Overview

Volumetric Uncertainty in Radiotherapy

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ABSTRACT:

The technologies available to identify anatomical structures (including radiotherapy target and normal tissue 'volumes'), and to deliver dose accurately to these volumes, have improved significantly in the past decade. However, the ability of clinicians to identify volumes accurately and consistently in patients still suffers from uncertainties that arise from human error, inadequate training, lack of consensus on the derivation of volumes and inadequate characterisation of the accuracy and specificity of imaging technologies. Inadequate volume definition of a target can result in treatment failure and, consequently, disease progression; excessive volume may also lead to unnecessary patient injury. This is a serious problem in routine clinical care. In the context of large multi-centre clinical trials, uncertainty and inconsistency in tissue-volume reporting will be carried through to the analysis of treatment effect on outcome, which will subsequently influence the treatment of future patients. Strategies need to be set in place to ensure that the abilities and consistency of clinicians in defining volumes are aligned with the ability of new technologies to present volumetric information. This review seeks to define the concept of volumetric uncertainty and propose a conceptual model that has these errors evaluated and responded to separately. Specifically, we will explore the major causes, consequences of, and possible remediation of volumetric uncertainty, from the point of view of a multidisciplinary radiotherapy clinical environment. Hamilton, C. S., Ebert M. A. (2005). *Clinical Oncology* 17, 456–464

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Introduction

The goals of contemporary conformal radiotherapy are to maximise tumour control and minimise complications in surrounding tissues. One of the key concepts in achieving this aim is to ensure that the physical (i.e. dose distribution) and geometric (i.e. three-dimensional space) dose delivery is accurate, reproducible over time and consistently defined. The principles underpinning these concepts have been well developed in the reports from the International Commission on Radiation Units and Measurements (ICRU) [1,2]. Thus, the concepts of gross tumour volume (GTV), clinical target volume (CTV) and planning target volume (PTV) have assisted clinicians greatly over the past decade in providing a uniform conceptual framework for volumetric delineation in radiotherapy practice. Recognition of organ movement, and a desire to separate biologic uncertainty from the physical uncertainty, led to later

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refinements of these concepts, in the form of the mobile target volume (MTV) and biological target volume (BTV) The BTV has conceptually undergone a further transformation, as the possibilities of biologically targeted boosts within the GTV have been suggested [3,4]. The ICRU has responded to the same problem of target volume movement by introducing the concept of an internal target volume (ITV) [2].

Any inaccuracies in delivering a three-dimensional dose–volume envelope to an intended internal volume should be regarded as geometric error or uncertainty. Geometric issues shall not be considered in detail in this review other than to emphasise that both geometric and volumetric uncertainty contribute to the total spatial uncertainty for a particular patient. Readers are referred to the many extensive reviews of geometric uncertainty [4–14].

Clinicians have long recognised the inherent difficulties in defining tumour-related volumes accurately and reproducibly. For example, even direct inspection by the naked eye, or by endoscopy combined with direct palpation, does not always result in easily definable and reproducible GTVs. If we add to this the multiplicity of uncertainties associated with commonly used imaging

modalities, it is readily apparent that clinical variation and inherent limitations in imaging techniques will consistently produce significant GTV variability and uncertainty [15]. In addition, reproducible and accurate estimates of locoregional microscopic tumour extension in various sites have also proven difficult over many years. For example, in early breast cancer, the combination of meticulous postoperative pathologic assessment and high-quality preoperative mammography failed to predict microscopic tumour extension beyond 2 cm from the primary site in 11% of cases [16]. Preoperative endo-rectal ultrasound, currently recognised as an essential staging tool for rectal cancer, has been reported as having a significant false-positive rate resulting from tumour-associated inflammation [17]. Extra-capsular extension of prostate cancer, undetectable by preoperative imaging, was reported in up to 35% of cases in a surgical series by Sohayda et al. [18]. Thus, for many common visceral malignancies, it has been well demonstrated that variable local microscopic extension commonly occurs, and that this extension is impossible to estimate accurately without extirpative surgery.

