MANUAL

EARL ACCREDITATION

VERSION 4.2

May 2023

This manual provides the background of the EARL Accreditation programs, detailed instructions of performing the necessary quality control tests and data submission process.

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REVISIONS

Date	Version	Description of changes
September 2010	1.0	Initial release
January 2015	1.1	Replaced reference to "FDG PET and PET/CT: EANM procedure guidelines for tumour PET imaging: version 1.0" with "FDG PET/CT: EANM procedure guideline for tumour PET imaging: version 2.0"
June 2020	2.0	EARL ^{18}F-FDG accreditation named EARL ^{18}F standards 1. Added EARL ^{18}F standards 2 accreditation and ^{89}Zr accreditation program. Removed the hard copy of the online questionnaire from the manual.
Oct 2020	2.1	Updates related to a new EARL database release for data submission and processing.
Jan 2021	3.0	Added EARL ^{68}Ga accreditation. Updated references to the upload with the new EARL accreditation database.
Feb 2021	3.1	Updated "EARL Research Ltd." to EANM Forschungs GmbH
Mar2021	3.2	Added section QC data limits of acceptability
May2021	3.3	Updated activity for calibration QC. Updated online box location on new web site. Updated url links for new web site.
Oct2021	4.0	Added automatic email reminder for the overdue QC on the 17th of the 2nd month of each quarter Removed phantom rental and shipping fee; referenced the web site for details on fees Updated abbreviation list Updated languages in the section for QC procedures Exchanged the word calibration with uniformity (phantom) Hoffmann 3D Brain phantom added ^{18}F/^{11}C Brain PET/CT accreditation ^{18}F PET/MRI accreditation
Jul2022	4.1	Added ^{89}Zr & ^{68}Ga for PET/MR Updated verbiage QC to data
May2023	4.2	^{89}Zr updated to be due once/year and upon software/hardware updates, dose calibrator updates/repair

ABBREVIATIONS

^{11}C	11-Carbon
^{18}F:	18-Fluoride
^{89}Zr:	89-Zirconium
AC-PET:	Attenuation corrected PET
BMI:	Body mass index
BSA:	Body surface area
BSREM:	Block sequential regularized expectation maximization
CT:	Computed tomography
FDG:	Fluorodeoxyglucose
FOV:	Field of view
^{68}Ga:	68-Gallium
GMWMr:	Grey matter to white matter ratio
LBM:	Lean body mass
MR:	Magnetic resonance
NAC-PET:	Non attenuation corrected PET
PET:	Positron emission tomography
QC:	Quality control
RCs:	Recovery coefficients
SOP:	Standard operating procedure
SRF:	Scan report form
SUV:	Standardised uptake value
SUVmax:	Maximum standardized uptake value
SUVmean:	Mean standardized uptake value
SUVpeak:	Peak[1] standardized uptake value

INTRODUCTION

Variability and reproducibility of standardized uptake value (SUV) and the factors affecting SUV as an imaging biomarker have been studied and documented[2,3]. EARL set up an accreditation program for ^{18}F-FDG-PET/CT imaging and launched it in July 2010. The aim was to help imaging sites meet the recommendations indicated in the EANM guideline, harmonize scanner performance, and minimize the effect of most of the technical factors affecting SUV variability. EARL accreditation enhances the quality standards of PET/CT investigations for daily clinical use and in multicenter clinical studies. The accreditation ensures similar performance of PET/CT systems within a multicenter setting by harmonizing the scans' quantification. Accreditation is given for a specific acquisition and reconstruction protocol on a designated PET/CT scanner and is valid only for the duration of continued data submission and re-validation by EARL. Quantitative values of SUVmean, SUVmax and in case of ^{18}F standards 2, SUVpeak from accredited scanners are comparable, exchangeable and PET/CT findings can be combined. The EARL ^{18}F-FDG-PET/CT accreditation program is endorsed by the European Organization for Research and Treatment of Cancer (EORTC) Imaging Group.

The EARL established performance specifications (EARL ^{18}F standards 1[4]) were recently updated to EARL ^{18}F standards 2[5]. EARL ^{18}F standards 2 allow sites to benefit from state-of-the-art PET/CT technology while still ensuring harmonized scanners performance. The quantitative results from EARL ^{18}F standards 1 accredited scanners are not directly comparable to results from scanners accredited using EARL ^{18}F standards 2, and a methodology has been proposed to translate the results from EARL ^{18}F standards 1 to standards 2[6]. This methodology is applicable to all PET/CT scanners, but the reconstruction parameters need to be adapted based on the specific equipment.

^{89}Zr-based tracers are becoming widespread with increasingly available supply, advances in radiochemistry and successful pilot studies in humans. Multicenter studies using ^{18}F-labelled tracers have demonstrated the need for standardization of image acquisition, reconstruction, analysis procedures and international harmonization programs. A similar approach can and should be applied with ^{89}Zr and ^{68}Ga based tracers.

