

EANM Dosimetry Committee guidance document: good practice of clinical dosimetry reporting

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Received: 30 June 2010 / Accepted: 4 July 2010
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Abstract Many recent publications in nuclear medicine contain data on dosimetric findings for existing and new diagnostic and therapeutic agents. In many of these articles, however, a description of the methodology applied for dosimetry is lacking or important details are omitted. The intention of the EANM Dosimetry Committee is to guide the reader through a series of suggestions for reporting dosimetric approaches. The authors are aware of the large amount of data

Electronic supplementary material The online version of this article (doi:10.1007/s00259-010-1549-3) contains supplementary material, which is available to authorised users.

These guidelines summarize the views of the Dosimetry Committee of the EANM and reflect recommendations for which the EANM cannot be held responsible. The recommendations should be taken in the context of good practice of nuclear medicine and do not substitute for national and international legal or regulatory provisions. The guidelines have been reviewed by the EANM Oncology Committee and the EANM Paediatrics Committee and have been brought to the attention of the National Societies of Nuclear Medicine.

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required to report the way a given clinical dosimetry procedure was implemented. Another aim of this guidance document is to provide comprehensive information for preparing and submitting publications and reports containing data on internal dosimetry. This guidance document also contains a checklist which could be useful for reviewers of manuscripts submitted to scientific journals or for grant applications. In addition, this document could be used to decide which data are useful for a documentation of dosimetry results in individual patient records. This may be of importance when the approval of a new radiopharmaceutical by official bodies such as EMA or FDA is envisaged.

Keywords Dosimetry · Targeted radiotherapy · Reporting

Introduction

As the number and breadth of nuclear medicine procedures expand, internal dosimetry is having an increasing impact on the development and clinical implementation of new and established radiopharmaceuticals. Comprehensive dosimetry studies of new radiopharmaceuticals are required to maintain the safety and the efficacy of diagnostic and therapeutic procedures. In addition, the licensing process for any new drug in nuclear medicine requires reliable and reproducible data on dosimetry.

A number of therapy procedures now take into account patient-specific dosimetry characteristics prior to treatment and in some cases administered activities are determined based on these calculations [1, 2]. It is becoming more widely recognized that, as with external beam radiotherapy, safe and effective treatment is dependent mainly on the absorbed doses delivered both to tumours and to critical organs.

In a recent communication, Nosedá and McLean [3] state that “if the aim of scientific publication is to disseminate scientific information that further advances our knowledge and to allow other researchers to use such information for expansion and possible improvements to the work, then every attempt should be made to include the most critical details in the published manuscript Many journals publish brief communications or short reports which, most likely owing to their small size and format, contain an extremely short methodology section or in many cases, no methodology at all to help explain exactly how the results were obtained by the investigators”.

Many recent publications in nuclear medicine contain data on dosimetric findings for existing and/or new diagnostic or therapeutic agents. However, in many of those articles, the description of the methodology applied for dosimetry is lacking or important details are omitted. At present, there are few guidelines regarding optimal practice of internal dosimetry, and methods can vary widely. A dosimetry study should allow reproducibility and possibly even improvement where results are promising, and can indicate when a ‘short cut’ in a procedure may introduce unnecessary and significant uncertainties. The validity of the results obtained from such a dosimetry study is dependent on the rigour and integrity with which such a study is reported.

Therefore, the purpose of this EANM Dosimetry Committee Guidance Document on “Good Practice of Dosimetry Reporting” is to provide recommendations to scientists and clinicians on how to *document* and *report* diagnostic, pretherapeutic and/or peritherapeutic clinical absorbed dose assessments. This includes the respective methodologies used for obtaining quantitative data, for generating activity–time curves and for calculating absorbed doses. Although diagnostic applications generally require less complex and accurate dosimetric methods than therapeutic applications, high-quality reporting is necessary in all cases. Preclinical dosimetry (i.e. cellular or animal) is not covered in this document, although concepts and recommendations presented here may also apply to that field.

