Water or Medium: Dose Specification in Trials and Real Life

T Kron¹,²,³, N Hardcastle¹,²
¹Peter MacCallum Cancer Centre, Department of Physical Sciences, Melbourne VIC 3000, Australia
²Centre for Medical Radiation Physics, University of Wollongong, Wollongong NSW 2500, Australia
³Sir Peter MacCallum Department of Oncology, University of Melbourne, Parkville VIC 3010, Australia

E-mail: Tomas.Kron@petermac.org

Abstract. Radiation dose is the therapeutic agent in radiotherapy where the objective is to maximise radiation dose to a target while minimising the dose to surrounding healthy tissues. Dose in this context is typically associated with the quantity “absorbed dose” as energy deposited per unit mass and measured in J/kg of tissue. However, even if high doses are delivered (no stochastic distribution considered) and photon or electron radiation is considered (no neutrons or heavy charged particles), there will be differences in the actual dose delivered to different tissue types as the stopping power for the electrons that deliver the vast majority of dose varies with elemental composition. Historically, radiation beam calibration and dose calculations were performed in water as a readily available, easily standardised material that closely matches the radiation properties of many human tissues. However, many superior dose calculation algorithms that have recently become available due to improved computer power (Monte Carlo Calculations, Acuros) calculate dose as deposited in the medium. The present paper examines arguments for both and proposes that based on the current scientific and political developments specification of dose as dose to medium would be the more robust and future proof choice.

1. Introduction

Due to faster computers and the use of GPU cards, radiation dose calculations in radiotherapy have developed rapidly in recent years. This facilitated the introduction of so called type C algorithms such as Monte Carlo Calculations [1] or linear Boltzmann transport equation solvers (Acuros XB) [2], which more closely model the physics of radiation transport and energy deposition [3]. Importantly, Type C algorithms utilise the elemental composition of tissues. This is in contrast to Type B algorithms such as collapsed cone convolution and pencil beam, which model interactions and dose deposition in different tissues as if each location of interest was water, but of electron and physical densities matching the material at that location. This is a widely used process that relies on conversion of image data (such as Hounsfield Numbers in a CT image) to electron densities, effectively converting complex photon interactions at photon kV images into electron densities that is the quantity of interest in MV photon interactions in matter and electron mediated dose deposition in water.

As the dose calculated and specified in water and medium is not identical, radiation oncologists and medical physicist need to decide what quantity is more relevant for their practice. This paper examines some of the arguments for both and aims to derive at a recommendation as to what may be more appropriate to consider for future use.
2. Dose specification options

2.1. Radiation transport and dose deposition
Dose delivery in a specified region of a patient depends on two physical processes: the transport of energy from the radiation source to the point of interest and the deposition of energy there. Radiation transport is governed by divergence of the beam and the interaction probability and interaction types in the material between the radiation source and the point of interest. In kV photon radiation there are several important interaction types and the secondary charged particles created travel not far enough to warrant separate consideration in a macroscopic dose calculation. As such only the photon interactions count and there is no doubt that material composition matters as atomic number will have a huge impact on the contribution of photoelectric effect to the attenuation and consequent dose deposition. In MV radiation elemental composition is less relevant for photon transport as Compton effect dominates. However, there are differences in stopping and scattering power for electrons, be it primary or secondary ones. This leads to differences in actual dose deposition between dose to water of different densities compare to dose to the medium.

2.2. Dose to water
Dose to water has been the backbone of dose measurements and specifications for a long time. Water is an easy medium to work with and readily available. Therefore, dose has traditionally been expressed as dose to water. In this case dose is specified as the dose that would have been received by water of an electron density derived by the material in which dose calculation is performed. For example, dose in lung becomes dose to water of a relative density of 0.3g/cm³ and dose to bone equals dose to water of a density of 1.3g/cm³. While this is not physically accurate it links nicely to typical dose calibrations by standard laboratories (which is in water) and is the only quantity available in conventional dose calculation algorithms of type B, such as pencil beam and convolution superposition.

It is important to note that the dose specification is not necessarily linked to the modeling of transport and algorithms such as Acuros allow to model transport in medium with conversion of the electron fluence at a given location into dose to medium or water independent of the radiation transport.

2.3. Dose to medium
Type C algorithms are more sophisticated and model radiation transport and dose deposition in the medium including atomic number and composition, which allows extension of the algorithm to lower energy X-rays. In megavoltage radiation, dose deposition depends on the number of photons (and their secondary particles) reaching a volume of interest. Accuracy improvements can result from consideration of radiation transport in the correct medium. However, the final step, the conversion of particle fluence to deposited dose can be made using stopping powers of the actual tissue or indeed any material of interest. Water is an attractive choice, as cells contain significant amounts of water, indirect DNA damage relies on radical formation in water and reference dosimetry is performed in water [4].

