

**Feasibility, safety, and efficacy of artificial carbon dioxide pneumothorax for computed tomography
fluoroscopy-guided percutaneous radiofrequency ablation of hepatocellular carcinoma**

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Informed consent: Our institution's Ethics Committee approved this retrospective study. The requirement for written informed consent for this study was waived because of its retrospective nature.

Ethical approval: All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Abstract

Purpose: To retrospectively assess the feasibility, safety, and efficacy of artificial carbon dioxide (CO₂) pneumothorax for computed tomography (CT) fluoroscopy-guided percutaneous radiofrequency (RF) ablation of hepatocellular carcinoma (HCC).

Materials and methods: This study included 26 sessions of 24 patients in whom the creation of artificial CO₂ pneumothorax was attempted to avoid the transpulmonary route during CT fluoroscopy-guided percutaneous RF ablation of HCC between April 2011 and December 2017. In these 26 sessions, 29 HCCs (mean tumor diameter: 12 mm, range: 6–22 mm) were treated.

Results: Adequate lung displacement after induction of artificial CO₂ pneumothorax was achieved in 23 of the 26 sessions (88.5%). In the remaining three sessions, transpulmonary RF ablation, transthoracic extrapulmonary RF ablation after switching to an artificial pleural effusion procedure, or RF ablation with electrode insertion in the caudal-cranial oblique direction was performed. No major complications were found. Among the 29 treated tumors, one (3.4%) showed local progression, and the other 28 (96.6%) were completely ablated at the last follow-up (mean follow-up period: 39.3 months, range: 7–78 months).

Conclusion: Artificial CO₂ pneumothorax for CT fluoroscopy-guided percutaneous RF ablation appeared to be a feasible, safe, and useful therapeutic option for HCC.

Keywords Artificial pneumothorax • Carbon dioxide • Computed tomography • Hepatocellular carcinoma • Radiofrequency ablation

Introduction

Radiofrequency (RF) ablation for hepatocellular carcinoma (HCC) is usually performed under ultrasonography (US) guidance because of its availability and real-time monitoring capability [1]. When HCCs are not visible using US or are not considered amenable to US-guided puncture, computed tomography (CT)-guided RF ablation is the treatment of choice [2]. However, CT-guided RF ablation often requires either transpulmonary RF ablation, which frequently results in pneumothorax [3–6] and may cause lung bleeding or air embolism [7, 8], or a complex non-axial path, which is technically more challenging [9].

Injection of gas in the pleural cavity to create an artificial pneumothorax may decrease the incidence of complications caused by transpulmonary RF ablation. Compared to air, carbon dioxide (CO₂) is a safer substance to use when injected into the pleural cavity. To our knowledge, few studies have investigated the effectiveness of artificial CO₂ pneumothorax for RF ablation of HCC. Therefore, more data are needed for determining the efficacy and safety of this procedure. The purpose of the present study was to retrospectively assess the feasibility, safety, and efficacy of artificial CO₂ pneumothorax for CT fluoroscopy-guided percutaneous RF ablation of HCC.

Materials and methods

Our institution's Ethics Committee approved this retrospective study (approval numbers: 3058 and 3058-01). Informed consent for CT fluoroscopy-guided percutaneous RF ablation with artificial CO₂

pneumothorax was obtained from all patients before treatment. The requirement for written informed consent for this study was waived because of its retrospective nature.

Patients

Between April 2011 and December 2017, 100 sessions of CT fluoroscopy-guided percutaneous RF ablation for HCC were performed at our institution. CT guidance for RF ablation was performed when HCCs were not visible using US or were not considered amenable to an US-guided puncture. In these patients, when the transpulmonary approach was required to insert the RF electrode into the target tumor in the scanning plane, the creation of an artificial CO₂ pneumothorax was attempted to avoid the transpulmonary route. One session was excluded due to the presence of pleural effusion before the procedure, and two sessions were excluded due to the use of artificial ascites in addition to the artificial CO₂ pneumothorax for pain relief. Two patients were treated twice by CT fluoroscopy-guided percutaneous RF ablation with artificial CO₂ pneumothorax for a newly developed HCC, 39 and 47 months after the first session, respectively. A single HCC was treated in 23 sessions, and two HCCs were treated in three sessions after the creation of artificial CO₂ pneumothorax. In total, 29 HCCs in 24 patients were treated during 26 sessions in this retrospective study to assess the feasibility, safety, and efficacy of artificial CO₂ pneumothorax for CT fluoroscopy-guided percutaneous RF ablation of HCC (Fig. 1).

The patients' backgrounds and tumor characteristics are summarized in Table 1. Twenty-three patients

with 28 HCCs had received transcatheter arterial chemoembolization with iodized oil (Lipiodol; Guerbet Japan, Tokyo, Japan) before RF ablation. The mean interval between transcatheter arterial chemoembolization and RF ablation was 27 days (range: 4–75 days). The remaining one HCC showed low attenuation on nonenhanced CT owing to the fat component. No patients had a history of ipsilateral thoracic surgery or severe respiratory insufficiency (e.g., severe pulmonary emphysema or interstitial pneumonia).

