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## Case Report

# The advantage of iron-containing fiducial markers placed with a thin needle for radiotherapy of liver cancer in terms of visualization on MRI: an initial experience of Gold Anchor

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## ABSTRACT

Radiotherapy for liver malignancy is increasing due to advances in radiotherapy technique. Visualization of the tumor as well as fiducial markers is essential. To see if improved visibility exists on computed tomography (CT) and magnetic resonance imaging (MRI), we evaluated an iron-containing fiducial marker. A patient with hepatocellular carcinoma and a patient with cholangiocarcinoma were enrolled. Pain caused by placement of marker and the best MRI sequence for visualization of both the fiducial marker as well as the liver tumor on MRI was evaluated. CT was obtained in 2.5-mm thickness, and MRIs were obtained in eight sequences (ie, T2-weighted image). 22G preloaded needles were used for marker placement in both patients; this caused little pain during placement under local anesthesia with xylocaine. No complication occurred in either patient. Both markers and tumors were well visualized by the same MRI sequence. The iron-containing fiducial marker is safe and useful for detecting fiducial markers in the liver and for registration using CT and MRI.

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## Introduction

There are various treatment methods for liver tumors; these include radio frequency ablation, transperipheral arterial chemical embolization (TACE), systemic chemotherapy, and radiotherapy [1]. Radiotherapy, particularly stereotactic ablative body radiotherapy (SABR), is commonly used for treating tumors located far from the body surface (i.e., deep tumors in the caudate lobe and

portal vein thromboses sometimes located near the diaphragm [2]). TACE or embolization using lipiodol are used for hyper vascular tumor such as hepatocellular carcinoma (HCC) to reduce the nutrient supply, from artery blood flow. That makes it difficult to treat the tumors by local chemotherapy. Some reports have stated that three-dimensional (3D) conformal radiotherapy can be successfully applied even if the portal vein is invaded by the tumor after SABR [3].

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In recent years, with the advancement of radiotherapy, improvement of treatment planning has become necessary before precise irradiation. It is sometimes difficult to track a tumor in the liver during radiotherapy. Therefore, fiducial markers are used to locate a tumor in the liver. Magnetic resonance imaging (MRI) is superior to computed tomography (CT) to delineate a liver tumor, which has led to the development of CT to MRI registration [4,5]. The outline of a tumor is delineated using MRI, and CT to MRI registration is guided by fiducial markers [6–8].

In general, detection of small fiducial markers in the liver is difficult by MRI. Use of a larger metal device can improve marker detection. However, a larger needle is required to place larger markers. The use of a larger needle increases the risks of bleeding, pain, discomfort, and tumor seeding.

Ferromagnetic metals are highly susceptible to MRI. The metals include iron, cobalt, nickel, and so on. Gold Anchor (GA) fiducial markers contain 0.5% pure iron in pure gold (Naslund Medical AB, Huddinge, Sweden), which voids the signal on MRI. A pilot study by Marsico et al. reported the usability of GA fiducial markers in the liver. However, the visibility on MRI was not addressed. To our knowledge, no study has reported the usefulness of a marker composed of 0.5% iron for detecting HCC or intrahepatic cholangiocellular carcinoma (CCC). We evaluated the pain, discomfort, bleeding, and safety during echo-guided insertion using 22G needle. Three weeks after, we investigated the GA fiducial markers in MRI for detection of HCC and CCC.

## Case reports

The study protocol was approved by the local institutional review board (approval no. 356), and written informed consent was received from the 2 patients discussed in this report.

### Patient 1: HCC

This case involved a patient with a background of hepatic cirrhosis (Child–Pugh class A) caused by chronic hepatitis C infection. The patient underwent repeated radio frequency ablation and TACE for HCC and was finally referred to our Radiotherapy Department for portal vein invasion.