EARL has added ^{89}Zr PET/CT accreditation in July 2020. It was initialized it in collaboration with the European Infrastructure for Translational Medicine (EATRIS). It aims at harmonizing PET/CT & PET/MR calibration and quantitative image quality using ^{89}Zr labeled pharmaceuticals. The ^{89}Zr accreditation is based on and derived from the procedures performed for the ^{18}F standards 1 accreditation which is a prerequisite for ^{89}Zr accreditation[7]. All ^{89}Zr reconstructions for quantification when referring to EARL accreditation should be done using the approved parameters for ^{18}F standards 1 accreditation.

In 2021 EARL released a ^{68}Ga PET/CT accreditation. Based on previous studies[8] this accreditation is derived from ^{18}F standards 2, which is a prerequisite for ^{68}Ga PET/CT accreditation. All ^{68}Ga reconstructions for quantification when referring to EARL accreditation should be done using the approved parameters for ^{18}F standards 2 accreditation[8].

In Q4 2021 we are starting ^{18}F/^{11}C Brain PET/CT accreditation program. It is based on a pilot study published by Verwer et. al.[9] In addition to already active, and in good standing ^{18}F

accreditation in accordance with either standards 1 or 2, for this accreditation Hoffman 3D Brain phantom images are required to be submitted once per year. This phantom simulates brain uptake of radiopharmaceuticals with a grey matter to white matter ratio (GMWMr) of 4.

In Q1 2022 ^{18}F PET/MR accreditation program was initiated. The accreditation is based on a pilot study published by Boellaard et. al.[10] This new program will have ^{18}F standards 1 and 2 same as the current PET/CT accreditation, and the same accreditation specifications will apply. The attenuation correction applied should be performed following the procedure recommended by your scanner manufacturer for phantom imaging. Each PET/MR scanner manufacturer has a specific phantom protocol in the scanner for uniformity and IQ phantoms. This accreditation only harmonizes the PET component, and not the attenuation correction, nor it checks/validates the attenuation correction method used in clinical studies. The ^{89}Zr & ^{68}Ga accreditations are available for PET/MR as of Q3 2022. Each PET/MR scanner manufacturer already has a specific phantom protocol set up in the scanner for uniformity phantom and IQ phantom.

MULTICENTER STUDIES

Participation in multicenter studies may mandate EARL Accreditation, in which case you are required to apply exactly the same reconstruction parameters for patient studies as used for the QC phantom (calibration QC and image quality QC), and which have been **approved by EARL**. Check with the study sponsor the specific standards required to participate.

After the first review of the submitted phantom QC data you may be advised by EARL to change your reconstruction settings (filters etc.). Please note that exactly the same reconstruction settings for which accreditation is given have to be used when reconstructing patient scans in the frame of a clinical trial requiring a specific EARL accreditation.

EARL PET/CT accreditation is given for a specific scanner and accreditation needs to be obtained separately for each scanner.

The series description should be as follows: **"EARLstandards_isotope_AC"** (i.e. **EARL1_18F_AC / EARL2_18F_AC / EARL1_89Zr_AC**). This allows tracking of the correct series in clinical trials. Additional reconstructions may be done for local use or for visual interpretation.

Recommendations for clinical acquisition times per bed in combination with dosage per kg patient weight can be found for various types of PET/CT scanners in the EANM imaging guideline[11].

ACCREDITATION PROCESS

All data for the accreditation is submitted via the EARL web site (https://earl.eanm.org). Your site's name will show as provided to EARL via an accreditation enrollment form (available on the EARL web site), and it is the name indicated on the accreditation certificate for your scanner (once accreditation is granted).

Upon enrollment you will receive EARL user credentials to log in via the EARL web site into your site's online box which can be found by navigating to Accreditation → Online box). A site can have multiple users with login credentials.

QC PROCEDURES

Calibration and Image Quality QC phantoms are required for obtaining ^{18}F based accreditation. Additional QC data have to be submitted outside of the scheduled quarterly submissions when there is a scanner hardware and/or software or dose calibrator updates/repairs.

- Calibration QC scan is required at initial accreditation and every quarter thereafter as defined in data submission timelines.
- Image quality QC scan is required at initial accreditation and once per year thereafter in the same quarter as the initial accreditation.
- ^{89}Zr calibration QC scanning is required at initial accreditation, and once per year thereafter in the same quarter as the initial accreditation, using the respective radiopharmaceuticals and the uniformity phantom.
- ^{68}Ga accreditations, calibration QC scanning is required every quarter using the respective radiopharmaceuticals and the uniformity phantom.
- For ^{18}F/^{11}CBrain PET/CT accreditation, in addition to already an active and in good standing ^{18}F accreditation, the Hoffman 3D Brain phantom images have to be submitted at initial accreditation and once per year thereafter in the same quarter as the initial Brain PET/CT accreditation.