The intention of these guidelines is to provide recommendations for reporting the data acquisition and processing necessary for dosimetry calculations, such that the methodology can be evaluated and reproduced. The description of or recommendations for optimal dosimetry methods are not the subject of this guidance document. A further aim of this document is to provide the reader with supplementary and comprehensive information for the preparation and submission of publications and reports containing data on internal dosimetry. A large amount of data are required to report a dosimetry procedure. In a clinical journal, data could be listed in appendices or - as

supplemental data - published online¹ as supplemental data. A general reference to dosimetry schema, for example the MIRD formalism, does not provide sufficient information to understand or replicate a dosimetry study.

The items addressed in these guidelines could also be used as a checklist by reviewers of manuscripts submitted to scientific journals or grant applications or for documentation of dosimetry results in individual patient records. This may be of importance when the approval of a new radiopharmaceutical by official bodies such as EMA or FDA is envisaged.

A prerequisite for generating data for dosimetric studies is the rigorous implementation of adequate quality control procedures as specified by, for example, the EANM guidelines on “Routine Quality Control Recommendations for Nuclear Medicine Instrumentation” [4]. This includes an appropriate documentation of the procedures and results.

A checklist containing questions with respect to all the suggested documentation is given in the [Appendix](#).

Suggested documentation

Equipment

General remark

All imaging and nonimaging devices used should be listed including manufacturer details.

Rationale If the manufacturers and devices are known it is easier for the reader to reproduce the data and to evaluate if the device is suited to fulfilling the technical requirements for the intended study.

Probe measurements

For quantification of whole-body retention, measurements are sometimes performed using an external probe. The following items should be documented:

- The operational mode of the probe (e.g. a simple counter or the use of gamma spectroscopy system) should be specified.
- If the probe is shielded and/or collimated, the geometric properties of the shielding/collimation (e.g. the thickness of the shielding or the useful field of view) should be given.

¹ In some journals it is also possible to submit additional material that also offers an opportunity to keep the manuscript short but provides enough detail for a proper evaluation of the methodology and the results.

- The geometry of the patient measurement should be described. This should include whether a fixed patient counter geometry is used, or whether the probe is hand-held. The patient orientation relative to the detector should also be given (e.g. whether the patient is supine, prone, or standing for anterior and/or posterior counting).
- An estimate of the Poisson noise propagation caused by patient and background count statistics should be provided.
- If more than one reading is taken at each time-point, the calculation used to return the mean value used should be given (e.g. arithmetic or geometric mean).

Rationale The sensitivity range of the device should be chosen such that the count loss due to dead-time effects can be accounted for and low activity measurements can be performed with the appropriate accuracy. Ideally, the count rate behaviour of the system should be known, and, if relevant to the purpose of the study, reported.

The geometric mean of anterior and posterior measurements can produce more accurate results than either used in isolation, particularly if the activity is not homogeneously distributed in the patient. The inverse square law effect can introduce large errors if sequential patient measurements are not performed with reproducible geometry.

Remarks

- Spectroscopy systems in high count rate situations might lead to erroneous data when using the built-in dead time corrections.
- Care should be taken to set up reproducible patient geometries.

Well counter measurements

Nonspectroscopic in-vitro measurements are no longer considered to be state-of-the-art. The geometry of the sample, the background, sensitivity and the window settings of the device should be documented. If peak-fit algorithms are used for the calculation, details or a reference should be given.

Rationale Erroneous measurements or faulty pieces of equipment can easily be detected when using gamma spectroscopy. Some well counters show a strong dependency on geometry. Care should be taken to set up reproducible sample geometries.

The use of peak-fitting algorithms, particularly for NaI detectors, might lead to erroneous results for overlapping peaks or for nuclides with several gamma rays due to the limited energy resolution of this type of detector.

