field (0028,0051) shall include the value "DECY" and Decay Correction field (0054,1102) shall be "START", which means that the images are decay corrected to the earliest Acquisition Time (0008, 0032).</p>
Scanning Workflow	Acquisition Device	<p>Shall be able to support Profile Protocol (Section 3) PET and CT order(s) of acquisition.</p>
		<p>Shall be able to pre-define and save (by imaging site) a Profile acquisition Protocol for patient acquisition.</p>
		<p>Shall be able to interpret previously-reconstructed patient images to regenerate acquisition protocol.</p> <p>Shall be configurable to store (or receive) acquisition parameters as pre-defined protocols (in a proprietary or standard format), to allow re-use of such stored protocols to meet multi-center</p>

Parameter	Entity/Actor	Specification
		specifications and to achieve repeatable performance across time points for the same subject.
CT Acquisition Parameters	Acquisition Device	Shall record all key acquisition parameters (technique) in the CT image header, using standard DICOM fields.
CT based attenuation correction	Acquisition Device	Shall record information in PET DICOM image header which CT images were used for corrections (attenuation, scatter, etc.).
PET-CT Alignment	Acquisition Device	Shall be able to align PET and CT images within ± 2 mm in any direction.
		Shall be able to align PET and CT images within ± 2 mm in any direction with a load up to 150 kg over the co-scan length.
Activity Concentration in the Reconstructed Images	Acquisition Device	Shall be able to store and record (rescaled) image data in units of Bq/ml and use a value of BQML for Units field (0054,1001).
Tracer Uptake Time	Acquisition Device	Shall be derivable from the difference between the Radiopharmaceutical Date Time field (0018,1078) (preferred) or Radiopharmaceutical Start Time field (0018,1072) and the Series Time field (0008,0031) or earliest Acquisition Time field (0008,0032) in the series (i.e., the start of acquisition at the first bed position), which should be reported as series time field (0008,0031).
PET Voxel size	Acquisition Device	See Section 4.3 (PET Voxel size) under the Reconstruction Software specification requirements.
CT Voxel size	Acquisition Device	Shall be no greater than the reconstructed PET voxel size. Voxels shall be square, although are not required to be isotropic in the Z (head-foot) axis. Not required to be the same as the reconstructed PET voxel size.
Subject Positioning	Acquisition Device	Shall be able to record the subject position in the Patient Orientation Code Sequence field (0054,0410) (whether prone or supine) and Patient Gantry Relationship Code field Sequence (0054,0414) (whether head or feet first).
Scanning Direction	Acquisition Device	Shall be able to record the scanning direction (craniocaudal v. caudocranial) into an appropriate DICOM field.

Parameter	Entity/Actor	Specification
Documentation of Exam Specification	Acquisition Device	<p>Shall be able to define the extent of anatomic coverage based on distance from defined landmark site (e.g. vertex, EAM). (both the landmark location (anatomically) and the distance scanned from landmark) would require DICOM tags).</p> <p>Shall be able to be reportable for future scanning sessions.</p> <p>The Acquisition Device shall record the z-axis FOV which represents the actual distance of scan anatomic coverage (cms).</p>
Differential Acquisition Time	Acquisition Device	Shall be able to acquire and record non uniform scan times dependent upon areas of clinical concern. Recording can be done through the use of Actual Frame Duration (0018,1242) and Frame Reference Time (0054, 1300).
DICOM Conformance	Acquisition Device	All image data and scan parameters shall be transferable using appropriate DICOM fields according to the DICOM conformance statement for the PET/CT scanner.
DICOM Data transfer and storage format	PET/CT Scanner or Display Workstation	<p>PET images shall be encoded in the DICOM PET or Enhanced PET Image Storage SOP Class, using activity-concentration units (Bq/ml) with additional parameters stored in public DICOM fields to enable calculation of SUVs.</p> <p>PET images shall be transferred and stored without any form of lossy compression.</p>

964

Parameter	Entity/Actor	Specification
DICOM Editing	Acquisition Device	<p>Shall be able to edit all fields relevant for SUV calculation and blood glucose before image distribution from scanner.</p> <p>Shall provide appropriate warnings if overriding of the current values is initiated.</p>

965

966 4.3. Reconstruction Software

967 Reconstruction Software shall propagate the information collected at the prior Subject Handling and
 968 Imaging Acquisition stages and extend it with those items noted in the Reconstruction section.

Parameter	Entity/Actor	Specification
Metadata	Reconstruction Software	Shall be able to accurately propagate the information collected at the prior stages and extend it with those items noted in the Reconstruction section.

969 Data can be reconstructed including all corrections needed for quantification as well as without scatter and
 970 attenuation correction. Analytical or iterative reconstruction methods should be applied. If the system is

971 capable of providing resolution recovery and/or time of flight, then the decision to ‘turn on’ or ‘turn off’
 972 this /these capabilities should be made prospectively, as dictated by the specific protocol, and should be
 973 consistent for a given subject across multiple time points.

974 Standardization of reconstruction settings is necessary to obtain comparable resolution and SUV recoveries
 975 across the same subject and inter-subject across sites.

Parameter	Entity/Actor	Specification
Data Corrections	Reconstruction Software	PET emission data must be able to be corrected for geometrical response and detector efficiency, system dead time, random coincidences, scatter and attenuation.
Reconstruction Methodology	Reconstruction Software	Shall be able to provide images without resolution recovery.
		Shall be able to indicate, for both TOF and Resolution recovery, if either are being used for purposes of image reconstruction.
Reconstruction Methodology / Output	Reconstruction Software	Shall be able to perform reconstructions with and without attenuation correction.
Data Reconstruction 2D/3D Compatibility	Reconstruction Software	Shall be able to perform reconstruction of data acquired in 3D mode using fully 3D image reconstruction algorithms. Shall be able to perform reconstruction of data acquired in 2D mode using 2D image reconstruction algorithms.
Quantitative calibration	Reconstruction software	Shall apply appropriate quantitative calibration factors such that all images have units of activity concentration, e.g. kBq/mL.
Multi-bed data	Reconstruction software	Shall combine data from multiple over-lapping bed positions (including appropriate decay corrections) so as to produce a single three dimensional image volume.
Voxel size	Reconstruction software	Shall allow the user to define the image voxel size by adjusting the matrix dimensions and/or diameter of the reconstruction field-of-view. Shall be able to reconstruct PET voxels with a size 4 mm or less in all three dimensions (as recorded in Voxel Spacing field (0028,0030) and computed from the reconstruction interval between Image Position (Patient) (0020,0032) values of successive slices). Pixels shall be square, although voxels are not required to be isotropic in the z (head-foot) axis.
		Shall be able to reconstruct PET voxels with a size of 3 mm or less in all three dimensions (as recorded in Voxel Spacing field (0028,0030)

Parameter	Entity/Actor	Specification
		and computed from the reconstruction interval between Image Position (Patient) (0020,0032) values of successive slices). Voxels shall be isotropic.
Reconstruction parameters	Reconstruction software	Shall allow the user to control image noise and spatial resolution by adjusting reconstruction parameters, e.g. number of iterations, post-reconstruction filters.
		Shall be able to record reconstruction parameters used in image DICOM header using the Enhanced PET IOD, developed by DICOM working group.
Reconstruction protocols	Reconstruction software	Shall allow a set of reconstruction parameters to be saved and automatically applied (without manual intervention) to future studies as needed.

976

977 4.4. Image Analysis Workstation

978 The image analysis workstation shall have the ability to receive and propagate the data output (imaging and
979 metadata) collected from the prior activities (Subject Handling, Image Acquisition, Reconstruction and Post-
980 Processing). With the input data, the analysis workstation (and software analysis tools) will be able to make
981 use of certain attribute values to perform certain measurements and computational analysis. The analysis
982 workstation and software may be coupled to the PET/CT scanner system or provided by a 3rd-party vendor.

Parameter	Entity/Actor	Specification
Metadata	Image Analysis Workstation	Shall be able to accurately propagate the information collected at the prior stages and extend it with those items noted in the Image Analysis Workstation section.
		Shall be able to display all information that affects SUVs either directly in calculation (e.g. patient weight, injected activity) or indirectly (uptake time, plasma glucose concentration).
Tracer Uptake Time: Display	Image Analysis Workstation	Shall be capable to display or include link to display the number of minutes between injection and initiation of imaging (as per derivation guidelines described in Section 4.2).

983

984 Input for Image Analysis is considered output of Reconstruction and Post processing software activity. If the
985 Image Analyst alters input data (e.g. zoom) this is considered part of Image Analysis activity. If this occurs,
986 the original input data will be maintained as a separate file, both to be stored, including description of
987 manipulation in an audit trail file or in a dedicated DICOM tag section (Section 3.2).

988

Parameter	Entity/Actor	Specification
Reference time	Image Analysis	Shall use either the Acquisition Time field (0008,0032) or

Parameter	Entity/Actor	Specification
for decay correction	Workstation	Radiopharmaceutical Start Time (0018,1072), if necessary. If a series (derived or not) is based on Acquisition Time decay correction, the earliest Acquisition Time (0008,0032) shall be used as the reference time for decay correction.

989

990 **4.4.1 Region of Interest (ROI) definition**

991 The scanner-display-analysis system shall provide a tool for the user to define both 2D and 3D regions of
 992 interest (ROIs). While the ROI can be drawn on processed images, the SUV calculation should be performed
 993 from unprocessed (raw) image data (See Section 3.3.2). These ROIs will then be used calculate SUV values
 994 as described in the next section.

995 The specifications below are for defined regions for the calculation of (1) average value within an ROI (i.e.
 996 SUVmean) (2) maximum value within an ROI (i.e. SUVmax) (3) average value within a fixed-size ROI (i.e.
 997 SUVpeak) (4) average value within a fixed-size ROI (i.e., SUVpeak), but with the location automatically
 998 selected to maximize the mean value. For SUVpeak measures, the use of partial voxel values to secure a
 999 1.2cm diameter sphere (or 1cc volume) ROI is appropriate and desirable.

1000

Parameter	Entity/Actor	Specification
Voxel Inclusion Policy	Analysis Tool	Shall describe voxel inclusion methodology and weighting policy including placement criteria and total volume.
		Use a method equivalent to weighting for partial voxels; fully included voxels use weight of 1.0. Weighting should be proportionate to volumes of voxels that are partly included.
ROI Specifications	Analysis Tool	Shall describe capabilities and limits of ROI specification and placement.
		Dimensions and center location of ROI (box, ellipse, or ellipsoid) shall be specifiable to ± 1 mm. For SUVpeak measures, the location within a target search region that yields the highest mean value of a 1 cc region shall be found automatically and reproducibly.
ROI Definition Tools	Analysis Tool	Shall provide a tool and user strategy to allow the placement of an ROI to determine the <u>average</u> value within the ROI. Shall provide a tool and user strategy to allow the placement of an ROI to determine the value and location of the voxel with the <u>maximum</u> value within an ROI. Shall provide a tool and user strategy to allow the placement of a 1 cm diameter ROI (either 2D or 3D) to determine the average value within the ROI.

Parameter	Entity/Actor	Specification
		Shall provide a tool and user strategy to allow automatic placement of a 1 cm diameter ROI (either 2D or 3D) such that the average value within the ROI is maximized.
Edge/Volume Detection	Analysis Tool	Shall provide threshold methods for defining an ROI based on image values. Shall clearly specify which threshold method is used and relevant parameters values.
		Three ROI definition methods shall be provided: Fixed value, % of maximum voxel, or edge detection/segmentation methods.
ROI saving/retrieve	Analysis/Archival	Shall have the capability to label, save, recall and edit ROIs.
		Shall have the capability to track tumor information across longitudinal scans. In addition to lesion (and normal reference region) identification, this may include cross time point mapping of lesions tracked on the basis of consistent anatomic and/or functional activity. Other lesion characteristics, such as lesion name (with consistent anatomic labeling), lesion location, ROI/VOI size, corresponding anatomic (CT) image or slice number, SUV metric(s) and assessment of tumor heterogeneity may also be tracked and captured using standard DICOM objects.
ROI Display Statistics	Analysis Tool	Shall have the capability to output to the screen display the selected statistics of the ROI. These include, but are not limited to: Area, volume, mean, maximum, minimum, standard deviation. Units can be selectable as activity concentration [Bq/ml] or SUV [g/ml] (See Section 3.4.3). Shall have the capability to display results with at least two decimal places.
		Shall output ROI Output Statistics to Structured Data Reporting DICOM files.
		Shall calculate results directly from the originally reconstructed voxels (not from interpolated and/or zoomed images).

1001 The workstation and repository shall be able to create, store and retrieve markups (i.e. ROIs) used for SUV
1002 measurements in accordance with a standard definition for ROIs that provides a known balance between
1003 precision and accuracy.

1004 **4.4.2 Calculation of Standardized Uptake Value (SUV)**

1005 The ROI definition and analysis software is responsible for SUV calculation, e.g. with decay correction to the
1006 appropriate reference time. Moreover, the manufacturer should implement both versions of SUV
1007 normalizations (body weight or lean body mass). Recommended vendor-neutral pseudo-codes for SUV

1008 calculation are given in Appendix G.

1009

Parameter	Entity/Actor	Specification
SUV Calculation	Analysis Tool	Shall have the capability to correctly calculate SUVs according to the vendor-neutral pseudo-codes for SUV calculation given in Appendix G.
Volume of Distribution Surrogate	Analysis Tool	Shall have the capability to calculate SUVs using as a surrogate for the Volume of Distribution: body weight, lean body mass, and body surface area (BSA). Lean body mass shall be calculated according to the formula of James [James 1976, Hallynck 1981]: Males: $LBM = 1.10(w) - 128(w^2/h^2)$ Females: $LBM = 1.07(w) - 148(w^2/h^2)$ Body surface area shall be calculated according to the Du Bois formula: $BSA (m^2) = (0.007184)((w)^{0.425})((h)^{0.725})$ [Vu 2002] Where w = weight in kg and h = height in cm.

