

# Percutaneous fiducial marker placement prior to stereotactic body radiotherapy for malignant liver tumors: an initial experience

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## ABSTRACT

The aim of this study was to describe our initial experience with a gold flexible linear fiducial marker and to evaluate the safety and technical and clinical efficacy of stereotactic body radiotherapy using this marker for malignant liver tumors. Between July 2012 and February 2015, 18 patients underwent percutaneous fiducial marker placement before stereotactic body radiotherapy for malignant liver tumors. We evaluated the technical and clinical success rates of the procedure and the associated complications. Technical success was defined as successful placement of the fiducial marker at the target site, and clinical success was defined as the completion of stereotactic body radiotherapy without the marker dropping out of position. All 18 fiducial markers were placed successfully, so the technical success rate was 100% (18/18). All 18 patients were able to undergo stereotactic body radiotherapy without marker migration. Thus, the clinical success rate was 100% (18/18). Slight pneumothorax occurred as a minor complication in one case. No major complications such as coil migration or bleeding were observed. The examined percutaneous fiducial marker was safely placed in the liver and appeared to be useful for stereotactic body radiotherapy for malignant liver tumors.

**KEYWORDS:** fiducial marker, percutaneous, SBRT, liver tumor

## INTRODUCTION

The treatment of liver metastases and primary liver tumors has evolved. Although surgery is the current standard treatment for localized surgically operable lesions [1], many patients with liver metastases cannot undergo surgical resection because of associated comorbidities, concerns about their age, the extent of the disease, or the patient's wishes. Alternative treatment approaches for unresectable liver metastasis and primary liver cancer include chemoembolization, radiofrequency ablation, cryotherapy, and the oral multikinase inhibitor sorafenib. Treatment choice is guided by the Barcelona Clinic Liver Cancer staging system and recommended treatment strategy [2].

Stereotactic body radiotherapy (SBRT) is a technique that allows the delivery of a precise dose of radiation to a tumor while sparing adjacent normal tissues. However, the movement of intra-abdominal organs due to respiration has hampered the use of SBRT. The insertion of a fiducial marker near to the tumor before radiotherapy allows respiratory motion to be tracked, thus enabling accurate dose delivery while the patient breathes freely [3]. Recently, the percutaneous insertion of fiducial markers has been described [4, 5], but experience of such procedures is still limited. This marker is made from gold, which makes it biocompatible and ensures it exhibits good contrast on X-ray images. In this study, we describe our initial experience with

this new fiducial marker and evaluate the technical feasibility, clinical efficacy, and safety of SBRT using this marker.

### MATERIAL AND METHODS

This study was part of a prospective SBRT study in which the CyberKnife G4 was used to treat liver tumors and was approved by the institutional review board. Written informed consent was obtained from all patients. Since the patient accrual for this SBRT study was relatively slow, we report our initial experience with a gold flexible linear fiducial marker (VISICOIL, RadioMed Corporation, Barlett, TN, USA) in this article. Between July 2012 and February 2015, 18 patients underwent percutaneous fiducial marker placement under computed tomography (CT) fluoroscopic guidance or ultrasonographic guidance before SBRT for liver tumors. The patients included 12 men and 6 women. Their median age was 68 years (range, 44–83 years), and all of them were inpatients. All of the tumors were pathologically or clinically diagnosed as malignant liver tumors.

#### Percutaneous fiducial marker placement technique

The technique is mostly common to that we previously reported for lung tumors [3]. First, all patients underwent diagnostic CT scans of their abdomen composed of 3–5 mm-thick contiguous axial tomographic sections. After reviewing these preliminary images, an appropriate puncture site and the optimal needle guidance method, i.e. CT fluoroscopic or ultrasound guidance, was determined in advance. The marker placement was performed during breath-holding under CT fluoroscopic guidance in 8 cases and under ultrasound guidance in 10 cases. The imaging parameters during CT fluoroscopy included a CT beam width collimated to 3 mm. One patient needed contrast-enhanced CT fluoroscopy during the procedure to delineate the tumor clearly. Ultrasonography was performed with a convex probe (2–5 MHz). A gold flexible linear marker containing an 18-gauge coaxial needle (0.75 mm in diameter and 5 mm in length, Fig. 1) was used as the fiducial marker. All patients received supplemental nasal oxygen, and their vital signs were monitored. Local anesthesia was achieved via the subcutaneous administration of 1% lidocaine. After confirming that the needle tip had reached the target lesion, the