Dose calibrators

The proper use of dose calibrators and the corresponding measures for determining the accuracy and linearity of the system, as well as for guaranteeing the traceability of activity, should be provided (e.g. the regular use of a traceable standard). Corrections applied to the equipment standard settings should also be given such as specific calibration factors.

Rationale Measurements should be traceable to a national or international standard. In addition, some isotopes (e.g. ^{90}Y , ^{123}I , ^{124}I) show a reading that is very strongly dependent on vial volume and height and syringe/vial ratio.

Gamma cameras

All gamma camera types, including details of the manufacturers and model (including year of manufacture), should be listed. This includes the number of heads, the crystal thickness and the collimator type used. The model variant should also be given where applicable, as should any relevant additional hardware used with the system. Information on the acquisition and processing software used (manufacturer, package, version) should also be provided.

Image quantification

Acquisition settings

The equipment parameters (i.e. number of heads used and matrix/pixel size), energy windows (number, thresholds), acquisition time and stopping conditions (i.e. count-based or time-based acquisitions) should be documented. For SPECT the number of projections, the orbit type and the rotation parameters (step and shoot vs. continuous, circular vs. noncircular, 180° vs. 360°) should be specified.

Phantom and calibration measurements

The phantom type (possibly manufacturer, volume, shape, if used in air or in scattering medium), the method of calibration (e.g. the conversion factor) and the respective activities used (e.g. in simulated tumours) should be specified in detail. It should also be stated if an absolute or a patient-relative calibration is used.

Rationale Sometimes a series of phantom measurements including known activities are performed and used for quantitative studies. Phantom specifications enable the assessment of the quality of the quantification process, especially when case-specific phantoms are constructed (e.g. see Lassmann et al. [5]).

If a patient-relative calibration is adopted, a detailed description of the method for ROI drawing (including the whole body or only the trunk, or other choices) is required, as well as other assumptions (e.g. fraction of activity in the trunk).

Sequential imaging

The methods for excluding variations in image quality and assuring reproducibility of patient positioning in subsequent imaging should be documented. If a standard of known activity is used this should be reported. If different pieces of equipment were used during sequential imaging, it must be stressed if and how results were made comparable.

Rationale The set-up of the equipment and the positioning of the patient might vary on a daily basis. The use of a standard source on sequential images could be used for improving the quality control procedures and/or the quantification (e.g. a thyroid phantom in the case of thyroid scans).

Conjugate view method

If, for planar imaging, the conjugate view method is applied, details should be provided on the methodology (e.g. ROI size and location, variations in ROI size). If corrections are applied to the quantification of activity in overlapping organs the corresponding methodology should be given. If, for some organs or organ systems, the conjugate view method is not used, the method used for attenuation correction should be described.

Rationale The use of pixel-wise conjugate views or organ-specific conjugate views in conjunction with transmission measurements or the use of external data such as CT for attenuation correction will heavily influence the quantification process. The quantification of organ uptake in planar images—particularly in the abdomen—is greatly influenced by the correction method for overlapping organs (e.g. kidneys and liver, see Jonsson et al. [6]).

Processing parameters (PET/SPECT)

If PET or SPECT is performed for quantification, the reconstruction method and the parameters used (cut-off frequency, number of iterations, number of subsets, post-filtering type and parameters) should be given. In addition, the reconstruction software manufacturer and version should be mentioned explicitly.

Rationale There is a strong influence of the image reconstruction method on the results (see, for example,

references [7–9]). Different methods of image reconstruction for a series of images (e.g. applying filtered back-projection for the first image and iterative reconstruction for the subsequent images) may lead to inaccurate and potentially nonreproducible quantification. In addition, references of image workstation/software, commercial or not, should be given in order to increase traceability and reproducibility.

Background correction (planar imaging)

It should be stated if and how background correction was performed on images.

Rationale For many radionuclides unspecific uptake (e.g. blood pool) can be observed. This contribution needs to be corrected for when quantifying organ uptake.