1010

1011 **4.4.3 Image Analysis Workstation Performance Specifications**

1012 The digital reference object (DRO), which is a synthetic PET (and CT) image, shall be used in order to
1013 evaluate conformance to the level of performance of analysis station/display station. Users should use the
1014 DRO (as per the DRO user's guide in Appendix F) to verify correct implementation of ROI placement, SUV
1015 calculations, and PET and CT image alignment.

Parameter	Entity/Actor	Specification
Performance Evaluation	Analysis Workstation	Shall use the DRO to verify adequate performance as described in Appendix F.
Analysis Accuracy	Analysis Workstation	For each of the specified ROIs in the DRO (Appendix F) the correct SUV values shall be replicated by the Analysis Workstation.
Alignment Accuracy	Analysis Workstation	The PET and CT DRO object shall appear perfectly aligned in the transverse, coronal, and sagittal views.
DICOM Conformance	Analysis Workstation	Shall be able to read and apply all mandatory DICOM PET IOD attributes, as well as any additional optional DICOM attributes specified in this profile (including those private attributes defined in Annex G for SUV calculation).

1016 **4.5. Software Version Tracking**

1017 Ideally, the PET/CT scanner should be able to build a list on the console of the dates of all software versions
 1018 (software changes that might impact quantitative accuracy would typically be inclusive of hardware
 1019 change). Furthermore, the scanner software version should be identified and tracked across time, with
 1020 updates and changes in scanner software noted during the course of the trial. At a minimum, Software
 1021 Versions should be manually recorded during the qualification along with the phantom imaging
 1022 performance data and the record should be updated for every software-upgrade over the duration of the
 1023 trial. This includes the flagging of the impact on quantification for now; in the future, record all software
 1024 version numbers in DICOM header.

1025

Parameter	Entity/Actor	Specification
Software Version tracking	Acquisition Device	Shall record the software version(s) used for acquisition and reconstruction in appropriate DICOM field(s).
Software version back-testing compatibility	Workstation	Shall provide mechanism to provide analysis of the image data using updated as well as prior (platform-specific) versions of analysis software.

1026

1027 **References**

1028 International Atomic Energy Agency (IAEA), Technical Report Series No. 454: Quality Assurance for
 1029 Radioactivity Measurement in Nuclear Medicine, IAEA, Vienna (2006).

1030 Medicare National Coverage Determinations Manual Chapter 1, Part 4 (Sections 200 – 310.1) Coverage
 1031 Determinations (Rev. 142, 02-03-12).

1032 http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads//ncd103c1_part4.pdf
 1033 Referenced 19 April 2012.

1034 QIBA UPICT Protocol: <http://qibawiki.rsna.org/index.php?title=UPICT>.

1035 Adams MC, Turkington TG, Wilson JM, Wong TZ. A systematic review of the factors affecting accuracy of
 1036 SUV measurements. *AJR Am J Roentgenol* 195(2):310-320, 2010. PMID: 20651185.

1037 Beaulieu S, Kinahan P, Tseng J, Dunnwald LK, Schubert EK, Pham P, Lewellen B, Mankoff DA. SUV varies with
 1038 time after injection in (18)F-FDG PET of breast cancer: characterization and method to adjust for time
 1039 differences. *J Nucl Med* 44(7):1044-1050, 2003. PMID: 12843218.

1040 Bland, JM and DG Altman. "Measurement Error Proportional To the Mean." *BMJ* 313, no. 7049 (1996): 106.

1041 Boellaard R. Standards for PET image acquisition and quantitative data analysis. *J Nucl Med* 50 Suppl 1:11S-
 1042 20S, 2009. PMID: 19380405.

1043 Boellaard R, O'Doherty MJ, Weber WA, Mottaghy FM, Lonsdale MN, Stroobants SG, Oyen WJ, Kotzerke J,
 1044 Hoekstra OS, Pruim J, Marsden PK, Tatsch K, Hoekstra CJ, Visser EP, Arends B, Verzijlbergen FJ, Zijlstra JM,
 1045 Comans EF, Lammertsma AA, Paans AM, Willemsen AT, Beyer T, Bockisch A, Schaefer-Prokop C, Delbeke D,
 1046 Baum RP, Chiti A, Krause BJ. FDG PET and PET/CT: EANM procedure guidelines for tumour PET imaging:
 1047 version 1.0. *Eur J Nucl Med Mol Imaging* 37(1):181-200, 2010. PMID: 19915839.

1048 Boellaard R. Need for standardization of 18F-FDG PET/CT for treatment response assessments. *J Nucl Med*

1049 52 Suppl 2:93S-100S, 2011. PMID: 22144561.

1050 Buckler AJ, Bresolin L, Dunnick NR, Sullivan DC, Aerts HJ, Bendriem B, Bendtsen C, Boellaard R, Boone JM,
1051 Cole PE, Conklin JJ, Dorfman GS, Douglas PS, Eidsaunet W, Elsinger C, Frank RA, Gatsonis C, Giger ML, Gupta
1052 SN, Gustafson D, Hoekstra OS, Jackson EF, Karam L, Kelloff GJ, Kinahan PE, McLennan G, Miller CG, Mozley
1053 PD, Muller KE, Patt R, Raunig D, Rosen M, Rupani H, Schwartz LH, Siegel BA, Sorensen AG, Wahl RL,
1054 Waterton JC, Wolf W, Zahlmann G, Zimmerman B. Quantitative imaging test approval and biomarker
1055 qualification: interrelated but distinct activities. *Radiology* 259(3):875-884, 2011. PMID: 21325035.

1056 Buckler AJ, Bresolin L, Dunnick NR, Sullivan DC. A collaborative enterprise for multi-stakeholder
1057 participation in the advancement of quantitative imaging. *Radiology* 258(3):906-914, 2011. PMID:
1058 21339352.

1059 Burger IA, Huser DM, Burger C, von Schulthess GK, Buck A. Repeatability of FDG quantification in tumor
1060 imaging: averaged SUVs are superior to SUVmax. *Nucl Med Biol* 39(5):666-670, 2012. PMID: 22381783.

1061 de Langen AJ, Vincent A, Velasquez LM, van Tinteren H, Boellaard R, Shankar LK, Boers M, Smit EF,
1062 Stroobants S, Weber WA, Hoekstra OS. Repeatability of 18F-FDG uptake measurements in tumors: a
1063 metaanalysis. *J Nucl Med* 53(5):701-708, 2012. PMID: 22496583.

1064 Delbeke D, Coleman RE, Guiberteau MJ, Brown ML, Royal HD, Siegel BA, Townsend DW, Berland LL, Parker
1065 JA, Hubner K, Stabin MG, Zubal G, Kachelriess M, Cronin V, Holbrook S. Procedure guideline for tumor
1066 imaging with 18F-FDG PET/CT 1.0. *J Nucl Med* 47(5):885-895, 2006. PMID: 16644760.

1067 Doot RK, Scheuermann JS, Christian PE, Karp JS, Kinahan PE. Instrumentation factors affecting variance and
1068 bias of quantifying tracer uptake with PET/CT. *Med Phys* 37(11):6035-6046, 2010. PMID: 21158315.

1069 Doot RK, Kurland BF, Kinahan PE, Mankoff DA. Design considerations for using PET as a response measure
1070 in single site and multicenter clinical trials. *Acad Radiol* 19(2):184-190, 2012. PMID: 22104290.

1071 Fahey FH, Kinahan PE, Doot RK, Kocak M, Thurston H, Poussaint TY. Variability in PET quantitation within a
1072 multicenter consortium. *Med Phys* 37(7):3660-3666, 2010. PMID: 20831073.

1073 Fletcher JW, Djulbegovic B, Soares HP, Siegel BA, Lowe VJ, Lyman GH, Coleman RE, Wahl R, Paschold JC,
1074 Avril N, Einhorn LH, Suh WW, Samson D, Delbeke D, Gorman M, Shields AF. Recommendations on the use
1075 of 18F-FDG PET in oncology. *J Nucl Med* 49(3):480-508, 2008. PMID: 18287273.

1076 Frings V, de Langen AJ, Smit EF, van Velden FH, Hoekstra OS, van Tinteren H, Boellaard R. Repeatability of
1077 metabolically active volume measurements with 18F-FDG and 18F-FLT PET in non-small cell lung cancer. *J*
1078 *Nucl Med* 51(12):1870-1877, 2010. PMID: 21078791.

1079 Gronenschild EH, Habets P, Jacobs HI, Mengelers R, Rozendaal N, van Os J, Marcelis M. The effects of
1080 FreeSurfer version, workstation type, and Macintosh operating system version on anatomical volume and
1081 cortical thickness measurements. *PLoS One* 7(6):e38234, 2012. PMID: 22675527.

1082 Hallett WA, Maguire RP, McCarthy TJ, Schmidt ME, Young H. Considerations for generic oncology FDG-
1083 PET/CT protocol preparation in drug development. *IDrugs* 10(11):791-796, 2007. PMID: 17968761.

1084 Hatt M, Cheze-Le Rest C, Aboagye EO, Kenny LM, Rosso L, Turkheimer FE, Albarghach NM, Metges JP,
1085 Pradier O, Visvikis D. Reproducibility of 18F-FDG and 3'-deoxy-3'-18F-fluorothymidine PET tumor volume
1086 measurements. *J Nucl Med* 51(9):1368-1376, 2010. PMID: 20720054.

1087 Jacene HA, Leboulleux S, Baba S, Chatzifotiadis D, Goudarzi B, Teytelbaum O, Horton KM, Kamel I, Macura
1088 KJ, Tsai HL, Kowalski J, Wahl RL. Assessment of interobserver reproducibility in quantitative 18F-FDG PET

1089 and CT measurements of tumor response to therapy. *J Nucl Med* 50(11):1760-1769, 2009. PMID: 19837757.

1090 Jackson T, Chung MK, Mercier G, Ozonoff A, Subramaniam RM. FDG PET/CT interobserver agreement in
1091 head and neck cancer: FDG and CT measurements of the primary tumor site. *Nucl Med Commun* 33(3):305-
1092 312, 2012. PMID: 22227560.

1093 Kamibayashi T, Tsuchida T, Demura Y, Tsujikawa T, Okazawa H, Kudoh T, Kimura H. Reproducibility of semi-
1094 quantitative parameters in FDG-PET using two different PET scanners: influence of attenuation correction
1095 method and examination interval. *Mol Imaging Biol* 10(3):162-166, 2008. PMID: 18408977.

1096 Kinahan PE, Doot RK, Wanner-Roybal M, Bidaut LM, Armato SG, Meyer CR, McLennan G. PET/CT
1097 Assessment of Response to Therapy: Tumor Change Measurement, Truth Data, and Error. *Transl Oncol*
1098 2(4):223-230, 2009. PMID: 19956382.

1099 Kinahan PE, Fletcher JW. Positron emission tomography-computed tomography standardized uptake values
1100 in clinical practice and assessing response to therapy. *Semin Ultrasound CT MR* 31(6):496-505, 2010. PMID:
1101 21147377.

1102 Krak NC, Boellaard R, Hoekstra OS, Twisk JW, Hoekstra CJ, Lammertsma AA. Effects of ROI definition and
1103 reconstruction method on quantitative outcome and applicability in a response monitoring trial. *Eur J Nucl*
1104 *Med Mol Imaging* 32(3):294-301, 2005. PMID: 15791438.

1105 Kumar V, Nath K, Berman CG, Kim J, Tanvetyanon T, Chiappori AA, Gatenby RA, Gillies RJ, Eikman EA.
1106 Variance of SUVs for FDG-PET/CT is greater in clinical practice than under ideal study settings. *Clin Nucl*
1107 *Med*. 2013 Mar;38(3):175-82. doi: 10.1097/RLU.0b013e318279ffdf. PMID 23354032 [PubMed - in process].

1108 Liu C, Pierce LA, Alessio AM, Kinahan PE. The impact of respiratory motion on tumor quantification and
1109 delineation in static PET/CT imaging. *Phys Med Biol* 54(24):7345-7362, 2009. PMID: 19926910.

1110 Lockhart CM, MacDonald LR, Alessio AM, McDougald WA, Doot RK, Kinahan PE. Quantifying and reducing
1111 the effect of calibration error on variability of PET/CT standardized uptake value measurements. *J Nucl Med*
1112 52(2):218-224, 2011. PMID: 21233174.

1113 Lodge M, Wahl, R. Characterizing the repeatability of oncology PET standardized uptake values. *J Nucl Med*
1114 54(2): 335, 2013.

1115 Mawlawi O, Erasmus JJ, Munden RF, Pan T, Knight AE, Macapinlac HA, Podoloff DA, Chasen M. Quantifying
1116 the effect of IV contrast media on integrated PET/CT: clinical evaluation. *AJR Am J Roentgenol* 186(2):308-
1117 319, 2006. PMID: 16423932.

1118 Minn H, Zasadny KR, Quint LE, Wahl RL. Lung cancer: reproducibility of quantitative measurements for
1119 evaluating 2-[F-18]-fluoro-2-deoxy-D-glucose uptake at PET. *Radiology* 196(1):167-173, 1995. PMID:
1120 7784562.

1121 Nahmias C, Wahl LM. Reproducibility of standardized uptake value measurements determined by 18F-FDG
1122 PET in malignant tumors. *J Nucl Med* 49(11):1804-1808, 2008. PMID: 18927325.

1123 Nakamoto Y, Zasadny KR, Minn H, Wahl RL. Reproducibility of common semi-quantitative parameters for
1124 evaluating lung cancer glucose metabolism with positron emission tomography using 2-deoxy-2-
1125 [18F]fluoro-D-glucose. *Mol Imaging Biol* 4(2):171-178, 2002. PMID: 14537140.

