

Advances in Radiation Therapy

a report by

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Radiation therapy has made significant advances over the past two decades. The beginning of the 1980s saw radiation therapy as a prescriptive medicine. Treatments using megavoltage X-rays were planned using the crude imaging tools available in the day. Radiation portals were typically defined using radiographic planar imaging, where only bony anatomy and large air cavities were visualized. The radiation oncologist used previous experience based on the tumor type, location, and extent (determined using planar imaging and palpation), to define the portals. Significant customization of the radiation portals based on a quantitative understanding of the patient's tumor geometry was not possible due to the poor access to three-dimensional (3-D) imaging modalities.

The advent of broader access to computed tomography (CT) and computing technology led to the first technological revolution in the 1980s. 3-D radiotherapy treatment planning (3DRTP), where the tumor is defined in 3-D using CT scans and the radiation portals are designed based on the 3-D tumor and normal organ shapes, was introduced and made rapid inroads into radiation therapy practice. The use of 3-D imaging allowed the radiation oncologist to customize the radiation dose distribution to the patient's specific tumor and normal organ geometry. Studies showed that in many cases, the earlier (called the 2-D approach) often underestimated the required beam portal size, causing underdosing of the tumor.

3DRTP also allowed a quantitative understanding of the radiation dose to critical structures. Physicians were provided with feedback on the radiation dose throughout the normal organs, and dose summary tools were invented that enabled the physicians to efficiently determine if the doses were within clinically acceptable limits.

3-D treatment plans were designed as models of the dose distributions that were to be delivered to the patient. As such, they suffered from two important limitations. First, the 3-D CT image was acquired at a specific point in time and, therefore, it only represented a 'snapshot' in time of the patient's tumor and normal organ positions.

As an example, the position of the prostate depends greatly on the fill status of the bladder and rectum. A CT acquired with a full rectum will show the prostate in a more anterior position than when the rectum is empty. Consequently, the treatment plan will be designed with the dose more anterior than the average tumor position and a 'geometric miss' could occur. Other similar tumor-positioning errors included patient positioning reproducibility and gradual tumor shrinking or tissue swelling that modified the size, shape, and position of the tumor. In order to combat these limitations, the concept of a tumor margin was defined. A margin was a 3-D expansion of the imaged tumor (gross tumor volume (GTV)) that was sufficiently large that the tumor would be positioned within the margin surface on a daily basis. The radiation dose was designed to encompass the margin volume (planning target volume (PTV)) rather than the imaged tumor volume. While this presumably guaranteed full irradiation of the tumor, it also led to treatment portals that irradiated more normal tissues than necessary given the tumor size and shape.

Secondly, the CT image could not show the entire extent of the tumor. Tumors typically invade with microscopic extensions, often infiltrating many centimeters from the bulky disease. The microscopic extensions cannot be visualized using CT imaging, so a method for identifying the suspected occult disease volume was developed, termed the clinical target volume (CTV). By definition, the CTV encompassed suspected tumor cells and its design was therefore less quantitative and required more clinical judgment to define than the GTV. Because the tumor burden was less in the CTV than the GTV, the dose required to sterilize the tumor in the CTV was assumed to be less than in the GTV. CTV doses were therefore often smaller than the GTV doses. The PTV margin concept was also applied to the CTV.

The second technological revolution occurred from treatment planning simulation studies conducted in the late 1980s. During that time, scientists identified the fact that the radiation dose distributions could be made significantly more conformal if the radiation fluence (intensity) from each beam could be optimized using software-based algorithms. Luckily, the linear

accelerators of the day were capable of delivering these optimized fluence patterns. This technology was labeled intensity modulated radiation therapy (IMRT), and it allowed the design of very conformal dose distributions. IMRT provided for the capability of irradiating tumors while sparing nearby surrounding normal organs.

The consequence of these revolutions is that the current state of the art is the fact that highly conformal radiation dose distributions (using IMRT) can be designed to an image dataset that is a snapshot of the patient geometry. While this has led to great improvements in the quality of treatment plans, the GTV is designed using bulky disease imaged using a single image dataset. These limitations are being overcome in the next generation of radiation therapy technology.

Improvements in Tumor Imaging

Improving tumor imaging is being actively investigated by radiology and radiation oncology departments and includes the development of molecular imaging, functional imaging, and biological imaging. The specific concepts behind these imaging categories overlap, but essentially, are that the imaging modalities will exploit highly sensitive imaging techniques to differentiate between tissue types. Some of these differentials are due to tumor physiology. For example, many tumors are more physiologically active, and therefore process more glucose, than the surrounding tissues. Positron emission tomography (PET) using ^{18}F -fluorodeoxyglucose, a glucose analog, provides highly sensitive images of active glucose uptake within rapidly growing tumors. It is expected that imaging advances will include the ability to determine aspects of the tumor environment, such as hypoxic state, and tumor dose response.

Removing the Limitations Associated With the Use of a Single Image Dataset

The use of the PTV concept allows the radiation dose distribution to encompass the tumor within the expected tumor positioning errors. An important technology, on-board imaging (OBI), is being developed that may allow monitoring of the tumor position for each treatment. OBI technology consists of imaging hardware attached to the linear accelerator that allows the acquisition of a 3-D CT image dataset. These 3-D CT images can be used to identify misalignments of the tumor, allowing the patient to be repositioned, placing the tumor in the planned position. In principal, this may allow for reduced PTV margins, leading to smaller high-dose volumes and correspondingly reduced normal tissue irradiation.

