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Report on validation of centres for imaging networks

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Abbreviations

WB	Whole Body
PVE	Partial Volume Effects
DT	Dead Time
RMH	Royal Marsden Hospital
NHSFT	National Health Service Foundation Trust
SPECT	Single Photon Emission Computed Tomography
CT	Computed Tomography
PMT	Photomultiplier Tube
MCA	Multichannel Analyser
HEGP	High Energy General Purpose
QC	Quality Control
OSEM	Ordered Subset Expectation Maximisation
AC	Attenuation Correction
TEWC	Triple-Energy Window Correction
RR	Resolution Recovery
NMI	National Metrology Institute
FOV	Field Of View
VOIs	Volumes Of Interest
GE	General Electric
FWHM	Full-Width-Half-Maximum
PMTs	Photo-Multiplier Tubes
UKW	Universitätsklinikum Würzburg
UMR	Philipps-Universität Marburg
IUCT-O	Institut Universitaire du Cancer de Toulouse

1. Introduction

The primary aim of this study is to obtain prospectively multi-centre data to establish the threshold absorbed dose required for a successful thyroid ablation and to develop novel tools to determine the range of absorbed doses delivered to potentially dose limiting organs.

The activity distribution within the patient as a function of time is measured to calculate absorbed dose distributions in the normal organs, thyroid remnants and associated lymph nodes. These activity measurements will be made with a combination of gamma camera imaging, whole body (WB) retention measurements and urine and blood sampling.

Accurate and reproducible quantitative gamma camera imaging is vital for normal organ and lesional dosimetry. In order to ensure comparability of absorbed dose measurements between participating centres, equipment set-up and calibration is required prior to patient recruitment. This includes calibration of all gamma cameras, dose calibrators, gamma counters and radiation monitoring equipment to be used in patient measurements.

Each Single Photon Emission Computed Tomography (SPECT) system is to be calibrated to correct for partial volume effects (PVE) as well as dead time (DT) exhibited at high count rates. Traceability to the relevant National Metrology Institute (NMI) will be ensured for all dose calibrator, gamma counter and radiation monitoring equipment calibrations. All calibrations are to be performed by a physicist from the Royal Marsden Hospital NHS Foundation Trust (RMH NHSFT) in collaboration with physicists at each site.

This report details the calibrations carried out at RMH NHSFT to ensure accurate and reproducible quantitative ^{131}I imaging at high count rates for use in patient dosimetry calculations. The subsequent development of the site set-up protocol, in collaboration with other participating centres, will ensure standardisation in quantitative imaging at all participating centres.

2. Assay equipment standardisation and calibration

A site set-up protocol has been developed to ensure that all equipment used in the quantification of patient activity is calibrated and optimised. The protocol is based on the site set-up protocol developed as part of the UK-based SEL-I-METRY trial (SEL-I-METRY 2015).

The following equipment, used in the acquisition of patient data at RMH NHSFT, has been calibrated:

Gamma cameras: 2 x Siemens Intevo SPECT/CT
Radionuclide calibrators: 1 x Capintec CRC-15R, 1 x Capintec CRC-55tR
WB retention probe: 3 x Southern Scientific Radhound energy compensated Geigers

The results of the equipment set-up and calibration at RMH NHSFT are detailed in this report. The protocol was further developed, in consultation with the other centres enrolled on the study, to establish a standardised calibration protocol that can be used by all participating centres.

2.1 Routine quality assurance

Prior to system calibration it was first ensured that all equipment that has the potential to affect quantification accuracy was functioning optimally. The tests listed in Table 1 were carried out prior to calibration of the systems.

Table 1 – Pre-calibration quality assurance tests.

Test	Undertaken within preceding:	Limits
Photopeak position	Month	Centred within peak energy window defined in Table 2
^{131}I intrinsic uniformity (20 Mcounts)	Month (allow time to correct artefacts where necessary)	Integral CFOV ≤ 4% Differential ≤ 3% NO MAJOR TUBE ARTEFACTS
^{131}I intrinsic uniformity at high count rates (~100 kcps; 20 Mcounts)		
^{99m}Tc intrinsic uniformity (20 Mcounts)		
Centre of rotation for High-Energy General Purpose (HEGP) collimators	Week	Within local limits
SPECT/CT system alignment, if applicable	Month	
Extrinsic HEGP flood	Month	
Routine quality control (QC) of weighing scales used in calibration	Week	
Routine QC of dose calibrators used in calibration	Day	

All pre-calibration tests were performed and the results were within the limits indicated.

