Preoperative computed tomography-guided percutaneous localization of ground glass pulmonary opacity with polylactic acid injection

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Keywords
Ground glass pulmonary opacity; percutaneous localization; polylactic acid; preoperative.

Abstract
Localization of a ground glass nodule is a difficult challenge for thoracic surgeons, especially for ground glass opacities (GGOs) less than 10 mm in diameter. In this study we implement a new method for preoperative localization of pulmonary (GGOs). From October 2013 to December 2014, computed tomography-guided percutaneous polylactic acid injection localizations were performed for five pulmonary nodules in five patients (2 men and 3 women; mean age, 59.8 years; range, 54–65 years). The injection was feasible in all patients and the localization effect was excellent. The total procedure duration was 12.6 minutes (range; 10–15) and the volume of polylactic acid injected was 0.38 mL. The wedge resections were easily and successfully performed in all five cases. The cutting margin was no less than 2 cm from the lesion. This technique is promising for the determination of GGO location in thoracoscopic surgery for wedge resection.

Introduction
Positive conclusions from the National Lung Screen Trials (NLST) were delivered in 2011, including: evidence that there is a tendency to promote lung cancer screening worldwide; more and more patients with ground glass opacities (GGOs) were diagnosed; and, in some cases, effective timely surgical intervention was required, because diagnosis of these small or faint lung nodules has remained a challenge with dedicated computed tomography (CT), fludeoxyglucose (FDG)-positron emission tomography (PET)/CT or even CT-guided percutaneous biopsy.1 Localization of a ground glass nodule is a difficult challenge for thoracic surgeons, especially for GGOs less than 10 mm in diameter. With the advent of video-assisted thoroscopic surgery (VATS), thoracotomy is no longer required for the excision of peripheral lung GGOs. However, VATS is limited to lesions that can be seen or palpated by the surgeon. Failure to visualize or palpate a lesion can lead to conversion thoracotomy rates of up to 46%.2 Many methods for localizing lesions have been reported in the literature, including CT-guided placement of hook wires, coil, methylene blue injection and intraoperative fluoroscopy, and ultrasound.3–10 The hook wire is most commonly used and the majority of these studies have involved solid pulmonary nodules. In these reports, the diameters of most lesions were over 10 mm or even larger. We present five cases of preoperative localization of pure GGOs less than 10 mm in diameter using polylactic acid injection adjacent to the lesion. This method allows for better palpation and visualization. To our knowledge, this is the first publication describing this method and specifically for GGOs less than 10 mm in diameter.

Patients and methods
The ethics committee of Xuanwu Hospital Capital Medical University approved this study. From October 2013 to December 2014, CT-guided percutaneous polylactic acid injection localizations were performed for five pulmonary nodules in five patients (2 men and 3 women; mean age, 59.8 years; range, 54–65 years). During routine physical examination, CT detected lesions in three patients, and two lesions were incidentally detected on CT because of symptoms of chest pain. Three patients were non-smokers, one a former smoker, and one a current smoker with a 20 pack-year habit. Characteristics of the nodules are summarized in Table 1.
Procedural details of polylactic acid injection localizations

All CT-guided percutaneous polylactic acid injections were performed two hours prior to VATS. Before the localization procedure, chest CT images were carefully reviewed to decide the most appropriate route to the target nodules for successful marking and lowest probability of complications. Procedural details of localizations performed in our study were as follows (Fig 1):

1. Each patient was placed on a CT table in a suitable position (supine or prone). Then, after placing a guide-wire mesh on the intended region of the chest wall, a preprocedural CT scan was performed.

Table 1 Characteristics of GGOs

| Characteristic                        | Value          |
|--------------------------------------|----------------|
| Maximum transverse diameter (mm)*    | 6.4 (5–8)      |
| Distance from the pleura (mm)*       | 16.4 (7–23)    |
| Location                             |                |
| RUL                                  | Alveolar epithelial hyperplasia |
| RUL                                  | Atypical adenomatous hyperplasia |
| RLL                                  | Atypical adenomatous hyperplasia |
| RLL                                  | Atypical adenomatous hyperplasia |
| RLL                                  | Adenocarcinoma-in-situ          |

*Data are means and range in parentheses. GGO, ground-glass opacity; RLL, right lower lobe; RUL, right upper lobe.

Figure 1 (a) Patient was placed on a computed tomography (CT) table in a prone position. A preprocedural CT scan was performed to locate the lesion 5 mm in diameter (arrow). (b) The needle tip (arrow) was accurately placed near the lesion. (c) A polylactic acid was injected through the needle. The instilled volume of polylactic acid was 0.5 mL, a ball was formed after injection (arrow). (d) After confirmation of the location, it is necessary to continue injecting while withdrawing the needle. A white membrane will form on the penetrating site surface of lung. The membrane (arrow) could indicate the location of GGO via video-assisted thoracoscopic surgery.
Based on preprocedural CT images, the skin entry site, exact intended site of injection, and needle route to the target were determined. The polylactic acid injection was to be placed 1 cm to the side of the lesion to ensure no influence on pathological result. After local anesthesia of the chest wall using 2% lidocaine, a 21-gauge needle was introduced to the planned polylactic acid injection site using sequential CT image guidance to guide the path, scanning only 10 cm around the lesion to avoid unnecessary radio exposure.