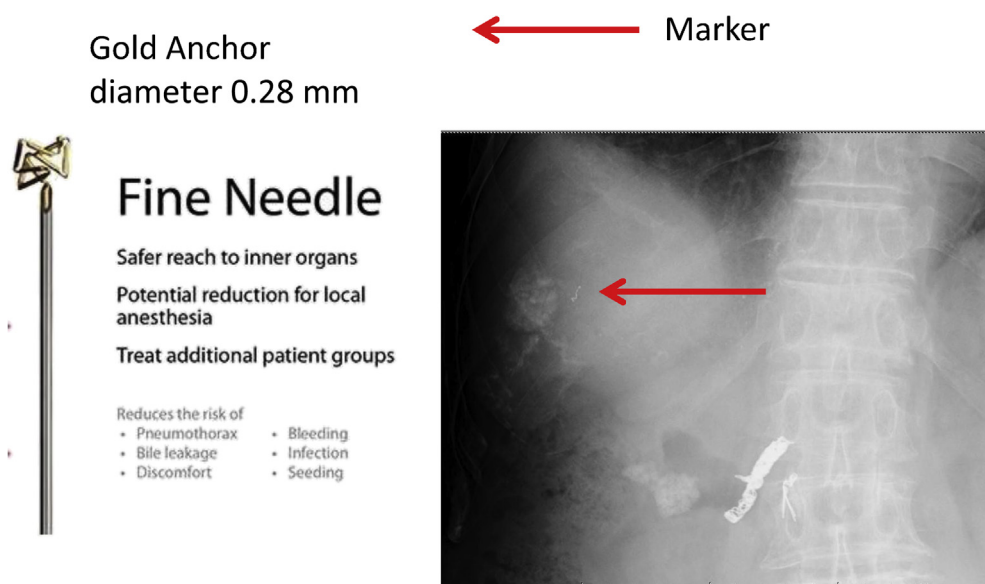
A hepatologist visualized the tumor in the liver by ultrasound. An iron-containing GA fiducial marker (Fig. 1) was placed 2 cm from the HCC using a 22G needle under local anesthesia (Fig. 1). The GA marker had a diameter of 0.28 mm and length of 10 mm (Fig. 2). The hepatologist with 30 years of experience opted for a 22G needle as a 25G needle would have been too flexible and difficult to insert. To prevent intrahepatic bleeding, astriction was performed about 8 minutes. Three weeks after placement, registration on CT and MRI was conducted (Fig. 3). Planning CT and cone-beam CT (CBCT) was shown in Fig. 4.

### Patient 2: CCC

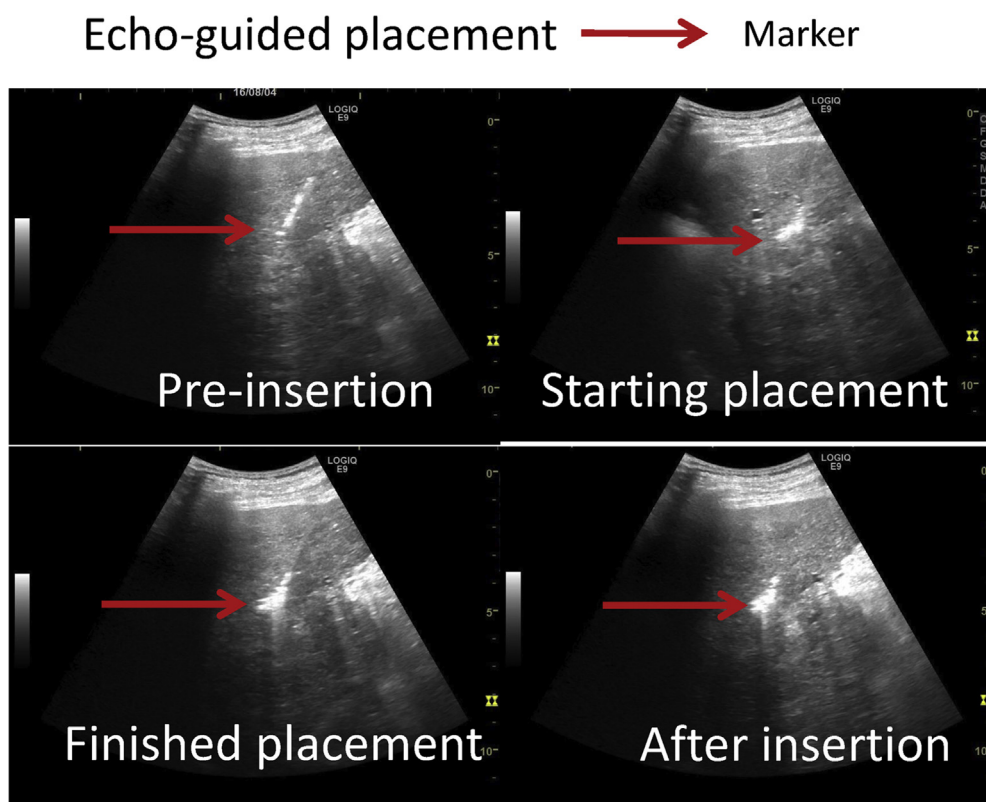
The second patient was referred to our Radiation Oncology Department for the treatment of CCC. In this patient, the bile duct was constricted and showed expansion of the intrahepatic bile duct (Fig. 4). Endoscopic retrograde biliary drainage was performed for placement of a 7 Fr, 9-cm tube (Fig. 4; upper right image) (Gadelius Medical K.K, Sapporo, Japan). Jaundice was relieved after endoscopic retrograde biliary drainage. A GA fiducial marker (diameter, 0.28 mm; length, 10 mm) was placed under echo-guided sonography using a 22G needle 2 cm from the tumor, similarly as that in patient 1.

