

Tumor track seeding: A new complication of fiducial marker insertion

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In the United States, lung cancer is the leading cause of cancer-related death. Candidates for tumor ablation using CyberKnife® require fiducial placement in or near the target tumor to achieve precision. Placing these reference points may lead to complications, including pneumothorax and/or hemorrhage. We report a new complication: the appearance of metastatic foci along the track of the fiducial marker. Since the marker was inserted by traversing the original primary tumor, we hypothesize that malignant cells were seeded along the track. In light of this new complication, current techniques for the insertion of fiducial markers should consider a peripheral approach when possible to avoid tracking of malignant cells.

Introduction

Lung cancer is the leading cause of cancer-related deaths in the United States (1). Among all treatment options for non-small-cell lung cancer, stereotactic radiosurgery with systems such as CyberKnife® is emerging as a possibility for patients who are medically unfit to undergo lung-tumor resection or for those whose tumor is unresectable. For precise tumor ablation, the CyberKnife® system may require fiducial marker placement in or near the target tumor (2). Placing these reference points may lead to several complications, such as pneumothorax (3) and hemorrhage (4). In this case study, we report a complication not previously described: the appearance of new metastatic focus in the area of the fiducial marker placement.

Case report

A 65-year-old male with a 100-pack-year smoking history initially presented with increasing shortness of breath. A chest CT showed a partially cystic right-upper-lobe lung nodule measuring 1.1 by 1.3 cm (Fig. 1A). A CT-guided biopsy confirmed non-small-cell lung carcinoma. PET/CT for staging showed hypermetabolic activity at the site of the nodule in the right upper lobe with SUV (max) of 3.8 without additional evidence of disease (Fig. 1B). The patient was staged T1N0M0 and was not a candidate for surgical resection secondary to COPD and a FEV1 less than 30%. The patient was treated with a combination of chemoradiation and completed 6300 cGy to the right upper lobe. At the three-month followup, PET/CT showed a slight progression of the right upper lobe tumor, with SUV (max) 2.8 but a size of 1.8 by 1.3 centimeters. However, six months later, a new CT showed enlargement of the known cancerous area to 2.3 by 4.3 centimeters; repeated PET/CT 3 days later showed an SUV (max) of 8.7 (Fig. 2).

It was decided that stereotactic body radiotherapy with CyberKnife would be a superior alternative to re-irradiation with conventional external-beam technique.

We therefore placed a CT-guided gold fiducial marker. Initially, a 17G-by-6cm guide needle was advanced into the lesion. We made three passes using a 20G-by-11 cm Temno biopsy needle, and confirmed the needle position using CT imaging. We then advanced the guide needle through the lesion to the deepest, most medial part of the tumor, and placed a single set of coupled gold fiducial markers (0.8 x 1.0 cm Civco®, Orange City, Iowa) (Fig. 3A). We then

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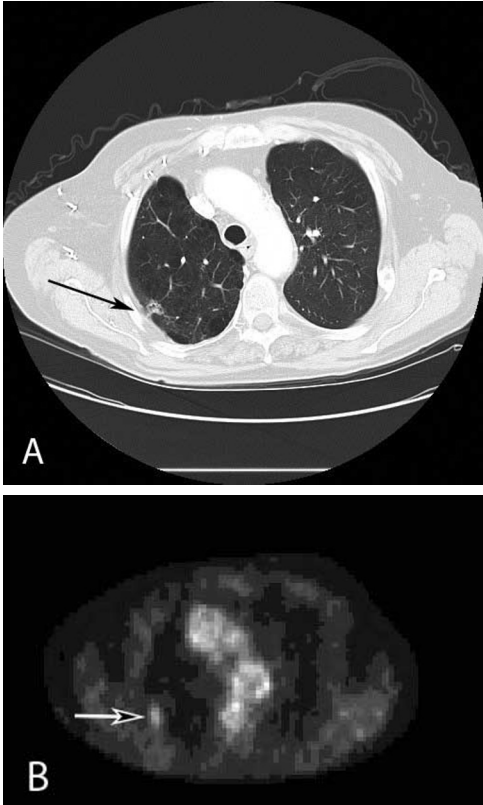


