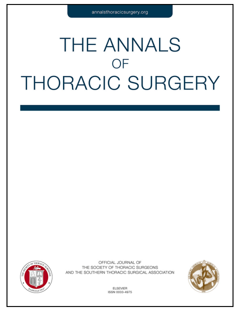
Accepted Manuscript



CT-Guided Percutaneous Radiotracer Localization and Resection of Indistinct/Small Pulmonary Lesions

Domenico Galetta, MD, PhD, Cristiano Rampinelli, MD, Luigi Funicelli, MD, Monica Casiraghi, MD, Chiara Grana, MD, Massimo Bellomi, MD, Lorenzo Spaggiari, MD, PhD

PII: S0003-4975(19)30624-1

DOI: https://doi.org/10.1016/j.athoracsur.2019.03.102

Reference: ATS 32594

To appear in: *The Annals of Thoracic Surgery*

Received Date: 4 December 2018

Revised Date: 19 March 2019

Accepted Date: 29 March 2019

Please cite this article as: Galetta D, Rampinelli C, Funicelli L, Casiraghi M, Grana C, Bellomi M, Spaggiari L, CT-Guided Percutaneous Radiotracer Localization and Resection of Indistinct/Small Pulmonary Lesions, *The Annals of Thoracic Surgery* (2019), doi: https://doi.org/10.1016/j.athoracsur.2019.03.102.

CT-Guided Percutaneous Radiotracer Localization and Resection of Indistinct/Small Pulmonary Lesions

Running Head: Lung Nodules Localization and Resection

Domenico Galetta, MD, PhD[1]

Cristiano Rampinelli, MD[2]

Luigi Funicelli, MD[2]

Monica Casiraghi, MD[1]

Chiara Grana, MD[3]

Massimo Bellomi, MD[2,4]

Lorenzo Spaggiari, MD, PhD[1,4]

[1]Division of Thoracic Surgery, European Institute of Oncology, IRCCS, Milan, Italy

[2]Division of Radiology, European Institute of Oncology, IRCCS, Milan, Italy

[3]Division of Nuclear Medicine, European Institute of Oncology, IRCCS, Milan, Italy

[4]Department of Oncology and Hematology-Oncology-DIPO, University of Milan, Milan, Italy.

Keywords: Lung Cancer Surgery, Computed tomography, Minimally invasive surgery

Word count: 4589

Corresponding Author:

Domenico Galetta, MD, PhD

Division of Thoracic Surgery

European Institute of Oncology

Via Ripamonti, 435, Milan, Italy

E-mail: mimgaletta@yahoo.com

Abstract

***Background**:* Detection of small pulmonary lesions has increased and often they are difficult to localize and resect. We present our mature experience with preoperative computer-tomography (CT)-guided radiotracer localization followed by resection of these lesions.

***Methods**:* Patients with pulmonary nodule smaller than 1 cm and/or deep below the visceral pleura underwent CT-guided injection of radiotracer technetium macroaggregates (99mTc-MAA) in/close to the lesion. A gamma probe was used to localize the marked area that was resected and in case of primary lung cancer, a lobectomy with nodal dissection was performed.

***Results**:* Between November 2007 and December 2017, 262 patients (196 men; median age 63 years) underwent preoperative radiotracer injection with a successful marking in all patients. Complications included 35 (13.4%) asymptomatic pneumothoraces, 36 (13.7%) parenchymal hemorrhage suffusions, and 2 (0.7%) mild allergic reactions to contrast medium. In all cases, except for 3, the gamma probe revealed the pulmonary lesion. Mean distance from the pleura was 10 mm (range, 0-40 mm). Pulmonary resection was performed by thoracoscopy in 212 (80.9%) cases, intentional thoracotomy in 42 (16.0%), converted thoracoscopy in 8 (3.1%). Mean pathological nodule size was 9.3 mm (range, 2.5-39 mm). 166 (63.4%) nodules were nonsolid, 64 (24.4%) were partially solid, and 32 (12.2%) had a solid morphology. Histology showed 16 (6.1%) benign and 246 (93.9%) malignant lesions (218 primary lung cancers).

***Conclusions**:* Preoperative radiotracer localization of small/indistinct pulmonary lesions is simple and feasible with a high rate of success. It may be an effective and attractive alternative in managing lung lesions.

