

PET/CT Digital Reference Object

Larry Pierce¹, Brian Elston¹, Dennis Nelson², David Clunie³, Paul Kinahan¹

¹ University of Washington - Department of Radiology

² MIM Software

³ CoreLab Partners

Version 05/29/2013
(Updated June 2019)

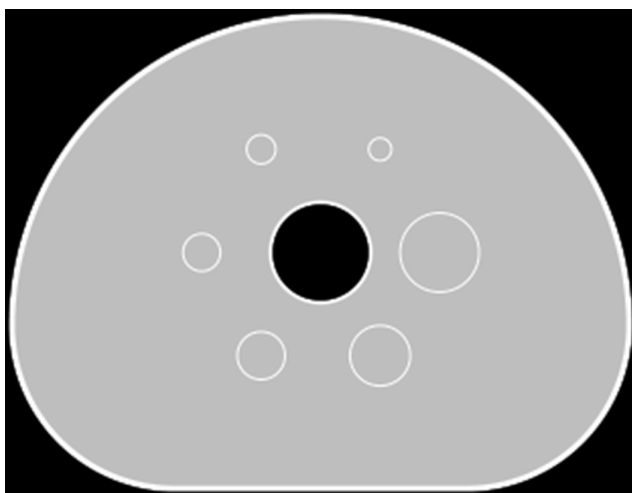
1 Project Description

The PET/CT Digital Reference Object (DRO) is a QIBA and RSNA sponsored artificially generated set of PET and CT DICOM files (a DICOM stack) of known voxel values and DICOM fields. The DRO is intended to check SUV computation fidelity and region of interest (ROI) analysis performance. This is motivated by the vendor-specific variations in the standardized uptake value (SUV) calculations as illustrated in Figure 2.

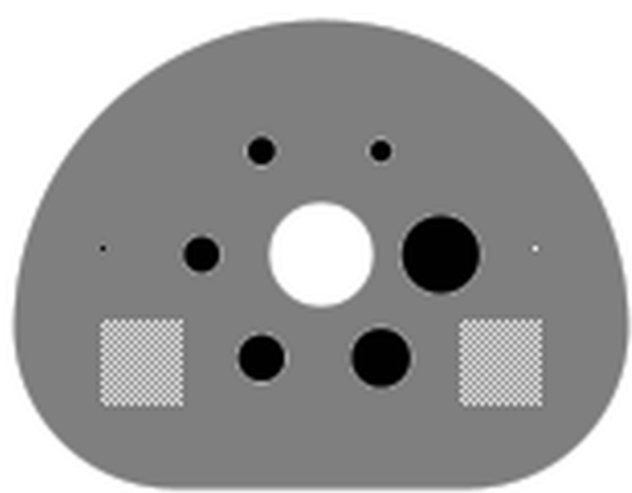
Two versions of the DRO are included in the current package, one “Male” (May 28, 2013 ; version number 20130528) and one “Female” (May 29, 2013 ; version number 20130529). This document will refer to the “Female” DRO except in Section 3.2.1, which describes the calculation of lean body mass.

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

Users of the DRO are asked to download the package, import the PET and CT objects into their viewing software, perform several region of interest (ROI) analyses, and compare the results to the SUV tables in Section 2.3. Additionally,



(a) Slice 40 of the CT DRO



(b) Slice 40 of the PET DRO

Figure 1: Slice 40 of the CT and PET DROs

users may wish to submit the results, as detailed in Section 2.2. Submitted results will be used for internal analysis only and will not be shared with anyone at any time.

Two DICOM stacks are provided in the 05/29/2013 (female) DRO package: a PET object and a CT object. Each image volume is modeled after the NEMA Image Quality (IQ) Phantom described in [1]. The PET object has added “test voxels” together with 2D and 3D “test patterns”. Axial and coronal views of the PET object are shown in Figure 3. Detailed descriptions of the CT and PET DROs are given in sections 3.1 and 3.2.

