CT Fluoroscopy–Guided Percutaneous Fiducial Marker Placement for CyberKnife Stereotactic Radiosurgery: Technical Results and Complications in 222 Consecutive Procedures

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ABSTRACT

Purpose: To evaluate technical outcome and safety of computed tomographic (CT) fluoroscopy–guided percutaneous fiducial marker placement before CyberKnife stereotactic radiosurgery.

Materials And Methods: Retrospective analysis was performed of 196 patients (106 men) undergoing CT fluoroscopy–guided fiducial marker placement in 222 consecutive procedures under local anesthesia from March 2006 to February 2012. Technical success was defined as fiducial marker location in the tumor or vicinity suitable for CyberKnife radiosurgery evaluated on postinterventional planning CT. Complications were classified per Society of Interventional Radiology (SIR).

Results: One hundred ninety-six patients (age, 61.5 y ± 13.1) underwent percutaneous placement of 321 fiducial markers (mean per tumor, 1.2 ± 0.5; range, 1–4) in 37 primary tumors and 227 metastases in the thorax (n = 121), abdomen (n = 122), and bone (n = 21). Fiducial marker placement was technically successful in all procedures: intratumoral localization in 193 (60.1%), at tumor margin in 50 (15.6%), and outside of tumor in 78 cases (24.3%; mean distance to marker, 0.4 cm ± 0.6; range, 0–2.9 cm). Complications were observed in 63 placement procedures (28.4%), including minor self-limiting pneumothorax (n = 21; SIR class B) and self-limiting pulmonary hemorrhage (n = 35; SIR class A), and major pneumothorax requiring thoracostomy/drainage insertion (n = 14; SIR class D) and systemic toxicity of local anesthetic drug (n = 1; SIR class D).

Conclusions: CT fluoroscopy–guided percutaneous fiducial marker placement can be performed with high technical success under local anesthesia in various anatomic regions. Although self-limiting in most cases, pneumothorax and pulmonary hemorrhage are frequently observed during fiducial marker implantation into lung tumors.

ABBREVIATIONS

COPD = chronic obstructive pulmonary disease, PET = positron emission tomography

Stereotactic radiosurgery is characterized by the delivery of a highly concentrated radiation dose to a small target volume within a single session, with minimal radiation exposure to neighboring tissue (1,2). The CyberKnife radiosurgery system (Accuray, Sunnyvale, California) is capable of applying megavoltage photon radiation to

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irregularly shaped targets in free-breathing patients. Bony structures are used as landmarks for brain and spine treatments, and radiopaque markers (ie, fiducial markers) implanted within or next to the target are used as landmarks during therapy for moving organs like lung or liver (3–5). To compensate for respiratory and other unintentional motions of the patient and target lesion, the system uses a stereotactic radiographic image-guided system to track the fiducial markers in real time and permanently adjust the focus of the radiation beam (2,6). Depending on the anatomic localization of the target, various guidance techniques have been described to perform fiducial placement before CyberKnife radiosurgery: surgical (7), bronchoscopic (8), endoscopic (9), transarterial (10), and image-guided percutaneous placement with the use of ultrasound (US) (11,12) or computed tomography (CT) (12,13). Although image-guided fiducial marker placement in the abdomen and pelvis is associated with a low complication rate (12), the reported pneumothorax rate after pulmonary fiducial marker insertion varies considerably (13,14). On the contrary, independent from the anatomic location, the technical success rate in terms of fiducial marker implantation within or in the vicinity of a tumor is high if CT is used as a guidance method (12,13).

The present retrospective study aimed to evaluate the technical outcome and complication rate of CT fluoroscopy–guided percutaneous fiducial marker placement in various anatomic sites at a single treatment center.

MATERIALS AND METHODS

The present work is a retrospective study of all consecutive patients who underwent fiducial marker placement in the thorax and abdomen under CT fluoroscopy guidance in a single institution from March 2006 to February 2012. Regarding the retrospective review of periinterventional imaging studies and clinical patient charts, our study was authorized by the institutional review board, and formal ethical approval was not required. The principles of the Declaration of Helsinki were followed. Informed consent by the patient or his or her legal guardian to undergo CT-guided fiducial marker placement was obtained 24 hours and directly before the intervention.

Study Population

Indication for CyberKnife radiosurgery was regularly discussed and confirmed within the multidisciplinary institutional tumor board, which included oncologists, surgeons, radiation oncologists, pathologists, and interventional radiologists. The following were required as inclusion criteria for CyberKnife radiosurgery. First, in resectable disease, other local ablative methods (eg, radiofrequency ablation) and operative treatment of the patient had been ruled out by the multidisciplinary team. Second, the radiation oncologists had confirmed the suitability of the tumor lesion(s) (in terms of tumor size, location, and number) and the patient (in terms of the ability to cooperate) for CyberKnife radiosurgery. In the lung and liver, a maximum of two and three tumor lesions were treated, respectively. Inclusion criteria for fiducial marker placement were (i) an unequivocal delineation of the tumor on CT, magnetic resonance (MR) imaging, or positron emission tomography (PET)/CT; (ii) safe accessibility of the tumor with the fiducial marker needle under CT fluoroscopy guidance; and (iii) inability to directly track the tumor by the radiosurgery system without fiducial markers.