2.2 Patient acquisition protocols

Patient acquisition protocols were set-up and saved on the SPECT/CT systems according to the parameters listed in

Table 2.

Table 2 – ^{131}I patient scanning parameters.

Parameter	**Suitable for ^{131}I**
Collimator	High-energy general purpose (HEGP)
Peak energy window (20%)	364 keV ± 10%
Low scatter energy window (6%)	318 keV ± 3%
High scatter energy window (6%)	413 keV ± 3%
Matrix	128 x 128
WB planar	
Acquisition mode	Continuous
Speed	20 cm/min
Auto-contouring	Deactivated
SPECT	
SPECT movement	Body Contour (or radius as close to patient as possible)
Projections	60 (6˚/projection)
Time per projection	60 s*
CT	Standard low-dose protocol (e.g. at RMH NHSFT: 130 kVp, 35 quality reference mAs, pitch 0.8, 19.2 cm collimation)

* acquisition time will be adjusted during patient scanning according to the count rate.

SPECT image reconstruction parameters were optimised to reach convergence of the smallest sphere as listed in Table 3.

Table 3 – optimised SPECT image reconstruction parameters for images reconstructed at RMH NHSFT.

Parameter	**Suitable for ^{131}I**
Reconstruction	Ordered Subset Expectation Maximisation (OSEM)
Attenuation Correction (AC)	CTAC if available, otherwise Chang (0.11 cm^{-1} @ 364 keV)
Scatter correction	Triple-Energy Window Correction (TEWC)
Iterations / subsets	40 / 4
Post-reconstruction filtering	None
Resolution recovery (RR)	Yes

A specific reconstruction protocol was created for these dosimetry images using the above parameters.

2.3 Radionuclide calibrators

The accuracy of radionuclide calibrators used in the assay of ^{131}I should be traceable to the relevant National Metrology Institute (NMI). In the UK the NMI is the National Physical Laboratory, which confirms the accuracy of its standards by comparisons with the NMIs in other countries. In accordance with UK guidelines (IPEM 2006), a subset of the calibration factors used at RMH NHSFT

are checked annually for the full range of radionuclide energies over a five year period and it is ensured that the calibrators read within ± 5% of the primary standard.

The SPECT system calibration will be made against readings from these calibrators. Therefore, the same calibrators should be used to assay patient doses as was used to calibrate the SPECT system.

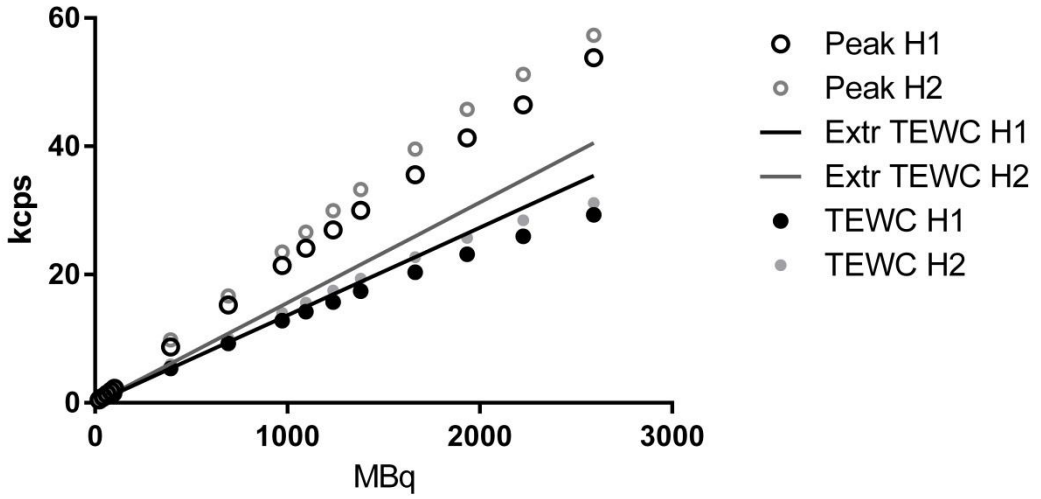
2.4 Gamma cameras

2.4.1 Dead time correction factor

DT factors are used to correct the acquired image for counts lost due to paralysis of the detector. High count rate test acquisitions ensure that the system correctly handles high activities of ^{131}I and identifies artefacts that may occur at high count rates. DT correction factors were determined according to the site set-up protocol; in brief this entailed planar scanning of a cylindrical phantom containing increasing activities of ^{131}I (nominally 20 to 2800 MBq), positioned centrally to the detector field-of-view (FOV). The correction factor at each activity level can then be determined from the ratio of the expected count rate, which is extrapolated from the sensitivity of the detectors at low count rates, to the measured count rate.

