

Preoperative localization of lung nodules: a comparative analysis of hookwire and radio-guided procedures

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Background: Histological diagnosis of pulmonary nodules requires surgical resection on many occasions. There are multiple localization strategies each with their own benefits and complications. The objective of this study is to compare preoperative lung nodule localization with hookwire and radiotracer injection (radioguided occult lesion localization, ROLL). To compare results, complications, and volume of the sample resected with both techniques.

Methods: Patients undergoing resection of pulmonary nodules with video-assisted thoracoscopy and presurgical localization with hookwire or ROLL were studied. Eighty-eight pulmonary nodules were resected in 76 patients: 52 with a hook wire and 36 with a radiotracer. The localization rate, the shortest distance between the nodule and the pleura, the intrapulmonary distance of the locator, the complications, the volume of the resection piece, and the histological result were all assessed. In addition, the factors that influence the volume of the surgical piece were analyzed.

Results: All the nodules were resected with both techniques. The intrapulmonary path of the locator is longer for the ROLL group (23.91 *vs.* 16.28 mm; P=0.04), with no differences in the distance from the nodule to the pleura. The rate of pneumothorax was significantly higher after the placement of a hook wire (69.2% *vs.* 24.2%; P<0.0001), while there were no differences in the presence of hemorrhage. The volume of the pieces resected using ROLL was more minor than with hookwire, although not statistically significant (20.19 *vs.* 34.26 cc; P=0.07).

Conclusions: Preoperative localization with the ROLL technique is safer than the placement of hookwire. In addition, the ROLL technique shows a tendency to obtain a smaller volume of resected tissue since the marking is not affected by the intrapulmonary route used during marker placement. ROLL technique allows to locate lung nodules with fewer complications than hookwire and probably gets smaller resection samples.

Keywords: Lung nodule; radioguided occult lesion localization (ROLL); hookwire; preoperative localization; video-assisted thoracoscopic surgery (VATS)

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Introduction

A pulmonary nodule is defined as a round or oval opacity less than 3 cm in size and surrounded by lung (1). There are multiple causes of pulmonary nodules, whether solitary or multiple. The detection of small-sized pulmonary nodules has increased in recent years due to the implementation of computed tomography (CT) devices with lower collimation and reconstruction thicknesses and reconstruction algorithms with maximum intensity projection (MIP) techniques (2). Detecting these nodules is essential in lung cancer screening programs and cancer patients. In the latter, the new targeted therapies or immunotherapy require a molecular determination that may require a histological sample. However, a percutaneous biopsy of these tiny lung lesions has lower performance than in larger volume nodules (3,4), and an excisional biopsy is required. This intervention can be performed by video-assisted thoracoscopic surgery (VATS), which provides a specific diagnosis (5).

Since hookwire marking was published in 1993 (6), multiple localization methods have been described in the literature, with the hookwire being the most widely used. However, the hookwire has a high yield with a morbidity of 13–14%, and the main disadvantage is the migration of the device (7-9). Therefore, in 2000, the marking of pulmonary nodules using radioguided occult lesion localization (ROLL) was described, which consists of injecting a radiotracer inside the nodule and subsequent intraoperative localization using a gamma detection probe (10). This technique had previously been used with great success in other pathologies such as breast nodules (11), allowing the volume of the resection pieces to be reduced (12).

Although some studies compare the effectiveness of different techniques for preoperative localization of pulmonary nodules to date (5,9,13,14), the factors that determine the performance of the ROLL technique compared to the hookwire and how they affect the performance of the ROLL technique, and the volume of the resected lung has not been studied.

The objective of our study was to evaluate the performance and complications of the ROLL technique compared to hookwire marking based on the characteristics of the nodule, the radiological approach, and its impact on the volume of lung parenchyma removed. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-552/rc).

Methods

Our work is a retrospective study in which the series of marking of pulmonary nodules intervened using ROLL has been compared, with prospective inclusion of patients (from November 2015 to September 2018) and the retrospective series of marking with hookwire for resection of pulmonary nodules in our center (from March 2012 to July 2019). In all cases, the need for a presurgical localization was decided by consensus in the multidisciplinary committee of lung neoplasms. The analysis was performed after the approval of the local ethics committee (Comitè d'Ètica de l'Hospital Clínic de Barcelona; HCB/2016/0147). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). In addition, all patients signed the informed consent before the interventional and surgical procedures.

