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Health informatics — Datasets and data structure for clinical and biological evaluation metrics in radiotherapy

Informatique de santé — Jeux de données et structure de données pour les métriques d'évaluation clinique et biologique en radiothérapie

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Foreword

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This document was prepared by Technical Committee ISO/TC 215, *Health informatics*.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

Radiotherapy or radiation therapy is a treatment method used mostly in cancer care. Due to rapid technical advances of the radiotherapy treatment modalities, it is becoming increasingly important to select an appropriate radiotherapy treatment modality for individual patients by considering patient conditions and the resources that are required.

In the case of external-beam radiation therapy (EBRT), where the therapeutic radiation beams are emitted from a machine outside the body of the patient, treatment planning is performed prior to treatment. When selecting a treatment modality from among possible candidates, treatment plans are made for the candidates, if necessary, and then the dosimetric indices and/or radiobiological metrics corresponding to the treatment plans are compared.

Tumour control probability (TCP) and normal tissue complication probability (NTCP) are among the metrics used in the comparisons. They are simple phenomenological models based on clinical observations which are described in ICRU 83[12] as clinical and biological evaluation metrics (CBEMs), along with other metrics such as equivalent uniform dose, conformity and homogeneity indices. Recently, more sophisticated models incorporating non-dosimetric patient factors, spatial dose metrics and -omics elements (e.g. radiomics and proteomics) have also received attention and some of them are starting to be referred to in clinical trials in some countries.

For wider and safer use of CBEMs in clinical practice and clinical trials, it is important to provide an effective framework for ensuring the traceability of calculated metrics. Standardization of data formats for reporting calculated CBEMs is one possible way. However, no attention has been paid to such standardization to date, while there is active research on new metrics or new models as well as increasing attention to transparent reporting of developed models.

This document describes datasets and data structure for the reporting of CBEMs, especially of simple model types of TCP and NTCP. Scientific aspects of reliability of CBEMs are not in the scope of this document. Because of the variety of CBEM models, when an evaluated CBEM is to be reported and/or referred to, it is important to report and/or refer to the value of the calculated CBEM along with information about the CBEM model itself as well as with dose information and non-dosimetric factors of the patient that are used in the calculation. It is also important to include descriptions about uncertainties, underlying assumptions, limitations and situations for application of the CBEM model. In general, the dose information of the treatment plan used in the calculations (dose-volume histogram (DVH) in most cases) is converted to match the model definition; for instance, adjusting the differences in fraction size between the plan of the patient and the reference fraction size of the CBEM model. This means that the apparent values of the doses (e.g. maximum dose and mean dose) used in the calculation are CBEM-model-specific. To ensure traceability, inclusion of the description about the process of such dose conversions along with the value of the representative dose values would be a great help. This document provides datasets and data structure for CBEM reporting by considering the above mentioned aspects.

While this document is not intended to cover the reporting of CBEMs by contemporary sophisticated models, the data structures described in this document can apply to the reporting of them as well.

Health informatics — Datasets and data structure for clinical and biological evaluation metrics in radiotherapy

1 Scope

This document reports on the datasets and a data structure for reporting clinical and biological evaluation metrics (CBEMs). The reporting of radiation dose estimates is outside the scope of this document.

This document is applicable to CBEMs for external-beam radiation therapy (EBRT) modalities, but not CBEMs for brachytherapy or molecular radiotherapy.

Various types of radiotherapy treatment modalities are available for cancer care. Consequently, there is a growing awareness of the need for objective schemes that will contribute to enable the selection of an appropriate radiotherapy treatment modality for individual patients. The use of CBEMs, the metrics associated with a certain radiotherapy treatment plan for a patient, is attracting attention for clinical purposes in the field of EBRT. In anticipation of the clinical use of CBEMs, the importance of research on clinical and scientific aspects of CBEMs is increasing, in concert with the importance of establishing a standardized data format for reporting of specifics of a CBEM.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

3.1
data element
unit of data that is considered in context to be indivisible

Note 1 to entry: The definition states that a data element is “indivisible” in some context. This means it is possible that a data element considered indivisible in one context (e.g. telephone number) can be divisible in another context (e.g. country code, area code, local number).