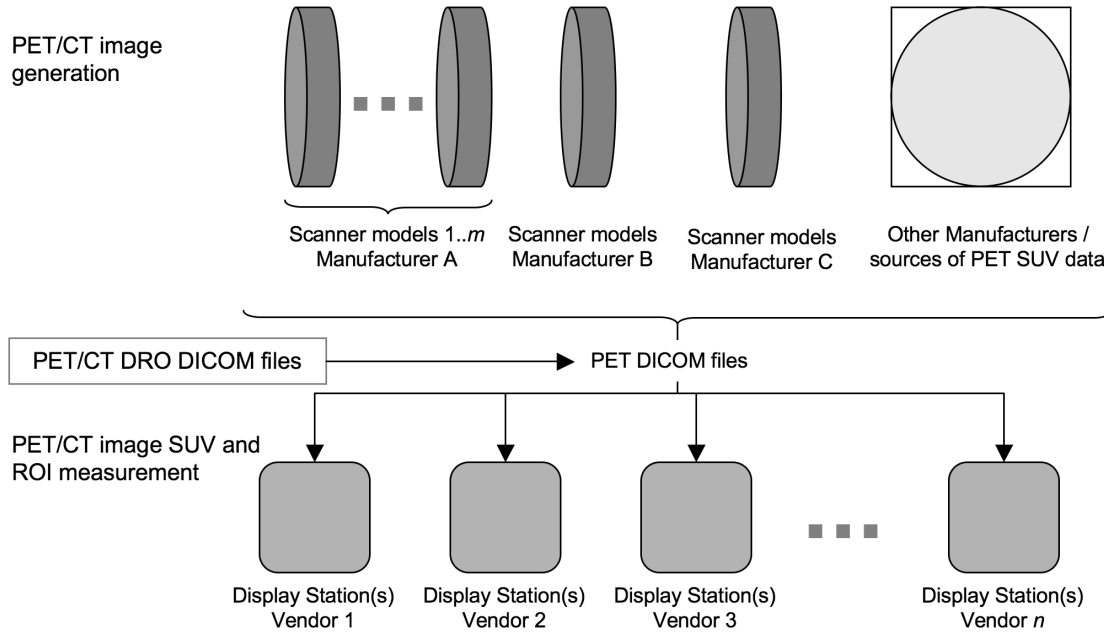


Figure 2: Flow of PET/CT DICOM image files in a heterogeneous manufacturer and vendor network. The insertion of digital reference objects (DROs) for testing validity of SUV and ROI analysis is also indicated.

2 Using the Digital Reference Object

Users of the Digital Reference Object are requested to:

1. Download the DRO (or import from CD) and the user report, as described in Section 2.1.1.
2. Verify the DRO files (Section 2.1.2).
3. Import the DRO into your viewing software (Section 2.1.3).
4. Perform ROI analysis of the DRO (Section 2.2).
5. Compare the results of the ROI analysis to the tables in Section 2.3.
6. (optional) Submit the completed report (Section 2.4).
7. (optional) Submit feedback on the DRO, the report, or general comments (Section 2.5).

2.1 Obtaining, Verifying, and Importing the DRO

2.1.1 Getting the 05/29/2013 DRO Package

The 05/29/2013 DRO package is named **DRO_20130529.zip** and can be downloaded from the DRO website:

<http://depts.washington.edu/petctdro/>

Alternatively, you can order a copy of the DRO on compact disk (CD) and have it mailed to you by sending an email request to the Imaging Research Laboratory at: petctdro@uw.edu

2.1.2 Verifying the DRO Package

1. Create a new folder and place the file **DRO_20130529.zip** in that folder.
2. Unzip the file **DRO_20130529.zip**
3. Verify that all files and directories are present:
 - A README file: **README.txt**
 - The User Report pdf: **DRO_REPORT.pdf**
 - The User Report MS Excel Spreadsheet: **DRO_REPORT.xls**
 - Two directories named **20130529_DRO_DICOM_female** and **20130528_DRO_DICOM_male** , each with two sub-directories:
 - (a) A directory named **DRO_CT_20130529** (**DRO_CT_20130528** for male) containing One Hundred Ten files numbered files named **000001** through **000110** (no file extensions)
 - (b) A directory named **DRO_PET_20130529** (**DRO_PET_20130528** for male) containing One Hundred Ten files numbered files named **000001** through **000110** (no file extensions)
 - The user guide (this document): **DRO_USER_GUIDE_20130529.pdf**
 - A presentation on the DRO given at the Society of Nuclear Medicine in 2012: **SNM2012_DROtalk.pdf**

2.1.3 Importing the DRO into your Software

1. Use your viewing software to import all DICOM files in the folder **DRO_CT_20130529**
2. Use your viewing software to import all DICOM files in the folder **DRO_PET_20130529**
3. Quickly scroll through the CT and PET DRO objects to verify that they have been properly imported.

