

An Overview of Image-Guided Radiotherapy (IGRT)

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Abstract

Image-guided radiotherapy (IGRT) has undergone a continuous evolution of refinements leading up to the sophisticated techniques currently implemented as standard treatment, in radiation oncology clinics. This paper aims to summarize, in a general fashion, the key advances that have resulted in the ability of radiation oncologists to deliver increased radiotherapy doses to tumors, reduce doses to normal tissues, limit treatment related toxicity/complications, and increase patient convenience.

Keywords: Radiotherapy; CT imaging; Prostate cancer

Introduction

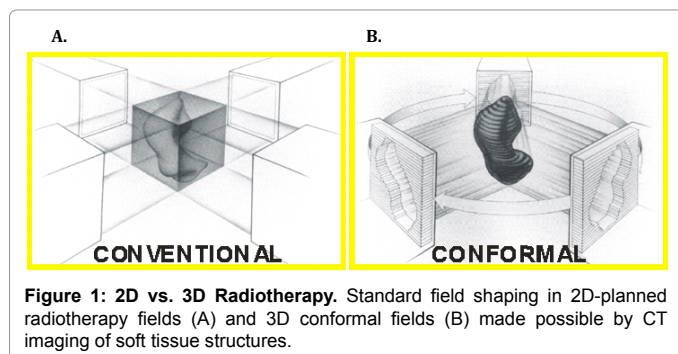
Radiotherapy (RT) in the modern era has always been image guided. Prior to the 1990's, the standard, available imaging incorporated into RT planning and targeting consisted of 2-dimensional plain radiographs of the treated region of interest. The anatomic position of the target regions as well as critical normal tissues was inferred from bony landmarks and whatever additional procedures could be used to improve targeting confidence: e.g. administration of oral contrast for delineation of upper gastrointestinal structures, enemas or rectal markers for lower GI tissue delineation, urinary contrast/catheter placement for genitourinary delineation, etc. The inability of such techniques to precisely define soft tissue anatomy resulted in high degrees of targeting uncertainty and subsequent large margins around any area of interest requiring treatment. The large volumes of normal tissues receiving the full prescription dose frequently limited the ability to deliver tumoricidal doses and were associated with high rates of treatment failure, toxicity, and complications.

The first major advance leading to what is regarded as modern image guided therapy was the incorporation of 3-dimensional treatment planning simulation. This generally refers to the incorporation of diagnostic-quality CT imaging as a direct part of the initial patient simulation process, allowing for accurate delineation of both target and normal critical soft tissue structures with the patient positioned and immobilized as they would be for daily RT treatment visits. Beams could now be more conformally shaped around targets and normal critical structures, and greater confidence in dose estimation with respect to both target coverage and risks to critical normal structures now existed (Figure 1). In no disease site has this concept been better illustrated than in prostate cancer where multiple prospective studies using 3D conformal RT have demonstrated improvement in clinical outcomes with the ability to safely escalate radiotherapy dose (Table 1) [1-3].

The increased conformity afforded by 3D treatment planning was taken a step further with the routine implementation of intensity modulated radiotherapy (IMRT). IMRT took advantage of multileaf collimation of individual RT beams in that numerous beam segments could now be generated for any given beam angle. The IMRT process involves precise, 3D delineation of all relevant target volumes and critical structures based on the initial planning CT scan. A series of priority weightings are then applied based on the clinician's specific goals of target coverage vs. normal tissue sparing. An inverse optimization algorithm is then carried out and a series of computer iterations results in an optimal solution and treatment plan. The end result (Figure 2), clinically, has been tightly conformal dose gradients and an ability to essentially "bend" isodose curves around critical structures in ways not possible with 3D conformal RT. Refinements in IMRT technique have led to techniques such as volumetric modulated arc therapy (VMAT) which has been shown in the context of lung stereotactic body radiotherapy (SBRT) to both decrease treatment time (by >50%), improve target dose coverage, and reduce total body exposure to ionizing radiation (Figure 3) [4]. It quickly became clear, however, that to fully exploit the dosimetric advantages of intensity modulation, confidence in targeting had to be maximized.

