Impact of Preoperative Marking Coils on Surgical and Pathologic Management of Impalpable Lung Nodules

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Background. The management of occult lung lesions, particularly subsolid opacities, is a new challenge because they are difficult to localize during surgery and the number of lesions detected by computed tomography (CT) is increasing.

Methods. Between February 2008 and December 2011, preoperative CT-guided marking with coils was systematically carried out to localize presumed impalpable nodules before video-assisted thoracoscopic surgery (VATS). The procedure feasibility, reliability, and safety as well as its impact on the resection volume and on the pathologic examination strategy were examined.

Results. This preoperative marking procedure was used for 68 nodules in 60 consecutive patients. The mean procedural time was 25 minutes/patient and complications included minimal asymptomatic pneumothorax (42 cases, 70%) and hemorrhagic suffusion (21 patients, 35%). Patients with non-retrieved coils during VATS required larger resection volumes (94.88 mm$^3$ vs 20.65 mm$^3$; $p = 0.008$). The presence of a coil loop in the pleural space was not statistically associated with higher resected lung volume. Primary pulmonary adenocarcinoma was found in 42 patients (71.2%). Five nodules were associated with atypical adenomatous hyperplasia. Pathologic examination was considered to be improved by the presence of a coil next to the lesion but not within it. Coil placement modified the pathology practices for intraoperative analysis, as tissue sampling in the immediate vicinity of the coil was preferred to systematic sampling.

Conclusions. Impalpable lung nodules can be safely marked with coils preoperatively to improve their surgical and pathologic management.

Surgery of small and subsolid lung lesions detected by computed tomography (CT) is a real challenge [1–3]. Indeed, most of these clinical situations require parenchyma-sparing resection using a minimally invasive approach such as video-assisted thoracoscopic surgery (VATS) to reduce a decline in lung function or because of multifocality or benignity [4–8]; however, most of the time they are difficult to localize during surgery. The number of lesions detected has increased dramatically over recent years with the widespread use of multidetector CT and the current intervention guidelines for the management of such lesions [9, 10]. Recent studies demonstrating the effectiveness and feasibility of lung cancer screening using repeated CT support the hypothesis of a persistent rise in the incidence of small lung lesion detection and surgical indication.

Although the morphologic appearance of subsolid opacities can help discriminate between benign and malignant lesions [10, 11], this information is not fully reliable and the removal of such opacities is recommended. However, surgery can lead to excessive parenchymal tissue sacrifice because the lesions are both difficult to see and to feel. Furthermore, the location of ground glass opacities is also a challenge for pathologists as they might not be visible or palpable during gross examination. Therefore, we hypothesized that the use of a coil would improve both surgery and pathologic examination of such small peripheral lesions. This study thus focused on the use of preoperative CT-guided impalpable nodule coil marking.

Material and Methods

Study Population

This single-center cohort study was performed between February 2008 and December 2011. Informed consent was read and signed by each patient before the procedure. The Nimes-Montpellier University Institutional Ethics Committee approved this data collection because of the
routine nature of this type of small lung lesion management and because it adhered to current guidelines [12] (Institutional Review Board approval number 1206-01).

Inclusion criteria were single or multifocal opacities presumed impalpable of unknown origin that were growing or stable for at least 3 months during follow-up CT. Both CT-guided marking with coils and VATS were decided by multidisciplinary consensus obtained during the weekly multidisciplinary lung cancer meeting, taking into account clinical history, nodule morphology, and international guidelines.