Patient population

Eighty-eight nodules belonging to 76 patients have been studied: 52 resected with hookwire and 36 with ROLL. *Table 1* collects the global demographic data grouped by technique, the distribution by lobes of the nodules, and the type of guide used in each group of patients.

Hookwire marking (Figure 1)

We used a specific marker for the lung (Léleman, Valencia, Spain). The markings were performed using CT fluoroscopy guidance (Sensation 16, Siemens Healthineers, Erlangen, Germany) in 18 cases or step-by-step technique in the remaining 34 cases. The step-by-step technique consists in introducing the needle a few millimeters and taking a CT image to ensure the correct positioning of the needle tip, and so on, consecutively until the needle reaches the nodule. Fluoroscopy-CT guidance consists in advancing the needle while CT is acquiring the image. With fluoroscopy-CT, the needle's tip's position can be controlled in real-time. Subsequently, a new CT scan was performed to determine the existence of complications and the exact location of the hookwire.

Marking with ROLL technique (Figure 2)

Chiva needles of 22-G and 9 or 16 cm in length (BD, Madrid, Spain) were used for marking. The tip of the needle was placed inside the nodule under CT fluoroscopy

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7

19

23

18

34 (38.6)

54 (61.4)

Global (n=76)	Hookwire (n=49)	ROLL (n=27)	Statistical significance
64.05 (10.14) [38–82]	62.47 (10.11) [38–82]	66.93 (9.89) [40–79]	NS
	27:22	17:10	NS
	27 (55.1)	22 (81.5)	P<0.05
88	52	36	
10.13 (4.59) [3–22]	10.29 (4.49) [4–22]	9.89 (4.78) [3–22]	NS
21	13	8	_

1

8

10

9

0 (0.0) 36 (100.0)

Table	1	Demographical	data
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Age (years), median (SD) [range]

Patients

Men:Women

Localization, n

RUL

RML

RLL

LUL

LLL

Type of quidance, n (%)

Step by step

Fluoroscopy-CT

Final diagnosis, n (%)

Prior neoplasm (n, %)

Number of resected nodules Size (mm), median (SD) [range]

Malignant70 (79.5)39 (75.0)31 (86.1)–Benign18 (20.5)13 (25.0)5 (13.9)–ROLL, radioguided occult lesion localization; SD, standard deviation, NS, non-significative; RUL, right upper lobe; RML, right middle lobe;

6

11

13

q

34 (65.4)

18 (34.6)

RULL, radioguided occult lesion localization; SD, standard deviation, NS, non-significative; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; CT, computed tomography; –, non-realized.

guidance, and the radiotracer was injected ([99mTc]Tc-MAA, 37–111 MBq, 0.2 mL; depending on whether the injection was performed on the same-day surgery or the previous one) mixed with 1 mL of iodinated contrast. Next, a new CT was performed to check the iodinated contrast's location and evaluate potential complications. Subsequently, a single-photon emission CT/CT (SPECT/CT) (InfiniaTM HawkeyeTM 4; GE Healthcare Milwaukee, WI, USA or Symbia Intevo Bold; Siemens Healthineers, Erlangen, Germany) with volumetric reconstruction was performed to verify the location of the radiotracer.

Analysis of the marking procedure

The following measurements were made: the size of the nodule, location according to the lobe, the smallest distance between the pleura and the nodule (pleural-distance; PD), the distance of the intrapulmonary path traveled by the marker (nodule-distance; ND), and marking complications,

for each group (Figure 3).

The nodule size was considered the maximum diameter in the lung window (*Figure 3A*, *3F*). The shortest distance to the pleura was considered regardless of the route used to mark the lesion (*Figure 3B*, *3G*). In both ROLL and hookwire, the ND was considered the path traveled by the needle or the hookwire from its access through the peripheral pleura until it reached the nodule (*Figure 3C*, *3H*). The following complications were recorded: pulmonary hemorrhage, pneumothorax, and need for drainage (*Figure 4*).