An automated messaging system will send an e-mail reminder on the 26th of the first month of each quarter to perform and to submit the QC data due (calibration QC, image quality QC, Brain QC) within the subsequent 3 weeks. Notify EARL via email in advance if you are unable to submit the QC data on time. Missing to submit the required QC data will result in your scanner(s) accreditation being put on hold (is no longer active), and you will be able to submit the QC data again in the subsequent quarter (i.e. in 3 months).

On the 17th of the 2nd month of the quarter an automatic email reminder will inform you of the QC expected and not submitted yet as requested. If you did not submit the IQ data as requested in the respective quarter, and after the reminder on the 17th of the 2nd month you still have not submitted it, you will receive a 3rd automatic reminder on the 1st of the first month of the next quarter, and will be asked to submit it in the respective data submission period for that quarter.

NOTE: All clocks (dose calibrator, scanner, department clocks) must be synchronized. It is required to measure or derive the residual activity in the syringe or administration system in order to allow EARL to correctly verify the scanner's calibration.

QC DATA LIMITS OF ACCEPTABILITY

- Calibration QC data for all programs has limits of acceptability of <10% deviation.
- Image Quality QC data limits of acceptability are listed on the EARL web site under Accreditation specifications.

- $^{18}F/^{11}C$ Brain PET/CT limits of acceptability are listed on the EARL web site under Accreditation Specifications.

^{18}F PET/CT AND PET/MR EARL STANDARDS 1 AND 2

Both standards can be used independently or in parallel. For either EARL ^{18}F standards 1 or 2 you need to submit the data described below in QC Procedures section. If you are already participating in EARL ^{18}F standards 1 and would like to add standards 2, you need to provide **only** an additional image quality ACPET reconstruction fulfilling the requirements to obtain RCs for standards 2.

You will need to upload a separate zip file containing the images used for the attenuation correction, NACPET and ACPET, for each of the ^{18}F standards under the respective link provided for this purpose (under Devices in your online box).

For PET/MR with respect to the attenuation correction, use the recommended procedure already set up by your scanner manufacturer. Each PET/MR scanner manufacturer already has a specific phantom protocol set up in the scanner for uniformity phantom and IQ phantom. For the PET component - radiopharmaceutical, the phantoms filling and acquisition, reconstruction, please use the same details as provided in the section below applicable for PET/CT

CALIBRATION QC

Calibration QC scan is performed using a cylindrical uniformity phantom. The exact internal volume of this phantom should be known and provided in the calibration QC scan report form. Refer to the end of this manual for a Calibration QC scan report form (SRF) example.

Materials required

- Dose calibrator
- Water or distilled water
- Cylindrical uniformity phantom with a diameter of approximately 20 cm (17 to 22 cm), and length sufficient to cover the entire axial field of view (FOV) of the scanner
- A syringe with precisely known activity of ^{18}F. At the time of measurement the activity should be >30MBq but <100MBq, ideally such that it will decay to around 70 MBq at the time of expected phantom acquisition

Preparation

- Fill the uniformity phantom completely with water (best to use distilled water) and remove 10 to 20 ml water from the phantom
- Inject the ^{18}F from the syringe into the phantom and flush it a few times to ensure that the activity is transferred into the phantom. Measure the residual activity of the empty syringe
- Close the phantom and shake it extensively to homogenize the activity throughout (no need to re-fill after shaking)

Calibration QC scan acquisition

- Position the phantom on the scanner bed, centrally in the FOV

- Perform scout and low dose CT for attenuation correction purposes using your standard of care patient scan settings.
- For PET/MR with respect to the attenuation correction, use the recommended procedure already set up by your scanner manufacturer for phantom scanning. Each PET/MR scanner manufacturer already has a specific phantom protocol in the scanner for uniformity phantom and IQ phantom.
- Acquire a PET scan of at least 2 bed positions at 5 min/bed. If using continuous bed motion, convert the speed to result in comparable parameters for 2 beds at 5min/bed. The rest of the scan's acquisition parameters should be set up as close as possible to your clinical acquisition protocol.
- Record the time indicated on the scanner console when the PET series acquisition starts and report it in the scan report form at the time of uploading the data via the EARL online box.

IMAGE QUALITY QC

Image quality QC scan is performed using a NEMA IEC body image quality phantom.

Materials required

- Dose calibrator
- Water or distilled water
- Bottle for measuring 1000 ml stock solution
- NEMA IEC body image quality phantom. If the phantom comes with a lung insert, place it into the phantom before filling. The lung insert should be filled with polystyrene beads, without water. Ensure that all of the spheres are positioned sequentially by increasing size on one axial plane
- A syringe with a long needle for filling the spheres with stock solution. The needle used should be blunt and at least 15 cm long to reach the spheres and not damage them during filling. A large volume syringe and 18 gauge or larger bore size needle will facilitate faster filling of the spheres
- Two ≤ 5ml syringes with precisely known activity of ^{18}F. The activity of ^{18}F in each syringe should be such that it will decay to around 20 MBq at the time of expected phantom acquisition
- Colored dye may be added to the stock solution in order to better visualize the filling of the spheres

