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Percutaneous computed tomography-guided cryoablation in the lung: a single institution series

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ABSTRACT

Purpose: The purpose of the present study is to report a single center's experience and to evaluate the efficacy and safety of Computed Tomography (CT)-guided cryoablation (CA) for the treatment of primary and metastatic lung lesions.

Material and Methods: Institutional database research from 01/04/2019 till 01/04/2020 identified 8 patients with primary or secondary lung lesions (n=15) who were treated by CT-guided CA and were evaluable for the 6 months follow-up. Technical and clinical success on a per tumour and per patient basis as well as complication rates were recorded. Neoplasmatic substrate included non-small-cell lung carcinoma (NSCLC) (n=2) and metastases from sarcoma (n=3), pancreatic (n=1) and colon (n=2) carcinoma. Mean patient age was 64.3 years (range 23-80 years) and male/female ratio was 5/3.

Results: Median size of the lesions was 1 cm (range 0.4-2.5 cm). Median number of tumours was 1.87 (range 1-4). The mean procedure time was 66.92 min (range 50-84 min), including local anaesthesia, cryoprobe(s) placement, ablation and postprocedural CT evaluation. Median length of hospital stay was 2.5 days (range 1-8 days). Local recurrence-free response (local tumour efficacy) of the treated lesions at 6 months was 93.33% (14/15) and 100% following a second cryoablation treatment for recurrent tumour. The rate of pneumothorax requiring pleural catheter placement was 25% (2/8). Additionally there were 3 grade 2 complication events during 13 procedures.

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Conclusions: The present study demonstrates that percutaneous CT-guided CA constitutes a safe and effective ablation technique for primary and metastatic lung lesions.

KEY WORDS | Lung; Cryoablation; Bronchogenic carcinoma; Metastasis

Introduction

Lung cancer is the commonest type of cancer in both sexes and a leading cause of death, constituting 19.4% of all cancer deaths [1]. In addition, the lung remains one of the most frequent sites of metastastic spread [2]. Apart from surgical options and radiation therapy, percutaneous ablation constitutes an additional alternative technique for local treatment of primary or secondary lung lesions [3, 4]. Currently, curative thermal ablation may be suggested for patients with non-small-cell lung carcinoma (NSCLC) stage I (T1N0M0) who are medically inoperable or refuse surgery [5]. As far as metastatic disease is concerned, oligometastatic patients with disease confined in <3 sites and <5 lesions can be managed effectively with percutaneous ablation [6]. A recent multicenter, prospective, single-arm, phase 2 study has proven safety and efficacy of percutaneous cryoablation (CA) for pulmonary metastases [7]. Ideal target for percutaneous ablation in the lung is a lesion <3.5 cm in diameter, fully surrounded by non-neoplastic aerated lung parenchyma [8, 9]. Size (<2 cm), number and location of the lesions along with disease-free interval and a ratio >4 in between the area of ablation induced ground-glass opacity (GGO) and total tumour volume size constitute significant success factors [10, 11].

CA utilises high pressure cables and cryoprobes in order to create super cooling of argon gas in temperatures <-25°C through rapid decompression of the gas and equilibrium of its pressure to ambient pressure [12]. Cell death results from an early phase, including breakdown of cellular and intracellular membranes, as well as protein denaturation followed by a late phase of vascular ischaemia [12]. Advantages of the technique include low peri- and post procedural pain as well as the ability to visualise the ice ball during the ablation session; all of these however are associated with increased cost and duration of the procedure. Specifically for lung CA, a triple freeze-thaw protocol seems to offer earlier identification of the imaging findings associated with the ablation, the promise of a shorter procedure time or larger zones of ablation, and theoretically, more effective cytotoxicity related to the additional freeze-thaw cycle; this specific protocol seems to result in low recurrence and complication rates [13, 14].

The purpose of the present study is to describe a single institution's experience upon percutaneous CA for primary and secondary lung lesions, focusing upon local tumour control and safety.