Procedures

Artificial CO₂ pneumothorax induction was performed by one of two interventional radiologists with 11 and 24 years of experience. CT systems used for the procedures were a 16-row multidetector CT instrument (Aquilion 16; Canon Medical Systems, Otawara, Japan) from April 2011 to November 2016, and an 80-row multidetector CT instrument (Aquilion PRIME; Canon Medical Systems, Otawara, Japan) from December 2016 to December 2017. The following settings were used when acquiring the CT fluoroscopic images: scanning speed 0.75-second (Aquilion 16) and 0.5-second (Aquilion PRIME) rotation time, tube voltage 120 kV, current 30 mA, collimation 4mm. All procedures were performed on an inpatient basis under conscious sedation. Fentanyl citrate (Fentanyl Injection; Janssen Pharmaceutical, Tokyo, Japan) was administered intravenously to induce moderate sedation, and 1% lidocaine was used for local anesthesia. Oxygen saturation, heart rate and rhythm, and blood pressure were monitored during the entire procedure. Oxygen was administered at a rate of 2 L/min through a nasal cannula. Patients were placed in the prone

position when the target tumor was located on the dorsal side, otherwise, patients were placed in the supine position.

Techniques of artificial CO₂ pneumothorax induction

Artificial CO₂ pneumothorax was induced by a one-step or two-step method according to the operator's preference.

One-step method

Under breath-holding after expiration, a 22-gauge needle or 18–20-gauge sheathed needle (Surflo; Terumo, Tokyo, Japan) was introduced into the liver surface at the lower end of the thoracic cavity, where no intervening lung tissue was present under CT fluoroscopic guidance. CO₂ was sucked into a sterile syringe through a sterile antibacterial gas filter from a CO₂ gas dispenser (Gaster; Gadelius Medical, Tokyo, Japan). A small amount of CO₂ was injected, and upon confirmation of CO₂ infusion into the thoracic cavity under CT fluoroscopy, additional CO₂ was injected until lung parenchyma was cleared from the route leading to the target tumor. If the CO₂ infusion occurred in the subcutaneous space or the abdominal cavity, the needle tip was adjusted to inject a small amount of CO₂ which was confirmed using CT fluoroscopy. If the CO₂ pneumothorax reduced in size during insertion of the RF electrode owing to absorption of CO₂, CO₂ was added.

Two-step method

Under breath-holding after expiration, a 22-gauge needle or 18–20-gauge sheathed needle (Surflo; Terumo, Tokyo, Japan) was introduced into the liver surface at the lower end of the thoracic cavity where no intervening lung tissue was present under CT fluoroscopic guidance. After CO₂ injection into the thoracic cavity was confirmed, another 22-gauge needle or 18–20-gauge sheathed needle was introduced into the created intrapleural space under CT fluoroscopy. Additional CO₂ was injected until lung parenchyma was cleared from the route leading to the target tumor (Fig. 2). If the CO₂ pneumothorax reduced in size during insertion of the RF electrode owing to absorption of CO₂, CO₂ was added.

RF ablation

RF ablation was performed using a 17-gauge internally cooled electrode with a 2- or 3-cm exposed tip (Cool-Tip RF ablation system; Medtronic, Minneapolis, MN, USA). The RF electrode was inserted into the target tumor through the created intrapleural space under CT fluoroscopic guidance. RF energy was applied using an impedance control algorithm. Multiple overlapping ablations were applied when required to achieve an adequate ablative margin. At the end of the RF ablation procedure, the electrode path was cauterized to prevent bleeding and tumor seeding during retraction of the electrode. Intrapleural CO₂ was aspirated through the needle until no more CO₂ could be aspirated. To evaluate the therapeutic response and complications, contrast-enhanced CT examinations of the lower chest and upper abdomen were performed

immediately after RF ablation.

Assessment and follow-up

Adequate lung displacement, complications, and local tumor progression were evaluated in addition to the patients' position, the total amount of CO₂ administered, and the amount of CO₂ aspirated at the end of the procedure. Adequate lung displacement was defined as completion of RF electrode placement to the target tumor in the scanning plane without passing through the lung using sufficient CO₂ injection. Major and minor complications were assessed in accordance with the Society of Interventional Radiology guidelines [10]. Local tumor progression and the emergence of new HCC tumors were monitored using multiphase contrast-enhanced CT or gadoxetic acid-enhanced magnetic resonance imaging, except in one patient who was monitored using non-contrast-enhanced CT, non-contrast-enhanced magnetic resonance imaging, and US after the procedure.

Results

The patients' position was supine in 20 (76.9%) sessions and prone in six sessions (23.1%). Artificial CO₂ pneumothorax was induced by a one-step method in nine sessions (34.6%) and by a two-step method in 17 sessions (65.4%).