2.2 Performing the ROI Analysis and Completing the Report

Open the DRO user report pdf: **DRO_REPORT_20130529.pdf** . Choose one of the following options to complete the DRO report:

1. Record your answers directly in the pdf document using annotations or a pdf editor.
2. Open the MS Excel file **DRO_REPORT_20130529.xls** and record your answers directly in the Excel spreadsheet. (Each line on the pdf document corresponds to a row on the MS Excel spreadsheet.)
3. Print the user report and write your answers on the printed report.

Follow the instructions in the report and record your answers. Save the completed report.

2.3 Acceptable SUV values for the ROI Analysis

For each of the female and male DRO, bounds for acceptable SUV measurements for each ROI are given in the tables below. Two sets of acceptance bounds are given: one for those software packages that report only one decimal place for ROI measurements, and a second set of bounds for software packages that report two or more decimal places for SUV measurements. Description of the bounds are given in Appendix E.

	ROI Max		ROI Min		ROI Mean		ROI STD	
	min	max	min	max	min	max	min	max
ROI 1	3.95	4.05	0.55	0.65	1.25	1.55	0.85	1.15
ROI 2	3.95	4.05	3.95	4.05	3.95	4.05	-0.05	0.05
ROI 3	4.05	4.15	0.95	1.05	0.95	1.05	0.15	0.35
ROI 4	0.95	1.05	-0.15	-0.05	0.95	1.05	0.05	0.15
ROI 5	0.85	0.95	0.05	0.15	0.45	0.55	0.35	0.45
ROI 6	0.85	0.95	0.05	0.15	0.45	0.55	0.35	0.45

Table 1: SUV Bounds for the 20190528 male DRO for software that reports one decimal place.

	ROI Max		ROI Min		ROI Mean		ROI STD	
	min	max	min	max	min	max	min	max
ROI 1	3.995	4.005	0.635	0.645	1.295	1.505	0.875	1.095
ROI 2	3.995	4.005	3.995	4.005	3.995	4.005	-0.005	0.005
ROI 3	4.105	4.115	0.995	1.005	1.015	1.035	0.235	0.325
ROI 4	0.995	1.005	-0.115	-0.105	0.985	0.995	0.085	0.115
ROI 5	0.895	0.905	0.095	0.105	0.465	0.535	0.395	0.405
ROI 6	0.895	0.905	0.095	0.105	0.475	0.525	0.395	0.405

Table 2: SUV Bounds for the 20190528 male DRO for software that reports two or more decimal places.

	ROI Max		ROI Min		ROI Mean		ROI STD	
	min	max	min	max	min	max	min	max
ROI 1	3.95	4.05	0.55	0.65	1.25	1.55	0.85	1.15
ROI 2	3.95	4.05	3.95	4.05	3.95	4.05	-0.05	0.05
ROI 3	4.05	4.15	0.95	1.05	0.95	1.05	0.15	0.35
ROI 4	0.95	1.05	-0.15	-0.05	0.95	1.05	0.05	0.15
ROI 5	0.85	0.95	0.05	0.15	0.45	0.55	0.35	0.45
ROI 6	0.85	0.95	0.05	0.15	0.45	0.55	0.35	0.45

Table 3: SUV Bounds for the 20190529 female DRO for software that reports one decimal place.

	ROI Max		ROI Min		ROI Mean		ROI STD	
	min	max	min	max	min	max	min	max
ROI 1	3.995	4.005	0.635	0.645	1.295	1.505	0.875	1.095
ROI 2	3.995	4.005	3.995	4.005	3.995	4.005	-0.005	0.005
ROI 3	4.105	4.115	0.995	1.005	1.015	1.035	0.235	0.325
ROI 4	0.995	1.005	-0.115	-0.105	0.985	0.995	0.085	0.115
ROI 5	0.895	0.905	0.095	0.105	0.465	0.535	0.395	0.405
ROI 6	0.895	0.905	0.095	0.105	0.475	0.525	0.395	0.405

Table 4: SUV Bounds for the 20190529 female DRO for software that reports two or more decimal places.

2.4 Submitting the Report

If you printed the report, scan the completed report to a .pdf file.

