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Image Guidance in Radiation Oncology Treatment Planning: The Role of Imaging Technologies on the Planning Process

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Radiation therapy has evolved from 2-dimensional (2D) to 3-dimensional (3D) treatments and, more recently, to intensity-modulated radiation therapy and image-guided radiation therapy. Improvements in imaging have enabled improvements in targeting and treatment. As computer-processing power has improved during the past few decades, it has facilitated developments in both imaging and treatment. The historical role of imaging from 2D to image-guided radiation therapy is reviewed here. Examples of imaging technologies such as positron emission tomography and magnetic resonance imaging are provided. The role of these imaging technologies, organ motion management approaches and their potential impacts on radiation therapy are described.
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Radiation therapy has been established as an effective local therapy for cancer. Over approximately the past half century, researchers in the field of radiation therapy have progressively used smaller fields with greater doses. This trend has been enabled by improvements in target definition and delivery. Computed tomography (CT) was the first innovation in target definition in that radiation oncologists were able to see the soft-tissue anatomy that they were irradiating; the development of CT-based 3-dimensional (3D) treatment planning in the 1980s led to significant improvements in sparing normal structures. More recently, intensity-modulated radiation therapy (IMRT) has permitted radiation oncologists to sculpt a 3D dose cloud around the target volume.[1,2] Current developments in stereotactic body radiation therapy extend this principle even further. More recently, image-guided radiation therapy (IGRT) has been developed. Historically, all radiation treatments are image guided, but the use of IGRT incorporates recent innovations in both target delineation and in-room corrections.

A variety of in-room correction systems are available commercially. The goal of all these systems is to ensure that the patient or, more specifically, the target organs, are positioned as planned relative to the treatment beam. A variety of systems exist, including imaging devices mounted in the floor to locate implanted fiducials during treament (eg, Cyberknife, Novalis), CT on rails (Siemens) megavoltage CT scanners (eg, Tomotherapy), electromagnetically implanted fiducuals (Calypso), cone beam CT systems (Varian Trilogy, Elekta Synergy).

Target delineation plays a major role in the treatment-planning process. A pioneering medical physicist, Harold Johns, said "If you can't see it, you can't hit it and if you can't hit it, you can't cure it." Improvements in imaging have led to improvements in target delineation and in turn, have driven the need for more accurate delivery and verification methods. To provide a perspective on the evolution of imaging and its role in treatment planning, we provide a brief historical review.

Historical Role of Imaging in Radiation Therapy

2D Era: Irradiation of Anatomical Regions

In the early era of radiation treatments, patients were placed on a radiation therapy simulator. These are now called "conventional simulators." A conventional simulator is an x-ray tube on a gantry which mimics the optical and alignment properties of linear accelerator. It is capable of both fluoroscopy and radiography. In the 2D era, contours of the patient anatomy were taken along the central axis of the beam using a solder wire and digitized into the treatment planning computers. The patient was positioned under fluoroscopic guidance, and the physician used the radiographs to draw shielding blocks. The blocks were then fabricated. The patient positioning was evaluated by creating a so-call portal film—the image generated using the beam from the treatment port. Image quality is

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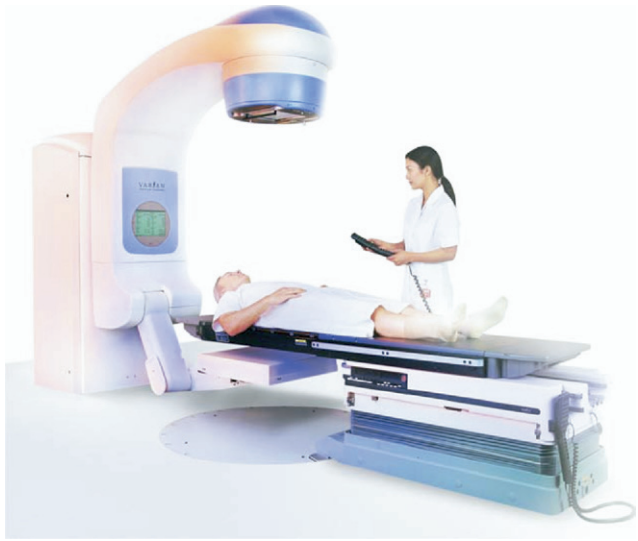

Figure 1 Illustration of a conventional simulator. (Image from http://varian.mediaroom.com/index.php?s = media_library&cat = 5. Copyright © 2007, Varian Medical Systems, Inc. All rights reserved.)

notoriously poor because the high energy of the beam results in very low contrast. Nevertheless, bony anatomy can be used to confirm that the portal image agrees with the planned simulation radiograph. Modern conventional simulators now have flat panel imaging systems and can be used for cone beam reconstruction as well (Fig. 1).

