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Has the use of computers in radiation therapy improved the accuracy in radiation dose delivery?

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Abstract. Purpose: It is well recognized that computer technology has had a major impact on the practice of radiation oncology. This paper addresses the question as to how these computer advances have specifically impacted the *accuracy of radiation dose delivery to the patient*.

Methods: A review was undertaken of all the key steps in the radiation treatment process ranging from machine calibration to patient treatment verification and irradiation. Using a semi-quantitative scale, each stage in the process was analysed from the point of view of gains in treatment accuracy. **Results:** Our critical review indicated that computerization related to digital medical imaging (ranging from target volume localization, to treatment planning, to image-guided treatment) has had the most significant impact on the accuracy of radiation treatment. Conversely, the premature adoption of intensity-modulated radiation therapy has actually degraded the accuracy of dose delivery compared to 3-D conformal radiation therapy. While computational power has improved dose calibration accuracy through Monte Carlo simulations of dosimeter response parameters, the overall impact in terms of percent improvement is relatively small compared to the improvements accrued from 3-D/4-D imaging. **Conclusions:** As a result of computer applications, we are better able to see and track the internal anatomy of the patient before, during and after treatment. This has yielded the most significant enhancement to the knowledge of “*in vivo*” dose distributions in the patient. Furthermore, a much richer set of 3-D/4-D co-registered dose-image data is thus becoming available for retrospective analysis of radiobiological and clinical responses.

1. Introduction

While historically, computer applications occurred mainly in the scientific realm, today computer applications are ubiquitous. The question as to whether this has had any societal impact is moot. One way of assessing this would be to see what happens if we turn off any application that involves computer usage; many activities in society today would come to a halt, as evidenced by unexpected failures in telecommunication networks. Because of the highly technical nature of radiation therapy, it was one of the first *medical* specialties to apply computers to routine clinical procedures [1]. This led to the initiation of the International Conferences on the Use of Computers in Radiation Therapy (ICCR), the first of which was held in 1966 in Cambridge, UK. References to each of the proceedings up until 2010 can be found in a book chapter by Van Dyk [1]. In the context of these ICCR conferences, the question being addressed in this paper is whether computer applications have actually impacted the accuracy of dose delivery to the patient in radiation therapy and, if so, how, and to what extent.

2. Methods

A true test of whether accuracy in dose delivery is affected by the use of computers in radiation therapy would be to do a controlled study analyzing dose delivery accuracy with and without computer assistance. However, it is obvious that this is effectively (and ethically) impossible since some of these procedures can simply not be executed ‘manually’ (e.g., IMRT optimization). The practical alternative is to use a logical, semi-quantitative analysis of the impact.

Since net accuracy is affected by multiple steps in the overall radiation therapy process, it is helpful to review the issues that impact dose delivery accuracy at each stage of that process and then to assess the impact of the role of computers on that stage. In terms of the steps in the radiation treatment



process, there are two broad considerations. The first deals with technology-related uncertainties such as radiation beam calibration and the commissioning of the radiation treatment planning system. The second relates to patient-related uncertainties including patient anatomy and its variation. These considerations are summarized in column 1 of Tables 1 and 2, respectively. A brief description of each step is found in column 2 of these Tables along with a description of accuracy and uncertainty issues in column 3.

3. Results

Column 4 of Tables 1 and 2 provides the authors' opinion of the impact of computers in radiation therapy in each stage of the calibration, commissioning or treatment process, based on a literature review. While this is admittedly subjective, it does provide an inventory of items to be considered in assessing gains or losses in dose accuracy. Figure 1 provides a graphical summary of the data in Tables 1 and 2.

4. Discussion

Historically, computer applications in radiation therapy have been most often linked to the treatment planning component of the treatment process. The 1987 ICRU Report 42 [2], *Use of Computers in External Beam Radiotherapy Procedures with High-Energy Photons and Electrons*, specifically produced "... a report on treatment planning and recording and documentation procedures ...". Little consideration was given to the other stages of the calibration, commissioning and the downstream treatment process involving the individual patient.