Attenuation correction

It should be stated if and how attenuation correction was performed on images.

Rationale There are many different ways of performing attenuation correction (e.g. the use of a transmission source for planar imaging or CT for SPECT). Presently there is no standard methodology for performing attenuation correction and the results may be greatly influenced by the way attenuation correction is done.

Scatter correction

It should be stated if and how scatter correction was performed on images.

Rationale There are many different ways of performing scatter correction (e.g. double energy or triple energy window techniques; see references [10, 11]). Presently there is no standard methodology for performing these corrections and the results may be greatly influenced by the way these corrections are done. Additionally, the way a specific scatter correction methodology was implemented (i.e. window width, window centre, correction coefficient, correction position within the processing algorithm, etc.) should be explicitly mentioned for the same reasons.

If pairs of isotopes (e.g. $^{90}\text{Y}/^{111}\text{In}$) are administered the methodology for correcting for cross-talk should be described.

Partial volume effect correction

It should be stated if and how the partial volume effect correction was performed on images.

Rationale For objects that are in the order of the system resolution or smaller the activity might be underestimated when no correction for the partial volume effect is performed [7, 12, 13].

Dead-time correction

When imaging of high activities is required (e.g. for peri-therapeutic dosimetry) the method for dead time correction should be indicated. The corresponding validation method should also be described.

Rationale When using gamma cameras in situations of high count rate, the dead-time or the manufacturer-implemented dead-time corrections might not give correct results (see reference [14] or [15]).

PET – Correction for “dirty” nuclides

It should be stated if and how corrections are made for nuclides with additional gamma emissions that will be detected within the coincidence window of the detector.

Rationale Standard quantification procedures for PET have been developed for ^{18}F -FDG and are not equally applicable to isotopes such as ^{86}Y and ^{124}I [16, 17]. It should be clearly stated if corrections were applied and if these were applied how they were implemented.

Biokinetics

Number of data points

The number and timing of data points acquired for either probe measurements or image data for each patient should be documented.

Rationale The accuracy of activity–time measurements from which dosimetry is calculated depends on the sampling of the data. Ideally, a minimum of three data points per phase are required to enable error estimation, and the accuracy of this estimation depends on the timing of these samples as well as on data integrity.

Suggestions for the optimal sampling time points for thyroid cancer dosimetry are given in the recommendations of the EANM Dosimetry Committee [18].

Fitting and integration procedures

The fitting and integration procedures should be given. A numerical value for the statistical fit criterion (such as chi-

squared) and the errors of the fit parameter should be documented for each patient.

Rationale The choice of the fit function and the result of the fit may greatly influence the integration of the activity–time curve and, subsequently, the calculation of the absorbed dose as has been shown, for example, by Flux et al. [19].

Extrapolation

Procedures for data extrapolation before the first and beyond the last data point acquired should be given. If a compartmental model is used, details of the model and the results of the fit procedures need to be described.

Rationale The procedure for data extrapolation influences the result. Estimating uptake function before the first point will also lead to inaccuracies. Using physical decay after the last data point is a conservative estimate (suited to radiation protection), but might not lead to the optimal results.

Remark Examples of how to choose the optimal fit function are given by, for example, Divoli et al. [20] and Glatting et al. [21].

Residence times

It is useful if the residence times for each patient are given individually.

Rationale If the residence times for each patient in addition to the administered activities are published a reanalysis of the patient data is feasible if new or different dosimetry and calculation methods become available.

Remark According to MIRD pamphlet 21 (“A generalized schema for radiopharmaceutical dosimetry – standardization of nomenclature”), “residence time” is replaced by “time-integrated activity coefficient” [22].

Dosimetry calculations

S-values

The source of the S-values - when using the absorbed fraction method² - should be documented. If other calculation methods for the calculation of the energy deposition patterns and geometric properties are used, detailed information on the computer codes used and the respective radiation transport parameters should be given.

