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calibration protocol using information from a multi-centre phantom study
between partners

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D2: A technical validation and calibration protocol using information from a multi-centre phantom study between partners

Introduction

The quantification of perfusion in PET is sensitive to acquisition parameters. This limits the usefulness of such measures, as they are not easily comparable between centres, or even between different acquisition types or image reconstruction protocols at a single centre. Additionally, this means that uncertainty exists in the source of variations between measurements. Currently, it is not known whether variations in perfusion measurements come from variations within the patient or variations due to scanner parameters.

Thus, it would be desirable to have a physical standard (phantom) with an associated calibration protocol written down for implementation across the wider PET community. This would lead to an improvement of the usage of physical standards as part of a routine perfusion PET measurements, implement quality control systems and enable the end user to understand key sources of uncertainty in their measurements.

Eventually, by implementing the protocol at multiple sites and systems with the use of the phantom, the differences in modelled perfusion values due to technical factors could be reduced after specific harmonisation measures are implemented.

Motivation and Aims

Our intent was to draft a calibration protocol for standard acquisition of dynamic PET perfusion measurements between different PET systems and imaging centres by using information from a multi-centre phantom study between partners.

Our aims were as follows:

1. Establish a technical validation and calibration protocol using information from a multi-centre phantom study between TPC and NPL

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2. Produce documentation relating to the relevant acquisition protocols and requirements to extract the necessary information about the imaging system used
3. Indicate what would be the necessary requirements to perform calibrations across sites which do not have access to the same equipment or same tracers

Eventually, these would allow to use the physical standard as a means of a calibration across different imaging sessions or imaging centres.

Materials and Methods

Test object: flow phantom

To investigate flow quantification accuracy, a flow phantom (DCE Dynamic Flow Phantom, Shelley Medical Imaging Technologies, Canada [1]) was used as shown in Figure 1. The phantom contains a water container, peristaltic pump, injection port, phantom shell, flow constrictor valves and flow meters. Flow inside the system is controlled with the peristaltic pump and the flow constrictor valves. The flow meters are used for reference recording.

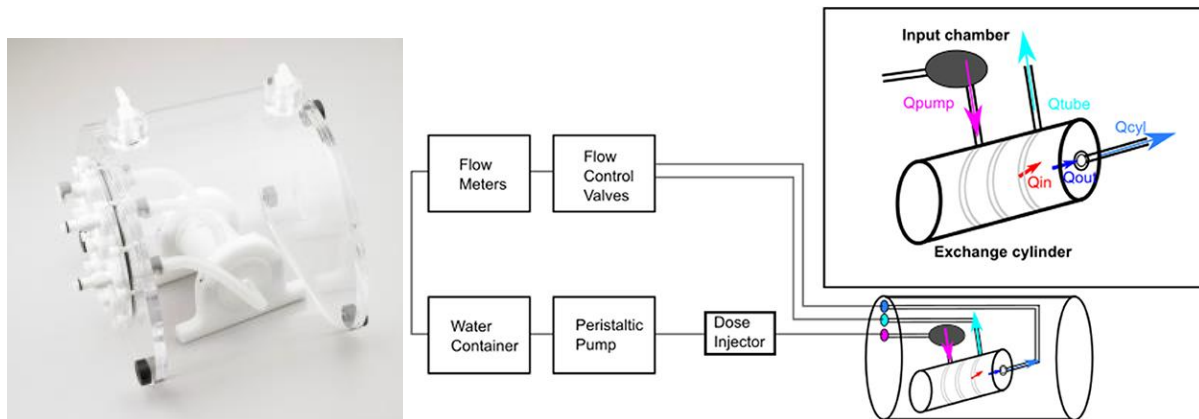


Figure 1: Image and working schematic of DCE Dynamic Flow Phantom, Shelley Medical

An input chamber and an exchange cylinder containing a perforated tube are located inside the shell, which has similar dimensions as the NEMA [2] image quality phantom. The input chamber models the left ventricle blood pool whereas the exchange cylinder and perforated tube model tracer exchange in myocardial tissue. These allow to measure input and tissue TACs for kinetic modelling.