### Image acquisition

After marker placement, CT (Optima CT580; GE Medical Systems, Milwaukee, WI) and MRI (Intera 1.5 Nova; Philips



**Fig. 1** – Radiograph after insertion. Characteristics of the iron-containing Gold Anchor fiducial marker, which can be placed spherically with a thin 22G or 25G needle. GA contains 0.5% iron and has high visibility on MRI. Visualization is good on simple X-ray images as well. GA, Gold Anchor; MRI, magnetic resonance imaging.



**Fig. 2 – Echo-guided placement.** Use of a 22G needle in echo-guided placement of the GA in the liver. The tip of the needle is distinct and the marker was detained in the liver. The marker is recognized as a high echo. After removal from the liver, visualization of the marker is good. GA, Gold Anchor.

Medical Systems, Eindhoven, The Netherlands) were performed with the following mentioned parameters. Images of the HCC patient are shown in Figs. 3 and 5, and images of the CCC patient are shown in Figs. 4 and 6.

#### Parameters for MRI

- 1) T2-weighted image (T2WI); T2-weighted fast spin-echo: repetition time (TR), 600 ms; echo time (TE), 150 ms; number of samples (signals) averaged (NSA), 1; number of phase encoding steps (PESs), 205; number of frequency encoding steps (FESs), 256; typical spatial resolution (TPR); frequency/phase, 1.72/1.37.
- 2) T2-weighted SPIR (T2WI SPIR); spectral presaturation with inversion recovery image. T2-weighted fast spin-echo: TR, 1200 ms; TE, 80 ms; NSA, 2; PES, 280; FES, 400; TPR; frequency/phase, 1.42/0.95 (Fig. 3; upper right image).
- 3) T2\*-2D-WI (T2\*-2D); T2\*-weighted 2-dimensional gradient echo: TR, 174 ms; TE, 14 ms; NSA, 2; PES, 217; FES, 272; TPR; frequency/phase, 1.61/1.29.
- 4) T2\*3D-WI (T2\*3D); T2\*-3D-weighted 3-dimensional gradient echo: TR, 37 ms; TE1, 14 ms; deltaTE, 7.3 ms; NSA, 2; PES, 218; FES, 272; TPR; frequency/phase, 0.55/0.54. Parameters for dynamic MRI: gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (gadolinium-EOB; Primovist injection syringe, Bayer AG, Leverkusen, Germany).
- 5) Dynamic T1-3D-weighted (FFE; fast field) echo: TR, 3.8 ms; TE, 1.86 ms; NSA, 1; PES, 216; FES, 224; TPR; frequency/phase, 1.73/1.56. Early-phase: 35 seconds with breath holding after

injection, portal venous phase: 60 seconds with breath holding after injection (Fig. 3; lower left image), parenchymal phase: 120 seconds with breath holding after injection.