1126 Nestle U, Kremp S, Schaefer-Schuler A, Sebastian-Welsch C, Hellwig D, Rube C, Kirsch CM. Comparison of
1127 different methods for delineation of 18F-FDG PET-positive tissue for target volume definition in
1128 radiotherapy of patients with non-Small cell lung cancer. *J Nucl Med* 46(8):1342-1348, 2005. PMID:

- 1129 16085592.
- 1130 Subramaniam R, et al. FDG PET/CT Liver SULmean: Inter-reader agreement and impact of placement of
1131 volume of interest. Radiology 2012 (in press).
- 1132 Vu TT. Standardization of body surface area calculations. Journal of Oncology Pharmacy Practice 8(2-3):49-
1133 54, 2002.
- 1134 Velasquez LM, Boellaard R, Kollia G, Hayes W, Hoekstra OS, Lammertsma AA, Galbraith SM. Repeatability of
1135 18F-FDG PET in a multicenter phase I study of patients with advanced gastrointestinal malignancies. J Nucl
1136 Med 50(10):1646-1654, 2009. PMID: 19759105.
- 1137 Wahl RL, Jacene H, Kasamon Y, Lodge MA. From RECIST to PERCIST: Evolving Considerations for PET
1138 response criteria in solid tumors. J Nucl Med 50 Suppl 1:122S-150S, 2009. PMID: 19403881.
- 1139 Weber WA, Ziegler SI, Thodtmann R, Hanauske AR, Schwaiger M. Reproducibility of metabolic
1140 measurements in malignant tumors using FDG PET. J Nucl Med 40(11):1771-1777, 1999. PMID: 10565769.
- 1141 Weber WA. Assessing tumor response to therapy. J Nucl Med 50 Suppl 1:1S-10S, 2009. PMID: 19380403.
- 1142 Weber, WA, CA Gatsonis, PD Mozley, LG Hanna, AF Shields, DR Aberle, R Govindan, DA Torigian, JS Karp, JQ
1143 Yu, RM Subramaniam, RA Halvorsen, BA Siegel, 6678 Research team ACRIN, and Research team MK-0646-
1144 008. "Repeatability of 18f-Fdg PET/CT in Advanced Non-Small Cell Lung Cancer: Prospective Assessment in 2
1145 Multicenter Trials." J Nucl Med 56, no. 8 (2015): 1137-43.
- 1146 Young H, Baum R, Cremerius U, Herholz K, Hoekstra O, Lammertsma AA, Pruim J, Price P. Measurement of
1147 clinical and subclinical tumour response using [18F]-fluorodeoxyglucose and positron emission tomography:
1148 review and 1999 EORTC recommendations. European Organization for Research and Treatment of Cancer
1149 (EORTC) PET Study Group. Eur J Cancer 35(13):1773-1782, 1999. PMID: 10673991.

1150

1151 **Appendices**

1152 **Appendix A: Acknowledgements and Attributions**

1153 This document is proffered by the Radiological Society of North America (RSNA) Quantitative Imaging
1154 Biomarker Alliance (QIBA) FDG-PET/CT Biomarker Committee. The FDG-PET/CT Biomarker Committee is
1155 composed of physicians, scientists, engineers and statisticians representing the imaging device
1156 manufacturers, image analysis software developers, image analysis facilities and laboratories,
1157 biopharmaceutical companies, academic institutions, government research organizations, professional
1158 societies, and regulatory agencies, among others. A more detailed description of the QIBA FDG-PET/CT
1159 group and its work can be found at the following web link: [http://qibawiki.rsna.org/index.php?title=FDG-](http://qibawiki.rsna.org/index.php?title=FDG-PET_tech_ctte)
1160 [PET_tech_ctte](http://qibawiki.rsna.org/index.php?title=FDG-PET_tech_ctte)

1161 The following were members of the QIBA FDG-PET/CT Biomarker Committee during the writing of this
1162 Profile (in alphabetical order):

1163

QIBA FDG-PET Biomarker Committee (in alphabetical order)

Paul E. Kinahan, PhD (Co-Chair)

University of Washington

Ling X. Shao, PhD (Co-Chair)**Richard L. Wahl, MD, FACR (Co-Chair)**

Keith Allberg
Ramsey D. Badawi, PhD
Stella M. Batalles, MD
Richard Baumgartner, PhD
Bernard Bendriem, PhD
Ronald Boellaard, PhD
John Buatti, MD
Chris Buckle, MD
Andrew J. Buckler, MS
Janice Campbell, PhD
Paul L. Carson, PhD
Michael E. Casey, PhD
Sung Chang, PhD
Sandra Chica, MD
Paul E. Christian
David A. Clunie, MBBS
Daniel Coiro
Patricia E. Cole, MD, PhD
Peter David Corr, MD
Barbara Croft, PhD
Shiva K. Das, PhD
Simon DeBruin, MSEE
Todd Deckard, MSEE
Jon DeVries, MBA
Robert K. Doot, PhD
Gary S. Dorfman, MD
Vinay A. Duddalwar, MD, FRCR
Richard M. Eaton, JD
Edward A. Eikman, MD
Brian Elston
Richard A. Frank, MD, PhD, FPPM
Kirk Frey, MD, PhD
Daniel Gagnon, PhD
Susan Galbraith, PhD
Constantine Gatsonis, PhD
Igor D. Grachev, MD, PhD
Michael Graham, PhD, MD
Donald P. Harrington, MA, MD
Markus T. Harz, PhD
Howard Higley, PhD
Otto Hoekstra, MD
John M. Hoffman, MD
Blaine C. Horvath, RT

Philips Healthcare**Johns Hopkins University**

RadQual, LLC
University of California, Davis
Instituto Cardiovascular de Rosario
Merck Research Laboratories
Siemens Medical Solutions USA
VU Medical Center, Amsterdam, NL
University of Iowa
University of Chicago
Elucid Bioimaging Inc.
Wm. Beaumont Hospital
University of Michigan Health System
Siemens
Amgen
Novartis
University of Utah/SNMMI QIBA Representative
PixelMed
Delfin Imagem
Eli Lilly and Company
UAE University
Duke University
Duke University
Segami Corporation
Vital Images, Inc.
Merge Healthcare
University of Pennsylvania
Weill Cornell Medical College
USC/Norris Comprehensive Cancer Center
Medical Imaging & Technology Alliance (MITA)
Moffitt Cancer Center
Washington University
GE Healthcare
University of Michigan
Toshiba
Astrazeneca
Brown University
GE Healthcare
University of Iowa
State University of New York
Fraunhofer MEVIS, Inst for Medical Image Computing
CCS Associates, Inc.
VU Medical Center, Amsterdam, NL
University of Utah
BioClinica, Inc.

William Howe, MD, PhD	Siemens Medical Solutions USA
Yuying C. Hwang, PhD	Amgen
Todd Johnson, MS	Vital Images, Inc.
Lisa R. Karam, PhD	NIST
Gary J. Kelloff, MD	Cancer Imaging Program, NCI
Robert Koeppe, PhD	University of Michigan
Steve Kohlmyer	GE Healthcare
Feng-Ming (Spring) Kong, MD, PhD	University of Michigan
Martin A. Lodge, PhD	Johns Hopkins University
Lawrence (Larry) R. MacDonald, PhD	University of Washington
Marianne Maffoni	TeraRecon, Inc.
Piotr Maniawski	Philips Healthcare
Paul Marsden, MD	King's College London
Timothy J. McCarthy, PhD	Pfizer
Alexander (Sandy) McEwan, MB	SNMMI
Colin G. Miller, PhD	BioClinica, Inc.
Matthew P. Miller, PhD	GE Healthcare
Michael A. Miller, PhD	Indiana University
Neru Munshi, PhD	PAREXEL International
Dennis Nelson, PhD	MIMvista Corp.
Sarah J. Nelson, PhD	University of California, San Francisco
Chuck Nortmann	Philips Healthcare
Miguel H. Pampaloni, MD	University of California San Francisco
Anshuman Panda, PhD	Mayo Clinic
Seong-Hoon Park, MD	Wonkwang University School of Medicine
Sonia H. Pearson-White, PhD	The Biomarkers Consortium, FNIH
Eric S. Perlman, MD	Perlman Advisory Group
Larry Alan Pierce, PhD	University of Washington
Lucy Pike, PhD	King's College London
Wolf S. Richter	Pharmtrace
Christina L. Sammet, PhD	Northwestern University
Steffen Sammet, MD, PhD	University of Chicago
Subhendra N. Sarkar, PhD, RT	Beth Israel Deaconess Hospital
Annette Schmid, PhD	PAREXEL International
Lalitha Shankar, MD, PhD	NIH
Barry A. Siegel, MD	Washington University in St. Louis
Debi Simone	GE Healthcare
Anand K. Singh, MD	Harvard-Massachusetts General Hospital
Anne M. Smith, PhD	Siemens Medical Solutions USA, Inc.
Juergen Soldner	Siemens Medical Solutions USA, Inc.
Rathan Subramaniam, MD, PhD	Johns Hopkins University
Daniel C. Sullivan, MD	Duke University
John J. Sunderland, PhD	University of Iowa
Fuk Hay Tang, PhD	Hong Kong Polytechnic University
Ukihide Tateishi, MD, PhD	Yokohama City University Graduate School of Medicine

Valerie Treyer, PhD	Consultant, Neuroscientist
Timothy G. Turkington, PhD	Duke University
Ronald Van Heertum, MD	BioClinica, Inc.
Matt Vanderhoek, PhD	Henry Ford Hospital
Ronald Van Heertum, MD	BioClinica, Inc.
Etienne Von Lavante, D.Phil	Mirada Medical
Wenli Wang, PhD	Toshiba
Wolfgang Weber, MD	Memorial Sloan-Kettering Cancer Center
Ralph Wickenhoefer, MD	Central Hospital German Armed Forces
Scott D. Wollenweber, PhD	GE Healthcare
John G. Wolodzko, PhD	BioClinica, Inc.
Roxanne Yaghoubi	Academy of Radiology Research
Jeffrey T. Yap, PhD	Harvard-Dana Farber Cancer Institute
Brenda Ye, MD	FDA
Terry S. Yoo, PhD	CDER
Kwon-Ha Yoon, MD, PhD	Wonkwang University
Helen Young, PhD	AstraZeneca
T. C. Zhao, PhD	TeraRecon, Inc.
Brian E. Zimmerman, PhD	NIST

1164

1165 The FDG-PET/CT Biomarker Committee is deeply grateful for the support and technical assistance provided
1166 by the staff of the Radiological Society of North America.

1167

1168 **Appendix B: Background Information for Claim**

1169 A number of publications report test-retest repeatability for tumor SUV measurements with FDG PET
1170 [1,2,3,4,5,6,7,8,9]. Table 1 lists these publications and summarizes some of their results. Comparing
1171 repeatability measurements from the various reports is complicated by the different methodologies
1172 employed in each study and also the different metrics used to characterize repeatability.

1173 Table 1. Selected repeatability parameters extracted from literature publications. Where multiple SUV
1174 types were reported, preference was given to SUVmax as this SUV definition was more comparable
1175 between studies. The column marked 'Inferred wCV' is an estimate of the within-subject coefficient of
1176 variation based upon the reported parameters and may not appear in the original manuscripts. Details of
1177 how these Inferred wCV values were derived are described in the text and in Table 2.

Publication	SUV Type	Repeatability Parameter	Parameter Value	Where in Manuscript	Inferred wCV	Comment
Minn 1995 [1]	SUVmean	Mean absolute percentage difference	10 %	Table 4	8.86 %	n=10. 1.2 x 1.2 cm ROI
Weber 1999 [2]	SUVmean	SD of the percentage difference	9.1 %	Table 2	6.43 %	n=16. 50 % isocontour VOI
Nahmias 2008 [5]	SUVmax	SD of the difference	1.14 SUV	Page 1806	Not available	n=26. Results reported in absolute SUV units
Kamibayashi 2008 [6]	SUVmax	Mean absolute percentage difference	16.1 %	Table 4	14.27 %	n=45. Two different PET scanners
Nakamoto 2002 [3]	SUVmax	Mean absolute percentage difference	11.3 %	Table 4	10.01 %	n=10
Krak 2005 [4]	SUVmax	Mean absolute percentage difference	13 %	Table 2	11.52 %	n=29
Velasquez 2009 [7]	SUVmax	Within subject coefficient of variation	11.9 %	Table 5	11.9 %	n=45. Multi-center study after centralized quality assurance and analysis
Hatt 2010 [8]	SUVmax	SD of the percentage difference	16.7 %	Table 2	11.81 %	n=17
Weber 2015 [10]	SUVmax	SD of differences of log-transformed SUV	0.16	Table 2	11.97 %	n=40. Multi-center study

1178

1179

1180 The region-of-interest (ROI) or volume-of-interest (VOI) methodology varied between publications. Minn et
 1181 al [1] report SUVmean derived from a fixed size 1.2 × 1.2 cm region-of-interest. Weber et al [2] report
 1182 SUVmean derived from a volume-of-interest defined by a 50% isocontour. The remaining papers report
 1183 SUVmax, although data for multiple ROI definitions were sometimes reported. Because SUVmax was more
 1184 commonly reported amongst these repeatability papers and was more comparable between studies, table
 1185 1 focused primarily on SUVmax.

1186 Nahmias and Wahl [5] report SUVmax but, unlike the other publications, they present their results in
 1187 absolute SUV units, as opposed to relative units. Direct comparison with the other reports was therefore
 1188 not possible. Kamibayashi et al [6] compared the repeatability of SUVs measured on different scanner
 1189 systems, whereas the other reports involve test-retest studies on the same scanner. For this reason the
 1190 Kamibayashi data were also not directly comparable with the other papers. The remaining publications
 1191 [3,4,7,8,10] are amenable to more direct comparison as they all report the repeatability of SUVmax, with
 1192 test and retest studies both performed on the same scanner system.

1193 A further complication when comparing reports is the different metrics used to characterize repeatability.
 1194 In table 1 we translate the reported repeatability measurements to a within-subject coefficient of variation
 1195 (wCOV) to allow a more direct comparison. Based on the data in the last 5 rows of table 1 [3,4,7,8,10], it
 1196 can be seen that the within subject coefficient of variation for SUVmax was in the range 10.0 – 12.0 %.

