Iodine-125 seed implantation treatment of lung metastases <2.5 cm using a 5-ml syringe as a guide

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Research

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Abstract

Background: Small lung metastases move with respiration, making localization difficult and often increasing the number of puncture. Accurate puncture can reduce trauma to lung tissue and accelerate patient recovery.

Objective: To present our experience with the technique of using a local anesthesia 5-ml syringe as a guide for computerized tomography (CT)-guided iodine-125 seed implantation (CT-ISI).

Methods: This was a retrospective study of patients with small metastatic tumors in the lung treated with CT-ISI between 12/2013 and 03/2018 at the Affiliated Hospital of the University. The patients were divided according to whether a 5-ml syringe was used as a guide during CT-ISI or not. The final follow-up was on March 31st, 2018. Implantation success and complications were examined.

Results: Nineteen patients were included. A total of 840 seeds were used, with 44.2±33.6 (range, 10-160) seeds per patient. The mean D90 for CT-ISI was 134.5±7.5 Gy. Treatment intervention for eleven patients was performed using a 5-ml syringe as a guide during CT-ISI. There were no differences in total dose and number of implanted seeds between the two groups, but the number of punctures per lesion was lower in the syringe group than in the no-syringe group (1.9±0.5 vs. 2.9±0.6, $P<0.001$), suggesting a higher puncture accuracy. One patient in the no-syringe group experienced grade 2 chest tightness, chest pain, intraoperative needle tract bleeding, and postoperative blood in sputum.

Conclusion: Puncture with a 5-ml syringe as a guide during CT-ISI is probably a more accurate option for patients with small (<2.5 cm) lung metastasis.

Background

Secondary lung tumors (or lung metastases) are common lung malignant lesions, with a frequency of 30%-55% of all cancer patients.[1, 2] Primary cancers that have the potential to metastasize to the lungs include bladder cancer, colon cancer, breast cancer, prostate cancer, sarcoma, Wilms tumor, and neuroblastoma.[1, 2]

There are currently no uniform guidelines in clinical practice for addressing small pulmonary metastases. Surgery of lung metastases is indicated only in highly selected cases in whom a curative intent is possible without damaging lung function.[2–5] Unfortunately, lung metastases are rarely solitary, and multiple metastatic tumors in the lungs often occur at the same time. In these cases, systemic treatments or radiation therapy are more often indicated,[6–9] but the use of stereotactic body radiotherapy (SBRT) is also limited due to radiation lung damage.[10, 11] On the other hand, iodine-125 seed implantation (ISI) treatment can be administered repeatedly, the local control rate is good, and the treatment can prolong the survival of patients with lung metastasis.[12] Especially in the case where lung metastasis is very small, and detection and treatment occur in a timely manner, it is easy to achieve a complete response

(CR).[13] Because early-detected metastases are small, the amount of seeds used is small, and radiation-induced lung injury is minimal.[13]

Direct needle puncture can be challenging due to the relatively small size of the lesions and their non-stationary positioning due to lung movement during respiration. Computed tomography (CT)-guided transthoracic needle biopsy is recommended for tissue biopsy of pulmonary lesions < 2 cm.[14] A meta-analysis found that the rate of major complications is low in CT-guided lung biopsy, but this risk increases with decreasing lesion size.[15–18]

Accurate puncture can reduce trauma to lung tissue and accelerate patient recovery. In our clinical work, we found that the use of a local anesthesia syringe as a guide improves the accuracy of the puncture method. In our hospital, 2% lidocaine is used for local anesthesia with an injection dose of 5 ml before CT-ISI is performed. After local anesthesia, the 5-ml syringe is not pulled out immediately but left at the site of local anesthesia. The small lesion in the lung is then co-located with this body surface marker. This is not only helpful to select the best puncture point, but also can provide a guide for the direction of the puncture needle. When larger syringes (such as 10 and 15 ml) are retained at the site of local anesthesia, the direction of the needle tip will be deviated due to gravity, which cannot provide an accurate guide for the implantation direction of the puncture needle.

