Efficiency of radioguided occult lesion localization for labelling surgical lung lesions☆

Eficacia de la localización radioguiada para el marcaje de lesiones pulmonares quirúrgicas ocultas

To the Editor:

In recent years, the need to diagnose and treat ever smaller lung lesions or nodules with a limited solid component has increased. Multiple endoscopic and image-guided diagnostic techniques are now at our disposal, but when these methods fail, the next step is diagnostic-therapeutic, preferably minimally invasive, surgery. However, the development of these techniques has contributed to an increased difficulty in locating small lesions. Finally, the need to repeat biopsies of previously diagnosed lesions also complicates their localization for surgery.

The objective of this study was to evaluate the feasibility and safety of using a radiolocalization technique for labeling hidden lung lesions.

Between September 2014 and September 2020, 45 patients from our hospital with pulmonary lesions suggestive of malignancy were selected consecutively and prospectively. Patients with lesions showing progressive growth on successive computerized tomography (CT) scans or pathological uptake on 18-fluorodeoxyglucose positron emission tomography-CT (PET-CT) were included. Lung lesions had to present any of the following characteristics: lesion less than 1 cm, subsolid lesion, or lesion at a depth of more than 1 cm. Lesions with a solid component measuring more than 2 cm were excluded. All cases were presented to the multidisciplinary oncology committee, who discussed the clinical case, need for surgical biopsy, and the possibility and feasibility of performing a CT-guided radiotracer labeling.

A lesion was defined as pure ground glass or lacking in solid component when it disappeared completely in the mediastinal window of the CT[1]. Lesions were defined as subsolid if the nodular component that remained visible in the mediastinal window of the CT was greater than 6 mm[1].

The lesion was labeled within 2 h before the intervention. The selected radiotracer was ^{99}TC-labeled macroaggregate albumin (LyoMAA Technoscan® 2 mg, Curium, Netherlands) with a half-life of 2–8 h and a particle size of 10–100 μm. Prior to injection of the tracer, local anesthesia consisting of 10 ml mepivacaine 1% was applied at the thoracic puncture site. A transthoracic puncture using a 22 G needle guided by CT without intravenous contrast material was then performed in or near the lesion. After checking the correct position of the needle with new CT slices, the radiotracer was injected. After injection, new slices were obtained to check for the absence of complications, such as pneumothorax or bleeding. Crossing of fissures and damage to pulmonary bullae were avoided during the puncture. After the procedure, the patient was transferred to the nuclear medicine unit, where a single photon emission computed tomography-CT (SPECT-CT) was performed (Discovery NM/CT 670®, GE Healthcare, Boston, US) to check that the tracer was positioned correctly, had not migrated to nearby areas, and was sufficiently active.

During surgery, the lesion was located using a detector probe (Navigator GPS®, RMD Instruments, US) and pulmonary resection was performed according to the standard technique. The approach route was selected according to the location and depth of the lesion and the presence of other lung lesions requiring palpation. On completion of resection, the lack of residual uptake at the resection margins (<10% of the peak) was confirmed and the specimen was sent to the pathology department. In patients whose lesion was consistent with lung carcinoma and who tolerated the procedure, the intervention was completed with anatomical lung resection.

Table 1
Histology of pulmonary nodules.

Histology	N
Primary lung carcinoma	
AIS	3
MIA	1
Invasive adenocarcinoma	16
Squamous carcinoma	1
Metastases	
Colon	13
Prostate	2
Melanoma	2
Gastric	1
Leiomyosarcoma	1
Benign	
Atypical adenomatous hyperplasia	2
Hamartoma	1
Miscellaneous	3
Total	46

AIS: adenocarcinoma in situ; AMI: minimally invasive adenocarcinoma.

Intra-surgical labeling and radiographic localization were performed in 46 nodules from 45 patients. The procedure was ruled out in 1 patient because of accidental aortic puncture. Mean age was 65.69 ± 7.14 years, 32 were men and 13 women. The mean size of the nodules was 8.8 ± 4.00 mm (range 0.6–20 mm) and the mean distance to the nearest pleura was 15.37 ± 14.39 mm (range 2–68 mm). The morphology of the nodules was ground glass, semi-solid, and solid in 22 (47.82%), 6 (13.04%), and 18 nodules (39.13%), respectively. Pathology findings are listed in Table 1. Fifteen patients underwent minimally invasive surgery, 27 thoracotomy, and 3 rethoracotomy. Two patients had affected margins: 1 was re-operated and another completed treatment with radiation therapy. Thirteen patients had post-puncture pneumothorax (28.8%), but none required pleural drainage. The only complication during the procedure was accidental aortic puncture that required no intervention due to the absence of bleeding after the event. The right upper lobe (34.78%, n = 16) was the most frequent site, followed by right lower lobe (32.6%, n = 15), left upper lobe (15.21%, n = 7), left lower lobe (13.04%, n = 6) and middle lobe (4.34%, n = 2).

Digital palpation has historically been the reference technique for locating lung lesions. However, more than half of lesions measuring less than 10 mm located at a depth of more than 5 mm can go unnoticed[2]. Several techniques have been developed for locating these lesions and performing minimally invasive surgery, bypassing the need for digital palpation. The most important of these are hook wire labeling, methylene blue labeling, ultrasound-guided intraoperative localization, and the most modern, radiolocalization.