- 6) Diffusion weighed images (b factor, 800); diffusion-weighted single-shot spin-echo: TR, 1200 ms; TE, 80 ms; NSA, 6; PES, 128; FES, 128; TPR; frequency/phase, 2.97/3.02.
- 7) Hepatobiliary phase (HBP); HBP was obtained 20 minutes after injection of EOB, T1-3D-weighted (FFE; fast field) echo: TR, 3.8 ms; TE, 1.86 ms; NSA, 1; PES, 244; FES, 272; TPR; frequency/phase, 1.40/1.55 (Fig. 3; lower right image).

#### Parameters for CT

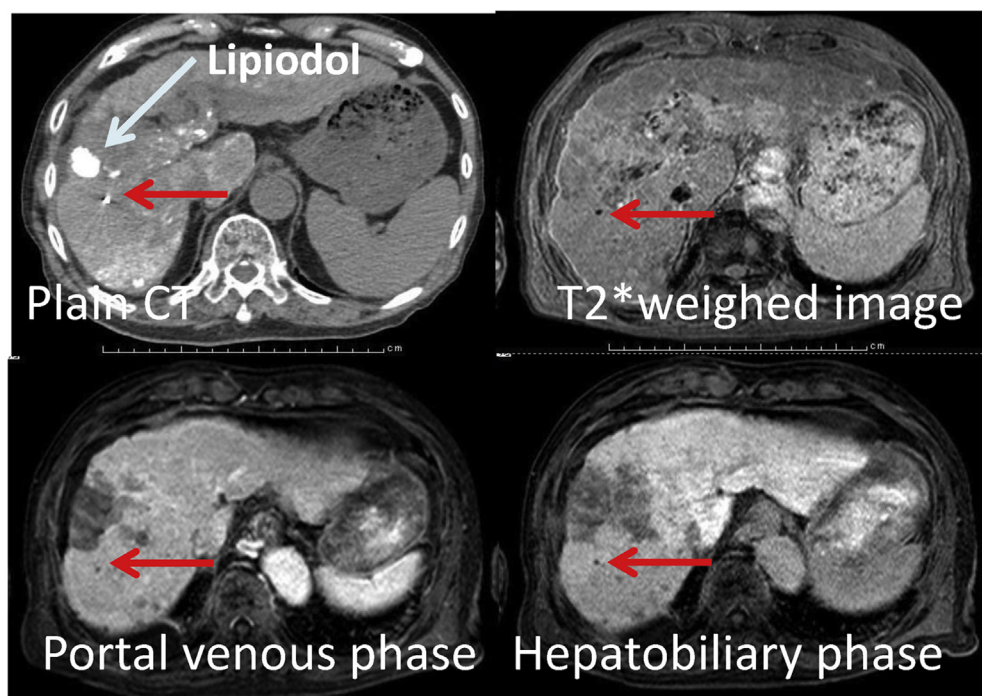
Planning CT: slice thickness, 1.25 mm; field of view, 40 cm × 40 cm; 460 mA; 120 kV. Cone-beam CT; slice thickness, 2.5 mm; number of pixels, 384 × 384; 80 mA; 125 kV. Novalis Tx system (Varian Medical Systems, Inc., Palo Alto, CA; Fig. 5).

## Results

### Patient 1

The GA fiducial marker was placed using a 22G needle and was sufficiently visualized by echo-guided sonography. After placing the GA, striction was performed about 8 minutes to prevent bleeding. There was no complication. Three weeks after marker implantation, registration on CT and MRI was performed.