The aim of the present study is to present our experience with the technique of using a local anesthesia 5-ml syringe as a guide for CT-ISI puncture. This could provide a simple method to improve the outcomes of CT-ISI of small lung lesions and avoid complications.

Methods

Study design and patients

This was a retrospective study of patients with small metastatic tumors in the lung treated with CT-ISI between December 2013 and March 2018 at the Department of Interventional Radiology of the Affiliated Hospital of the University. This retrospective study was approved by the ethics committee of the Affiliated Hospital of the University. The use of patient information was approved by our institutional review board, which waived a requirement for patient informed consent.

The inclusion criteria were: 1) highly suspected diagnosis of metastatic tumors in the lung based on patients' history of cancer and on clinical, imaging, and/or pathological characteristics of the lesions; 2) underwent CT-ISI; 3) the largest diameter of the lesions was <2.5 cm; and 4) complete clinical data.

The exclusion criteria were: 1) emphysema or a large lung bubble near the metastasis; 2) unstable cardiorespiratory function, blood coagulation disorder, or active infection; or 3) Eastern Cooperative Oncology Group performance status (ECOG PS) ≥3.

Grouping

The patients were divided into two groups according to whether a 5-ml syringe was used as a guide during CT-ISI or not.

CT-ISI

The radioactivity of the iodine-125 seeds (CIAE-6711; Chinese Atomic Science Institution, Beijing, China) used in this study was 2.59×10^7 Bq. The ISI treatment plan system (TPS; KL-SIRPS-3D) and gun-type implantation device were from the Institute of Medical Science and Technology (Beijing, China). Disposable 5-ml syringes and 18 G puncture needles (Cook Medical, Bloomington, IN, USA) were used for local infiltration anesthesia and puncture. The lung lesions were scanned by CT at 3-mm intervals using a 64-slice CT scanner (Siemens, Germany) for intraoperative and postoperative follow-up.

One radiation physicist and two interventional radiologists generated the treatment plan (TP) for each pulmonary metastasis using the TPS in order to determine the number of seeds to be implanted and the ideal implantation location. The planning target volume was defined as 0.5 cm of expansion external to the gross tumor volume. The prescribed dose was 135 Gy, which was chosen based on our previous studies.[12, 13] Local anesthesia was administered with a 5-ml syringe (2% lidocaine; Yimin, Yichang, China) at the body surface location marker (Figure 1 A,B, Figure 2 A and Figure 3 A). An 18 G needle was then punctured into the pulmonary metastasis with or without the 5-ml syringe as a guide (Figure 1 C,D,E,F, Figure 2 B,C and Figure 3 B,C,D) and Iodine-125 seeds were implanted (Figure 2 D and Figure 3E). As in our previous study, the seeds were placed 0.5-0.8 cm apart in line with the TPS to the best extent possible. The seed radiotherapy treatment radius of iodine-125 is about 1 cm, according to the manufacturer's instructions. Thus, for lesions ≤1 cm, the entire lesion can be fully included in the treatment range even if the lesion is only punctured at the edge. For larger lesions, if the puncture location could not fully cover the lesion, the puncture was considered failure and had to be performed again after adjusting the position or path of the puncture needle. Post-implantation dose verification was performed to verify the therapeutic dose according to the TPS and assessment of peripheral tissue (bronchial and vascular) damage. A D90 (dose contains 90% of the target volume) value of >135 Gy at the last implantation was regarded as successful.