Surgical procedure

Patients were referred to the operating room immediately after hookwire localization and between 2 and 18 hours after ROLL marking. In all cases, the procedure was started with VATS. In the hookwire-marked nodules, access to the mechanism was identified at the parietal and visceral pleural levels, and the nodule was resected with safety margins



Figure 1 Hookwire marking procedure of a pulmonary nodule using CT guidance. (A) 5-mm solid nodule (white circle) located in the apical segment of the right lower lobe. (B) The hookwire introducer is placed under CT-fluoroscopic guidance passing adjacent to the nodule (black arrow) and leaving the end slightly medial to the lesion (white arrow). (C) Through the introducer, the hookwire is deployed, opening beyond the nodule (white arrowhead). (D) Once the introducer device has been removed, the hookwire is definitively placed, leaving the pulmonary nodule located between the spiral (white arrowhead) and the visceral pleura. (E) Coronal plane reconstruction shows that the hookwire spiral's opening surrounds the internal portion of the pulmonary nodule (white circle). CT, computed tomography.

around the distal end and resecting the lung parenchyma that was crossed by the hookwire. For the ROLL technique, a gamma detector probe (Navigator GPS, Dilon Medical Technologies, Newport News, VA, USA) was introduced through one of the VATS accesses. Radiotracer activity was detected inside the lesion, and the absence of significant activity in the surgical bed was assessed. In addition, we collected the following variables: type of resection, VATS success, need for reconversion to thoracotomy, and marker displacement. We consider a successful VATS when the surgeon was able to locate the nodule without any other measure (reconversion to thoracotomy, palpation...).

Pathological evaluation

The presence of the nodule within the surgical piece was verified perioperatively, and the volume of the resected lung was calculated. The volume of the surgical piece (in cubic centimeters) was calculated using a prolate ellipse volume calculation: height × width × length (all in centimeters) × $\pi/6$ (15).



Figure 2 Marking procedure with the ROLL technique. (A) 5-mm solid nodule located in the apicoposterior segment of the culmen (white circle). (B) The nodule is punctured with a 22-G needle using fluoroscopy-CT guidance. In the image, it can be seen that the tip of the needle is inside the nodule (white arrow). (C) SPECT/CT images in a lung window where it can be verified that all the radiotracer activity is inside the nodule (white arrow). (D,E) SPECT/CT volume-rendering reconstructions in the coronal (D) and sagittal (E) planes that allow determining the location of the radiotracer (white circle) that serves as a guide for the surgeon. ROLL, radioguided occult lesion localization; CT, computed tomography; SPECT, single-photon emission CT.

Statistical analysis

Results are reported as absolute number and frequency for qualitative variables and as mean and standard deviation (SD) or median and range for continuous variables. Student's *t*-test was used to compare continuous variables and the Chisquare test or Fisher's exact test for qualitative variables. The relationship between the volume of the piece and the distances from the nodule (PD and ND) for each group were determined using a simple linear regression study. The level of significance was considered at 5%. The analyzes have been carried out with the statistical program StatCrunch (Pearson Education 2020).

Results

Preoperative location

All of the nodules were resected during surgery: 52 nodules, corresponding to 49 patients, by hookwire



Figure 3 Radiological analysis of marking procedures. (A-E) Marking of a solid nodule with hookwire. (A) 9-mm solid nodule in the right upper lobe (white circle). (B,G) The white line reflects the minimum distance between the pleura and the nodule. (C,H) Placement of the hookwire introducer under CT-fluoroscopic guidance until reaching the periphery of the nodule (white arrow). The white line reflects the distance of the intrapulmonary path of the introducer until it reaches the node. (D) Final position of the hookwire is located adjacent to the nodule (arrowhead). In this example, it can be seen how the intrapulmonary path of the harpoon does not correspond to the shortest distance to the pleural surface. (E) Coronal reconstruction demonstrating the intimate contact between the hookwire coil and the pulmonary nodule 1 (arrowhead). (F-I) Marking of solid nodule with ROLL technique. (F) 3-mm solid nodule located in the posterior basal segment of the right lower lobe (white circle). (G) The white line indicates the shortest distance between the pleura and the nodule. (H) Puncture of the nodule using a 22-G needle and fluoroscopy-CT guidance. The white arrow indicates the point of the needle inside the nodule, and the white line indicates the distance of the intrapulmonary path of the needle until reaching the lesion. (I) The black arrowhead indicates the iodinated contrast material injected together with the radiotracer, which is inside the nodule and in its vicinity. CT, computed tomography; ROLL, radioguided occult lesion localization.

marking and 36 nodules, in 27 patients, by ROLL. No significant differences were observed in the size of the nodules (*Table 1*) or the PD (*Table 2*) between both groups. ND was significantly higher in ROLL-labeled nodules than in hookwire-marked nodules.