Abstract Word count: 249

In the last decades, thoracic surgeons are faced more and more with the management of an increasing number of patients with small lung nodules due to a diffuse use of computed tomography (CT) scans in daily clinical practice [1-6]. These patients are evaluated based on patient and imaging characteristics to determine the probability of the nodule being malignant [7].

The early diagnosis of these small pulmonary nodules is important because in cases of lung cancer the prognosis of these patients is correlated with their size [8,9]. However, preoperative attempts to obtain a cytological or histological diagnosis through transbronchial or transthoracic needle biopsy and positron emission tomography (PET) scans do not always allow definitive exclusion of the malignant nature of these lesions [10,11]. Patients with a solitary small lung nodule that is highly suspicious for primary lung cancer undergo wedge resection, intraoperative pathological evaluation, followed by a lobectomy, if proven malignant.

Traditionally, these patients underwent a thoracotomy followed by palpation of the lung and eventually resection of the lesions. Patients with a nodule that was >5 mm away from the pleura that was <1 cm in size had about 63% chance of needing thoracotomy to remove the nodule [12]. However, the advancement of both video-assisted thoracoscopic surgery (VATS) and robotic-assisted minimally invasive procedures has led to the development of advanced localization techniques to avoid thoracotomy.

Advanced localization techniques are performed with either transbronchial or transthoracic localization. The most common transbronchial technique utilizes electromagnetic navigation bronchoscopy to place a fiducial marker with concurrent methylene blue dye injection. On subsequent thoracoscopic examination, the lesion can be identified with methylene blue on direct visualization and the fiducial can be identified with fluoroscopy [13]. Another option is to perform transthoracic localization with CT-guidance by a radiologist who leaves a hookewire [14-16], microcoil [17-19], dye and contrast dye [20-24] or radiotracer in the nodule immediately prior to surgical resection [25-30]. This latter method has been largely used in our Institution since 2007. It consists in the preoperative percutaneous placement of a technetium (^{99}TC) radiotracer in or near the lung lesion using CT guidance with subsequent thoracoscopic localization by endoscopic radio probe. This technique has been modified by other authors [26-28] who used ^{99}TC macro-aggregated albumin (MAA) that stayed localized in lung parenchyma for 18-24 hours.

The purpose of this study was to evaluate the results of our consolidated experience in terms of feasibility, safety, and efficacy of the procedure of preoperative CT-guided radiotracer localization followed by resection of small, indistinct, or non-palpable pulmonary lesions.

PATIENTS AND METHODS

Study Patients

The proposal to place ^{99}TC radionuclide to guide subsegment lung resection was approved by our Institutional Review Board. All patients with small pulmonary nodules who were enrolled to receive preoperative CT-guided radiotracer localization followed by resection were informed of the procedure's benefits, risks, and limitations and gave their written approval.

Between November 2007 and December 2017, 262 consecutive patients underwent radiotracer injection followed by thoracoscopic localization for solitary undiagnosed lung nodules. Patients who had more than one nodule requiring localization were excluded from this study.

Indication for Tumor Localization

Indications for surgical biopsy of the small or ill-defined pulmonary lesion were the presence of a PET positive nodule or a nodule increasing in size in subsequent CT scans even if PET was negative. Patients were selected for the radiotracer procedure in the following cases: a) when solid nodules were present, localization was recommended for small (diameter <10 mm) or deeply located (distance from the visceral pleura >10 mm) nodules; b) subpleural cavitary lesions and ground glass opacities (GGOs) were localized regardless of their size and depth.

Technique of preoperative CT-guided radiotracer localization

The technique of preoperative localization of lung lesions by the use of preoperative CT-guided percutaneous placement of ^{99}TC radiotracer has been previously reported [29, 30]. Briefly, a radiologist experienced in interventional techniques performed CT-scan localization (Figure 1A). Positioning of patients in the CT scanner was performed to achieve the shortest direct path from the skin to the pulmonary lesion to be marked. Images acquired to localize the lesion were 1.25 mm thick without contrast medium. When possible, a direct and vertical needle trajectory was used to reach the target lesion. After injection of local anesthetic, the correct placement of the tip of a 25G needle in or near the nodule was verified with a further series of 12 to 20 images (Figure 1B). Once this was confirmed, 0.2 to 0.3 mL of a solution composed of 0.1 to 0.15 mL ^{99}TC-MAA (MAASOL; GE Healthcare, Buckingamshire, UK) and 0.1 to 0.15 mL nonionic iodinated contrast medium was injected. Depending on the time interval between localization and the planned surgery, 4 μg to 9 μg human serum albumin macro aggregates labeled with 7 to 15 MBq eluted ^{99}TC-MAA were used. A further CT scan was performed at the end of the injection procedure to define the distribution of the contrast medium, which also allowed us to check for any iatrogenic pneumothorax (Figure 1C). An immediate postprocedure nuclear medicine scintigram was obtained to confirm the intraparenchymal location of the radiotracer (Figure 1D).