Follow-up and evaluation of clinical effectiveness

Patients were monitored using continuous electrocardiogram for 6 h after seed implantation, with appropriate symptomatic treatment for chest tightness, chest pain, blood in sputum, vomiting, fever, etc. Generally, the patients were discharged within 2 days after implantation. The final follow-up was on March 31st, 2018. The follow-up time was calculated from the first-ever treatment of pulmonary metastases with CT-ISI to the last follow-up or death. Chest CT enhancement examinations were used to evaluate the maximum diameter of the metastatic pulmonary lesions (Figure 3F), to screen for new lesions, and to assess radiation-induced lung injury at 1, 3, 6, and 12 months after CT-ISI. Radiation lung injury was evaluated according to the National Cancer Institute’s Common Terminology Criteria for Adverse Events, version 4.0 (CTCAE 4.0). [19]

Statistical analysis

Continuous variables were expressed asmeans ± standard deviations (SD) and were analyzed using the Student t-test. Categorical variables were presented as frequencies and percentages and were analyzed using the chi-square test or Fisher's exact test, as appropriate. Two-sided P-values <0.05 were considered statistically significant. GraphPad Prism, version 5 (GraphPad Software Inc., San Diego, CA, USA) was used for statistical analysis.

Results

Tumor characteristics

Nineteen patients were included. Table 1 presents their characteristics. They had a total of 50 small (<2.5 cm) lung lesions, with 2.6±2.2 (range, 1-10) metastases per patient. The lesion size was 1.6±0.4 cm. The mean time between diagnosis by CT scan of the primary tumor and the first discovery of pulmonary metastasis was 12.7±4.8 (range 8-21) months. Three patients also had liver metastasis, and two had bone metastasis.

CT-ISI

CT-ISI was performed 37 times in those 19 patients, with 2.3±0.7 punctures (range, 1-5) per lesion. A total of 840 seeds were used, with 44.2±33.6 (range, 10-160) seeds per patient. The mean D90 for CT-ISI was 134.5±7.5 Gy (Table 2).

Use of the 5-ml syringe to guide metastasis access

Treatment intervention for eleven patients was performed using a 5-ml syringe as a guide during CT-ISI (median 2, range 1-5 times) in 28 lung metastases. Eight patients received treatment without the 5-ml syringe during CT-ISI (median 2, range 1-4 times) in 22 lung metastases. There were no differences between the two groups regarding the characteristics of the patients (Table 1), except that the syringe group had a higher frequency of males. There were no differences in total dose and number of implanted seeds between the two groups, but the number of punctures per lesion was lower in the syringe group than in the no-syringe group (1.9±0.5 vs. 1.9±0.6, P<0.001), suggesting a higher puncture accuracy.

Complications

All patients tolerated the procedures well. No CT-ISI-related deaths occurred, and no patients needed premature procedure terminations. Only one patient treated without a 5-ml syringe experienced grade 2 chest tightness, chest pain, intraoperative needle tract bleeding, and postoperative blood in sputum. All of the complications were mild to moderate and required only symptomatic treatment (Table 3).

Follow-up

The median follow-up period was 13 months, ranging from 8 to 27 months. During follow-up, four patients died, one patient was lost to follow-up, and 14 survived. One patient in the no-syringe group experienced subcutaneous tumor implants.

Discussion

Small lung metastases move with respiration, making localization difficult and often increasing the number of punctures for access. Accurate puncture can reduce trauma to lung tissue and accelerate patient recovery.[15–18] The objective of the present study was to present our experience with the technique of using a local anesthesia 5-ml syringe as a guide for CT-ISI. The results suggest that puncture with a 5-ml syringe as a guide during CT-ISI is probably a more accurate option for patients with small (< 2.5 cm) lung metastasis.

Stage IV cancer is incurable, but highly selected may undergo surgery of isolated lung metastasis.[2–5, 20, 21] Unfortunately, lung metastases are usually small and multiple, and generally, do not have obvious clinical symptoms.[1, 2] Small asymptomatic lung metastases may be simply followed, and more aggressive options can be kept for symptom control once the lesions become symptomatic.[6–9, 22] Systemic therapy and radiotherapy can be used for lesion control.[6–9] During the treatment of metastases with SBRT, the risk of radiation-induced lung injury is high.[23, 24] Percutaneous ablation, either using radiofrequency or ICI, may reduce the patient treatment load and have good outcomes.[12, 13, 25–27]

