

Application of efficient Monte Carlo photon beam simulations to dose calculations in voxelized human phantoms

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Valorization

The socioeconomic value of the research presented in this thesis can best be understood in the context of two broad fields operating within the spheres of health care and public health: the field of Radiotherapy and the field of Radiation Protection. In general, more attention has been given to Radiotherapy because there is an urgency to improve the treatment of a disease which is likely to touch us all in some manner, it intersects significantly with other areas of medicine (*e.g.*, radiology, oncology), and, historically, it has consumed more private and public funds. In keeping with this, this Valorization will focus mainly on the applications of the above research to Radiotherapy. However, a section on its implications for the field of Radiation Protection is included at the end.

In order to focus this discussion about the socioeconomic value of the research in this thesis, Figure 1 gives a breakdown of the areas of relevance covered here. The reader is encouraged to refer back to this figure.

Radiotherapy

According to the World Health Organization (WHO)[2], cancer is second only to heart disease as global cause of death, with the most common cancers being, in order, lung, liver, colorectal, stomach and breast. In 2015, cancer was responsible for 8.8 million deaths worldwide, with the number of new cases expected to rise by approximately 70% over the next two decades. Moreover, approximately 70% of cancer deaths occur in low-to-middle-income countries, thus placing the greatest cancer care burden on the societies that can least afford it.

Radiotherapy is one of the three pillars of cancer treatment, which also comprise chemotherapy and surgery. It is estimated that 50% of newly diagnosed cancer cases require radiotherapy, and that radiotherapy, alone or in conjunction with surgery and/or chemotherapy, is responsible for 40% of cancer cures[3]. Unfortunately, radiotherapy is a costly treatment modality. In the US, the median cost of a course of radiation therapy can range from USD 8,600 for breast cancer to USD 18,000 for prostate cancer[4]. Add to this the average cost of purchasing

research in this thesis	radiotherapy				radiation protection
	R&D			clinical	
	improving accuracy	understanding RBE	new techniques & technologies	beam commissioning	
history by history statistics					
directional bremsstrahlung splitting					
HOWFARLESS					
directional source biasing					
CBCT skeletal dose calculations					
D_m vs D_w as specifier of dose to sensitive tissue in bone					
Use of Burlin cavity theory to calculate D_m (Discussion)					

Figure 1: Areas of socioeconomic relevance for the research presented in this thesis. Note that, given the importance of valid uncertainty estimates in MC, history by history statistics[1] are inseparable from development and applications of EGSnrc and are, thus, relevant across all areas.

a linear accelerator (approximately USD 2.5 million, factoring in facility costs) and personnel costs, and it can easily be seen that the need outstrips capacity in most low-to-middle-income countries.

EGSnrc

Monte Carlo (MC) simulations continue to play a large role in the development of modern radiotherapy technology. As the most widely-used general purpose MC code in radiotherapy research, EGSnrc has figured in the development of the state-of-the-art of radiotherapy for techniques ranging from brachytherapy to image-guided radiotherapy (IGRT).

Insofar as much of the research contained herein is integral to EGSnrc, then, it, too, has contributed and continues to contribute to the ongoing development of radiotherapy. For the purposes of this Valorization, it is understood that many of the socioeconomic contributions of the research here are delivered through the vehicle of EGSnrc.

As an aside, however, note that EGSnrc is now public domain software (as of 2016), and, therefore, the algorithms described in this thesis have devolved into this domain, where they are currently being put to use by researchers, engineers and developers across the world developing future applications for Radiotherapy, Radiation Protection, Food Irradiation, and other fields beyond the scope of this work.

Improving Accuracy

While improving accuracy would seem to be a self-evident goal for radiotherapy, there is very little quantitative data indicating the degree to which regular systematic errors in practice affect treatment outcome. As mentioned in the Discussion of this thesis, AAPM Task Group 105[5] has stated that errors of 5-7% may have repercussions for tumour control probability (TCP) and normal tissue complication probability (NTCP). And while this seems like an easily attainable margin of error, one must be aware of the many steps in treatment planning over which inaccuracies may accrue. Thus, it is incumbent on practitioners to improve the accuracy of every step of the treatment planning process.

Since MC is the most accurate method of determining radiotherapy dose, it has been embraced as the method of choice for treatment planning, with the stakeholders in its successful implementation including radiation oncologists, clinical physicists, manufacturers of treatment planning systems (TPSs) and treatment devices and, of course, patients. In addition, MC calculated dose is increasingly used as the quantity of interest in preclinical research platforms, such as small animal irradiators. Considerable resources continue to be devoted to expanding the role of MC in the clinic, but, as noted in the Discussion, more is required.