Off-line Image Guidance

Off-line image-guided radiotherapy (IGRT) refers to imaging modalities that enhance targeting accuracy without the patient physically present on the treatment table. In its most basic form, this begins with a 3D CT simulation based on which initial target volumes and critical structures may be identified. This delineation is greatly enhanced by the incorporation of other advanced imaging modalities based on the disease site being treated. Notable examples include the evolving role of MRI for prostate cancer [5] and its standard role in the delineation of primary brain tumors. Likewise, metabolic imaging in the form of positron emission tomography (PET) scans, most notably in the context of definitive RT for lung cancers, has been shown to



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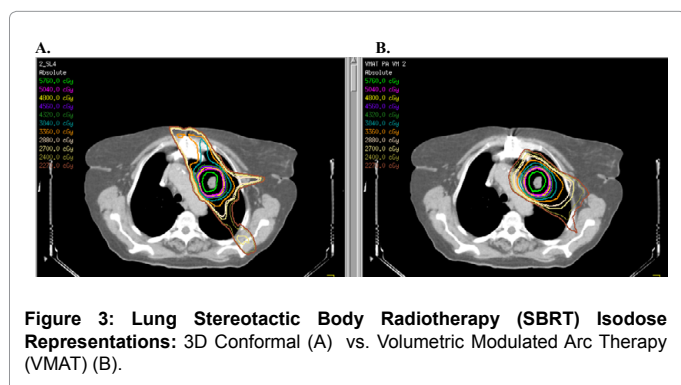
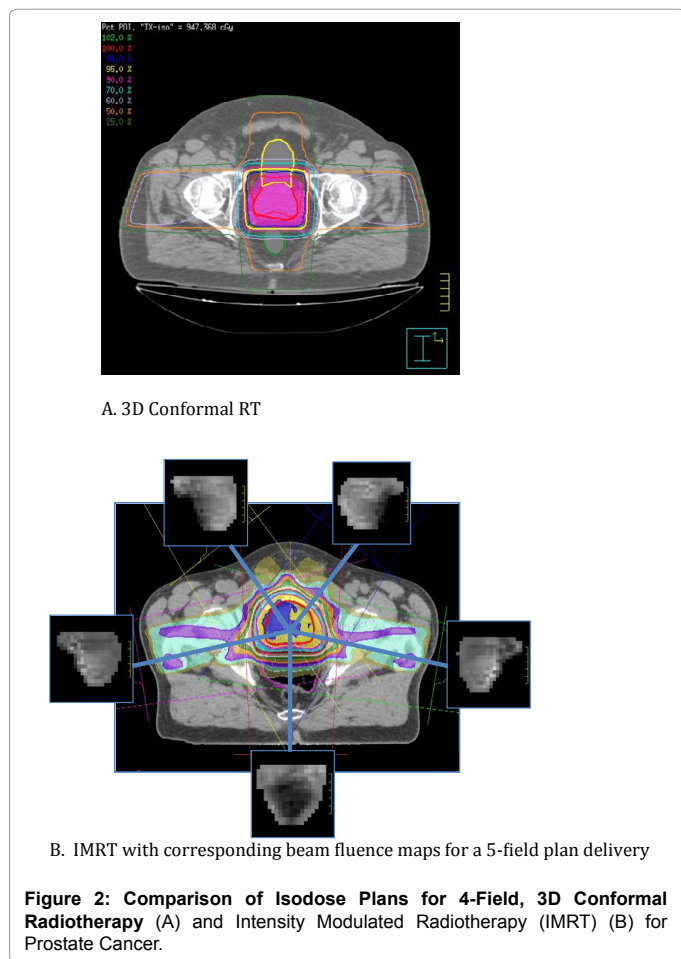
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Study	Design	N	Findings
MD Anderson (Kuban et al. [1])	70 vs. 78 Gy	301	59% vs. 78% 8 year failure free survival; 15% vs. 7% 8 yr. clinical failure
Massachusetts Gen. (Zeitman et al. [2])	70.2 vs. 79.2 Gy	392	61.4% vs. 80.4% 5 yr. PSA control
Netherlands (Peeters et al. [3])	68 vs. 78 Gy	664	54% vs. 64% 5 yr. failure free survival
RTOG 0126	70.2 Gy vs. 79.2 Gy	~1500	Not yet reported; accrual completed

Table 1: Prospective randomized trials demonstrating improved outcomes in prostate cancer with dose-escalated, 3D conformal radiotherapy.



enhance the accuracy of primary tumor delineation (differentiating from synchronous intrapulmonary pathology such as atelectasis) as well as identification of involved hilar or mediastinal lymph nodes [6,7].