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The input and tissue TACs can be measured by a volume-of-interest (VOI) analysis, defined for the input chamber and exchange cylinder. The TACs are used for image-based flow modelling based on a two-compartment kinetic (one-tissue compartment) model as implemented in the phantom flow quantification software (QuantifyDCE 1.1, Shelley Medical Imaging Technologies, Canada, [1]).

Phantoms were purchased separately by each site. The initial protocol was assessed at TPC and later adapted by NPL to investigate the feasibility of implementing multi-centre measurements using a different PET/CT system and radiotracer.

Measurements performed at TPC and NPL

The protocol was repeated in TPC using the Discovery D690 and Discovery MI PET/CT systems and in NPL using the Mediso AnyScan SCP. Flow meter calibration and flow rates were fixed for all studies. Due to the COVID-19 travel restrictions imposed at the time of the study, the phantom imaging protocol was recorded in TPC and shared for NPL for reproducibility. At the time the study was conducted at NPL, remote video conferencing was used to ensure proper set-up and imaging of the phantom.

In TPC, data from two PET/CT systems was collected. The digital Discovery MI with four detector rings (DMI-20) and the analog Discovery 690 (D690) (GE Healthcare, US) PET/CT systems were used as in [3,4].

In the NPL, two datasets were collected using the Mediso Anyscan SCP (Mediso, Hungary).

PET measurements at each site were performed using dynamic PET acquisition in list-mode. CT-based attenuation correction was used at both sites. $^{15}\text{O}\text{-H}_2\text{O}$ with an automatic dispenser (Hidex Oy, Finland) was used at TPC with target activity of 500 MBq, whereas $^{18}\text{F}\text{-FDG}$ with manual injection was used at NPL, with target activities of 100 MBq and 200 MBq in the respective studies. The acquisition time used for TPC was 4 minutes and 40 seconds, following the clinical protocol, NPL collected for 10 minutes and 6 minutes due to the longer $^{18}\text{F}\text{-FDG}$ half-life and variations in the injection protocol used.

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Manual injection protocols were established at NPL to investigate sources of variation due to injected volumes and activity. The first considered an injected volume of 2 ml with 100 MBq of ^{18}F -FDG which was injected over approximately 2 seconds. The second was an injected volume of 0.5 ml containing 200 MBq of ^{18}F -FDG injected in less than 1 second.

At TPC, the default values the vendor recommended with iterative reconstruction available on the system were used. For the dynamic acquisitions of 4 min 40 s, list-mode data was binned into 24 time-frames of 14x5 s, 3x10 s, 3x20 s and 4x30 s. At NPL there was no default vendor recommendations and therefore the same temporal reconstruction settings were used with the vendor supplied 3D OSEM reconstruction algorithm. All data corrections including decay, attenuation, scatter, randoms and dead-time were performed.

Protocol description

A template of the final protocol is given entirely in Appendix 1. An experimental acquisition sequence was defined as follows, for imaging a range of different flow values (low, medium, high) between the systems. The pump values from low to high flow are 150 ml/min, 200 ml/min and 250 ml/min. The amount of flow to the cylinder is adjusted by adding constriction by the flow control valves by $Q_{\text{cyl}} = 80\%, 60\%, 40\% \text{ and } 20\% \times Q_{\text{pump}}$. This totals to 12 measurement points per individual PET/CT system. Finally, the phantom should be calibrated before each measurement. For recording, a template for the measurement recording were prepared and it is given entirely in Appendix 2.

In the below paragraphs, we will describe the specific steps in conducting the protocol between centres and systems.