## CT and MR images ← Marker



**Fig. 3 – CT and MR images.** CT and MRI: comparisons of 3 representative MRI sequences. T2\*-weighted image: the position of a marker is well visualized on MRI. Dynamic-enhanced portal venous phase: the GA and tumor invasion are visible. Hepatobiliary phase (after contrast media dosage, about 20 minutes). The GA and tumor are well visualized as compared to the portal venous phase. The hepatobiliary phase was best for recognition of both the tumor and GA. CT, computed tomography; GA, Gold Anchor; MR, magnetic resonance; MRI, magnetic resonance imaging.

The CT and MR images of the patient with HCC are shown in Figure 3. The GA marker was well depicted on CT, T2\*-WI, portal venous phase, and hepatobiliary phase at 20 minutes after injection of gadolinium-EOB. In addition, GA was well depicted on planning CT and cone-beam CT (Fig. 5). A radiotherapy plan was made with registration on CT and MRI after echo-guided placement of the GA fiducial marker. Localized radiotherapy treatment (SABR; 48 Gy/4 fractions) was performed for HCC for 4 days in the following week using the Novalis Tx system.

#### Patient 2

GA was well visualized in planning CT and MRI (Figs. 4 and 6). Image registration of planning CT and MRI was performed after echo-guided placement of the GA marker (Fig. 6). Because the duodenum was too close to the intrahepatic bile duct carcinoma, SABR was judged as impossible, and 3D-conformal radiotherapy of 50-Gy/25 fractions was performed using the Novalis Tx system.

#### Discussion

Takeda et al. reported that the 3-year local control rate of liver cancer was 96.3%, the 3-year liver-related cause-specific

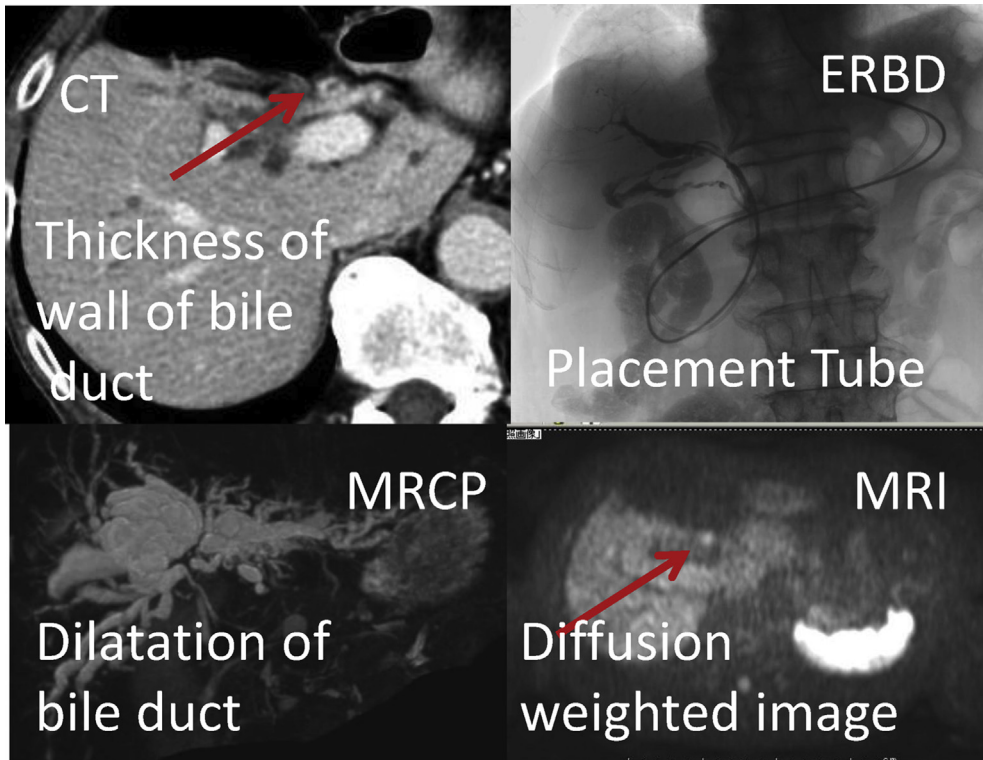
survival rate was 72.5%, the overall survival rate was 66.7%, and toxicity was tolerable [9]. The use of SABR is expected to increase as this method advances in the future.

