

Innovation and the future of advanced dosimetry: 2D to 5D

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Abstract. Recent years have witnessed a remarkable evolution in the techniques, capabilities and applications of 3D dosimetry. Initially the goal was simple: to innovate new techniques capable of comprehensively measuring and verifying exquisitely intricate dose distributions from a paradigm changing emerging new therapy, IMRT. Basic questions emerged: how well were treatment planning systems modelling the complex delivery, and how could treatments be verified for safe use on patients? Since that time, equally significant leaps of innovation have continued in the technology of treatment delivery. In addition, clinical practice has been transformed by the addition of on-board imaging capabilities, which tend to hypo-fractionation strategies and margin reduction. The net result is a high stakes treatment setting where the clinical morbidity of any unintended treatment deviation is exacerbated by the combination of highly conformal dose distributions given with reduced margins with fractionation regimens unfriendly to healthy tissue. Not surprisingly this scenario is replete with challenges and opportunities for new and improved dosimetry systems. In particular tremendous interest exists in comprehensive 3D dosimetry systems, and systems that can resolve the dose in moving structures (4D) and even in deforming structures (5D). Despite significant progress in the capability of multi-dimensional dosimetry systems, it is striking that true 3D dosimetry systems are today largely found in academic institutions or specialist clinics. The reasons will be explored. We will highlight innovations occurring both in treatment delivery and in advanced dosimetry methods designed to verify them, and explore current and future opportunities for advanced dosimetry tools in clinical practice and translational research.

1. Introduction

The sophistication capability and complexity of radiation treatments has increased dramatically in recent years. Three main engines of innovation initiated much of the early phase of this transformation. The first originated in the theoretical world, with the discovery and development of mathematical tools to optimize the radiation fluence for a desired dose prescription and normal tissue tolerance [1, 2]. Then came innovations in computer control and electro-mechanical hardware components needed to implement the delivery of fluence-modulated radiation treatments (e.g. IMRT) [3, 4]. The third engine can be attributed to the addition of ‘on-board’ imaging, in the form of cone-beam-CT capability with the patient in treatment position just prior to treatment [5-7]. Continued innovations in fluence optimization and delivery techniques have led to a range of advanced treatment techniques available at the present time, including IGRT, MRI-guided therapy, VMAT and RapidArc, gating techniques, flattening-filter-free high dose-rate treatments, through to dynamic couch motion treatments [8]. Importantly these techniques have transformed clinical practice, and regularly enable exquisite dose conformation to tumor and substantial dose sparing to healthy structures, even in the most irregularly shaped settings.

The net results of these advances and innovations are substantial gains in clinical capability, flexibility, and efficacy for many patients. However, the price is an elevated potential for errors, and



substantially more difficult treatment commissioning and verification procedures. The difficulty of comprehensive verification and commissioning of advanced treatments has now far exceeded the capabilities of conventional dosimetry systems [9]. These topics have received significant recent attention in the literature and at the congressional level in the United States government [10, 11]. Independently, the Imaging and Radiation Oncology Core Houston (IROC Houston, formerly the Radiological Physics Center [RPC]) reported unacceptably high failure rates for dosimetry credentialing in national clinical trials for several IMRT treatments: 18% for head and neck (7%, 4 mm gamma criteria) and 32% for spine (5%, 3 mm criteria) [12]. The high failure rates despite a generous passing criteria are alarming, and a wake-up call, suggesting the quality and accuracy of implementation of advanced treatments like IMRT must be improved. These failures were detected with sparse sampling on a pair of orthogonal 2D film-planes normalized with thermoluminescent dosimeter (TLD) point measurements, which will miss errors in regions that were not sampled, thereby representing an overly optimistic perspective.

In addition to the challenges of treatment commissioning and verification, the advent of on-board imaging created new concerns arising from the tendency to shrink ‘safety’ margins historically added to allow for patient set-up errors. The ability to shrink margins has the potential to reduce normal tissue toxicity, and hence open the possibility for significantly hypo-fractionated treatments in the curative setting which would have been deemed untenable prior to the on-board imaging era. However, there are real concerns the tendency to shrink margins may lead to the phenomena of ‘marginal miss’, and a loss of local control. Such concerns have been reported in prostate cancer [13], orbital lymphoma [14], breast and head-and-neck cancer [15-18]. The problem of how to verify accurate dose delivery in moving tumors is a challenge ideally suited to 3D dosimetry, and several studies have been reported [19-22]. Similarly, high resolution 3D dosimetry techniques have potential for a defining role in determining and characterizing the dosimetry of small fields [23-25].

