Dosimetry challenges and opportunities in modern radiation therapy

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Abstract. Modern radiation therapy (RT) includes conformal therapy, intensity modulated radiation therapy, proton therapy, image-guided radiation therapy, adaptive radiation therapy (ART), and recently magnetic-resonance guided radiation therapy and, upcoming, 4π radiation therapy. These techniques show the continual increase in complexity of radiation therapy techniques which, coupled with a stagnant medical physics workforce, means that the amount and complexity of work per physicist has increased and is likely to increase in the foreseeable future. Three distinct challenges can be identified that need to be addressed. First, is the recent commercial development of automated multi-metastases stereotactic radiosurgery (SRS) techniques. These techniques plan and irradiate a number (up to approximately 20) brain lesions in one treatment session, typically employing one isocenter. The spatial accuracy specifications for SRS imply that attention to the angular accuracy is more critical for these treatments than conventional SRS or other treatment methods. In parallel, our and other groups are developing 4π techniques, which is a proposed method for optimizing both beam angles and intensity fluence to provide x-ray based dose distributions with unparalleled compactness and conformality. One cost to deliver these dose distributions is the added requirement to not only rotate the couch but also shift the couch to increase the number of available beam angles. These two techniques will require efficient and quantitative dose distribution measurements of relatively large volumes for, at least, end to end testing of multi-metastases and 4π treatments. Finally, magnetic resonance guided radiation therapy has led to a resurgence in the development of on-table ART, which requires that the medical physicist compare two calculated treatment plans and efficiently and effectively determine if differences between those treatment plans are clinically significant. Modifying and improving existing tools will be critical to the safe and effective on-table ART.

1. Introduction

What are the characteristics of modern radiation therapy (RT)? If we define modern RT to include those techniques in current clinical practice as well as those that are on the immediate horizon, it encompasses 3D conformal therapy, intensity modulated radiation therapy (IMRT), brachytherapy, proton therapy, and magnetic-resonance guided radiation therapy (MRgRT). There is even a company that is developing a PET-guided radiation therapy machine. On the surface, dosimetry challenges for these techniques appear relatively straightforward. We have been conducting dosimetry measurements for all but the PET-guided system for at least a few years, and in the case of conformal therapy, for decades, so are there any significant new challenges to manage? I would postulate that the answer to this is yes, and it comes from a confluence of factors that include increasing dose delivery complexity, decreasing manpower resources, increasing automation, and decreasing time to manage and evaluate results.
Increased complexity can be seen by comparing conformal therapy treatment plans to fixed-field IMRT to VMAT type deliveries. Sophisticated motion coordination is required to deliver an integrated dose distribution with an absolute dose to within 5%, and the subsequent dose delivery complexity increases the chances that errors will exist within the system, errors that need to be detected before they cause a clinically relevant dose delivery error. Complexity is also increasing with respect to how we manage the patients on the table. Modern linear accelerators are essentially robots, capable of simultaneously moving multiple systems, including the patient couch, gantry, and multileaf collimator, in a choreographed dance that is intended to further increase either dose conformation and/or treatment speed. The addition of routine couch motion makes measurement-based dosimetry more complicated, yet more important than before.

Decreasing manpower resources is a function of two features, a stable workforce, and an increasing workload. In our clinic, we have found that physics-based responsibilities continue to increase, while the number of physicists in our staff does not increase. Given the expected growth in treatment options, this deficit is not likely to stabilize. More complex treatment planning and delivery options, coupled with an increase in both on-table and off-table adaptive therapy, will increase the workload for medical physicists.

Part of the complexity increase is due to the ability to automate complex workflows. All modern linear accelerators are essentially robots. They operate using a centralized computer system that manages multiple subsystems in a way that allows these subsystems to choreograph their function. This has been coupled with newly developed optimization tools and advances in computer hardware, to enable computations that a few years ago would have been at best impractical.

Much of the rationale in advancing the hardware and software in RT is to enable the process of adaptive radiation therapy (ART), which can be defined as adjusting the treatment plan due to changes in patient morphology or functional status. ART is typically subdivided into online and offline (or on-table and off-table), describing whether the new treatment plan will be applied to the fraction in which the new information was acquired, or at some point in the future, typically the next fraction [1]. In either case, the time allotted to evaluate dose distributions is greatly reduced relative to the typical workflows.