While OBI seems to provide the ideal tool to significantly reduce the PTV margins, there are some

Figure 1: An example of the use of PET-based functional imaging to modify the radiation dose distribution for a cervical cancer patient. (a) A PET-positive cervical lymph node is identified on the PET scan and the delineated structure is transferred directly to the treatment planning CT scan (b). (c) The radiation dose distribution is modified to boost the PET-positive lymph node while delivering a conventional dose to the lymph node bed

Figure 1a

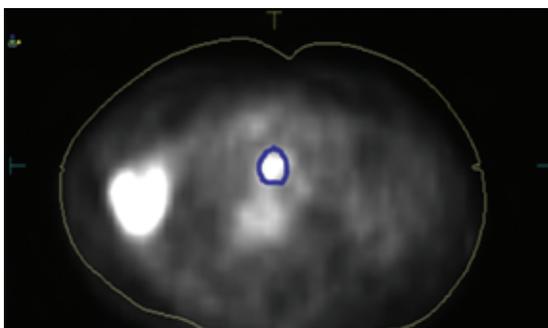
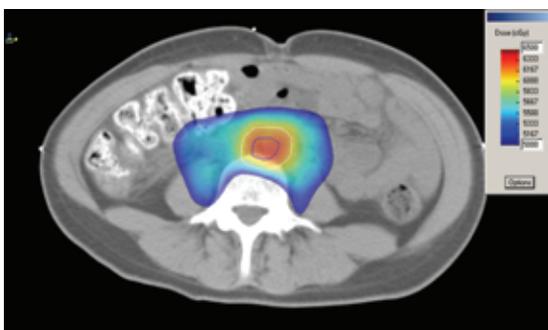


Figure 1b



Figure 1c



challenges that need to be met before it comes into widespread use. In order for therapists to use the image data to reposition the patient, they need to have efficient and effective tools to evaluate the tumor position relative to the planned position. The current commercial tools are relatively crude and need significant improvements.

Physicians also need to access the registration results at convenient locations (as opposed to requiring them to travel to the treatment unit for the review process). This access requires a database system that can deal with the large image datasets and will transfer the image information efficiently to the physician.

The use of OBI promises to be a definite advance in patient positioning but it has some significant technical limitations. The image acquisition process uses the linear accelerator gantry rotating around the patient. The time of acquisition is typically one minute; longer than a patient can hold their breath and long enough for other physiologic processes (e.g. digestion) to significantly move internal organs. This motion results in image artifacts that can disturb or completely destroy the image quality. The number of tumor sites is limited where OBI imaging will guarantee high-quality images that can be relied on for daily positioning. Research is being conducted to analyze the raw image data to reduce motion artifacts.

Another technical limitation is that the imaging modality uses kilovolt or megavolt X-rays and therefore the soft-tissue contrast is limited. Many tumors in the abdomen or pelvis cannot be visualized using these modalities.

treatment plan based on the actual radiation response as compared against the expected response. For example, if the tumor is expected to regress at a specific rate and the tumor regresses slower, increasing the dose fractionation may be appropriate. Conversely, if the tumor regresses more rapidly than expected, the dose fractionation or total dose could be reduced.

The customization of the treatment plan during therapy is an exciting potential advance in radiation therapy practice. There is anecdotal evidence that some tumor regression may cause the tumor to leave the high-dose region. Having the capability to vary the total dose or dose fractionation with respect to variations in tumor response rates may improve the local control and complication rates for many sites.

Breathing Motion

As mentioned earlier, one of the challenges to accurate imaging is the management of breathing motion. Breathing motion also causes other difficulties for conformal therapy or IMRT. The motion of the tumor during the initial CT imaging will cause artifacts, leading to errors in determining the shape of the tumor.

With OBI, there is the potential for adjusting the treatment plan to changes in the tumor size or position based on 3-D image datasets.

Adaptive Radiation Therapy

An important potential advance that can take place with the implementation of OBI involves the periodic review of the image datasets to determine if the tumor has regressed significantly. Some tumors, such as cervical cancer and Hodgkin's lymphoma, are very radiosensitive and regress dramatically throughout therapy. The initial treatment plan may be inappropriate part way through the course of therapy. In the past, review of the relationship between the treatment plan and the tumor was limited to monitoring the patient's weight or how well they fit into custom-fabricated immobilization devices. With OBI, there is the potential for adjusting the treatment plan to changes in the tumor size or position based on 3-D image datasets. This process is termed adaptive radiation therapy (ART). ART includes replanning for geometric changes, but can also be used to modify the patient's

Breathing motion of the tumor during treatment causes the radiation beam to be larger than the tumor cross section. Techniques are being developed to quantify the breathing motion to allow for a more accurately designed radiation beam. These techniques are also being used to gate the linear accelerator to effectively limit breathing motion, as well as investigating the option of tracking the tumor motion with the radiation beam.

Conclusions

This is an exciting time in radiation therapy. The industry has the ability to deliver customized, highly conformal dose distributions and is implementing the capability of collecting 3-D images prior to each treatment. Advances in radiology imaging techniques will be used to improve the ability to identify otherwise microscopic disease, aid in the definition of the GTV, and ultimately improve local control and cure rates. ■

Photographed with the cooperation of Edward Hospital, Naperville, Illinois.



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