The images were reconstructed according to the parameters listed in Table 3. No artefacts were seen at high activities Figure 1 depicts the count rates obtained from 21 to 2593 MBq ^{131}I. The count rates were lower for head 1 due to the attenuation from the patient bed. The measured count losses with respect to the extrapolated count rates were comparable for each head.

a)



b)

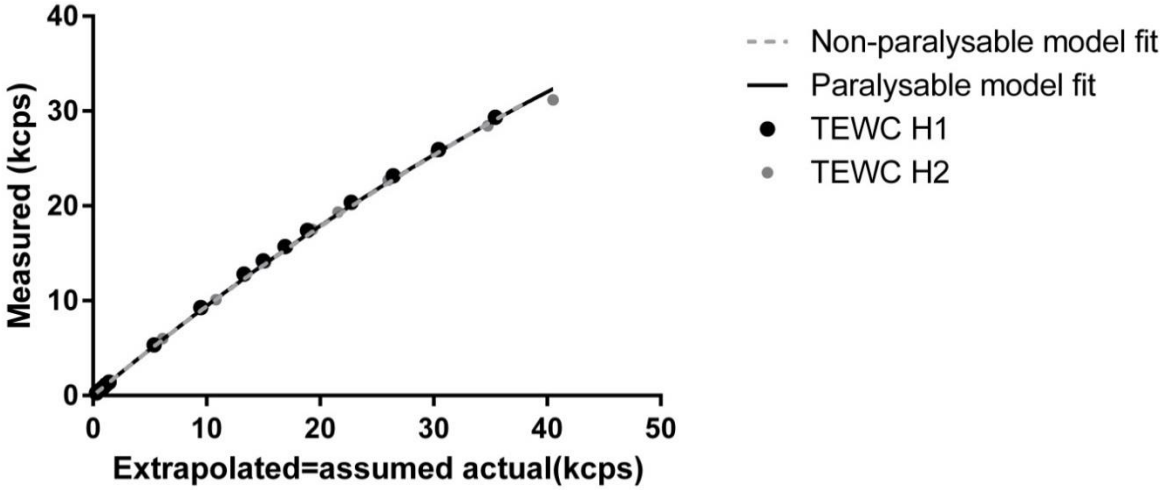


Figure 1 – measured TEWC photopeak energy window count rates a) for each head as a function of activity and b) as a function of the extrapolated count rate showing the paralysable and non-paralysable model fit.

The non-paralysable DT model provided a good fit to the extrapolated count rate versus the measured count rate. The non-paralysable DT correction factor is given by:

$$\frac{n}{m} = \frac{1}{(1-m\tau_n)} \qquad \text{Equation 1}$$

where n is the extrapolated count rate, m is the measured count rate (kcps) and τ_n is the non-paralysable DT of the system. A value of 0.0058 ± 0.00020 ms fit this data with an r^2 value of 0.992.

Additionally the paralysable model was fit to this data:

$$m = ne^{-n\tau} \qquad \text{Equation 2}$$

where τ is the paralysable DT of the system, calculated to be 0.0056 ± 0.00012 ms (standard error of 0.00016) with an r^2 value of 0.999.

The DT factors as a function of the measured count rate are shown in Figure 2.