The overwhelming uncertainty that goes unstated in all currently recognised staging systems (TNM, UICC, AJC, FIGO), and the ICRU documents, relates to the phenomenon of occult metastatic disease. Apart from the often-recognised importance of securing good local control, this problem dominates most solid tumour definitive and adjuvant therapy in relation to survival and disease-free related survival outcomes. Understandably, this uncertainty is rarely stated in all voluming schemes and assessments of volumetric or geometric uncertainty. A semi-quantitative graded assessment of these biologic uncertainties for site-specific clinical scenarios might assist in the overall understanding of the context and aim of treatment, rather than the usual simplistic subdivision into adjuvant/radical and palliative aims of treatment (Table 1).

Apart from the uncertainties of metastatic disease assessment, the other largest source of volumetric uncertainty relates to the seemingly unavoidable problem of clinician variability. It is important that clinician variability may be at an inter- or intra-clinician level, or both [15,19–35].

Volumetric uncertainty can also extend to critical organs (organs at risk [OAR]). Apart from the obvious problem of potential overdose, variation in OAR outlining produces dose–volume histogram (DVH) data (including mean doses, V_{20} , equivalent uniform doses and, possibly, bioeffect predictions), which may be, at best, unsuitable for comparison of results and, at worst, dangerous. Volumetric uncertainty also involves the integration of a variety of clinical factors with anatomical, learned clinico-pathologic concepts and imaging information, usually in the environment of a three-dimensional radiotherapy planning system

Table 1 – Suggested shorthand annotation of risk categories for local, regional and distant occult disease

Risk of	Low (≤10%)	Mod (10–25%)	High (≥ 25%)
Local extension outside GTV	L1	L2	L3
Regional extension outside GTV	R1	R2	R3
Distant disease outside GTV	D1	D2	D3

GTV, gross tumour volume.

(RTPS). For example, the radical treatment of non-small cell carcinoma of the lung may involve the generation of a plan that produces an 'unacceptable' V_{20} . The clinician may physically or biologically reduce doses, margins and/ or one or more treatment volumes. Thus, a complex feedback loop may be set up on the basis of questionable DVH complication data and clinical 'hunch'.

The final implication of volumetric uncertainty from any cause, is that it potentially represents a systematic error. The typical reported magnitude of inter-clinician variation commonly exceeds that of geometric systematic error, and will clearly have tumour control implications for some patients. These issues become even more critical as we adopt three-dimensional conformal radiotherapy and intensity-modulated radiotherapy techniques in greater numbers of treatment sites.

Data Sources and Search Strategy

The authors have drawn on personal and collegiate publication record at their own and other institutions. Personal and published research experience in the context of quality assurance from randomised clinical trials, and the report prepared by the British Institute of Radiology (Geometric Uncertainties in Radiotherapy) [36], have also been incorporated in the review. The international literature was searched using PubMed, using the following search terms: 'quality assurance', 'variation', 'delineation', 'outlining', 'segmentation', 'inter-clinician', 'intra-clinician', 'dosimetry', 'GTV', 'PTV', 'randomised trial' in the context of radiotherapy.

Overview of Volumetric Uncertainty

The development of affordable, high-quality, multi-slice computed tomography imaging with the appropriate slice width, interval, reconstruction techniques and intravenous contrast use will enable excellent visualisation of GTV in a variety of body sites. Known anatomical and imaging limitations, particularly in the mediastinum, abdomen and pelvis, produce known diagnostic difficulties and sources of uncertainty in differentiating tumour from normal tissue anatomy [37–40]. Anecdotal experience, literature and

¹ Within this review, the manual definition of volumes on radiographic images will be referred to as 'delineation', whereas the general concept of the definition of three-dimensional structures and their volume information shall be referred to as 'voluming'.