Research in this thesis with direct application to improving the accuracy of radiotherapy includes the implementation of history by history statistics in EGSnrc[1] and directional bremsstrahlung splitting (DBS)[6] (see Figure 1). As stated in the Discussion, the former has proven its utility in all applications of EGSnrc and is of direct relevance to assessing the accuracy of a simulation, where robust uncertainty estimates are required. Considering the design and development of more accurate TPSs and techniques, then, it is easy to see that, to the extent that EGSnrc plays a role in their development, so does this method of estimating uncertainty. Directional bremsstrahlung splitting (DBS), meanwhile, has emerged as the de-facto technique for efficient photon and X-ray beam simulations and, thus, plays a key role in such TPS development tasks as: 1) development and testing of MC dose calculation engines, 2) verification of virtual source models, 3) providing phase space data libraries.

No discussion of accuracy would be complete without some mention of the occasional radiotherapy accidents, stemming from human error and/or machine failure, that result in large treatment errors with acute health repercussions. While the WHO estimates that only 3,125 patients worldwide were affected by such incidents between 1976 and 2007[7], the results are alarming and tend to generate press headlines. Although, strictly speaking, such errors fall outside the definition of accuracy as used in this thesis, EGSnrc and other MC simulations are commonly used to simulate these incidents in an attempt to reproduce the levels of overdose/underdose and to help ensure that the errors are not repeated. In this way, then, the

research in this thesis also comprises a part of the larger effort to insure against such accidents.

Understanding Radiobiological Effect (RBE)

Given radiotherapy's long history and, in recent decades, relative efficacy, surprisingly little is known about the biological mechanism(s) whereby ionizing radiation destroys tumour cells. Although promising strides have been made in recent years—for example, it is now understood that ionizing effects occur in water-bound DNA and on a scale of nm—this is an area that continues to be of great interest to oncologists, radiobiologists and medical physicists. For it is thought that a more complete understanding of RBE will, in turn, inform the design of more effective radiotherapy techniques.

It is at this intersection of Radiobiology and Radiation Physics that the debate continues over whether dose to water-in-medium, D_w , or dose to medium, D_m , is a more accurate representation of RBE. The study on whether D_w or D_m is a better estimator of dose to sensitive skeletal tissue[8] presented in this thesis contributes directly to this debate by offering numerical evidence in favour of D_w . While the calculation of D_w using Burlin cavity in a mouse phantom, presented in the Discussion, offers a potential general methodology for converting D_m to D_w .

In addition, the study on additional dose due to cone beam CT (CBCT) imaging in IGRT[9] presented here contributes, through its deconstruction of skeletal dose into dose to red bone marrow (RBM) and bone surface cells (BSC) to our understanding of RBE.

New Radiotherapy Techniques & Technologies

Monte Carlo continues to operate at the forefront of Radiotherapy research, providing a tool that can be used to study new techniques and devices and assisting in the design and QA of new protocols. Thus, MC, and EGSnrc in particular, is of direct interest to physicists and engineers involved in the design and testing of new radiotherapy technologies, which, ultimately, will have an impact on the practices of clinicians and the quality of treatment received by patients.

Several studies in this thesis are relevant to the continuing development of radiotherapy technology. By providing physicists and engineers with a means to efficiently simulate photon beams, directional bremsstrahlung splitting[6] is implicated in any development effort involving high energy photons or X-rays making use of EGSnrc. Directional source biasing[10], meanwhile, with its efficient simulations of Co-60 treatment heads, provides a potential means for commissioning units using the relatively new image-guided radiotherapy (IGRT) technology of MRI combined with Co-60 treatment. Revealing a significant increase in dose to radiosensitive bone surface cells when CBCT is used with IGRT, the dose calculations presented

in chapter VI[9] provide motivation for improvements in this IGRT technique. Finally, the protocol for using Burlin cavity theory to compute D_w from D_m presented in the Discussion is anticipated to comprise part of a larger body of research that will guide the development of preclinical research tools.

Additionally, the costliness of radiotherapy (see above) has led to a renewed interest in the use of Co-60 treatment heads, especially in low- and middle-income countries, where purchasing the number of LINACs required to meet the treatment requirement is beyond reach. This, then, does not represent the development of a new technology but the re-emergence and refinement of an older technology to meet a current need. The design and commissioning of such units will require efficient MC simulations of Co-60 sources, and in this directional source biasing[10] may play a role.

Beam and TPS Commissioning

In addition to expanding and refining radiotherapy techniques, MC, and EGSnrc, is used by clinical physicists in the task of commissioning beams and TPSs. Commissioning is an essential process in establishing a new treatment head and/or TPS in a clinic and ensures that: a) the treatment beam delivers the expected dose and b) the TPS provides an accurate estimate of the delivered dose. Thus, commissioning has a direct impact on the successful operation of a radiotherapy clinic.