1197 Table 2 summarizes the relationships that were involved in converting the published repeatability
 1198 parameters to within-subject coefficient of variation.

1199

1200 Table 2. Relationships used to compare repeatability metrics found in the literature.

Parameter	Symbol	Relationship	Comment
Percentage difference	D	$100 \times (SUV_2 - SUV_1) / 0.5 \times (SUV_1 + SUV_2)$	Test-retest difference expressed as a percentage of the mean
Mean absolute percentage difference of D	D_MAD	Mean of D over all subjects	D is the absolute value of D
Standard deviation of D	D_SD	Standard deviation of D over all subjects	$D_SD = D_MAD / \sqrt{(2/\pi)}$ for normally distributed data
Within subject coefficient of variation	wCV	$D_SD / \sqrt{2}$	Reflects repeatability of a single measurement
Within subject coefficient of variation	wCV	$100(\exp(s_w)-1)$	s_w is the within-subject standard deviation of differences of log-transformed data. This derivation leads to asymmetric repeatability coefficients [11]
Repeatability Coefficient where differences are Normally distributed	RC	$100(1.96 \times \sqrt{2} \times wCV)$	Reflects 95 % limits of repeatability for the difference between two measurements
Repeatability Coefficient where the logarithm of the differences are Normally distributed	RC	$100(\exp(\pm 1.96 \times \sqrt{2} \times s_w)-1)$	Asymmetric repeatability coefficients [11]

1201

1202

1203

1204

1205

1206

1207

1208

One assumption that was made during these conversions was that the percentage difference (D) between test-retest SUV measurements was normally distributed with zero mean. While this assumption may not be strictly applicable over a wide range of SUVs, it is an assumption that is implicitly being made whenever 95% limits of repeatability are employed [7,8]. Applying this same assumption to the studies that report the mean absolute percentage difference (D_MAD) allows their results to be simply related to the other publications that report the standard deviation by $D_MAD = \text{sqrt}(2/\pi)D_SD$, as shown below.

$$\begin{aligned}
 D_MAD &= \frac{1}{\sigma\sqrt{2\pi}} \int_{-\infty}^{\infty} |x - \mu| e^{-\frac{(x-\mu)^2}{2\sigma^2}} dx \\
 &= \frac{2}{\sigma\sqrt{2\pi}} \int_0^{\infty} (x - \mu) e^{-\frac{x-\mu^2}{2\sigma^2}} dx \\
 \text{let } r &= \frac{(x - \mu)^2}{2\sigma^2}, \text{ and } dr = \frac{(x - \mu)}{\sigma^2} dx, \text{ and limits are unchanged } \int_{x=0}^{x=\infty} \rightarrow \int_{r=0}^{r=\infty} \\
 \text{then,} \\
 D_MAD &= \sqrt{\frac{2}{\pi}} \sigma \int_0^{\infty} e^{-r} dr = \sqrt{\frac{2}{\pi}} \sigma e^{-r} \Big|_0^{\infty} = \sqrt{\frac{2}{\pi}} \sigma [1 - 0] = \sqrt{\frac{2}{\pi}} \sigma \approx 0.80\sigma
 \end{aligned}$$

1209

1210

References

1211

1212

1213

1214

1215

1216

1217

- 1 Minn H, Zasadny KR, Quint LE, Wahl RL. Lung cancer: reproducibility of quantitative measurements for evaluating 2-[F-18]-fluoro-2-deoxy-D-glucose uptake at PET. *Radiology*, 196, 1 (1995), 167-173.
- 2 Weber WA, Ziegler SI, Thodtman R, Hanauske A-R, Schwaiger M. Reproducibility of metabolic measurements in malignant tumors using FDG PET. *J Nucl Med*, 40, 11 (1999), 1771-1777.
- 3 Nakamoto Y, Zasadny KR, Minn H, Wahl RL. Reproducibility of common semi-quantitative parameters for evaluating lung cancer glucose metabolism with positron emission tomography using 2-deoxy-2-[18F]fluoro-D-glucose. *Mol Imaging Biol*, 4 (2002), 171-178.

1218 4 Krak NC, Boellaard R, Hoekstra OS, Twisk JWR, Hoekstra CJ, Lammertsma AA. Effects of ROI definition
1219 and reconstruction method on quantitative outcome and applicability in a response monitoring trial.
1220 Eur J Nucl Med Mol Imaging, 32, 3 (2005), 294-301.

1221 5 Nahmias C, Wahl LM. Reproducibility of standardized uptake value measurements determined by 18F-
1222 FDG PET in malignant tumors. J Nucl Med, 49, 11 (2008), 1804-1808.

1223 6 Kamibayashi T, Tsuchida T, Demura Y, et al. Reproducibility of semi-quantitative parameters in FDG-PET
1224 using two different PET scanners: influence of attenuation correction method and examination interval.
1225 Mol Imaging Biol, 10 (2008), 162-166.

1226 7 Velasquez LM, Boellaard R, Kollia G, et al. Repeatability of 18F-FDG PET in a multicenter phase 1 study
1227 of patients with advanced gastrointestinal malignancies. J Nucl Med, 50, 10 (2009), 1646-1654.

1228 8 Hatt M, Cheze-Le Rest C, Aboagye EO, Kenny LM, Rosso L, Turkheimer FE, Albarghach NM, Metges JP,
1229 Pradier O, Visvikis D. Reproducibility of 18F-FDG and 3'-deoxy-3'-18F-fluorothymidine PET tumor
1230 volume measurements. J Nucl Med., 51 (2010), 1368-1376.

1231 9 Kumar V, Nath K, Berman CG, Kim J, Tanvetyanon T, Chiappori AA, Gatenby RA, Gillies RJ, Eikman EA.
1232 Variance of SUVs for FDG-PET/CT is greater in clinical practice than under ideal study settings. Clin Nucl
1233 Med. 2013 Mar;38(3):175-82. PMID 23354032

1234 10 Weber, WA, CA Gatsonis, PD Mozley, LG Hanna, AF Shields, DR Aberle, R Govindan, DA Torigian, JS Karp,
1235 JQ Yu, RM Subramaniam, RA Halvorsen, BA Siegel, 6678 Research team ACRIN, and Research team MK-
1236 0646-008. "Repeatability of 18f-Fdg PET/CT in Advanced Non-Small Cell Lung Cancer: Prospective
1237 Assessment in 2 Multicenter Trials." J Nucl Med 56, no. 8 (2015): 1137–43.

1238 11. Bland, JM and DG Altman. "Measurement Error Proportional to the Mean." BMJ 313, no. 7049 (1996):
1239 106.

1240

1241 **Appendix C: Conventions and Definitions**

1242 ***Convention Used to Represent Profile requirements***

1243 Requirements for adhering to this Profile are presented in tables/boxes as shown in the example below.
1244 Shaded boxes are intended future requirements, and are not at this time required for adhering to the
1245 Profile. Bold text is used for requirements that are formatted as checklists, which are provided in Appendix
1246 I. The format used is the following:

Parameter	Entity/Actor	Specification
		Normative text: Clear boxes are current requirements
		Shaded boxes are intended for future requirements
		Bold text indicates requirements included in checklists (Appendix I)

1247

1248 Items within tables are normative (i.e. are required in order to be compliant with the QIBA protocol). The
1249 intent of the normative text is to be prescriptive and detailed to facilitate implementation. In general the

1250 intent is to specify the final state or output, and not how that is to be achieved.

1251 All other text outside of these tables is considered informative only.

1252 A condensed table from section 3.2.1.2 'Subject Positioning' is reproduced below as an illustrative example.

1253

Parameter	Entity/Actor	Specification
Respiratory motion minimization	Technologist	If the patient is observed to take a deep breath during the CT scan it should be documented and a repeat CT study should be considered.
Respiratory motion minimization	PET/CT Scanner	The PET/CT scanner shall provide methods to minimize the PET image errors introduced by respiratory motion.
Breathing and motion non-conformance	Technologist	The Technologist shall document issues regarding subject non-conformance with breathing and motion.
		The Technologist shall document issues regarding subject non-conformance with breathing and motion using the common data format mechanism (Appendix E).

1254

1255

1256 **Definitions**

1257 18F-FDG or FDG: 2-deoxy-2-(18F)fluoro-D-glucose, a glucose analog, with the positron-emitting radioactive
1258 isotope fluorine-18 substituted for the normal hydroxyl group at the 2' position in the glucose molecule.
1259 FDG is the most commonly used (>90%) radiotracer in PET imaging.

1260 Accreditation: Approval by an independent body or group for broad clinical usage (requires ongoing
1261 QA/QC) e.g. ACR, IAC, TJC (listed below).

1262 AC: Attenuation Correction. Attenuation is a an effect that occurs when photons emitted by the radiotracer
1263 inside the body are absorbed by intervening tissue. The result is that structures deep in the body are
1264 reconstructed as having falsely low (or even negative) tracer uptake. Contemporary PET/CT scanners
1265 estimate attenuation using integrated x-ray CT equipment. While attenuation-corrected images are
1266 generally faithful representations of radiotracer distribution, the correction process is itself susceptible
1267 to significant artifacts.

1268 Conformance: Meeting the list of requirements described in this document, which are necessary to meet
1269 the measurement claims for this QIBA Profile.

1270 CRF: Case Report Form (CRF) is a paper or electronic questionnaire specifically used in clinical trial research.
1271 The CRF is used by the sponsor of the clinical trial (or designated CRO etc.) to collect data from each
1272 participating site. All data on each patient participating in a clinical trial are held and/or documented in
1273 the CRF, including adverse events.

1274 CT: X-ray computed tomography (CT) is a medical imaging technique that utilizes X-rays to produce
1275 tomographic images of the relative x-ray absorption, which is closely linked to tissue density.

1276 DICOM: Digital Imaging and Communications in Medicine (DICOM) is a set of standards for medical images
1277 and related information. It defines formats for medical images that can be exchanged in a manner that
1278 preserves the data and quality necessary for clinical use.

1279 Dose: Can refer to either radiation dose or as a jargon term for 'total radioactivity'. For example, 10 mCi of
1280 ¹⁸F-FDG is often referred to as a 10 mCi dose.

1281 FDG: See ¹⁸F-FDG.

1282 LBM: Lean Body Mass is calculated by subtracting body fat weight from total body weight. The Lean body
1283 mass (LBM) has been described as an index superior to total body weight for prescribing proper levels
1284 of medications and for assessing metabolic disorders.

1285 mCi: millicuries. A non-SI unit of radioactivity, defined as 1 mCi = 3.7×10^7 decays per second. Clinical
1286 FDG-PET studies inject (typically) 5 to 15 mCi of ¹⁸F-FDG.

1287 MBq: megabecquerel. An SI-derived unit of radioactivity defined as 1.0×10^6 decays per second.

1288 Metabolic Response / Metabolic Disease. A classification based on the visible level of FDG uptake
1289 associated with malignant solid tumors. There are several specific classifications depending on the
1290 criteria used:

- 1291 • CMR: Complete Metabolic Response. A complete resolution of FDG-PET uptake within the tumor
1292 volume so that it is indistinguishable from the surrounding normal tissue.
- 1293 • PMR: Partial Metabolic Response. A reduction in FDG uptake. The thresholds used for this
1294 determination depend on the criteria used. Two such criteria are the EORTC [Young, 1999] and
1295 PERCIST [Wahl, 2009] proposals.
- 1296 • PMD: Progressive Metabolic Disease. An increase in FDG uptake relative to a predefined threshold.
- 1297 • SMD: Stable Metabolic Disease. No change in FDG uptake relative to predefined thresholds.

1298 PERCIST: PET Response Criteria for Solid Tumors [Wahl, 2009]. A framework proposed for using FDG-PET
1299 imaging as a cancer therapy response criteria for solid tumors. Proposed as a more accurate alternative
1300 to RECIST for several types of solid tumors.

1301 PET: Positron emission tomography (PET) is a tomographic imaging technique that produces an image of
1302 the in vivo distribution of a radiotracer, typically FDG.

1303 PET/CT: Positron emission tomography / computed tomography (PET/CT) is a medical imaging system that
1304 combines in a single gantry system both Positron Emission Tomography (PET) and an x-ray Computed
1305 Tomography (CT) scanners, so that images acquired from both devices can be taken nearly-
1306 simultaneously.

1307 Profile: A QIBA Profile is a document that describes a specific performance Claim and how it can be
1308 achieved. A Profile consists of one or more Claims and associated Details.

- 1309 • Claims: tell a user what can be accomplished by following the Profile.
- 1310 • Details: tell a vendor what must be implemented in their product; and tell a user what procedures
1311 are necessary.

1312 QA: Quality Assurance. Proactive definition of the process or procedures for task performance. The
1313 maintenance of a desired level of quality in a service or product, esp. by means of attention to every
1314 stage of the process of delivery or production.

1315 QC: Quality Control. Specific tests performed to ensure target requirements of QA program are met.
1316 Typically by testing a sample of the output against the specification.

1317 Qualification: Approved by an independent body or group for either general participation in clinical
1318 research (ACRIN-CQIE , SNM-CTN others) or for a specific clinical trial (requires ongoing QA/QC). This
1319 includes CROs, ACRIN, SNM-CTN, CALGB and other core laboratories.

1320 RECIST: Response Evaluation Criteria in Solid Tumors (RECIST). A set of published rules that define when
1321 cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progression") during
1322 treatments. Based on anatomical size changes of solid tumors. Commonly used but also controversial.

1323 ROI: Region of interest. A region in an image that is specified in some manner, typically with user-controlled
1324 graphical elements that can be either 2D areas or 3D volumes. These elements include, but not limited
1325 to, ellipses, ellipsoids, rectangles, rectangular volumes, circles, cylinders, polygons, and free-form
1326 shapes. An ROI can also be defined by a segmentation algorithm that operates on the image.
1327 Segmentation algorithms include, but are not limited to, fixed-value thresholding, fixed-percentage
1328 thresholding, gradient edge detection, and Bayesian methods. With the definition of an ROI, metrics are
1329 then calculated for the portion of the image within the ROI. These metrics can include, but are not
1330 limited to, mean, maximum, standard deviation, and volume or area. Note that the term ROI can refer
1331 to a 2D area on a single image slice or a 3D volume. In some cases, the term ROI is used to refer to 2D
1332 area and the term volume of interest (VOI) is used to refer to a 3D volume. In this Profile the term ROI is
1333 used to refer to both 2D areas and 3D volumes as needed.