Adequate lung displacement after induction of artificial CO₂ pneumothorax was achieved in 23 of 26

sessions (88.5%). In one session (3.8%), pleural adhesion prevented adequate lung displacement from the path of the electrode (Fig. 3), and transpulmonary RF ablation was performed. In one session (3.8%), lung displacement was inadequate after the induction of artificial CO₂ pneumothorax, and transthoracic extrapulmonary RF ablation was performed after switching to an artificial pleural effusion procedure. In one session (3.8%), CO₂ was infused on the outside of the parietal pleura, and CT fluoroscopy-guided RF ablation with electrode insertion in the caudal-cranial oblique direction was performed to avoid lung parenchyma (Table 2). In two patients who were treated twice using CT fluoroscopy-guided percutaneous RF ablation with artificial CO₂ pneumothorax 39 and 47 months after the first session, pleural adhesion was not observed, and adequate lung displacement after induction of artificial CO₂ pneumothorax was achieved.

The total amount of CO₂ administered was 300–3000 mL (mean: 1006 mL). The amount of CO₂ aspirated at the end of the procedure was 0–500 mL (mean: 99 mL; the data were not available for five sessions) (Table 2). In the case in which a total CO₂ volume of 3000 mL was administered, CT immediately after RF ablation showed small residual pneumothorax, although the amount of CO₂ aspirated at the end was 100 mL.

In two sessions (7.7%), HCC in the Spiegel lobe was treated after the creation of artificial CO₂ pneumothorax (Fig. 4).

No major complications were found. In one session (3.8%), the patient complained of dyspnea after the creation of artificial pneumothorax, but her oxygen saturation was maintained above 97%, and RF ablation

was continued. Oxygen saturation did not obviously decrease in any patient. CT scans obtained immediately after RF ablation revealed small residual pneumothorax in 25 sessions (96.2%). In seven sessions, chest radiographs were obtained on the same day or the next day. In these assessments, no pneumothorax was noted in two sessions, and a small residual pneumothorax that required no further treatment was noted in five sessions. No definite real pneumothorax was identified. Residual pleural effusion was observed in one case that involved switching to an artificial pleural effusion procedure. CT scans obtained immediately after RF ablation revealed small residual subcutaneous emphysema in 23 sessions (88.5%). The vasovagal reaction was observed after the creation of CO₂ pneumothorax in one session (3.8%), which improved after intravenous administration of atropine sulfate. Other complications related to the creation of CO₂ pneumothorax were not observed. With respect to the complications related to RF ablation, minor complications were observed in four sessions (15.4%), including intra-abdominal hemorrhage in two sessions (7.7%), restlessness in one session (3.8%), and vomiting in one session (3.8%) (Table 2). In the one session of restlessness, non-contrast-enhanced CT was performed instead of contrast-enhanced CT to evaluate the therapeutic response and complications immediately after RF ablation.

The mean follow-up period after RF ablation was 39.3 months (median: 36 months, range: 7–78 months). One tumor (3.4%) showed local tumor progression at four months after RF ablation, and the recurrent tumor was treated by US-guided percutaneous RF ablation at another hospital. The other 28 tumors

(96.6%) showed complete ablation at the last follow-up (Table 2).

Discussion

We reviewed cases where an artificial pneumothorax with CO₂ was used to avoid the complications caused by transpulmonary RF ablation. To our knowledge, artificial CO₂ pneumothorax for percutaneous thermal ablation of HCC has only been reported by Hermida et al. [11]. A case of massive cerebral arterial air embolism induced by artificial pneumothorax using air was reported during a medical thoracoscopy [12]. Favelier et al. [9] reported a case where an artificial CO₂ pneumothorax was successfully used for an adrenal biopsy procedure. Because CO₂ is highly soluble in blood, it is associated with a lower risk of air embolism than air. CO₂ insufflation is safely applied in thoroscopic surgery [13–15]. Additionally, the small size of residual CO₂ pneumothorax does not warrant aspiration after the procedure since it is spontaneously absorbed and subsequently eliminated through respiration [9]. Moreover, CO₂ has a lower thermal conductivity than air allowing it to provide excellent thermal insulation [16].

Our study achieved adequate lung displacement above the level of the target tumor after induction of artificial CO₂ pneumothorax in 23 of 26 sessions (88.5%). Successful induction of artificial pneumothorax was reported in all six cases by De Baère et al. [17] and in all 28 cases by Hermida et al. [11]. Fujiwara et al. [18] reported that the lung was moved away successfully from the puncture route on the axial CT view in 14

of 17 cases (82.4%), and the base of the lung did not move away fully in three of 17 cases (17.6%). Our results were similar to those reported by Fujiwara et al. [18].

In one session, pleural adhesion prevented adequate lung displacement from the path of the electrode. The patient had no history of thoracic surgery, and it was difficult to predict pleural adhesion using preoperative CT findings. No previous study has reported the prevention of lung displacement by pleural adhesion during RF ablation of liver tumors. In terms of artificial pneumothorax for needle biopsy of the mediastinum and pulmonary hilum, Scalzetti [19] reported that pleural adhesion prevented adequate lung displacement in two of 21 patients (9.5%). If adhesion is expected preoperatively, it is presumed that the lung does not move sufficiently. If the lung does not move due to adhesion during CO₂ infusion, transpulmonary puncture [3–6] or caudal-cranial oblique puncture [20, 21] should be considered without injecting too much CO₂. In patients with severe pleural adhesion, transpulmonary RF ablation is unlikely to cause a serious pneumothorax.