Complications

Complications derived from marking are described in *Table 2*. We found a higher percentage of pneumothorax in the hookwire group, although pneumothorax was asymptomatic in all cases. Hookwire migration occurred in 3/52 hookwire-tagged cases (5.8%) while none of the ROLL cases did. In the cases of migration of the hookwire, pulmonary resection was completed due to the presence of a pulmonary hematoma at the puncture site.

Surgical intervention

All nodules were located and resected that represents a successful CT localization of 100%. Only in one case of ROLL did it have to be converted to thoracotomy because the nodule was very central (1/36: 2.8%), representing a VATS success of 97.2%. There were no other intraoperative complications in any of the cases attributable to the markings.

Pathological study: volume of the surgical piece

The results relative to the volume of the piece are described in *Tables 2,3*. There is a good correlation between the PD and the volume of the piece in the ROLL group (r=0.53; P=0.001), while there is no correlation for the hookwire group. We found no correlation between the volume of the piece and the



Figure 4 Marking using the ROLL technique of two nodules, one in each lung, for resection in the same surgical act. (A) 7-mm solid nodule located in the medial segment of the middle lobe (white circle). (B) Puncture with a 22-G needle inside the nodule. (C) Confirmation CT scan after radiotracer injection showing contrast deposition inside the nodule (white arrow) and mild hemorrhage in the needle track (white arrowhead). (D) 6-mm solid nodule in the upper segment of the lingula (white circle). (E) Puncture with a 22-G needle inside the nodule. (F) Verification CT showing the deposition of contrast material inside the nodule (black arrow) and a small anterior pneumothorax (black arrowheads). ROLL, radioguided occult lesion localization.

Table 2 Distance of the nodules, complications related to the	procedure, and volume of the resected lung globally sample and according to groups	

	Global	Hookwire	ROLL	Statistical significance
Distances related to the nodule	e, mm			
PD, median ± SD [range]	9.36±8.07 [0-43]	10.13±7.47 [0-29]	8.25±8.87 [0-43]	NS
ND, median ± SD [range]	19.36±15.57 [0–97]	16.28±11.46 [0–55]	23.91±19.51 [0–97]	P=0.042
Complications				
Pneumothorax	44 (50.0)	36 (69.2)	8 (24.2)	P<0.0001
Pulmonary hemorrhage	41 (46.6)	25 (48.1)	16 (44.4)	NS
Volume of the resected lung, c	с			
Global	-	34.26 (52 nodules)	20.19 (36 nodules)	P=0.072
PD >0 mm	-	35.66 (48 nodules)	20.91 (33 nodules)	P=0.086

ROLL, radioguided occult lesion localization; PD, distance to the pleura; SD, standard deviation; ND, distance of the pulmonary path of the needle; NS, non-significative; cc, cubic centimeters; –, non-realized.

 Table 3 Relationship of the distances with the volume of the resected lung

Volume	Global	Hookwire	ROLL
Volume of the resected lung and PD	R=0.16, (P=0.13)	R=0.08, (P=0.56)	R=0.53, (P=0.001)
Volume of the resected lung and ND	R=0.05, (P=0.67)	R=0.13, (P=0.37)	R=0.10, (P=0.56)

ROLL, radioguided occult lesion localization; PD, distance between the nodule and the pleura; ND, distance of the intrapulmonary path of the needle.



Figure 5 Marking of a pulmonary nodule using the ROLL technique. (A) 7-mm nodule located in the posterior basal segment of the right lower lobe (white arrow). (B) Verification CT scan after radiotracer injection showing the intralesional disposition of the contrast material (black arrow) and hemorrhage in the puncture tract (white arrow). (C,D) Comparative diagram of the eventual resection of the same nodule according to the technique used. (C) Using the ROLL technique, despite the puncture path, the surgeon can perform a small wedge resection that only considers the location of the nodule and the shortest distance to the visceral pleura (triangle). (D) By using hookwire marking, in this same case, we would force a resection of the entire parenchyma crossed by the locator, which would significantly increase the volume of the piece (rectangle). ROLL, radioguided occult lesion localization; CT, computed tomography.