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departmental-based teaching all provide each radiation oncologist with a variable view on the likely uncertainties in GTV delineation or microscopic extension given any given tumour stage, grade and anatomical location. Comparisons can be made with fractionation surveys and a recently published survey of radiation oncologists' understanding of organ tolerance doses. On the basis of a few studies and a wide variety of anecdotal experience and departmental training, significant inter-clinician variation in organ tolerance doses [41,42] has been found. To illustrate this uncertainty in relation to normal tissues, we know that significant differences have been reported in the most appropriate methodology for outlining the rectum. This applies to its three-dimensional structure, external and internal outlines, and superior and inferior extent. This problem assumes particular importance when comparing international results or in a randomised trial setting, where strict DVH-based protocols or comparisons are required in order to achieve valid comparisons on acute and late toxicity data associated with any given protocol [43,44].

Volumetric uncertainty may also arise from RTPS software design. Differing mathematical approaches to interpolation algorithms and volume expansion algorithms may mean that volumetric comparison between clinicians and different centres may not be strictly comparable. Differing DVH reduction calculation algorithms also have

the potential to produce non-consistent results for international comparison, between departments and in a randomised trial setting. The various DVH-related statistics (e.g. mean dose, V_{20} , V_{30} , V_{50}) may also potentially be calculated in different ways in various RTPS [45–47]. Excessive reliance on auto-contouring algorithms in RTPS may produce one-off errors, particularly in the lung where collapse or consolidation may produce erroneous lung volumes.

Differences between departments in their scanning protocols, grey-scale settings and window or level settings may contribute further to volumetric uncertainty at an interdepartmental level. Just as it was apparent to the profession some decades ago of the need to standardise dose specification to allow uniform reporting and comparison of results, similar considerations now apply in relation to scanning and delineation protocols for common tumour sites.

Fig. 1 provides a flow-chart of sources of volumetric uncertainty. It can be seen that the process of volume definition and assessment represents a complex feedback phenomenon via the treating clinician, radiation therapist, physicist or dosimetrist. As radiation oncologists gradually shift from conventional dose tolerance figures [48] towards tolerances based on sub-volume irradiation levels (e.g. V_{20} , V_{30} , V_{50}), the requirement for robust population-based or large randomised trial data becomes ever more significant.

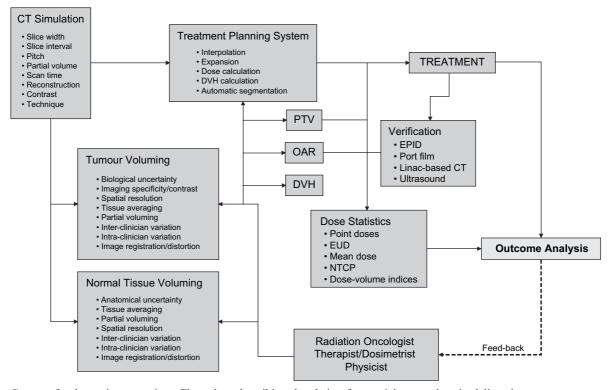


Fig. 1 — Causes of volumetric uncertainty. Flow-chart describing the chain of potential uncertainty in delineating gross tumour volume, planning target volume, clinical target volume and organs at risk. It should be noted that this system has the facility to feedback voluming information, in relation to individual patients and global practice. CT, computed tomography; CTV, clinical target volume; DVH, dosevolume histogram; EPID, electronic portal imaging device; EUD, equivalent uniform dose; NTCP, normal tissue complication probability; OAR, organs at risk; PTV, planning target volume.

Other imaging techniques have the possibility to improve the accuracy of computed tomography simulator-based GTV delineation. In particular, positron emission tomography scanning has shown promise in a number of sites, including lung, head and neck, and cervical cancer [49–53]. Magnetic resonance imaging has also been shown to produce smaller and more reproducible GTV delineation in prostate and other cancers [54–59]. The definition of the extent/boundaries of disease or anatomical structures depends extensively on the contrast [60], as well as the specificity achievable with any given imaging modality. Where a variety of modalities are used between centres for the same sites, the variations in these parameters will influence the resulting variation in volume definitions.