Email the completed pdf form or Excel spreadsheet and any screenshots to jkoudelik@rsna.org with subject: “Completed DRO Report”. Include your name and institution in the body of the email.

Contact the Imaging Research Laboratory at the University of Washington with any questions or comments at:

email: petctdro@uw.edu

Phone: 206-543-0517

Fax: 206-543-8356

2.5 User Feedback

A primary purpose of this project is to evaluate the display statistics of various hardware and software configurations used in medical imaging. It is known that these systems vary (often in a number of subtle ways), but to what extent, how, and what impact this could potentially have on patient care is not well understood in the field. As a result your feedback is critical to helping establish reference material describing the display characteristics of the equipment that your institution operates with. We hope this study will improve understanding of how patient information is presented to service providers such as yourself, and as such we greatly value your input and feedback.

3 Description of the CT and PET DROs

There are two DROs in the 05/29/2013 package: a CT object, and a PET object. Screenshots of these objects can be seen in Figure 3.

Each image volume is modeled after the NEMA Image Quality (IQ) Phantom [1], as described in ***NEMA Standards Publication NU 2-2006 ; Performance Measurements of Positron Emission Tomographs***. 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.

3.1 The CT Object

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

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.

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 Figure 3(a). **NOTE:** Partial volume effects will alter the voxel values near the borders of different regions.

3.2 The PET Object

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

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.

Each region in the object is assigned an activity concentration in a manner that allows for control of the computed SUV_{bw} values.

The voxels interior to the phantom body have an SUV_{bw} value of 1.00. The voxels interior to the six hot spheres have an SUV_{bw} value of 4.00. The voxels corresponding to the polymethylmethacrylate shell and the exterior of the phantom body and interior to the lung insert have an SUV_{bw} value of 0.00. **NOTE:** Voxel values at the borders of different regions represent weighted averages of those regions, and therefore may take on values other than 0.00, 1.00, or 4.00 (partial volume effects).

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 SUV_{bw} value of 4.11. The test voxel closest to the largest hot sphere in slice 40 is set to an SUV_{bw} 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.

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

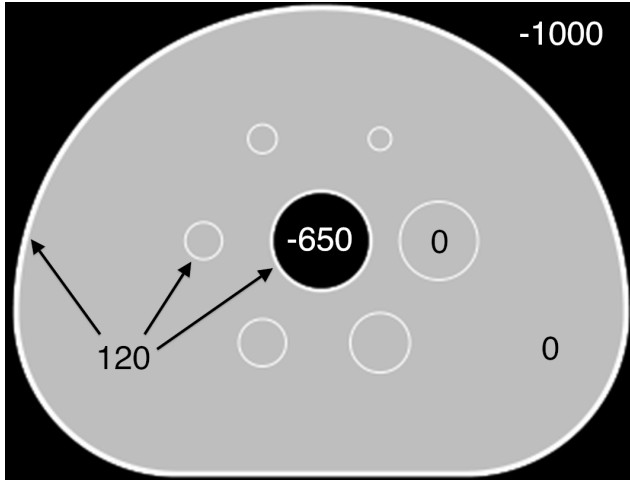
Each test pattern consists of a checkerboard of voxels with alternating SUV_{bw} values of 0.10 and 0.90. Both the 2D square and 3D cubic test patterns have edge measurements of 40 mm.

The SUV_{bw} values of each region of the PET DRO are shown in Figure 3(b).

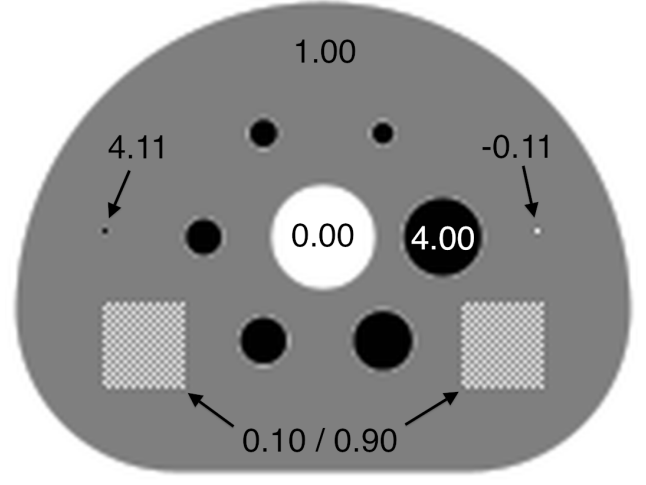
3.2.1 Lean Body Mass Calculations for the Male and Female DROs