Figure 1: A. 65-year-old male with small cell lung cancer. A. Right-upper-lobe lung nodule on axial lung windows of initial chest CT. Irregularly shaped peripheral nodule measures 1.1 by 1.3 cm. Technique: Siemens 64-slice CT scanner, 120 kV, 250 mAs, 5mm sections, noncontrast scan. B. PET/CT for staging showed hypermetabolic activity (SUV [max] 3.8) at the site of the nodule in the right upper lobe, axial plane (arrow). Technique: Scan was performed 60 minutes after injection of 12-16 mCi of FDG tracer, with the following parameters: Siemens 64-slice CT scanner 120 kVp, 250mAs, 5-mm slice thickness, and CT-based attenuation correction algorithm using two iterations and 8 subsets.

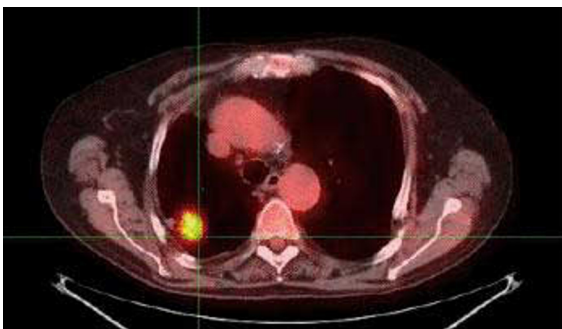


Figure 2: Right-upper-lobe lesion. PET/CT showed a definite progression of the right-upper-lobe tumor, with the mass now measuring 2.3 by 4.3 centimeters with a SUV (max) of 8.7. Technique: Scan was performed 60 minutes after injection of 12-16 mCi of FDG tracer, with these parameters: Siemens 64-slice CT scanner, axial plane, 120 kVp, 250mAs, 5mm slice thickness, and CT-based attenuation correction algorithm using two iterations and 8 subsets.

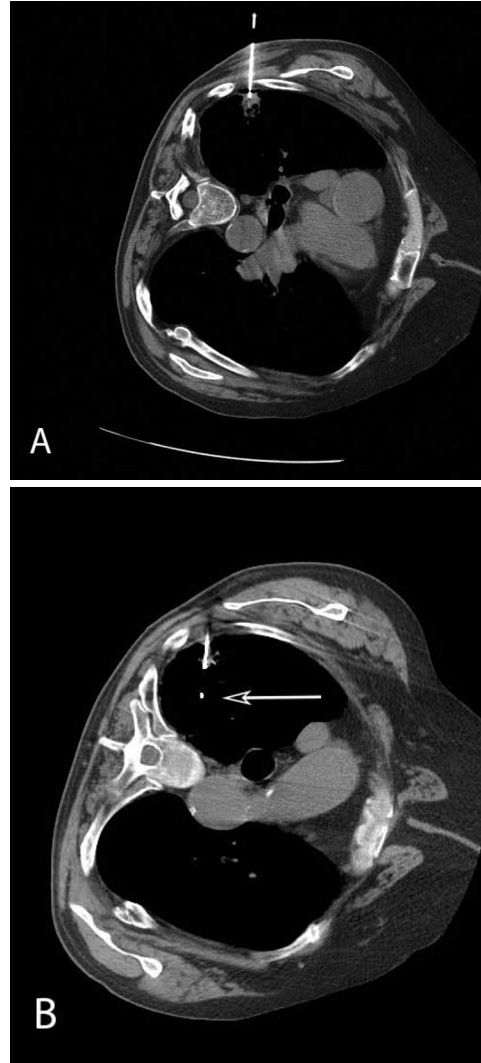


Figure 3: CT-guided biopsy and fiducial marker placement. A. Single set of coupled gold fiducial markers were placed in the deepest part of the mass, passing through the malignant tissue in the axial plane. An additional set of coupled fiducial markers was placed in the lung adjacent to the most cephalad aspect of the cavitory portion of the abnormality and deep to it. Technique: Siemens 64-slice CT scanner, 120 kV, 250 mAs, 5mm sections, non-contrast scan during fiducial marker placement. B. Single set of coupled gold fiducial markers were placed in the deepest part of the mass, passing through the malignant tissue in the axial plane. An additional set of coupled fiducial markers was placed in the lung adjacent to the most cephalad aspect of the cavitory portion of the abnormality and deep to it (arrow). Technique: Siemens 64-slice CT scanner, 120 kV, 250 mAs, 5mm sections, noncontrast scan during fiducial marker placement.