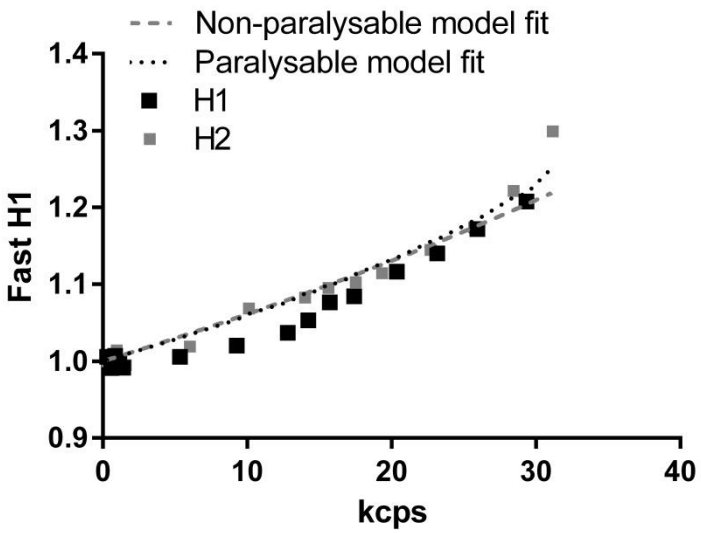


Figure 2 – DT correction factors.

For ease of implementation, and given the agreement between the two models, the non-paralysable DT correction factors are to be used with TEWC data at RMH NHSFT.

2.4.2 Partial volume correction factors

Calibration factors are needed to correct for partial volume and resolution effects that affect the activity concentrations measured in the reconstructed SPECT images. Factors were determined in accordance with the site set-up protocol for 1, 2, 3, 4, 5 and 6.3 cm diameter cylinders filled with an accurately determined concentration of ^{131}I positioned within a water-filled body-shaped phantom. The phantom was scanned according to the patient scanning parameters detailed in

Table 2.

Volumes of interest (VOIs) were delineated by specifying the physical dimensions of each cylinder and positioned to encompass the inner surface as seen on the CT image. The mean counts in each VOI were divided by the scan duration and cylinder activity concentration (0.24 MBq/ml) to give the count rate per unit activity concentration.

Figure 3 depicts an RMH NHSFT calibration curve for ^{131}I cylinders reconstructed with parameters listed in Table 3.

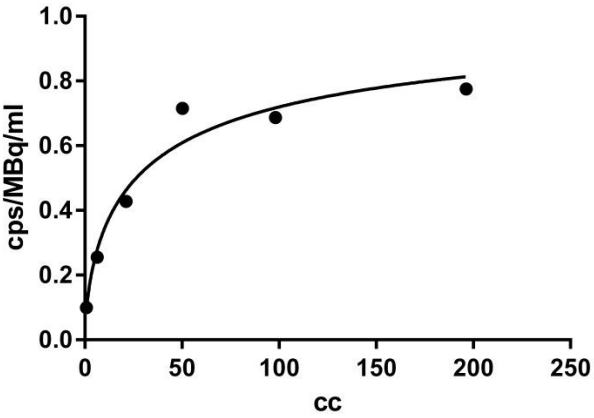


Figure 3 – ^{131}I SPECT image partial volume correction.

The PVE correction factors, RC, were derived by fitting the curve specified in Equation 3:

$$RC_{fit} = \frac{\alpha}{\left[1+\left(\delta/x\right)^{\beta}\right]}$$ Equation 3

where *x* is the cylinder volume and α, δ and β are fitting coefficients. α represents the plateau of the curve and was estimated from the total counts per voxel in an 8 cm cylindrical VOI positioned about the largest four cylinders divided by the activity concentration. α was constrained to 1.072 ± 0.0352 cps/MBq/ml. The coefficients of fit, β and δ were found to be 0.6379 ± 0.0949 and 32.53 ± 5.97 respectively.

2.5 WB retention monitors

Ceiling mounted detectors installed 2 meters above the patient bed are used in the determination of WB retention and absorbed dose. A compensated Geiger is used for high count-rate measurements and a NaI detector for low count-rate measurements. Both detectors are calibrated for ^{131}I and undergo a constancy check with a long half-life ^{226}Ra source on a weekly basis, in accordance with EANM guidelines (Sokole 2010).

2.6 Protocol development

2.6.1 Manufacturer dependent gamma camera performance at high count rates

The gamma cameras listed in Table 4 will be used in the acquisition of patient data.

Table 4 – Gamma camera models to be used in the acquisition of patient data at each centre.