3D Era: Target Volume Definitions

When CT was introduced, radiation oncologists were eager to implement it clinically. For the first time, they could now view where the radiation was going and, with the help of physicists and industry, they could calculate the actual dose sent to the organs. As shown in Fig. 2, it was now possible to simulate the effect of different blocking and beam shaping, as well as beam geometry and beam weighting before treating patients. An optimal plan that could deliver a uniform radiation dose to the tumor could be calculated and delivered. The 3D treatment planning era had begun. As computer graphics became more sophisticated and the computer processing speeds increased, more sophisticated analytical tools became widely available.

The specific position of the patient is crucial as the CT scan serves to provide a model for treating the patient. Specifically, the CT scan is acquired so that the radiation oncologist can delineate the tumor, the surrounding organs at risk and apply a margin around the tumor. Specific nomenclature has been developed for target definition.[3,4] The gross tumor volume (GTV) includes the full extent of the tumor as defined by any imaging or fused studies. The clinical tumor volume (CTV) includes the GTV and a margin for microscopic extent of the disease. The CTV can be quite large if nodal involvement is suspected. The planning target volume (PTV) includes a margin that envelops the CTV to account for day to day variations in setup and internal organ motion. The prescription dose is to the PTV, ensuring that the tumor is enveloped by at least this dose of radiation.

CT simulators are essentially diagnostic CT scanners with 2 additional features. First, a flat table top, usually fabricated from carbon fiber, is used to mimic the flat table top of the treatment console and, second, a set of trackable lasers are mounted for helping position the patient. During CT simulation, the radiation oncologist will choose an isocenter, a position on the patient that marks the point at which all the radiation beams will intersect. Historically, this position was close to the geographical the center of the tumor, but with recent advances in treatment planning, localizing within a few cm of the center is sufficient. The radiation oncologist works on a CT simulation workstation, which has special software for reviewing the individual slices and for contouring on them. The software also is able to send a set of coordinates back to a set of trackable lasers, which move to a specific set of coordinates on the patient. A set of tattoos, each the size of the laser light beam cross-section, are then marked on the patient to form an orthogonal set of coordinates. Identical lasers are used on the treatment linear accelerator to perform the initial optical alignment of patients for treatment. After obtaining the CT data set, the physician then completes the contouring of the target and organs at risk. This information is then sent to the planning group, consisting of dosimetrists and physicists.

IMRT/IGRT Era: Dose Sculpting and Target Motion Management

In the past decade, the combination of computer controlled accelerators and innovations in planning lead to the development of IMRT. There are 2 key features to IMRT; the first is inverse planning. In the 3D era, the geometry of the tumor and organs at risk would be reviewed, and a skilled planner would vary gantry angles, collimation, blocking, beam weights, etc. to produce the best possible plan after several trial and error attempts. With increased computer power, medical physicists began

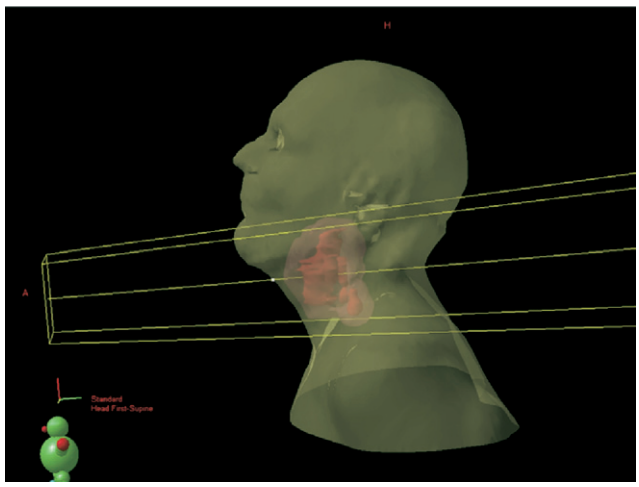

Figure 2 Volumetric rendering showing external patient anatomy, GTV (in red) and PTV expansion (in pink). (Image courtesy of Montefiore Medical Center.)