The May 29, 2013 (20130529) Digital Reference Object is referenced as “Female” in the DICOM header, with a height of 1.665 meters and a weight of 59.94 kilograms. These values result in an lean body mass conversion factor of exactly 0.75 using the formula $SUV_{lbm} = SUV_{bw} \times \left[1.07 - 148 \left(\frac{w}{h^2}\right)\right]$ where w is the weight in kilograms and h is the height in centimeters. Thus, all SUV_{lbm} measurements are **exactly** 0.75 times the SUV_{bw} measurements.

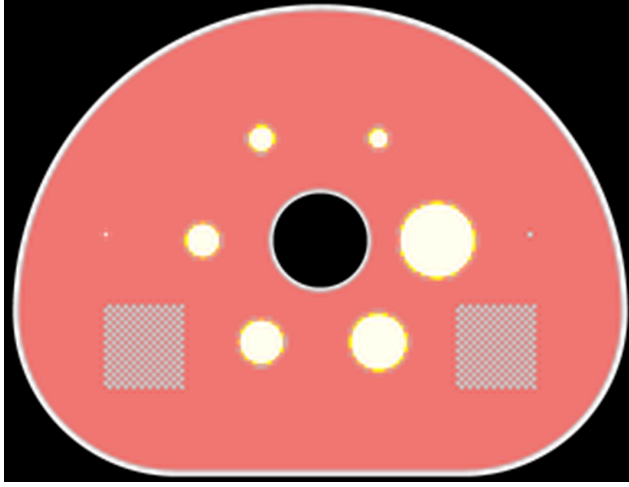
The May 28, 2013 (20130528) Digital Reference Object is referenced as “Male” in the DICOM header, with a height of 1.65 meters and a weight of 70 kilograms. These values result in an lean body mass conversion factor of approximately 0.77 using the formula $SUV_{lbm} = SUV_{bw} \times \left[1.10 - 128 \left(\frac{w}{h^2}\right)\right]$ where w is the weight in kilograms and h is the height in centimeters. Thus, all SUV_{lbm} measurements are **approximately** 0.7709 times the SUV_{bw} measurements.



(a) The CT DRO showing Hounsfield Units of each structure.



(b) The PET DRO with the SUV_{bw} values of each structure.



(c) Image fusion of the CT and PET DROs.



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

Figure 3: Views of the CT and PET DROs.

4 Acknowledgements

This work was supported by a grant from the RSNA Quantitative Imaging Biomarkers Alliance (QIBA).

References

- [1] Daube-Witherspoon ME et al., “PET Performance Measurements Using the NEMA NU 2-2001 Standard” *J Nucl Med* 2002 43:1398-1409
- [2] The NEMA DICOM standard: <http://medical.nema.org>
- [3] David Clunie’s DICOM FAQ: <http://www.dclunie.com/medical-image-faq/html/index.html>
- [4] Pseudocode for computing SUV_{bw} from QIBA: http://qibawiki.rsna.org/images/e/e8/SUV_vendorneutral_pseudocode_20091106_DAC.doc
- [5] Gronenschild, Ed *et al.* “The Effects of FreeSurfer Version, Workstation Type, and Macintosh Operating System Version on Anatomical Volume and Cortical Thickness Measurements” *PLOS One* 7(6): e38234. doi:10.1371/journal.pone.0038234
- [6] L Pierce, B Elston, D Clunie, D Nelson, P Kinahan “A Digital Reference Object to Analyze Calculation Accuracy of PET Standardized Uptake Value” *RSNA Radiology* Vol. 277 No. 2 (2015)

APPENDICES

A Version Identification and DICOM Field Assignment in the DRO

Each IRL-released version of the DRO is differentiated by inserting an official “Version Date” into the five DICOM fields:

StudyDate	(0008,0020)
SeriesDate	(0008,0021)
AcquisitionDate	(0008,0022)
Manufacturer	(0008,0070)
StudyDescription	(0008,1030)

The official version date of each DRO is given in the YYYYMMDD DICOM DateTime format. This is done to differentiate versions of the DRO while allowing multiple instances of each version (with different UID) for debugging purposes.