made a second pleural puncture parallel to the first puncture, 3 cm cephalad. We advanced a 17G-by-6cm guide needle into the lung, inferior to the cavitory portion of the abnormality and deep to it. We placed an additional set of coupled fiducial markers at this location (Fig. 3B).

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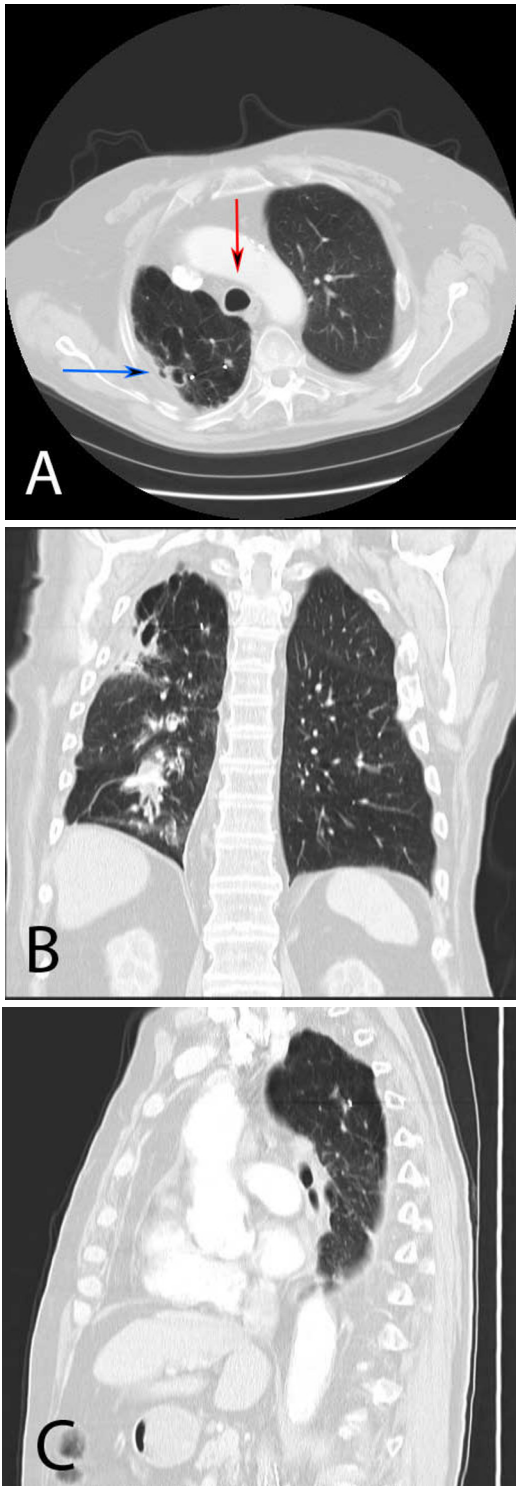


Figure 4: After fiducial placement and subsequent stereotactic radiosurgery. CT scan shows fiducial marker is in place (original mass at red arrow; new mass with adjacent fiducial at blue arrow) and around it is now a new 7.2 mm foci of disease, just medial to the marker. Technique: Siemens 64-slice CT scanner, 120 kV, 250 mAs, 5mm sections, non-contrast scan. A: Axial. B: Coronal reformat. C: Sagittal reformat.