Based on previous studies by our team, pulmonary metastases of 1–2 cm in size can be diagnosed and located in the lungs, and patients are able to tolerate treatment.[12, 13] Nevertheless, access to small lesions (< 2.5 cm) is prone to failure, but methods for the accurate positioning of the access needle are scarce. Penetrating directly through the rib into the lesion for seed implantation is contrary to the intention of minimally invasive therapy, and we do not recommend this approach.[28] Computed tomography fluoroscopy-guided percutaneous Iodine-125 seed implantation has been studied, but it is advisable to apply this approach cautiously for small lesions < 2.5 cm.[29] Novel 3D-printing template technologies can be used to guide the puncture and solve the problems of the continuous respiration-associated movements of the lungs,[30, 31] but it requires printing systems, CAD software, and the ability/experience to use them.

Iodine-125 seed implantation is often carried out under local anesthesia, and it is difficult to locate the small lesions in the lungs during respiration. Han et al.[32] were the firsts to use a puncture needle to localize the tumors during CT-ISI for the treatment of primary lung cancer. We further improved this technique by using a conventional surface marker combined with CT scan line positioning. When a 5-ml syringe was used for local anesthesia, the syringe was inserted in the direction of the metastasis and placed on the skin, followed by a CT scan to determine the location of the metastasis. Using a local anesthesia syringe as a guide, the ISI puncture needle can more easily access the target metastasis regardless of lung movement. Moreover, the syringe can aid in anchoring the small metastases, reducing the degree of small metastases movement.

In the present study, the use of the syringe led to a smaller number of punctures per lesions to achieve a successful ISI. Because the average number of puncture was lower, the procedure-related complications for the syringe was smaller than the no-syringe group. Most of the complications were Grade 1. The only patient with grade 2 complications was in the no-syringe group, but this observation is anecdotic and cannot be used for the conclusion. One patient in the no-syringe group experienced subcutaneous tumor implants, which was considered to result from multiple punctures. Therefore, reducing the number of punctures and improving the accuracy of punctures can reduce the risk of tumor metastasis.

The present study has some limitations. This was a retrospective analysis study with a short follow-up period. In addition, this was a single-center study with a limited sample size. Furthermore, there is a selection bias since only the patients with small metastases (< 2.5 cm) were included. We focused on the accuracy and complications of the use of a 5-ml syringe as a guide during CT-ISI, and survival analysis was not performed in this study. A large sample multi-center cohort study is warranted to evaluate the long-term outcomes associated with this very simple method to improve the accuracy of CT-ISI.

Conclusion

Puncture with a 5-ml syringe as a guide during CT-ISI could improve the accuracy of puncture and was not associated with any additional complications in patients with small (< 2.5 cm) lung metastases.

Abbreviations

CR
Complete response
CT
computerized tomography
CT-ISI
computerized tomography-guided iodine-125 seed implantation
D90
Dose contains 90% target volume
ISI
iodine-125 seed implantation
PD
progressive disease
PR
partial response
RR
response rate

SBRT
stereotactic body radiotherapy
SD
stable disease
TPS
treatment-planning system

Declarations

Ethics approval and consent to participate: This retrospective study was approved by the ethics committee of the Affiliated Hospital of Jiangnan University. The use of patient information was approved by our institutional review board, which waived a requirement for patient informed consent.

Consent for publication: Written informed consent to publish this information was obtained from study participants.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing financial interests exist.