fiducial marker was deployed, and then the needle was removed (Fig. 2). Only one fiducial marker was placed in each patient. After the procedure, CT or cone-beam CT was performed to determine whether any complications such as pneumothorax or bleeding had occurred.

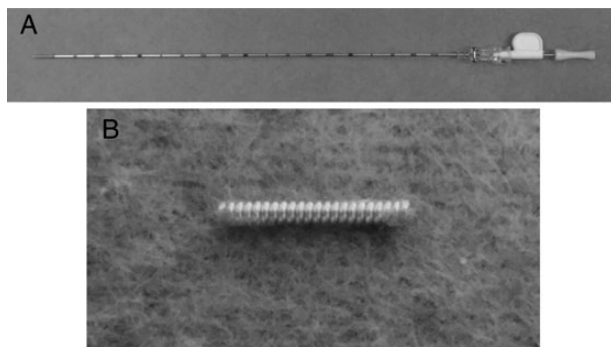


Fig. 1. The gold flexible linear fiducial marker (VISICOIL). (A) An 18-gauge coaxial introducer needle containing the gold flexible linear fiducial marker. (B) The gold flexible linear fiducial marker.

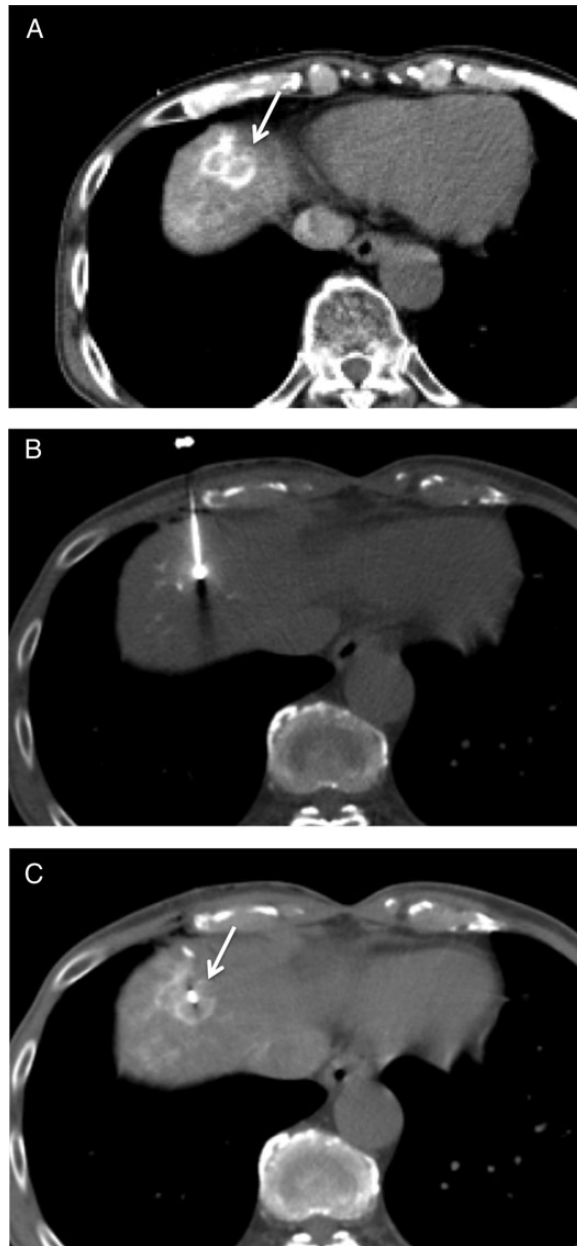


Fig. 2. A 73-year-old man with metastasis from carcinoma of the ampulla of Vater. (A) CT image shows a hypervascular tumor in S8 (arrow). (B) CT image shows the percutaneous insertion of the gold flexible linear fiducial marker. (C) CT image shows the successful placement of the gold flexible linear fiducial marker (arrow) in the tumor.