Material and Methods

Patient characteristics

Institutional database research from 01/04/2019 till 01/04/2020 identified eight (8) patients with primary or secondary lung lesions (n=15) who were treated by CT-guided CA. Inclusion criteria included patients ≥18 years old with primary or metastatic pulmonary disease, confirmed either by prior biopsy or through imaging (defined as new or growing nodules in cases of histologically proven primary cancer); up to 5 intrapulmonary or pleural lesions with a maximum size of 3.5 cm; Karnofsky Performance Scale (KPS) score ≥60, coagulation parameters within normal limits and a life expectancy of >3 months. All included patients and lesions should have been evaluable for the 6 months follow-up. Exclusion criteria included uncontrollable primary or metastatic disease outside the lung, non-compliance of patients, uncontrollable INR, systematic or local inflammation, severe pulmonary fibrosis or respiratory distress at rest, poorly controlled pleural effusion, expected survival less than 3 months, Eastern Cooperative Oncology Group (ECOG) performance status score less than 3 and presence of a medical or psychiatric illness that would preclude informed consent or follow up.

Each patient underwent laboratory tests (including renal function and coagulation tests) at least 24 h prior to the percutaneous ablation session. The patients were fully informed about the procedure, the possible complications and the surgical and medical alternatives

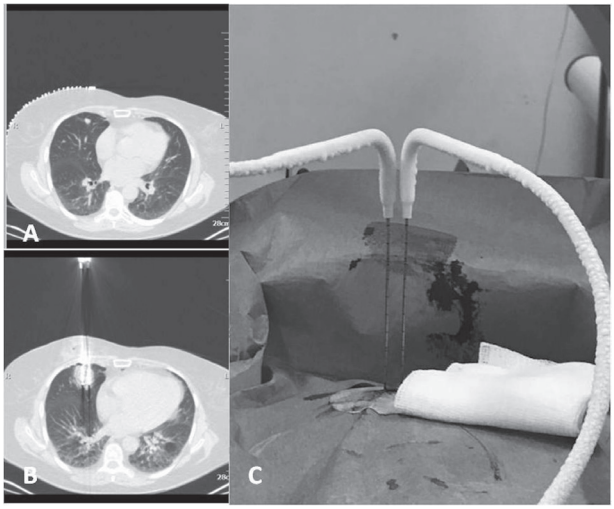

Fig. 1. *Oligometastatic sarcoma female patient undergoing percutaneous lung cryoablation.* ***A:*** *Computed Tomography axial scan illustrating the metastatic nodule (1 cm in diameter) in the right lung.* ***B:*** *Computed Tomography axial scan illustrating the two cryoprobes on each side of the lesion (chopsticks technique) and the resultant ground glass opacity covering the lesion with safety margins >5 mm.* ***C:*** *Two IceSpheres cryoprobes were placed parallel one to the other.*

available; informed written consent was obtained in all cases.

Percutaneous cryoablation procedure

According to the Infection Department of our Hospital, each patient received intravenously, 45-60 minutes before the cryoablation session, a dose of antibiotics (Amoxycillin 1 g + Clavulanic acid 0.2 g). Cryoablation was always performed in an inpatient setting under local anaesthesia (10 cc of 2% Lidocaine Hydrochloric on skin, subcutaneous tissues and pleura) and intravenous analgesia (1 g paracetamol diluted in 100 ml of normal saline was administered during the procedure). CT guidance with sequential scanning (120 Kv peak, 240 mAs wavelength and 2 mm slice thickness) was used for planning, targeting and intra-procedural modification during the CA session. Under extended local sterility, CA was performed with percutaneous approach in all cases. After the initial CT scan, skin entry point was selected. Depending on the size of the lesion, one or more cryoprobes (ICE FC Cryoablation system, Boston Scientific, Marlborough, Massachusetts, United States) was/were inserted in the lesion of interest and the approach was evaluated with sequential CT scans **(Fig. 1)**. Once in the correct location, a triple freeze-thaw protocol was applied [13, 14]. Intermittent, short, ice ball monitoring CT scans were obtained every 3-5 minutes during freezing and following the passive thaw **(Fig. 2)**. Axial, coronal, and sagittal images were reformatted intermittently to further evaluate whether the tumour was fully encompassed by the ice ball and whether the ice ball involved adjacent anatomic structures. CT assessed any potential immediate complications during and at the end of the cryoablation treatment.

Table 1. Definitions of index tumour response according to the SOLSTICE study [5].