4.1. Calibration and commissioning process

4.1.1. Beam calibration

Basic radiation dosimetry has been, and continues to be the major focus in national standards calibration laboratories, for external quality assurance review agencies, as well as for medical physics professionals involved in developing dosimetry/calibration protocols. In 1976, ICRU Report 24 [3] showed that hospital beam calibrations in photon beams had uncertainties of 1.0 to 2.5% (optimally) or 2.3 to 4.9 % (minimally). In 1984, Svensson [4] indicated that beam calibrations could be performed with an uncertainty of 1.4 to 3.4% depending on whether they were cobalt-60, megavoltage x-ray or electron beams. A 2011 review by Andreo [5] showed that the determination of absorbed dose in a water phantom for therapeutic beams can be performed with an accuracy of 1 to 2% depending on the beam (photons or electrons) and whether the ionization chamber was calibrated in a primary or secondary standards laboratory. Some of the improvements in calibration protocols relate to the use of revised fundamental dosimetric factors generated with Monte Carlo techniques that are computer intensive. Thus, one could argue that computers have aided in the reduction of absolute dose calibration uncertainties by perhaps 1 to 4%.

Table 1. An evaluation of *the impact of the use of computers on the dose delivery accuracy* specifically for technology-related aspects of external beam radiation therapy using a five-star scale with one star representing minimal impact and five stars representing major impact.

1. Activity	2. Brief Description	3. Accuracy & Uncertainty Issues	4. Estimated Impact
Calibration protocol	<ul style="list-style-type: none"> Data/parameter generation 	<ul style="list-style-type: none"> Dependent on protocol Dependent number of particle histories for Monte Carlo 	**
Beam calibration	<ul style="list-style-type: none"> Use water phantom & detector positioning 	<ul style="list-style-type: none"> Distance determinations Detector reading 	*
Beam commissioning	<ul style="list-style-type: none"> Use of computer controlled detection system 	<ul style="list-style-type: none"> Detector positioning Detector size Detector response 	**
Treatment planning system commissioning	<ul style="list-style-type: none"> Entry of data Data fitting to determine model parameters In phantom analysis 	<ul style="list-style-type: none"> Data transfer Data fitting Algorithm limitations 	*****

4.1.2. Treatment planning system commissioning.

Treatment planning system applications are very computer intensive because the 3-D/4-D dose distribution must be determined in a heterogeneous time-dependent absorber – the patient. Modern systems use 3-D scatter integration techniques or Monte Carlo simulations. For many years, even into

Table 2. An evaluation of *the impact of the use of computers on the dose delivery accuracy* specifically for the patient-related steps for external beam radiation therapy using a five star scale with one star representing minimal impact and five stars representing major impact. TPS = treatment planning system; OAR = organ-at-risk

1. Activity	2. Brief Description	3. Accuracy & Uncertainty Issues	4. Estimated Impact
Diagnosis/clinical evaluation	<ul style="list-style-type: none"> Tumor pathology/staging Use of imaging 	<ul style="list-style-type: none"> Imaging limitations (resolution, sensitivity) False positives/negatives (specificity) 	****
Therapeutic decisions	<ul style="list-style-type: none"> Cure/palliation Treatment modalities/techniques 	<ul style="list-style-type: none"> Physician decision making Statistical analysis of clinical trials 	*
Treatment prescription/directive	<ul style="list-style-type: none"> Dose prescription including normal tissue dose-volume constraints 	<ul style="list-style-type: none"> Radiobiological outcome data Limitations on dose-volume data for both tumours & normal tissues Radiobiological models 	*
Patient positioning & immobilization for imaging	<ul style="list-style-type: none"> Laser positioning Patient support, positioning, & immobilization 	<ul style="list-style-type: none"> Laser accuracy on CT & other imaging units Congruence with therapy machine isocentre Stability of immobilization devices Patient comfort & compliance 	*
Imaging for treatment planning	<ul style="list-style-type: none"> Set-up patient Generate images for target & normal tissue localization 	<ul style="list-style-type: none"> Imaging limitations, e.g., resolution, interpretation of pixel signals Image fusion accuracy 3-D/4-D considerations 	*****
Contouring (image segmentation) of target volumes & organs at risk	<ul style="list-style-type: none"> Use ICRU concepts of GTV, CTV, ITV, PTV, PRV 	<ul style="list-style-type: none"> Limitations of imaging and segmentation Limitations of knowledge of microscopic spread not seen in images Uncertainties associated with CTV to PTV margins Inter- and intra-observer variations of target/normal tissue delineation 	**
Treatment planning (forward or inverse)	<ul style="list-style-type: none"> Dose calculations Treatment optimization 	<ul style="list-style-type: none"> Quality of beam data measurements Quality of TPS commissioning TPS algorithm accuracy in different regions and densities Degradation in accuracy with IMRT fields (e.g. small segments) 	***
Physician approval of treatment plan	<ul style="list-style-type: none"> Plan acceptability, esp. regarding tumor dose uniformity or acceptable doses to OARs Use of DVHs 	<ul style="list-style-type: none"> Physician knowledge/experience Clarity of communication between planner and physician Decision-making influenced by quality of printouts and graphic displays 	***
Data transfer & file management	<ul style="list-style-type: none"> Done manually in 2-D era Done through departmental network in 3-D/IMRT/MLC era 	<ul style="list-style-type: none"> Data transfer has little impact on accuracy/uncertainties unless a gross error occurs (e.g., wrong patient ID, wrong MLC configuration) More of an impact on reducing significant errors compared to manual copying of data Computers required for complex 3-D/IMRT plans 	*
Plan validation/checking	<ul style="list-style-type: none"> For 2-D, would be check of plan & MU For IMRT, phantom measurement or independent calculation 	<ul style="list-style-type: none"> Dependent on accuracy of 2nd check Has little impact on accuracy other than a confirmation and quality assurance to intercept gross errors 	**
Treatment machine set-up/immobilization/verification imaging (e.g., IGRT)	<ul style="list-style-type: none"> Use same immobilization at imaging for planning and in treatment room 	<ul style="list-style-type: none"> Patient set-up uncertainties should be determined in each department for each technique IGRT reduces both systematic and random uncertainties 	*****
Treatment dose delivery, possibly with <i>in vivo</i> dosimetry	<ul style="list-style-type: none"> Dose is delivered with appropriate field sizes, gantry rotations, shielding, MLC settings, etc. 	<ul style="list-style-type: none"> Machine dosimetry calibration Reproducibility of patient set-up Accuracy of <i>in vivo</i> dosimetry system Adaptive therapy protocol QA audits for IMRT delivery show significant variations at the 7%/4 mm accuracy levels 	**