### Evaluation of the success rate and complications

Technical success was defined as successful fiducial marker placement at the intended site. The target site was chosen by consensus by an interventional radiologist and a radiation oncologist before the procedure. Clinical success was defined as the completion of SBRT without the marker dropping out of position. The following complications were evaluated: coil migration, pneumothorax, bleeding and death. Marker position was checked by CT or cone-beam CT images taken immediately after placement and planning CT images taken before radiotherapy. Migration of a marker before radiotherapy was defined as its displacement exceeding 3 mm from the initial position on CT images; the marker position within or relative to the tumor was evaluated. During radiotherapy, migration of a marker was evaluated by comparing abdominal plain X-ray images at an inspiratory phase in the supine position taken after marker placement with fluoroscopy images taken at an inspiratory phase of the treatment system; thereby the marker position was evaluated in relation to the rib bones and diaphragm. It was difficult to evaluate subtle displacements of the marker by fluoroscopy images alone, especially once radiotherapy was started, because the size of the tumor and the surrounding tissue could change with treatment. Therefore, when migration of the marker that could influence treatment accuracy (e.g. >3 mm) was suspected by fluoroscopy, CT scanning was scheduled for further evaluation to determine whether the displacement was significant or not.

### RESULTS

The characteristics of patients, tumors and fiducial marker placement are summarized in Table 1. The median tumor size was 35.5 mm

**Table 1. Summary of patients, tumors and fiducial marker placement**

Patients ( <i>n</i> = 18)	
Male/Female	12/6
Median age (range)	68 (44–83)
Tumors ( <i>n</i> = 18)	
Size (mm) – Median of maximum length (range)	35.5 (11–88)
Type	
Hepatocellular carcinoma	5
Liver metastasis (Colon/Gastric/Others)	13 (6/2/5)
Site	
S1/4/6/7/8/1&8/3&4/4&8/7&8	1/3/1/1/7/2/1/1/1
Fiducial marker placement ( <i>n</i> = 18)	
CT fluoroscopic/US guidance	8/10
Inside/near the tumor	11/7

S1 = Caudate lobe, S3 = Ventrolateral segment of the left lobe, S4 = Medial segment of the left lobe, S6 = Posteroinferior segment of the right lobe, S7 = Posterosuperior segment of the right lobe, S8 = Anterosuperior segment of the right lobe.

(range, 11–88). The 18 tumors consisted of 5 hepatocellular carcinomas (28%) and 13 liver metastases (72%). The target sites for marker insertion were as follows: inside the tumor in 11 cases (61%) and near the tumor in 7 cases (39%). The fiducial marker placement was successful in all cases (100%, Fig. 2); thus, the technical success rate was 100% (18/18). The median hospitalization period was 2 days (range: 2–5). Two patients underwent radiofrequency ablation of another lesion after fiducial marker placement; therefore, their hospitalization period was 5 days. SBRT was successfully performed in all 18 cases, and none of the markers was judged to have dropped out of its position. No patients underwent CT for evaluation of the marker position during the radiotherapy course. Thus, the clinical success rate was 100% (18/18). The median period between marker implantation and SBRT was 16 days (range: 0–31).

No major complications, such as bleeding or marker migration, occurred (0%, 0/18). One patient developed mild pneumothorax; however, the SBRT was performed as planned because the pneumothorax disappeared after a few days' observation. Thus, the minor complications rate was 6% (1/18).

### DISCUSSION

In SBRT for liver lesions, techniques for controlling tumor motion are required because the bowel and stomach, which have a perforation risk, lie close to the liver. There are two main methods for reducing the uncertainty regarding the positions of liver tumors [6]. One is to minimize tumor motion via the inhalation of oxygen, abdominal compression, learning of regular respiratory patterns, or breath-holding techniques [7–9]. The other technique, which is more sophisticated, is target gating or target chasing, during which the movements of the skin surface or other markers are monitored [10, 11]. The placement of the gold flexible fiducial markers near or inside a tumor is considered to be the most direct version of this method. In the present study, fiducial markers were inserted before tumor-tracking SBRT (using a CyberKnife G4) during abdominal compression to improve the accuracy of localization.