Conducting the imaging protocol

Preparations of the phantom and the PET imaging system should be conducted according to the instructions provided by the vendor. To conduct the imaging protocol:

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1. Calibrate the peristaltic pump and flow meters
2. Connect the phantom as detailed
3. Set-up the phantom on the imaging pallet, so that during scanning only the phantom is in the imaging field of view
4. Use a circulating reservoir and test for possible leaks
5. Set the phantom for recirculation at high rate
6. Ensure as many bubbles as possible are removed by inverting and rotating the phantom while the pump is running
7. Secure the phantom to the bed
8. Perform a CT scan which contains the whole phantom body
9. If extensive air is seen inside the phantom, repeat air removal
10. After air removal, setup the water reservoirs and waste either in circulation or waste mode, depending on the type of radiotracer used
11. Set flow to desired rate and ratio using pump and valve controls, after which system is ready for active scanning
12. Perform a scout CT and try to align the PET stack so that the phantom heart compartment is centered in the PET field of view
13. Perform anatomical CT and CT for attenuation correction for the phantom
14. Perform PET scanning in dynamic acquisition mode
 - Name the PET acquisition in a format which is identifiable later
 - Set dynamic acquisition length according to site protocol
 - Mark all positions in the CT and PET scan for future reference and to ensure that any repeated scans are not off position
 - Prepare the PET scan, but do not yet start the scan
15. Prepare either an automatic injector or a syringe to the injection port, ensuring that the activity has been previously calibrated to the same standard as the PET system
16. Perform injection and start the PET scan upon injection
17. In case of long-lived isotopes, flush the system between scans
18. Return to (11) to perform the next flow rate
19. Reconstruct images using default parameters and the iterative reconstruction algorithm provided by the vendor

Data analysis procedure

The suggested method to analyse the data is to use the QuantifyDCE software provided with the phantom to calculate image-derived flow values by kinetic modelling,

The modelling of image-derived flow values is based on TACs measured by a volume-of-interest (VOI) analysis using a two-compartmental model. VOI delineation is conducted by selecting the centre point of the input chamber and exchange cylinder from the PET images. Spherical region-of-interests (ROIs) at the centre points with a specific diameter for input chamber and exchange cylinder are automatically produced and the VOI is delineated by searching all pixel values corresponding a certain threshold range within the ROI.

The model implementation is given in detail in [5] and [6]. The model contains four parameters, delay, ISF, q_{in} and q_{out} which are solved using the standard approach of non-linear least-squares fitting. The modelled parameters for rate constants q_{in} and q_{out} in units of min^{-1} can then be converted to final image-derived flow values Q_{in} and Q_{out} (units of ml/min) when they are multiplied by the cylinder volume ($V_{cyl} = 161 \text{ ml}$).

Thus, Q_{in} ($Q_{in} = V_{cyl} \times q_{in}$) represents the flow from the perforated tube to the exchange cylinder and Q_{out} ($Q_{out} = V_{cyl} \times q_{out}$) the flow out from the exchange cylinder.

Further protocol refinement

Further refinement of the protocol shall address the following items:

1. Cross-validation of ^{18}F -FDG and ^{15}O -H₂O measurements at TPC and NPL should be performed using the phantom to calibrate the acquisitions between sites which do not have access to ^{15}O -H₂O.
2. For sites which do not have access to automatic power injector, further work needs to be conducted for determining the optimum approach of delivering the bolus by hand injection.
3. Finally, further work is also needed to match the reconstruction parameters across different PET/CT systems, especially of systems of different vendors.

Conclusions

A calibration protocol for standard acquisition of dynamic PET perfusion measurements using a flow phantom was developed and successfully conducted at both NPL and TPC.

References

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- [5] Gabrani-Juma, H. et al. Validation of a Multimodality Flow Phantom and Its Application for Assessment of Dynamic SPECT and PET Technologies. *IEEE Trans. Med. Imaging* 36, 132–141 (2017).
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Appendix 1: Protocol for PET scanning with the Shelley dynamic phantom

Information below can also be found in word document: "19SIP04_D2_appendix1.docx"

1. Setup

Calibration of Peristaltic pump and flow meters should be performed according to appropriate manuals.

Connect phantom as detailed in Shelley manual, excluding MRI components.

