Percutaneous Implantation of Fiducial Markers for Imaging-Guided Radiation Therapy

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OBJECTIVE. The use of imaging-guided radiation therapy (IGRT) to treat thoracic and abdominal tumors is increasing. In this article, we review the process of IGRT and describe techniques to implant fiducial markers in the optimal geometry.

CONCLUSION. Implantation of fiducial markers can be challenging. A better understanding of the physics of IGRT can help optimize fiducial marker placement for precise tumor targeting.

Imaging-guided radiation therapy (IGRT) integrates imaging into the radiation treatment planning and delivery to allow more precise localization and targeting of tumors. Respiratory motion is a major source of uncertainty with target localization. As radiotherapy evolves into exploiting hypofractionated courses of treatment using large doses of radiation per fraction, precision is crucial for both treatment efficacy and safety.

CyberKnife (Accuray, Inc.) is an IGRT system that uses orthogonal x-rays to visualize radiopaque fiducial markers implanted in the tumor for real-time tracking during the entire treatment cycle. As experience with IGRT grows, most radiology practices will become involved in fiducial marker implantation for thoracic and abdominal tumors. In this article, we attempt to provide a better understanding of the CyberKnife system from a radiologist’s perspective and to describe techniques to implant fiducial markers in the optimal geometry.

The CyberKnife System

To better understand optimal fiducial marker placement, it is important to review the process of IGRT. Traditional stereotaxy requires rigid immobilization of the target tumor to determine spatial coordinates for precision guidance. IGRT, on the other hand, separates the process of localization from immobilization and tracks the target in real time.

The CyberKnife consists of a lightweight linear accelerator mounted on a maneuverable robotic arm combined with real-time imaging guidance. Images from two orthogonal x-ray systems are electronically registered to digitally reconstructed radiographs derived from the treatment planning CT, and anatomic translation and rotation in the three axes are measured (Fig. 1). The robotic manipulator then compensates for these differences and retargets the radiation beam to maintain spatial precision [1–3]. However, tumor location during the respiratory cycle may vary several centimeters [4–10], and this variable requires additional tracking.

The CyberKnife uses a system called Synchrony, a continuous respiratory system capable of delivering precise radiation throughout the respiratory cycle. Adjustments for respiratory variations are made by coupling the motion of previously implanted radiopaque fiducial markers with chest wall excursions. The fiducial markers act as internal radiographic landmarks that maintain a fixed relationship within the tumor and with each other.

Orthogonal radiographic views of the fiducial markers during treatment coupled with digitally reconstructed radiographs of the fiducial markers from the treatment planning CT can accurately specify spatial position and orientation during the entire treatment cycle. The relative relationship between the movements of the chest wall and of the fiducial markers is used to create a predictive model that is continuously updated throughout the treatment cycle. When the target moves, this process detects the change and corrects the beam pointing in real time.
Placement of Fiducial Markers

Typically, three to five radiopaque gold fiducial markers are implanted in and around the tumor to be treated. Individual markers measure approximately 0.8 × 5 mm and can be introduced percutaneously via a 19-gauge introducer needle. Other agents such as platinum coils can be used; their utility in lung tumors (Fig. 2) is described later. To aid introduction of the fiducial markers via a 19-gauge needle, the fiducial markers can be cut in half before autoclaving and sterilization; however, this is not necessary. Occasionally, fiducial markers cannot be advanced beyond the hub of the needle or are obscured by blood, making the procedure time-consuming. In these situations, using a small curved Kelly forceps and choosing a vertical trajectory so that gravity can help “drop” the fiducial marker can help decrease procedure time.

For the orthogonal x-ray systems of the CyberKnife system to identify individual fiducial markers, it is important that the markers are not placed superimposed on each other in 45° oblique views. This potential problem is best avoided by imaging the tumor in 3D and placing the fiducial markers in different octants (Figs. 3 and 4). This placement strategy may require two skin entry sites; however, in most cases, just torquing the needle should suffice. If two fiducial markers are superimposed in the 45° angle view, the CyberKnife system will interpret them as a single marker (Fig. 5). If two markers are inadvertently placed so that they appear superimposed on an orthogonal view, placement of an additional marker may be required.