Preparation

Stock solution for the spheres (filling the spheres with approximately 20kBq/ml):

- Fill the bottle with exactly 1000 ml water (best to use distilled water)
- Inject the ^{18}F from one of the syringes into the bottle and flush it a few times to ensure the activity is transferred into the bottle. Measure the residual activity in the empty syringe
- Homogenize the solution in the bottle
- Using the syringe with the long blunt needle, fill all the spheres with the homogenized solution from the bottle, ensuring no air bubbles remain within the spheres

Background compartment of the NEMA IEC body phantom (filling the background with approximately 2kBq/ml, aiming to achieve 1:10 background to sphere activity ratio):

- Fill the background compartment completely with water (best to use distilled water)
- Remove 30ml water from the background compartment of the phantom
- Inject the ^{18}F from the second syringe into the background compartment and flush the syringe a few times to ensure the activity is transferred into the phantom. Measure the residual activity in the empty syringe
- Close the phantom and shake it extensively to homogenize the activity throughout the background compartment (no need to re-fill after shaking)

Image quality QC scan acquisition

- Position the phantom on the scanner bed, centrally in the FOV (in both horizontal and vertical direction relative to the gantry) using the scanner lasers such that the center of each sphere is located in a single transverse plane
- Perform scout and low dose CT for attenuation correction purposes (CTAC) using your standard of care patient scan settings.
- For PET/MR with respect to the attenuation correction, use the recommended procedure already set up by your scanner manufacturer for phantom scanning. Each PET/MR scanner manufacturer already has a specific phantom protocol in the scanner for uniformity phantom and IQ phantom.
- Acquire a PET scan of at least 2 bed positions and 5 min/bed. If using continuous bed motion, convert the speed to result in compatible parameters for 2 beds at 5min/bed. The rest of the scan's acquisition parameters should be set up as close as possible to your clinical acquisition protocol
- Record the time indicated on the scanner console when the PET series acquisition starts and report it in the scan report form at the time of uploading the data via the EARL online box

CALIBRATION AND IMAGE QUALITY QC SCAN RECONSTRUCTIONS

Reconstructions should be performed as applied in clinical practice (attenuation, scatter, normalization, decay, dead time corrections, time of flight, point spread function, etc.). Upon data analysis EARL may suggest some changes in order to harmonize the scanner performance in the accreditation program. If you reference EARL accreditation in the clinical scan report, a reconstruction with the approved EARL parameters should be used for the quantitative assessment. An additional site-specific standard of care reconstruction could be used for the visual interpretation of the scans.

^{89}Zr PET/CT AND PET/MR ACCREDITATION

In order to obtain ^{89}Zr accreditation you have to have EARL ^{18}F standards 1 accreditation in place, and in addition, once per year you have to submit the calibration QC for ^{89}Zr using the methodology described below which is similar to the ^{18}F calibration phantom procedure. Based on Kaalep et.al.[5] and Makris et. al.[12] ^{89}Zr RCs are directly related to the RCs obtained with ^{18}F. At this time IQ data is not required to be submitted for the ^{89}Zr accreditation.

Considerations and specific issues as compared to ^{18}F

Despite similarities in procedures and execution of the experimental QC studies between the ^{18}F and ^{89}Zr accreditation, there are several specific issues for ^{89}Zr activity preparation and image data collection:

1. Dose calibrator or administration system related issues:

- Dose calibrators or other systems for assessing patient specific activities are not calibrated for ^{89}Zr. On some systems settings for ^{89}Zr are not available. This means that ^{89}Zr is not known to the system and that settings such as half-life are not available. In the latter case these settings should be provided first and stored as ^{89}Zr settings before performing the QC experiments for the EARL accreditation. In this case a calibration factor needs to be derived. The calibration factor converts the (incorrect) activity read from the dose calibrator or administration system into correct ^{89}Zr activity. Preferably this calibration factor should be saved into the dose calibrator or administration system settings in order to read the correct ^{89}Zr activity directly from that system. If saving in the system is not possible, you should design a local procedure to guarantee that correct ^{89}Zr activity is prepared including the use of the above-mentioned calibration factor. The calibration factor will be verified as part of the ^{89}Zr accreditation procedure.
- It is essential that during the QC experiments the exact same settings and procedures are followed as during preparation and administration of patient activities.

