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# 4D CT-based radiation treatment planning—the coming of age of real-time imaging

**By Dwight E. Heron, M.D.**

## LEARNING OBJECTIVES

*Upon completion of this activity, participants should be able to:*

- Describe the current state of radiation therapy for thoracic and abdominal tumors.
- Review the concepts of target definition in conformal radiation therapy planning.
- Explain the dosimetric impact of target and/or organ motion in radiation treatment planning.
- Review the early clinical experience with 4D CT-based radiation treatments.

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Since the early 1980s, spurred by the introduction of supercomputing technologies, 3D radiation planning has been considered an affordable and elegant delivery option for radiation. Newer advances prompted by computed tomography and 3D reconstruction now allow views of tumors and their relationships to other vital structures. This enables physicians to generate a "beam's eye view" of the target and surrounding structures from the perspective of the entering radiation beam. As a result, 3D views of the prescribed radiation dose cloud to the target and normal tissues can be optimized to further enhance the therapeutic ratio.

Although 3D conformal radiation therapy (3D CRT) has revolutionized the oncologic use of radiation, its effectiveness is limited by respiratory motion and the impact that has on imaging and radiation treatment planning.[1,2] Several researchers have shown that even with quiet respiration, lung tumors can move significantly, causing potential inaccuracies in treatment delivery.[3,4] Without an effective way to image and evaluate the consequences of respiration on tumor and nearby critical structures, advanced conformal radiation techniques such as intensity-modulated radiotherapy (IMRT) are not possible.

## TARGET DEFINITION

As a general principle, the goal of CRT is to deliver the intended dose to the target with as little dose as possible leaking out to the

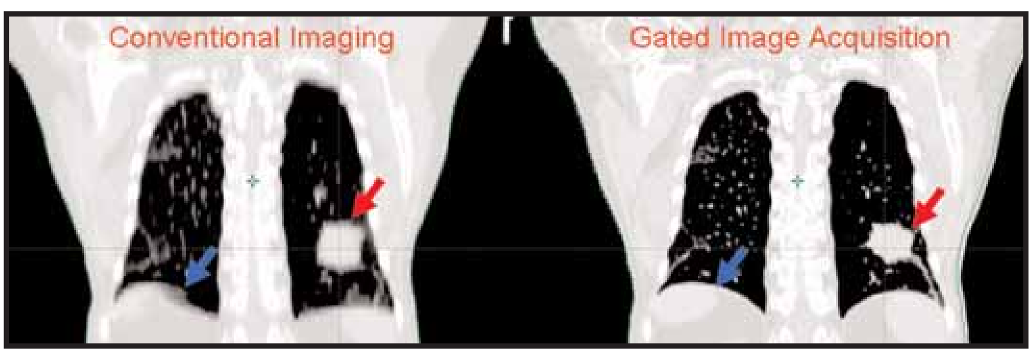


***Figure 1**. Distortion images seen in nongated (left) and gated 4D CT acquisition (right). Note the larger volume and blurred border (red arrows) and scalloped ("mushroom") dome of the right hemidiaphragm (blue arrows) compared to gated image acquisition.*

***Figure 2****. 4D CT setup with CCD camera and reflective box placed 3 to 5 cm below xiphoid process.*

surrounding tissues. This depends heavily on accurate delineation of the target volume. The International Commission on Radiation Units and Measurement has provided guidelines on the definition of target volumes used for treatment planning.[5] These volumes include the gross tumor volume (GTV), the clinical target volume (CTV), which accounts for clinical microscopic extension of disease, and a planning target volume (PTV), which accounts for setup uncertainties, tumor motion, and dosimetric buildup of radiation.

In fact, the greatest uncertainty in thoracic radiotherapy is respiration-induced motion of the target.[6,7] It is within the PTV that tumor motion—and organ motion, for that matter—influence treatment-related toxicities such as radiation pneumonitis, which may result from a PTV expanded to encompass the range of motion of the tumor. Failure to encompass the tumor within the PTV will result in a geographic miss and undoubtedly in local failure. The need for precise target definition is paramount when highly conformal radiation techniques such as IMRT or radiosurgery are being considered.

Helical CT has shortened imaging time and may reduce the volume averaging that results in a "blurred" image of moving structures when scanning the thorax or abdomen with standard techniques. However, these ungated acquisitions do not give a true representation of many target volumes. Researchers have shown that contouring of tumor and normal lung in patients with lung cancer can produce large intra- and interobserver variations.[8,9] Others have shown that positron emission tomography (PET) can decrease this variability in contouring by clearly distinguishing metabolically active tumor from the adjacent atelectatic lung.[10-12] Nonetheless, ungated PET scanning is also subject to volume averaging, which may result in a larger-than-accurate GTV.

To overcome these challenges, dynamic imaging techniques have been developed to more accurately depict target and organ motion. Clear knowledge of the true kinetics of these volumes of interest can significantly improve radiation treatment planning by providing a detailed map of trajectories throughout the respiratory or physiologic cycle.