The increasing complexity of RT leads to increased demands to conduct ever more sophisticated dosimetry analyses. They are required to be quantitative comparisons that yield the data needed for safety evaluation, while being conducted within the workflow’s time constraints. Figure 1 shows a schematic of the challenge we are dealing with. The amount of time allowed to measure or calculate and evaluate doses has decreased steadily. Most measurements in the 2D era were conducted as part of the systematic management of the machines. The amount of time to review the measurements could be measured in days to weeks. 3D conformal radiation therapy brought with it the use of multileaf collimators [2] and their attendant dosimetric complexity. IMRT presented the most rapid increase in dosimetric complexity, initiating mandatory per-patient measurements that had a turn-around time of one or a few days [3]. Early on, the number of data points that were being measured was dozens (exclusive of films), but modern systems acquire on the order of 1000 data points. On-table adaptive radiation therapy does not allow for pre-treatment measurement-based quality assurance, so it compares multiple calculations in an attempt to determine if the instructions for the linear accelerator will produce the desired dose distribution [4]. These calculations can have more than 1,000,000 points to compare, at the same time that this evaluation has to be conducted in less than a few minutes to be inserted into the clinical workflow. This evolution from few to many points and the reduction of available time will stress existing resources and will require new support tools for the physicist.

In summary, there are two principal challenges to address in dosimetry: 1) Increased planning and delivery complexity to manage and 2) Increased evaluation challenges without increased resources.

2. Complexity
As previously stated, the complexity of RT has increased dramatically from the late 1980s to the present. Dosimetry tools have been developed to aid us in managing this increased complexity, but there are new
challenges that have been recently introduced or are about to be introduced that may make the existing systems insufficient to assure that dose distribution delivery has sufficient accuracy.

On the first front, there has been a recent development of commercial multi-metastases irradiation that treats many brain metastases in a single or few treatments. The treatment planning aspects of this are not substantially different than the planning of single or few metastases, but due to limitations in the MLC design, in order to isolate the radiation dose distribution in each metastasis, the planning system sometimes has to split the treatment into multiple passes. Still, as long as the planned dose distributions are clinically acceptable, are there any fundamental differences in the QA of these treatments than there are for other stereotactic treatments? Figures 2 and 3 shows examples of multi-metastasis treatment plans from vendors that are commercializing this technique.

The QA specifications for traditional stereotactic radiosurgery of brain metastases can be found in the AAPM report 54 [5]. They stated that the accuracy of a linear accelerator (as of 1995) set up for stereotactic radiosurgery was 1.0 mm. More recently, the AAPM published the report from Task Group 142 [6], within which it also specified that for stereotactic radiosurgery, the isocenter accuracy be 1.0 mm. Couch angle was specified to be accurate to within 1°. When treatment planning is conducted to irradiate a single lesion, or a few closely spaced lesions, the ultimate spatial accuracy of the treatment is dominated by the isocenter tolerance. However, when a large number of metastases are being treated, these may be distributed throughout the brain. Assuming that the volume being treated extends approximately 15 cm (the typical size of the human brain), if the isocenter is placed in the middle of the brain, some lesions may be as far as 7.5 cm from isocenter. A 1° couch angle error will move the dose distribution farthest from isocenter 1.3 mm from its intended location, much greater than the accuracy specified at isocenter. Similar errors would be caused by errors in the gantry angle, although given that most stereotactic treatments include couch rotation, the impact on the location accuracy of the resulting dose distribution is more complex and would include degrading the dose falloff as well as localization accuracy. Similarly, an error in the collimator angle would yield a combination of localization inaccuracy and dose falloff degradation.

Given that the current specifications for gantry, collimator, and couch accuracy can lead to unacceptable spatial errors in the delivered dose distributions, the specifications for these quantities needs to be updated for the single isocenter irradiation of multiple metastases. In addition, the delivery of these complex dose distributions requires an additional level of scrutiny than more traditional radiation therapy methods. 3D dosimeters are uniquely suited for such measurements. They can simultaneously determine spatial localization accuracy and dose distribution conformality (i.e. the dose falloff) for all of the irradiated lesions. There are no other techniques that would efficiently and definitively determine the delivered dose distribution end-to-end accuracy.

Similarly, there will soon be a class of radiation dose distributions that will take advantage of the robotic nature of modern commercial linear accelerators. Tran et al [7] determined recently that if a dose optimizer was allowed to simultaneously optimize beam directions and fluences, the resulting dose distributions would be not only conformal, but much more compact. They termed this new technique $4\pi$, referring to the number of steradians in a sphere and suggesting that the beams can come from all directions. $4\pi$ therapy employs a complicated dance between the couch and gantry motions, including couch shifts to expand the number of beam directions that can be employed without collision between the gantry and the couch or patient. The added dynamic degree of freedom of couch shifting, as well as the range and number of non-coplanar beams, will greatly stress dosimetry validation. As with multi-metastasis therapy, a technique that can validate the delivered dose distribution accuracy, including the spatial accuracy and the dose distribution conformality, will be critical to safely introducing $4\pi$ therapy.

