New tool improves 4D radiation therapy for lung cancer

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Using a 4D computed tomography technique, it is possible to trace a tumor’s 3D trajectories during a breathing cycle, increasing the probability of a successful treatment.

Despite all efforts, lung cancer is still the leading cause of cancer-related deaths in the United States. About 80% of all primary lung cancers are non-small cell lung carcinomas (NSCLC). At the present time, the optimal treatment for patients with primary early-stage NSCLC in which the cancer has not migrated to distant parts of the body is complete surgical resection. Unfortunately, only a quarter of all patients have this valuable option. For patients with early stage, medically inoperable disease, radiation therapy is the treatment of choice. For locally advanced NSCLC, especially those cases involving the mediastinum (the partition between the left and right thoracic cavities) concomitant radiation therapy and chemotherapy (radio-chemotherapy) is the preferred treatment.

Although significant technological progress has been made in radiation therapy in recent years, the five-year survival rate for patients with early stage NSCLC remains at about 15%. More accurate definition of the tumor volume and better control of the internal organ motion during respiration can improve local control of radiation therapy.

Clinical measurements using target tracking or image-guided techniques have shown that a tumor can move significantly during a free breathing cycle. Depending on its location, a tumor can move from a few millimeters to several centimeters. Intensity modulated radiation therapy (IMRT) involves highly conformal radiation dose distribution with steep gradients. If respiratory motion is not carefully modeled during the treatment planning phase, IMRT could miss the target. If the treatment includes dose escalation, radiation pneumonitis and esophagitis could result, leading to an increased risk of complications.

To account for this periodical respiratory motion and avoid missing the target, the most common approach is to add a population-derived safety margin to the gross tumor volume (GTV) to obtain a planning target volume (PTV). However, such a one-size-fits-all approach neglects the basic fact that respiratory motion is anisotropic and patient-dependent. In addition, during a free breathing computed tomography (CT) simulation, images could be acquired at any phase of a breathing cycle. This is particularly the case for the common single-slice CT scanners. A low rotation rate produces images with poor interslice correlation. With such a generalized uniform margin, a PTV based on such CT images may either include more normal lung tissue than required or miss the GTV altogether at certain phases of a breathing cycle.

Another approach to tumor movement due to respiration is gating using an infrared sensor placed on the patient’s chest surface. The radiation beam is turned on when the patient’s breath...
enters a pre-determined phase window. End-exhalation is usually chosen because the breath tends to stay slightly longer than at end-inhalation, and thus is more reproducible. Studies have shown, however, that the movement of the PTV does not necessarily follow the sinusoidal movement of the external sensor.

Recently, respiration correlated CT (4DCT) has been developed and implemented in radiation oncology. The time information required for 4D imaging can be obtained prospectively or retrospectively using respiratory motion gating or tracking techniques. With 4DCT, it is now possible to trace a tumor’s 3D trajectories during a breathing cycle using a technique called the maximum intensity projection (MIP). The tumor volume is defined as the union of these 3D trajectories and is called the internal target volume (ITV) (see Figure 1).

Intuitively, there should be a CT data set at a certain phase in which the GTV is optimally located in the ITV. In this case, optimal location means that in this specific phase, the margins or separations between the GTV and the ITV are the largest. These margins also distribute most uniformly so that the GTV has the minimum probability of moving out of the ITV during the course of a radiation treatment, providing a minimum probability of a target miss. Assuming that patient setup uncertainties prior to treatment are completely random and homogeneous, we introduce a novel parameter called the phase impact factor (PIF) to quantitatively search for such an optimal phase during a free breathing CT simulation for 4D radiation therapy (4DRT). The PIF is defined as:

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\text{PIF} = \frac{\text{Variance of Margin}}{\text{Mean Margin}}
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Once the CT images with the optimal phase are determined, an IMRT plan is computed and optimized using the inverse treatment planning technique. The PIF could be used as the most conservative phase data selection criterion in 4D radiation therapy for lung cancer (see Figure 2). The PIF is expected to offer a safer CT data set than the most commonly used phase-averaged CT images.

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**References**