Surgical Treatment

The surgical procedure was performed within 24 hours from the nodule localization with ^{99}TC-MAA, either on the same day or the next day. The patient was placed in the lateral decubitus position after that a general anesthesia with single-lung ventilation was induced. Video-thoracoscopic camera was usually introduced in the VII intercostal space. A second thoracoscopic incision or small anterior utility thoracotomy was then performed for the introduction of the endoscopic gamma detecting probe (Neo 2000; Neoprobe, Dublin, OH) (Figure 2A) which allowed to identify the exact location of the nodule passing its over the surface of the involved lung (Figure 2B). In some cases, this procedure was performed trough a lateral muscle-sparing thoracotomy. The identification of the nodule was based on the maximum signal intensity by both a numeric and an acoustic signal (Figure 2C). The identified ^{99}TC marked area was lifted up and a long clamp was positioned below this area. The lung parenchyma below the clamped zone was checked by radioprobe (Supplemental File 1,A) and if the signal was absent or very low respect to the marked nodule, the stapler was placed here and fired (Supplemental File 1,B), and the specimen was removed in an endobag. The radioprobe was used to confirm the absence of signal in the remaining lung (both stapled line and nearby parenchyma) (Supplemental File 1,C) and to determine scintigram counts of the resected specimen (Figure 2D). A frozen-section examination of the resected lesion was performed. Patients with a confirmed diagnosis of primary lung cancer underwent immediate lobectomy or segmentectomy followed by nodal dissection.

RESULTS

Characteristics of Patients and Pulmonary Lesions

Between November 2007 and December 2017, 262 patients with ill-defined or not palpable pulmonary lesions underwent CT-guided radiotracer placement, with a successful marking in all the patients, and radio-guided surgical biopsy. Table 1 depicts the general characteristics of the study participants. There were 196 male and 66 female patients, with a median age of 63 years (range, 19 to 79). The mean nodule size was 9.3 mm (range, 2.5-39 mm). Radiological aspects of the pulmonary nodules were as follows: in 166 cases (63.4%) they were non-solid with GGO aspect; in 64 cases (24.4% they were partially solid, and in 32 cases (12.2%) they were solid lesions.

Localization Procedure

No significant complications occurred in relation to CT-guided marking of the lesion, except for a) 35 patients (13.4%) who developed a small asymptomatic pneumothorax (demonstrated only by post-procedural CT and ranging from few millimeters to 3.0 cm) all managed conservatively except two requiring chest tube placement before surgery; b) 36 patients (13.7%) who presented a parenchymal hemorrhage suffusion which did not need neither surgical intervention, nor blood transfusion; c) and two cases (0.7%) who had mild allergic reaction after the percutaneous injection of contrast medium controlled by of steroid administration. Of these patients, four had simultaneously a pneumothorax associated with hemorrhage suffusion.

All radiotracer injections were confirmed with scintigraphy which showed that 248 patients (94.6%) had a correct radiotracer positioning while 14 patients (5.4%) had a mild extravasion of radiotracer into the pleura or diffusion into the surrounding area of the target; however, that did not interfere with the detection of radiotracer at surgery. 105 patients (40.1%) underwent surgery on the same day of the localization procedure, and 157 patients (59.9%) the day after the localization procedure. The reduction of radioactive signal related to the 6-hour half-life of ^{99}TC-MAA in the delayed cases did not affect our ability to localize lesions.