"Complete" response	tumour ablation zone disappearance or reduction of at least 75%
"Partial" response	tumour ablation zone reduction of 30% to 75%
"Stable disease"	tumour ablation zone reduction less than 30%
"Local failure"	tumour ablation zone increase of greater than 20% compared to the smallest diameter or the appearance of nodular enhancement

Outcome measures

Imaging and clinical follow-up were performed at 1 week and at 1, 3, 6 and 12 months post CA. The chest CT performed at 1 month served as the post-treatment baseline study. According to the methodology of the SOLSTICE study, technical success was defined as a zone of ground glass opacity or consolidation encompassing the targeted tumour with ≥5 mm circumferential ablative margin. According to the same methodology, tumour response was calculated comparing the sum of the largest diameter of ablation zones. **Table 1** includes the definitions for local tumour efficacy.

The definition of complications was assigned according to the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) classification system [15].

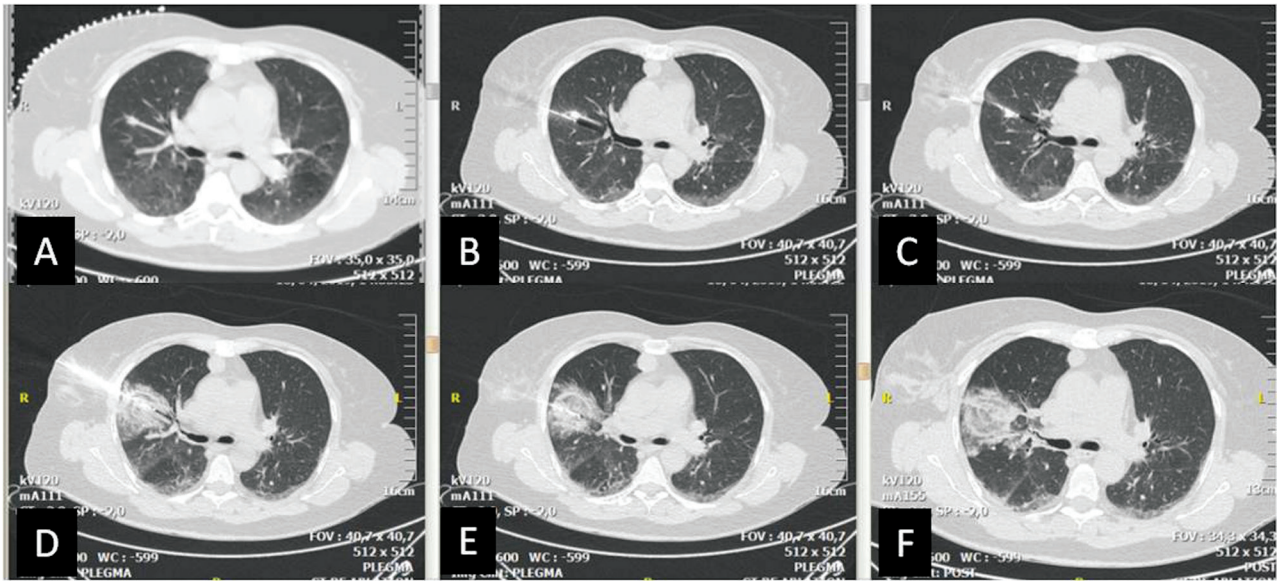

Fig. 2. *Oligometastatic sarcoma female patient undergoing percutaneous lung cryoablation.* ***A:*** *Computed Tomography axial scan illustrating the metastatic nodule (1 cm in diameter) in the right lung (notice the vessel right medially to the nodule).* ***B, C:*** *Computed Tomography axial scan illustrating the two cryoprobes on each side of the lesion (chopsticks technique).* ***D, E:*** *Computed Tomography axial scan during freezing cycle illustrating the resultant ground glass opacity covering the lesion with safety margins >5 mm.* ***F:*** *Computed Tomography axial scan post cryoablation session evaluating lack of complication events and illustrating the resultant ground glass opacity covering the lesion with safety margins >5 mm.*

Results

Five out of 8 patients treated received systematic therapy during the ablation and study period. Neoplasmatic substrate included NSCLC (n=2) and metastases from sarcoma (n=3), pancreatic (n=1) and colon (n=2) carcinoma. Mean patient age was 64.3 years (range 23-80 years) and male/female ratio was 5/3. Median size of the lesions was 1 cm (range 0.4-2.5 cm). The mean procedure time was 66.92 min (range 50-84 min), including local anaesthesia, cryoprobe(s) placement, ablation and postprocedural CT evaluation. Median length of hospital stay was 2.5 days (range 1-8 days).