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Authors' contributions: JL Z, YX G participated in the sequence alignment. ZQ S participated in the design of the study and performed the statistical analysis. LJ Z, QG X, J L conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1. Characteristics of the patients with small lung metastasis treated with CT-ISI

Patient characteristics	All (n=19)	With Syringe (n=11)	Without syringe (n=8)	P
Men (%)	12 (63.2)	9 (81.8)	3 (37.5)	0.048
Age (years)	56.1±16.7	58.0±10.2	53.5±23.6	0.578
Primary tumor, n (%)				7.827
Hepatocellular carcinoma	7 (36.8)	6 (54.6)	1 (12.5)	
C olorectal adenocarcinoma	5 (26.3)	2 (18.2)	3 (37.5)	
Ovarian cancer	3 (15.8)	1 (9.1)	2 (25.0)	
Hypopharyngeal squamous cell carcinoma	1 (5.3)	0	1 (12.5)	
Pancreatic adenocarcinoma	1 (5.3)	1 (9.1)	0	
Esophageal squamous cell carcinoma	1 (5.3)	0	1 (12.5)	
Synovial sarcoma	1 (5.3)	1 (9.1)	0	
Treatment history, n (%)				
Local excision	13 (68.4)	9 (81.8)	6 (75.0)	0.718
Chemotherapy	19 (100.0)	11 (100.0)	8 (100.0)	1.000
Transcatheter arterial chemoembolization	13 (68.4)	9 (81.8)	4 (50.0)	0.141
Radiotherapy	5 (26.3)	1 (9.1)	4 (50.0)	0.079
Time of first pulmonary metastasis (months)	12.7±4.8	12.4±4.6	13. 3±5.3	0.703
Lesion size (cm)	1.6±0.4	1.7±0.5	1.6±0.4	0.744
Number of lesions	2.6±2.2	2.6±2.5	2.8±1.8	0.849
Follow-up time (months)	14.5±6.0	13.3±5.6	16.1±6.5	0.323

Table 2. Puncture results

	All	With syringe	Without syringe	P
D90 (Gy)	134.5±7.5	135.9±6.5	132.6±8.8	0.362
Number of implanted seeds	44.2±33.6	44.6±42.0	43.8±19.2	0.961
Number of punctures per lesion	2.3±0.7	1.9±0.5	2.9±0.6	<0.001

Table 3. Complications with or without 5 ml syringe as a guide for CT-ISI treatment

Complications (grade 1/2), n (%)	With syringe	Without syringe
Intraoperative chest tightness	1 (9.1)	3 (37.5)
Intraoperative chest pain	1 (9.1)	3 (37.5)
Intraoperative bleeding [a]	0	3 (37.5)
Post-operative blood in sputum	1 (9.1)	4 (50.0)
Post-operative fever	1 (9.1)	1 (12.5)
Post-operative vomiting	1 (9.1)	1 (12.5)
Seed migration	0	0
Radiation-induced lung injury	2 (18.2)	3 (37.5)
Puncture related complications	3 (27.3)	6 (75.0)

[a] Including massive bleeding and needle tract bleeding.

Based on the Common Terminology Criteria for Adverse Events, version 4.0.