Regarding exclusion criteria for CT fluoroscopy–guided fiducial marker placement, the quality improvement guidelines of the Society of Interventional Radiology for percutaneous needle biopsy were applied (15). In particular, relative contraindications included significant coagulopathy that could not be adequately corrected, severely compromised cardiopulmonary function (in the presence of emphysema, chronic obstructive pulmonary disease [COPD], or previous lung surgery) or hemodynamic instability, lack of a safe pathway to the lesion, and inability of the patient to cooperate with or to be positioned for the procedure.

A total of 196 individual patients (90 women, 106 men; mean age, 61.5 y ± 13.1 [standard deviation]; age range, 12–87 y) underwent fiducial marker placement under CT fluoroscopy guidance in 222 consecutive sessions. The total number of tumor lesions was 264, including 37 primary tumors and 227 metastases. **Tables 1** and **2** show the characteristics of the patient population and target lesions, respectively.

Periinterventional Imaging and Image Guidance

Before CT fluoroscopy–guided fiducial marker placement, previous cross-sectional images not older than 2 weeks, such as CT, MR imaging, or PET/CT, were checked by an experienced interventional radiologist and an experienced radiation oncologist in all patients. All procedures were performed by using a SOMATOM Sensation 16 or SOMATOM Definition AS+ CT scanner (Siemens, Erlangen, Germany) with CT fluoroscopy (CARE Vision CT; Siemens) capability. Each patient underwent pre- and postinterventional CT of the involved organ region. For planning of the needle trajectory, the preinterventional CT scan included 5-mm slices, and coronal and sagittal reconstructions. A contrast-enhanced CT scan including a portal venous phase was acquired in case of parenchymal tumor lesions (eg, liver metastases). An arterial phase was added for better visualization of hypervascularized tumors (eg, hepatocellular carcinoma) and arteries along the needle access route.

Fiducial marker placement was performed under intermittent quick-check CT fluoroscopic acquisitions,

Table 1. Population Characteristics in Patients Who Underwent CT Fluoroscopy–Guided Fiducial Seed Placement (N = 196)

Characteristic	Value
Age (y)	
Mean ± standard deviation	61.5 ± 13.1
Range	12–87
Sex	
Female	90 (45.9)
Male	106 (54.1)
Tumor entity	
Colorectal carcinoma	63 (32.1)
Bronchial carcinoma	38 (19.4)
Breast carcinoma	15 (7.7)
Renal cell carcinoma	14 (7.1)
Hepatocellular carcinoma	12 (6.1)
Pancreatic carcinoma	10 (5.1)
Adenocarcinoma (unknown origin)	4 (2)
Urothelial carcinoma	4 (2)
Cholangiocellular carcinoma	3 (1.5)
Leiomyosarcoma	3 (1.5)
Ovarian carcinoma	3 (1.5)
Prostate carcinoma	3 (1.5)
Carcinoma of unknown primary	2 (1)
Esophageal carcinoma	2 (1)
Melanoma	2 (1)
Neuroendocrine tumor	2 (1)
Squamous cell carcinoma	2 (1)
Cervical carcinoma	1 (0.5)
Endometrial carcinoma	1 (0.5)
Ewing sarcoma	1 (0.5)
Lipoblastomatosis	1 (0.5)
Nasopharyngeal carcinoma	1 (0.5)
Malignant peripheral nerve sheath tumor	1 (0.5)
Multiple myeloma	1 (0.5)
Parotis carcinoma	1 (0.5)
Pleural mesothelioma	1 (0.5)
Primitive neuroectodermal tumor	1 (0.5)
Thymic carcinoma	1 (0.5)
Thyroid carcinoma	1 (0.5)
Testicular carcinoma	1 (0.5)
Tonsillar carcinoma	1 (0.5)

Values in parentheses are percentages.