Operative and Perioperative Results

At surgery, pulmonary resection of the lung undetermined nodule was performed by thoracoscopy in 212 patients (80.9%) and by intentional thoracotomy in 42 cases (16.0%). Intentional thoracotomy was performed for deep nodules that the surgeon believed were not removable by the thoracoscopic stapling technique. The nodules were not palpable at open thoracotomy and required radioprobe guidance for localization and successful excisional biopsy. Eight patients (3.1%) required conversion to open thoracotomy and biopsy after thoracoscopic assessment of the nodule's actual location by the operating surgeon judged the nodule was too deep for thoracoscopic wedge excision (Table 2). In every case a frozen section of the nodule was performed and the surgical procedure was then completed according to the result of the pathological examination. Table 2 reported the histology of the biopsied nodules. There were 16 cases (6.1%) of benign lesions while malignant lesions were encountered in 246 cases (93.9%). Of these, 218 patients (83.2%) had a primary lung cancer while 28 patients (10.7%) had a metastatic lesion. All patients found to have primary lung cancer underwent an immediate lobectomy and lymph node complete resection or, if severe emphysema was present, underwent a segmentectomy or a wide wedge resection. Overall, lobectomy was performed in 187 patients, segmentectomy in 11 cases, and wedge resection in 64 cases. A frozen section of the surgical margins of the initial wedge resection of the 246 malignant cases was also performed and in no of these there was microscopic neoplastic disease. Neither intraoperative nor postoperative mortality occurred. Postoperative complications were reported in 32 cases (12.2%) and included prolonged air leaks (n=24), atrial fibrillation (n=6), pulmonary embolism (n=1), and transient ischemic attack (n=1).

COMMENT

As the use of CT becomes widespread in clinical practice, the frequency of encountering small or faint lesions on CT is increased [31]. Low-dose CT greatly increases the likelihood of detection of small nodules, and 51.7% of detected lung cancers found during baseline screening were GGO [32]. According to some authors, these small nodules may be safely followed with serial CT scans to assess for their growth; some of these nodules, particularly those less than 5 mm, are said to be unlikely to be malignant. However, there is an increasing rate of malignancy in nodules greater than 5 mm. In some experiences, is reported that a 12% of patients with nodules between 5.0 and 9.0 mm were diagnosed with malignancy at follow-up [32]. It is intuitive that the risk of malignancy increases with the increasing diameter of the pulmonary nodule. Given these data, it is essential to definitively establish a diagnosis for small lung nodules in high-risk patients.

The accurate early diagnosis of these small nodules is challenging, even with dedicated CT, PET-CT, or image-guided percutaneous biopsy [10, 11]. We have not found percutaneous biopsy to be useful for these lesions, particularly for sub centimeter nodules. Others have reported a significant risk of false-negative results and complications with this technique [33]. The most accurate means for obtaining a definitive tissue diagnosis for suspicious, small nodules remains the surgical excision biopsy.

VATS resection remains the preferred surgical procedure for both diagnosis and, in selected cases, treatment of pulmonary nodules. One of the major problems often encountered during VATS is localization of the target nodule, which depends on its location, size, and characteristics such as nodule consistency. Further, when small nodules are located more than 2 cm below the pleural surface, it is difficult for surgeon to determine their exact location during operation [34]. Failure to localize pulmonary nodules often results in the conversion of VATS to open thoracotomy with a conversion rate ranging from 54% up to 63% for subcentimeter nodules [12, 35].

Several preoperative and intraoperative techniques have been described for nodule localization when performing VATS [13-30]. These procedures include metallic hookwire localization under CT guidance, CT-guided micro-coil, a localization technique using barium or staining with methylene blue, and endothoracic pulmonary sonography. These methods are generally effective but burdened with significant rates of failure and complications: a) dye placement is limited by diffusion away from the nodule and difficulty in visualization in patients with extensive anthracotic pigmentation; b) the injection of liquids that are not soluble may be a potential risk of embolism and cerebrovascular accidents if these inadvertently reach the systemic circulation [22]; c) there is an high incidence of dislodgement of the hookwire or micro-coil during transportation to the operating room or during lung deflation for thoracoscopy, inducing pneumothorax, or during the maneuvers for pulmonary surgical resection, thereby rendering the procedure unsuccessful. Moreover, probably due to this dislodgement, the hookwire technique may lead to intrapulmonary hemorrhage, pleuritic pain, and air embolism.