Inter- and Intra-clinician Variation

The problem of inter- and intra-clinician variation in the practice of medicine is widespread. It is now recognised that, for a variety of reasons (*vide supra*), it is not possible to regard the GTV or BTV as precise, well-demarcated, three-dimensional volumes [5,6,61,62]. For that reason, many of the causes of intra- and inter-clinician variation will not be able to be corrected on a systematic basis. Every effort should be made, however, to understand, measure or grade these variations, and account for them in protocol design [23,31,32,50].

There are some causes of inter- and intra-clinician variation where improvements can be made. Denham et al. [63] showed that variations in the understanding of the term 'PTV' accounted for a significant amount of inter-clinician variation. Significant differences in allowances for random error were also apparent. In a second related study, experienced radiation oncologists produced significant intra-clinician variation in target volume delineation in lung cancer [19]. This study suggested that non-stagerelated variables affected volume delineation. These studies pointed to the necessity for uniform application of the ICRU volumetric criteria. For example, 62% of clinicians who indicated, before the planning exercise, that they would include microscopic disease in their target volume, actually complied with this and, conversely, 45% of clinicians who said that they did not intend to include microscopic disease extensions, seemed to include microscopic disease on their planning computed tomography. Other studies of inter-clinician variation have pointed to similar issues in sites other than lung cancer. Seddon et al. [23] reported inter-clinician variation, particularly about the prostatic apex, superior prostate, seminal vesicles, and superior rectum, in the context of the MRC RT-01 Randomised Prostate Cancer Trial. Currently, the exact contributions of non-stage-related factors in contributing to this observed variation is a matter of speculation. Rigorous design of large-scale blinded exercises will be required to assess this phenomenon more accurately.

The contribution of computer-based RTPS hand-eye coordination skills in this context is also unknown. Testing and validation of hand-eye co-ordination and spatial anatomical skills has been applied in surgical disciplines, and may be useful in indicating the cause of inter- and intra-clinician variation in volumetric delineation in radiation oncology [64-67]. Three-dimensional reference grids superimposed on computed tomography planning anatomy may provide some additional guidance for clinicians [68]. Recent, large-scale, quality-assurance reviews of phase III radiotherapy trials have provided additional evidence that inter-clinician variation in clinical care and radiotherapy technical delivery form a small but significant area for ongoing clinical attention [21,23,69]. This phenomenon is surprisingly demonstrated in treatment scenarios where PTVs can be specified rigorously in terms of bony anatomy, which should not be misinterpreted. Widder et al. [21] reported considerable variation in treatment volumes despite detailed treatment guidelines in their pre-trial dummy run for an Austrian rectal cancer trial.

Technical Issues in Volume Definition

When presented with diagnostic imaging information, an individual can only be expected to provide outlines derived from the information present in the images. As such, although computed tomography has set standards in three-dimensional imaging, alternative imaging modalities can frequently provide anatomical information that far exceeds that available in computed tomography (in particular magnetic resonance imaging as discussed elsewhere in this review).

There are other technical contributions to volumetric uncertainty in addition to issues associated with the amount of information presented in diagnostic images and human intervention in defining volumes.

Resolution

The relationship between the physical extent of a radiotherapy field and the treatment volume depends upon the resolution of various stages of the imaging-planningtreatment process. In the first instance, is the resolution of the imaging used to define volumes [70]. In computed tomography, the resolution in the imaged plane will often be less then 0.5 mm (meaning that the basic imaging element, or pixel, is 0.5 mm wide). Depending on the generation of scanner used, however, the resolution in any other plane will at best be half of the slice thickness, which could vary between tenths of a mm to (more typically) 10 mm or more. This should be contrasted with the resolution achievable with a multi-leaf collimator (possibly 5 mm or more, including definition of the beam penumbra). As such, a high resolution in an image plane may well be redundant for treatment purposes in some instances (smallfield treatments such as radiosurgery demanding higher resolution). However, for assessing delivered dose, a high resolution is desirable, as the error associated with volume calculation falls off with increasing resolution.