Table 2. Distribution of Tumor Lesions (N = 264) for CT Fluoroscopy–Guided Fiducial Seed Placement by Organ Region

Organ	No. of Lesions	No. of Pts.
Thorax		
Lung	112 (42.4)	105
Pleura	4 (1.5)	2
Mediastinum	3 (1.1)	3
Thoracic wall	2 (0.8)	2
Abdomen and pelvis		
Liver	105 (39.8)	86
Pancreas	6 (2.2)	5
Retroperitoneal space	3 (1.1)	3
Lesser pelvis	2 (0.8)	2
Lymph node	2 (0.8)	2
Muscle	2 (0.8)	2
Adrenal gland	1 (0.4)	1
Spleen	1 (0.4)	1
Bone		
Thoracic cage (ribs, sternum)	18 (6.8)	16
Other bones	3 (1.1)	3

More than one treated tumor lesion or organ region is possible in one procedure. Values in parentheses are percentages.

with the use of low-milliampere CT fluoroscopy at a tube current–exposure time product of 10 mAs (16,17). Precautions with respect to radiation protection of the operator during CT fluoroscopy included aprons, thyroid shields, and eyeglasses of 0.5-mm lead equivalent. An additional shield was put onto the lower half of the patient before sterile draping to reduce scattered radiation. With respect to radiation protection of the operator's hand, during CT fluoroscopy, angular beam modulation (Hand Care; Siemens) was activated, ie, the radiation exposure was switched off between the ten o'clock and two o'clock position of the x-ray tube. For assessment of complications and three-dimensional planning of the CyberKnife radiosurgery procedure, after fiducial marker placement, a contrast-enhanced or unenhanced CT scan with 1-mm axial reconstructions was performed.

Procedure

All procedures were performed by one of the board-certified authors, each of whom had interventional experience of at least 5 years at the time of the intervention. In patients with intrapulmonary tumor lesions, monitoring with pulse oximetry was generally applied during the intervention. In case of cardiorespiratory comorbidities such as emphysema/COPD or previous lung surgery, the procedure was performed with standby of an anesthesiologist. After sterile draping and disinfection of the skin overlying the planned needle entry point, local anesthesia with 10–20 mL of 2% mepivacaine hydrochloride (Scandicain; AstraZeneca, Wedel, Germany) was applied. After a small skin incision was made, the 18-gauge applicator needle (CP Medical, Portland, Oregon) with a length of 20 cm was then introduced and advanced to the tumor lesion under intermittent quick-check CT fluoroscopy. At the beveled tip, the applicator needle contained bone wax, which acted as a safety measure against inadvertent marker placement, as well as a 1 × 3-mm gold fiducial marker. When the preloaded needle had been satisfactorily introduced, a rubber spacer was removed at the end of the applicator needle, and the gold fiducial marker was

delivered by pushing the central mandrin into the needle. Because the CyberKnife system uses orthogonal x-rays at 45° to vertical to track the tumor and the fiducial markers, the markers should be placed in a noncollinear array in different sectors of the tumor to specify a three-dimensional space enclosing the tumor (18). For this purpose, in case of large tumor lesions (ie, diameter > 3 cm), as many as three further markers were implanted in analogy to the description of Bhagat et al (14). The number of fiducial markers used in each case was at the discretion of the interventional radiologist performing the procedure. The markers did not have to be positioned within the tumor lesion, but in the vicinity. Fiducial marker placement within 1 cm of the lesion was regarded as acceptable for targeting. If a fiducial marker showed immediate migration or was unintentionally misplaced, additional markers were inserted until at least one marker remained within or adjacent to the target lesion. Gold fiducial markers are known to cause a perturbation of the dose distribution in their vicinity (19). For the CyberKnife scenario (ie, multiple 6-MV beams from different directions), a moderate increase near the fiducial marker surface can be expected. Therefore, fiducial markers inside the target volume increase inhomogeneity. This is in agreement with the CyberKnife dose prescription approach, in which low prescription isodose lines (60%–80%) and high inhomogeneity are preferred.

After the postinterventional CT scan, all patients without complications or with minor complications (ie, class A or B complications according to Society of Interventional Radiology [SIR] criteria [15]) were sent back to the ward for clinical monitoring for 24 hours. Patients with major complications (SIR class C or D; eg, thoracostomy tube placement after transthoracic fiducial marker placement requiring prolonged admission or catheter exchange) were monitored under appropriate treatment until their complete recovery.

Simulation of the radiosurgery procedure with the use of the CyberKnife treatment planning system was performed by a team of radiation oncologists and medical physicists in the days following the fiducial marker placement procedure. By using the CT scan acquired after the marker placement procedure, the tumor volume and sensitive anatomic structures were identified and outlined, followed by the calculation of an appropriate radiation dose. In addition, the position of the fiducial markers in relation to the tumor and neighboring structures was localized. This allowed the precise tracking of the robotic system during delivery of the therapeutic radiation dose (4).

Assessment of Technical Outcome and Complications

In a retrospective analysis of patients' imaging studies available in the local picture archiving and communication system, radiology reports, and remaining medical records, two experienced interventional radiologists evaluated the technical success and complications associated with CT fluoroscopy–guided fiducial marker placement. Technical success was defined as placement of one or more fiducial markers suitable for tracking of the tumor in a free-breathing patient during treatment simulation and treatment. The necessity of a further referral of the patient to the interventional radiology unit for placement of additional fiducial markers in the same tumor lesion (as a result of migration of the primarily implanted marker) was regarded as a technical failure. Complications of the fiducial marker placement procedures were classified according to SIR Standards of Practice Committee classification of complications by outcome (15).