2. PET/CT and PET/MR systems

- Most PET/CT scanners calibrated for ^{18}F provide quantitatively accurate activity and activity concentration data for ^{89}Zr as well (assuming that the correct isotope settings are used during acquisition). On some scanners ^{89}Zr isotope setting may not be automatically available. If ^{89}Zr settings are not available, your PET/CT vendor should provide and enter these settings (e.g. it becomes available as dedicated ^{89}Zr isotope listing or defined as ‘other’) into the system. The correct settings for ^{89}Zr on the PET/CT scanner should be implemented before applying for ^{89}Zr EARL accreditation. Please note that for ^{89}Zr both the positron abundance and half-life are different compared to those of ^{18}F.
- During the evaluation of the ^{89}Zr calibration experiments, the total activity in the phantom as measured by the PET/CT scanner will be derived. As (EARL ^{18}F standards 1 accredited) PET/CT scanners provide quantitatively accurate activity estimates for ^{89}Zr as well (taking above considerations into account), the PET/CT scanner will be used as the site-specific activity assessment standard (Kaalep *et al.*, EJNMMI Phys. 2018). Use directly any discrepancy between the dose calibrator or administration system activity read, and the activity derived from the PET/CT scanner to adjust the calibration/efficiency factor for the dose calibrator or administration system reads (see point 1).
- For PET/MR with respect to the attenuation correction, use the recommended procedure already set up by your scanner manufacturer. Each PET/MR scanner manufacturer already has a specific phantom protocol set up in the scanner for uniformity phantom and IQ phantom. For the PET component - radiopharmaceutical, the phantoms filling and acquisition, reconstruction, please use the same details as provided in the section below applicable for PET/CT.

3. Preparing solutions for filling phantoms.

- In most cases ^{89}Zr will be labeled to a pharmaceutical, usually antibodies or fragments. Not all patient radiopharmaceuticals dissolve well in water and/or the radiopharmaceutical may stick to phantom wall and administration lines/systems. In order to avoid activity sticking, specific preparations are needed to ensure that all activity enters the phantom and that the activity remains well dissolved in water during the experiments. Bovine and human serum albumins may be used to coat the inner walls of the phantoms prior to filling it with water and the ^{89}Zr solution to avoid sticking of the radioactivity to the phantom wall.

Materials

- Dose calibrator
- Water or distilled water
- Cylindrical calibration phantom with a diameter of approximately 20 cm (17 - 22 cm), and length sufficient to cover the entire axial FOV of the scanner
- A syringe with precisely known activity of ^{89}Zr solution. The activity of ^{89}Zr should be such that it will decay to around 37 MBq by the time of expected phantom acquisition. The activity may be prepared in any form, i.e. labeled to any antibody provided that activity can be well dissolved and mixed in the water solution
- A PET/CT or PET/MR scanner already accredited for EARL ^{18}F standards 1 and in good standing

Preparation

- Fill the calibration phantom completely with water (best to use distilled water) and remove 10 to 20 ml water from the phantom
- After measuring the full syringe, inject the ^{89}Zr activity into the phantom and flush the syringe a few times to ensure the activity is transferred into the phantom. Measure the residual activity of the empty syringe
- Close the phantom and shake it extensively to homogenize the activity throughout (no need to re-fill after shaking)

^{89}Zr calibration scan acquisition

- Position the phantom on the scanner bed, centrally in the FOV
- Perform scout and low dose CT for attenuation correction purposes (CT-AC) using your standard of care patient scan settings
- Acquire a PET scan consisting of at least 2 bed positions of at least 5 min/bed position. The rest of the scan's acquisition parameters should be set up as close as possible to your clinical acquisition protocol for ^{89}Zr studies
- Record the time indicated on the scanner console when the PET series acquisition starts and report it in the scan report form at the time of uploading the data via the EARL online box

Reconstructions

Reconstructions should be performed with attenuation, scatter, normalization, decay, dead time corrections as applied in clinical practice. Upon data analysis EARL may suggest some changes in order to harmonize the scanner performance in the accreditation program.

^{68}Ga PET/CT AND PET/MR ACCREDITATION

In order to obtain ^{68}Ga accreditation you have to have EARL ^{18}F standards 2 accreditation in place, active, and in addition every quarter you have to submit the calibration QC for ^{68}Ga using the methodology described below which is similar to the ^{18}F calibration phantom procedure. At this time IQ data is not required to be submitted for the ^{68}Ga accreditation.

Considerations and specific issues as compared to ^{18}F

Below are several specific points worth emphasizing for ^{68}Ga activity preparation and image data collection:

- Dose calibrator or administration system have to be set for ^{68}Ga. It is essential that during the QC experiments the exact same settings and procedures are followed as during preparation and administration of patient activities.
- Most PET/CT and PET/MR scanners calibrated for ^{18}F provide quantitatively accurate activity and activity concentration data for ^{68}Ga as well (assuming that the correct isotope settings are used during acquisition). On some scanners ^{68}Ga isotope setting may not be automatically available and you (or your PET/CT or PET/MR vendor should provide) should enter these settings (e.g. it becomes available as dedicated ^{68}Ga isotope listing or defined as 'other') into the system. The correct settings for ^{68}Ga on the PET/CT or PET/MR scanner should be implemented before applying for ^{68}Ga EARL accreditation. Please note that for ^{68}Ga both the positron abundance and half-life are different compared to those of ^{18}F.
- During the evaluation of the ^{68}Ga calibration experiments, the total activity in the phantom as measured by the scanner will be derived. EARL ^{18}F standards 2 accredited scanners provide quantitatively accurate activity estimates for ^{68}Ga as well, and the scanner will be used as the site-specific activity assessment standard[8]. Directly use any discrepancy between the dose calibrator or administration system activity read, and the activity derived from the scanner to adjust the calibration/efficiency factor for the dose calibrator or administration system reads.
- For PET/MR with respect to the attenuation correction, use the recommended procedure already set up by your scanner manufacturer. Each PET/MR scanner manufacturer already has a specific phantom protocol set up in the scanner for uniformity phantom and IQ phantom. For the PET component - radiopharmaceutical, the phantoms filling and acquisition, reconstruction, please use the same details as provided in the section below applicable for PET/CT.