ND in either of the two groups (Figure 5, Table 3).

In the ROLL group, a smaller piece volume was observed, even for non-subpleural nodules, than in the hookwire group, although without statistically significant differences.

Discussion

Surgical resection of pulmonary nodules is an essential tool in managing primary and metastatic pulmonary lesions. Small nodules require a localization technique for intraoperative identification, such as the hookwire, the most common and first to be used, and the ROLL, with more than 20 years of experience (16,17). Our results demonstrate 100% resection success for both techniques but with a lower rate of complications with ROLL.

Other techniques have been described, such as palpation, ultrasound, or dyes. Palpation is the one that presents the worst detection rates, between 24-28% (14), being useful in solid nodules, larger than one centimeter in size, and located near the anterior or lateral walls of the chest (5,6). Dyes allow the location of lung lesions even by endobronchial puncture, but they present difficulties such as pleural diffusion (4%), confusion with other pigments

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such as anthracosis (18) and have a lower localization rate (86%). However other series published had demonstrated better results with dye injection that can reach 95% (19-21). Ultrasound, like other techniques, has better results than palpation [100% in some series (5)], although with the difficulty of ultrasound interpretation and the need for the collapse of the lung parenchyma, up to 40 minutes from the pleural incision (5). Hookwire marking achieves better results than palpation, 94% (14), but has some drawbacks such as migration and the appearance of symptomatic pneumothorax. In addition, localization with hookwire determines the volume of resection for the surgeon since the entire intrapulmonary trajectory of the marker must be removed (5). The ROLL technique, which has reported detection rates of 99-100% in series with long experience (16,17), requires a gamma detector probe in the operating room, a specialist in Nuclear Medicine to guide the surgeon during the resection, and a scintigraphy post tracer injection, not available at all centers. One drawback is the possibility of pleural diffusion of the radiotracer, which would prevent the location of the nodule (5). Other localization methods are less used, such as radioactive seeds, lipiodol, or coils (14,22) or combining methods as fluorescent iodized emulsion and hookwire (23). The meta-analysis by Park et al. (14) showed that the best results were obtained with lipiodol labeling compared to hookwire and microcoils. However, lipiodol presented more complications than microcoils, so the latter was considered the best option. Hookwire localization presented a 98% success rate since it was also possible to locate the nodule in cases with migration due to the hemorrhage caused during implantation. The review by Zaman et al. advises against palpation due to its worse results and highlights radiotracers as the best marking method due to their high precision with few complications (9).

In our study, localization using ROLL was more precise than using a hookwire since the hookwire moved in 5.8% of cases. However, the overall resection rate in both cases was 100% since, in the cases in which the hookwire migrated, the hemorrhage in the puncture tract allowed the nodule detection. This percentage is within what was previously published (0.4–9%) (6,7,24,25). The migration of the hookwire has been related to the patient's movements [especially in nodes anterior to the scapula (26)], cough (27) and the short pleura-node distance (28). Pleural migration of the radiotracer for ROLL (5) has also been described, mainly in subpleural lesions (29), both in peripheral and fissural pleura, as with coils. In our series we did not have any cases of radiotracer migration. We believe that this is due to the injection of the radiotracer inside the nodule and not in its vicinity. This fact probably prevents the tracer from migrating to the pleura even in subpleural nodules.

VATS was converted into a mini-thoracotomy during the resection of a nodule due to central location, representing a 2.8% similar to that described in the literature (16).

Although the volume of resected parenchyma is lower in the ROLL group, the differences are not significant, probably due to the sample size. Nevertheless, the volume of the piece may have an impact in these patients, mainly with a history of oncology, since they could require new lung resections, and preservation of lung parenchyma is important.

In the analysis of the volume of the part, the PD shows a good correlation with the volume of the part. ND does not correlate with volume with either technique. This shows that resection with ROLL allows obtaining a size of the piece that is only affected by the relationship of the nodule with the pleura and not by the lung distance traveled by the needle. Probably, the path traveled by the needle is what determines the volume of parenchyma resected when using the hookwire (5), but not when using ROLL, since it allows the surgeon to choose the best approach, which will be the closest to the pleura. We must point out that, in our series, the distance of the intrapulmonary path of the needle is more significant than that reported in other works with ROLL (30,31). This has allowed us to resect subpleural lesions adjacent to the fissural or mediastinal pleura.