The first 3D dosimetry systems were developed in response to the dramatic increase in complexity represented by IMRT described above. The first commercial IMRT system, The Peacock from Nomos Inc, treated patients tomographically, a 2 or 4cm slice at a time, after which the patient was indexed to treat the next slice. Understanding the dosimetry at inter-slice junctions and the accuracy of computer modeling of the dose from a rotational modulated delivery of many small fields was a huge challenge quite beyond the dosimetry systems of the time. The first attempts to verify these dose distributions in 3D were with polymer gel dosimetry [26, 27], based on pioneering work of Maryanski and Gore [28, 29]. Since these early works, polymer gel dosimetry continues to be refined, and has been used successfully [30, 31] with both MRI [32], x-ray-CT [33, 34], and optical-CT readout [34-36]. Innovations in polymer gel dosimeters continue to this day, with new formulations exhibiting increased dose sensitivity and less sensitivity to oxygen [38]. In 2006 a new radiochromic plastic dosimetry system PRESAGE was reported [38]. The potential advantages included reduced light scatter enabling more accurate optical imaging, and greater versatility arising from oxygen insensitivity. PRESAGE has been extensively characterized and used in many dosimetry applications [8, 40-48]. PRESAGE was not the first radiochromic dosimeter however, with earlier Fricke gels having practical limitations of signal diffusion [49-55]. Today recent innovations in radiochromic dosimeters offer exciting potential for further improvements [8, 56-58].

The innovations described above (fluence modulation and on-board imaging) opened new avenues of clinical potential, including dose accumulation in deforming organs, and on-line adaptive procedures. Responding to these developments, 3D dosimetry researchers developed deformable dosimeters with ability to measure and validate dose in deforming dosimeters [22, 59-61] and deformable-image-registration algorithms [62].

In parallel to 3D dosimetry techniques based on chemical dosimeters (polymer gels, plastics, etc) other researchers investigated transit dosimetry: an approach which reconstructs the actual delivered 3D dose from measurements made by on-board flat-panel-detectors acquiring transmission projections during treatment [63-65]. This approach has the significant advantage of an in-vivo measurement of the

treatment dose. Efforts have been made to acquire similar capability with chemical dosimeters [66], but without the directness of the EPID approach.

3D dosimetry requirements have also emerged in other areas of clinical and pre-clinical work. 3D dosimetry has tremendous potential in the challenging world of proton and heavy particle therapy. Several groups have investigated proton dosimetry with chemical dosimeters [67-70], but substantial challenges remain in obtaining accurate readings in the Bragg peak. These challenges have led to innovative alternative approaches. Liquid and solid scintillators [71, 72] have shown very promising potential and results. Brachytherapy is a field where high resolution 3D dosimetry systems have been developed and applied to characterize sources and shields, verify monte-carlo calculations, and other aspects with useful effect [73-80]. The pre-clinical world of micro-radiation-treatments has grown tremendously in the last 5 years, with many research groups investigating aspects of complex treatments in small animals. Substantial innovations have been made incorporating 3D printing technology and ultra-high resolution 3D dosimetry [81-83].

2. Conclusions

In conclusion, this presentation will review highlights from key clinical and pre-clinical advances in treatment capability, and responding innovations in the field of 3D and multi-dimensional dosimetry. A number of 3D dosimetry systems are in use at the present time, based on competing or complimentary approaches including chemical systems (polymer and radiochromic), scintillating systems (liquid and solid) and electronic systems (e.g. transit dosimetry with EPIDS, and diode and ion chamber arrays). It is apparent that much progress has been achieved, but also that the goal of widespread clinical implementation remains elusive, and many challenges have not been comprehensively solved. A number of 3D dosimetry systems still require substantial expertise to achieve clinical grade results in a consistent fashion. Some chemical dosimetry systems exhibit batch-to-batch differences in sensitivity and stability, making consistent dosimetry challenging, and demanding high tolerances for manufacturing practices. One approach to addressing these challenges is the emergence of remote dosimetry [84] services, and there are at least three commercial services at the present time from the main manufacturers of chemical dosimetry systems MGS Research, Modus Medical, and Heuris Inc. It is also apparent that there is substantial room for innovation and improvement in many aspects of 3D-5D dosimetry spanning the gamut of materials, read-out, analysis software, and in the economic and practicality of techniques transferrable to the non-specialised clinic.

3. References

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