Radiotherapy and Oncology xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Review

The influence of tissue composition uncertainty on dose distributions in brachytherapy

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ARTICLE INFO

Article history:
Received 29 August 2017
Received in revised form 31 December 2017
Accepted 5 January 2018
Available online xxxx

Keywords:
Review
Brachytherapy
MBDCA
Elemental composition
Tissue heterogeneity
Mass energy-absorption coefficient

ABSTRACT

Background and purpose: Model-based dose calculation algorithms (MBDCAs) have evolved from serving as a research tool into clinical practice in brachytherapy. This study investigates primary sources of tissue elemental compositions used as input to MBDCAs and the impact of their variability on MBDCA-based dosimetry.

Materials and methods: Relevant studies were retrieved through PubMed. Minimum dose delivered to 90% of the target (D_{90}), minimum dose delivered to the hottest specified volume for organs at risk (OAR) and mass energy-absorption coefficients (μ_{en}/ρ) generated by using EGSnrc "g" user-code were compared to assess the impact of compositional variability.

Results: Elemental composition for hydrogen, carbon, oxygen and nitrogen are derived from the gross contents of fats, proteins and carbohydrates for any given tissue, the compositions of which are taken from literature dating back to 1940–1950. Heavier elements are derived from studies performed in the 1950–1960. Variability in elemental composition impacts greatly D_{90} for target tissues and doses to OAR for brachytherapy with low energy sources and less for ^{192}Ir-based brachytherapy. Discrepancies in μ_{en}/ρ are also indicative of dose differences.

Conclusions: Updated elemental compositions are needed to optimize MBDCA-based dosimetry. Until then, tissue compositions based on gross simplifications in early studies will dominate the uncertainties in tissue heterogeneity.

Clinical standards of brachytherapy (BT) dose calculation have traditionally been based on report number 43 issued in 1995 by the American Association of Physicists in Medicine (AAPM) termed TG-43 [1]. In the TG-43 based dose calculation process the affected malignant tissue, the surrounding radiation sensitive healthy organs, BT seeds, needles and applicators are considered to be water for simplification. This simplification overlooks the alteration of photon fluence and absorption of dose by different tissues, BT seeds, needles or applicators. TG-43 report was followed by an updated protocol, TG-43U1 [2] in 2004.

Newly developed model-based dose calculation algorithms (MBDCAs) provide a detailed and more accurate method for calculation of absorbed dose in heterogeneous systems such as the human body [3–5]. These algorithms include collapsed-cone convolution (CCC) [4], grid-based Boltzmann solver (GBBS) [6] and Monte Carlo (MC) [7] methods. However, to obtain accurate dose distributions, a correct geometrical description, density and tissue composition of the patient, a model of the BT seeds and the implanted BT applicators with appropriate density and material composition are needed as inputs to these MBDCAs. AAPM released a report in 2012, TG-186, providing guidance for the use of MBDCAs [8]. According to TG-186 guidelines, MBDCAs should replace the water based TG-43 dosimetry. MBDCAs generally require voxel by voxel assignment of tissue density and elemental composition (mass fraction of each element composing the tissue). The patient geometry is obtained via a computed tomography (CT) image, which is imported into the dose calculation software where it is represented as a voxelized geometry. Tissue physical density is obtained from the CT images of the treated anatomy using a Hounsfield Unit (HU) to density calibration. Similar information is required for the radiation source and needles/applicators. However, modelling of the applicators is generally more detailed, requiring mesh models or computer aided design models for finer replication of the applicators [9,10]. As opposed to external beam

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https://doi.org/10.1016/j.radonc.2018.01.007
0167-8140/

radiotherapy, a voxelized model for BT applicators might be too coarse in spatial resolution [8].

Accurate dosimetry with MBDCAs requires detailed knowledge of the atomic composition of the irradiated tissue. For a given tissue, different elemental compositions have been reported in the literature, giving rise to different effective atomic numbers and interaction cross-sections. TG-186 recommends the use of elemental compositions published in Report 46 of the International Commission on Radiation Units (ICRU 46) [11]. For the majority of tissues described in ICRU 46, with the notable exception of breast calcifications, elemental compositions are identical to those listed in the publication of Woodard and White (W&W) [12] as shown in Appendix A. Other exceptions simply imply that data were only present in one of both publications. This is the case for prostate tissue, where elemental composition is available in the work of W&W but not in ICRU 46. It is therefore reasonable to state that elemental compositions of tissues involved in prostate, breast and other cancer sites targeted by BT have not been systematically updated between both publications. Moreover, the work of W&W is not itself a primary tissue analysis of elemental composition, but rather a reassessment of results published by Report 23 of the International Commission on Radiation Protection (ICRP 23) [13]. ICRP 23, in its turn draws data from studies undertaken at the University of Tennessee and the Oak Ridge National Laboratory (ORNL). The implications of this methodology in obtaining elemental compositions are analysed in this review, after which suggestions for more modern techniques are presented in the discussion.