The main advantage of the intraoperative thoracoscopic ultrasonography technique for the localization of pulmonary nodules is that it does not require preoperative procedures. Unfortunately, this technique has an intrinsic limitation due to the absence of propagation of ultrasound in the presence of air. Therefore, in patients with emphysematous lung, in case of incomplete pulmonary collapse and in case of the presence of small and deep lesions, the rate of successful localization is seen to reduce significantly. Moreover, its success is operator-dependent [36].

In the literature are reported few experiences with the use of the percutaneous injection of radiotracer [26-30]. We perform CT-guided radiotracer injection using ^{99}TC-MAA solution, modifying the technique described by Grogan [28], by adding a small amount of nonionic iodinated contrast medium to the radiotracer which allowed (a) to visualize the contrast medium distribution in relation to the nodule and (b) better guides the intraoperative localization performed by the surgeon.

CT-guided percutaneous radiotracer localization seems to overcome many of the limitations of the previous mentioned techniques, has a high success rate, and has fewer and acceptable procedure-related complications. The marking of the nodule with a radiotracer is possible in any portion of the lung and does not interfere with the histological examination. Furthermore, the technique can increase the accuracy of the resection by verifying in real time the absence of radioactivity just above and below the stapler line, thus assuring an adequate oncological margin. Other advantages of this technique are the following: it does not require intraoperative fluoroscopy, does not require a skilled ultrasonographer, and uses an available radionuclide (lung scan), available radio probes (breast sentinel node procedures), available CT technology, and available thoracoscopic technology.

Some pitfalls have been experienced but have been adjusted for. The first one, occurring in 4 cases in our experience, is the possibility of an extravasation of the radiotracer inside the lung parenchyma in case of bullous emphysema adjacent to the nodule. This can lead to a wider area of radioactivity, which reduces the precision of the resection. In our experience, we preferred to convert to a small thoracotomy, with the nodule nonetheless found inside the radioactive area. On the basis of this experience, we can say that bullous emphysema around the target lesion could be considered the only true contraindication for this technique. However, we overpass this risk by leaving the radiotracer near the target area and performing the lung resection according the exact visualization of CT scans which guide us to the correct identification of the lung area that must be resected.

A second pitfall also described by other authors [26, 28], and occurred in 10 patients of our experience, is the spillage of the radiotracer into the pleural space, which may happen if the radiotracer is injected near the pleural surface of a major fissure, or more frequently if a pneumothorax develops during injection. This increases the ground radioactivity, thus enabling the correct localization of the lesion, even if, as occurred in our experience, part of the radiotracer was correctly injected within the nodule. We overcame this pitfall by adopting routine post-CT-placement nuclear medicine scintigram to confirm parenchymal placement of the radiotracer.

A third pitfall could be considered the relatively short half-life of the radionuclide, which may lead to some difficulties in scheduling injection procedure and operation. Preoperative marking of the lesion should be followed by surgical resection, either immediately or within a few hours. Thus, in case the planned operation must be postponed, radiotracer could have dissolved the day after its introduction and no longer be detectable. In our experience, this problem has been overcome with the ^{99}TC MAA solution that does not dissipate rapidly into the lymphatic system or surrounding parenchyma. In fact, we successfully localized nodules up to 15-20 hours after the injection of the contrast. In our experience about 60% of patients were operated on the day after the radiotracer injection without difficulty to detect the marked area.

Evaluating the risks of this procedure, we have to underline the possibility to develop a pneumothorax like all procedures that require CT-guided placement. In our experience, in all the cases in which this happened (n=25, 9.6%), it was small and asymptomatic except for two cases requiring a chest drain placement before surgery.

The rate of detection through videothoracoscopic approach was high in our experience reaching the rate of 80.9% (n=212). Even during the open approach, the method was useful for the correct localization of the nodule, which was resected through simple wedge resection or typical segmentectomy. Another important point to consider is the risk of pleural dissemination due to the presence of positive surgical margins with initial wedge resection. Pathologic data on the surgical margins of the initial wedge resection of the 246 malignant cases revealed that in no of these there was microscopic neoplastic disease on the resected margins. This data confirm that our technique of nodule identification and resection may be considered a safe procedure without risk of pleural dissemination.

At the light of our mature experience, we can affirm that the radiotracer localization technique is safe and effective, as evidenced by the acceptable rate of minor complications after the radiotracer injection, by the absence of intraoperative and perioperative morbidity and mortality, and the high rate of malignancy in resected nodules (93.9%). Our use of the localization procedure for both VATS and thoracotomy shows that this is a versatile technique that can be applied to various surgical approaches.

