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Full Length Research Paper

Exploring the efficacy of CT-Guided percutaneous microwave ablation in lung tumors: An initial study

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To assess the feasibility and safety of percutaneous microwave ablation of the lung in rabbits, percutaneous puncture and lung microwave ablation were performed in seven New Zealand white rabbits under computed tomography (CT) guidance. Technical feasibility and complications were evaluated. Two rabbits were sacrificed immediately and gross and microscopic pathology was analyzed. The remaining rabbits received CT scans 1 week and 3 months later. CT scans showed the ablation size was 1.1 ~ 1.6 cm immediately after ablation. The lesions shrank slightly 1 week later. After 3 months, the ablation lesions involuted significantly and even disappeared. Mild pneumothorax was found in 2 rabbits but resolved spontaneously 1 week later. Histologic changes in the microwave lesions were observed which were characterized by the central necrosis and edema of surrounding tissues. It is feasible and safe to perform CT-guided percutaneous microwave ablation of the lung in rabbits. Although further study is still required; microwave ablation can be used as a minimally invasive and effective therapeutic technique in patients with lung tumors.

Key words: Lung, computed tomography, microwave ablation.

INTRODUCTION

Lung cancer is one of the most common malignancies worldwide, and the current therapies include surgery, radiation therapy and chemotherapy (Fry et al., 1999; Hsu et al., 1996; Robert et al., 1999; Machtay and Friedberg, 1997). Surgical intervention is usually performed in patients with cancers at early-stage and remains the primary curative technique (Fry et al., 1999; Hsu et al., 1996). Nevertheless, surgical treatment is frequently limited in clinical practice due to concomitant chronic obstructive broncho-pneumopathy and/or other associated diseases (Downey, 1999). Under this condition, minimally invasive treatments often receive great attention as is happening in thermal ablation which includes radiofrequency ablation (RFA), microwave ablation (MA), laser ablation (LA), etc. Microwave ablation (MA) has been successfully used in the treatment of hepatocellular carcinoma (Liang and Wang, 2007; Curley et al., 2000), metastatic liver cancer (Liang et al., 2003; Lencioni et al., 1998), renal tumors (Liang et al., 2008) and other solid tumors (Wood, 2002; Anzai et al., 1995; Wang et al., 2009). Theoretically, lung tumors can be treated with thermal ablation because the surrounding air in the adjacent normal parenchyma provides an insulating effect, thus facilitating energy concentration within the tumor tissues. Recently, the efficacy and safety of stereotactic radiation therapy (SRT) has been reported (Grills et al., 2010). Radiofrequency ablation (RFA) is also a well-established modality in the treatment of unresectable liver tumors (Higgins and Berger, 2006) and recently, several authors have evaluated RFA for the treatment of primary and metastatic lung cancer (Lencioni et al., 2004). However, SRT has its side effects such as radiation pneumonitis, pulmonary fibrosis, radiation myelitis, mucocutaneous reactions (stomatitis, esophagitis, enteritis, cystitis) and

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weakness, fatigue, dizziness, headache, anorexia, nausea, vomiting and other reactions. In addition, the

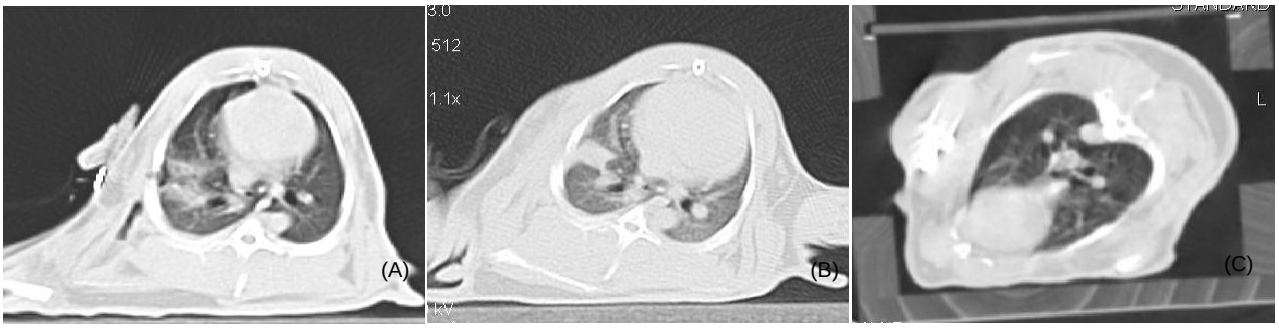

Figure 1. Microwave ablation of rabbit lung. A) Immediately after ablation, CT scans showed the ablation lesion was ground glass opacity with blurry margin and had heterogeneous density. B) One week after ablation, the lesions shrank slightly, and C) Three months after ablation, the lesion disappeared.

radio sensitivity is related with the tumor cell proliferation cycle and the pathological grade.