Phantom was arranged on Therapy pallet such that during scanning, the pump and injection port are located outside the rear of the camera whilst the phantom remains in the PET bore. A general layout is shown in Figure 2



Figure 2: General layout of Dynamic phantom on therapy pallet.

NB: The minimum amount of pipework was used.

2. Preparation and CT scan:

1. Setup phantom using recirculating reservoir and test (including leak check). Ensure as many bubbles as possible are removed by inverting and rotating the phantom shell
2. Firmly secure phantom to the bed
3. Disconnect reservoir and waste bucket, sealing ends of inlet and outlet pipes with suitable connectors. Place all pipework on the patient couch outside the FOV of the CT
4. Perform CT scan which encompasses the whole phantom body

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5. Check for bubbles in the system and repeat steps 1-4 until all significant bubbles are removed
6. Perform low- and high-resolution CT scans of phantom
7. Move phantom to the PET measurement position by performing a 1 second, 1 FOV scan centred over the heart compartment of the dynamic phantom. Record this position for future reference
8. Reconnect reservoir and waste bucket, taking care not to move phantom
9. Resume recirculation of water at a high rate (500 ml/min), checking to ensure no significant bubble pass through the system
10. Set flow to desired rate and ratio using pump and valve controls
11. System is ready for active scanning

3. Performing a dynamic PET scan with ^{18}F -FDG

1. Using the same protocol in which the CT was acquired, create a dynamic PET acquisition
 - a. PET acquisition should be named using the following format:
PT_PERCENTAGE_PUMPFLOW_CYLFLOW
2. Acquisition should be set to 10-minute continuous scan
3. Copy the positioning from the test PET scan performed during setup
4. Draw up ~ 100 MBq ^{18}F -FDG in ~4 ml to a 10 ml syringe and measure activity on calibrator
 - a. Record activity and reference time on spreadsheet
5. Turn recirculate valve to waste container
6. 'Prepare' the scan
7. Connect syringe to injection port, do not open the valve
8. Press 'go' to start the scan
9. Wait 5 s
10. Open injection valve and Inject activity over 2-3 s
11. Close injection valve and remove syringe
12. Measure syringe residue on calibrator and record value and reference time on spreadsheet
13. Following completion of scan, open all valves completely and increase pump flow rate to flush system
14. After ~5 minutes return system to recirculate and reduce flow rate
15. Process can be restarted if new active scan is required

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Appendix 2: Template for measurement recording

A template for recording the measurements is provided in the excel spreadsheet:
"19SIP04_D2_appendix2.xlsx"

The screenshot below shows what the template looks like:

DATE		Imaging Protocol for (Insert name) PET/CT system			
Collection: LIST-mode Qcyl = 80 %, 60 %, 40 % and 20 % * Qpump Start scan immediately from injection (SS) Measure the dose administration time (DAT) [s] Dose (target) = 500 MBq Tracer = O-15H2O					
Measurement	Parameter		Test 1	Repeate	Unit
	Qpump	Reference	150	150	mL/min
			30	30	mL/min
	Qtube	Before			mL/min
		After			mL/min
	Qcyl	Reference	120	120	mL/min
		Before			mL/min
		After			mL/min
	SS				s
	DAT				s
	Dose				MBq
	Input peak				s
Measurement	Parameter		Test 1	Repeate	Unit
	Qpump	Reference	200	200	mL/min
			40	40	mL/min
	Qtube	Before			mL/min
		After			mL/min
	Qcyl	Reference	160	160	mL/min
		Before			mL/min
		After			mL/min
	SS				s
	DAT				s
	Dose				MBq
	Input peak				s
Measurement	Parameter		Test 1	Repeate	Unit
	Qpump	Reference	250	250	mL/min
			50	50	mL/min
	Qtube	Before			mL/min
		After			mL/min
	Qcyl	Reference	200	200	mL/min
		Before			mL/min
		After			mL/min
	SS				s
	DAT				s
	Dose				MBq
	Input peak				s