Finally, the recent commercial introduction of MR-guided radiation therapy introduces limits in the use of traditional dosimetry systems (such as scanning ionization chambers) and in the processes used to align and localize the detector systems (since there is a relatively deep bore and the alignment lasers are displaced from isocenter). The impact of the magnetic field on ionization chambers and other dosimetry systems is being determined and is likely a strong focus of this meeting.
3. More work, less time

The commercial introduction of MRgRT brought along with it a new emphasis on the clinical potential of on-table adaptive radiation therapy (ART). ART requires that up-to-date images be acquired, resegmented, and the planned treatment be recalculated using the new images, or at least the new image segmentation. If the treatment plan is deemed unacceptable, it is reoptimized and the new plan used for that fraction. Given that these treatments are universally IMRT, a patient-specific QA would be required, but a measurement-based approach is unfeasible. Therefore, clinics have employed a calculation-based method to assure that the radiation dose distribution to be delivered will closely match the planned dose [4]. The operational parameters being sent to the linac are transmitted to an independent dose calculation engine that recomputes the dose distribution and compares it to the planned dose. The medical physicist then determines whether the doses are clinically similar and approves the treatment to proceed. As mentioned above, dose distributions can have millions of points to compare, and the physicist has seconds to conduct the comparison, so improved dose comparison techniques will be required.

The comparison is being made between two dose distributions that are computed on the patient model. This provides opportunities not present in most dose distribution comparisons, namely the ability to compare doses within organ systems [8]. The dose comparison can be made with the clinical tolerances in mind. For example, if a critical structure dose is well below tolerance, the dose comparison specification could be relaxed, since even under the relaxed criteria, an overdose would not be occurring. On the other hand, much of the body is not segmented, so care would be needed to assure that the dose distributions are evaluated in all tissues, not just those near tolerance. There are no generally accepted methods for conducting these types of evaluations, but extensions of current systems are often employed, such as dose distribution overlays, dose differences, and $\gamma$ evaluations. Since these are conducted in 3-dimensions, the limitations in human vision and computer displays, means that the physicist would need to scroll through the multiple slices to evaluate the entire dose distribution.

Tools, such as the $\gamma$ tool, were developed to efficiently sift through dose distribution comparisons and highlight regions of discrepancy. Unfortunately, most dose distribution comparisons were unable to pass all measurement points for even reasonable passing criteria, so compromise techniques were developed, such as to allow a predetermined fraction of points to fail the dose comparison test [9]. While this approach was efficient, it turned out that the sensitivity to clinically relevant dose errors was quite poor, in part due to the lack of dose and spatial specificity of such criteria. Given that the medical physicist will have very little time to compare two high spatial resolution dose distributions, optimizing the dose comparison workflow will be critical to detecting subtle but clinically relevant errors. Scrolling and closely inspecting the dose distribution is an impractical method for determining whether the dose distribution differences are clinically relevant, especially given that most calculation algorithms are unable to meet the typical $\gamma$ comparison criteria in all conditions.

The analysis of dose distributions for on-table adaptive therapy is further complicated by the fact that for MRgRT, the dose distributions will be calculated using Monte Carlo, which by its nature has statistical noise. As previously published by Low and Dempsey [10], $\gamma$ has sensitivity to noise that depends on the assignment of the reference and evaluated distributions, and if the evaluated distribution has significant noise, then $\gamma$ is underestimated. $\gamma$, or other dose comparison criteria will need to be adjusted to manage the statistical noise.

4. Conclusions

There are three domains in which 3D dosimetry will need development, the implementation of SRS for non-isocentric lesions, $4\pi$ radiation therapy, and on-table adaptive radiation therapy. The first two will require development of relatively large 3D dosimeters for, at least, end to end system tests. The last will require a re-tuning of dose distribution comparison techniques to enable the effective comparison of hundreds of thousands to millions of dose points in a very short time. These challenges will provide opportunities for further research and development in the area of 3D dosimetry.
Figure 1. Schematic showing the increased amount of data to analyse and the decreased amount of time allocated to analyse those data. This illustrates the increasing workload that physicists have to measure and analyse dosimetry data.

Figure 2. Image from the Varian website representing their implementation of multi-metastasis irradiation therapy (https://www.varian.com/sites/default/files/resource_attachments/HyperArcBriefOverview_RAD10424A_SecuredMarch2017.pdf). Note that lesions throughout the brain are being simultaneously irradiated. Meeting current stereotactic radiosurgery accuracy specifications will require improvements in 3D dosimetry.

Figure 3. Image showing BrainLab’s multi-metastasis treatment planning. Image courtesy of Dr. Nzhde Agazaryan, Ph.D.
5. References

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