Figure 3 Illustration of multileaf collimator. This model has 120 leaves that are individually computer controlled. (Image from http://www.varian.com/orad/prd056.html. Copyright © 2007, Varian Medical Systems, Inc. All rights reserved.)

to try to solve the inverse problem, that is, given a 3D model of the target and surrounding organ at risk, find the optimal combination of x-rays and beam angles to deliver the radiation. The second and most striking feature of IMRT is that radiation intensities are modified by the use of a multileaf collimator (MLC; Fig. 3).[5] These devices consist of sets of tungsten leaves driven by individual motors. The position of leaves can be controlled and used to shape virtually any intensity distribution. Two types of delivery have been available, segmented often-called step and shoot and dynamic. In segmented IMRT, the leaves move to form a shape, the beam is turned on for a certain exposure, and then a new shape and a different exposure is delivered. The sum of these exposures produces an IMRT field. In dynamic delivery, the leaves move while the beam is on; gaps between the leaves result in the desired delivery. Recently, Tomotherapy has introduced a new approach for treatment that uses helical delivery with a binary MLC to create the intensity modulation; this system permits a greater degree of freedom for delivering the treatment over fixed gantry approaches. In turn, some vendors (Elekta and Varian) have recently introduced a commercial version of intensity modulated arc therapy, which permits modulated therapy while the linear accelerator gantry rotates around the patient.[6]

Figure 4 shows the comparison of dose distribution on 3D and IMRT plan. The color wash begins at the threshold prescription isodose level. The structures that the physician has contoured are outlined in red. The difference in volume of healthy tissue receiving prescription dose is dramatically reduced using IMRT. IMRT has revolutionized radiation oncology; it permitted tumor dose escalation, which, in principle, should lead to increased local control rates while at the same time allowing for mathematical constraints of normal tissue doses in the inverse planning process.

Role of Imaging Technologies

In the IMRT/IGRT era, when only outlined structures (GTV, CTV and PTV) are in the radiation dose prescription volume, target delineation is the crucial input data to the treatment planning process. If the target definition by imaging is inaccurate, the rest of the planning and delivery approach is rendered ineffective. Non-CT-based imaging technologies have begun to play a role in helping with target delineation. For instance, magnetic resonance imaging (MRI)[7] and positron emission tomography/computed tomography (PET/CT)[8-12] are playing new roles in helping the radiation oncologist define the GTV.

MRI plays an important role in defining targets because of its greater soft-tissue contrast. For instance, it has been demonstrated that the prostate is difficult to define on CT and is often overcontoured (by approximately 30% by volume) when using CT.[13] MRI enables the radiation oncologist to separate the prostate from the periprostatic fat, thereby permitting focusing of the radiation to the correct target volume. The resolution of MRI is approximately 1 mm and a cell is approximately 10 microns in width, meaning that, in one

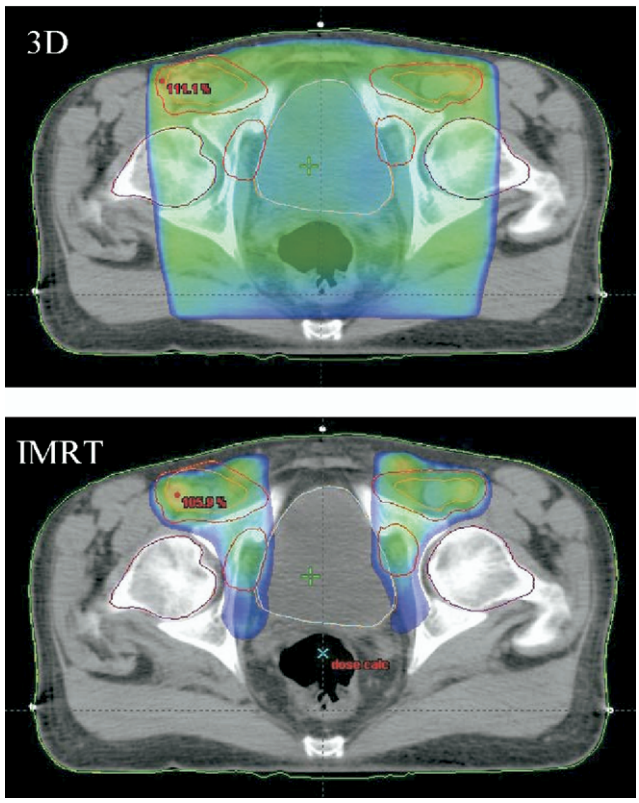

Figure 4 Comparison of dose distributions on 3D and IMRT plan. The color wash begins at the threshold prescription isodose level. (Image courtesy of Montefiore Medical Center.)

