EDITORIAL

Complexity of advanced radiation therapy necessitates multidisciplinary inquiry into dose reconstruction and risk assessment

To cite this article: Wayne Newhauser 2010 Phys. Med. Biol. 55

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EDITORIAL

Complexity of advanced radiation therapy necessitates multidisciplinary inquiry into dose reconstruction and risk assessment

The availability of low-cost, high-performance computing is rapidly transforming the landscape of cancer research. Computational techniques are playing an increasingly important role and have become the third major method of scientific inquiry, supplementing traditional methods of observation and theory. This evolution began in the 1940s when high-performance computing techniques were developed for military applications, including radiation transport calculations. These same basic methods are still widely utilized in a broad spectrum of computational problems in medicine, including radiation cancer therapy (Rogers 2006, Spezi 2010) and radiologic diagnostic imaging (Doi 2006, Kalender 2006). Supercomputing is also now being used to study the genetics and genomics of cancer (Geurts van Kessel 2010), with application to gene sequencing (Mardis 2008), genome-wide association studies (Pearson and Manolio 2008), biomolecular dynamics (Sanbonmatsu and Tung 2007) and systems biology (Wolkenhauer et al 2010).

The extensive and growing body of literature is evidence of a remarkable expansion of activity and enormous boost to cancer research from the application of high-performance computing. Early successes were facilitated by inexpensive computing resources and advances in modeling algorithms. Many contemporary models require extensive approximations and phenomenological approaches. In fact, many critical problems remain computationally intractable; the underlying physical and biological processes are simply too complex to model with contemporary theory and computing capacity. In the future, a vast stream of new insights will flow from studies that use increasingly exact models and first-principles approaches. Hence, in the war on cancer the present status of computational research could be summarized as the beginning of the beginning. For these reasons, there is a vital need for scientists and clinicians to periodically discuss progress and future plans regarding computational cancer research, particularly research involving supercomputing.

In April 2010, a symposium entitled ‘4th Joint Symposium on Computational Medical Physics: The Nexus of Research on Cancer, Radiation, and Supercomputing: Dawn of a Golden Age?’ was convened at Rice University in Houston, Texas. One objective of this symposium was to provide researchers and clinicians with an overview of recent progress in advanced radiation therapy. Another was to review basic concepts and methods from a wide variety of disciplines related to cancer radiation therapy, including supercomputing, physics, informatics, imaging, and epidemiology. The symposium featured current issues and controversies and, in particular, a review of recent advances in research on proton and photon therapies. Sessions included Current Issues in Proton Therapy for Pediatric Cancers; Current Issues in Advanced Radiotherapy for Prostate Cancer; Charged Particles in Space and Military Applications; Recent Advances in Radiation Epidemiology; Advanced Computing Techniques: Perspectives from Cancer Researchers and Computer Scientists; Radiobiologic, Dosimetric, and Outcomes Modeling; Imaging and Informatics, and a Young Investigators’ Symposium. The complete program is available at www.regonline.com/joint_symposium.
Editorial

This editorial symposium was attended by more than 100 delegates who delivered 47 oral presentations. The delegates included leading scientists and clinicians from the fields of epidemiology, particle physics, medical physics, mathematics, oncology, and cancer prevention.

This issue of *Physics in Medicine and Biology* contains 13 original research articles based on selected presentations from the symposium. Each article underwent the journal’s usual rigorous peer review process; we are grateful to the many individuals who contributed to this issue, including the publishing editor, board members, referees, and of course the authors, all of whom generously shared their time and expertise.

The majority of articles from the symposium are interrelated and focus on dose and risk assessments related to radiation exposures from advanced radiation therapies. These research topics have become increasingly complex and require the combined expertise of researchers with highly specialized and diverse investigational skills. Innovative multidisciplinary teams will be needed to achieve breakthroughs and, ultimately, to translate the research into clinical practice (Disis and Slattery 2010). The symposium’s scientific goals included fostering and promoting such multidisciplinary teams, which will work to solve these complex problems and thereby improve cancer outcomes.