Figures

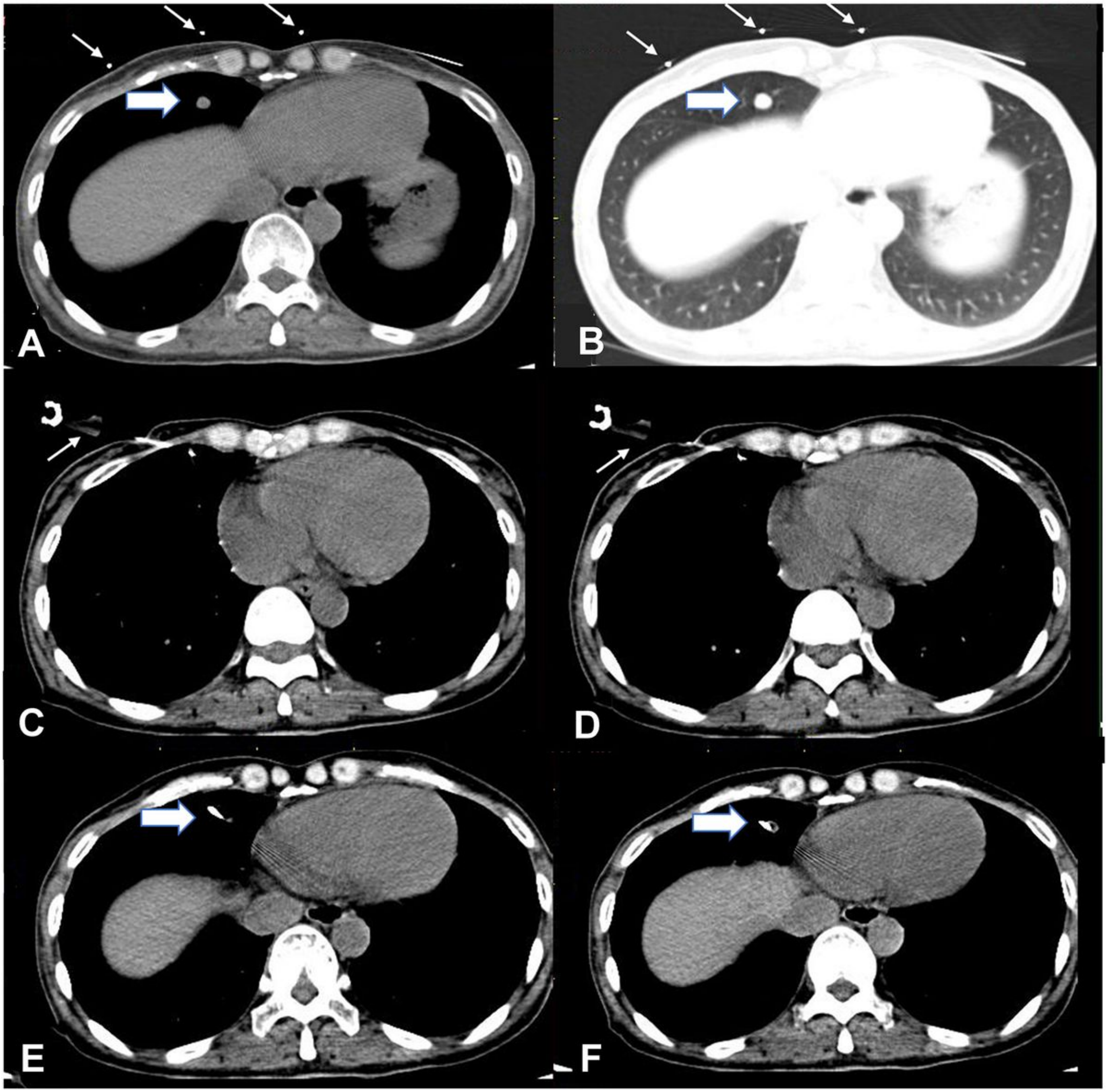

Figure 1

Treatment of pancreatic cancer lung metastasis by iodine-125 seed implantation. According to the body surface localizationof the 5-ml syringe used for local anesthesia and after the computed tomography (CT) scan, the 5-ml syringe was found to be near the lung metastasis (diameter of 1 cm) in the three layers (layer thickness of 3 mm). Then, according to the syringe as the selection, an 18 G needle was used to access the lesion at first try to deliver the seeds. (A,B) The fine white arrow indicates the body surface marker. The broad arrow indicates the lung metastasis. (C, D) The fine white arrow indicates the

5-ml syringe used as a guide. (E, F) The broad arrow indicates the 18 G needle punctured into the lung metastasis.