3. Dose to water or dose to medium?
In principle one can be converted into the other using stopping powers [5]. However, this introduces additional uncertainties, and in the case of conversion from calculated dose to medium back to water, yields different results to calculating dose to water in the first place [6]. As such it is preferable to select one dose specification and stick with it, a process that is also recommended for clinical trials [7]. Fortunately, the differences between dose to water and dose to medium are generally small for human tissues [8]. Differences in lung are usually less important than the changes attributable to better modelling of charged particle disequilibrium in type C algorithms. The largest difference occurs in cortical bone where differences of up to 11% have been reported, [5] and careful discussions between
clinicians and physicists are required [9]. In an ideal world, one would like to specify dose in a way that correlates best with the biological effects of interest. Unfortunately, it is unlikely that the clinical data will be available in the near future that would allow deciding this. As such, other criteria must be used:

a) Understanding the relationship between ‘dose’ and clinical outcomes is based on dose to water calculation [10]. However, conversion of Dm to Dw will not necessarily give this same result, and may result in a dose that is even further from experience gained over many years using Type B dose calculation algorithms to specify dose to water [6].

b) It can be argued that the DNA in cells, the ultimate target of radiation effects, is surrounded largely by water and at least indirect radiation damage to DNA is proportional to the creation of free radicals in water [11]. However, this argument would not apply as well to hypoxic cells where potentially the energy deposition in the phosphorus back bone of DNA becomes more important. On the other hand, the relevance of dose to a medium also becomes a matter of discussion in the context of bone where critical cell compartments such as osteoblasts and osteoclasts are close to calcium rich bone but consist themselves of water. This makes the decision of which specification of dose in millimetre size voxels is more relevant rather difficult.

c) There is a conceptual link to reference dosimetry, which is performed in water [4, 12]. However, it needs to be remembered that most reference dosimetry is actually performed using air filled ionisation chambers and that the stopping power ratio used in Bragg-Gray cavity theory to correct dose in air to dose to water is on of the larger contributors to uncertainty in reference dosimetry. This becomes even more obvious in the case of electron relative dosimetry where the need for an ‘ionisation to dose’ conversion is a result of a measurement in air with the desire to obtain dose to water [13].

d) At least in the context of Monte Carlo calculations there is hope for reduced uncertainty in avoiding converting from dose to medium to dose to water specification [14].

e) Dose delivered using other radiation qualities will be easier using a dose to medium environment; while experience with protons and particularly high LET charged particles is still missing, there is no doubt that kV X-rays would be easier combined with MV radiotherapy if dose to medium was used. This is important not only for brachytherapy but also image guidance using kV based CBCT systems.

f) CT allows determination of electron densities and not necessarily media. This argument becomes less convincing as future planning may actually be based on other imaging modalities such as magnetic resonance imaging (MRI) where media could be easier to determine than electron densities. However, this also highlights the additional complication that even nominally identically tissues may have different elemental compositions in patients and the association of medium and such elemental composition to real tissues may be ambiguous [14].

Given these arguments, it appears that both dose to water and dose to medium could be justifiably used for photon and electron dose description as long as it is made clear what is measured and how the measurement is used. Pedro Andreo summarises the considerations regarding the choice of dose specification very nicely in a recent article [14]. He concludes: “Considering … current developments in advanced dose calculation methods, planning in terms of dose-to-tissue should be the preferred choice, under the expectancy that progress in the field will gradually improve some of the crude approximations…” [14]. This also reflects the thinking that current limitations of dose to medium calculations such as a limited number of discrete tissues specified in dose calculations and publications of the International Commission on Radiation Units and Measurements (ICRU) [15, 16]. No doubt this will improve over time as the gradual transition between media with change of CT number employed in modern dose calculations demonstrates.
Considering all these points most clinical trials organisations are currently recommending the use of dose to medium as the ‘native’ environment for the most accurate radiation transport and dose calculation methods currently available [7]. This has also been the conclusion of a recent AAPM report [17].

4. Conclusion
The discussion about dose to water or medium specification has been going on for nearly 20 years [18]. It can be argued that the discussion in itself has contributed to a better understanding of the objectives of dose optimisation in radiotherapy. However, while both ‘dose to water’ and ‘dose to medium’ have some justification, it is concluded that dose to medium appears to be the more future proof solution.

5. Acknowledgement
The authors would like to thank the Peter Mac Foundation for support of a cloud-based radiotherapy treatment planning system that calculates dose to medium (or water).

6. References
[1] Rogers D W 2006 Phys. Med. Biol. 51 R287-301
[2] Han T et al 2011 Med. Phys. 38 2651-64
[3] Zhou C et al 2017 Radiat. Oncol. 12 80
[4] IAEA 2000 IAEA Technical report series N398 (Vienna: International Atomic Energy Agency)
[5] Siebers J V et al Phys. Med. Biol. 45 983-95
[6] Reynaert N et al 2018 Phys. Imag. Radiat. Oncol. 5 26-30
[7] Gladstone D J et al 2016 Int. J. Radiat. Oncol. Biol. Phys. 95 1344-5
[8] Healy B et al 2003 Med. Phys. 30 2282-91
[9] Hardecastle N et al 2019 Phys. Imag. Radiat. Oncol. 11 92-7
[10] Hall E and Giaccia A 2005 Med. Phys. 26 1847-70
[11] Klevenhagen S 1993 Physics and dosimetry of therapy electron beams. (Madison: Medical Physics Publishing)
[12] Andreo P 2015 Phys. Med. Biol. 60 309-37
[13] Siebert B R 2006 Radiat. Prot. Dosim. 121 3-11
[14] Ibott G S et al 1997 Med. Phys. 24 1249-54
[15] Kry S F et al 2020 Med. Phys. 47 e53-64
[16] Liu H et al 2002 Med. Phys. 5 922-4