1334 SUV: Standardized uptake value. A measure of relative radiotracer uptake within the body. Typically
1335 defined for a time point t as $SUV(t) = r(t)/(d'/V)$, where $r(t)$ is the measured radioactivity concentration
1336 within the ROI (typically in units of kBq/ml), d' is the decay-corrected injected radioactivity (or 'dose'),
1337 and V is a surrogate for the distribution volume. Typically, patient weight or lean body mass are used
1338 for V .

1339 Notes:

- 1340 1. The SUV can change over time, so measuring $r(t)$ at a consistent time point is recommended.
- 1341 2. Either body weight or lean body mass are used for a surrogate for the distribution volume, so the
1342 SUV units are g/ml (Section 3.4.3)
- 1343 3. For a uniform distribution of radiotracer, the SUV everywhere would be exactly 1 g/ml.
- 1344 4. The measured SUV statistic is typically one of the following:
 - 1345 i. SUVmean: The average SUV within the ROI.
 - 1346 ii. SUVmax: The maximum SUV within the ROI.
 - 1347 iii. SUVpeak: The average SUV within a fixed-sized ROI, typically a 1 cm diameter sphere. The
1348 spheres location is adjusted such that the average SUV is maximized.
 - 1349 iv. TLG: Total lesion glycolysis. The summed SUV within the ROI.

1350 TOF: Time of Flight (TOF) is a PET imaging technique utilizing differential annihilation photon travel times
1351 to more accurately localize the in vivo distribution of a radiotracer.

1352 UPICT: Uniform Protocols For Imaging in Clinical Trials (UPICT). A RSNA-QIBA initiative that seeks to provide
1353 a library of annotated protocols that support clinical trials within institutions, cooperative groups, and
1354 trials consortia. The UPICT protocols are based on consensus standards that meet a minimum set of

1355 criteria to ensure imaging data quality.

1356 VOI: Volume of interest. See definition for ROI.

1357

1358 *Organizations*

1359 AAPM: The American Association of Physicists in Medicine is a member society concerned with the topics
1360 of medical physics, radiation oncology, imaging physics. The AAPM is a scientific, educational, and
1361 professional organization of over 8,000 medical physicists.

1362 ACR: The 36,000 members of |include radiologists, radiation oncologists, medical physicists, interventional
1363 radiologists, nuclear medicine physicians and allied health professionals.

1364 ACRIN: The American College of Radiology Imaging Network (ACRIN) is a program of the American College
1365 of Radiology and a National Cancer Institute cooperative group. Focused on cancer-related research in
1366 clinical trials.

1367 CLIA: Clinical Laboratory Improvement Amendments: Accreditation system for establishing quality
1368 standards for laboratory testing.

1369 CQIE: The Centers of Quantitative Imaging Excellence (CQIE) program was developed by ACRIN in response
1370 to a solicitation for proposals issued in December 2009 by SAIC-Frederick on behalf of the National Cancer
1371 Institute (NCI). The primary objective of the CQIE Program is to establish a resource of 'trial ready' sites
1372 within the NCI Cancer Centers Program that are capable of conducting clinical trials in which there is an
1373 integral molecular and/or functional advanced imaging endpoint.

1374 CRO: Contract Research Organization A commercial or not-for-profit organization designated to perform a
1375 centralized and standardized collection, analysis, and/or review of the data generated during a clinical trial.
1376 Additional activities which may be performed by an imaging core lab include training and qualification of
1377 imaging centers for the specific imaging required in a clinical trial, development of imaging acquisition
1378 manuals, development of independent imaging review charters, centralized collection and archiving of
1379 images received from study sites, performing pre-specified quality control checks/tests on incoming images
1380 and development and implementation of quality assurance processes and procedures to ensure that
1381 images submitted are in accord with imaging time points specified in the study protocol and consistent with
1382 the quality required to allow the protocol-specified analysis /assessments

1383 CTN: The Clinical Trials Network (CTN) was formed by SNMMI in 2008 to facilitate the effective use of
1384 molecular imaging biomarkers in clinical trials.

1385 EANM: The European Association of Nuclear Medicine (EANM) constitutes the European umbrella
1386 organization of nuclear medicine in Europe

1387 EARL: EANM Research Ltd (EARL) was formed by EANM in 2006 to promote multicentre nuclear medicine
1388 and research.

1389 ECOG-ACRIN: A National Cancer Institute cooperative group formed from the 2012 merger of the Eastern
1390 Cooperative Oncology Group (ECOG) and the American College of Radiology Imaging Network (ACRIN).

1391 EORTC: The European Organization for Research and Treatment of Cancer or EORTC is an international non-
1392 profit organization that develops, coordinates, and stimulates cancer laboratory and clinical research in
1393 Europe.

1394 EMA: European Medicines Agency is a European Union agency for the evaluation of medicinal products.

1395 Roughly parallel to the U.S. Food and Drug Administration (FDA), but without FDA-style centralization.

1396 FDA: Food and Drug Administration is responsible for protecting and promoting public health in the U.S.
1397 through the regulation and supervision of food safety, tobacco products, dietary supplements, prescription
1398 and over-the-counter pharmaceutical medications, vaccines, biopharmaceuticals, blood transfusions,
1399 medical devices, electromagnetic radiation emitting devices, and veterinary products.

1400 IAC: The Intersocietal Accreditation Commission (IAC) provides accreditation programs for Vascular Testing,
1401 Echocardiography, Nuclear/PET, MRI, CT/Dental, Carotid Stenting and Vein Center.

1402 MITA: The Medical Imaging & Technology Alliance is a division NEMA that develops and promotes
1403 standards for medical imaging and radiation therapy equipment. These standards are voluntary guidelines
1404 that establish commonly accepted methods of design, production, testing and communication for imaging
1405 and cancer treatment products.

1406 NCRI: National Cancer Research Institute. The National Cancer Research Institute (NCRI) is a UK-wide
1407 partnership between the government, charity and industry which promotes co-operation in cancer
1408 research among the 22 member organizations for the benefit of patients, the public and the scientific
1409 community.

1410 NEMA: National Electrical Manufacturers Association is a forum for the development of technical standards
1411 by electrical equipment manufacturers.

1412 NIST: National Institute of Standards and Technology is a measurement standards laboratory which is a
1413 non-regulatory agency of the United States Department of Commerce.

1414 QIBA: Quantitative Imaging Biomarkers Alliance. The Quantitative Imaging Biomarkers Alliance (QIBA) was
1415 organized by RSNA in 2007 to unite researchers, healthcare professionals and industry stakeholders in the
1416 advancement of quantitative imaging and the use of biomarkers in clinical trials and practice.

1417 RSNA: Radiological Society of North America (RSNA). A professional medical imaging society with more than
1418 47,000 members, including radiologists, radiation oncologists, medical physicists and allied scientists. The
1419 RSNA hosts the world's largest annual medical meeting.

1420 SNMMI: Society of Nuclear Medicine and Molecular Imaging (formerly called the Society of Nuclear
1421 Medicine (SNM)). A nonprofit scientific and professional organization that promotes the science,
1422 technology and practical application of nuclear medicine and molecular imaging. SNMMI represents 18,000
1423 nuclear and molecular imaging professionals worldwide. Members include physicians, technologists,
1424 physicists, pharmacists, scientists, laboratory professionals and more

1425 TJC: The Joint Commission (TJC) accredits and certifies health care organizations and programs in the
1426 United States.

1427 USP: United States Pharmacopeial Convention establishes written and physical (reference) standards for
1428 medicines, food ingredients, dietary supplement products and ingredients in the U.S.

1429

1430 **Appendix D: Model-specific Instructions and Parameters**

1431 The presence of specific product models/versions in the following tables should not be taken to imply that
1432 those products are fully compliant with the QIBA Profile. Conformance with a Profile involves meeting a
1433 variety of requirements of which operating by these parameters is just one. To determine if a product (and
1434 a specific model/version of that product) is compliant, please refer to the QIBA Conformance Document for

1435 that product.

1436 ***D.1. Image Acquisition Parameters***

1437 The following technique tables list acquisition parameter values for specific models/versions that can be
1438 expected to produce data meeting the requirements of Section 3.6.4 ('Phantom Imaging').

1439 These technique tables may have been prepared by the submitter of this imaging protocol document, the
1440 clinical trial organizer, the vendor of the equipment, and/or some other source. (Consequently, a given
1441 model/version may appear in more than one table.) The source is listed at the top of each table.

1442 Sites using models listed here are encouraged to consider using these parameters for both simplicity and
1443 consistency. Sites using models not listed here may be able to devise their own acquisition parameters that
1444 result in data meeting the requirements of Section 3.6.4 and conform to the considerations in Section 4. In
1445 some cases, parameter sets may be available as an electronic file for direct implementation on the imaging
1446 platform.

1447 ***D.2. Quality Assurance Procedures***

1448 Examples of recommend quality assurance procedures are shown for specific GE, Philips, and Siemens
1449 PET/CT scanners in the tables below.

QA procedures and schedules for Philips Gemini TF, V3.3 and V3.4					
Device	QA Procedure	Frequency	Performance Requirement	Operator	
CT	Tube Calibration	Daily		Staff	
	Air Calibration	Daily		Staff	
	Noise: On head phantom	Daily	No artifacts. Water 0 ± 4 CT	Staff	
	Noise and Artifacts. On body phantom	Daily	No artifacts. Teflon pin = 890 ± 50 CT Water 0 ± 4 CT	Staff	
	Contrast scale and artifacts	Monthly	No artifacts. Large Acrylic pin diameter is 50 ± 1 mm. All 7 resolution holes visible. Five of the six low contrast aculon pins detectable. Water 0 ± 4 , Nylon 100 ± 15 , Polyethylene 75 ± 15 , Teflon 1016 ± 50 , Acrylic $+140 \pm 15$, Lexan $+116 \pm 15$	Staff	
	Impulse Response	Advanced test as needed	Width at 50% Max of the Impulse Response profile should be $1.45 \text{ mm} \pm 0.10 \text{ mm}$.	Physicist/service	
	Slice thickness	Advanced test as needed	Average of aluminum strips within tolerance of values stated in manual.	Physicist/service	
	PET	System Initialization	Daily	Completion of program	Physicist/service
		Baseline collection (analog offsets of all photomultiplier channels)	Daily	Values within range. Success message	Staff
		PMT gain calibration	Daily	All PMTs calibrated within target gain. No Failed message.	Staff
Energy test and analysis		Daily	Energy centroids approximately 100. FWHM < FWHM threshold.	Staff	
Timing test		Daily	Agreement with system timing against the calibration settings	Staff	
Emission sinogram collection and analysis		Daily	Completion of program	Staff	
Automated System Initialization		Daily, prescheduled to shorten daily QC	Values within range.	Staff	
AutoQC	Daily, prescheduled to shorten daily QC	visually inspect for non uniformities	Staff		
Uniformity check	Monthly		Staff		
SUV calibration	Every 6 months, after recalibration, when SUV validation shows discrepancy		No warning message for calgen program	Staff	
SUV validation	Every 2 months, when PM is performed		ROI average should be 1.0 (0.9 - 1.1).	Staff, service	

QA procedures and schedules for GE Discovery ST, STE, Rx and Discovery 600/700 series PET/CT systems					
Device	QA Procedure	Frequency	Performance Requirement		
Computers	System reboot	Daily or as needed	N/A		
	CT tube warm up	Daily or after 2 hours of inactivity	N/A		
	Air calibrations (fast cals)	Daily			
	Generator calibrations	Daily			
CT	Contrast Scale	Acquire scans daily	The difference in CT numbers between the Plexiglas resolution block and water = 120, variation 10%		
		Acquire scans daily	The standard deviation for an ROI in the 1.6mm bar pattern should equal 37 ± 4 for the standard algorithm		
		Acquire scans daily	CT number for water of 0 ± 3 HU for the center ROI. The uniformity difference between the Center ROI and the average of the edge ROIs should be 0 ± 3 for Small Body (0 ± 10 maximum deviation if Large Body is used). Noise in the center of the image to approximately equal 4.3 ± 0.5 .		
	CT QA phantom	Acquire scans daily	Slice thickness should not vary by more than ± 1 mm from the expected value		
		Acquire scans daily			
		Acquire scans daily			
	PET	Full system calibration	After tube replacement or as PM		
			Daily		
		PET Daily Quality Assurance (DQA)	Coincidence	Daily	
			PET coincidence mean	Daily	
PET coincidence variance			Daily		
Singles			Daily		
PET singles mean			Daily		
PET singles variance			Daily		
Deadtime			Daily		
PET mean deadtime			Daily		
Timing			Daily		
PET timing mean			Daily		
Energy			Daily		
PET energy shift			Daily		
PET singles update gain	Weekly	Contrast value for a 3 mm object is less than 5 HU. Typical variation is ± 0.5 HU.			
Clean database	Weekly				
PET 2D normalization	Quarterly (if appropriate for the system)				
PET 2D well counter correction	Quarterly (if appropriate for the system)				
PET 3D normalization and well counter correction	Quarterly				
Establish new DQA baseline	Quarterly				
Ge-68 source pin replacement	Every 18 months				