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Volume Averaging

This is intimately associated with resolution, although it is also highly dependent on the imaging technique used to define volumes. Nuclear medicine based techniques (positron emission tomography and single photon emission computed tomography) produce images in which the relationship between image signal and the actual anatomy or function being imaged is blurred as a result of the method used to obtain images. In computed tomography, this is principally caused by an averaging of anatomical structure at the resolution of the image used. In PET, in particular, the resolution is inherently limited by the volume averaging introduced by the range of the positrons producing the image. For ¹⁸FDG imaging, this range is about 1–2 mm. Thus, definition of volumes must incorporate this volume averaging, which can result in a demonstrable variation in delineation.

Calculational Methods

Treatment planning and virtual simulation systems present and handle volumetric data in different ways. This can lead to uncertainties in volume information based on inter-slice extrapolation and interpolation, volume expansion algorithm, volume calculation, interpolation and data storage.

Inter-slice Extrapolation and Interpolation

Owing to the typically poorer resolution of imaging data out of the imaging plane (e.g. along the scan direction, usually the superior-inferior axis in computed tomography), presentation or calculation of volumetric data will often use interpolation for anatomical regions between slices. This will also be the case when outlining is carried out on only a selection of slices and information on intervening slices is interpolated. The method used for such interpolations may be system-specific, and can lead to differences between systems. Also, different methods of accounting for end-of-structure partial volume effects (accounting for the part of a structure that may or may not extend to the image slice adjacent to the last slice on which the structure is visible) can lead to appreciable differences in volume definition, especially when the image slice thickness is large. Ackerly et al. [71] found a discrepancy of 6-12% in volume for the same structure defined on different planning systems, where the discrepancy was caused by the method used for extrapolation of the volume at the outer slices (at 10 mm slice thickness).

Volume Expansion Algorithm

Treatment planning systems will typically provide automated methods for deriving one volume from another, using volume expansion, for example, in order to add a margin. Many alternative methods are available for making such a calculation, with different methods trading off calculation speed with accuracy.

Volume Calculation

Part of the analysis of volumetric data, including calculation of dose—volume information, is the calculation of the actual volume of an outlined structure. Planning systems will trade off speed against accuracy in using alternative methods for calculating volume. Such methods are also used to determine the centre-of-mass of a volume, which may be used in defining points of interest or treatment isocentres.

Interpolation and Data Storage

Analysing volumetric data may involve storing or exporting the data-defining volumes. In such instances, interpolation methods may be used to smooth or complete data. Again, such methods may vary between planning systems.

The definition of a volume inherently includes these effects which are convolved with the uncertainties contributed by human intervention. Quantification of these effects can be made, at least in computed tomography-based planning, by carrying out studies that use geometrically known phantoms with well-defined boundaries between different media types. The uncertainties introduced by these effects will also be amplified through image distortion or registration errors [59,72–77].

Strategies to Evaluate and Reduce Volumetric Uncertainty

Relatively few studies have included a sufficient sample size to enable a systematic assessment of the three-dimensional aspects of volumetric uncertainty. Analysis of the potential clinical effects, including values of parameters derived for dose–volume models, is restricted to general or theoretical scrutiny [78–83]. Most studies of clinician delineation involve relatively small surveys, and results are commonly displayed in a two-dimensional format. Available or emerging methods, however, are allowing more thorough evaluation or reduction of volumetric uncertainties.