On a per lesion basis, technical success was achieved in 93.33% (14/15) of evaluable tumours. Repeat treatment of an index tumour was performed in 1 patient. Local recurrence-free response (local tumour efficacy) of the treated lesions at 6 months was 93.33% (14/15) and 100% following a second cryoablation treatment for recurrent tumour. On a per patient basis, at 6 months follow-up overall treatment response was complete for 87.5% (7/8) and stable for 12.5% (1/8) with secondary per patient effectiveness of 100% (8/8).

The rate of pneumothorax requiring pleural catheter placement was 25% (2/8). Additionally, there were 3 grade 2 complication events (pneumothoraces requiring nothing but observation) during 13 procedures. During the follow-up period there were no deaths related to the procedure or to disease progression.

Discussion

The present study adds to the growing number of case series showing that percutaneous CT-guided CA is an efficacious and safe technique in terms of achieving local tumour control and recurrence-free response on both per lesion and per patient basis for both primary and secondary pulmonary disease [7, 16-19]. Similar to other studies, in the present case series, the treatment of primary and metastatic pulmonary disease with CA was successful and well tolerated; one major difference of the present study is that all patients were treated under local anaesthesia, resulting however in no significant differences concerning the efficacy and safety rates [7, 19]. Our overall rate of pneumothorax necessitating pleural catheter (25%) was comparable to that of other cryoablation (18.8-26%) and heat-based lung ablation (5-62%) studies [5, 7, 19-26]. There seems to be a relation between the risk of pulmo-

nary complications and the application of multiple devices [5].

There is no doubt that peri- and postprocedural pain is limited during cryoablation in comparison to heat based techniques, thus enabling the procedure to be held under moderate or mild anaesthesia. This is an essential advantage, as these patients in their vast majority are not able to undergo procedures under general anaesthesia due to co-morbidities. Another advantage of cryoablation is the visibility of the ice ball in the form of ground glass opacity; notice however that cytotoxic temperatures are achieved at least 5 mm more medially than the visible edge of this ground glass opacity where the temperature is 0°C.

Heat-based ablation techniques (mainly radiofrequency and microwaves) have been extensively studied in the lung [8-10, 20-22]. When compared to other heat-based techniques, cryoablation is governed by clearly longer intraprocedural time and a more complex set up regarding the pressurised gas. In cases with a high risk of bleeding (patients with coagulopathies or severe emphysema), in our department heat thermal techniques are usually preferred over CA. Das et al. showed that both CA and microwave were comparably effective, with similar survival benefits in patients with advanced NSCLC (stages IIIb/IV) and small tumours (size less than 3 cm); in addition, cryoablation technique offered the advantage of reduced intra-procedural pain [23]. A metanalysis by Jiang et al. showed that radiofrequency and microwave lung ablation were more effective than CA in terms of local progression rate, with no significant difference regarding the complication rates [24]. However, this meta-analysis included CA studies not using the triple freeze-thaw protocol. Triple freeze-thaw protocol for lung tumour cryoablation constitutes standard of practice in our department, as it has proven to lead to both lower recurrence and complication rates, with a minimal extension of the procedural time (6 min) [13, 14]. Alveolar spaces are not a good conductor of thermal energy and the additional cycle extends the solid freeze zone in the lung. Thus, parenchymal haemorrhage, which is caused in early thaw cycles, increases the zone of ablation in subsequent cycles by allowing thermal energy conduction via blood products in the alveolar spaces [13, 14].

A major limitation of the present study is including primary and metastatic pulmonary lesions in the same patient pool. Other limitations include its retrospective design, small sample size (due to which only lesions up to 2.5 cm in diameter are included), and relatively short follow-up period. It has to be noted though, that in Greece cryoablation became available for clinical practice approximately 1 year ago.

In conclusion, our experience provides preliminary evidence that CA is a safe and effective technique in the treatment of primary and metastatic pulmonary tumours. **R**

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Ethical approval
Institutional Review Board approval was waived based on the retrospective nature of the study.
Conflict of interest
The authors declared no conflicts of interest.

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