For some years, MC calculations have been used for direct comparison with measurement and for providing simulated beam data for use by TPSs. Also, MC-calculated correction factors are used in dose calculation protocols. This indicates the extent of the role that MC plays in radiotherapy practices and also the confidence that clinicians have in current MC algorithms.

Several of the studies in this thesis are relevant to commissioning activities. Once again, DBS[6] is an important technique for any commissioning activity involving photon beams. The HOWFARLESS algorithm for fast DOSXYZnrc dose calculations in homogeneous phantoms[11] is also useful for calculating depth-dose curves and dose profiles for comparison with measurement. Directional source biasing[10] (DSB) has a potential role in commissioning Co-60 units.

Moreover, DSB is of potential relevance to clinics and primary standards labs, such as the National Research Council of Canada, where Co-60 provides the accepted standard beam quality for ion chamber calibration, because it makes routine comparison between measured and calculated ion chamber doses feasible.

Radiation Protection

While cancer treatment and diagnosis represent the most systematically directed application of radiation to the human body, they by no means represent the only sources of radiation exposure. Of course, the most dramatic examples of radiation exposure historically have come from nuclear reactor incidents and the atomic bombs dropped by the US on Hiroshima and Nagasaki at the end of World War II. Though the application of a systematic study of the effects of radiation and accompanying efforts to minimize risk to the public would seem to be quite beside the point in most of these events, useful data on the long-term effects of radiation exposure have been gleaned from these tragedies. These data have allowed researchers working in the field of Radiation Protection to estimate the risks associated with unintended exposure to various sources of radiation, including naturally occurring terrestrial and cosmic sources, as well as occupational risks for those who work with or close to radiation (*e.g.*, nuclear power workers, health care workers).

The International Commission on Radiological Protection (ICRP) estimates that the additional risk of cancer death due to exposure to radiation is 5.5% per Sievert (Sv)[12], where a Sievert is the SI unit for dose equivalent and is equal to absorbed dose scaled by a quality factor, depending on the type of radiation, and the radiobiological effect. The exposure limits currently proposed by the ICRP[12] are 1 mSv/yr for the general public and 20 mSv/yr for radiation workers. Note that these limits apply to intentional or accidental exposure and, thus, are over and above unavoidable exposure to radiation occurring naturally in the environment. Governments of some countries, including Canada, use these same exposure limits. While it is a somewhat tired adage to equate the lifetime risk represented by exposure to 1 mSv/yr to one-fifth that of smoking a lifetime total of 75 cigarettes[13], it nevertheless puts the risks represented by these exposure limits into perspective. Quite apart from any scientific/actuarial basis for these limits, however, most public policy is informed by the perception of radiation as generally dangerous, and so these represent absolute upper limits for guidelines adhering to the practice of keeping exposure as low as reasonably allowable, or the so-called ALARA principle.

Given the uneasy balance between perceived and actual risk, then, it is important from both public safety and policy perspectives that: 1) the public be shielded from unintended exposure to human-manufactured sources of radiation as much as possible and 2) policy be guided by an understanding of potential sources of exposure and radiobiological effects.

While the design of radiation shielding structures, such as LINAC bunkers, generally does not require the accuracy available in MC simulations, there is, nevertheless, an ongoing role for EGSnrc in determining the dose distribution around an irradiating device and, hence, the

material and layout of the shielding structure.

The research in this thesis, however, is more pertinent to the goal of understanding radiobiological effects and mitigating exposure where possible. In quantifying additional dose to red bone marrow and bone surface cells, the dosimetric study of the routine use of CBCT imaging in IGRT[9] motivates guidelines for the use of this particular imaging modality. The study on D_m versus D_w as an accurate representation of dose to sensitive tissue in bone[8], meanwhile, presents a quantitative argument for D_w as a better estimator of RBE and, consequently, risk in the case of unintended or avoidable exposure. By this same token, the research on estimating D_w presented in the Discussion may also be directed towards a method for estimating risk from radiation exposure.

Other Applications

Although EGSnrc has been developed with therapeutic, diagnostic and radiation protection applications in mind, the above discussion by no means represents the full extent of its societal role, and, by extension, the role of much of the research in this thesis. For example, companies designing LINACs for industrial purposes, such as food irradiation and equipment sterilization, make use of EGSnrc simulations to optimize accelerator design, determine shielding requirements and maximize throughput.

It is expected that, as the capabilities of EGSnrc evolve and expand in response to interest in new applications of ionizing radiation and new treatment modalities (see the Discussion), the research described in this thesis will find other applications of socioeconomic consequence heretofore unseen.

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