In one session (3.8%), lung displacement was inadequate after the induction of artificial CO₂ pneumothorax, and transthoracic extrapulmonary RF ablation was performed after switching to an artificial pleural effusion procedure. RF ablation with artificial pleural effusion is reported to be a safe and feasible therapy in US-guided RF ablation [22, 23]. Artificial pleural effusion may be effective to clear the dependent part of the lung from the route of the electrode.

In our study, HCC in the Spiegel lobe was treated after the creation of artificial CO₂ pneumothorax in two

sessions (7.7%). In previous reports, artificial pneumothorax was mainly used for tumors in the hepatic dome; to our knowledge, its use for tumors in the Spiegel lobe has not been reported. A tumor in the Spiegel lobe is difficult to puncture due to its deep position and carries a risk of pneumothorax, intrapulmonary bleeding, or air embolism, but risk can be reduced by using artificial pneumothorax. Therefore, artificial pneumothorax can expand the indications for RF ablation.

We accessed the thoracic cavity with a one-step or two-step puncture for the creation of an artificial CO₂ pneumothorax. A 22-gauge needle or 18–20-gauge sheathed needle was introduced into the liver surface at the lower end of the thoracic cavity where no lung parenchyma intervened. Hermida et al. [11] used a 14-gauge Veress needle to access the pleural space. They reported that <1 min was necessary to reach the pleural cavity. A Veress needle provides rapid access to the pleural space, but even a blunt-tipped needle can lead to lung damage in cases of pleural adhesion [18]. The one-step method is simple, but the needle tip easily touches the surface of the lung, and it is difficult to maintain a stable position. In contrast, the two-step method makes it easier to inject additional CO₂ through the second needle in a stable position, especially when more than one HCC is treated in one session.

The total amount of CO₂ administered was 300–3000 mL (mean: 1006 mL) in this study. In the case in which a total CO₂ volume of 3000 mL was administered, CT immediately after RF ablation showed small residual pneumothorax, although the amount of CO₂ aspirated at the end was 100 mL. We occasionally needed to add CO₂ during the RF electrode insertion owing to artificial pneumothorax shrinkage after lung

parenchyma was cleared from the route leading to the target tumor. These findings suggested that CO₂ was absorbed during the procedure. Favelier et al. [9] reported that a chest CT scan performed 30 min after the procedure demonstrated almost complete spontaneous resorption of the CO₂ pneumothorax. Hermida et al. [11] injected 200–2000 mL of CO₂ to create an artificial CO₂ pneumothorax. In the reports that used air to create an artificial pneumothorax, the amount of air administered was 30–600 mL (median: 200 mL) [18] and 200–800 mL (mean: 566 mL) [17]. The amount of CO₂ administered may be larger than that of air because CO₂ is absorbed during the procedure, although no study to date has reported this difference.

No major complications related to the creation of CO₂ pneumothorax were observed in this study.

Previous studies also did not report any major complications related to artificial pneumothorax in percutaneous thermal ablation of liver tumors [11, 17, 18]. In this study, one patient complained of dyspnea after the creation of the artificial pneumothorax, but the oxygen saturation was maintained above 97%.

Hermida et al. [11] reported that oxygen saturation remained high and stable in all patients. CO₂ injection should be performed carefully, paying special attention to the risk of dyspnea or circulatory changes [18].

Dyspnea may occur in cases that require a large amount of CO₂ to clear the lung from the route leading to the target tumor. Therefore, this method can be contraindicated in patients with severe respiratory insufficiency, and it is preferable to minimize the amount of CO₂ injected into the intrapleural space.

However, artificial CO₂ pneumothorax, even in dyspnea, can be controlled by discontinuing CO₂ injection or aspirating CO₂ [24] and is considered a low-risk approach. Further study is needed to establish the safety

of artificial CO₂ pneumothorax.

In this study, local tumor progression was identified in one of 29 HCCs (3.4%) with a median follow-up period of 36 months. In previous studies, local tumor progression was reported to be 0% (median follow-up period: 9.5 months) [18] and 10.7% (median follow-up period: 13.1 months) [11]. Based on a longer follow-up period, our study showed that CT fluoroscopy-guided percutaneous RF ablation with artificial CO₂ pneumothorax achieved obvious good local control of HCC.

This study has several limitations. First, a retrospective design was used. Second, the study was conducted at a single institution with a small sample population. Third, it was presumed that the therapeutic efficacy of RF ablation was reinforced by transcatheter arterial chemoembolization.

In conclusion, artificial CO₂ pneumothorax for CT fluoroscopy-guided percutaneous RF ablation appeared to be a feasible, safe, and useful therapeutic option for HCC.