There are no such side-effects in the thermal ablation (thermal therapy); therefore, SRT and thermal ablation can not replace with each other and we have to select an appropriate treatment according to the specific circumstances of each patient. Although experimental and clinical studies regarding percutaneous RFA of lung cancer have been reported (Lee et al., 2003; Thanos et al., 2006), there have few reports on MA. We performed computed tomography (CT)-guided MA of the normal lung in rabbits to evaluate the feasibility and safety of this technique.

MATERIALS AND METHODS

Animals and ablation procedures

The whole study protocol was approved by the animal research committee of the hospital before study. Seven New Zealand white rabbits (male, 2.5 ~ 3 kg) were anesthetized using an intramuscular injection of ketamine hydrochloride (40 mg/kg) and xylazine hydrochloride (5 mg/kg) before ablation. Before the treatment used in tumor models, firstly, we must understand the efficacy and safety of the microwave ablation using in lung tissue *in vivo* in order to provide reliable ablation experimental parameters after tumor ablation. Therefore, we used the model without lung diseases. A delivery system (KANGYOU Microwave Energy Sources Institute, Nanjing, China) with the microwave frequency of 2,450 MHz and an output power of 10 ~ 80 W which was based on the isolated experiment before and the size of rabbit lung tumor model was used. A 15-guage rigid internally cooled microwave antenna was applied for ablation. After anesthesia, rabbits were placed in a supine position on a table for CT (LightSpeed, GE Healthcare). The antenna was percutaneously inserted into the right pulmonary parenchyma. Ablation was performed at one site per animal. The emission power was 30 W and ablation lasted for 3 min.

CT scan

Spiral CT was performed using a 1-mm collimation immediately, 1 week and 3 months after MA. One week and 3 months later, the rabbits only received CT scan. Complications such as pneumothorax, hemothorax and thermal injury of the chest wall were also monitored by CT scan.

Histopathologic examination

Immediately after ablation, two rabbits were sacrificed with an overdose of ketamime and xylazine, and the lungs harvested. Gross observation was performed on all rabbits and gross specimens were cut in a plane similar to that in spiral CT. For macroscopic examination, two observers measured the central discolored region of coagulation necrosis with calipers in each sample and discrepancies resolved by consensus. Tissues were then fixed in 10% formalin for hematoxylin-eosin (HE) staining for microscopy.

RESULTS

MA

In all rabbits, the puncture was easy and successful. Under the CT guidance, the antenna was placed in an appropriate position in the pulmonary parenchyma to prevent damage to other organs. All rabbits tolerated the MA well and awoke from anesthesia without undue delay.

CT scan

Immediately after ablation, CT scans showed the ablation lesions were ground glass opacity with blurry margin and had heterogeneous density. The lesion size varied from 1.1 to 1.6 cm. One week after ablation, the lesions shrank slightly. Three months after ablation, the lesions became significantly shrank or even disappeared (Figure 1). Mild pneumothorax was found in 2 rabbits and resolved without treatment 1 week later (Figure 2).