[SOURCE: ISO/IEC 11179-1:2023, 3.3.4, modified — Example deleted.]

3.2
Digital Imaging and Communications in Medicine
DICOM
standard for the communication and management of medical imaging information and related data

Note 1 to entry: The DICOM Standard facilitates interoperability of medical imaging equipment.

Note 2 to entry: DICOM is defined in ISO 12052.

[SOURCE: ISO/IEC 39794-16:2021, 3.16]

3.3
dose fractionation
method of administration of radiation in which the absorbed dose is divided into two or more fractions separated in time

[SOURCE: IEV ref 881-11-18]

3.4
dose-volume histogram
DVH
dose as a distribution-function or frequency-function over a specified volume

[SOURCE: ICRU 50, modified — Abbreviated term "DVH" added.]

3.5
endpoint
<primary> principal indicator(s) used for providing the evidence for clinical performance, effectiveness or safety in a clinical investigation

[SOURCE: ISO 14155:2020, 3.22]

3.6
intensity-modulated radiation therapy
IMRT
treatment procedure requiring, in general, the coordinated control of photon or electron fluence, beam orientation relative to the patient, and beam size of the external beam, either in a continuous or a discrete manner, and as pre-determined by a *treatment plan* (3.12)

Note 1 to entry: The primary purpose of IMRT is to improve the conformity of the dose distribution to the planned target volume, while minimizing dose to surrounding healthy tissue.

[SOURCE: IEC 60976:2016, 3.2.7]

3.7
numerical value equation
numerical quantity value equation
mathematical relation between numerical quantity values, based on a given quantity equation and specified measurement units

[SOURCE: ISO/IEC Guide 99:2007, 1.25, modified — Examples deleted.]

3.8
radiotherapy
radiation therapy
therapy that uses ionizing radiation to kill cells and shrink pathological tissues

Note 1 to entry: Radiation may be delivered by a machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body near cancer cells (brachytherapy) or from radiopharmaceutical administered to the patient (molecular radiotherapy).

[SOURCE: ISO 12749-6:2020, 3.3.2]

3.9
radiotherapy treatment planning system
RTPS
device, usually a programmable electrical medical system including its associated peripherals, that is used to simulate the application of radiation to a patient for a proposed radiotherapy treatment

Note 1 to entry: It usually, but not necessarily, provides estimations of absorbed dose distribution in human tissue using a particular algorithm or algorithms. These algorithms provide simulations of radiation that is typically from, but not necessarily limited to, medical electron accelerators, gamma beam therapy equipment, or in brachytherapy from radioactive sources.

[SOURCE: IEC 62083:2009, 3.1.6]

3.10
region of interest
ROI
sub-dataset picked out from the entire dataset for a specific purpose

[SOURCE: ISO 20263:2017, 3.1.24]

3.11
relative biological effectiveness
RBE
<of radiation> ratio of the absorbed dose of a reference radiation to the absorbed dose of the radiation of interest, generally X-ray or gamma ray, that produces the same level of biological effect

Note 1 to entry: The term should only be used in radiobiology.

[SOURCE: IEV ref 881-17-03]

3.12
treatment plan
all patient and dosimetric information that is intended for use by appropriately qualified persons for the purpose of prescribing or administering *radiotherapy* (3.8), including any information to be transmitted to other equipment

Note 1 to entry: A printed or plotted treatment plan is referred to as a treatment plan report.

[SOURCE: IEC 62083:2009, 3.1.8]

3.13
treatment planning
process of establishing the *treatment plan* (3.12)

[SOURCE: IEC 62083:2009, 3.1.9]

4 Abbreviated terms

CBEM	clinical and biological evaluation metric
CI	confidence interval
DICOM	Digital Imaging and Communications in Medicine
DVH	dose-volume histogram
EBRT	external-beam radiation therapy
IMRT	intensity-modulated radiation therapy
LOINC	Logical Observation Identifiers Names and Codes (Regenstrief Institute, Inc.)
NTCP	normal tissue complication probability
RBE	relative biological effectiveness
ROI	region of interest
RTPS	radiotherapy treatment planning system
TCP	tumour control probability

5 CBEMs in EBRT

5.1 General

EBRT is a form of radiotherapy for delivering a beam or beams of ionizing radiation from outside the body of patients. There are several different types of modalities of EBRT (EBRT modality) regarding beam types and ways of forming dose distributions in the patient body, each provided by a specific device or system. For specific patients, a suitable EBRT modality is selected among those available by considering the patient condition and the resources required. Recently, the use of CBEMs for treatment plans of EBRT has been gaining attention in clinical practice and for research purposes.