RESULTS

Technical Outcome

CT fluoroscopy–guided percutaneous fiducial marker placement was performed in 222 consecutive sessions involving 196 individual patients with 264 tumor lesions (37 primary tumors and 227 metastases; **Fig 1**). One hundred seventy-five patients underwent only one session of fiducial marker placement. As a result of newly diagnosed tumor lesions in the course of their disease, 18 patients underwent two sessions, two underwent three sessions, and one underwent five sessions of fiducial marker placement before radiosurgery. The distribution of underlying tumor entities and organ systems/organs affected by the target lesions is summarized in **Tables 1** and **2**. The mean number of tumor lesions treated in one session was 1.3 ± 0.8, with a mean tumor diameter of 2.3 cm ± 1.2 cm (range, 0.5–6.5). The total number of fiducial markers implanted was 321, with a mean number of fiducial markers per tumor lesion of 1.2 ± 0.5 (range, 1–4). On CT immediately after CT fluoroscopy–guided marker placement, the localization of the fiducial markers (N = 321) in relation to the tumor lesion was as follows: intratumoral in 193 cases (60.1%), at the tumor margin in 50 cases (15.6%), and outside of the tumor in 78 cases (24.3%). In all 196 patients, CyberKnife treatment was possible after a single session of CT fluoroscopy–guided marker placement, without any cases of relevant secondary marker migration preventing successful treatment planning and treatment. The mean time interval between fiducial marker placement and CyberKnife radiosurgery treatment was 3.4 days ± 3.3 (range, 0–21 d). **Table 3** summarizes the characteristics and technical outcomes of CT fluoroscopy–guided marker placement in 264 tumor lesions.

Complications

In 63 of 222 CT fluoroscopy–guided marker placement procedures (28.4%), SIR-defined complications

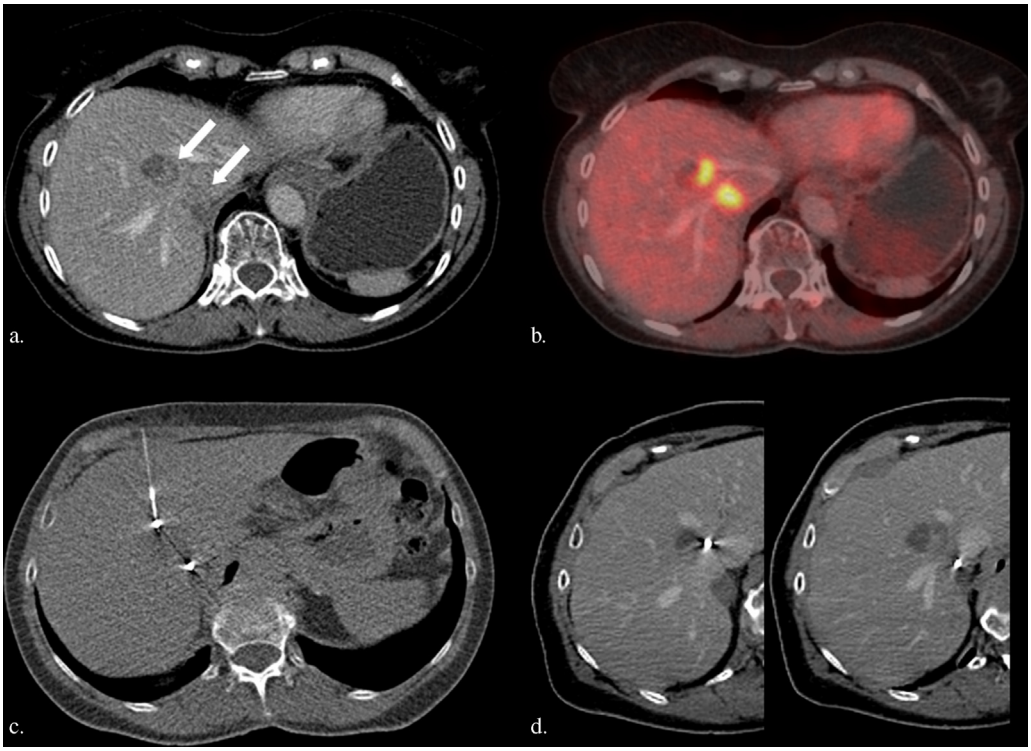

Figure 1. Images from a 69-year-old woman with a history of colorectal cancer 1 year earlier who had undergone radiofrequency ablation of two liver metastases in segments VII and VIII neighboring the vena cava and the large liver veins. Contrast-enhanced portal venous CT scan shows two slightly enhancing local recurrences (arrows) at the margin of the ablation areas **(a)**. On PET/CT, a corresponding hypermetabolism of both metastases is depicted **(b)**. Two fiducial seeds are implanted within the lesions under CT fluoroscopy via an 18-gauge needle **(c)**. The portal venous CT scan performed after the intervention for planning of CyberKnife radiosurgery shows correct intratumoral localization of both fiducial seeds **(d)**. (Available in color online at *www.jvir.org*.)