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Fig. 1 Study flow chart

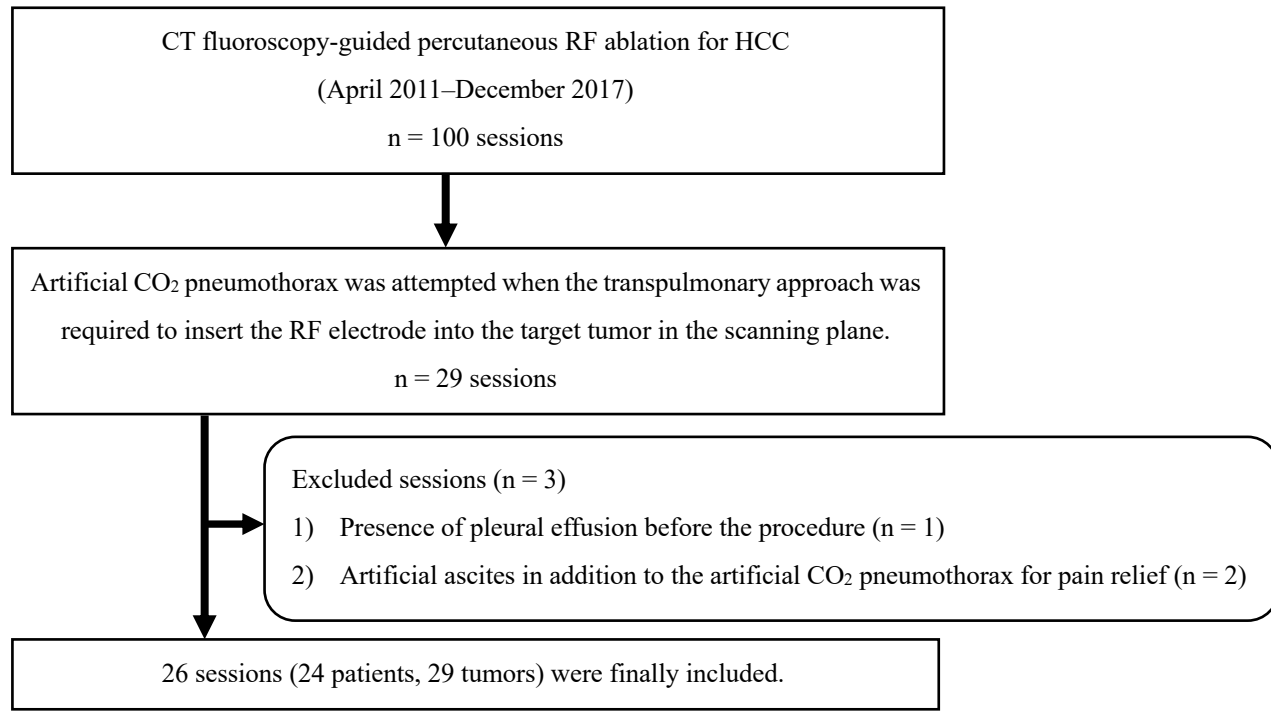
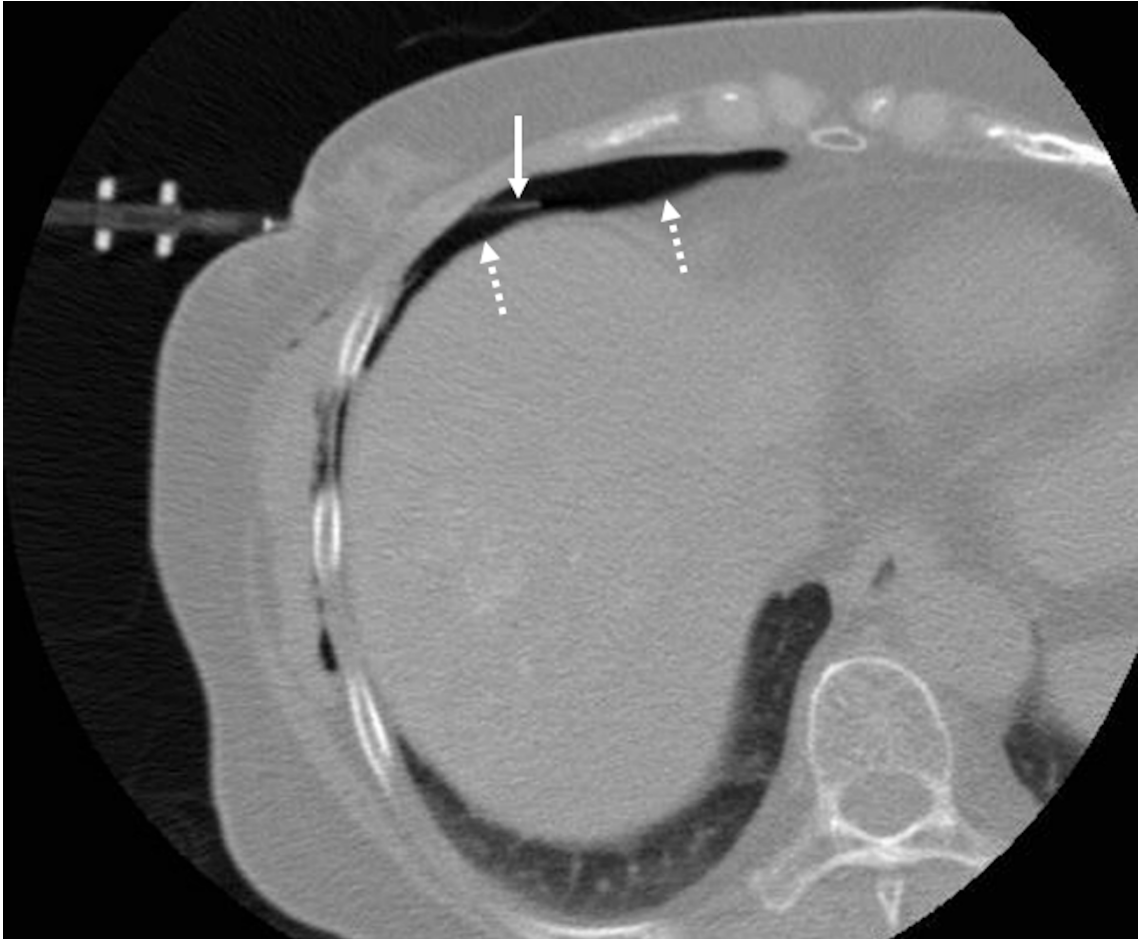