QA procedures and schedules for Siemens Biograph 6/16 Hi-Rez, Biograph 16 Truepoint, Biograph 16 Truepoint with TrueV, PET Syngo 2010A, Biograph mCT					
Device	QA Procedure	Frequency	Performance Requirement	Operator	
Computers	Restart computers	Daily at Startup	N/A	Staff	
	Clear scheduler	Daily	N/A	Staff	
	Clear network, local, and film queues	Four times daily	N/A	Staff	
	Archive patient data	Daily	N/A	Staff	
CT	System cleanup/defragmentation	Weekly	N/A	Staff	
	CT Cleanup/Calibration	Daily, after 60 minutes of full load, within 1 hour of patient scan		Staff	
	CT Quality	Water HU	Daily	Results stated as "in tolerance"	Staff
		Pixel noise	Daily	Water HU = 0 +/- 4	Staff
Tube voltages		Daily	Results stated as "in tolerance"	Staff	
PET	PET Daily QC	Daily	Daily vs. standard chi-square <10, no patterns or artifacts	Staff	
		Daily	Pass/fail comparison against expected scanner min/mean/max	Staff	
		Daily	No visual artifacts or unusual patterns	Staff	
		Daily	Pass/fail	Staff	
	Scanner cross calibration	System quality report	Weekly	Pass/fail	Staff
		Partial detector setup: generate crystal region maps/energy profiles	Quarterly	Pass/fail	Staff
		Full detector setup and time alignment	When Ge-68 phantoms are replaced		Staff
		Calculate the Cross Calibration Correction Factor	When Ge-68 phantoms are replaced		Staff
		Recalibrate the current Ge-68 phantom and ECF	When Ge-68 phantoms are replaced		Staff
		Normalize and calibrate the scanner	When Ge-68 phantoms are replaced		Staff
CT constancy and	Monthly as part of maintenance plan			Service	

1453 **Appendix E: Data Fields to be Recorded in the Common Data Format**

1454 **Mechanism**

1455 The list below comprises meta-information (i.e. in addition to image values of kBq/ml) that is necessary for
1456 quantitatively accurate (i.e. known and minimal uncertainties) of PET SUVs. The intent here is to list what
1457 information should be captured rather than the mechanism itself. The format and corresponding
1458 mechanism of data capture/presentation is currently unspecified, but ranges from paper notes, to scanned
1459 forms or electronic data records, to direct entry from the measurement equipment (i.e., the PET/CT
1460 scanner or auxiliary measurement devices such as the dose calibrator) into pre-specified DICOM fields.
1461 Ideally all of the specified meta-data will be captured by direct electronic entry to DICOM fields, after
1462 suitable modification of the DICOM format for PET imaging.

1463 The concept endorsed here is that the needed meta-data is identified. Through revisions of this Profile, the
1464 DICOM standard, and technology the meta-data is inserted into the analysis stream (Figure 3) in a more
1465 direct manner and technology and accepted standards evolve.

- 1466 • The needed information, where feasible, is listed in order from least frequently changing to most
1467 frequently changing.
- 1468 • In all cases note whether measurements are made directly or estimated. If the latter case, note the
1469 source of information and the date and time (e.g. if subject cannot be moved from bed to measure
1470 weight or height).

1471 Data fields to be recorded:

- 1472 1. Site specific
 - 1473 a. Site information (include name and/or other identifiers)
 - 1474 b. Scanner make and model
 - 1475 c. Hardware Version numbers
 - 1476 d. Software Version numbers
 - 1477 e. Confirmation that scanner used was previously qualified (or not)
- 1478 2. Protocol specific
 - 1479 a. PET
 - 1480 i. Duration per bed
 - 1481 ii. Bed overlap
 - 1482 iii. Acquisition mode (2D or 3D)
 - 1483 iv. Reconstruction method
 - 1484 b. CT technique
- 1485 3. Scanner specific QA/QC
 - 1486 a. Most recent calibration factors (scanner)
 - 1487 b. Scanner daily check values
 - 1488 c. most recent clock check
 - 1489 d. most recent scanner QA/QC
- 1490 4. Subject exam specific
 - 1491 a. Height
 - 1492 b. Weight
 - 1493 c. Fasting time assessment
 - 1494 d. Blood glucose concentration and time of sampling
 - 1495 e. Pre- and post-injection assayed activities and times of assay

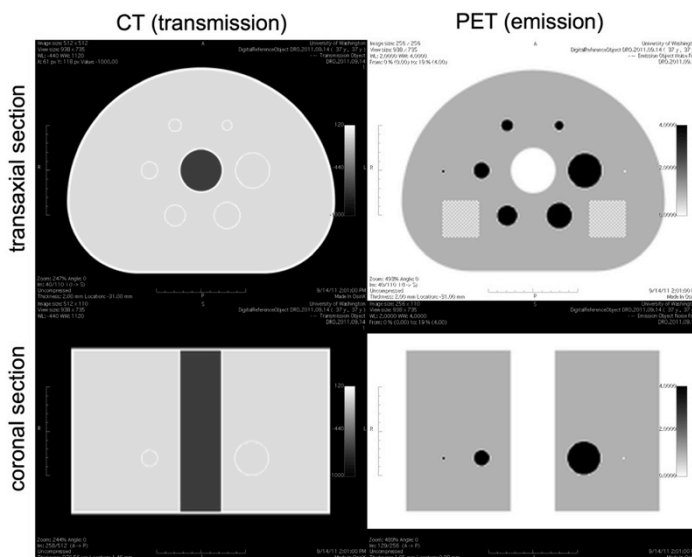
- 1496 f. Injection time
- 1497 g. Site of injection (and assessment of infiltration)
- 1498 h. Net injected activity (calculated including decay correction)
- 1499 i. Uptake time

1500 **Appendix F: Testing PET/CT Display and Analysis Systems with the FDG-PET/CT**
 1501 **Digital Reference Object**

1502 The PET/CT Digital Reference Object (DRO) is a synthetically generated set of DICOM image files of known
 1503 voxel values for positron emission tomography (PET) and x-ray computed tomography (CT). The PET/CT
 1504 DRO is intended to test the computation of standardized uptake values (SUVs) by PET/CT display stations. It
 1505 is also intended to test region of interest (ROI) calculations and alignment between the PET and CT images.
 1506 This is motivated by vendor-specific variations in PET DICOM formats used for SUVs. The development of
 1507 the PET/CT DRO is supported by the Quantitative Imaging Biomarker Alliance (QIBA).

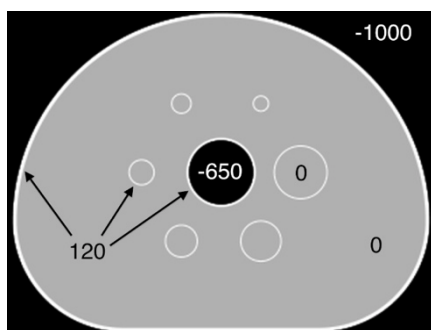
1508 The primary goals and objectives of the PET/CT Digital Reference Object are to support the QIBA FDG-PET
 1509 'Technical Validation' efforts for Profile development. This will be done by (1) evaluation and validation of
 1510 SUV calculations in PET images, (2) evaluation and validation of ROI calculations and (3) providing a
 1511 common reference standard that can be adopted and modified by PET/CT scanner and display station
 1512 manufacturers.

The PET and CT components of the Images of the DRO are each a set of DICOM format files, one file per image slice. Each set of files are typically grouped as a stack to form an image volume. Representative sections through the CT and PET image volumes are shown below.

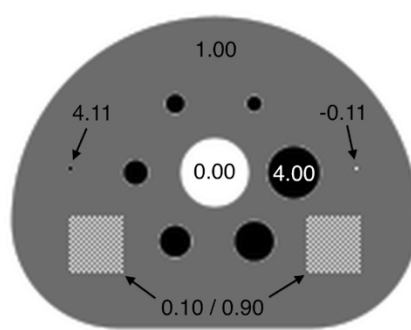


The synthetic test object is based on, but is not identical to, the NEMA NU-2 PET test phantom [J Nucl Med, vol. 43 no. 10 1398-1409, 2002]. The PET object has added 'test voxels' together with 2D and 3D 'test patterns'. In each object, the thickness of the exterior shell is 3 mm, the thickness of the hot sphere walls is 1 mm, and the thickness of the lung insert wall is 2mm.

1513
1514



The CT DRO showing Hounsfield



The PET DRO with the SUVbw

Units for each structure.

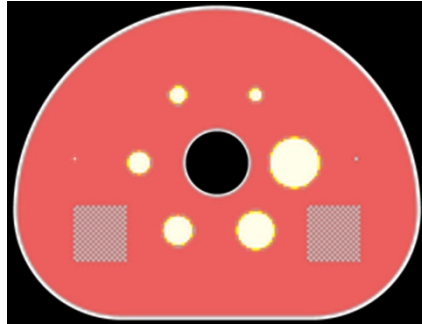
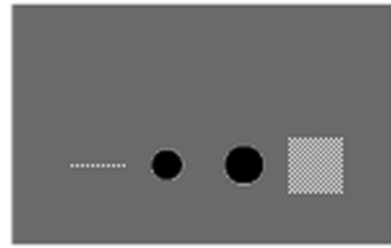


Image fusion of the CT and PET DROs showing perfect alignment

values of each structure.



Coronal view of the PET DRO showing the 2D test pattern in slice 40 (left) as well as the 3D cubic test pattern (right)

1515

1516

Structure of the CT and PET DROs.

1517

The CT Object

1518

The CT object is $512 \times 512 \times 110$ voxels, and is stored in 110 DICOM files named 000001.dcm through 000110.dcm , numerically ordered so that 000001.dcm corresponds to slice 1 in the image volume.

1520

The CT object has a reconstruction diameter of 500 millimeters and an axial extent of 220 millimeters, resulting in a voxel size of $500/512 \times 500/512 \times 2$ ($0.9765625 \times 0.9765625 \times 2.0$) millimeters³.

1522

The interior of the phantom body and the interiors of the hot spheres have voxels with values of 0 Hounsfield Units (HU), simulating water in the body and the interior of the hot spheres. The shell of the body, lung insert wall, and hot sphere walls have voxels set to 120 HU, simulating polymethylmethacrylate. The voxels interior to the lung insert are set to -650 HU, simulating lung attenuation material. The voxels exterior of the phantom body are set to -1000 HU, simulating air. These values are indicated in the above figure. NOTE: Partial volume effects will alter the voxel values near the borders of different regions.

1528

1529

The PET Object

1530

The PET object consists of a $256 \times 256 \times 110$ voxel image volume stored in 110 DICOM files named 000001.dcm through 000110.dcm, similar to the CT object described above.

1532

The PET object has a reconstruction diameter of 500 millimeters and an axial extent of 220 millimeters, resulting in a voxel size of $500/256 \times 500/256 \times 2$ ($1.953125 \times 1.953125 \times 2.0$) millimeters³.

1534

The voxels interior to the phantom body are set to an SUV value of 1.00. The voxels interior to the six hot spheres are set to an SUVbw value of 4.00. The voxels corresponding to the polymethylmethacrylate shell and the exterior of the phantom body and interior to the lung insert are set to an SUVbw value of 0.00. NOTE: Partial volume effects will alter the voxel values near the borders of different regions.

1538

There are two test voxels in slice 40 of the DRO. The test voxel furthest from the largest hot sphere in slice 40 is set to an SUVbw value of 4.11. The test voxel closest to the largest hot sphere in slice 40 is set to an SUVbw value of -0.11. NOTE: There is no polymethylmethacrylate shell surrounding the test voxels in the PET object, and no partial volume effects surrounding the test voxels. An SUV less than zero is possible when using PET image reconstruction methods such as analytic filtered back projection.

1540

1541

1542

1543 There are two test patterns in the PET DRO, a square (2D) checkerboard pattern in slice 40, and a cubic (3D)
1544 checkerboard pattern centered in slice 40. The 3D cubic test pattern appears closest to the largest hot
1545 sphere in an axial view of slice 40.

1546 Each test pattern consists of a checkerboard of voxels with alternating SUVbw values of 0.10 and 0.90 Both
1547 the 2D square and 3D cubic test patterns have edge measurements of 40 mm. The SUVbw values of each
1548 region of the PET DRO are shown in the above figure.

1549 Users of the DRO are asked to download the package, import the PET and CT objects into their viewing
1550 software, perform region of interest (ROI) analyses, and submit the results back to this website.

1551

1552 **Procedure**

1553 Users of the Digital Reference Object are requested to:

- 1554 1. Download the DRO (or import from CD) and the user report form.
- 1555 2. Verify the DRO files are present.
- 1556 3. Import the DRO into the viewing software.
- 1557 4. Perform ROI analysis of the DRO.
- 1558 5. Submit the completed report and store a copy locally.

1559

Digital Reference Object Analysis Sheet - Version 10/31/2011

You may record your answers directly on this form or by filling out the accompanying Excel spreadsheet. The numbers on each line indicate the corresponding rows and columns of the Excel spreadsheet.

1 Basic Information

Fill out the basic information for the test. Include a brief description of the workstation and its hardware, the software being tested, and the makes and models of the primary scanners that supply the images viewed on the workstation used for this test.

ROW	Item	Value
6	Name of Institution	
7	Name of person testing software	
8	Email or Phone contact	
9	Date of test	
10	Workstation used for test (Serial #)	
11	Description of hardware (Hardware Version)	
12	Make and model of monitor	
13	Software Manufacturer	
14	Name of software being tested	
15	Version of software	
16	Makes and models of primary scanners	

Load the DRO into your viewing software. Using an axial view, advance to **slice 40**, which contains the two test voxels and both test patterns as shown in Figure 1. Record the type of SUV that you are measuring (or 'Unknown') and the number of decimal places that the software reports for the SUV value. Record the type of ROI that your software uses (2D or 3D). Record the ROI measurement units and indicate if it is a diameter, an area, a volume, etc..

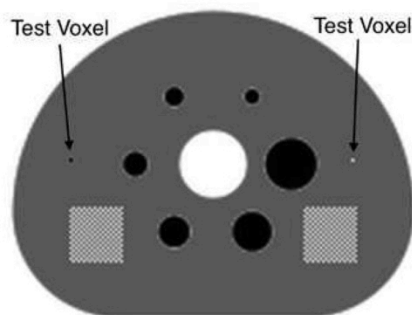


Figure 1: You should see both the hot and cold test voxels and the two square test patterns in slice 40.