Quantification of Uncertainties

Seddon et al. [23] have reported larger studies that enable the calculation of three-dimensional 'maps' of the standard deviation of specified volumes. Giraud et al. [15] have reported a similar study comparing the outlining of lung tumours by diagnostic and therapeutic radiologists. Regions on the 'map' showing the greatest 'disagreement' could then be addressed by educational, quality assurance and newer imaging and technical strategies. Remeijer et al. [84] have developed computational methods for generating statistics regarding inter- and intra-observer outlining variations, based on the three-dimensional information of delineated structures. These methods allow distinction of random and systematic volume uncertainties introduced by observers, including their dependencies on delineation method or modality. Such techniques are not currently easily integrated into routine quality assurance, and audit practice within the environment of the RTPS. RTPS manufacturers might be encouraged to develop built-in tools that enable these analyses across a large patient database.

Trials, Dummy-runs and Databases

The requirement to export a DICOM (NEMA 2001) or RTOG (based on the AAPM standard) [85] format dataset, and separately analyse three-dimensional variation (interclinician, intra-clinician or temporal), means that largescale analysis of delineation variations remains effectively a research tool. In the context of larger inter-centre comparative studies, as being undertaken by several collaborative trials groups, there are possibilities to use such databases across multiple clinicians and institutions. Methods for quantifying the variation of outlining, volume generation and calculation and dose-volume assessment across large-scale multi-centre databases are now emerging and, in some cases, are well established. Several trials groups have developed tools for retrieving treatment planning information, including radiographic data, outlined structures and dose distributions using RTOG and DICOM data exports from treatment planning systems [61,86–91]. Many others remain unpublished. Readers for these data formats have been developed, allowing comparison of all submitted data in a common format. An alternative may also be to use a common treatment planning system that can be shared over multiple trials sites [92]. In the context of trials, the use of such systems can include pre-trial dummy-runs using digital diagnostic data to ascertain variations in protocol interpretation and structure delineation.

The advantage of evaluating delineation data in the context of a multi-centre trial is that a specific protocol is being used with definition of the volumes to be delineated. Testing of protocol adherence can be achieved by using 'test' data sets to be compared against benchmark outlines for credentialing of participating sites. Before the advent of database systems collecting digital planning data during trials, the possibilities for examining trends in delineation (as well as dosimetric parameters) were reduced to manual examination of hardcopies. In combination with clinical outcome data obtained in a large trial, there will be the possibility to look at the clinical implications of volumetric differences between participants and algorithmic differences between treatment planing systems.

The Physical Process of Delineation

Improvements might also be obtained by making the process of volume delineation within the RTPS more consistent. Steenbakkers *et al.* [86] have reported on a keystroke monitoring system, which allows file capture of a clinician's sequence of tool use within the RTPS. This may be useful as a quality-assurance tool or as a real-time prompt for parameters such as margins (manual or auto), grey-scale selection, window selection and OAR. It might also be used to prompt clinicians to view all appropriate re-constructions, digitally reconstructed radiographs or other specialised rendered views.

Consensus on Delineation

Probably the greatest gains to be made in this area relate to the development and introduction of site-specific scanning, and delineation of guidelines that could be reasonably applicable to most radiotherapy departments internationally. If these were developed by an international multidisciplinary panel, we would have greater assurance that even though the regions of 'disagreement' might not be 'correctly' specified by the guidelines, there would surely be less variation. These type of guidelines are now being published, and are often well developed in the clinical trial setting [93,94]. Such guidelines will be crucial to enable valid comparison of treatment results. This applies particularly to the reporting of normal tissue toxicity, based on DVH data. Rigorous validation of DVH metrics and the current biological modelling of normal tissue toxicity will only be possible if large international DVH data sets are compiled. These will be meaningless if scanning and delineation methods differ.

Table 2 outlines a possible template for such international site-specific guidelines. These guidelines may incorporate an atlas of high-quality, computed tomography images with typical representative CTVs and OARs. Effective peer-auditing of three-dimensional RTP clinician practice will also require high-quality digital projection in a large departmental multidisciplinary environment in order to carry the principles of two-dimensional film and chart review into the 21st century.