The version date is user-editable in the source code header files (see Section D) along with Patient Information and other fields. Users can change the version date format to fit their own identification purposes.

A.1 Released Versions of the DRO

20110914: The September 14, 2011 version of the DRO was released in October of 2011. It was found to have numerous errors in the DICOM fields, and was promptly removed from the website. An email notice was sent to inform users of the errors.

20111031: The October 31, 2011 version of the DRO was released in November of 2011 and is an update and correction to the 20110914 version. Alterations to the 20110914 version include:

1. Fixes made to incorrectly reported and repeated DICOM fields from the Sept. 14, 2011 version
2. New UID structure implemented
3. New DRO versioning structure implemented (see Section A)
4. New software versioning implemented
5. Implementation of a DRO verification checklist for DICOM validity and Quality Control (see Section B)

20121019(female) and 20121027(male): Addition of female object to test male and female lean body mass calculations. Added contact information and website information to image comments field of the DICOMs.

20130529(female) and 20130528(male): Supersedes the **20121019(female)** and **20121027(male)** previously released versions. Naming conventions were changed to make them easier to identify, and a correction to the height was made (the previous versions erroneously listed the height in centimeters).

B DRO Verification and Quality Control

Starting with the October 31, 2011 version of the DRO (20111031), a quality control checklist was implemented in order to ensure the validity and compatibility of the DRO. This checklist was signed off by Brian Elston, Larry Pierce, and Paul Kinahan and the records filed at the Imaging Research Laboratory.

This checklist includes:

1. Testing all DRO slices (each DICOM file) from the PET and CT objects using a bash script and the dicom3tools package provided by David Clunie (<http://www.dclunie.com/dicom3tools/dciodvfy.html>). Each of these PET and CT DICOM files is tested using:
 - (a) **dcentvfy**: To ensure entry-level attribute consistency.
 - (b) **dciodvfy**: To ensure that no errors are reported.
 - (c) **dctable**: Critical attributes (InstanceNumber, SliceLocation, ImagePositionPatient, SeriesTime, AcquisitionTime, FrameReferenceTime) are tabulated for manual review.

2. Several DICOM files are chosen from both the PET and CT objects and **andump** is used to manually review all DICOM fields and ensure that each field is accurate and that the length of each DICOM field matches the length of the intended value.
3. Visual checks of the DRO, including verification of the pixel values in various slices of the PET and CT objects. This includes testing of the test voxel and test pattern SUV values and scrolling through the PET and CT DRO in the axial, sagittal, and coronal dimensions.
4. Fusing the PET and CT objects and scrolling through the fused image in the axial, sagittal, and coronal dimensions in order to look for anomalies in the DRO and ensure proper image fusion.
5. Testing the DRO by performing the ROI analysis in Section 2.2 and verifying that the reported numbers are within the expected range.
6. Sending the DRO files to David Clunie for additional verification.

C How SUV_{bw} is Calculated

For a given voxel value measured in Becquerels per milliliter, the SUV_{bw} value for that voxel is defined as

$$SUV_{bw} = \frac{(\text{Bq/mL}) \times w \times 1,000}{\text{Decayed Dose}} \quad (1)$$

and Bq/mL is computed from the DICOM stored data by

$$(\text{Bq/mL}) = m \cdot d + b \quad (2)$$

where d is the stored voxel data (from DICOM field (7FE0,0010)), m is the rescale slope (DICOM field (0028,1053)), b is the rescale intercept (DICOM field (0028,1052)), and w is the patient's weight in kilograms (DICOM field (0010,1030)). The decay corrected dose given to the patient is computed as

$$\text{Decayed Dose} = (\text{Injected Dose}) \times 2^{-\text{Decay Time}/\text{Half Life}}$$

The Decay Time is computed as the difference in time from when the radiopharmaceutical was injected into the patient (DICOM field (0018,1072)) to when the scan began (DICOM field (0008,0031)). The radiopharmaceutical half life is measured in seconds and is stored in DICOM field (0018,1075). The injected dose is stored in DICOM field (0018,1074).

In an ideal setting, the software process flow would look like this:

1. Software retrieves the voxel data stored in DICOM stack
2. Software reads the DICOM fields needed to convert voxel data to SUV (rescale slope, patient weight, etc.)
3. Software converts stored voxel values into SUV values according to Equations 1 and 2 above
4. Software correctly displays the converted voxel values in SUV units on the screen
5. Software correctly computes and reports the max, min, mean, SD, and any other statistics for an ROI drawn on the image

Using the DRO gives known data for step one of this process.