At least three markers that do not appear superimposed on orthogonal views are required to give positional information about the tumor. Similarly, fiducial markers placed in a cluster appear as one marker, diminishing the utility of the treatment planning CT (Fig. 6). A minimum of 1.5 cm between fiducial markers is recommended; however, this spacing is not always possible. On the other hand, because the CyberKnife treatment planning CT uses a 20-cm field of view, fiducial markers placed too far from the tumor may not be adequate (Fig. 7). Hardware can obscure the fiducial markers; hence, fiducial markers should not be placed over the hardware at a 45° axial orientation.

Artifact from the fiducial markers can obscure a small tumor completely, especially in tumors with low tumor-to-parenchyma contrast (Fig. 8). For such tumors, it is preferable to place the fiducial markers around the periphery of the tumor rather than directly in the tumor. This approach may still create artifacts that decrease visibility of the target lesion; however, fusion of planning CT images with PET images may help show the contours of the target lesion in the presence of artifacts. A similar approach can be used for hard-to-reach tumors, for example, liver dome, in which the fiducial markers can be placed inferior to the tumor provided there is not a substantial difference between respiratory movements of the fiducial markers versus the actual tumor (Fig. 9).

The CyberKnife can measure to an accuracy of 0.1 mm; it is vital that inflammation due to percutaneous placement of the fiducial markers resolve so that the spatial resolution of the markers at the time of CT simulation is the same as during the treatment (Fig. 10). In addition, fiducial markers can migrate (Fig. 11A–11C). Consequently, a 1-week interval between fiducial placement and treatment planning CT is recommended to decrease the possibility of fiducial misregistration and ensure precise targeting of the tumor.

Migration is most often seen in fiducial markers implanted in the lung. This higher likelihood of migration may be due to the higher incidence of pneumothorax after percutaneous interventions in patients with poor lung re-serve [11], which results in fiducial markers “dropping” into the pleural space. To overcome this problem, our group has implanted platinum microcoils percutaneously instead of gold seeds (Fig. 11D) because the former appear to be more stable in lung parenchyma, allowing a more predictable and precise CyberKnife treatment planning CT. The disadvantage of microcoils is the possibility that the configuration of the coil itself may change over time. In our experience, a short microcoil with a tight configuration overcomes this issue; however, our experience is limited. Titanium vascular clips have also been successfully used in partial-breast irradiation using the CyberKnife; however, these clips usually lack sufficient contrast and may be difficult to track.

Besides alternative fiducial agents, alternative methods of introduction and implantation have also been explored.Bronchoscopic implantation of fiducial agents for lung tumors is well documented [12]. The risk of causing a pneumothorax is miniscule, which is a significant advantage in patients with compromised lung function. Similarly, implantation with endoscopic sonog-raphy guidance has been described for the pancreas, where a transgastric approach is often preferred over a percutaneous approach to avoid going through the small bowel or colon [13, 14].

In summary, implantation of fiducial markers can be challenging. A better understanding of the physics of IGRT can help optimize fiducial marker placement for precise tumor targeting.

References


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Fig. 1—Photograph shows CyberKnife (Accuray, Inc.) imaging-guided radiation therapy system. Two orthogonally placed x-ray sources are mounted on ceiling, and detectors are mounted below patient table. Central linear accelerator is mounted on maneuverable robotic arm. These detectors create digitally reconstructed radiographs that are used for tumor localization and anatomic translation in three planes. (Courtesy of Accuray, Inc., Sunnyvale, CA)

Fig. 2—Tools for fiducial marker implantation.
A, Photograph shows radiopaque gold fiducial markers, measuring 0.8 × 5 mm; markers can be introduced via 19-gauge thin wall or conventional 18-gauge introducer needle. Microcoils measuring 3 or 4 mm in diameter can also be used as fiducial markers.
B, Photograph shows fiducial markers loaded in 19-gauge introducer needle with use of hemostat.