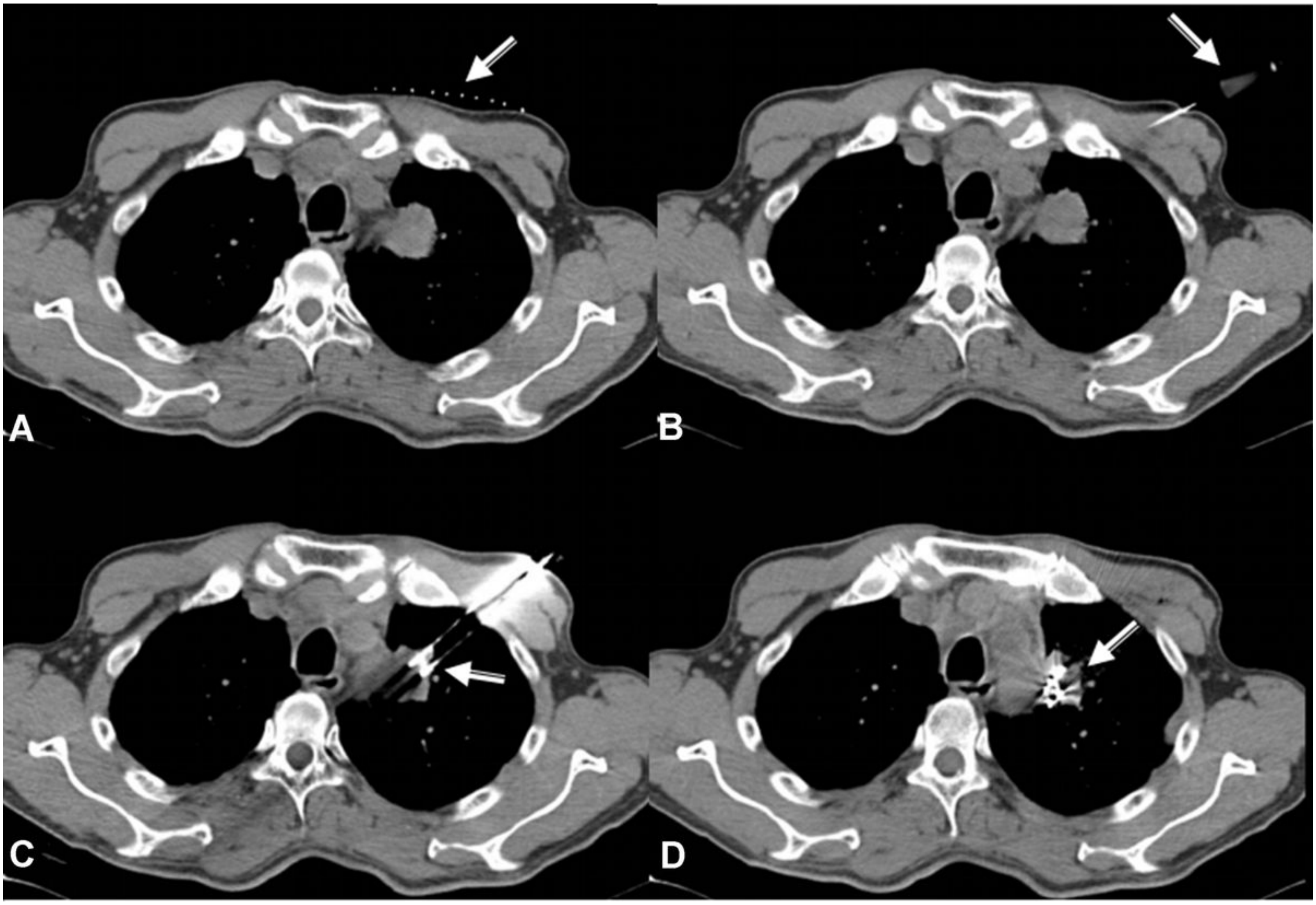

Figure 2

A 60-year-old male underwent regular chemotherapy. He then underwent repeated local seed implantation. (A) The body surface marker. (B) A 5-ml syringe was left at the site of local anesthesia. (C) An 18 G needle was punctured into the pulmonary metastasis. (D) The implantation was completed.