The following two points should be emphasized: (1) the safety of using the thin needle to place the fiducial marker in the liver by echo-guided imaging and (2) increasing the visibility of fiducial marker as well as tumor on MRI by comparing some sequences.

Although the range of fiducial markers varies, the most commonly used is a diameter of 0.35-1.1 mm. It is relatively easy to identify a large marker on both CT and MRI. However, with a large needle diameter, the frequency of dissemination and the incidence of significant complications will increase [8]. In addition, the risk of hemorrhage is particularly high in patients with cirrhosis. The thinnest needle size for GA placement is 25G. Tumor dissemination caused by a 25G needle can be clinically ignored.

Both 25G and 22G needles can be used to place a GA with spherical and linear shapes. The GA can also be zigzag shaped delivered from needle on purpose. The actual diameter of a spherical GA is approximately 2 mm. However, the signal void on MRI is approximately 5 mm. Therefore, it is easy to detect a GA on MRI and to do registration on CT and MRI.

We previously compared MRI sequences for detecting seeds in low-dose late brachytherapy of the prostate and concluded that contrast-enhanced T1-WI was the best of the 5-element



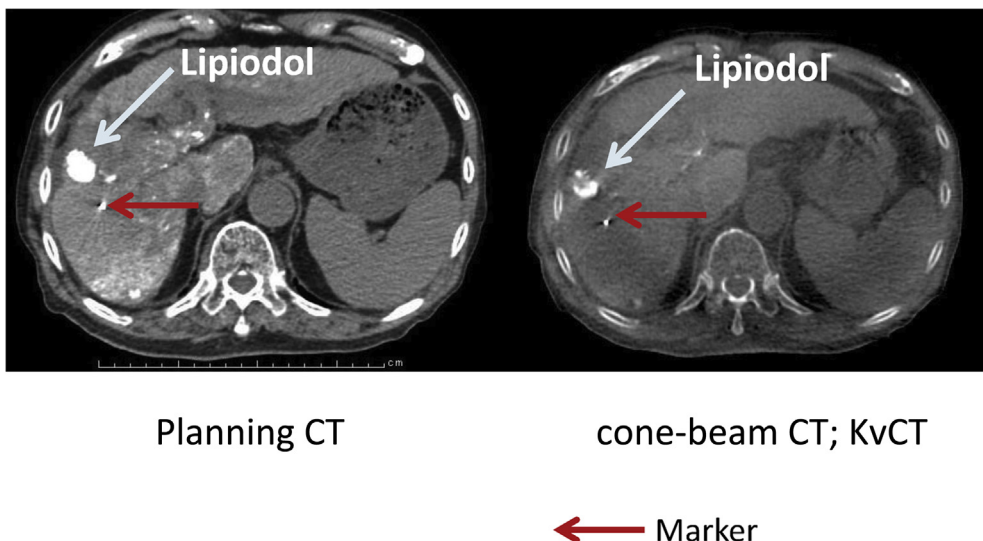
**Fig. 4 – Cholangiocarcinoma improvement in jaundice before treatment. For cases of jaundice, a drainage tube was placed before radiotherapy. CT, computed tomography; MRI, magnetic resonance imaging.**

sequence (T1-WI, T2-WI, T2\*-WI, contrast-enhanced T1-WI, and fat-suppressed contrast-enhanced T1-WI) [5].