Fig. 2 Artificial carbon dioxide (CO₂) pneumothorax induction with the two-step method: (a) An 18-gauge sheathed needle (arrow) is introduced into the liver surface at the lower end of the thoracic cavity with no intervening lung tissue under computed tomography (CT) fluoroscopic guidance. A small amount of CO₂ is injected. (b) Another 18-gauge sheathed needle (arrow) is introduced into the created intrapleural space (dashed arrows). (c) A radiofrequency (RF) electrode (arrowhead) is inserted into the target tumor (arrow) through the created intrapleural space (dashed arrows). (d) Contrast-enhanced CT obtained immediately after RF ablation shows a non-enhancing area (dashed arrows) surrounding the target tumor (arrow) with dense Lipiodol accumulation

a



b



c



d

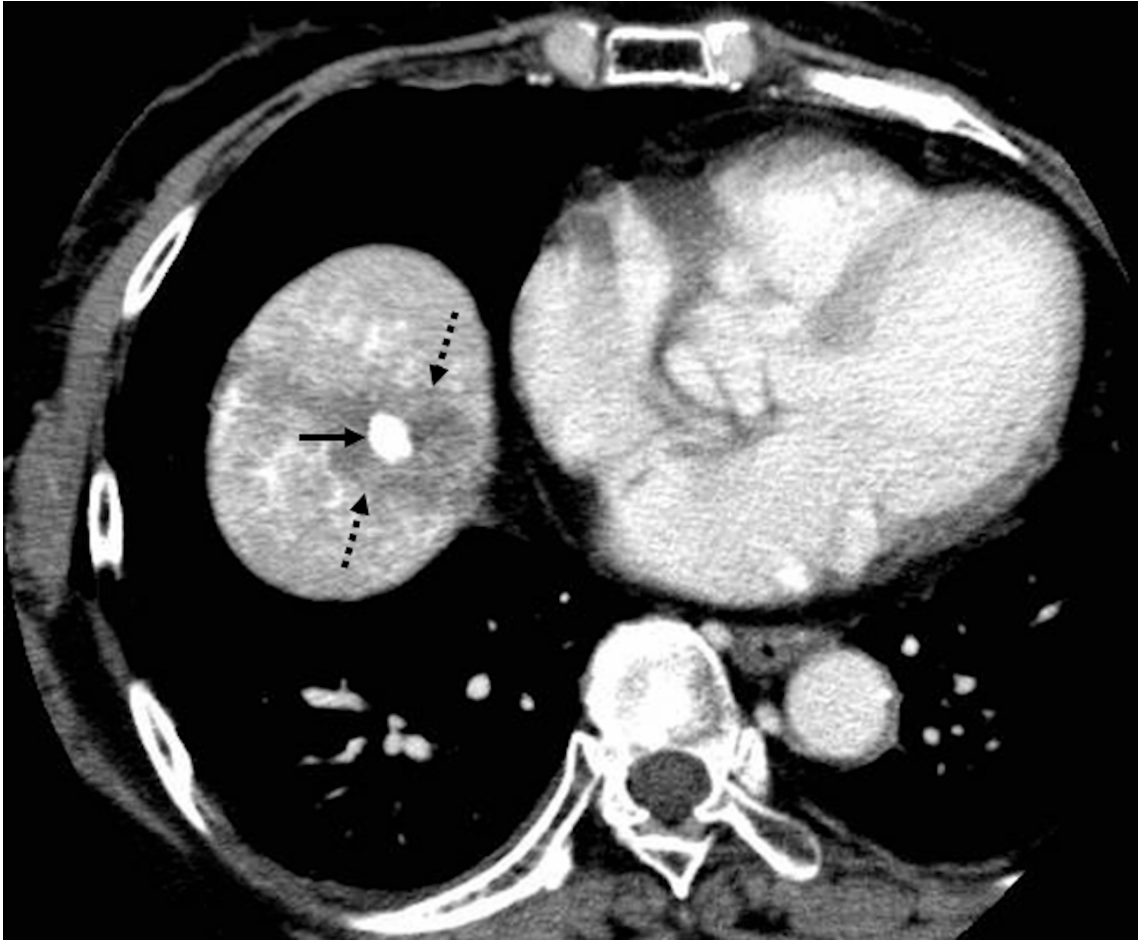


Fig. 3 Image of a hepatocellular carcinoma showing partial Lipiodol accumulation (arrowheads) in Couinaud's segment VIII in a man in his 70s. Pleural adhesion prevents adequate lung (arrows) displacement from the path of the electrode