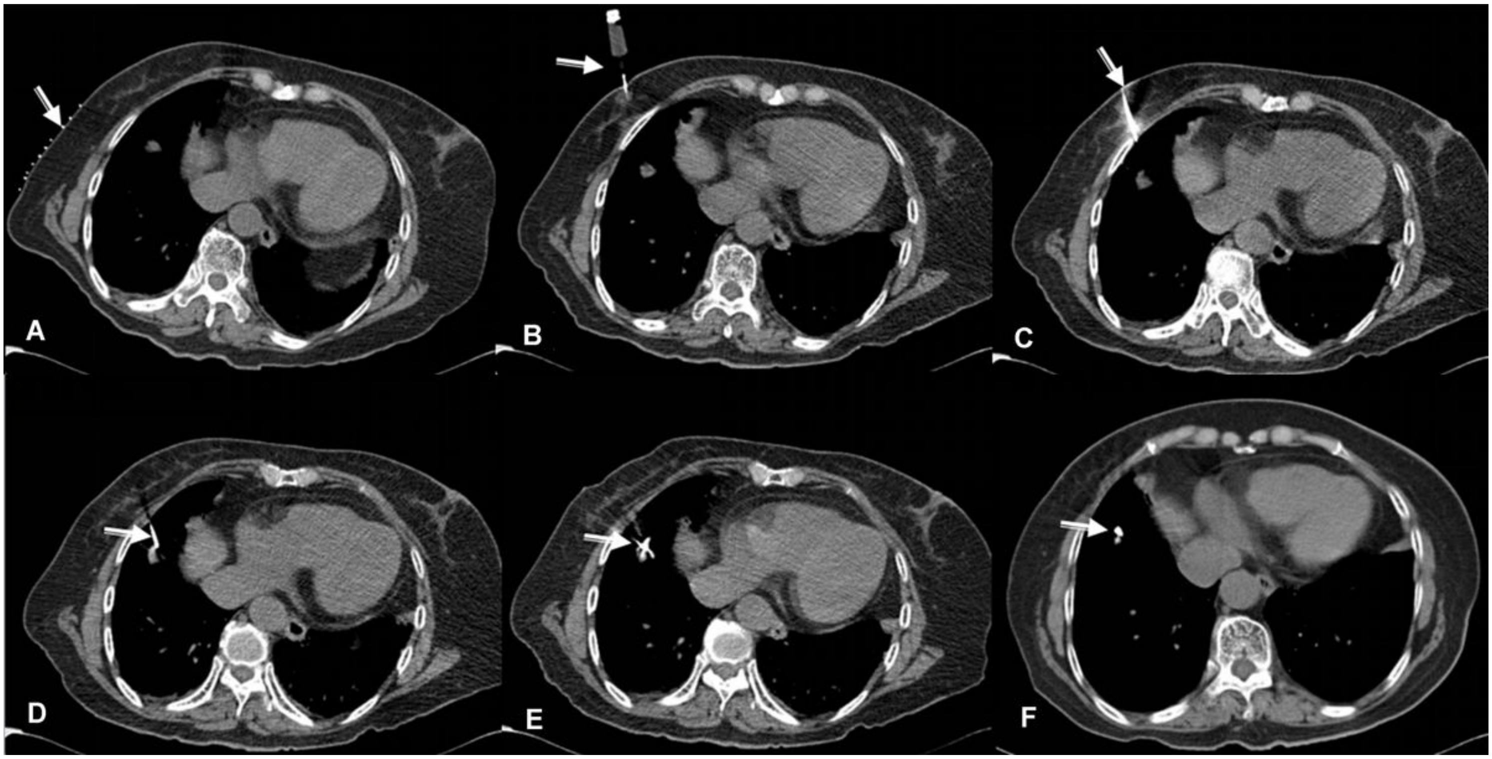

Figure 3

A 70-year-old female underwent regular chemotherapy. She underwent local seeds implantation due to recurrent pulmonary metastases. (A) The body surface marker. (B) A 5-ml syringe was left as a guide after local anesthesia. (C, D) An 18 G needle was punctured into the lesion. (E) Seeds were implanted. (F) The lesion disappeared and only a seed remained at 1 month after implantation.