Preparing solution for filling the phantom

In most cases ^{68}Ga will be labeled to a pharmaceutical.

Materials

- Dose calibrator
- Water or distilled water
- Cylindrical uniformity phantom with a diameter of approximately 20 cm (17 - 22 cm), and length sufficient to cover the entire axial FOV of the scanner (for scanner with axial FOV up to 30cm)

- A syringe with precisely known activity of ^{68}Ga solution. The activity of ^{68}Ga should be such that it will decay to around 37 MBq by the time of expected phantom acquisition The activity may be prepared in any form, i.e. labeled to any pharmaceutical provided that activity can be well dissolved and mixed in the water solution
- A PET/CT or PET/MR scanner already accredited for EARL ^{18}F standards 2 and in good standing

Preparation

- Fill the calibration phantom completely with water (best to use distilled water) and remove 10 to 20 ml water from the phantom
- After measuring the full syringe, inject the ^{68}Ga activity into the phantom and flush the syringe a few times to ensure the activity is transferred into the phantom. Measure the residual activity of the empty syringe
- Close the phantom and shake it extensively to homogenize the activity throughout (no need to re-fill after shaking)

^{68}Ga calibration scan acquisition

- Position the phantom on the scanner bed, centrally in the FOV
- Perform scout and low dose CT for attenuation correction purposes (CTAC) using your standard of care patient scan settings (for PET/MR see above)
- Acquire a PET scan consisting of at least 2 bed positions of at least 5 min/bed position. The rest of the scan's acquisition parameters should be set up as close as possible to your clinical acquisition protocol for ^{68}Ga studies.
- Record the time indicated on the scanner console when the PET series acquisition starts and report it in the scan report form at the time of uploading the data via the EARL online box.

Reconstructions

Reconstructions should be performed with attenuation, scatter, normalization, decay, dead time corrections as applied in clinical practice. Upon data analysis EARL may suggest some changes in order to harmonize the scanner performance in the accreditation program.

^{18}F/^{11}C Brain PET/CT accreditation

^{18}F/^{11}C Brain PET/CT QC scan is performed using the Hoffman 3D Brain phantom. In order to obtain ^{18}F/^{11}C Brain PET/CT accreditation you have to have either EARL ^{18}F standards 1 or 2 accreditation in place, active, and in addition once per year you have to submit the Brain PET/CT Hoffman 3D Brain phantom images acquired using the methodology described below.

Materials required

- Dose calibrator
- Water or distilled water
- Bottle for measuring 1500 ml solution.
- Hoffman 3D Brain image quality phantom. This phantom comes with multiple inserts that should be placed into the phantom before filling it. It is an anthropomorphic phantom containing a 1140 mL single compartment, representing the entire brain. This

phantom simulates a grey matter to white matter ratio (GMWMr) of 4. The fillable volume is a factor of 4 smaller in areas representing WM than in areas representing GM. This is achieved with extra plastic layers within WM regions that are thin enough to be indiscernible on PET images (due to partial volume effects), yet lower the fillable volume in those regions, leading to lower apparent activity concentrations on the PET images.

- A syringe with a long needle for filling the phantom with solution from the bottom up. The needle used should be blunt and long to reach the bottom of the phantom and not damage it during filling. A large volume syringe and larger bore size needle will facilitate faster filling of the phantom from the bottom up.
- A syringe with precisely known activity of ^{18}F (use of FDG or any other ^{18}F labelled radiopharmaceutical is allowed, as long as it does not stick to the phantom). The activity of ^{18}F in syringe should be ~50 MBq calibrated for the intended scan start time.

Preparation

Stock solution (filling the phantom with ~33kBq/ml calibrated for the intended scan start time):

- Fill the bottle with exactly 1500 ml water (best to use distilled water).
- Inject the ^{18}F from the syringes into the bottle and flush it a few times to ensure the activity is transferred into the bottle. Measure the residual activity in the empty syringe.
- Homogenize the solution in the bottle.
- Using the syringe with the long blunt needle, fill the phantom from the bottom up (to minimize air pockets formation) with the homogenized solution from the bottom up, ensuring no air bubbles remain within the phantom.