## STRATEGIES TO ASSESS MOTION

Even with conformal techniques such as 3D CRT, geometric and physiologic distortions of tumor and organs as a result of respiratory or organ motion are often encountered (Figure 1). These distortions can result in underdosing disease or overdosing nearby normal and critical tissue. Conventional radiation treatment planning has historically compensated for these geometric and respiration-induced movements by expanding the margins around a tumor to minimize the risk of missing the disease, the so-called "geographic miss." In doing so, more normal tissue was subject to unintended but necessary irradiation to minimize the risk of failure. Ironically, the need for these expanded margins has arguably limited potentially curative doses of radiation for a variety of tumors, including lung cancer, in order to avoid treatment-related side effects such as pneumonitis and esophagitis. Large margins have also resulted in lower doses to the disease because of concerns about radiation-induced transverse myelitis of the spinal cord.

## HARDWARE SPECS FOR 4D RADIOTHERAPY

At the heart of the 4D CT solution are three key components. One of these is a CT scanner capable of performing gated acquisition of data sets. Ideally, the CT should be a multislice helical scanner. Additionally, a marker system is necessary to temporally link the individual axial images of the 4D CT to a specific phase of the respiratory cycle. Possible marker systems include implanted fiducials with radiographic localization or external markers with optical CCD detection, such as the Real-Time Position Management respiratory gating system (RPM), from Varian Medical Systems of Palo Alto, CA (Figure 2). Unlike implanted fiducials, such external marker systems are designed to approach motion tracking noninvasively by correlating the movement of a marker block with internal organ motion linked to the respiratory cycle. These scans usually generate a large number of images (about 1500), which must be sorted. Consequently, a sufficiently fast imaging workstation is the third component necessary to ensure efficient processing and sorting for radiation treatment planning.

## 4D CT IN RADIATION TREATMENT PLANNING

Moving targets or organs can result in marked distortion in anatomic and functional imaging during data acquisition.[13-16] Imaging modalities operated in a "slow" mode relative to the moving object are likely to record a blurred image that is a summation of the object's range of motion while the scan was obtained. Although this may be useful in radiation therapy planning (2D and 3D), this blurring, or volume averaging, fails to give a true representation of the tumor volume and configuration, which is necessary if techniques such as IMRT are to be used. Conversely, if the imaging technique is "too fast" relative to the moving object, an apparently disjointed, noncontiguous object may be portrayed as the target volume (Figure 1). The magnitude of these artifacts, which are readily seen on any helical or nonhelical CT scan, is the result of a complex interplay between the CT data acquisition period and the respiratory cycle. Neither of these outcomes is acceptable for modern therapy planning if precision radiation therapy is the goal.

A technology panel of the American Society for Therapeutic Radiology and Oncology (ASTRO) proposed 4D radiotherapy be defined as "the explicit inclusion of the temporal changes in anatomy during imaging, planning and delivery of radiation therapy."[17] By definition, therefore, the acquisition of multiple CT data sets over several respiratory cycles, the sorting ("binning") of these axial images as a function of respiratory phase for treatment planning, and modification of the standard delivery mechanism are all necessary to fulfill these criteria.

There are several techniques for acquiring the 4D data set. Prospective respiratory-gated image acquisition obtains each CT scan at a specific phase of the respiratory cycle. These prospective acquisitions are triggered by a particular phase of respiratory cycles and together will build the complete 4D data set. Alternatively, retrospective reconstruction of the imaging data can be achieved by dynamic image acquisition linked to the rhythmic, coached breathing of the patient. These images are then sorted retrospectively into the individual phases to create a 4D data set for treatment planning. Once sorted on the imaging workstation, the degree of organ or target motion can be assessed and a decision made regarding the need for gated or ungated treatment.

## MANAGING MOTION DURING TREATMENT

Several strategies have been developed in an attempt to reduce the size of the margins around tumors, thereby improving the therapeutic ratio. These techniques include tumor tracking,[18,19] breath-hold technique,[20] active breathing control,[21,22] abdominal compression, and 4D CT-based gating.

*Breath-hold technique*. The breath-hold technique, either at deep inspiration or deep expiration, has been used as a strategy to minimize motion artifact both at the time of radiation simulation and image acquisition and during treatment.[23] While a fairly crude (though effective) method for managing motion, the breath-hold technique has some limitations. First, respiratory function in lung cancer patients is often significantly compromised, thereby limiting their ability to perform breath-hold for any significant period of time. In our experience, patients frequently become fatigued, and the amplitude (i.e., depth) of their breath-hold becomes increasingly shallow on successive attempts. Also, extended treatment times are required because of frequent interruptions and the need for rest breaks. For these reasons, we have not adopted breath-hold as a standard approach for patients with thoracic or abdominal malignancies.

