EARL procedure for assessing PET/CT system specific patient FDG activity preparations for quantitative FDG PET/CT studies.

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The EANM guideline for quantitative FDG PET and PET/CT studies, published in the January 2010 issue of the European Journal of Nuclear Medicine and Molecular Imaging (referred to as '2010 guideline' in the remainder of document), provides recommendations for FDG activity as a function of scanner type, acquisition mode, bed overlap, scan duration and patient weight. Equations as well as a table are given to allow users to determine the optimal dosage to be administered to the patient. This standardized activity is based on the acquisition mode, acquisition time per bed position, the weight of the patient and the amount of bed overlap. Using the guideline, the standardized FDG activity can be derived once the patient's weight is known and the scan duration per bed has been decided upon.

In the presently published 2010 guideline a provision was already made to account for improvements in scanner technology. Indeed, time of flight (ToF) is now available on more systems, high definition reconstruction techniques have been released and systems with extended axial fields of view (>18 cm) and thus higher sensitivities have become available. The guideline already indicates that in these cases other (lower) FDG activities may be given to the patient, but that the imaging site has to demonstrate that this does not result in loss of image quality or quantification. The 2010 guideline however, only defined an allowed range of SUV recovery coefficients which can be determined using the recommended quality control procedures for calibration and image quality/SUV recovery. In this document a more specific procedure is suggested to optimize and assess lower limits for FDG activity for new PET/CT systems that does not only consider recovery factors but also the signal to noise ratio.

FDG optimization procedure.

The calibration QC described in the present 2010 guideline should be followed as is. The main purpose of the calibration QC measurement is to verify a proper calibration between the PET/CT system and the dose calibrator that is used to measure the FDG activity that will be given to patients examined in that imaging center. Preferably, calibration factors should be independent from dosages and/or the reconstruction method applied. When this is not the case they should be determined separately for each setting used in clinical practice.

In the 2010 guideline, a procedure is given to assess image quality/SUV recovery based on the modified NEMA image quality phantom. After filling the phantom, an activity

concentration of about 2 kBq/ml is obtained in the large background compartment of the phantom and an activity concentration of about 20kBq/ml in the spheres at the intended time of the phantom scan. The 'background' activity concentration of 2kBq/ml can be expected for a 75kg patient who received a 300 MBq activity and is scanned at 1 hour p.i. (including some urine clearance of FDG). Scanning the same phantom (thus filling it once) several times at various intervals provides scans with lower activity concentrations in the phantom, thus mimicking lower FDG dosage. The purpose of the newly proposed procedure below is to assess to which level FDG activity can be reduced while keeping image quality and quantification accuracy within acceptable limits.

The proposed modified procedure is thus as follows:

- Prepare IQ phantom as indicated in the 2010 guideline and SOPs
- Start the first PET/CT study of the phantom when background activity concentration equals 2 kBq/ml (acceptable range 1.8-2.2) using an acquisition time per position of 10 min per bed. The start time of the first experiment will be referred to as the IQ-QC reference time or T0. Note that PET scanners have the highest sensitivity in the center of the axial field of view. For multi-bed i.e. whole-body studies, the overlapping bed positions exhibit a uniform sensitivity which only drops at the beginning and the end of the total scan. The calculations are to be performed in this uniform sensitivity region. Therefore, all the spheres of the phantom should be completely in the field of view for 2 consecutive bed positions. In case sites want to use shorter bed durations, than an additional 2 bed PET/CT study, as described above, should be performed using the minimally intended shorter bed duration, directly after the first experiment.
- Next, several additional experiments using exactly the same phantom will be performed every hour. Use the minimal scan duration (time per bed) as intended to be used in the clinic. At T0 the phantom represents a patient that has been administered with about 300 MBq and about every 1 hours after T0 the experiment resembles a patient scanned with about 66% of the activity. Thus at T0 the experiment resembles a patient study with 300MBq, at T0+1h this is 205 MBq, at To+2hr 140 MBq, at T0+3h 97 MBq and, finally, at T0+4h 66MBq. Additional delayed phantom studies may be collected in case FDG activities lower than 66 MBq for a 75 kg patient are intended or desired (in combination with the intended shorter acquisition time per bed!).
- After collection of all the phantom data, the first acquired dataset (thus at T0 and with 10 min emission scans per bed position) should be reconstructed and analyzed such that specifications for SUV recoveries as published on the EARL website are met. High count data are firstly used to optimize image reconstruction settings for harmonized image quantification. The 2010 guideline provides an exact description of the procedures and data analysis methods that need to be followed. Analysis software can be provided as research tool upon request.
- Subsequently, all other phantom studies/scans will be reconstructed using the same reconstruction method and settings as the ones applied above and that meet the EARL specifications for recovery coefficients (please see website for the new EARL specifications for recovery coefficients).

- Finally, all reconstructed image data will be analyzed as described in the 2010 guideline. SUV recoveries as a function of sphere size will be determined and compared with the specifications given in the guideline.
- Data collected at later time points will suffer from increased noise levels. This could be reflected in an upward bias of SUV recovery coefficients. Therefore, only those scans that provide SUV recovery coefficients that remain within the specified acceptable range (see 2010 guideline) represent an FDG activity in combination with the applied acquisition time per bed acceptable to be used for a 75kg patient.
- In addition to the recovery coefficient, the COV of voxel values within three 3 cm rectangular VOI's per plane, drawn in 3 axial image planes that visualize the six spheres (thus 9 rectangular ROI in total) and positioned in the uniform background compartment of the phantom, and within the section of uniform and maximum sensitivity profile of the performed whole body scan, should remain lower than 15 %. The COV, which is the standard deviation divided by the mean of the pixel values within the VOI, is first derived for every single rectangular VOI (n=9) and the final COV parameter is obtained by taking the average of these 9 COV values. The final average COV should remain below 15%.
- The phantom dataset, having the lowest activity concentration that still meets the above 2 criteria (unbiased SUV recoveries and COV < 15%) indicates the minimally allowable FDG activity to be used for a 75kg patient in combination with the minimally intended acquisition time per bed being applied during the phantom studies.
- During patient examination FDG activity should be adapted to patient weight using linear scaling, i.e. divide by 75 and multiply with the patient weight. Likewise, FDG activity may be adjusted when using different acquisition time per bed than those applied for the phantom study, using linear scaling*. A longer scan duration can still be proportionally adjusted with lower FDG activity per weight. However, in the new procedure only increases of the time per bed durations compared with the one tested are allowed.

* At present there is no sufficient published data to support deviation from linear scaling between activity, weight and time per bed. Although some preliminary (unpublished) reports suggest that FDG activity should be scaled with the squared patient weight, other reports suggest absence of any activity-weight relationship (Watson *et al.*, JNM 2005). Discrepancy may be caused by the activity ranges applied (Europe: ~185 MBq for 75 kg subjects, USA: ~370 MBq for 75 kg subjects). Consequently, despite the known limitations of linear scaling of weight, time per bed and FDG activity, the authors propose to still apply linear scaling as a first order approximation in order to minimize difference in image quality between subjects as a suboptimal, yet better alternative of not scaling at all.