Histopathologic changes

On gross section, lesions were oval, surrounded the

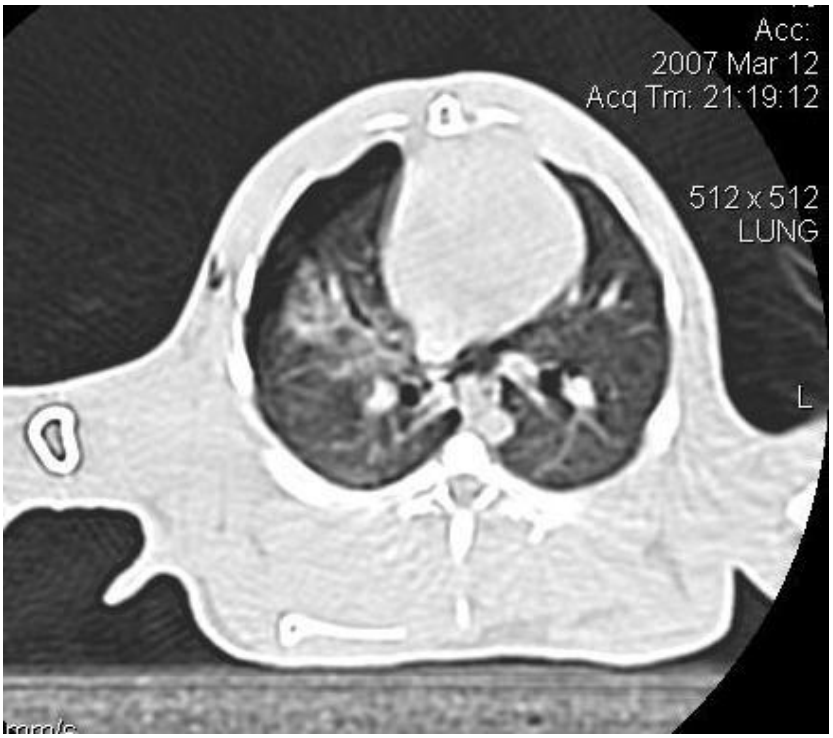

Figure 2. Mild pneumothorax was found after ablation immediately.

puncture site and comprised of three zones. One was the central zone, measuring 2 ~ 3 mm in diameter which appeared grossly as a dark-brown charred band. Microscopically, the central zone showed a thin stripe of a central cavity with the surrounding alveolar structure disappearing. Another was the coagulated zone, a pale-brown area surrounding the central zone and 1.0 ~ 1.4 cm in thickness. Microscopically, the alveolar wall destruction and cellular degeneration were noted. The remaining zone was the congestive zone which was 1 ~ 3 mm in thickness, light-red and located adjacently to the coagulation zone. Tissue congestion, edema and effusions in the periphery alveolar spaces were also observed on microscopic examination (Figure 3).

DISCUSSION

Lung cancer is the leading cause of tumor-related death and has relatively poor prognosis in most patients. Although, improvement of therapy has increased the survival; 1.35 million new cases are diagnosed annually worldwide and approximately 85% of them die of this disease within 5 years (Soto et al., 2000). Surgical intervention is usually regarded as the preferred therapy. However, in clinical practice only about one-third of patients are eligible for surgical intervention because the majority of lung cancer patients are older than 70 to 75 years and frequently have concomitant cardiopulmonary and/or other diseases. Unfortunately, chemotherapy and external beam radiation have not greatly improved the prognosis of patients with unresectable disease, but contribute to substantial toxicity especially for those with comorbidities (Marino et al., 1995). Hence, effective minimally invasive options like thermal ablation should be developed for tumor therapy. Percutaneous image-guided ablation with thermal energy sources such as RF, MA, high-intensity focused ultrasonography (US) and laser have recently received increasing attention as minimally invasive strategies for local treatment of solid malignancies (Dodd et al., 2000; Gazelle et al., 2000; McGahan and Dodd, 2001; Goldberg et al., 2000). It can control the regions with coagulation necrosis with a single application to an area as large as 3 to 5 cm depending on the blood flow in the treated tissue (Goldberg et al., 1998). The cells in a hypoxia environment with limited blood supply such as those in the center of necrotic tumors may be resistant to chemotherapy and external-beam radiation therapy but more sensitive to thermal ablation because heat increases the sensitivity under the hypoxic condition and heat dissipation decreased due to poor perfusion (Dupuy et al., 2002, 2001). Lung tumors seem to be suitable for thermal ablation because the surrounding air in the adjacent normal lung parenchyma provides an insulation leading to energy concentration within the tumors (Goldberg et al., 1995). RF ablation remains the most widely used thermoablative technique worldwide. Goldberg et al. (1995) first evaluated the