ROW	Item	Value
20	SUV Type (BW, LBM, BSA)	
21	Number of decimal places	
22	ROI Type (2D, 3D)	
23	Recording ROI Area or Diameter?	

2 ROI Analysis of the DRO

For each of the following six ROIs (shown in Figure 2), record the maximum, minimum, mean, standard deviation for the voxel SUV values. Also record either the diameter or area of each ROI (if recording area, record the volume for ROI 6).

- (1) Draw a circular ROI with an area of 490 mm² (diameter=25 mm), concentric with the smallest hot sphere.
- (2) Draw a circular ROI with an area of 490 mm² (diameter 25 mm), concentric with largest hot sphere.
- (3) Draw a circular ROI with an area of 490 mm² (diameter 25 mm), concentric with the hot test voxel.
- (4) Draw a circular ROI with an area of 490 mm² (diameter 25 mm), concentric with the cold test voxel.
- (5) Draw a circular ROI with an area of 490 mm² (diameter 25 mm), centered within the single plane test pattern nearest the hot test voxel.
- (6) Draw a spherical (3D) ROI with a volume of 2,600 mm³ (diameter 25 mm), centered within the 3D block test pattern nearest the cold test voxel.

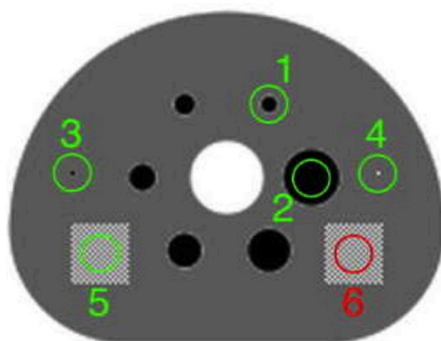


Figure 2: ROIs for the DRO analysis. The cross-section of the sphere in the 3D test pattern (on the right) is shown in red.

COL:		C	D	E	F	G
ROW	ROI	Max	Min	Mean	STD	Diam or Area
28	ROI 1					
29	ROI 2					
30	ROI 3					
31	ROI 4					
32	ROI 5					
33	ROI 6					

Appendix G: Vendor-neutral Pseudo-codes for SUV Calculation

G.1 Generic version

This appendix contains the consensus opinion on the generic form of SUV calculation from PET DICOM images. A generic pseudo-code is used with "///" signifying the beginning of a comment field to the end of the line. This version assumes the PET IOD is being used and not the Enhanced PET IOD: units are BQML, no private data elements required, series time is OK. Updated as of September 28, 2012. The most up to date version is maintained on the QIBA FDG-PET Wiki page (http://qibawiki.rsna.org/index.php?title=Standardized_Uptake_Value_SUV). Note that this is based on our most complete understanding at this time, but requires careful validation if implemented. In particular, it is strongly recommended not to use Series Date and Series Time for decay correction.

```
// SUV cannot be calculated if any of the specified DICOM attributes are missing or empty or zero
if Corrected Image (0x0028,0x0051) contains ATTN and DECAy and Decay Correction (0x0054,0x1102) is START {
    if Units (0x0054,0x1001) are BQML {
        half life = Radionuclide Half Life (0x0018,0x1075) in Radiopharmaceutical Information Sequence (0x0054,0x0016) // seconds
```



```

1580     if Series Date (0x0008,0x0021) and Time (0x0008,0x0031) are not after Acquisition Date (0x0008,0x0022) and Time (0x0008,0x0032) {
1581         scan Date and Time = Series Date and Time
1582         start Time = Radiopharmaceutical Start Time (0x0018,0x1072) in Radiopharmaceutical Information Sequence (0x0054,0x0016)
1583         // start Date is not explicit ... assume same as Series Date; but consider spanning midnight
1584         decay Time = scan Time – start Time      // seconds
1585         // Radionuclide Total Dose is NOT corrected for residual dose in syringe, which is ignored here ...
1586         injected Dose = Radionuclide Total Dose (0x0018,0x1074) in Radiopharmaceutical Information Sequence (0x0054,0x0016)// Bq
1587         decayed Dose = injected Dose * pow (2, -decay Time / half life)
1588         weight = Patient's Weight (0x0010,0x1030) // in kg
1589         SUVbwScaleFactor = (weight * 1000 / decayed Dose)
1590         // Rescale Intercept is required to be 0 for PET, but use it just in case
1591         // Rescale slope may vary per slice (GE), and cannot be assumed to be constant for the entire volume
1592         SUVbw = (stored pixel value in Pixel Data (0x7FE0,0x0010) + Rescale Intercept (0x0028,0x1052))* Rescale Slope (0x0028,0x1053)
1593         * SUVbwScaleFactor // g/ml
1594     }
1595 }
1596 }
1597

```

1598 G.2 Robust version

1599 This appendix contains the consensus opinion on the most robust form of SUV calculation from PET DICOM
1600 images. Updated as of September 28, 2012. The most up to date version is maintained on the QIBA FDG-
1601 PET Wiki page (http://qibawiki.rsna.org/index.php?title=Standardized_Uptake_Value_SUV). Note that this
1602 is based on our most complete understanding at this time, but requires careful validation if implemented.
1603 In particular, it is strongly recommended not to use Series Date and Series Time for decay correction.

```

1604
1605 // SUV cannot be calculated if any of the specified DICOM attributes are missing or empty or zero
1606 if Corrected Image (0x0028,0x0051) contains ATTN and DECAy and Decay Correction (0x0054,0x1102) is START {
1607     if Units (0x0054,0x1001) are BQML {
1608         half life = Radionuclide Half Life (0x0018,0x1075) in Radiopharmaceutical Information Sequence (0x0054,0x0016) // seconds
1609         if Series Date (0x0008,0x0021) and Time (0x0008,0x0031) are not after Acquisition Date (0x0008,0x0022) and Time (0x0008,0x0032) {
1610             scan Date and Time = Series Date and Time
1611         }
1612     } else { // may be post-processed series in which Series Date and Time are date of series creation unrelated to acquisition
1613         if GE private scan Date and Time (0x0009,0x100d,"GEMS_PETD_01") present {
1614             scan Date and Time = GE private scan Date and Time (0x0009,0x100d,"GEMS_PETD_01")
1615         }
1616     } else {
1617         // else may be Siemens series with altered Series Date and Time
1618         // either check earliest of all images in series (for all bed positions) (wrong for case of PETSyngo 3.x multi-injection)
1619         scan Date and Time = earliest Acquisition Date (0x0008,0x0022) and Time (0x0008,0x0032) in all images of series
1620         or
1621         // back compute from center (average count rate ) of time window for bed position (frame) in series (reliable in all
1622         cases)

```

```

1623 // Acquisition Date (0x0008,0x0022) and Time (0x0008,0x0032) are the start of the bed position (frame)
1624 // Frame Reference Time (0x0054,0x1300) is the offset (ms) from the scan Date and Time we want to the average
1625 count rate time
1626 if (Frame Reference Time (0x0054,0x1300) > 0 && Actual Frame Duration (0018,1242) > 0) {
1627     frame duration = Actual Frame Duration (0018,1242) / 1000 // DICOM is in ms; want seconds
1628     decay constant = ln(2) / half life
1629     decay during frame = decay constant * frame duration
1630     average count rate time within frame = 1/decay constant * ln(decay during frame / (1 - exp(-decay during
1631     frame)))
1632     scan Date and Time = Acquisition Date (0x0008,0x0022) and Time (0x0008,0x0032)
1633     - Frame Reference Time (0x0054,0x1300) /1000 + average count rate time within frame
1634 }
1635 }
1636 }
1637 start Time = Radiopharmaceutical Start Time (0x0018,0x1072) in Radiopharmaceutical Information Sequence (0x0054,0x0016)
1638 // start Date is not explicit ... assume same as Series Date; but consider spanning midnight
1639 decay Time = scan Time - start Time // seconds
1640 // Radionuclide Total Dose is NOT corrected for residual dose in syringe, which is ignored here ...
1641 injected Dose = Radionuclide Total Dose (0x0018,0x1074) in Radiopharmaceutical Information Sequence (0x0054,0x0016) // Bq
1642 decayed Dose = injected Dose * pow (2, -decay Time / half life)
1643 weight = Patient's Weight (0x0010,0x1030) // in kg
1644 SUVbwScaleFactor = (weight * 1000 / decayed Dose)
1645 }
1646 else if Units (0x0054,0x1001) are CNTS {
1647     SUVbwScaleFactor = Philips private scale factor (0x7053,0x1000, " Philips PET Private Group")
1648     // if (0x7053,0x1000) not present, but (0x7053,0x1009) is present, then (0x7053,0x1009) * Rescale Slope
1649     // scales pixels to Bq/ml, and proceed as if Units are BQML
1650 }
1651 else if Units (0x0054,0x1001) are GML {
1652     SUVbwScaleFactor = 1.0 // assumes that GML indicates SUVbw instead of SUVlbm
1653 }
1654 }
1655 // Rescale Intercept is required to be 0 for PET, but use it just in case
1656 // Rescale slope may vary per slice (GE), and cannot be assumed to be constant for the entire volume
1657 SUVbw = (stored pixel value in Pixel Data (0x7FE0,0x0010) + Rescale Intercept (0x0028,0x1052))* Rescale Slope (0x0028,0x1053) * SUVbwScaleFactor // g/ml
1658

```

1659 Appendix H: Consensus Formula for Computing Lean-Body-Mass Normalization 1660 for SUVs

1661 It is important that the PET community is consistent in its computation of SUV_{LBM} , particularly in light of the
1662 recent article by Wahl et al. (1) that proposes using SUV_{LBM} as part of the PERCIST criteria to monitor
1663 treatment response.

1664 Two different formulas for estimating male Lean Body Mass-normalized SUV (SUV_{LBM}) are currently being

1665 used in the PET community. The two variations of the formula for estimating LBM for males are as follows:

1666
$$\text{LBM(male)} = (1.10 \times \text{Weight}) - 128 \times (\text{Weight} / \text{Height})^2 \quad [1]$$

1667
$$\text{LBM(male)} = (1.10 \times \text{Weight}) - 120 \times (\text{Weight} / \text{Height})^2 \quad [2]$$

1668 Where the units for weight are kg, and the units for height are cm. Only one formula is being used for the
1669 calculation of female LBM (2,3):

1670
$$\text{LBM(female)} = (1.07 \times \text{Weight}) - 148 \times (\text{Weight} / \text{Height})^2 \quad [3]$$

1671 Both versions for estimating male lean body mass (equation 1 from Hallynck et al. (2) and equation 2 from
1672 Morgan and Bray (3)) are based on the original work of James (4), which in turn were derived from a fit of
1673 (weight/height²) to percentage body fat as measured by skin fold measurements. Equation 1 is the version
1674 widely used by the pharmacology community and can be considered the 'correct' version (5-7).

1675 The second version of the equation [2] can be traced back to an article by Morgan and Bray (3), in which
1676 the formula presented by Hallynck et al. (2) is likely misquoted, since the article (2) is referenced elsewhere
1677 in Morgan and Bray (3) without discussion of the difference in formulas where 120 was substituted for 128
1678 as a coefficient. The first incorporation of this formula for computing LBM into SUV calculations was
1679 described in Sugawara et al (8), which cites the Morgan and Bray paper (3). It is this version of the formula
1680 for males, with 120 as the coefficient, that has been sometimes quoted in the PET literature. Sugawara et al
1681 (8) used only data for female patients, which cites the formula for estimating female LBM by Morgan and
1682 Bray (3), which in turn matches the Hallynck et al. (2) paper.

1683 Although the impact of this difference in coefficient is relatively minor for patients with a normal body mass
1684 index (BMI (kg/m²) = (weight/height²), it does vary as a function of the patient's weight / height ratio. For
1685 example, for a patient of height 180 cm and weight 75 kg (BMI: 23) the value of SUV_{LBM} as computed by the
1686 two formula would differ by less than 1.5 % for regions with an SUV_{LBM} of ~1. However, for a male patient
1687 of the same height but weighing 150 kg (BMI: 46), the difference in SUV_{LBM} for the same regions would be
1688 ~7 %.

1689 In comparing equations [1] and [2], it is recommended that equation [1] be used in preference to equation
1690 [2]. However, although the James (2) is the most commonly used data source for equations estimating
1691 LBM, it is well known that it is incorrect for extreme BMI values (5-7). Janmahasatian et. al (5) have
1692 proposed alternative equations for LBM:

1693
$$\text{LBM(male)} \text{ (kg)} = (9270 \times \text{Weight}) / (6680 / (216 \times \text{BMI})) \quad [4]$$

1694
$$\text{LBM(female)} \text{ (kg)} = (9270 \times \text{Weight}) / (8780 / (244 \times \text{BMI})) \quad [5]$$

1695 These revised formulas for LBM have achieved some acceptance in the pharmacology community (6,7), and
1696 future versions of this Profile may recommend equations [4] and [5] instead of equations [1] and [3]. There
1697 are also continuing efforts to come up with more accurate methods for estimating LBM, through direct
1698 measurement on a per-patient basis using CT (9). However, the different methods providing estimates of
1699 LBM typically have unknown levels of bias and variance. Thus consistency and standardization are likely to
1700 yield larger improvements in study power for clinical trials, when compared to potential improvements in
1701 accuracy of LBM estimation.

1702 References

1703 1. Wahl, R., Heather, J., Kasamon, Y., Lodge, M. (2009) From RECIST to PERCIST: Evolving Considerations for
1704 PET Response Criteria in Solid Tumours. JNM 50(5); 122S-150S.

1705 2. Hallynck TH, Soep HH, Thomis JA, Boelaert J, Daneels R, Dettli L. (1981) Should clearance be normalized
1706 to body surface or lean body mass. Br J clin Pharmac 11: 523-526.

1707 3. Morgan, D., Bray K. (1994) Lean Body Mass as a predictor of drug dosage: Implications for Drug Therapy.
1708 Clinical Pharmacokinetics 26(4); 292-307.

1709 4. James, W. (1976) Research on Obesity. London. Her Majesty's Stationary Office.