MBDCAs have intrinsically the potential to offer treatment plans with more accurate dosimetry, but they are highly dependent on the accuracy of information provided as input [14]. As MBDCAs are becoming available in the clinic, and we are departing from water based dosimetric materials, there is a need for precise and updated elemental composition of tissues. The aim of this review was to assess past studies for the reported variation in elemental composition for target volume and organs at risk (OAR) and the impact of these heterogeneities on absorbed dose. The importance of elemental composition for absorbed dose for low and high energy radionuclides and low energy electronic brachytherapy sources in MBDCAs, and the difference in dose between the water-based TG-43 formalism and MBDCAs is discussed. Results for μ_{en}/ρ coefficients generated for several tissues will serve as an illustration to supplement results on dose metrics obtained by previous research.

Methods

Literature search

Keywords used in searching past literature include "tissue heterogeneity", "model-based dose calculation algorithms", "TG-186", "Monte Carlo", "dose heterogeneity", "low energy brachytherapy" and other concepts related to model-based dosimetry for BT. Most studies were retrieved in PubMed. Articles were selected according to, although not restricted to, the following criteria:

- Is the impact of tissue heterogeneity on dose distribution investigated?
- Are different elemental compositions compared?
- Are dose metrics obtained from TG-43 and TG-186 compared?
- Considerations for organs at risk.

Mass energy-absorption coefficients

The "g" usercode included in the MC software "electron gamma shower" developed by the National Research Council of Canada (NRCC), EGSnrc, was used to generate values of μ_{en}/ρ coefficients for the tissues of interest [15]. To accomplish this, input data such as elemental tissue composition, incident energies and cross-sections for different interactions must be provided to the usercode. Data gathered from the scientific literature [11–13] have been used to collect elemental compositions of water, air and other tissues (see Appendix A for list of materials as well as Figs. 1–5).

PEGS4, a pre-processor for EGS, is used to create tissue data sets needed by EGSnrc. To be able to produce this data set, the element-by-element mass fractions of the tissue of interest and the energy cutoffs of 1 keV for photons and 512 keV for electrons are incorporated into a PEGS4 input file. Selected compositions for use in the PEGS4 files were taken from ICRU 46 when possible and from W&W if not available within ICRU 46.

In addition to the generated PEGS4 data set, an EGSnrc input file containing specifications regarding the choice of the cross-section library, energy spectra, scattering options as well as other relevant parameters was created. The XCOM based photon interaction cross-section library was chosen [16]. Incident kinetic energies ranged from 1.5 keV to 1.5 MeV. μ_{en}/ρ for each energy level specified within the EGSnrc input file are generated using "g". Every tissue is accompanied by its own unique PEGS4 input file, PEGS4 data file and EGSnrc input file. Results are then compared to the NIST database [17] for certain tissues for validation.

Results

Literature review

Studies investigating the influence of the variation in elemental composition on BT dose distribution heterogeneity for breast, prostate, gynaecological, lung and head & neck cancer have been reviewed. Tables 1–3 show some of the reported results for minimal dose delivered to 90% of the target organ (D_{90}) for TG-43 based dose to water in water $D_{w,w}$ and TG-186 MBDCAs based dose to medium in medium $D_{m,m}$ or dose to water in medium $D_{w,m}$. Other metrics include minimum dose to the high dose region x cm^3 ($D_{x\text{-}cm3}$) and minimum dose delivered to x% (D_x) for OAR. The variations between TG-43 and TG-186 metrics are defined as $\frac{TG186-TG43}{TG43}\times 100\%$. If results for different MBDCAs are compared (eg A vs B), the percent difference is computed as $\frac{|A-B|}{TG43}\times 100\%$.

Mass energy-absorption coefficient

Tissues considered for analysis (Appendix A) are broadly classified into three categories:

- Upper body thorax tissues, those relevant to breast cancer treatment
- Lower body tissues, those relevant to prostate cancer treatment
- Other tissues, which are relevant to other cancer treatments

It is noteworthy that this categorization is mostly intended to make the graphical presentation of results more practical. Tissues do not belong exclusively to one category: it is quite possible that a material belonging to the "upper body" category may be incorporated into prostate cancer treatment, and vice versa.

μ_{en}/ρ ratios of non-water materials to water are plotted $\left(\text{i.e. } \left(\frac{\mu_{en}}{\rho}\right)_{tissue}\Big/\left(\frac{\mu_{en}}{\rho}\right)_{water}\right)$ as a function of photon energy. Although results were produced for energies up to 1.5 MeV, the plots are truncated at 250 keV for clarity of illustration. The ratios are approximately constant above 250 keV.

Please cite this article in press as: Mann-Krzisnik D et al. The influence of tissue composition uncertainty on dose distributions in brachytherapy. Radiother Oncol (2018), https://doi.org/10.1016/j.radonc.2018.01.007