If the needle tip was accurately placed, the inner core of the needle was withdrawn and polylactic acid was injected through the needle. The average instilled volume of polylactic acid was 0.38 mL (range, 0.3–0.5 mL).

Post-procedural CT was performed to identify the exact location and characteristics of the injected polylactic acid ball. Polylactic acid forms a ball immediately after injection. After confirming the location, it is necessary to continue injecting while withdrawing the needle. A white membrane forms on the penetrating site surface of the lung. The membrane could indicate the location of the GGO, as once the polylactic acid ball has hardened it becomes palpable. According to the relationship between the polylactic acid ball and target lesion on CT scan, the surgeon can determine the range of wedge resection.

**Results**

The injection was feasible in all patients, as well as the localization effect, with 12.6 minutes (range; 10–15) total procedure duration, and 0.38 mL volume of polylactic acid injected (Table 2). The wedge resections were quickly, easily, and successfully performed in all cases, and the cutting margin was no less than 2 cm from the lesion. It is very convenient to find the lesion by the newly formed membrane on the lung surface, and it is also easy to locate the lesion by palpating the artificial ball. In one patient, quick pathology diagnosed adenocarcinoma-in-situ; therefore, we performed two, four, seven, and 10 lymph node samplings to determine negative pathology. We considered wedge resection to be curative for this 5 mm lesion. Preoperative localization confirmed the thoracoscopic findings and decreased the examination time. Working with a polylactic acid ball-firing stapler is easy. Few complications were observed. One of the patients developed a small pneumothorax during the localization procedure. No intrapulmonary hemorrhage occurred. No complications occurred after surgery. The mean duration of the postoperative stay was three to four days. The final histological diagnosis was benign in four cases, adenocarcinoma-in-situ in one case (Table 1).

**Discussion**

Video-assisted thoracoscopic surgery is a minimally invasive surgical solution for the resection of pulmonary nodules. However, VATS wedge resection can be challenging in cases where the nodule is too small or too far from the pleural surface, or lacks sufficient density to be palpable by the surgeon. Many methods for localization of lesions have been described in the literature. CT-guided methylene blue injection has been reported; however, it is limited by the rapid spread of the dye through the lung parenchyma, making it difficult to determine the cutting margin. Intraoperative endoscopic ultrasound has also been used to identify peripheral nodules, but the false negative rate was up to 40%.

Mack et al. first described the hook wire needle localization of pulmonary nodules. According to the literature, it became the most popular technique, although some procedures were performed with modifications. Wire dislodgement and local pulmonary hemorrhage were major complications of this method. Wire dislodgement may make the surgical procedure even more difficult. Finley et al. have reported the use of coils in recent years. However, the complications of hook wire are not solved by this new microcoil. The distance between the wire tip and the pleura should be greater than 30 mm, a factor demonstrated to correlate with successful wire localization. When the lesion is close to the lung surface, it is difficult for the wire to dock.

Polylactic acid is one of the ideal biomedical polymer materials. With no animal origin causing an immunogenicity reaction, it has good biocompatibility. After United States Food and Drug Administration approval in the 1990s, the polylactic acid system has been widely used in biomedical fields, such as in hormone drugs, the controlled release system of carrier materials, and repair materials. In clinical trials, it has proven safe and effective, biodegradable, and absorbable by the human body. Polylactic acid becomes solid immediately when encountering water; thus making it an excellent material for GGO location. When injected beside the lesion in the lung, a solid ball will form, which is very easy to be palpated and held by surgical instruments. When injected while withdrawing the needle, a small amount of polylactic acid will form a white membrane on the lung surface of penetrating site, which is distinctive under thoracoscopic view. Compared with the hook wire, polylactic acid is less invasive and more suitable for superficial GGOs. The average distance of GGOs from the pleura in this study was 16.4 mm.

In summary, we have described preoperative polylactic acid injection for the localization of GGOs, resulting in easy

| Table 2: Procedural details of localization |
|-------------------------------------------|
| Total procedure duration (minutes)* | 12.6 (range; 10–15) |
| Volume of polylactic acid (mL)*        | 0.38 (range; 0.3–0.5) |

*Data are means and range in parentheses.
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and successful surgical resection. Although the number of cases in this study was small, the advantages of this method are such that we suggest this technique will be promising for GGO location in facilitating thoracoscopic surgery for wedge resection.

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