A pilot study of the role of TC-99 radionuclide in localization of pulmonary nodular lesions for thoracoscopic resection

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Objective: Video-assisted thoracic surgery (VATS) is an interesting and emerging procedure for diagnosis and treatment of peripheral pulmonary nodules. However, thoracoscopy has limits in the detection of small nodules, below the pleural surface, deep in the lung parenchyma, which cannot be seen as much as palpated. Methods to localize such lesions, including the methylene blue injection or the introduction of a hooked-wire under the radiological vision, have some advantages but a lot of limitations. We are developing a new technique for the detection of pulmonary nodules smaller than 2 cm, deep in the lung parenchyma. Methods: The technique consisted of an intra-lesional injection of 0.3 ml of solution of 99mTc-labelled human serum albumin microspheres (5–10 MBq) under the CT-scan guide, 2 h before surgery. During thoracoscopy a 11 mm diameter-collimated probe connected to a gamma ray detector (Scinti Probe MR 100 – Pol.hi.tech., Aquila – Italy), is introduced by a 11.5 mm trocar and the pleural surface of the suspected area was scanned. A hot-spot indicated the presence of the injected nodule and as a consequence, the area to be resected. Results: from June 1997 to June 1999 we treated 39 patients with small pulmonary nodules. The patients were 27 men and 12 women with a mean age of 60.8 years (range: 13–80). In 19 cases the anamnesis was positive for synchronous or metachronous malignant neoplasm. The mean surgical procedure length was 50 min (range 20–100 min). In all the cases the nodule was resected and the resection margins were pathologically free of tumour. Histological examination showed 21 benign lesions and 18 malignant lesions (seven metastases and 11 primary lung cancers). Nine pts with primary lung carcinoma underwent a completion lobectomy by open surgery. Conclusions: Radiolocalization by gamma-probe allows the detection and exeresis of small nodules in a easy and safe way. Future and predictable advances in radio-marked monoclonal antibodies, as well as in the development of endoscopic beta-detector probe, will offer a more effective method for detection of primary and metastatic tumours, targets of thoracoscopic resections. © 2000 Elsevier Science B.V. All rights reserved.

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1. Introduction

In the United States up to 40% of solitary pulmonary nodules (SPN) are reported to be malignant [1]. Traditional non-operative approaches as broncoscopy or the transthoracic needle aspiration biopsy (TNAB) in some case are not successful especially when the nodule is less than 10 mm or benign [2,3]. In the last years, thoracoscopic resection of small indeterminate pulmonary nodules has been performed widely as a diagnostic and therapeutic tool. The limit of this minimally invasive technique is the difficulty to localize the deep intraparenchymal lesions, not being possible a direct finger palpation. Several techniques to overcome such problem have been described. Percutaneous hookwire placement or methylene blue staining under radiological vision, and intra-operative ultrasound have been utilized with good results [4–9], but not without complications or failures.

We are developing a new technique to detect those nodules neither visible nor palpable with endoscopical instruments and this paper reports our preliminary experience.

2. Materials and methods

Patients with small pulmonary nodules (less than 2 cm in
The pulmonary nodules were localized by means of 5 mm thick high resolution axial computed tomographic (CT) sections. Local anaesthesia of the thoracic wall was performed and then, under CT guidance, a 22G needle was introduced into the lesion or just in contact with it. At this moment, 0.3 ml of a solution composed by 0.2 ml of $^{99m}$Tc-labelled human serum albumin microspheres (5–10 MBq) and 0.1 ml of non-ionic contrast was injected. Before the injection, the solution was preserved into a special leaded syringe for radioprotection.

Then the patient was transferred to the operating room. Under general anaesthesia – with orotracheal selective intubation – and with the patient in lateral position, we induced the pneumothorax and introduced a 7 mm trocar for the videothoracoscope, usually in the sixth or seventh intercostal space along the midaxillary line. After a first exploration of the pleural space we positioned a second 11.5 mm trocar, whose placement was planned according to the radiological site of the nodule and the position of the lobes on thoracoscopic vision. Through this trocar, a 11 mm diameter-collimated probe connected to a gamma ray detector unit (Scinti Probe MR 100, Pol.hi.tech., L'Aquila, Italy) was introduced. First an area of the lung, far from the suspected one, was scanned to reset the system, then we approached the pleural surface of the target area to localize the radioactive source. Gamma ray emissions, detected by the probe, were converted into digital as well as audio signals. The audible signal increased proportionally to the radioactivity and on a monitor its value was contemporaneously visible both in numeric and graphic representation (Fig. 1).