² Traditionally called “MIRD scheme“ or “MIRD method“

Rationale The accuracy of absorbed dose calculations relies on the accuracy and proper use of S-values. For organ/tumour mean absorbed dose calculations, the use of tabulated standard S-values with patient-specific organ mass corrections might be sufficient. The use of standard S-values without organ mass corrections in the context of targeted radiotherapy dosimetry is considered poor practice [23].

If the scope of the study requires the determination of absorbed dose gradients within a given organ/tissue, i.e. a voxel-based calculation, the computing approach (type, code) and the corresponding validation process should be reported.

Mass (or volume) determination

For individual mass (or volume) assessments of organs/lesions the respective methods should be provided. If density corrections are applied, they should also be reported. In case of differences between the morphological and the functional volume of organs or lesions, the volume chosen for dosimetric calculation should be described, as well as the reason for that choice.

Rationale The accuracies of different methods for organ/lesion mass determination vary considerably and depend strongly on the quantification method. A detailed discussion of the use of SPECT/PET for volume determination can be found in the ICRU report 67 [24].

Tumour dosimetry

Data should be provided on how the absorbed dose to a specific tumour or lesion in a patient was calculated.

Rationale In many publications the self-dose of a radionuclide in a homogeneously filled sphere is used as a first-order approximation of a tumour. An example of this application is the use of the sphere model of OLINDA/EXM [25] which only provides tumour self-doses for spherical tumours, and does not provide data on tumour cross-doses to or from other organs. Lesions/tumours, however, can vary in shape and size; therefore, if other geometries are considered this information should be given (see, for example, reference [26]). Details of the methodology used to determine the tumour volume should be given.

Absorbed doses (results)

The results of the absorbed dose calculations in individual patients should be given. If the results are expressed in Gy/MBq, then the injected activity should be reported. If dose–volume histograms or isodose curves are calculated the results should be provided.

Rationale In many published articles only mean values (and or ranges) for organ absorbed doses are given. Sometimes even the residence times are averaged before the actual absorbed dose calculation. Tabulating these data allows the reader to draw his/her own conclusions as to the validity of the assessments of the absorbed dose. A proper assessment of the measurement uncertainties and the uncertainties associated with the subsequent calculations should be considered as a basic scientific standard.

If commercially available computer codes (e.g. OLINDA/EXM) are used it should be stated which code and version and, if applicable, which variables and/or input data (e.g. the kind of phantom, the input data, the mass corrections) have been used for the calculation of the absorbed dose.

The calculation of dose–volume histograms or isodose curves provides a measure of inhomogeneous dose distributions.

Remark If radiobiological calculations are performed (see below) the physical quantity “absorbed dose” should also be provided.

The number of significant digits in the resulting values for absorbed doses should not exceed the errors of the underlying process.

Statistical errors

If possible, error margins including the results of a propagation of error calculation should be included.

Rationale Many dose calculations rely on experimental data that have uncertainties due to measurement limitations (e.g. instrument uncertainty). In some cases the data are modelled by an analytical fit function in order to obtain the area under the curve. The uncertainties of the experiment are propagated in this process.

One would expect that, in the near future, a rigorous calculation of the propagation of error (or propagation of uncertainty), including the fit process, will be performed and the errors reported.

Radiobiological parameters

When using the “biologically effective dose” (BED), or the “equivalent uniform dose” (EUD), the radiobiological parameters applied should be reported as well as their source and the reason for that choice. The formula for the calculation should also be reported.

Remark A description of the basic radiobiological formalism in the context of internal dosimetry is given by Dale [27] and O’Donoghue [28].

Miscellaneous

Confounding factors

In some cases confounding factors such as the use of recombinant human TSH in the case of differentiated thyroid cancer or renal protection agents (e.g. sometimes used during treatments with radiolabelled peptides) might alter the biokinetics of a given radiopharmaceutical. This information should be provided.