In conclusion, we have reported here our results of a large-experience in using radiotracer localization and subsequent radioprobe-guided excision in 262 patients with small or undefined pulmonary nodules. All nodules were successful localized and excised; most of them were malignant, 83.2% being primary lung cancer. Excised benign nodules were a very small amount (6.1%); thus, we believe that high rate of resected primary lung cancers justifies the use of this technique in patients with the clinical and radiologic suspicious of lung cancer.

References

1. Bai C, Choi CM, Chu CM, et al. Evaluation of pulmonary nodules: clinical practice consensus guidelines for Asia. Chest 2016;150:877-93.

2. National Lung Screenin Trial Research Team, Aberle DR, Adams AM, Berg CD, et al. Reduced lung cancer mortality with low-dose computed tomographic screening. N Engl J Med 2011;365:395-409.

3. Lehman SJ, Abbara S, Cury RC, et al. Significance of cardiac computed tomography incidental findings in acute chest pain. Am J Med 2009;122:543-9.

4. Erasmus JJ, Connolly JE, McAdams HP, et al. Solitary pulmonary nodules: Part I. Morphologic evaluation for differentiation of benign and malignant lesions. Radiographics 2000;20:43-58.

5. Erasmus JJ, Connolly JE, McAdams HP, et al. Solitary pulmonary nodules: Part II. Evaluation of the indeterminate nodule. Radiographics 2000;20:59-66.

6. McWilliams A, Tammemagi MC, Mayo JR, et al. Probability of cancer in pulmonary nodules detected on first screening CT. N Engl J Med 2013;369:910-9.

7. Chan EY, Gaur P, GE Y, et al. Management of the solitary pulmonary nodule. Arch PAthol Lab Med 2017;141:927-31.

8. Birim O, Kappetein AP, Takkenberg JJ, van Klaveren RJ, Bogers AJ. Survival after pathological stage Ia non small cell lung cancer: tumor size matters. Ann Thorac Surg 2005;79:1137-41.

9. Port JL, Kent MS, Korst RJ, Libby D, Pasmantier R, Altorki NK. Tumor size predicts survival within stage IA non-small cell lung cancer. Chest 2003;124:1828-33.

10. Kozower BD, Meyers BF, Reed CE, Jones DR, Decker PA, Putnam JB Jr. Does positron emission tomography prevent non therapeutic pulmonary resections for clinical stages IA lung cancer? Ann Thorac Surg 2008;85:1166-9.

11. Kothary N, Lock L, Sze DY, Hofmann LV. Computed tomography-guided percutaneous needle biopsy of pulmonary nodules: impact on nodule size on diagnostic accuracy. Clin Lung Cancer 2009;10:360-3.

12. Suzuki K, Nagai K, Yoshida J, et al. Video-assisted thoracoscopic surgery for small indetermined pulmonary nodules. Indications for preoperative marking. Chest 1999;115:563-8.

13. Bolton WD, Howe H 3rd, Stephenson JE. The utility of electromagnetic navigational bronchoscopy as a localization tool for robotic resection of small pulmonary nodules. Ann Thorac Surg 2014;98:471-5.

14. Saito H, Minamiya Y, Matsuzaki I, et al. Indication for preoperative localization of small peripheral pulmonary nodules in thoracoscopic surgery. J Thorac Cardiovasc Surg 2002;124:1198-202.

15. Gonfiotti A, Davini F, Vaggelli L, et al. Thoracoscopic localization techniques for patients with solitary pulmonary nodules: hook wire versus radio-guided surgery. Eur J Cardiothorac Surg 2007;32:843-7.

16. Ciriaco P, Negri G, Puglisi A, et al. Video-assisted thoracoscopic surgery for pulmonary nodules: rationale for preoperative computed tomography-guided hookwire localization. Eur J Cardiothorac Surg 2004;25:429-33.

17. Chen YR, Yeow KM, Lee JY, et al. CT-guided localization of subpleural lung lesions for video-assisted thoracoscopic surgery (VATS). J Formos Med Assoc 2007;106:911-8.