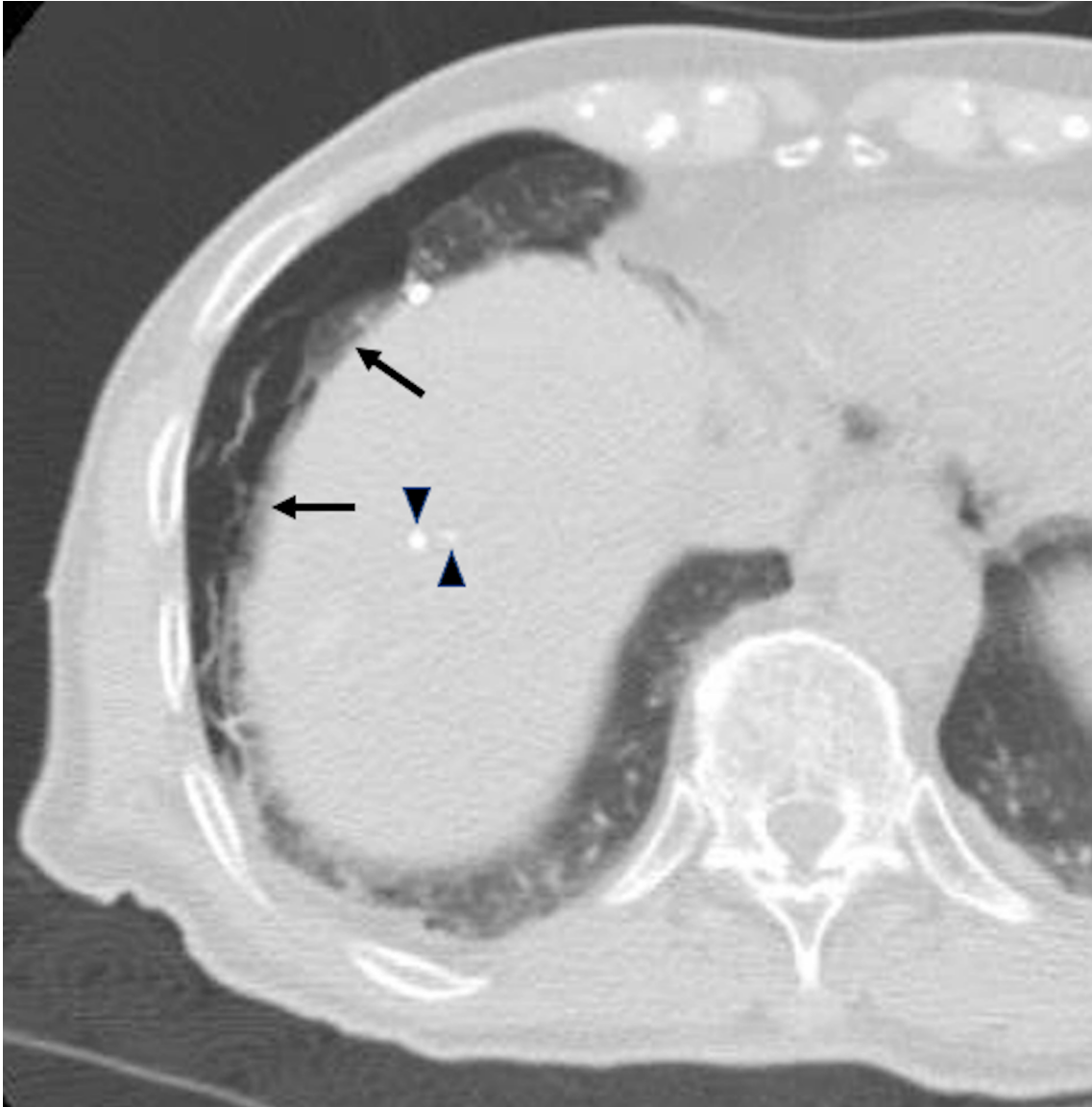


Fig. 4 Image of a hepatocellular carcinoma showing dense Lipiodol accumulation in the Spiegel lobe of a man in his 60s. A radiofrequency electrode (arrowhead) is inserted into the target tumor (arrow) through the created intrapleural space (dashed arrows)