External audit

It should be stated if an external audit of the data and the calculation procedures (including processing software) has been performed. A successful external audit will raise the confidence of the reader with respect to the results.

Choice of radionuclide and radiopharmaceutical

When using different isotopes for pretherapeutic dosimetry and for therapy the possible deviations in biokinetics need to be discussed.

Units

Are the units used appropriate for the purpose? Are all units SI units? The publication of absorbed doses describing deterministic radiation effects should be clearly separated from the use of dosimetry when reporting stochastic effects of ionizing radiation.

Remark The degree of accuracy needed for dosimetry differs between the diagnostic use of a radiopharmaceutical and its use for therapy. Often the stochastic effects are described by the “effective dose” (units millisieverts) utilizing conservative estimates and extrapolations in this context. For reporting deterministic effects, the absorbed dose should be given in gray, possibly corrected for dose rate and fractionation using the BED, in a realistic dose calculation model.

Conclusion

These guidelines on reporting dosimetric methods and results provide a comprehensive overview of the acquisition and processing of images quantitatively for dosimetric purposes and of the subsequent steps needed for a proper dosimetric assessment of nuclear medicine diagnostic and therapeutic agents. Applying the checklist given in the [Appendix](#) will guide the authors of reports and publications through the necessary steps so that the reproducibility of the

results will be warranted and other researchers will be enabled to use such information for expansion and possible improvements to the work.

Acknowledgment This work was developed under the close supervision of the Dosimetry Committee of the EANM (K. Bacher, M. Bardiès, C. Chiesa, G. Flux, M. Konijnenberg, M. Lassmann, S. Palm [observer from the IAEA], S.-E. Strand, and L. Strigari).

We would like to thank S. Baechler, A. Chiti, M. Guy, C. Greaves, and the national societies of nuclear medicine for their helpful comments and suggestions.

Appendix: Documentation checklist

Procedure	Yes	No
Probe Measurements		
Is the probe used as a simple counter?		
In conjunction with gamma spectroscopy?		
Is the probe shielded and/or collimated?		
Are the geometric properties of the shielding/collimation given?		
Is the geometry of the patient measurement given?		
Are the background counts without any sources present given?		
Are the sensitivity and the window settings documented?		
Is the sensitivity range of the device provided?		
Are the dead time characteristics of the system known?		
Well Counter Measurements		
Are the geometry of the sample, the background, sensitivity and the window settings of the device documented?		
Dose Calibrators		
Are the QC procedures implemented and documented?		
Are measurements performed with traceable calibrated sources?		
Are the appropriate corrections for geometry dependencies done?		
Gamma-Cameras		
Gamma camera make (name of the manufacturer) and model (+ year)		
Crystal thickness		
Energy window(s) (number + range of each)		
Pixel size / Matrix size		
Number of heads used for the acquisition		
Software version		
Collimator		
Stopping conditions		
ROI location and size		
Corrections for overlapping organs		
Background correction		

Table (continued)

Procedure	Yes	No
Method of scatter correction		
Method of attenuation correction		
Dead time correction		
SPECT		
Number of projections		
Orbit type		
Rotation parameters		
Reconstruction parameters		
Software used		
Partial volume effect correction		
PET		
Correction for “dirty” nuclides		
Phantom and Calibration Measurements		
Method of calibration		
Phantom type		
Activities used		
Biokinetics		
Number of data points for each patient		
Fitting procedures incl. error of fit parameters		
Treatment of the AUC before the first and after the last data point		
Residence Time		
Given for each patient individually?		
Dosimetry Calculation		
Computer and software		
Source of S-Values		
Mass determination – described how?		
Tumour dosimetry performed and described how?		
Is geometric or cross-talk corrections to tumour dosimetry applied?		
Propagation of error calculation performed		
Miscellaneous		
Is the choice of nuclides justified?		
Is there an external audit?		
Are the units used appropriate for the purpose?		
Are the confounding factors included?		

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