For more information on DICOM fields and SUV calculations from DICOM fields, see:

- The NEMA DICOM standard: <http://medical.nema.org>
- David Clunie's DICOM FAQ: <http://www.dclunie.com/medical-image-faq/html/index.html>
- Pseudocode for computing SUV_{bw} from QIBA: http://qibawiki.rsna.org/images/e/e8/SUV_vendorneutral_pseudocode_20091106_DAC.doc

D Creation of the DRO

The size, position, and shapes (i.e. physical geometry) in the NEMA IQ phantom are saved as exact mathematical formulae, and are hard-coded in the DRO algorithm.

The parameters of the creation process are defined in three input files to the executable program. The Command Parameter File defines characteristics of the physical geometry and SUV_{bw} (PET) or Housefield Units (CT). A Header Input File specifies DICOM header field values for the generated voxel geometry, though a subset of these are image dependent (e.g. Rows, PixelSpacing, RescaleSlope, etc.) and thus are set in-code in the application. A read-only UID file contains a uniquely assigned DICOM UID prefix, and is used to assure the DRO has unique DICOM header fields where appropriate. The UID prefix is assigned from a sub-range that has been specifically allocated for your use, and thus is stored in a read-only file that should not be modified.

Both the PET and CT DROs are created using the same two-step process. The first step is to generate the voxel values for the image volume. Values for each object in the phantom are defined by the user (in the Command Parameter file). For example, the user can designate the Hounsfield Units of the polymethylmethacrylate shell of the CT DRO or the SUV_{bw} measure of the six hot spheres in the PET DRO.

In the PET object, the user can control the SUV_{bw} values for:

- The six spheres (all have the same activity)
- The background
- The body
- The center rod lung insert (usually set to zero)
- An optional single hot voxel
- An optional single cold voxel

In the CT DRO, the user can designate the Hounsfield Units of:

- The interior of the spheres (usually set to water)
- The polymethylmethacrylate shell (includes sphere and lung insert walls)
- The lung insert
- The body (usually set to water)

Similarly, the user can define other fields that will affect the DROs image, and also will be reflected in the DICOM header. These include (but are not limited to):

- Reconstruction Diameter
- Image size (x,y, and z) (can be different for PET and CT DROs)
- Slice Thickness
- Number of fine-division oversampling for calculating voxel values
- Optional test pattern, placement, and extent (single slice area and volume)

From these values the algorithm then sub-divides the image volume into the user-defined voxel size and slice thickness. Each image voxel is oversampled, and the algorithm numerically integrates the hard-coded formulae to determine the value for that voxel.

In the second step, after the voxel values have been calculated, the image information (voxel size, slice thickness, etc.) is combined with user defined header values (from the Header Input file) to compute and populate all of the necessary DICOM header fields for the PET and CT modalities.

The Header Input File is composed of a series of key-value pairings specifying DICOM key header tags to be assigned a designated value. DICOM tags are preceded with ‘**DCM_**’, which references a given (group, element) tag within the

DCMTK DICOM toolkit. A subset of these tags (eg. `DCM_MediaStorageSOPInstanceUID`, `DCM_StudyInstanceUID`, etc.) are dependent on timestamps, slice information, or other programatic information, and thus cannot be set by the user through the Header Input file. There are also image dependent fields that should not be set by the user (but they are allowed to), which generate a warning.

There is support for sequences (both single level and nested) using a simple parsing mechanism. Key-value pairings are allowed to have an empty value. Private tags can be specified directly through (group, element) designations with a specified value and type (which defaults to 'LO' if not specified).

In this version, only strictly necessary DICOM fields are populated, with a few exceptions, such as kVP in the transmission object.