**CT-Guided Marking Procedure**

Lesions were marked with coils the day before or, more frequently (48 patients, 80%), just a few hours before performing VATS. The CT-guided marking was performed preoperatively using a 64-multidetector CT scan (VCT LightSpeed 64; GE Healthcare, Milwaukee, WI) by an interventional radiologist experienced in image-guided needle interventions (S.B.). Local anesthesia with buffered lidocaine (n = 58) or general anesthesia (n = 2; pediatric patients) was administered. Patients were placed in the most suitable position for transparietal access (prone, n = 18; supine, n = 10; lateral, n = 32 positions). A coaxial 17G needle (Bard) was first positioned through or beside the nodule. One or more platinum coils (6/3 mm; Tornado, Cook Medical, Bloomington, IN) were dropped into the needle and pushed in with a stiff guide wire (Amplatz, Cook Medical). The cost of 1 coil is 97 € (128 USD) exclusive of tax. There are no extra costs of any nature for radiologic procedures charges in our academic institution. Coils were inserted through the needle under iterative control to check the exact coil placement and the appearance of any complication. As a peripherally inserted coil can be dislodged during thoracoscope insertion, more than 1 coil was placed if the initial coil was considered to be insufficiently well anchored. The CT control scan at the end of the procedure was carried out for each patient. The marking procedure was considered technically successful when 1 or more coils were inserted adjacent to or inside the nodule (Fig 1A-C). After the fourth patient, the marking technique was modified and coils were placed in the 5 to 10 mm perimeter around the lesion but not through the nodule itself. Placing a coil loop in the pleural space was tested as a specific criterion for improving surgical tracking of nodules (Fig 2). The data registered were the following: procedure duration, clinical symptoms (dyspnea, hemoptysis, chest pain or any other occurrence), and CT data; presence of a pneumothorax, pleural effusion, alveolar hemorrhage or any other complication. Follow-up; thoracic follow-up CT was performed on all patients between 3 to 6 months after the surgical procedure. The presence of a remaining nodule was systematically assessed.

**Surgical Procedures**

The procedure was carried out with patients placed in the lateral position with the lung to be operated on uppermost, under general anesthesia, and with respiration monitoring. Three trocars were inserted in the pleural space for VATS. When the preoperatively inserted coil was located, a wedge resection was performed first. Excised specimens were then immediately sent for intraoperative examination. The VATS lobectomy was subsequently carried out when required, based on the pathology examination. Coil and coil loop visualization or identification during VATS, excised parenchymal volume, and complications were recorded.

**Surgical Pathology Analysis**

All wedge specimens were submitted to intraoperative frozen-section pathologic examination. First, the pathologist located the coils at gross examination. As coils caused hardening, a tissue block sampling was done around the coil. In the case of a missing coil (fallen during surgery or removed by the surgeon), the entire specimen was systematically sampled; the pathologic procedure consisted of systematic tissue sampling every 5 mm.

**Statistical Analysis**

As the excision volume did not distribute normally for our population, nonparametric statistics were used to minimize the effect of extreme values (2 patients with lobectomy). Correlations between the excised volume and the distance nodule-pleural space were carried out using the Spearman rank correlation test. The same test was also used for excised lung volume and nodule size comparison. Univariate analyses (Kruskal-Wallis and Wilcoxon tests) were used to analyze the relationship between excision volume and coil loop visualization during VATS. A p value less than 0.05 was considered to indicate a statistically significant difference.

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Fig 1. Transverse, non-enhanced chest computed tomography scan in a 56 year old man (A) before, (B) during, and (C) after coil insertion. Coils were inserted beside the target lesion with the final loop in the pleural space.
Results

CT-Guided Marking Procedure

Between February 2008 and December 2011 (46 months), 60 consecutive patients (20 men and 40 women) were enrolled. The median age at the time of the procedure was 57 years (range: 12 to 83 years). Computed tomography scans revealed a maximal transverse diameter of the nodules or ground glass opacities ranging from 1.8 mm to 50 mm (mean 9.89 mm /7.5 mm). The distance from the parietal pleura to the edge of the nodule at CT ranged from 0 to 34 mm (mean 7 mm).

Finally, 68 nodules (29 ground glass opacity, 17 part solid nodules, 22 solid nodules <1 cm) were successfully marked by CT-guided placement of 1 to 6 coils/patient (mean = 3.2). Of the 68 marked nodules, 60 had a coil loop in the pleural space that was visible during the post-procedure CT scan. All marking procedures were carried out without major complications with a mean duration of 24.95 minutes per patient (range: 10 to 63 minutes).

