MEDIRAD

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Guidelines and recommendations for quantitative I-131 imaging and dosimetry

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1. Introduction

The overall objectives of MEDIRAD Work Package 3 (WP3) are to develop and implement the tools necessary to establish, for the first time in a multicentre setting, the range of absorbed doses delivered to healthy organs in patients undergoing thyroid ablation and the threshold absorbed dose required for thyroid ablation. This will enable patient-specific treatment planning that will minimise the risk to the patient while ensuring a successful outcome.

The protocol for a future large-scale epidemiological study of the effect of low absorbed doses from the irradiation of normal organs by internal radionuclide sources will be developed as part of WP3. This will potentially allow individualised risk/benefit treatment planning for these procedures. As a preparatory step for future clinical trials and studies, recommendations and protocols have been developed for the calculation of absorbed doses from internal ^{131}I sources.

To achieve these objectives, the following aims were identified:

- Gamma camera characterisation for high activity quantitative imaging to enable standardised collation of quantitative image data and absorbed dose calculations obtained at different centres.

- Dosimetry and kinetic modelling for 100 patients to establish the range of absorbed doses delivered to thyroid remnants and to normal organs from fixed levels of administered activity.

As part of WP3, imaging and data collection study protocols were developed (D3.1). Furthermore, a report on the validation of centres for the imaging network (Deliverable 3.2) and results of the site set-up measurements were collated (Milestone 23). Recommendations and guidelines based on the findings of WP3 are provided in the following.

2. Guidelines and recommendations for quantitative I-131 imaging and dosimetry

2.1 Quantitative I-131 imaging in a multi-centre setting

Prior to each centre participating in a study, standardised pre-study gamma camera set-up and calibration measurements (including dose calibrator and gamma counters) should be performed for each camera to be used in the study. This will ensure that image data collected from each participating centre is consistent and that the absorbed doses computed based on these images will be comparable between sites. Experience from the MEDIRAD WP3 MRT clinical trials have shown that site set-up measurements may need to be adapted locally. Radiation protection guidance in different countries and centres varies substantially and may require specific changes to the site set-up protocols. These requirements should be discussed prior to the start of site set-up measurements to ensure standardisation across sites. Complexity and time required for measurements should be based on resources available at each centre.

Each site must have access to a SPECT or SPECT/CT system, which will be calibrated to correct for partial volume effects and dead time in ^{131}I imaging during a site visit. Standard operating procedures (SOPs) for the calibration of equipment including radionuclide calibrators, ceiling mounted monitors or dose rate meters to measure whole-body activity retention and gamma cameras for quantitative SPECT/CT should be developed. Those protocols should be developed based on the assessment of available resources and experience at each centre. (1)

As part of the development of those SOPs data anonymization and transfer should be decided upon to comply with data protection legislation such as the general data Protection regulation (GDPR) in the European Union.

Site set-up measurements should be performed according to National Electrical Manufacturers Association (NEMA) standards wherever possible. Furthermore accuracy of ancillary equipment in the quantification chain must be assessed as part of the process that will include clock synchronization, traceability of radionuclide calibrators and accuracy of weighing scales. (1) Radionuclide calibrators used should be traceable to an appropriate national primary standard.

Gamma camera and SPECT/CT calibration should be performed using similar correction methods for attenuation and scatter across centers. Site set-up protocols must, therefore, define the phantom set up, radionuclide activities to be used, acquisition and reconstruction parameters and analysis methods. In addition, sites should perform a range of quality assurance tests prior to the site set-up measurements. This may include Photopeak position, intrinsic uniformity for I-131 and Tc-99m, centre of rotation for the collimators used, SPECT/CT system alignment (if applicable), extrinsic collimator flood, QC of weighing scales and dose calibrators used in these measurements. For radioiodine, a gamma camera and SPECT/CT calibration protocol was proposed in Ref. (2) as part of WP3. The protocol includes dead-time, recovery curve and sensitivity measurements.

Recovery factors are required for the correction of partial volume and resolution effects in the reconstructed SPECT image. Measurements may be performed using a cylindrical IEC head phantom (inner diameter 19.7 cm, inner height 18.3 cm). Sphere inserts should be used which are large enough to ensure that the plateau of the recovery curve can be measured. In Ref. (2) the use of six 3D-printed sphere inserts was used with internal diameters of 1.0, 1.7, 2.8, 3.7, 5.0 and 6.5cm was proposed. Internal volumes of all spheres should be accurately measured using the weight difference of empty and filled spheres. Spheres should be filled with a solution of water, I-131, potassium iodide and sodium thiosulphate. The activity concentration in the spheres must be based on the expected activity concentration in tissues of interest.

System volume sensitivity used to assess the system's response to a uniform concentration of activity should be measured using a large cylindrical or body-shaped phantom with a volume greater than 6 liters. The volume of the phantom must be accurately measured using the weight of water required to completely fill the phantom. Total activity in the phantom should be low enough to avoid dead-time effects (i.e. 40 MBq in Ref. (2)).

Dead-time factors should be determined to correct the acquired image counts for counts lost due to detector paralysis. For details of dead-time measurement protocols see Refs (2, 3).

2.2 Imaging & reconstruction protocol

The dosimetry imaging parameters should be stored in a protocol on the SPECT system. Calibration factors will be specific to that protocol; therefore trial patient images are only to be acquired on systems that have been specifically set-up and calibrated. Adequate correction methods should be used for attenuation and scatter correction.