Training

The inevitable increase in use of established (computed tomography/magnetic resonance imaging) and newer

Table 2 - Possible template for site-specific voluming guidelines

Scope of guidelines	Medical aims and introduction Staging workup, histology General treatment strategy and scheduling
CT Sim	Patient position, couch, immobilisation, treatment aids Skin markers, fiducial markers Upper/lower scan levels Slice thickness/width Contrast oral/IV
Secondary planning imaging	PET, MRI, Ultrasound Fusion techniques
Volume definition	GTV, CTV, PTV, BTV Expansion techniques Biologic uncertainty Outlining tools, window, level settings
OAR definition	Upper/lower levels Expansion techniques, addition or subtraction volumes Motion/margin uncertainty Paired/single organ
Geometric error	Definitions, assessment Decision models and correction

BTV, biological target volume; CTV, clinical target volume; GTV, gross tumour volume; MRI, magnetic resonance imaging; PTV, planning target volume.

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imaging modalities (positron emission tomography) implies that the congruence of diagnostic and therapeutic radiology will increase over the next 2 decades. Highquality and comprehensive training for radiation oncologists will require a thorough theoretical and practical understanding of all these imaging techniques in relation to the imaging of all cancer types and normal anatomy. Training curricula and examinations should be designed to reflect this increased need. This will reflect an increased infrastructure requirement for high-quality digital access to diagnostic and planning images throughout radiotherapy departments. The role of the oncological radiologist in teaching will obviously become increasingly crucial. Adequate access to contemporary three-dimensional RTPS terminals for trainees also remains problematic in many centres. Limited upfront capital and software upgrade budgets often mean planning terminals are used exclusively for service work, and teaching may take a back seat. In particular, RTPS are not designed primarily as a teaching tool. For instance, three-dimensional volumetric comparison of the trainee compared with a 'gold standard' is often cumbersome on commercially available radiotherapy planning systems. In addition, group teaching around a typical radiotherapy planning system screen is not viable. Dedication of a RTPS terminal and digital projection in a tutorial situation may be a luxury that is unaffordable by many departments. PC-based physicians' review stations or terminal-emulating programs may provide some solutions to this problem. Ideally, educators at both an under- and post-graduate level should have access to a portable physicians' review programme, which is suitable for networking in a workshop situation or projection as a high-quality digital display. Few affordable DICOM viewers offer the volumetric delineation tools that are found on typical high-end RTPS. In addition, incompatibilities between commercial systems and other DICOM viewing platforms are significant. The Australian Faculty of Radiation Oncology has developed a CD-based threedimensional planning module, where trainees are able to volume typical clinical cases using OSIRIS [95] software and compare on tiled screens their volume with an instructor's gold standard. A higher quality DICOM viewer with the facility to three-dimensionally superimpose the students' and teachers' volume would represent a significant advance. As such, software developed in Australasia, for the purpose of analysing digital treatment planning information ('SWAN') [90], is also being implemented to facilitate the teaching of principles of anatomical outlining. RTOG and DICOM imports can be used to provide cases for student revision, providing, in addition to outlining facilities, dosimetric display and DVH calculation, methods for comparing outlines to 'gold standards' and facilities for adding-on a user's own index calculation algorithms. Similar software has been developed at the Washington University Medical Center [91].

Large-scale multidisciplinary teaching is urgently needed, particularly in relation to pelvic and thoracic imaging. Possibilities for workshop-based, tutorial, or self-directed teaching again requires a suitable DICOM viewing

and delineation platform. The manufacturers of RTPS may have large educational opportunities in this area. Additionally, professional journals and publishers have a clear role in providing an educational framework to highlight and seek remedies for issues such as volumetric uncertainty.

Conclusions

The issue of volumetric uncertainty has been well identified in radiotherapy, and methods of quantifying and minimising this uncertainty are being developed. This overview is a prelude to a series of publications in this journal, which will examine these methods in detail and hopefully promote consensus on how to effectively introduce those methods and, in turn, produce more reliable and consistent response data.

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