The most detailed and sophisticated imaging, however, cannot account for variability in positions of targets and critical structures due to physiologic organ motion and technical setup variability. These factors can only be accounted for when a time factor is considered. Techniques have evolved that this may be accomplished in the off-line setting, the most notable disease site examples for which these have been employed are lung and prostate cancer [8,9].

Lung Cancer–Off-Line Image Guidance

Tumor motion due to respiration needs to be considered every time radiotherapy is used in the management of intrathoracic tumors. 4D CT scans [8] are now routinely employed at the time of RT treatment planning simulation for primary lung cancers. This technique involves the acquisition of CT chest imaging at coordinated phases of the respiratory cycle and allows for precise quantification of the direction and amplitude of target motion. This allows for the generation of a precise integrated gross target volume to which no additional margin for tumor motion needs to be considered. Additional expansions need only consider microscopic extension of the tumor and setup inaccuracy. The end result of this process is the generation of a planning target volume to which the definitive dose prescription will be delivered. If constructed appropriately, the gross tumor plus any microscopic extension of disease should never lie outside this volume.

Prostate Cancer–Off-Line Image Guidance

It has long been recognized that the prostate is not a static target that its position in the pelvis is subject to variable anatomic shifts based most notably on the degree of rectal filling/emptying with stool and bowel gas. Historically, this has been managed using off-line adaptive techniques that have been employed and described extensively for a number of years now. This involves the integration of multiple helical CT scans acquired early in the treatment course and subsequent quantification of shifts in the prostate position due to both organ motion and setup variability. In the off-line setting, the alternative approach would be to simply apply a margin around the prostate ± seminal vesicles wide enough to account for any organ motion and setup uncertainty that may occur across the entire population. In implementing this approach, it was possible to generate patient-specific planning target volume margins that were shown, in the vast majority of cases, to reduce the volume of bladder and rectum being treated [9,10]. While not widely employed, the fact that adaptive radiotherapy for prostate cancer has been implemented since the late 1990’s has afforded the opportunity to illustrate the long-term clinical value of image guidance in terms of ability to escalate RT dose, decrease normal tissue toxicity, and improve disease control [11].

On-line Image Guidance

Adjunct technology built into contemporary linear accelerators now routinely includes cone beam CT, a technique through which volumetric soft tissue image acquisition can be achieved with the patient precisely positioned and immobilized on the linear accelerator

treatment table. This now allows for precise quantification and correction (in real-time) of interfraction variability due to organ motion and patient setup inaccuracy. While patient positioning may certainly be manually corrected by radiotherapy technical staff, accelerator technology has evolved to the point that robotic table shifts and rotations may be automatically implemented based on detected variations in 3-dimensional target location. That is, no manual correction is required and adjustments can be made remotely from the treatment console.

To optimize the utilization of cone beam CT, however, there is one additional variable to be considered, and that is intrafraction motion. This may be minimized using immobilization maneuvers, examples of which would include abdominal compression for thoracic tumors [12] or placement of a rectal balloon for prostate cancer [13]. Additional measures would include real-time target monitoring, which may be achieved through multiple modalities including ultrasound, infrared tracking beacons (Calypso®), [14] or continuous kilo voltage imaging of implanted fiducial markers associated with technologies such as CyberKnife®. With these measures implemented, the monitoring system is typically linked to the linear accelerator such that movement of the target beyond a pre-set tolerance will trigger a shutoff of the treatment beam.