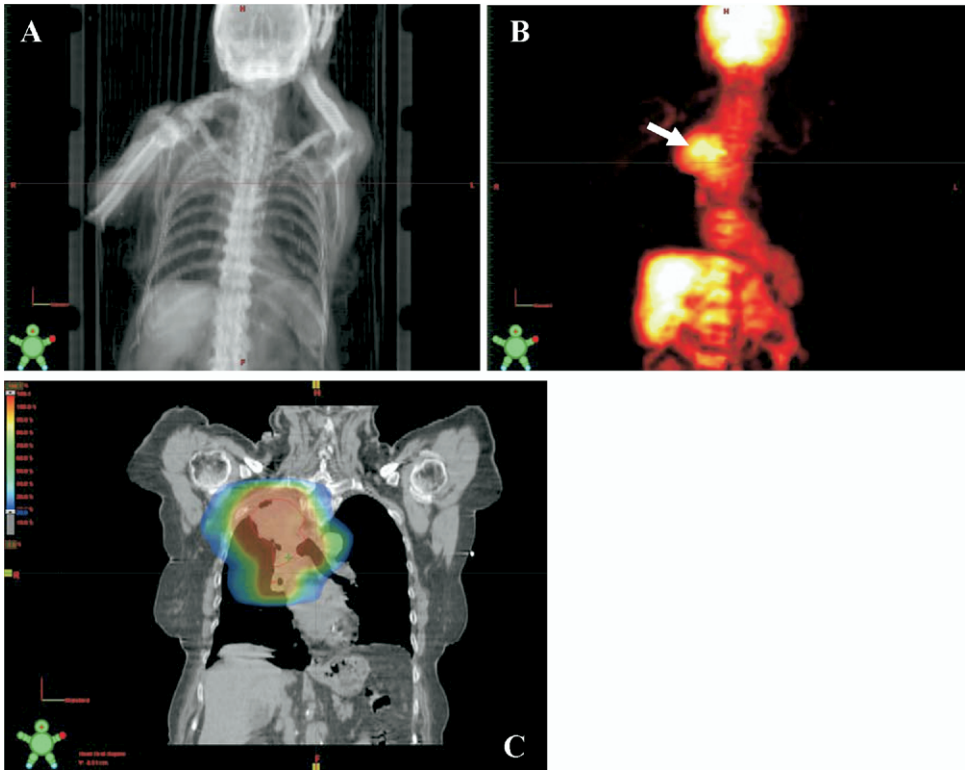

Figure 5 Target delineation of lung cancer by PET-CT in treatment planning. (A) Coronal view of CT image. (B) Intense uptake seen on PET image. Note that the both set of images were acquired in single PET/CT scan. (C) GTV delineation (red line) and isodose distribution (color wash). (Image courtesy of Montefiore Medical Center.)

cubic millimeter, there are approximately 1 million cells. For the oncologist to find that cancer cell, molecular imaging methods are required. PET has potential to provide this level of information. A new nomenclature, called "biological target volume," has been suggested to define PET defined volumes.[14]

PET has played an extraordinary role in nonsmall cell lung cancer staging and treatment. For nonsmall cell lung cancer, there was substantial variation between the target definition of different radiation oncologists. With PET, target delineation in lung between has been shown to be much more consistent.[15] Figure 5 shows an example of how PET/CT makes target delineation clearer. However, it may not mean that these results are accurate. No imaging system has been shown to be 100% perfect (eg, to not have false positives) in defining any target volume. PET provides supplemental information to the radiation oncologist who integrates the information with all other studies to define the PTV. In addition to lung cancer, PET has also been used to plan esophagus and head and neck cancers.

In facilities with PET scanners only, radiation oncology patients are set up in the PET scanner and the resulting images were fused to the planning CT, acquired on a CT simulator. Typically, a flat table top is added to the PET scanner and a radiation therapist accompanies the patient for setup. Despite these efforts, uncertainties in the registration process remain. With PET/CT scanners, hardware solves the registration problem between the PET and CT automatically and accurately. Some centers have modified PET/CT scanners have created PET/CT simulators by adding a flat tabletop and trackable lasers to the PET/CT.

Motion also plays a major role in target definition. For tumors that move several centimeters with a patient's respiration, the PTV margin must be drawn to encompass the entire range of motion, thereby increasing the toxicity of the radiation and limiting the overall dose that can be delivered. Recently, methods to reduce the effect of respiratory motion have been developed including breath hold during treatment, "gating" in which the beam is turned on or off in synchrony with the respiratory cycle[16] and "tracking" in which the beam follows the tumor based on imaging technology.[17,18] Planning is performed using a 4D CT, ie, a CT that takes multiple volumetric images and sorts them according to the breathing cycle to produce a 3D movie loop- the 4th D refers to time.[19] Similar technology is currently being applied to PET/CT systems.[20,21]

The most common tracer for PET is fluorodeoxyglucose labeled with radioactive fluorine. Other tracers based on ^{11}C and ^{18}F also are being developed to aid radiologists in the imaging of angiogenesis, hypoxia, and apoptosis. Together, these developments have the potential to provide information about tumor metabolism, location, and treatment response and thereby improve the effectiveness of radiation treatments for patients in the future.

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