Regarding complications, we detected a high percentage (50%) of pneumothorax in cases marked with a hookwire. The rates published in the literature range between 5.9% (32) and 68.0% (7), in this previous study with 4.6% of pleural drainage prior to surgery. In our series, no patient developed symptomatic pneumothorax or required a pleural drainage tube placement prior to surgery. According to the meta-analysis by Park *et al.* (14), the mean rate of pneumothorax after placement of a hookwire was 35%, being higher than that identified when using coils (16%) or lipiodol (31%).

We found no significant differences regarding postprocedural pulmonary hemorrhage between both groups. The percentage of hookwires that caused pulmonary hemorrhage is within the range reported in previous publications: 1.3% (33) to 41.6% (34). Postprocedural bleeding seems to be inherent to the marking and not to the type of procedure. In contrast, in the meta-analysis by Park (14), differences were found between the percentage of bleeding between the hookwire (16%), lipiodol (12%), and the coils (6%). According to Ichinose *et al.* (7), an intrapulmonary needle path greater than 25 mm is a risk factor for developing hemorrhage and hemoptysis.

On the other hand, patients who require marking of several nodules tend to present more complications if the hookwire is used (26). In our series, we only located several nodules in the same patient using ROLL, without any serious associated complications.

Another critical element is the cost of the technique. Localization with ROLL is cheaper, as it had been published, than marking with a hookwire or with coils (22) and, with the new hybrid equipment, it is possible to reduce the time and cost of the examination by being able to perform the procedure in the same Nuclear Medicine department using a SPECT/CT with incorporated fluoroscopy (35) or to assess the margins intraoperatively, using a portable gamma camera (36).

Our work has some limitations. In the first place, it is a comparative analysis of two techniques, in which one of them has been performed prospectively (ROLL) while the evaluation of the data of the hookwire resection is retrospective. However, the same radiologists have carried out the assessment of complications and the measurement of distances for all the cases in the series. Another potential limitation would be the limited number of patients reviewed. It would be expected that, with a more significant number of patients in both techniques, but especially in the ROLL arm, it would be possible to demonstrate that hookwire marking determines more significant resection volumes, which, in our series, is only a trend. Finally, it is a single-center study, which guarantees the homogeneity of the methodology and the data collected but lacks external validity.

Among the strengths of this study, the comparison between the ROLL technique within the same center stands out, therefore without bias from the surgical team. Most of the published articles refer to a single type of marker, and the comparative studies compare the results carried out in different works or compare the hookwire with other localization techniques, but not with ROLL, except for Gonfiotti *et al.* (13), who also did not find differences in the successful marking between both techniques. In contrast, in our series, we have detected a more significant number of complications with the hookwire. Gonfiotti *et al.* had 16% of cases of displacement of the hookwire prior to resection that prevented the nodule's location and only 4% of pleural diffusion of the radiotracer that did not allow detection (13), higher than those observed in our series. Our work demonstrates that both markers offer a high success rate in the resection of pulmonary nodules, but the ROLL technique allows more minor tissue resection and is associated with a lower rate of complications. In addition, it does not limit the patient's mobility since the chest wall externalizes no element, nor does it condition the volume of tissue that must be removed or the surgical approach. The intrapulmonary path of the needle does not affect the result of the procedure and allows the marking of several lesions in the same lung or both in the same act. In addition, the ROLL technique provides greater flexibility in surgical programming, being able to schedule these patients first thing in the morning, having scheduled the day before. However, prospective, randomized, multicenter studies are needed to compare the different types of markers and to confirm these findings with external validity.

Conclusions

The location of pulmonary nodules with hookwire and using ROLL offer an excellent resection rate with the ROLL technique. The rate of complications is lower with ROLL technique. The intrapulmonary path traveled by the needle does not affect the volume of the surgical piece, and the only important thing is the distance at which the pleural nodule is located, so this technique allows the resection of deep nodules with maximum preservation of healthy lung parenchyma.

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Footnote

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Ethical Statement: The authors are accountable for all

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aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The analysis was performed after the approval of the local ethics committee (Comitè d'Ètica de l'Hospital Clínic de Barcelona; HCB/2016/0147). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). In addition, all patients signed the informed consent before the interventional and surgical procedures.

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