*Active breathing control*. Active breathing control (ABC) is a semi-invasive technique for suspending respiration at a predefined phase of the respiratory cycle. The ABC setup consists of a set of flow monitor and scissor values for controlling both inspiration and expiration. A "T-tube" mouthpiece connected to the ABC device continually monitors the patient's tidal volumes in real-time. At preselected phases of the respiratory cycle, the ABC device may be activated to immobilize respiration, thereby minimizing tumor motion. It has previously been shown that tumor motion can be eliminated using this method,[24] allowing for reductions in margin size when planning target volumes for liver cancer. Several other authors have demonstrated the feasibility of ABC for the treatment of lung, breast, and other abdominal tumors.[25-30]

*4D CT-based gated treatments.* 4D CT-based gated radiation therapy treatments are less invasive and less restrictive in nature than the other two delivery methods. In lieu of restrictive or interventional respiration, a 4D CT-based gating approach involves coached breathing with the radiation beam gated as a function of respiratory phase. In practical terms, problems often encountered with the breath-hold technique in patients with already compromised lung function can be readily avoided with this method. Respiratory fatigue and a shifting breath-hold amplitude are usually not prominent features of gated treatments.

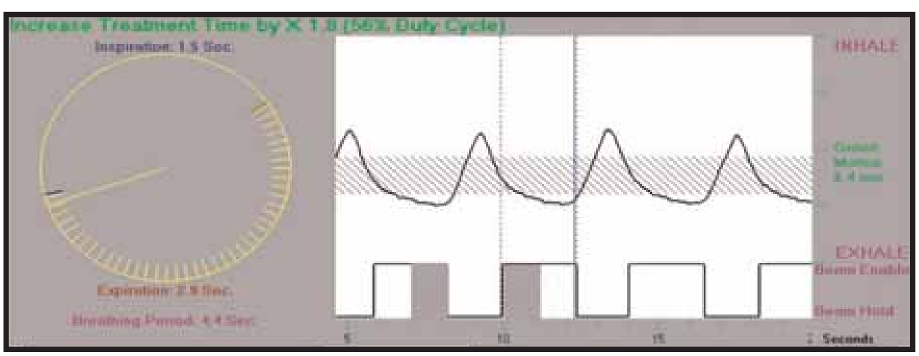

***Figure 3***. *RPM depicting respiratory waveform and radiation delivery on end-expiratory phase.*

However, for this treatment approach to work, the patient must be able to follow visual and/or auditory cues to produce a consistent respiratory waveform (Figure 3).

## UNIVERSITY OF PITTSBURGH EXPERIENCE

The University of Pittsburgh Cancer Institute implemented a 4D CT-based radiation therapy program in January 2004. Since that time, more than 250 4D CT scans have been performed to assess a variety of tumors and any associated organ motion in the thorax and abdomen. Using a quadslice GE Lightspeed Qx/i CT scanner in axial cine mode along with the RPM system, patients are first imaged in free-breathing mode for the helical scan. They are then trained to follow auditory coaching ("breathe in") for a five-minute period to establish a stable breathing cycle. We have found that both dual coaching ("breath in, breathe out") and multimodality coaching (visual bars) are confusing to patients and more likely to compromise the reproducibility of the breathing cycle, which is crucial for linking the 4D data set. The entire 4D CT simulation takes 20 to 30 minutes and includes patient setup and training. This is well within the typical simulation time at our center.

To complete the motion study evaluation, the acquired axial CT images and the respiratory phase during which they are obtained are transferred to GE Medical Systems' AdvantageSim workstation. A software application on the workstation can be used to sort the images according to the respiratory phase during which they were acquired. A tool allows the user to choose the best image for each phase at each location. Once these images are assembled, a 3D image set is generated and can be viewed dynamically in the axial, sagittal, and coronal planes. These images can be looped to create a 3D movie depicting the motion of the regions of interest. The tumor can be identified and contoured at each phase and the images transferred to the radiation therapy planning system for plan development.

Our preclinical and clinical experience has indicated that reduction in tumor motion to 5 mm or less using gating techniques enables the clinician to use IMRT to treat tumors in the thorax and abdomen. For abdominal tumors, the motion of the liver, spleen, and kidneys is predominantly in the superior-inferior direction with an average range of motion of approximately 13 mm. Direct knowledge of these organs has made it possible to deliver a novel program using whole abdominal IMRT (WAIMRT). Both the dosimetric and clinical outcomes suggest significant improvement in toxicities compared with conventional 2D and 3D approaches.

In treating non-small cell lung cancer with IMRT, which is made possible only by 4D CT's ability to assess motion, we have found the incidence of grade 3 esophagitis to be rare. Similarly, cases of grade 1 or 2 esophagitis were mostly resolved within two months of completing treatment. There were no patients with clinically evident radiation pneumonitis.

There are clearly some limitations in the use of 4D CT in its current form. Regardless of acquisition mode, errors sometimes happen and manifest as the "mushroom" effect, where scalloping of the chest wall or diaphragm is seen. These occur when images are incorrectly matched to their respiratory phase and have to be manually removed from the data set. Additionally, there are errors in the imaging data set at the extremes of respiration; i.e., end-inspiration and end-expiration. As the technology advances, it is likely that these shortcomings will be resolved.

## CONCLUSION

4D CT represents a major advance in radiation therapy planning and is a powerful and precise tool for identifying and studying respiration-induced tumor and organ motion. This approach to treatment planning further individualizes patient assessment as it defines patient-specific tumor margins. As the tumor and organ kinetics are likely to be unique to each patient, the advanced treatment plans that can be generated with this modality will be inherently distinctive for each patient. Seeing is truly believing. ■

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