	Camera 1	Camera 2
RMH NHSFT	Siemens Intevo SPECT/CT	Siemens Intevo SPECT/CT
UKW	Siemens Symbia T2 SPECT/CT	Siemens Intevo Bold SPECT/CT
UMR	Siemens Symbia S SPECT	
IUCT-O	GE Discovery 670 SPECT/CT	

Siemens gamma cameras switch to high count rate modes automatically. General Electric (GE) cameras require an engineer to set-up “fast mode” for each radionuclide to avoid saturation of the detector at high count rates. In setting-up GE cameras for high count rate ^{131}I imaging as part of the SEL-I-METRY trial the following issues have been noted when operating in “fast mode”:

- Linear degradation of image uniformity either side of the count rate used for calibration, which becomes clinically unacceptable (>3%) within 10 kcps of the calibration count rate.
- Increase in peak full-width-half-maximum (FWHM) with count rate to approximately 10% at 100 kcps.

Qualitative analysis showed event pile-up towards the centre of the photo-multiplier tubes (PMTs) at very high count rates as well as streaking between the centre of the PMTs, seen more prominently in the horizontal direction.

In February 2018 GE found a solution to this issue and, after recalibration, the systems now exhibit a constant uniformity with increasing count rate. RMH NHSFT will continue to collaborate with GE when setting up centres throughout Europe equipped with GE gamma cameras to ensure no further issues are encountered with “fast mode”.

2.6.2 Variations in local radiation protection rules

Through discussions with the other centres already recruited to this study it became apparent that the proposed method of calculating DT correction factors will not be possible. Due to local radiation protection rules all three centres restrict the activities of liquid ^{131}I that can be handled by staff to

less than 1 GBq. Patients recruited in these centres will be administered a nominal fixed activity of 3.7 GBq and, according to the patient acquisition protocol, could potentially be scanned as early as four hours post-administration.

In consultation with the other centres, a protocol has been developed to image 3.7 GBq ^{131}I in capsule form located within a scatter phantom. The phantom containing the capsule will be imaged at regular intervals as the activity decays (approximately eight weeks) to obtain the range of count rates depicted in Figure 1b.

2.6.3 Calibration factor validation

To demonstrate that reproducible quantitative accuracy is achieved with site specific calibration factors a validation will be performed. An anthropomorphic head and neck phantom, utilising non-spherical objects of varying activity concentrations to represent thyroid remnants and salivary glands, will be used for this validation. A low activity concentration will be added to the background to replicate the clinical scenario. The data acquired with this phantom will be used to determine intercentre reproducibility as well as quantitative accuracy.

2.6.4 Additional gamma counting equipment for blood samples

For 20 patients recruited at UKW regular blood samples will be collected to enable the calculation of the blood absorbed dose. The activity in the blood samples will be quantified within a well counter cross-calibrated to the dose calibrator as well as the SPECT/CT.

The well counter will be cross-calibrated to the dose calibrator, thereby achieving traceability to the relevant NMI, using three 0.2 mL aliquots, prepared from a stock solution with an activity concentration of 100 kBq/mL. The mean of the three count rate measurements and the known activity concentration, determined with the dose calibrator, will be used to determine the calibration factor of the well counter.

A 0.2 mL aliquot, taken from the stock solution used to calibrate the SPECT/CT, will also be measured in the well counter. Three measurements will be taken within two weeks as the aliquot decays, each measurement being at least 3-4 days apart. It will be ensured that each measurement of activity with the well counter is within ±5% of the decay corrected activity measured on the dose calibrator. Deviations greater than ±5% will result in recalibration of the well counter.

2.6.5 Reconstruction optimisation

The reconstruction parameters listed in Table 3 have been optimised to reach convergence for the smallest sphere for OSEM based reconstructions carried out on the Siemens Symbia workstation at RMH NHSFT. The reconstruction parameters will need to be optimised at each centre and will be dependent upon whether single or dual-modality imaging was utilised as well as manufacturer specific correction options.

Site specific optimised reconstruction protocols will be created by the local physicist to be used for reconstruction of all images related to this study. Each centre will also send raw data to IUCT-O for centralised analysis with commercially available software.

3. Conclusion

A protocol has been developed to enable sites across Europe to carry out quantitative imaging at high count rates of ^{131}I. This protocol was used to calibrate the equipment used in the acquisition of patient data at RMH NHSFT. In collaboration with other participating centres across Europe, the protocol was developed to take into account variations in equipment and local radiation protection procedures.

The development of this protocol allows the first European network able to perform standardised quantitative radioiodine imaging for dosimetry to be established.

4. References

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