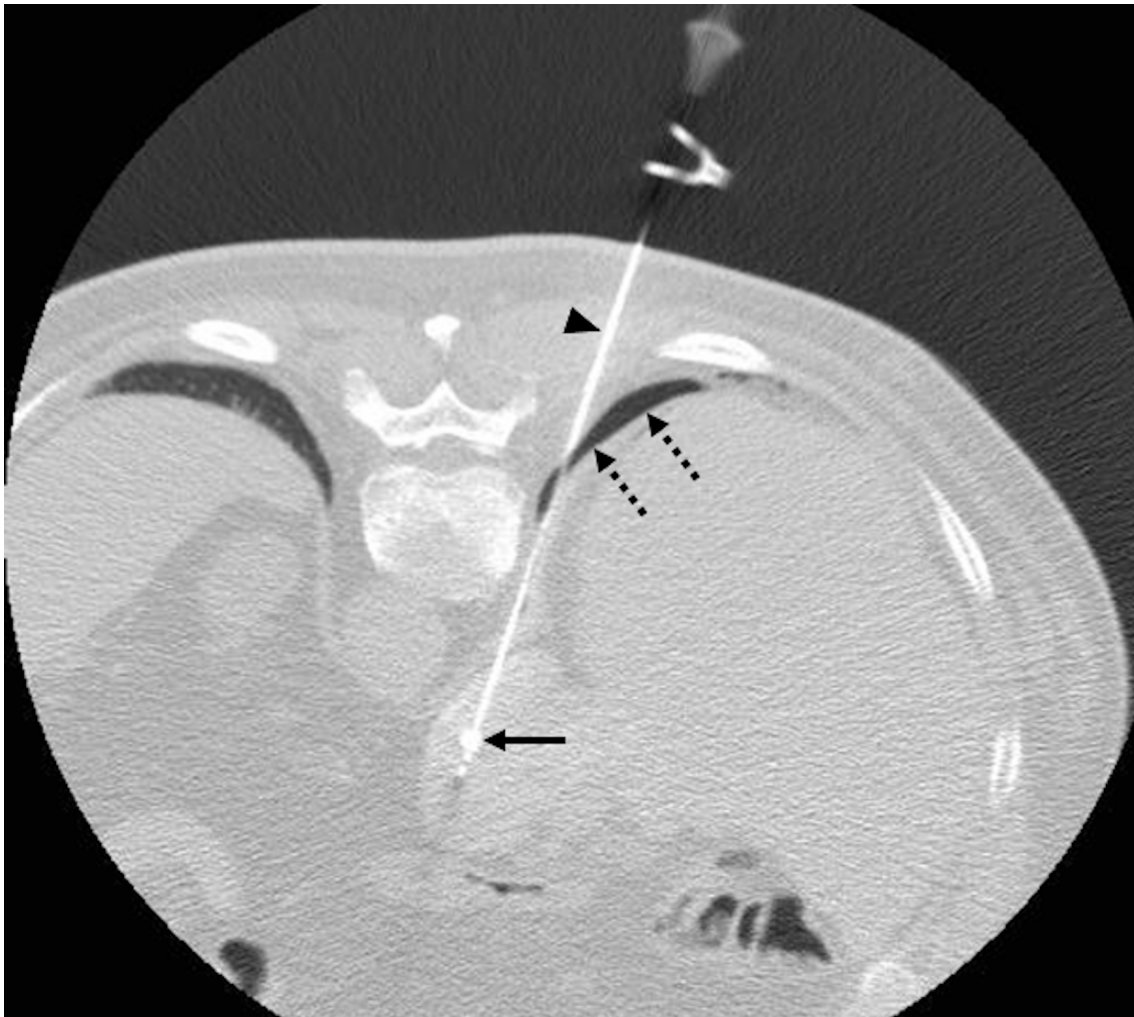


Table 1 Characteristics of the 24 patients and 29 tumors in 26 sessions

Age (years)	
Mean (range)	74 (58–85)
Sex	
Male	14 (58.3)
Female	10 (41.7)
Cause of liver damage	
Hepatitis C virus	16 (66.7)
Alcoholism	5 (20.8)
Hepatitis C virus + Alcoholism	2 (8.3)
Autoimmune hepatitis	1 (4.2)
Child-Pugh class	
A	18 (75.0)
	<20 sessions>
B	6 (25.0)
	<6 sessions>
No. of tumors	

1	23 sessions (88.5)
2	3 sessions (11.5)
Tumor size (mm)	
Mean (range)	12 (6–22)
Location (No. of tumors)	
Couinaud's segment I	3 (10.3)
Couinaud's segment III	1 (3.4)
Couinaud's segment IV	3 (10.3)
Couinaud's segment VII	5 (17.2)
Couinaud's segment VIII	17 (58.6)

Note—Except where otherwise indicated, data are presented as number (%)

Table 2 Results of CT fluoroscopy-guided RF ablation with artificial CO₂ pneumothorax

Adequate lung displacement (No. of sessions)	
Yes	23 (88.5)
No	3 (11.5)
Total amount of CO ₂ administered (mL)	
Mean (range)	1006 (300–3000)
Amount of CO ₂ aspirated (mL) ^a	
Mean (range)	99 (0–500)
Complications (No. of sessions)	
<i>Related to the creation of CO₂ pneumothorax</i>	
Dyspnea	1 (3.8)
Vasovagal reaction	1 (3.8)
<i>Related to RF ablation</i>	
Intra-abdominal hemorrhage	2 (7.7)
Restlessness	1 (3.8)
Vomiting	1 (3.8)
Follow-up period (months)	
Mean (median, range)	39.3 (36, 7–78)

Local tumor progression (No. of tumors)

Yes	1 (3.4)
No	28 (96.6)

Note—Except where otherwise indicated, data are presented as number (%)

CT computed tomography, *RF* radiofrequency, *CO₂* carbon dioxide

^aThe data were not available for five sessions