Forty-two patients (70%) experienced minimal or moderate pneumothorax. All pneumothoraces were clinically neutral but 2 out of the 42 patients required chest tube insertion (3.3%) to allow the safe marking of a second nodule. Small areas of ground glass opacity or consolidation attributed to bleeding within the lung during post-procedure CT scans were observed in 21 of 60 (35%) patients, without any hemoptysis. No air embolism was recorded.

Surgical Procedure

The marked nodules were identified during surgery using 1 or more of the following signs: Direct identification by visual assessment of the coil loop in the pleural surface; or indirect signs such as small hematoma or induration identification using palpation. The surgical procedures are summarized in Table 1. Fifty-seven patients underwent VATS wedge excision. The excised lung volume was known for 52 patients (7 missing data). After intraoperative pathologic analysis, wedge excision was followed by VATS lobectomy on 17 patients, by segmentectomy for 1 patient, and by pneumonectomy because of bifocal lesions in 1 case. A large probabilistic resection was done in cases where coils were not visible at the time of surgery using intraoperative pathologic examination in order to ascertain the presence of the nodule in the resected parenchyma. Lobectomies were performed in the following 2 instances: (1) when invasive components were detected; or (2) when the marking coil failed to detect the lesion.

The pneumonectomy was justified as follows. Wedge resection was performed in the first phase of the surgical process for ground glass opacity of the left upper lobe; however, intraoperative frozen-section pathologic examination demonstrated the invasive characteristic of this ground glass opacity and therefore a lobectomy was needed. In the second phase of the surgery, a conversion into pneumonectomy was decided as the ground glass opacity had an invasive component and the patient suffered from another solid mass in the lower lobe. Wedge excision was not possible for 2 patients who had nodules situated at 23.9 mm and 34 mm from the pleural space, respectively.

One patient experienced 2 cardiac arrests during anesthetic induction, but was successfully resuscitated. However, the surgery was cancelled. In the 59 patients who underwent surgery, 58 of the 67 marked nodules could be correctly identified during VATS. In 9 nodules, the marking coils could not be visualized by the surgeon either because they had been dislodged during the thoracoscope insertion in the pleural space or because they were situated too deep in the parenchyma to be seen. The 2 patients who had primary lobectomy were among these 9 patients.

A significant volume of excised lung tissue was saved when successful intraoperative coil visualization was possible. Indeed, Table 2 shows lower excised lung

Table 1. Summary of Procedures of 60 Patients With 68 Marked Nodules Included in This Study

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No.</th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wedge</td>
<td>38</td>
<td>Malignant tumor n = 25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Benign lesion or AAH n = 13</td>
</tr>
<tr>
<td>Wedge + segmentectomy</td>
<td>1</td>
<td>Minimally invasive adenocarcinoma</td>
</tr>
<tr>
<td>Wedge + lobectomy</td>
<td>17</td>
<td>In situ (n = 10) or invasive adenocarcinoma (n = 7)</td>
</tr>
<tr>
<td>Wedge + pneumonectomy (bifocality)</td>
<td>1</td>
<td>In situ adenocarcinoma + invasive carcinoma</td>
</tr>
<tr>
<td>Lobectomy</td>
<td>2</td>
<td>In situ adenocarcinoma</td>
</tr>
<tr>
<td>Cancelled surgery</td>
<td>1</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

AAH = atypical adenomatous hyperplasia.
volume when there was a coil detection (94.88 mm³ ± 84.26 vs 20.65 mm³ ± 17.06, p = 0.0081). A positive correlation was found between the volume of excised lung tissue and nodule size (p = 0.5455, p < 0.0001). The distance between the nodule and the pleural space and a coil loop in the pleural space did not correlate significantly with the excised volume.