Percutaneous fiducial marker placement has been widely performed, but some complications such as marker migration (which might cause delayed or inappropriate treatment) have been reported [4, 5]. For example, a previous study described cardiac embolization due to the migration of a nester embolization coil that was used as a fiducial marker [12]. Unlike traditional cylindrical gold seed fiducial markers, for which the migration rate was reported to be 5% [13], the marker used in this study is flexible and has a coiled design, which might reduce the incidence of fiducial migration. In our study, no marker migration was observed; thus, this gold flexible linear fiducial marker seems to be superior. However, pneumothorax occurred in one case, and a previous report found that percutaneous insertion of the gold flexible linear fiducial marker into the lungs is associated with a high risk of pneumothorax [3]. In our experience, the needle included with the gold flexible linear fiducial marker is not sharp enough, and it is more difficult to penetrate the pleura and tumors with this needle than with a biopsy needle. Therefore, it might be necessary to improve the shape of the needle.

Ohta *et al.* [14] previously reported that the transarterial placement of a fiducial marker resulted in a low complications rate (2%) and a high technical success rate (100%). However, complications such as femoral pseudoaneurysms have also been reported to occur

after angiography [15]. In addition, some of the transarterial marker procedures failed, and the outcomes of such procedures were considered to depend on the tumor site and the anatomy of the hepatic artery. Celiac artery stenosis makes it difficult to identify the hepatic artery [16, 17]. Therefore, the tumor site and the anatomy of the hepatic artery should be confirmed with CT and angiography. On the other hand, Brook *et al.* [18] reported that the complications rate for percutaneous fiducial marker placement in the abdomen or pelvis was 4.3% (8/188); there were five minor complications (small hematomas in four cases, pneumothorax in one case) and three major complications (bleeding in two cases, sepsis in one case). Percutaneous fiducial marker placement might exhibit a higher complication rate than transarterial placement. The main benefit of percutaneous marker placement is that it is easy to place the marker in the target position and does not take much time. This study did not aim to compare transarterial and percutaneous procedures. Therefore, there is a clear need for additional research to address this issue. At this time, the fiducial marker placement method should be decided based upon a consensus being reached between radiation oncologists and interventional radiologists after consideration of the tumor location and the anatomy of the hepatic artery, which should be confirmed with CT and angiography.

Ultrasound-guided marker placement is an alternative to marker placement under CT [5]. Ultrasound enables real-time monitoring and comfortable handling during intra-abdominal procedures. In addition, ultrasound involves a lower radiation dose than CT fluoroscopic guided procedures. However, the deep part of the liver cannot be clearly observed using ultrasound. Furthermore, the skill of the operator and the efficiency of the ultrasound machine vary among hospitals. Therefore, the implantation method should be discussed on an individual basis.

Three or more fiducial markers were used in the cases described in the literature [5]. In our study, however, only one marker was used based on the consensus of an interventional radiologist and a radiation oncologist. Complications such as pneumothorax might occur more frequently when multiple fiducial markers are inserted percutaneously. One marker is considered to be sufficient because the gold flexible linear fiducial marker is less likely to migrate [3]. In this study, no signs of migration were observed, and all patients underwent radiotherapy without any problems. In future, the complications rate and the frequency of recurrence after radiotherapy should be analyzed with respect to the number of markers employed.

In conclusion, the new gold flexible linear fiducial marker is useful for percutaneous insertion because of its good stability. In this study, we were unable to determine the local control rate of patients undergoing SBRT with this fiducial marker due to the short follow-up periods involved. It is therefore necessary to observe our patients for a longer period to evaluate the clinical usefulness of this marker.

#### CONFLICT OF INTEREST

The authors state that there are no conflicts of interest to report.

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