As part of MEDIRAD WP3 the following imaging protocol was developed for quantitative I-131 imaging:

- Collimator: High Energy (HE)
- Photopeak-energy window: 364 keV ± 10%
- Lower scatter-energy window: 318 keV ± 3%
- Higher scatter-energy window: 413 keV ± 3%

- SPECT(/CT) matrix: 128 × 128
- SPECT movement: Body contour
- Projections: 2 × 30 (6° projection)
- Time per projection: Adjusted based on patient activity in field-of-view
- CT: Standard low-dose protocol

A proposed I-131 imaging schedule is shown in Table 1.

Table 1: Post-RAIT patient dosimetry scanning schedule.

Hours post-^{131}I admin.	**Mandatory**	**Optional**
6 ± 2 h		WB planar and/or 1-2 bed SPECT(/CT)*
24 ± 4 h	WB planar	1-2 bed SPECT(/CT)*
48 ± 4 h	WB planar and 2-bed SPECT(/CT)*	
72 ± 12 h	WB planar	1-2 bed SPECT(/CT)*
96 ± 12 h	WB planar	1-2 bed SPECT(/CT)*
168 ± 24 h		WB planar and/or 1-2 bed SPECT(/CT)*

* SPECT(/CT) range: base of skull to top of thigh

To perform absorbed dose calculations for target and normal tissues, the acquisition of images over several days following therapy may be necessary. This may involve return trips to the hospital for patients depending on the length of the in-patient stay and may add to the workload of already busy departments. Image acquisition schedules should be standardised as much as reasonably practicable, but may therefore allow for local differences in the availability of resources and patient pathways.

Reconstruction should be performed using iterative reconstruction with the parameters optimised for a specific study or disease site. An example reconstruction protocol as used in Ref. (2) would be OSEM (4 iterations, 10 subsets) with CT attenuation correction (or Chang with 0.11 cm^{-1} @ 364 keV) and triple-energy window (TEW) scatter correction.

2.3 Lesion/organ dosimetry

SPECT images should be quantified and corrected for dead time as presented in Section 2.1. If WB, CT and SPECT DICOM images are anonymised for a study, all header data describing the SPECT(/CT) system used to acquire the data will need to remain. This will be required to apply the correct calibration factors.

Dosimetry can be performed for volumes-of-interest (VOIs) or on a voxel-by-voxel basis. For VOI-based dosimetry, the outlining techniques must be well defined and should be based on anatomical imaging in conjunction with visible uptake on the SPECT images (4). Outlining by a trained radiologist is advised.

Dosimetry methodologies developed for a clinical study should include appropriate uncertainty analysis and should either be standardised across centres or carried out at a central dosimetry hub. For further details refer to Ref. (2).

2.4 Whole-body dosimetry

Whole body retention measurements are used to calculate radiation protection restrictions and whole body doses. A ceiling mounted detector is recommended to facilitate reproducibility.

An initial background reading for 600 seconds should be acquired prior to the therapy administration. Immediately following administration, 60 second measurements for the patient lying prone and then supine should be performed. A second reading should be performed immediately after the first void. As many whole body retention measurements as practical should be performed to allow calculation of the absorbed dose with the maximum accuracy.

3. Dosimetry MRT multi-centre clinical studies recommendations

Clinical studies performed in a multi-centre setting are essential to ensure wider input into the trial design and data analysis and to collect sufficient data to achieve the statistical significance required. Authors from WP3 have provided a summary of the physics aspects of setting up a multi-centre clinical trial involving imaging-based dosimetry in Ref. (1). A quality assurance plan should be implemented to allow for the collation of results from the individual centres.

The following six recommendations were provided by authors of WP3 in Ref (5) to provide guidance on the set up and successful running of multicentre MRT studies, based on the experience of the multicentre MEDIRAD WP3 clinical study:

Recommendation 1: Clinical trial quality assurance plans, including the site set-up measurements and dosimetry, should be drawn up und implemented for any MRT clinical trials involving a component of dosimetry as it is routine practice in external beam radiotherapy.

Recommendation 2: Communication between key staff at each centre is essential to ensure that experience and resources are shared.

Recommendation 3: Standardisation of image acquisition and dosimetry protocols should be achieved as far as reasonably practicable. Nevertheless, local differences such as the availability of resources such as SPECT or SPECT/CT systems should be taken into account.

Recommendation 4: Standardised gamma camera calibration methodologies and image acquisition and reconstruction protocols should be developed to be used across trials with similar dosimetry aims.

Recommendations 5: Data transfer facilities for DICOM data and associated non-DICOM data should be set up. Non-DICOM data includes data collected on case report forms. Data transfer must be established and validated before the clinical trial commences.

Recommendations 6: Standardisation of dosimetry methodologies including uncertainty analysis should be achieved across sites participating in the trial. If this cannot be achieved, dosimetry calculations should be carried out at a central dosimetry hub.

4. Conclusion

As part of WP3, a site set-up protocol was developed for high-activity quantitative I-131 imaging which may be used in future studies. Furthermore, WP3 have developed imaging protocols and schedules for a patient cohort treated with I-131 for thyroid cancer. Dosimetry methodologies were developed and implemented in an open-source dosimetry software package.

5. Recommendation References

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