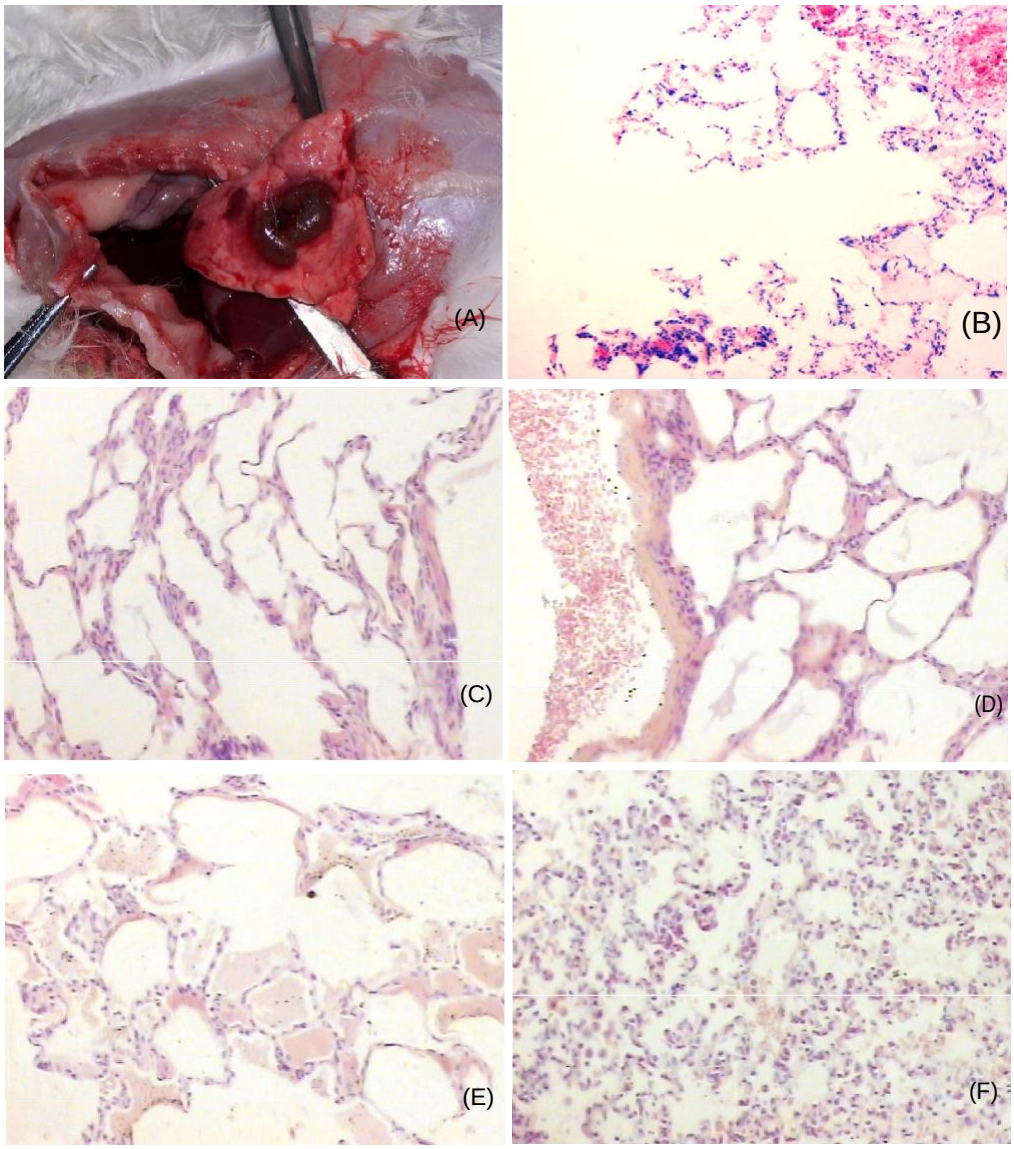

Figure 3. A) Photograph of gross specimen shows that microwave lesion is well visualized; B) The central zone showed a thin stripe of a central cavity, with the surrounding alveolar structure disappearing (HE × 100); C) In the coagulated zone, a pale-brown area surrounding the central zone, the alveolar wall destruction and cellular degeneration were noted (HE × 100); D, E) Tissue congestion, edema and effusions in the periphery alveolar spaces were also observed in the congestive zone, which located adjacently to the coagulation zone (HE × 100); and F) Normal alveolar structure surrounding ablation lesions (HE × 100).

feasibility and safety of RFA of normal pulmonary tissue in rabbits. In another study of them, they assessed the RFA in experimentally induced pulmonary malignancies (Goldberg et al., 1996).