18. Powell TI, Jangra D, Clifton JC, et al. Peripheral lung nodules: fluoroscopically guided video-assisted thoracoscopic resection after computed tomography-guided localization using platinum micro coils. Ann Surg 2004;240:481-8.

19. Mayo JR, Clifton JC, Powell TI, et al. Lung nodules: CT-guided placement of microcoils to direct video-assisted thoracoscopic surgical resection. Radiology 2009;250;576-85.

20. Vandoni R, Cuttat JF, Wicky S, et al. CT-guided methylene-blue labeling before thoracoscopic resection of pulmonary nodules. Eur J Cardiothorac Surg 1998;14:265-70.

21. Nomori H, Horio H, Naruke T, Suemasu K. Fluoroscopy-assisted thoracoscopic resection of lung nodules marked with lipiodol. Ann Thorac Surg 2002;74:170-3.

22. Watanabe K, Nomori H, Ohtsuka T, et al. Usefulness and complications of computed tomography-guided lipiodol marking for fluoroscopy assisted thoracoscopic resection of small pulmonary nodules: experience with 174 nodules. J Thorac Cardiovasc Surg 2006;132:320-4.

23. Magistrelli P, D'Ambra L, Berti S, et al. Use of India ink during preoperative computed tomography localization of small peripheral undiagnosed pulmonary nodules for thoracoscopic resection. World J Surg 2009;33:1421-4.

24. Moon SW, Wang YP, Jo KH, et al. Fluoroscopy-aided thoracoscopic resection of pulmonary nodule localized with contrast media. Ann Thorac Surg 1999; 68:1815-20.

25. Chella A, Lucchi M, Ambrogi MC, et al. A pilot study of the role of TC-99 radionuclide in localization of pulmonary nodular lesions for thoracoscopic resection. Eur J Cardiothorac Surg 2000;18:17-21.

26. Ambrogi MC, Melfi F, Zirafa C, et al. Radio-guided thoracoscopic surgery (RGTS) of small pulmonary nodules. Surg Endosc 2012:26:914-9.

27. Daniel TM, Altes TA, Rehm PK, et al. A novel technique for localization and excisional biopsy of small or ill-defined pulmonary lesions. Ann Thorac Surg 2004;77:1756-62.

28. Grogan EL, Jones DR, Kozower BD, Simmons WD, Danielm TM. Identification of small nodules: technique of radiotracer-guided thoracoscopic biopsy. Ann Thorac Surg 2008;85:S772-7.

29. Bellomi M, Veronesi G, Trifirò G, et al. Computed tomography preoperative radiotracer localization of nonpalpable lung nodules. Ann Thorac Surg 2010;90:1759-65.

30. Galetta D, Bellomi M, Grana C, Spaggiari L. Radio-guided localization and resection of small or ill-defined pulmonary lesions. Ann Thorac Surg 2015;100:1175-80.

31. Swensen SJ, Jett JR, Hartman TE, et al. CT screening for lung cancer: five year prospective experience. Radiology 2005;235:259-65.

32. Henschke CL, McCauley DI, Yankelevitz DF, et al. Early Lung Cancer Action Project: overall design and findings from baseline screening. Lancet. 1999:354:99-105.

33. Midthun DE, Swensen SJ, Jett JR. Clinical strategies for solitary pulmonary nodules. Ann Rev Med 1992;43:195-208.

34. Mack MJ, Hazelrigg SR, Landreneau RJ, Acuff TE. Thoracoscopy for the diagnosis of the indeterminate solitary pulmonary nodule. Ann Thorac Surg 1993;56:825-30.

35. Cardillo G, Regal M, Sera F, et al. Videothoracoscopic management of the solitary pulmonary nodule: a single-institution study on 429 cases. Ann Thorac Surg 2003;75:1607-11.

36. Mattioli S, D'Ovidio F, Daddi N, et al. Transthoracic endosonogrphy for the intraoperative localization of lung nodules Ann Thorac Surg 2005;79:443-9.