In summary, modern image-guided radiotherapy has been the culmination of a series of innovations in treatment delivery that have sequentially reduced the sources of uncertainty associated with three variables: initial delineation of tumor and critical structure extent/anatomy; target motion; and patient setup inconsistencies. Future directions to improve RT dose delivery will likely include dynamic consideration of tumor response and anatomic changes occurring on a patient-by-patient basis throughout a treatment course. While accounting for changes in general anatomy due to factors such as weight loss will only enhance the accuracy of RT delivery, adapting treatment fields/dose calculations to changes in target volumes due to tumor response will require prospective study to define the optimal timing at which to implement changes. Likewise, safe reductions in the sizes of target volumes will need to be defined specifically for different disease sites along with identifying the optimal imaging modalities required to define them.

References

1. Kuban DA, Tucker SL, Dong L, Starkschall G, Huang EH, et al. (2008) Long-term results of the M. D. Anderson randomized dose-escalation trial for prostate cancer. *Int J Radiat Oncol Biol Phys* 70: 67-74.
2. Zietman AL, DeSilvio ML, Slater JD, Rossi CJ Jr, Miller DW, et al. (2005) Comparison of conventional-dose vs high-dose conformal radiation therapy in clinically localized adenocarcinoma of the prostate: a randomized controlled trial. *JAMA* 294: 1233-1239.
3. Peeters ST, Heemsbergen WD, Koper PC, van Putten WL, Slot A, et al. (2006) Dose-response in radiotherapy for localized prostate cancer: results of the Dutch multicenter randomized phase III trial comparing 68 Gy of radiotherapy with 78 Gy. *J Clin Oncol* 24: 1990-1996.
4. Matuszak MM, Yan D, Grills I, Martinez A (2010) Clinical applications of volumetric modulated arc therapy. *Int J Radiat Oncol Biol Phys* 77: 608-616.
5. Rasch C, Barillot I, Remeijer P, Touw A, van Herk M, et al. (1999) Definition of the prostate in CT and MRI: a multi-observer study. *Int J Radiat Oncol Biol Phys* 43: 57-66.
6. Nestle U, Walter K, Schmidt S, Licht N, Nieder C, et al. (1999) 18F-deoxyglucose positron emission tomography (FDG-PET) for the planning of radiotherapy in lung cancer: high impact in patients with atelectasis. *Int J Radiat Oncol Biol Phys* 44: 593-597.
7. van Der Wel A, Nijsten S, Hochstenbag M, Lamers R, Boersma L, et al. (2005) Increased therapeutic ratio by 18FDG-PET CT planning in patients with clinical CT stage N2-N3M0 non-small-cell lung cancer: a modeling study. *Int J Radiat Oncol Biol Phys* 61: 649-655.
8. Keall P (2004) 4-dimensional computed tomography imaging and treatment planning. *Semin Radiat Oncol* 14: 81-90.
9. Yan D, Jaffray DA, Wong JW (1999) A model to accumulate fractionated dose in a deforming organ. *Int J Radiat Oncol Biol Phys* 44: 665-675.
10. Yan D, Lockman D, Brabbins D, Tyburski L, Martinez A (2000) An off-line strategy for constructing a patient-specific planning target volume in adaptive treatment process for prostate cancer. *Int J Radiat Oncol Biol Phys* 48: 289-302.
11. Brabbins D, Martinez A, Yan D, Lockman D, Wallace M, et al. (2005) A dose-escalation trial with the adaptive radiotherapy process as a delivery system in localized prostate cancer: analysis of chronic toxicity. *Int J Radiat Oncol Biol Phys* 61: 400-408.
12. Heinzerling JH, Anderson JF, Papiez L, Boike T, Chien S, et al. (2008) Four-dimensional computed tomography scan analysis of tumor and organ motion at varying levels of abdominal compression during stereotactic treatment of lung and liver. *Int J Radiat Oncol Biol Phys* 70: 1571-1578.
13. van Lin EN, Kristinsson J, Philippens ME, de Jong DJ, van der Vight LP, et al. (2007) Reduced late rectal mucosal changes after prostate three-dimensional conformal radiotherapy with endorectal balloon as observed in repeated endoscopy. *Int J Radiat Oncol Biol Phys* 67: 799-811.
14. Kupelian P, Willoughby T, Mahadevan A, Djemil T, Weinstein G, et al. (2007) Multi-institutional clinical experience with the Calypso System in localization and continuous, real-time monitoring of the prostate gland during external radiotherapy. *Int J Radiat Oncol Biol Phys* 67: 1088-1098.

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