Table 3. Characteristics and Technical Outcome of CT Fluoroscopy–Guided Fiducial Seed Placement in 264 Tumor Lesions

Characteristic/Parameter	Value
Total tumor lesions	264
Primary tumor	37
Metastasis	227
Lesions treated in one session	1.3 ± 0.8
Tumor diameter (cm)	2.3 ± 1.2
Minimum	0.5
Maximum	6.5
Total implanted fiducial seeds	321
Fiducial seeds implanted per lesion	1.2 ± 0.5
Median	1
Minimum	1
Maximum	4
Localization of fiducial seed	
Seed within tumor	193 (60.1)
Seed at tumor margin	50 (15.6)
Seed outside of tumor	78 (24.3)
Distance from tumor margin to seed (cm)	0.4 ± 0.6
Minimum	0
Maximum	2.9

Values presented as mean ± standard deviation where applicable. Values in parentheses are percentages.

(15) occurred, as summarized in **Table 4**. During 14 of 105 procedures (13.3%) with pulmonary fiducial marker placement, a pneumothorax occurred that required thoracostomy tube insertion (instantaneous insertion of pigtail drainage catheter under CT fluoroscopy, n = 7; surgical thoracostomy tube insertion, n = 7) and a prolonged admission of at least 48 hours until complete recovery of the patient (SIR class D complication; **Fig 2**). In contrast, in 21 procedures (20%), after pulmonary fiducial marker placement, only a small pneumothorax was observed, which resolved without further therapy during the days following the intervention (SIR class B). This corresponds to an overall pneumothorax rate of 33.3% (35 of 105 sessions with pulmonary fiducial marker placement). Small peritumoral alveolar hemorrhage without hemoptysis was seen in 32 procedures (30.5%), and major bleeding developed in three patients (2.9%), followed by transient hemoptysis. In all cases, hemoptysis resolved within 30 minutes after the intervention (SIR class A). A combination of peritumoral alveolar hemorrhage and pneumothorax occurred in seven of the aforementioned 63 procedures.

After the application of the local anesthetic drug and successful fiducial marker placement in a pulmonary metastasis of renal-cell carcinoma, one 71-year-old woman

Table 4. Minor and Major Complications According to SIR Quality Improvement Guidelines (15)

Complication	No. of Pts.	Complications	
		Minor	Major
Lung	105	–	–
Pneumothorax	–	21 (20)*	14 (13.3)†
Pulmonary hemorrhage	–	35 (33.3)‡	–
Systemic toxicity of local anesthetic drug	–	–	1 (0.9)§

Values in parentheses are percentages.
*Pneumothorax without necessity of further intervention (class B complication).
†Pneumothorax requiring chest tube or pigtail drainage placement (class D complication).
‡Self-limiting pulmonary hemorrhage (class A complication).
§Successfully treated by infusion of Lipofundin for systemic binding of local anesthetic drug (class D complication).