Fig. 3—65-year-old man with non–small cell lung carcinoma in right upper lobe of lung.
A–C, Coronal reconstruction of unenhanced chest CT images show appropriately placed fiducial markers in x, y, and z planes. H = head (cranial), F = foot (caudal).
Fig. 4—48-year-old man with hepatic metastases from colorectal carcinoma in segment I.
A–D, Unenhanced CT images show sequential axial sections through liver with appropriately placed fiducial markers in x, y, and z planes.

Fig. 5—60-year-old woman with 1.5-cm hepatic metastasis from colorectal carcinoma (not shown in these images) in segment V.
A and B, Axial unenhanced CT images of liver show three of four fiducial markers are collinear 45° right anterior oblique view. These fiducial markers would register as single marker on some digitally reconstructed radiographs obtained for planning imaging-guided radiation therapy. H = head (cranial), F = foot (caudal).
Fig. 6—38-year-old woman with hepatic metastasis from breast carcinoma in segment IVB.
A, Axial contrast-enhanced CT image shows 1.2-cm hepatic metastasis in segment IVB.
B, Contrast-enhanced CT image at same level as A after fiducial marker implantation shows clustered fiducial markers obscure metastasis and would also be indiscernible as individual markers on digitally reconstructed radiographs obtained for planning imaging-guided radiation therapy.

Fig. 7—52-year-old woman with hepatocellular carcinoma in segment VI. Axial CT image shows that anteriormost fiducial marker is too far (> 7 cm) from tumor. Because CyberKnife system (Accuray, Inc.) uses small field of view (20 cm), fiducial markers should be placed near tumor.

Fig. 8—75-year-old man with pancreatic tail adenocarcinoma.
A, Axial contrast-enhanced CT image shows small hypodense mass in tail of pancreas.
B, Axial unenhanced CT image obtained at same level as A after fiducial marker implantation shows markers placed in tumor cause beam-hardening artifact that obscures margins of tumor.
Percutaneous Implantation of Fiducial Markers for IGRT

Fig. 9—62-year-old man with previously chemoembolized hepatocellular carcinoma in segment VIII with peripheral recurrence. Fiducial markers were not placed directly in tumor because of difficulty advancing needle to superior aspect of tumor.
A, Axial contrast-enhanced CT image shows one fiducial marker placed in mid aspect of tumor.
B, Axial contrast-enhanced CT image shows two additional markers placed just inferior to tumor. Of note, retained ethiodized oil from previous chemoembolization can also obscure fiducial markers and should be considered.

Fig. 10—84-year-old woman with left lower lobe non–small cell lung carcinoma.
A, Axial unenhanced CT image obtained before fiducial marker implantation shows tumor.
B, Axial unenhanced CT image shows localized pulmonary hemorrhage after implantation of fiducial markers. Hemorrhage completely obscures tumor.
C, Axial CT image obtained 1 week after fiducial marker implantation shows resolution of pulmonary hemorrhage. Tumor margins are easily discernible, enabling appropriate targeting by imaging-guided radiation therapy.
Fig. 11—42-year-old woman with left lower lobe non–small cell lung carcinoma.
A, Axial unenhanced CT image shows tumor and implanted fiducial markers.
B, Axial unenhanced CT image obtained 1 week after fiducial marker placement for treatment planning. Image shows that all implanted fiducial markers fell into pleural cavity.
C, Anteroposterior chest radiograph obtained at same time as B highlights importance of waiting 1 week before imaging-guided radiation therapy planning and treatment because fiducial markers can migrate or settle for up to 1 week.
D, Patient returned because markers had migrated. Axial CT image shows use of microcoils as fiducial markers. Four 3-mm-wide vortex coils were implanted via 19-gauge introducer needle.
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