The first clinical study on lung malignancies in humans was reported at the end of the 1990s. Soon after, some studies on the effects of RFA on lung tumors were reported. Available results show RFA of lung tumors is feasible and effective, and can improve the short-term survival and decrease the incidence of complications (Kelekis et al., 2006; Ambrogi et al., 2006). Microwave ablation offers some benefits of RF ablation and has several other theoretical advantages in increasing effectiveness in the treatment of tumors. The potential benefits of microwave technology include consistently high intratumoral temperature, large tumor volume for ablation, short ablation time, ability to use multiple applicators, improved convection profile, optimal heating of cystic masses and less procedural pain. In addition, microwave ablation does not require the placement of grounding pads (Simon et al., 2005). Radiofrequency ablation (RFA) is one of the methods in the treatment of

cancer. Microwave ablation may be applied for the same indications as RF ablation, but has several advantages in energy delivery. Most importantly, microwave propagation is not limited by charred tissue and, therefore, tissue temperatures can be elevated to very high levels (>150°C) without impairing energy deposition. High temperatures are more likely to overcome vascular mediated cooling and create larger and more lethal ablation zones with shorter treatment times (Pascal et al., 2010; Andreano et al., 2010). RF current may cause pacemaker malfunction, so the patients with cardiac pacemaker were banned in RFA treatment. Thus, despite the RFA treatment of lung cancer has achieved good results; we still need a systematic study on microwave ablation on the treatment of lung cancer. For these reasons, we conducted percutaneous MA using CT guidance to evaluate the technical feasibility and safety. There was no morbidity or mortality in our study, similar to the previous study (Goldberg et al., 1995). In addition, all animals received the percutaneous MA successfully. Only mild pneumothorax was noted during the ablation in 2 animals and resolved spontaneously without treatment 1 week later. There were no major complications such as severe pneumothorax and acute respiratory distress syndrome. Although, hematoma is a complication of MA, but not observed in on the present study by CT scan. This may be attributed to the potential of hemostasis induced by thermal coagulation of MA.

In addition, it should be noted that there is no tumor in these animals and thus we can select an appropriate site to place the antenna without considering the location of tumor. So, the puncture is easy and the puncture time minimized which is also beneficial for the decrease of post-ablation complications. It is difficult to perform MA and the incidence of complications will be increased. In addition, a study on RFA suggests that some complications are related to the tumor location (Thanos et al., 2006). For example, the thermal injury of bronchi during the ablation can induce the coagulation necrosis of bronchial wall and result in bronchial obstruction and obstructive penumonic consolidation. In this study, there were not any peri-operative treatment in these animals, and the emission power was 30 W and ablation lasted for 3 min. An oval ablation area, > 1 cm in diameter was obtained on gross section. Alveolar structure destruction, even absence and cellular degeneration were shown in microscopic examination. These findings confirmed the feasibility of MA. One of the limitations of our study is that the relationship between the output power and the size of ablation area was not evaluated. The reason that high output power was not used is that the rabbit lung is not big enough. The purpose of this study was to assess the feasibility and safety of percutaneous MA of the pulmonary tissues. The safety of procedure can not be ensured once the output power is too high. So the emission power was set at 30 W. However, the size of tumors in clinical cases is usually 3 cm or larger. Further studies are required to investigate the selection of appropriate output power for ablation according to the lesions. Another limitation is that it is difficult to evaluate the pain and fever in animal models, which, however are frequently encountered in the treatment of liver cancer. CT scan is a useful method to determine the location of probe and the complications.

It is easy to determine the ablation site and prevent puncture induced hemorrhage. But it may slightly overestimate the lesion size because the edema may mask the margins of ablation zone which shows more variable histologic changes with congestion and hemorrhage close to its center and edema in its outer regions. So, CT enhancement scan may be more practicable to determine the ablation area.

Conclusion

Our study has demonstrated that it is feasible and safe to perform CT-guided percutaneous MA of the lung. Although further study is still required in experimental tumor models and clinical trials; this method represents a minimally invasive and effective therapeutic technique in with the treatment of lung tumors.

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