5.2 CBEMs

In ICRU 83[12], the concept of CBEM is described in the section of "Level 3 Reporting" for intensity-modulated radiation therapy (IMRT). IMRT is one EBRT modality, however, the described concept of the CBEM can also be applicable to other EBRT modalities. In ICRU 83[12], TCP, NTCP and combination metrics of TCP and NTCP are described. This document examines TCP and NTCP as CBEMs but does not examine combination metrics of these two.

The CBEM is a metric which is associated with a treatment plan. Multiple CBEMs can be associated with one treatment plan, e.g. on metrics for different endpoints and/or by different CBEM models.

A schematic figure of the calculation process of a CBEM is shown in Figure 1. A CBEM is calculated using a CBEM model which is expressed as one or multiple numerical value equations. The input to the equations is the radiation dose information of a region of interest (ROI) for a treatment plan, which corresponds to the definition of the CBEM model. In particular cases, it can be multiple ROIs. If the model requires information regarding patient factors, this is also input for the calculations.

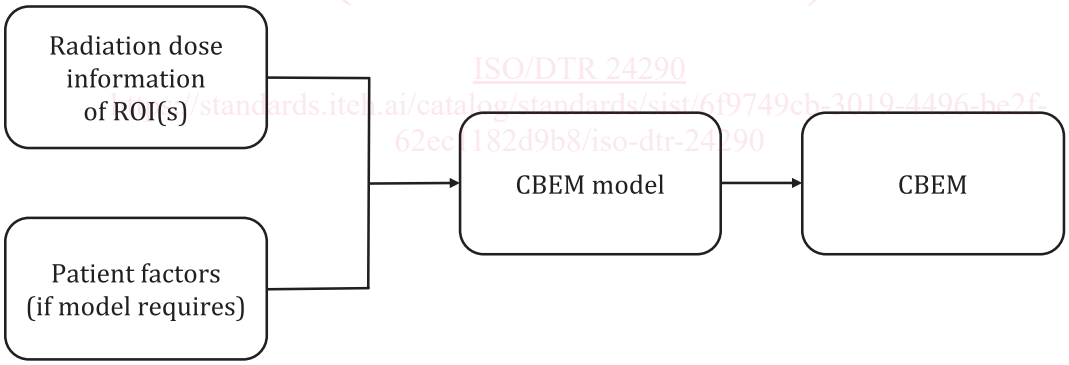


Figure 1 — Schematic of the CBEM calculation process

When the type of a CBEM is TCP, the ROI is the tissue volume that contains the tumour to be treated, depending on the definition of the TCP model. When the type of a CBEM is NTCP, a ROI is one or plural of normal tissues near the tumour. Radiation dose information of a ROI typically is either of the DVH, or one or more dose-volume indices specific to the CBEM model. Examples of such values include average doses, maximum doses or indices calculated from the DVH.

Before being input in the CBEM calculations, it is necessary to consider conversion of radiation dose information (dose conversion) under appropriate assumptions. Examples of such considerations include but are not limited to dose conversions in relation to the differences in radiation beam types and treatment schedules (number of fractions and prescription doses per fraction) between the target plan for the CBEM calculations and plans used for participants in the CBEM model development study. Scientific aspects of dose conversions are not covered in this document, however, data elements for narrative descriptions of assumptions in connection with dose conversions are provided in the datasets described in this document.