Table 1. *Clinical and radiological characteristics of the population*

Variable	Number
Patient population	262
Male/Female	196/66
Median age (range)	63 years (19-79)
Mean nodule size (range)	9.3 mm (2.5-39)
Mean pleural distance (range)	10 mm (0-40)
Nodule morphology (%)	
Non solid	166 (63.4%)
Partially solid	64 (24.4%)
Solid	32 (12.2%)
Radiological complications	63 (24%)
Aymptomatic pneumothorax	35 (13.4%)
Parenchymal hemorrhage soffusion	36 (13.7%)
Mild allergic reaction to c.m.	2 (0.7%)
Radiotracer confirmation at scintigraphy	
Correct	248 (94.6%)
Extravasation	14 (5.4%)

c.m. = contrast medium

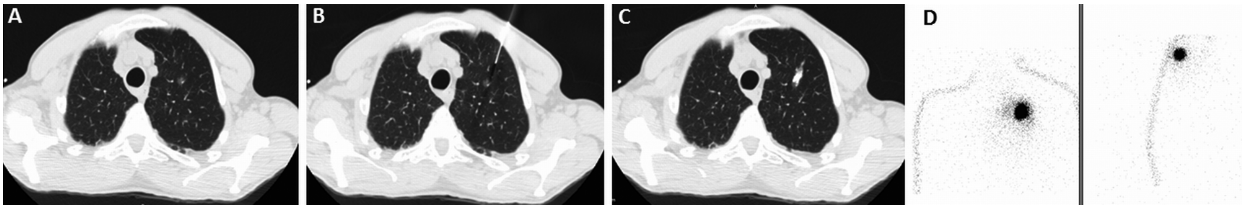
Table 2. *Surgical and Pathological Characteristics of the Population*

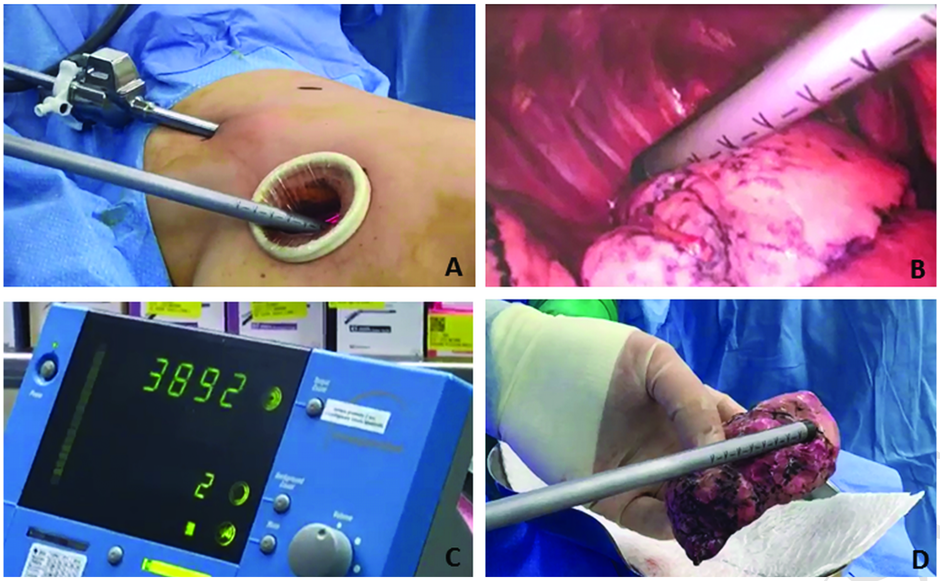
Variable	**Number**
Patient population	262
Time of the surgical resection	
Same day of injection	105 (40.1%)
Day after injection	157 (59.9%)
Pulmonary resection technique	
Thoracoscopy	212 (80.9%)
Intentional Thoracotomy	42 (16.0%)
Converted Thoracoscopy	8 (3.1%)
Histology (%)	
Benign	16 (6.1%)
Malignant	246 (93.9%)
Primary lung cancer	218 (83.2%)
Metastasis	28 (10.7%)

Figure Legends

Figure 1. CT images of the percutaneous placement of technetium and scintigram exam. A. CT scan localization of the GGO in the left upper lobe. B. Placement of needle tip near the GGO. C. CT scan at the end of procedure. D. Scintigram showing the correct placement of the radiotracer.

Figure 2. Surgical technique of identification of the marked nodule. A. Introduction of the gamma probe under thoracoscopic vision. B. Identification of the marked nodule by the gamma probe. C. Visualization of the maximum intensity of the numeric radioactivity signal. D. Identification the nodule directly on the resected specimen.


A
B
C
D


A
B
3892
2
C
D