Hook wire labeling helps localize up to 97% of the lesions, although the wire can move in up to 48% of cases[3]. Gonfiotti compared the use of hook wires with radiolocalization and found no statistically significant differences (84% vs 96%). Both methods were superior to digital palpation, which located only 24% of lesions[4]. The use of other techniques, such as endothoracic ultrasonography[5] or labeling by injecting contrast agents such as methylene blue[6], have also been described. The main advantage of ultrasonography is the absence of complications[7], but its use is limited by interoperator variability and diagnostic difficulties in very emphysematous parenchyma.

In conclusion, radioguided localization of hidden lesions is, in our experience, a safe and effective technique that is useful in the

☆ Please cite this article as: Garcia-Reina S, Fernández E, Lafuente Carrasco S, Margelí V, Gómez C, Moragas G, et al. Eficacia de la localización radioguiada para el marcaje de lesiones pulmonares quirúrgicas ocultas. Arch Bronconeumol. 2021;57:711–712.

resection of small, intraparenchymal lesions, achieving adequate margins using conventional or minimally invasive surgery.

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https://doi.org/10.1016/j.arbr.2021.09.005
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Respiratory Manifestations in Primary Immunodeficiencies: Findings From a Pediatric and Adult Cohort

Manifestaciones respiratorias en las inmunodeficiencias primarias: hallazgo de una cohorte pediátrica y adulta

Dear Editor,

Primary immunodeficiencies (PIDs) are a heterogeneous group of more than 400 inherited immune system disorders, with overall prevalence 1/1000–1/5000.[1] At any age, recurrent-to-persistent respiratory infections are often the first presenting sign of PIDs.[2] Poor defense from opportunistic or non-opportunistic pathogens, as well as non-infectious complications may significantly impact morbidity and mortality of the conditions, even when early detected.[3]

In PIDs, type, outcome and severity of the underlying defect might influence type and severity of patients' respiratory phenotypes, but only few studies documented this.[4]

In this report, we compared the respiratory manifestations and the chest imaging findings from a cohort of pediatric and adult patients from a tertiary level hospital, a major referral for PID, located in Campania region, in Southern Italy. In order to describe the respiratory phenotypes in different PID groups and to investigate their prevalence, we conducted a retrospective study over a three-year period, from mid-2018 to mid-2020 and created a database of 269 patients with PID including 182 children (mean age, 9 ± 4 years; 67% of the total) and 87 adults (mean age, 20 ± 6.5 years; 33% of the total). According to the underlying diagnosis, patients were allocated to three groups: cellular immunity defects [Group 1, $n = 48$, 17.9% of the total, including Ataxia–Teleangiectasia (A–T), partial DiGeorge syndrome (pDGS), or Severe Combined Immune-deficiencies (SCID) before treatment]; humoral immunity defects [Group 2, $n = 203$, 75.5% of the total, including Common Variable Immune-deficiency (CVID), X-linked Agammaglobulinemia (XLA), or selective IgA Deficiency (sIgAD)]; innate immunity defects [Group 3, $n = 18$, 6.6% of the total, including Chronic Granulomatous Disease (CGD), *STAT1* gain of function, hyper IgE Syndrome, *MYD88* Deficiency, or congenital neutropenia]. We analyzed variables including gender, type of PID, age at diagnosis, age at onset of respiratory symptoms, diagnostic delay (the time elapsed between the onset of respiratory symptoms and the diagnosis of PID), history of upper (i.e. rhinosinusitis and/or otitis) or lower (i.e. bronchitis and/or pneumonia) airway infections, chest imaging phenotypes (at X-ray or Computed Tomography or Magnetic Resonance Imaging).[5] In our study population, Groups 1 and 3 included only children, while Group 2 was composed of both pediatric and adult patients with humoral immunity defects.

Comparisons between groups were performed applying t-test for numerical variables and chi-test for categorical variables.

The age at onset of respiratory symptoms was significantly higher in Group 2 than Groups 1 and 3 ($P < .001$; Fig. 1A). In more than half of the cases, a diagnosis of cellular immunity defect was established, in nearly 90%, of cases in the first decade (Fig. 1B). A wide variability of age at diagnosis was found in cases with humoral immunity defects, while patients with defects of innate immunity were diagnosed always before adolescence. The diagnostic delay was lower in patients with cellular immunity defects than in other groups ($P < .01$; Fig. 1C). Rhinosinusitis was more common in Group 2, with a significant difference when compared to Groups 1 and 3 ($P < .05$), and otitis was more frequent in Group 1. No significant difference in the prevalence of lower airway infections was found among all groups (Fig. 1D).

In order to investigate whether a different localization of airway infections in each disease group was associated with a specific immunological defect, we compared the prevalence within subgroups. In Group 1, upper airway infections were more frequent in A-T patients, while lower airway infections were more prevalent among SCID patients (Fig. 1E–F). Within the pediatric patients from Group 2, we compared the prevalence among XLA, CVID and sIgAD, and found that rhinosinusitis was more prevalent in the CVID subgroup ($P < .05$) (Fig. 1G). Within Group 3, patients with CGD or other innate immunity disorders showed higher prevalence of pneumonia in the CGD subgroup (Fig. 1H).