Immediate postprocedure images displayed mild parenchymal hemorrhage at the inferior fiducial placement site. No pneumothorax was identified on a followup chest radiograph. Following the fiducial placement, the patient completed stereotactic body radiotherapy to the right upper lobe. He received 6000 cGy in three fractions of 2000 cGy each. Followup CT three months after the marker placement indicated that the primary mass remained stable in size. However, it also showed a small, 0.7cm nodule directly adjacent to the more medially located fiducial marker that was not present on prior studies (Fig. 4).

Followup PET/CT (Fig. 5A) demonstrated the dominant lesion to be less FDG-avid than in the previous study. The new, smaller 0.72cm lesion adjacent to the medially located fiducial marker showed increased metabolic activity and interval growth (Fig. 5B).

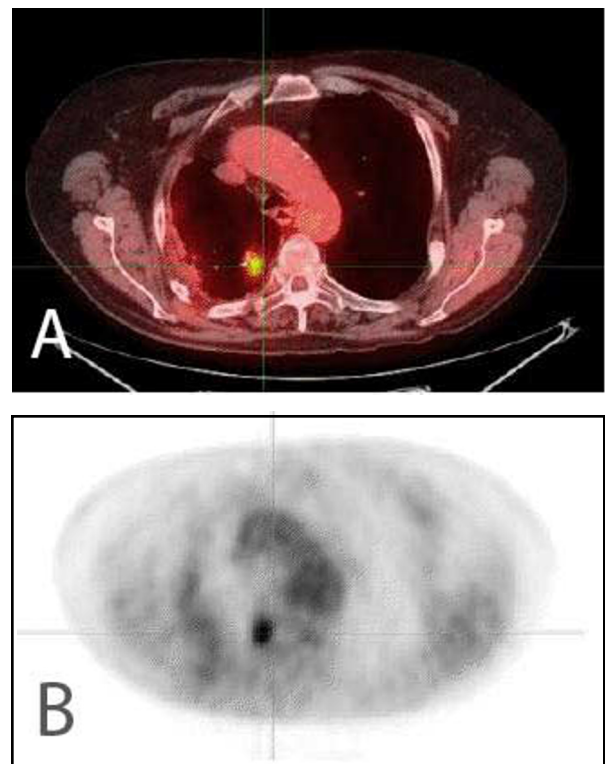


Figure 5: Followup PET/CT (A) and PET only (B) demonstrated the dominant lesion to be less glucose-avid (slightly out of plane). The new, smaller lesion adjacent to the medially located fiducial marker showed increased metabolic activity and interval growth in the axial plane. (Fiducial marker is obscured by metabolic activity.) Technique: Scan was performed 60 minutes after injection of 12-16 mCi of FDG tracer, with the following parameters: Siemens 64 slice CT scanner, 120 kVp, 250mAs, 5-mm slice thickness, and CT-based attenuation correction algorithm using two iterations and 8 subsets.

A presumptive diagnosis of tumor progression at the site of fiducial marker was made. The new lesion was not biopsied, and further treatment continued with the current markers (Fig. 6).

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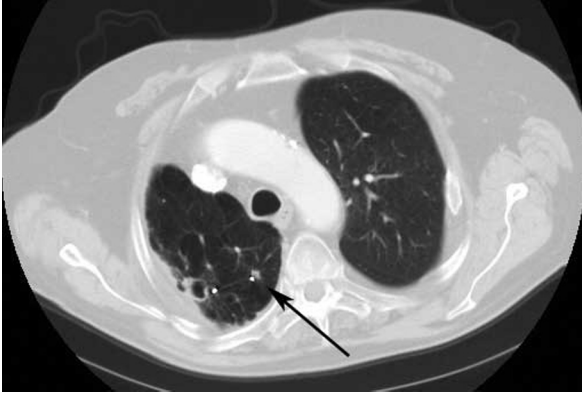


Figure 6: After fiducial placement (arrow shows marker) and subsequent stereotactic radiosurgery. CT 3 months later in the axial plane. Note formation of a new 7.2-mm mass adjacent to the fiducial marker which was not previously appreciated. Technique: Siemens 64-slice CT scanner, 120 kV, 250 mAs, 5mm sections, non-contrast scan and 8 subsets.