**Pathologic Analysis**

When the coil was identified in the surgical specimen, tissue sampling was done in the area next to the coil (n = 45 nodules). The routine technique of serial sampling was used in other cases (n = 14). Tissue damage (modification of the nodule structure) due to laceration by the coil placed in the nodule was reported in the case of 1 patient. Analysis of the surgical specimens from the 59 patients (Table 3) revealed the presence of a malignant lesion in 51 nodules (45 patients, 76.3%), including 42 adenocarcinomas out of which 12 of these (11 patients) had an invasive component. Five nodules were diagnosed as atypical adenomatous hyperplasia (AAH) in 3 patients. The AAH was found unexpectedly in 11 resections. Moreover, 16.4% of the nodules had a lesion of benign origin.

**Comment**

This prospective study demonstrated that a small peripheral nodule marking procedure using coils was feasible, safe, and not too time-consuming as all presumed impalpable lung nodules were accessible for puncture and coil placement. Our preoperative marking procedure facilitated the localization of non-visible or impalpable nodules for conservative diagnosis and curative surgery. Coils were detected in 86% (58 of 67) of cases during VATS and the excision volume was smaller every time the surgeon managed to retrieve the coils. The distance of a nodule from the pleural space was not associated with the excision volume, nevertheless; only 2 primary lobectomies were required for undetectable nodules deeply situated at 23.9 mm and 34 mm from the pleural space. The sample size and the low variability of distances from pleural surface between nodules may explain why the resected specimens did not vary with the depth of the nodule.

Our goal was to insert a coil loop into the visceral pleura to improve visual detection at VATS. By its very nature, this procedure induces minimal pleural separation. Moreover, this phenomenon did not affect patients inasmuch as they were transferred to the operating room after the procedure. Two out of the 42 patients required chest tube insertion (3.3%) only to allow the safe marking of a second nodule. A coil loop in the pleural space facilitated the visual identification of the marking site, but was not statistically associated with smaller excision volume. The surgeon could generally detect the original placement of the coil even when there was no pleural loop, thanks to the presence of limited localized bleeding or local surface deformation.

Several strategies carried out using transthoracic CT approaches have been developed to help detection of impalpable nodules during VATS with promising results [13–18]. Although the use of ink and hook wires can improve lesion identification, there are limits to the benefits of these procedures, in particular due to dye diffusion and wire migration. Our preoperative procedure of coil insertion differs slightly from the coil technique described by Mayo and colleagues [19]. First, in most patients, more than 1 coil had to be inserted around the nodule as their final position was sometimes difficult to predict due to the specific anatomic characteristics of the lung parenchyma and the use of coils that are normally used for vessel embolization. Coils can be dislodged when they revert to their original shape, as previously reported by Yoshida and colleagues [20].
In the first 4 patients, coils were placed through the nodule according to the Mayo technique, but in the fourth patient this led to tissue laceration which made pathologic reporting difficult. Indeed, because the structure of the nodule is an important criterion for differential diagnosis between AAH and adenocarcinoma [21, 22], the marking technique was rapidly modified and coils were placed in the 5 to 10 mm perimeter next to the lesion in order to avoid tissue damage. When bleeding occurred, it was away from the target lesion and thus did not damage the specimen. In other cases, the presence of a coil was subjectively judged to be helpful by our university pathologist. During gross examination, nodules were generally just slightly or not at all palpable and thus the presence of the coil facilitated the sampling procedure for the intraoperative frozen-section pathologic examination. Moreover, this marking was also useful to confirm that the target lesion had been removed because lung specimens can harbor hidden lesions, as indicated also by the associated diagnosis of AAH in 11 cases in this study.

Limitations of the Study
The main limitation of this prospective study was the absence of a control group. The impact of such a marking procedure on the resulting postoperative pulmonary function should now be evaluated in a randomized trial. Moreover, we did not systematically assess the impact of such a procedure on the time it took for pathologic analysis or patient-related outcome including anxiety and pain. We also lacked sufficient data to give recommendations on the limits related to the nodule itself such as depth, diameter, density, and number of nodule. Fluoroscopic and sonographic techniques were not used in this study. The success rate may be improved using these techniques whenever the marking procedure is not correctly identified.

Conclusions
Impalpable lung nodules are a real challenge for both surgeons and pathologists. Coil marking is a safe and effective technique, optimizing both impalpable nodule removal using VATS and pathologic examination.

References