1710 5. Janmahasatian S, Duffull SB, Ash S, Ward LC, Byrne NM, Green B. Quantification of lean bodyweight. Clin
1711 Pharmacokinet 44(10):1051-1065, 2005. PMID: 16176118.

1712 6. Han PY, Duffull SB, Kirkpatrick CM, Green B. Dosing in obesity: a simple solution to a big problem. Clin
1713 Pharmacol Ther 82(5):505-508, 2007. PMID: 17952107.

1714 7. Hanley MJ, Abernethy DR, Greenblatt DJ. Effect of obesity on the pharmacokinetics of drugs in humans.
1715 Clin Pharmacokinet 49(2):71-87, 2010. PMID: 20067334.

1716 8. Sugawara, Y., Zasadny, K., Neuhoff, A., Wahl, R. (1999) Reevaluation of the SUV for FDG: Variations with
1717 body weight and methods for correction. Radiology 213; 521-525.

1718 9. Chan T. Computerized method for automatic evaluation of lean body mass from PET/CT: comparison
1719 with predictive equations. J Nucl Med 53(1):130-137, 2012. PMID: 22128325.

1720

1721 **Appendix I: QIBA FDG PET/CT Imaging Site and Scanner Checklists**

1722

1723 **QIBA FDG PET/CT Imaging Site**

1724 The following checklist may be used to ascertain a PET imaging site's qualification for quantitative imaging
1725 according to the QIBA FDG PET/CT profile. Answers may be provided either as "current practice" or as
1726 "feasible", depending on the context, but it should be made clear both which was expected and how the
1727 site answered.

1728

<i>Site and Personnel Qualifications</i>		
1.	The site is accredited (ACR, IAC, TJC, etc.) or has Qualified status for clinical trials (ECOG-ACRIN, SNMMI-CTN, EARL, CROs, etc.)	__ yes __no
2.	The site has the support of technologists, physicists, and physicians experienced in the use of FDG-PET/CT, and meeting the qualifications described below.	__ yes __no
3.	Technologists: PET studies are performed by technologists whose certification is equivalent to the recommendations published by the representatives from the Society of Nuclear Medicine Technologists Section (SNMTS) or the American Society of Radiologic Technologists (ASRT) and should also meet all local, regional, and national regulatory requirements for the administration of ionizing radiation to patients.	__ yes __no

4.	Physicists: The medical physicist is 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.	__ yes __no
5.	Physicians overseeing and interpreting PET/CT scans are qualified by the ABR (Diagnostic and/or Nuclear Radiology) or American Board of Nuclear Medicine (ABNM) or equivalent within the United States or an equivalent entity appropriate for the geographic location in which the imaging study(ies) will be performed and/or interpreted.	__ yes __no
Imaging Procedures		
6.	Patient height and weight are entered into scanner during PET/CT acquisition.	__ yes __no
7.	Blood glucose is measured for each patient within 2 hours preceding FDG administration. Measured value and measurement time are documented.	__ yes __no
8.	If and when glucose threshold is exceeded, the reason shall be documented.	__ yes __no
9.	For each patient, the pre-injection FDG activity is measured and injected and residual activity is measured. Initial and residual measurement times and injection time are entered into the console.	__ yes __no
10.	FDG is administered through a 24-gauge or larger indwelling catheter placed anatomically remote to any sites of suspected pathology, preferably in an antecubital vein. Intravenous ports should not be used, unless no other venous access is available. In the case of manual administration, a three-way valve system should be attached to the intravenous cannula so as to allow at least a 10 cc normal (0.9% NaCl) saline flush following FDG injection. For automated injection devices alternate flushing mechanisms are allowed.	__ yes __no
11.	For follow-up scans, patients are imaged with the same workflow (i.e. patient handling, imaging acquisition, image processing, and image analysis) as for baseline scans.	__ yes __no
12.	The FDG uptake time (from injection to scan) is 60 minutes, with an acceptable range of 55-75 minutes. When repeating a scan on the same subject, uptake time for the 2 nd scan is within 10 minutes of that for the first scan.	__ yes __no
13.	If the patient is observed to take a deep breath during the CT scan it is documented and a repeat CT study is considered.	__ yes __no
14.	When a patient is rescanned, the same scan direction is used.	__ yes __no
15.	Reconstructed PET images, with and without attenuation correction, and CT images are archived at the imaging site.	__ yes __no
QA/QC		

16.	The site performs all PET/CT scanner QA/QC procedures recommended by the manufacturer and at the recommended frequency (e.g., daily, weekly, quarterly) and assures that the output values are acceptable.	__ yes __no
17.	Daily QA procedures are performed prior to any subject scan.	__ yes __no
18.	A water or water-equivalent phantom is scanned and evaluated daily and acceptable output is ensured.	__ yes __no
19.	Dose calibrator constancy is evaluated daily on the F-18 setting. Day-to-day differences no greater than 2.5% are allowed. Cs-137, Co-57, or simulated F-18 may be used.	__ yes __no
20.	The dose calibrator accuracy is evaluated monthly with measured values differing no more than 2.5% from the actual source value. Cs-137, Co-57, or simulated F-18 may be used.	__ yes __no
21.	Dose calibrator linearity is assessed at least annually over a range of 37-1110 MBq, with deviation of no more than 2.5% over the entire range.	__ yes __no
22.	Scales for patient weight measurement are evaluated annually or after any repair by qualified personnel, with error no more than 2.5% from expected values using a NIST-traceable or equivalent standard.	__ yes __no
23.	The glucose measuring device is measured and tested according to a CLIA-approved, CLIA-cleared, or equivalent (if outside the United State) procedure.	__ yes __no
24.	The PET/CT scanner computer and all clocks in the imaging facility used to record activity/injection measurements are synchronized to standard time reference within +/-1 minute. Synchronization of all clocks used in the conduct of the FDG-PET/CT study is checked weekly and after power outages or civil changes for Daylight Savings (North America) or Summer Time (Europe).	__ yes __no
25.	Quantitative Calibration Accuracy: PET scanner quantitative accuracy relative to the dose calibrator is verified quarterly and after scanner upgrades, maintenance or repairs, new setups and modifications to the dose calibrator via a uniform phantom scan of activity measured in the dose calibrator, achieving a large central ROI mean SUV value of 1.0 (acceptable range 0.9-1.1).	__ yes __no
26.	Axial Uniformity: Using a uniform cylinder phantom or equivalent shall obtain a slice-to-slice variability of less than 10% for the slices within the central 80% of the axial FOV.	__ yes __no
27.	PET Resolution: Cold rods (as in the Jaszczak or ACR PET phantoms) of diameter 9.5 mm or smaller must be visible. A hot cylinder (as in the ACR PET phantom) of 12 mm or smaller must be visible OR the 13 mm sphere of the NEMA image quality phantom must be visible.	__ yes __no
28.	PET noise: In a uniform phantom of 0.1 to 0.2 μ Ci/ml F-18 concentration the coefficient of variation of voxel values within a rectangular or circular region of at least 3 cm (side or diameter) must be no greater than 15% for all slices within the central 80% of the axial FOV.	__ yes __no
<i>Specific Personnel Responsibilities</i>		

29.	A technologist or physicist assesses uniformity (within-plane and across slices) and compares with previous results. Quarterly and following software upgrades.	__ yes __no
30.	A technologist or physicist shall perform the Quantitative Calibration Accuracy test. Quarterly and following software upgrades or changes to the dose calibrator	__ yes __no
31.	A physicist shall perform and document performance of a quantitative assessment (using a phantom with differing size defined targets such as the ACR or NEMA IQ phantoms processed with routine image reconstruction protocols) for lesion resolution. Annually.	__ yes __no
32.	A physicist Shall perform a quantitative assessment of image noise in phantom images to be of consistent and acceptable quality. Annually.	__ yes __no

1729

1730

1731 QIBA FDG PET/CT Scanner Checklist

1732 The following questionnaire/checklist may be used to ascertain a PET scanner's qualification for
 1733 quantitative imaging according to the QIBA FDG PET/CT Profile.

1734

	Parameter	Specification	Pass?
1.	Calibration factors	All necessary calibration factors needed to output PET images in units of Bq/ml shall be automatically applied during the image reconstruction process.	
2.	PET Scanner calibration	Shall be able to be calibrated according to the following specifications: Using a uniform cylinder containing F-18 in water solution (ideally using the same solution 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).	
3.	Weight	Shall be able to record patient weight in lb 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.	
4.	Height	Shall be able to record patient height in feet/inches or cm/m as supplied from the modality worklist or operator entry into scanner interface. Shall be stored in Patient Size field (0010,1020) in the DICOM image header, as per DICOM standard.	
5.	Administered Radionuclide	Shall be able to enter the radionuclide type (i.e. F-18) by operator entry into the scanner interface and through predefined protocol. Shall be recorded in Radionuclide Code Sequence (0054,0300) in the DICOM image header [e.g. (C-111A1, SRT, " ¹⁸ Fluorine")].	
6.	Administered Radiotracer	Shall be able to record the radiotracer (i.e. FDG), as supplied by operator entry into the scanner interface. Shall be recorded in Radionuclide Code Sequence field (0054,0300) in the DICOM image header, e.g. (C-B1031, SRT, "Fluorodeoxyglucose F ¹⁸ ").	
7.	Administered Radiotracer radioactivity	Shall be able to enter the administered radioactivity, in both MBq and mCi, as supplied by operator entry into the scanner interface. Shall be recorded in Radionuclide Total Dose field (0018,1074) in the DICOM image header in Bq.	
8.	Administered	Shall be able to record the time of the start of activity injection as supplied by	

	Radiotracer Time	operator entry into the scanner interface. Shall be recorded in Radiopharmaceutical Start Date Time field (0018,1078) (preferred) or Radiopharmaceutical Start Time field (0018,1072).	
9.	Decay Correction Methodology	Encoded voxel values with Rescale Slope field (0028,1053) applied shall be decay-corrected by the scanner software (not the operator) to a single reference time (regardless of bed position), which is the start time of the first acquisition, which shall be encoded in the Series Time field (0008,0031) for original images. Corrected Image field (0028,0051) shall include the value "DECY" and Decay Correction field (0054,1102) shall be "START", which means that the images are decay-corrected to the earliest Acquisition Time (0008, 0032).	
10.	Scanning Workflow	Shall be able to support Profile Protocol (Section 3) PET and CT order(s) of acquisition. Shall be able to pre-define and save (by imaging site) a Profile acquisition Protocol for patient acquisition.	
11.	CT Acquisition Parameters	Shall record all key acquisition parameters (technique) in the CT image header, using standard DICOM fields.	
12.	PET-CT Alignment	Shall be able to align PET and CT images within ± 2 mm in any direction.	
13.	Activity Concentration in the Reconstructed Images	Shall be able to store and record (rescaled) image data in units of Bq/ml and use a value of BQML for Units field (0054,1001).	
14.	Tracer Uptake Time	Shall be derivable from the difference between the Radiopharmaceutical Date Time field (0018,1078) (preferred) or Radiopharmaceutical Start Time field (0018,1072) and the Series Time field (0008,0031) or earliest Acquisition Time field (0008,0032) in the series (i.e., the start of acquisition at the first bed position), which should be reported as Series Time field (0008,0031).	
15.	PET Voxel size	See Section 4.3 (PET Voxel size) under the Reconstruction Software specification requirements.	
16.	CT Voxel size	Shall be no greater than the reconstructed PET voxel size. Voxels shall be square in transaxial dimensions, although are not required to be isotropic in the Z (head-foot) axis. Not required to be the same as the reconstructed PET voxel size.	
17.	Subject Positioning	Shall be able to record the subject position in the Patient Orientation Code Sequence field (0054,0410) (whether prone or supine) and Patient Gantry Relationship Code field Sequence (0054,0414) (whether head or feet first).	
18.	DICOM Conformance	All image data and scan parameters shall be transferable using appropriate DICOM fields according to the DICOM conformance statement for the PET/CT scanner.	
19.	DICOM Data transfer and storage format	PET images shall be encoded in the DICOM PET or Enhanced PET Image Storage SOP Class, using activity-concentration units (Bq/ml) with additional parameters stored in public DICOM fields to enable calculation of SUVs. PET images shall be transferred and stored without any form of lossy	

		compression.	
20.	Metadata	Shall be able to accurately propagate the information collected at the prior stages and extend it with those items noted in the Reconstruction section.	
21.	Data Corrections	PET emission data must be able to be corrected for geometrical response and detector efficiency, system dead-time, random coincidences, scatter and attenuation.	
22.	Reconstruction Methodology	Shall be able to provide images without resolution recovery.	
23.	Reconstruction Methodology / Output	Shall be able to perform reconstructions with and without attenuation correction.	
24.	Data Reconstruction 2D/3D Compatibility	Shall be able to perform reconstruction of data acquired in 3D mode using fully 3D image reconstruction algorithms. Shall be able to perform reconstruction of data acquired in 2D mode using 2D image reconstruction algorithms.	
25.	Quantitative calibration	Shall apply appropriate quantitative calibration factors such that all images have units of activity concentration, e.g. kBq/mL.	
26.	Multi-bed data	Shall combine data from multiple over-lapping bed positions (including appropriate decay corrections) so as to produce a single three-dimensional image volume.	
27.	Voxel size	Shall allow the user to define the image voxel size by adjusting the matrix dimensions and/or diameter of the reconstruction field-of-view. Shall be able to reconstruct PET voxels with a size 4 mm or less in all three dimensions (as recorded in Voxel Spacing field (0028,0030) and computed from the reconstruction interval between Image Position (Patient) (0020,0032) values of successive slices). Voxels shall be square in transaxial dimensions, although voxels are not required to be isotropic in the z (head-foot) axis.	
28.	Reconstruction parameters	Shall allow the user to control image noise and spatial resolution by adjusting reconstruction parameters, e.g. number of iterations, post-reconstruction filters.	
29.	Reconstruction protocols	Shall allow a set of reconstruction parameters to be saved and automatically applied (without manual intervention) to future studies as needed.	

1735