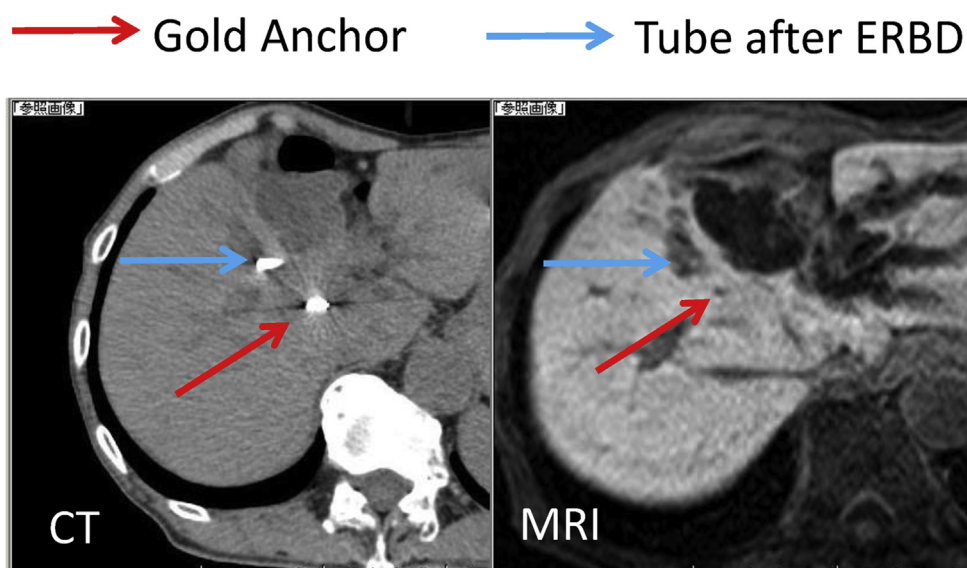
GA contains of 0.5% iron, and visualization by MRI is superior to that of fiducial markers that do not contain iron. GA has been widely used since 2012, and visualization by MRI is better than with a conventional fiducial marker, because iron is a strong magnetic substance. Magnetic susceptibility artifacts refer to a variety of MRI artifacts that share distortions or local signal change due to local magnetic field in homogeneities

from a variety of compounds. Dynamic-enhanced portal venous phase and hepatobiliary phase were used to identify tumor invasion. We used those 2 sequences in all cases.

GA was well visualized in T2\*-WI; therefore, we challenged similar 3 sequences as in the following. TR and TE of the T2\*-WI were changed 3 times (T2\*: TR, 128/174/220 ms; TE, 9.2/14/18 ms; flip angle, 25°; matrix, 272 × 217; field of view, 350 × 300; section thickness, 4 mm; acquisition, 25/34/43 seconds). Dynamic contrast-enhanced phase (after contrast



**Fig. 5 – Planning CT and cone-beam CT. Registration of planning CT for therapeutic CT; KvCT; recognition of GA is good by cone-beam CT (Novalis TX). CT, computed tomography.**



**Fig. 6** – After placement CT and MR images. Planning CT and hepatobiliary phase MRI, recognition of a marker is good in both images and registration was easily performed. CT, computed tomography; MR, magnetic resonance; MRI, magnetic resonance imaging.

media infusion), 30, 60, 120 seconds; hepatobiliary phase (after contrast media infusion), 20 minutes; 3D-T1TFE: 3D-T1 turbo field echo; TR, 3.8 ms; TE, 1.86 ms; flip angle, 12°; matrix, 224 × 272; field of view, 350 × 280; section thickness, 2.5 mm; acquisition, 16 seconds.

Detection of GA is best visualized on T2\*-WI with a TR/TE of 174/14 ms. The hepatobiliary phase was the best for detection of the tumor spread as well as GA. However, visibility of GA was also possible in the early dynamic phase and hepatobiliary phase. During the release of GA fiducial markers in 2012, there have been few reports of MRI with phantoms from overseas and no report of a comparison of human MRI examinations. Pain can be reduced with the use of a thin 22G or 25G needle, and an iron-containing marker is particularly useful for registration on CT and MRI in daily practice.

## Conclusion

We report the characteristics of iron-containing fiducial marker to the liver. Thin needle (22G–25G) reduces adverse event. As compared to the more commonly used markers, the iron-containing fiducial marker composed of 99.5% gold and 0.5% iron makes visualization in MRI easy, which helps planning CT and MRI registration also easy and precise.

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