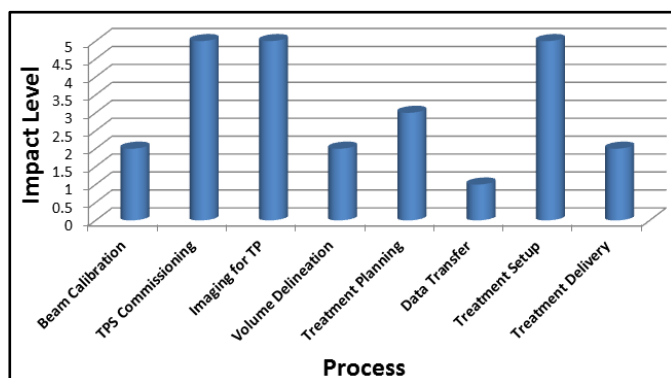


Figure 1. Graphical representation of the impact of computers on dose delivery accuracy for the different stages of the radiation treatment process using a five star scale, with one star representing minimal impact and five stars representing major impact.

the 2000s, tissue inhomogeneity corrections were not performed in many cancer centres. Today such calculations are performed more routinely and have reduced absolute dose delivery uncertainties from as much as 20% without any heterogeneity corrections to a few percent with convolution-superposition or Monte Carlo calculations [6]. Thus improvements in accuracy by as much as 15 to 20% have been noted. These represent potentially large inconsistencies and systematic offsets in the dose delivered in patients during the past decades of clinical experience. In some cases, it invalidates or at least impairs retrospective analysis of clinical dose-response results from the past era in radiation therapy.

4.2. Patient-related process

4.2.1. Imaging for diagnosis, treatment planning and target volume delineation

Imaging technologies have evolved dramatically in the last decades driven by the evolution of computer technologies. The use of 3-D imaging has allowed for very significant improvements in the ability to define target volumes and critical structures so that dramatic improvements can be made in normal tissue sparing with a potential for escalation in tumour doses [7-9]. This has also been extended to 4-D considerations to allow for intra-fraction motion of both tumour and normal tissue zones especially in lung [10]. It is very difficult to quote accuracy improvements in dose delivery; however, it is worth noting that improvements in target volume delineation have significantly decreased the likelihood of a “geographic miss”.