To help clarify how the 13 articles each contribute to the goal of improving cancer outcomes, a brief digression is necessary. The proportion of patients surviving their cancers for five years or more is large and increasing (Jemal *et al* 2009). Unfortunately, in survivors who received radiation therapy, the prevalence of radiogenic late effects is likewise large and increasing (cf Altekruse *et al* 2010, Meadows *et al* 2009, Hudson *et al* 2009, Friedman *et al* 2010), with the potential to become a public health issue of considerable scale (Travis 2006). A multitude of late effects are associated with radiation exposure, including the development of second cancers, cardiac toxicity, cognitive deficits, and musculoskeletal growth abnormalities in children. In modern radiation therapy, much effort is devoted to developing personalized treatments that control the tumor while minimizing acute toxicities to surrounding healthy tissues; comparatively less attention has been paid to minimizing late effects (Durante and Loeffler 2010). In recent years, however, there has been an encouraging increase in research activities seeking to quantify radiation exposures (Stovall *et al* 2006) and the associated risks of late effects from modern external-beam therapies (Xu *et al* 2008).

In this issue, Zhang *et al* (2010) report on Monte Carlo and analytical models to predict the stray radiation exposure in a patient receiving proton radiotherapy. In this study, the authors focused on stray neutron radiation that emanated from the treatment unit. Despite the complexity of high-energy neutron dosimetry, the authors succeeded in developing a relatively simple analytical model to predict these exposures. This finding is important because, with further development, it could provide a method to predict stray radiation exposures as an enhanced form of routine treatment planning. Fontenot *et al* (2010) report on methods to evaluate uncertainties in comparative risk assessments; knowledge of uncertainties is vital to determine the limits of applicability in these assessments, which may in turn affect clinical and policy decisions. Howell *et al* (2010a) report on the accuracy of a widely used radiation treatment planning system. In particular, they investigated the system’s dosimetric accuracy outside the treatment beam, e.g. due to scatter and leakage radiation from external-beam photon therapy. This study provides important illustrative evidence of the need to carefully validate dose algorithms in out-of-field regions. In a related study, Howell *et al* (2010b) developed a methodology to estimate doses to partially in-field and out-of-field organs. Scarboro *et al* (2010) report on the impact of organ size and position on out-of-field dose estimates. Taddei *et al* (2010a) report on the targeting accuracy of a novel device that can be used to treat age-related macular degeneration, the leading cause of blindness in the developed world. Taddei *et al* (2010b) report on the risks of radiogenic second cancers following proton and photon
radiation therapies for liver cancer. Taddei et al (2010c) also compare the risks of radiogenic second cancers from secondary neutrons for a boy and a girl after receiving craniospinal irradiation with passively scattered proton beams.

Scanned-beam proton therapy is presently considered the technologically most complex beam delivery approach and is used in only a few centers worldwide. Coutrakon et al (2010) reported on an investigation of dosimetric errors associated with the delivery of scanned proton beams. Titt et al (2010) report on a novel method to adjust the size of scanned proton beams. This study is important because our inability to produce very small beam spot sizes has been an obstacle to realizing the full clinical potential of this technique. Yepes et al (2010) report on the speedup and accuracy of a fast proton dose algorithm that uses an array of graphics processing units; this technique represents a nascent low-cost alternative to the traditional approach of high-performance computing using central processing units.

Radiation exposures from kilovoltage computed tomography (CT) procedures have increased dramatically, with the fraction of collective effective dose from CT exposures rising from 3% in the early 1980s to 49% in 2006 (NCRP 2009). Proton CT is an emerging technology that may enable reductions in both proton range uncertainties and the imaging dose to the patient relative to comparable kilovoltage CT techniques. Erdelyi (2010) reports on uncertainties in electron densities estimated using proton CT.

Finally, Cheung et al (2010) report on the suitability of advanced composite fiducial markers for localization of the prostate in proton therapy. Their analysis is particularly important because approximately 60% of the proton treatment capacity in the United States is used for patients with prostate cancer.

The symposium was the fourth of a series entitled ‘Symposia on Computational Cancer Research’. The symposia have alternately been hosted by The University of Texas M D Anderson Cancer Center, Rice University, and Northern Illinois University. The fifth joint symposium will be held in Houston, on 5–7 April 2011, and will focus on survivorship issues after childhood cancers (www.regonline.com/5thjointsymposium). On behalf of the symposium organizing committee, I hope to see you there.

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Chairman of 4th Joint Symposium Organizing Committee and Guest Editor

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