Scan acquisition

- Position the phantom on the scanner bed, such that the brain compartment is in the same orientation as the brain would be for a patient in head-first supine position. Align the phantom centrally within the FOV (in both horizontal and vertical direction relative to the gantry) using the scanner lasers.
- Perform a scout and ensure that the phantom is centered within one PET bed position.
- Perform low dose CT for attenuation correction purposes (CTAC) using your standard of care patient scan settings.
- Acquire a one bed Brain PET scan of 30 min.
- Record the PET series acquisition start time indicated on the scanner console, and report it in the scan report form at the time of uploading the data via the EARL online box.

Reconstructions

Reconstruct the PET data into one 30 min frame. For the first data submission, the scan's reconstruction parameters should be same as your clinical reconstruction parameters for **^{18}F/^{11}C Brain PET/CT and not using resolution modeling (PSF off)**. Reconstructions should be performed with attenuation, scatter, normalization, decay, dead time corrections as applied in clinical practice. Upon data analysis EARL may suggest some changes in order to harmonize the scanner performance in the accreditation program.

QC SCANS SUBMISSION

All phantom images must be provided in uncompressed **DICOM format and exported directly from the scanner**. If exported from a post processing workstation, the original DICOM files must not be modified in any way. DICOM files must fulfil the 'DICOM conformance statement' of the PET/CT scanner manufacturer.

For each QC scan, three DICOM series are required. A DICOM series is defined as a stack of files, where one file is generated for each axial slice. Submit the following:

- Attenuation correction CT
- Non attenuation corrected PET (NACPET) data
- Attenuation corrected PET (ACPET) data

If you are participating in both ^{18}F accreditations, upload the IQ ACPET series for each of the two ^{18}F standards under the respective link provided for this purpose. You do not have to upload the attenuation correction and the NACPET series under both standards, only under one of the two is sufficient.

Create a zip archive (preferably using WinZIP) containing all series for each separate QC data set (i.e. one zip for the calibration, 2nd zip for the IQ, etc.). Upload the zip file within the respective online QC scan report form. The currently uploaded QC documents can be reviewed as read only within the online box. Submit the scan report form with the corresponding zip archive via the online box. The maximum upload size for each separate upload is 500 MB. If your zip file exceeds this, please contact EARL for assistance.

The QC data is submitted via the EARL web site: https://earl.eanm.org **Accreditation→**Online box.

It is recommended to save all raw data (calibration and the image quality QC scans) and it is necessary to have it available until EARL has approved your QC results. You could be asked to perform additional reconstructions using different settings in the course of the harmonization process of the scanner. Raw data should be saved in either sinogram or listmode (whichever is applicable on your scanner), including all other data files (normalization, low dose CT or processed one etc.) necessary for (quantitative) reconstruction of the images.

EARL FEEDBACK AND RESULTS OF QC MEASUREMENTS

Information about the QC results acceptance or rejection is provided via email. In the online box you can check the status of the submitted data and review the details of the QC, including you can see graphs for the RCs of the IQ QC. If the submitted QC data meets the respective accreditation requirements, accreditation will be granted and your site's name and address will be listed on EARL's website in the Centres of Excellence network (https://earl.eanm.org, Accreditation → Centres of Excellence network). You will receive an accreditation certificate and signet. An accreditation certificate for the accredited scanner is provided via the online box upon accreditation granted each quarter, and you can also download the signet this way. The accreditation certificate contains your institution name, the department, scanner make, mode, and the serial number, the quarter in the respective year when it was printed.

You are allowed to use the accreditation signet (see an example below) on your correspondence and website. The accreditation signet will be available to download upon successful accreditation, and as soon as the head of imaging/nuclear medicine department has signed the "signet policy".

If the submitted QC data does not meet the respective accreditation requirements, you will receive suggestions with changes of the reconstruction parameters, or possible additional acquisition. You can find those in your online box under Devices → view (for the respective QC data) → view validation status.

DATA SUBMISSION TIMELINES

The following timelines for QC data submission are applicable for all EARL accreditations every year:
Quarter 1: 26Jan – 16Feb
Quarter 2: 26Apr – 16May
Quarter 3: 26Jul – 16Aug
Quarter 4: 26Oct – 16Nov

Schedule the QC measurement early in the respective EARL defined quarters, allowing you sufficient time to repeat the QC, if necessary.

Please inform EARL as soon as possible if you are unable to submit the QC data according to the deadlines due to unforeseen circumstance (i.e. phantom is damaged or scanner is not operational, problems with IT etc.), or if you need more time due to scanner re-calibration. Please inform EARL in the case of a scanner replacement, major recalibration or upgrade and/or if you wish to get accreditation for an additional scanner.

RENTAL OF PHANTOM

If you do not own a NEMA IEC body image quality phantom necessary for the image quality QC, or the Hoffman 3D brain phantom, EARL could lend you one. If you would like to borrow a phantom from EARL, please contact us well in advance via email: earl@eanm.org. EARL will arrange for the shipping of the phantom to you and commission transport insurance. The rental fee for borrowing a phantom can be found on the EARL web site in the section Fees. In addition, there will be shipping and delivery cost as well. You will receive an invoice for the total upon delivery confirmation by the shipping carrier. It is expected that you acquire and submit the IQ data withing 5 business days using the EARL NEMA borrowed phantom.