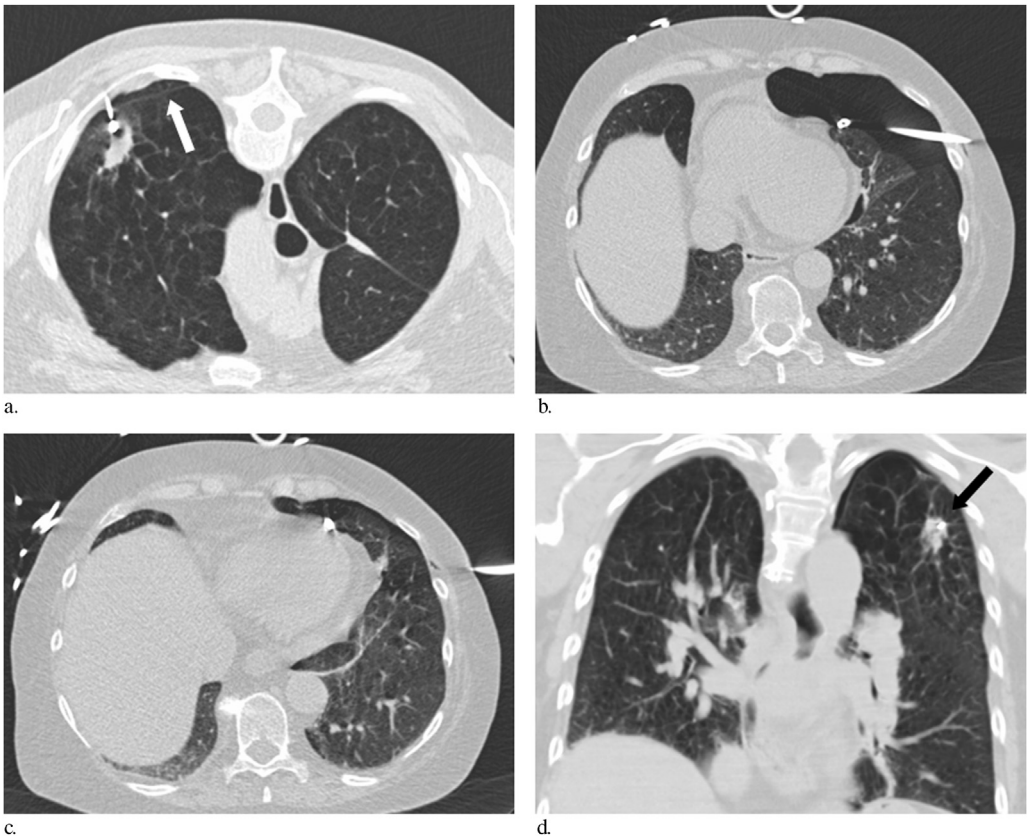

Figure 2. Images from a 66-year-old woman with COPD, a history of non–small-cell lung cancer, and a new tumor in the left upper lobe. One fiducial seed is inserted into the tumor under CT fluoroscopic guidance with crossing of the fissure (arrow) in prone position of the patient **(a)**. Although the initial control CT scan did not show a marked pneumothorax, a few minutes after the procedure, severe dyspnea developed and the patient was intubated by the anesthesiologists. Under CT fluoroscopy, a tension pneumothorax was confirmed and immediately treated by insertion of a 14-F pigtail drainage in supine position **(b)**, which relieved the pneumothorax instantly **(c)**. The final CT scan confirmed a correct intratumoral localization of the fiducial seed **(d)** (arrow).

showed a small, clinically asymptomatic hemorrhage within the needle access path on postinterventional CT (Fig 3). The patient additionally showed signs of systemic toxicity, with disorientation, dysphasia, and hypertension. After instantaneous intravenous infusion of Lipofundin (B. Braun, Melsungen, Germany) by the anesthesiologists for the purpose of systemic binding of the local anesthetic drug, the patient was transferred to the intensive care unit for further monitoring. The patient was discharged the following day after complete remission of symptoms (SIR class D). Other than the aforementioned complications, no procedure-related permanent adverse sequelae or deaths occurred in the present series.

DISCUSSION

The efficacy and complications associated with percutaneous CT-guided placement of fiducial markers before