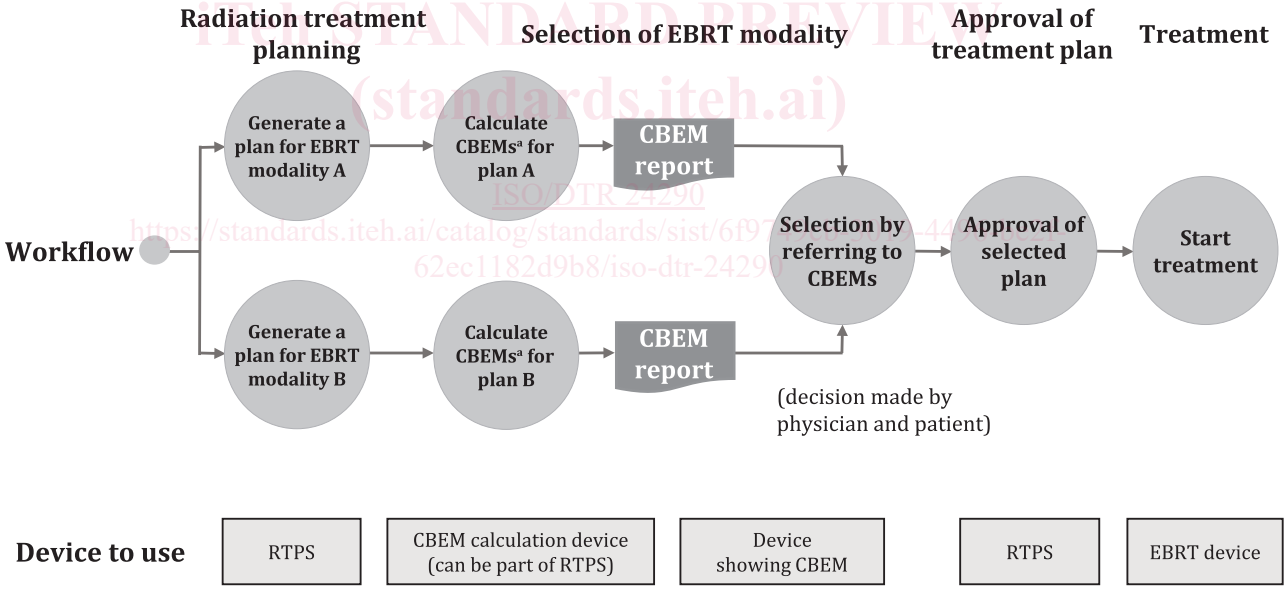
Examples of patient factors for CBEM calculations include information related to age, sex, diagnostics of the disease and pre-treatment health conditions. In most cases, these are treated as dummy variables (i.e. 0 or 1) in the calculations of the CBEMs.

5.3 Use case of CBEMs

5.3.1 Selection of the EBRT modality

An example of the workflow for selecting an EBRT modality for a specific patient by referring CBEMs is shown in Figure 2. For the patient, treatment plans for two candidate modalities A and B are generated by qualified persons such as physicians and medical physicists, by using different radiotherapy treatment planning systems (RTPSs). Information of the treatment plans is stored in the RTPS as electronic files. The information for this can be assessed by a CBEM calculation device through the file server functions of the RTPS.

For the two treatment plans, CBEMs, namely TCP and NTCP, are calculated by a qualified person using the CBEM calculation device. Through the graphical user interface of the CBEM calculation device, the qualified person(s) carefully selects the CBEM models suitable for the patient and the treatment plans, and then performs dose conversions by considering assumptions based on relevant aspects. The calculated results of the TCPs and NTCPs are stored as electronic files, as CBEM reports for the respective treatment plans. In the CBEM reports, the detailed information of the used models, the underlying assumptions of the models, information of the treatment plans, assumptions and adopted schemes for dose conversions, and some patient factors are included.



[a] CBEMs: TCPs and NTCPs about different complications. The same CBEM models are used for both treatment plans.

Figure 2 — Use case of CBEMs in the selection of an EBRT modality for a patient

Then the information in the CBEM reports for the two treatment plans are shown through a CBEM referring device by the same or different qualified person(s), possibly with the patient, to decide which EBRT modality or treatment plan to select. The selected treatment plan is approved, and it is used for the treatment.

5.3.2 Clinical trials

In clinical trials, CBEMs can be used to stratify patients into different risk groups, reduce the bias related to the type of EBRT and improve objectivity. However, before using the CBEMs for these purposes, it is