Discussion

Non-small-cell lung cancer is thought to occur secondary to repeated assaults on the lung tissue. It occurs in over 1.2 million individuals a year, 160,000 of whom are in the United States. It has a slight male predilection, which may be due to a higher percentage of male smokers than female smokers in past decades. The average age at diagnosis is around 70 years, and affected individuals often have tobacco, radon, and asbestos or particulate-matter exposures. Patients typically present with cough, and may have hemoptysis depending on the location of the lesion. Chest radiography may reveal a solitary pulmonary nodule, mass, pleural effusion, lung collapse, or mediastinal or hilar fullness. CT of the chest shows in greater detail the size, location, and extent of primary tumor and evaluates for hilar and/or mediastinal lymphadenopathy and distant metastases within the thoracic region. Transbronchial ultrasound may theoretically be used for diagnosis, but is not used commonly in practice. The main form of treatment is surgical resection with adjuvant chemotherapy and radiation. The prognosis varies based on the size of the tumor, the presence of metastasis, and the severity of the patient's symptoms, but overall prognosis is poor. Furthermore, many patients have poor lung function, making resection next to impossible. Stereotactic radiosurgery systems such as CyberKnife® are emerging as a possibility for patients who are unable to undergo lung-tumor resection or who have unresectable disease.

The CyberKnife® stereotactic radiosurgery system is a frameless, image-guided device with a 6-megavolt linear accelerator. This is mounted on a robotic arm to administer radiation to a tumor from different trajectories while minimizing dosage to adjacent normal tissue. It is emerging as a new option for patients with unresectable disease and is an effective treatment for non-small-cell lung cancer. Furthermore, it avoids the need for breath holding because it com-

pensates for changes in tumor position during the normal respiratory cycle, which in patients with severe lung disease can be an issue. In stereotactic radiotherapy and radiosurgical systems such as CyberKnife®, fiducial markers are necessary to allow precise tumor targeting. Complications of fiducial marker placement include pneumothorax (most common), hemorrhage, hemoptysis, and fiducial marker migration.

We present a case of what we believe to be tumor-track seeding secondary to fiducial placement, with subsequent formation of a new metastatic focus. We hypothesize that the placement of the fiducial marker through the original tumor may have led to seeding of malignant cells at the very end of the track, leading to the development of a new tumor nodule around the gold fiducial marker. Although (to the best of our knowledge) no current literature has mentioned this as a possible complication of fiducial marker placement, we believe that the second metastatic focus was due to a collection of tumor cells by the tip of the fiducial marker insertion instrument, which on its insertion and/or removal deposited these cells at the end of its path. We have arrived at our conclusion based on the similarity of the technique used for transthoracic needle biopsy and transthoracic fiducial placement. Although a rare complication of needle biopsies, tumor seeding of the pleural space and the skin has been reported. However, when disseminated through the needle tract, malignant cells rarely mature into tumor masses, as it is generally believed that most lung cancer cells have a low potential to grow in the pleural space. Indeed, Tomiyama et al surveyed 9,783 lung biopsies and found only 6 cases (0.061%) of tumor seeding at the site of the biopsy route (5). Overall, the incidence of tumor seeding leading to the formation of metastasis has been reported to be less than 1% (6), but a study from Sawabata has shown that fine-needle aspiration leads to spread of malignant cells in 60% of cases (7). In this paper, the development of new foci of disease at the site of the track was not explored, however. Furthermore, it has been suggested that the risk of tumor implantation depends on track size. Therefore, the use of large-bore needles or thoracoscopy ports potentially carries a relatively higher risk of tumor seeding (6).

Although tumor seeding may be common, implantation metastasis is rare and should not be a contraindication to fiducial marker placement. Creation of a new foci of disease maybe a rare but serious complication of fiducial marker placement when placement involves going through the tumor focus. Hence, current techniques for the insertion of fiducial markers may want to consider a peripheral approach to the tumor if possible to avoid tracking of malignant cells and the possibility of the formation of new disease foci.

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