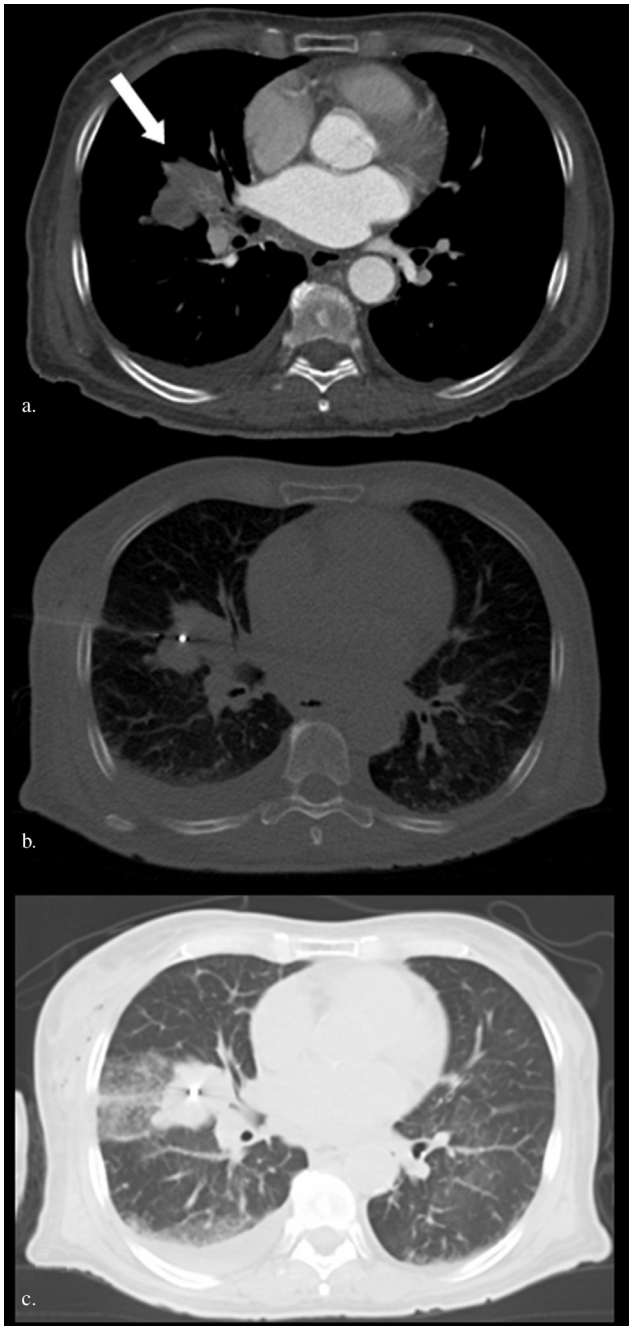

Figure 3. Images from a 71-year-old woman with a history of renal-cell cancer and a large metastasis (arrow) in the middle lobe abutting the right hilum **(a)**. Under CT fluoroscopy, a fiducial seed was successfully implanted within the tumor **(b)**. The CT scan conducted after the procedure revealed a major hemorrhage along the needle access path remaining clinically asymptomatic **(c)**. Immediately after the procedure, the patient began to show signs of systemic toxicity associated with the local anesthetic drug, with disorientation, dysphasia, and hypertension. After instantaneous intravenous infusion of Lipofundin (B. Braun) by the anesthesiologists for the purpose of systemic binding of the local anesthetic drug, the patient was transferred to the intensive care unit for further monitoring, and was discharged the following day after complete remission of symptoms.

stereotactic radiation therapy and radiosurgery have been evaluated in several clinical investigations and technical reports (12–14,20,21). In 188 consecutive patients, Brook et al (12) investigated the complication rates of CT- and US-guided fiducial marker placement in the abdomen with an 18-gauge delivery needle alone or with concomitant biopsy via a 17-gauge guiding sheath. The overall complication rate was 4.3%. Although the patient groups did not differ significantly regarding minor complication rates, number of markers per patient, and technical success, the only major complications were observed in patients with combined biopsy and marker placement procedures in renal or liver tumors under CT guidance. These results are in line with the present findings, as, in our patient series undergoing CT fluoroscopy–guided marker placement in nonpulmonary tumors without a concomitant biopsy, we did not observe any minor or major complications.

With respect to the frequency of pneumothoraces and the necessity of chest tube placement in patients undergoing CT-guided fiducial marker placement in pulmonary neoplasms, reported rates vary considerably (**Table 5**) (13,14,18,20,21). Pneumothorax rate ranges between 4.8% (13) and 67% (14), and frequencies of chest tube placement range between 2.4% (13) and 22% (14).

In analogy to the findings by Brook et al (12), in the study by Yousefi et al (20), concomitant core needle biopsy at the time of fiducial marker placement was associated with a significantly increased pneumothorax rate (64% vs 26% without biopsy; $P = .03$). Postprocedural CT demonstrated pulmonary hemorrhage in 19% of patients, whereas all but two patients remained clinically asymptomatic.

In comparison, in our patient series with pulmonary target lesions, a major alveolar hemorrhage with transient hemoptysis was seen in three patients. However, in all cases, hemoptysis was self-limiting within a time interval of 30 minutes after the procedure.

In their patient series with pulmonary, pancreatic, and hepatic tumors, Kothary et al (18) underlined that the overall complication rate of 5% was within the reported range for percutaneous biopsies (15). However, the rate of pneumothoraces requiring a chest tube (16%) exceeded the suggested threshold of 10% but paralleled previous results (20) focusing on the subpopulation of patients with lung tumors often associated with COPD. Localized self-limiting pulmonary hemorrhage was found in 18% of the lung implantations.

Bhagat et al (14) reported a still higher frequency of pneumothoraces (67%) and pneumothorax-related further interventions (22%). Remarkably, there was a significant difference in the pneumothorax rate associated with the use of 18-gauge (14 of 17 patients; 82%) versus 19-gauge (four of 10 patients; 40%) needles ($P = .01$).

Table 5. Pneumothorax and Chest Tube Rates in Pulmonary Fiducial Marker Placement (13,14,18,20,21)

Study, Year	No. of Pts.	Pulmonary Marker Placement	Fiducial Delivery Needle Diameter (Gauge)	No. of Fiducial Markers	Pneumothorax (%)	Chest Tube (%)
Yousefi et al (20), 2007	48	48*	18–20	2–6	33	12.5
Kothary et al (18), 2009	132	44*	19	3–5	45	16
Bhagat et al (14), 2010	28	28*	18–19	1–7	67	22
Sotiropoulou et al (13), 2010	105	42†	18	1–5	4.8	2.4
Patel et al (21), 2013	89	64*	19	1–4	33	9

*Number of patients.
†Number of lesions.