DRO: Software process

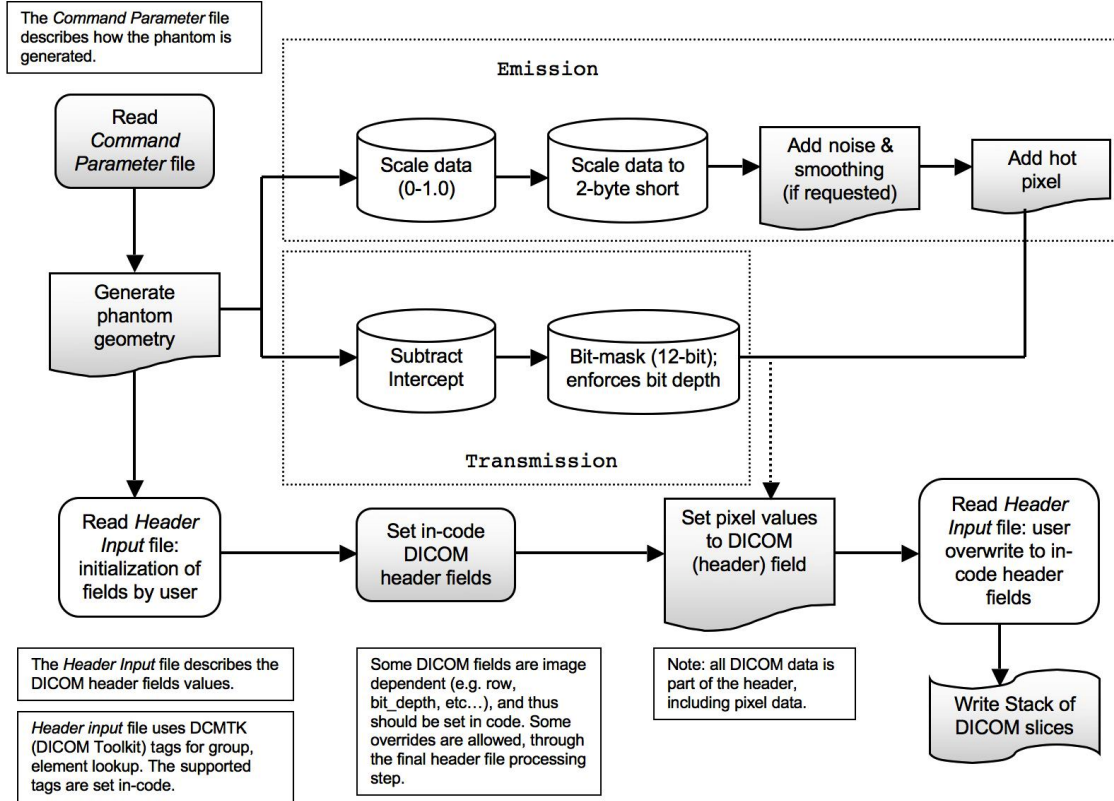


Figure 4: Workflow Diagram of the DRO creation process

E Determination of SUV Acceptance Bounds

To determine acceptable values for the SUV metrics performed for the DRO, each ROI test was performed using multiple ROI centers and diameters. This was done since it is unlikely that every software and user will create precisely the same ROIs for each DRO SUV test.

For each ROI and measurement, the ROI measurement was performed with the theoretically perfect ROI (exactly centered at sphere centers and test voxel centers, etc.). 2D ROIs (ROIs 1–5) were then perturbed by ± 3 mm in 0.5 mm increments in both the x - and y -directions (moving the ROI center on the square grid of 0.5 mm points). For each ROI center position, the diameter of the ROI was similarly perturbed by ± 3 mm. The 3D ROI (ROI 6) included an additional perturbation in the z -direction by ± 3 mm in 0.5 mm increments.

All ROI measurements were taken with all combinations of ROI center and diameter perturbations. This was done using whole-voxel inclusion (if the center of a voxel is in the theoretical ROI, then the entire voxel is considered to be

a part of the ROI). This was then repeated using partial-voxel inclusion using a $10 \times 10 \times 10$ up-sampling of each DRO voxel (and performing the center-inclusion method on sub-voxels as detailed above).

When ROI 2 has an oversized diameter and large deviation from the true center, as described above, the ROI will intersect the sphere wall. This leads to unrealistic measurements for ROI 2. Any ROI perturbation of ROI 2 that intersected the sphere wall was omitted.

For each ROI and measurement, the minimum and maximum ROI measurement was determined from the list of computed values. These values were then rounded to 1 decimal place. The lower bound of the acceptable SUV measurement values is computed as the rounded value minus 0.05. The upper bound of the acceptable SUV measurement values is computed as the rounded value plus 0.05.

For software that reports two or more decimal places for SUV measurements, the minimum and maximum values from the list of measurements were rounded to two decimal places and bounds were computed by ± 0.005 .