NEMA IEC body & Hoffman 3D Brain phantom receive instructions:

- Upon receipt of the phantom, please check the content of the box for completeness (an inventory list and packing instructions are enclosed) and intactness of the box contents. In case you notice damage of the transport box, please inform EARL and the mail carrier **immediately** and indicate the damage on the delivery confirmation via email at earl@eanm.org. Claims, which are reported later, will not be covered by the insurance. In case the phantom box seems to be OK at first sight and you notice a damage of the content afterwards – you need to notify EARL/the insurance **within 5 days after receipt of the phantom**. Please take pictures of the damage in order to provide evidence. Please note that these actions need to be taken in order to secure insurance coverage.
- In case the phantom is broken or damaged during the use of the phantom, please inform EARL immediately and check with your hospital if you have appropriate insurance to cover the damages.
- Before you send the phantom on to another site or back to EARL, please check again the content of the box for completeness and intactness and ensure that the phantom is packed and labeled exactly in the same way as you received it.
- Please keep the phantom until EARL arranges its transport.
- The delivery will be organized by EARL. Please do not use any other delivery services.

ACCREDITATION FEE

The fee for the accreditation program is per calendar year/per site/per scanner/per accreditation program (regardless of when the accreditation process starts within the calendar year), covering the costs for the initial accreditation procedure and maintaining the status of an EARL accredited Center of Excellence. For up-to-date information of the fee, please check the EARL web site under Fees. EARL will send you an invoice via email specifying an invoice number. Please reference the invoice number when transferring the payment.

The accreditation fee needs to be transferred to the following account:
ERSTE Bank
Bank code: 20111
IBAN: AT90 2011 1828 5173 8400
BIC: GIBAATWWXXX

ACCREDITATION ON HOLD

Please submit QC data on time as noted above in the timelines section. If the deadlines are disregarded, your PET/CT accreditation is no longer active. Re-entry into the accreditation program is possible, as soon as you are able to fulfil these requirements again in the next respective quarter as defined above. At the start of each quarter EARL updates the Centers of Excellence network on the web site. If your accreditation is not active at the time of this update, your center will not be listed. It will be listed when your accreditation is reactivated but no earlier than the next quarter when again the list updated (start of the 3rd month of each quarter).

The following information will be required to be provided at the time of uploading the QC scans:

SCAN REPORT FORMS

- The scan report forms (calibration, image quality, Brain PET/CT) can be found in the online box.
- It is required to fill in every field of the scan report form and to use the format noted in the fields. Your web browser may propose values, which you have entered previously, please check if those values apply for the current measurement.
- You are only allowed to submit the scan report form together with the corresponding phantom images.
- If you have problems with uploading the QC documents, please check your firewall and/or discuss this problem with your IT representative at your department.

CALIBRATION QC SCAN REPORT FORM

- Volume of calibration phantom (ml)
- PET acquisition start (read from console) at (hh:mm:ss) on (YYYY:MM:DD)
- Activity (MBq) at (hh:mm:ss) on (YYYY:MM:DD)
- Residual activity (MBq) at (hh:mm:ss)

IMAGE QUALITY QC SCAN REPORT FORM

Stock solution for spheres:

- Activity (MBq) at (hh:mm:ss) on (YYYY:MM:DD)
- Residual activity (MBq) at (hh:mm:ss) on (YYYY:MM:DD)
- Final volume (bottle + syringe) (ml)

Filling of background compartment of the phantom:

- Activity (MBq) at (hh:mm:ss)
- Residual activity (MBq) at (hh:mm:ss)

PET or PET/CT scan acquisition:

- PET acquisition start time (read from console) at (hh:mm:ss) on (YYYY:MM:DD)

^{18}F/^{11}C BRAIN PET/CT SCAN REPORT FORM

- Volume of stock solution (ml)
- PET acquisition start (read from console) at (hh:mm:ss) on (YYYY:MM:DD)
- Activity (MBq) at (hh:mm:ss) on (YYYY:MM:DD)
- Residual activity (MBq) at (hh:mm:ss) on (YYYY:MM:DD)
- Please confirm that you did not use resolution modeling (PSF) for this reconstruction? (select) (Confirm/Not confirmed)

APPENDIX

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

R.Boellaard[1], A.T. Willemsen[2], B.Arends[3], E.P. Visser[4].

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4.Department of Nuclear Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands.

The EANM guidelines for quantitative FDG PET and PET/CT studies, published in the January 2010 and updated in 2015 issue of the European Journal of Nuclear Medicine and Molecular Imaging 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 published guidelines 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 guidelines, 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 EANM 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 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 EANM 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 guidelines provide 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 guidelines. SUV recoveries as a function of sphere size will be determined and compared with the specifications given in the guidelines.
- 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 EANM 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.

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