With respect to a reduced pneumothorax and chest tube rate in comparison to the works by Kothary et al (18) and Bhagat et al (14), Patel et al (21) particularly underlined their "single puncture technique" for the placement of three fiducial markers at one time, combined with a reduced total number of implanted markers. Sotiropoulou et al (13) described the lowest pneumothorax (4.8%) and chest tube (2.4%) rates associated with the use of 18-gauge needles reported so far.

As Wu et al (22) have pointed out, there are several patient- and lesion-related technical factors affecting the pneumothorax rate in CT-guided needle biopsy of the chest that can be transferred to the scenario of pulmonary fiducial marker placement: These include COPD and the lack of a history of ipsilateral surgery (23), an increased depth of the lesion from the skin or a long needle path ($>$ 4 cm) (23–25), a small lesion size (23,26), as well as an increased number of pleural punctures and a wider insertion angle of the needle (ie, less perpendicular to the pleura) (25).

Bhagat et al (14) identified a small lesion size (P = .03), missing pleural contact of tumor lesion (P = .04), and the use of 18-gauge needles (P = .01) as factors significantly increasing the pneumothorax rate in fiducial marker placement. Remarkably, mean needle trajectory length, median number of implanted markers, median number of needle adjustments, and the presence of emphysema were not found to have a statistically significant influence on the rate of pneumothoraces (without or with the necessity of chest tube placement).

In the present patient series, we aimed to minimize the influence of the aforementioned risk factors by penetrating the pleura with the fiducial marker needle only once under strict breath-holding of the patient and by avoiding a wide insertion angle of the needle. In addition, the mean number of implanted fiducial markers per pulmonary tumor lesion was lower (mean, 1.2 ± 0.5; median, 1) than in the studies by Kothary et al (median number of fiducial markers per tumor, 4) (18), Yousefi et al (20) (mean number of fiducial markers per tumor, 3.68; median, 4), and Bhagat et al (14) (as many as seven fiducial markers per tumor) given a mean pulmonary tumor size of 2.2 cm ± 1.1 (range, 0.7–5.8 cm).

Remarkably, in contrast to the works by Brook et al (12), Kothary et al (18), and Yousefi et al (20), we administered only local anesthesia (without concomitant moderate sedation with intravenous midazolam and fentanyl), ensuring sufficient patient cooperation in all procedures. In addition, in contrast to the study by Patel et al (21), the planning CT for CyberKnife treatment was routinely performed immediately after the marker placement procedure with the actual treatment session being scheduled for the following day. Only in case of major complications such as a pneumothorax requiring chest tube placement and a prolonged patient observation on the ward was an additional planning CT performed a few days later after clinical recovery of the patient.

As a limitation of the present study, we did not quantify fiducial marker migration rate, whereas a relevant delayed fiducial displacement was ruled out during fiducial tracking and CyberKnife treatment was possible by using the implanted fiducial markers in all cases. In case of a displacement or a suboptimal placement of the first fiducial marker being evident under CT fluoroscopy, a further fiducial marker was implanted immediately. The low mean and median numbers of implanted fiducial markers per tumor lesion, as well as the high ratio of fiducial markers implanted within the tumor (60.1%) or at the tumor margin (15.6%), underline the high technical success rate feasible in our patient series treated under local anesthesia and CT fluoroscopic guidance. In addition, in all patients, a subsequent therapy planning and CyberKnife treatment were possible after a mean time interval of only 3.4 days ± 3.3. This high primary technical success rate is in line with the results of Brook et al (12) and Sotiropoulou et al (13), which reported technical success rates of 99.5% and 98.4%, respectively. Previous studies have observed migration rates between 4.8% (12) (nine of 188 patients; various tumor locations) and 9.1% (18) (four of 44 patients; pulmonary tumors). Fiducial marker migration is usually observed within 1 week of implantation (27), and is most often observed to the pleural space or extrapleural soft tissue (21), with a significantly higher rate of affected patients undergoing concomitant core biopsy (12). Bhagat et al (14) identified an increased risk of fiducial marker migration with shorter distances from the pleura to the deposition site (P = .04), and with fiducial marker placement outside the tumor lesion (P = .03).

In conclusion, the present study underlined that CT fluoroscopy–guided percutaneous fiducial marker

placement can be performed under local anesthesia with high technical success in terms of an intra- or peritumoral fiducial marker implantation in various organs and anatomic regions. Most frequently observed complications are pneumothoraces and pulmonary hemorrhages occurring during fiducial marker placement in lung tumors, with the majority of them being self-limiting and only a minority of pneumothoraces requiring chest tube placement and a prolonged hospital admission. Although all procedures were successful regarding the location and number of implanted fiducial markers allowing subsequent CyberKnife radiosurgery, the overall complication rate could potentially be reduced by the use of fiducial marker needles with diameters smaller than 18-gauge.

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