4.2.2. Treatment planning and treatment delivery per se (excluding image-guidance)

A major component of dose delivery accuracy to the patient can be assessed by performing end-to-end phantom tests where an anatomical phantom is scanned, planned and treated as if it were a patient. A number of reports have appeared describing such results from multiple institutions [6,11-14]. The conclusions are: (1) simpler dose calculation algorithms (those that do not integrate scatter in 3-D nor handle electron transport) can be inaccurate by as much as 20% in absolute regional dose, (2) 3%/3 mm criteria of acceptability at the $k=1$ (~1 st. dev.) is reasonable for 3-D conformal radiation therapy (CRT), (3) even with more sophisticated algorithms, as many as 30% of institutions can fail the 7%/4mm criteria of acceptability set by the Radiological Physics Center (RPC) for IMRT dose delivery upon their first attempt [13], and (4) dose delivery accuracy of 5%/4mm should be achievable at the $k=1$ level (meaning that $\sim\frac{1}{3}$ of situations lay outside these criteria). Furthermore, an examination of the variation in IMRT dose prescription, treatment planning, dose recording, and dose delivery among 803 brain, head-and-neck, and prostate cancer patients who were treated with different treatment planning systems at five different medical institutions indicated significant variations [15]. This raises concerns about the validity of comparing clinical outcomes from IMRT patients and suggests the need for national and/or international guidelines for dose prescription, dose computation, and reporting for meaningful clinical trials in IMRT. *Thus, in summary, dose delivery accuracy has actually been degraded as radiation therapy procedures have moved into the more sophisticated IMRT delivery procedures perhaps prematurely.*

4.2.3. Treatment delivery.

(a) *Image-guidance*. Image-guided radiation therapy (IGRT) uses imaging in the treatment room and allows for treatment adjustments to account for geometric deviations, both systematic and random. A recent review by Bujold *et al.* [16] demonstrated “that higher-quality dose delivery enabled by IGRT results in higher clinical control rates, reduced toxicity, and new treatment options for patients that previously were without viable options”. As with target volume delineation, it is very difficult to quote numerical magnitudes for dose delivery uncertainties associated with geometric displacement uncertainties; however, it is clear that these could be very significant because they are generally in high dose gradient regions, more than 5%/mm, near the tumour or normal tissue structures. IGRT would not be possible without digital technology; hence the “major impact” rating in our evaluation.

(b) *Intra-fraction motion*. With large CTV to PTV margins, slight tumour motion is relatively insignificant in terms of dose delivery variations. However, with reduced margins, higher dose prescriptions and tumour tracking technologies, the time component has become an extremely relevant consideration in ensuring full and accurate dose delivery to the target while simultaneously keeping normal tissue doses at acceptable levels. A recent review showed that for early staged lung cancers biologically equivalent doses (BED) of 72-80 Gy delivered with conventional techniques have been increased to 100-140 Gy using stereotactic body radiation therapy (SBRT), with tumour tracking or beam-gating techniques [17]. They reported that the average amplitudes of superior-inferior tumour motion were larger than 10 mm in approximately 33% of lung cancers. Clearly this could result in unacceptable dose variations if the treatments were delivered without image guidance and automated beam delivery, all heavily dependent on computer technologies.

4.2.4 Treatment evaluation and follow-up.

In view of the rich set of image data that are generated daily and that can be stored for later evaluation, patient follow-up analysis allows for the generation of much improved dose-response information both for tumour and normal tissues. Dose-volume analysis can now be performed as never before. Two of the 11 research priorities recommend by the Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) working group included (1) establishment of large continually growing data bases with full access to the 3-D dose matrix and linkage to biomarkers and clinical outcome and (2) development of methods for recording actual delivered dose (i.e., in an individual patient after fractionated radiotherapy) [18]. Both of these priorities are now possible with modern computer technology and are already being implemented [19-21]. Note, however, that proper controls for the accuracy of recorded 3-D/4-D dose distributions must still be applied (e.g., variations in dose algorithm accuracy for different IMRT situations).

5. Conclusions

While dose calibration procedures have yielded relatively small improvements in dose delivery accuracy (perhaps 1-4%) based on computer generated fundamental dosimetry parameters, it is clear that the combination of better dose calculation algorithms and digital imaging have had a more significant impact on dose delivery and geometric accuracy. Thus, the move into 3-D CRT allowed for very significant improvements in accuracy in targeted dose delivery. However, the implementation of IMRT combined with small field dosimetry difficulties has (temporarily) reduced the overall dose delivery accuracy to the point that, on their first attempt, 20 to 30% of institutions were not able to pass the 7%/4 mm criteria set by the RPC.

As a result of computer applications, we are better able to see and track the internal anatomy of the patient before, during and after treatment. This has yielded the most significant enhancement to the overall dose delivery accuracy of radiation therapy of individual patients. Furthermore, a much richer set of 3-D/4-D co-registered dose-image data are becoming available for retrospective analysis of radiobiological and clinical responses paving the way to personalized radiation therapy.

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