Once the area with the higher value of radioactivity was identified, a third trocar was introduced, choosing the site which allowed maximum manoeuvrability of endostapler devices (Endopath 35 mm, Ethicon) for the wedge resection. Before firing a careful instrumental palpation of the identified area was always performed. Moreover, any residual radioactivity was searched with the probe below the stapler to assess the right depth of the resection (Fig. 2). Once the wedge resection was performed the nodules were extracted from the pleural cavity into an endoscopic bag through the largest port-hole, to avoid tumour seeding to the chest wall. Frozen section examination was immediately performed and in case of a primary lung cancer, if the patient had adequate pulmonary reserve, a completion lobectomy through a thoracotomy completed the procedure.

3. Results

From June 1997 to June 1999, 39 patients with solitary or multiple small pulmonary nodules were treated. They were 27 males and 12 females with a mean age of 60.8 years (range 13–80). In 19 cases an history of synchronous or...
metachronous malignancy was reported. Bronchoscopy had been always performed. Preoperatively five patients underwent CT-guided TNAB, which was inconclusive in all cases. In 27 cases the nodule was solitary. All patients had nodules within 3 cm of the visceral pleura surface or near an edge of a pulmonary lobe, so that resection by stapler devices was always possible. Nineteen nodules were localized in the left lung (ten in the lower and nine in the upper lobe) and 20 in the right lung (nine in the lower, eight in the upper and three in the middle lobe). The mean size was 8.3 mm (range 4–19) and the mean distance from the pleura was 13 mm (range 6–30). During labelling procedure we didn’t experience any major complication apart six cases of asymptomatic pneumothorax.

The surgical procedure started from 60 to 190 min (mean 130) after the labelling. Localization by gamma-probe was successful in all cases; after the detection, 11 nodules were also palpable by endoscopic devices. The mean operation length was 50 min. (range 20–100). Nine patients with an histo-pathological diagnosis of lung cancer to frozen sections, and without functional contraindications, underwent a completion lobectomy via thoracotomy, in the same surgical stage. The mean drainage period was 2 days (range 1–5) and the mean post-operative hospital stay was 3 days (range 2–6).

Neither mortality nor morbidity related to the overall procedure was observed.

Histopathologically 21 nodules (54%) were benign, 7 (18%) metastatic and 11 (28%) were primary lung tumors (Table 1).

4. Discussion

Nowadays thoracoscopic procedures have completely

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replaced open surgery in the diagnosis of pulmonary, pleural and mediastinal diseases and in the treatment of benign nodules.

Some controversy still remains regarding the treatment of malignancy both primary and secondary. Limits of thoracoscopy are the adequacy of the resection in case of primary lung cancer and the necessity to palpate all the lung parenchyma to search other lesions not appreciable to CT in case of pulmonary metastases [10]. On the other hand, the suspicion of a solitary pulmonary metastasis is not a contra-indication to a thoroscopic resection because not all solitary pulmonary nodules, in patients with an history of malignant neoplasm, are necessarily a metastasis. In our series 11 of 19 nodules (58%) in patients with synchronous or metachronous malignancy were benign lesions or primary lung tumours.

Thoracoscopic resection of small peripheral pulmonary nodules is an easy and quick procedure when the nodule is in contact with the pleural surface. In this case it is generally visible on thoroscopic exploration or palpable with endoscopic instruments. On the contrary, when the nodule is either too small or too deep beneath the pleural surface, failure in localization and, as a consequence, conversion to open surgery can occur. And this appears to be more frequent if the distance between the nodule and the nearest pleural surface is more than 5 mm and in the case of a 10 mm nodule or less in size [11].

To avoid such difficulties, several techniques have been developed for preoperative or intraoperative localization of deep nodules. Percutaneous hookwire placement and methylene blue injection under CT guidance have been widely utilized alone or in association [4–9]. Results obtained with these procedures were generally good but not without failures or complications. Hookwire displacement, as much as the impossibility to recognize methylene blue coloration on the pleural surface, are responsible of the considerable conversion rate to open surgery, as reported by many authors [5–8,12]. Radioguided searching of the nodule allowed, in our experience, to detect all lesions injected. Time elapsed between methylene blue labelling of the nodule and thoracoscopy has been reported to affect the density of coloration of the target area, as a consequence the resection should always be performed within 3 h from the labelling [8]. The radionuclide we utilized to label the lesion (99Tc) had an half-life of 6 h, increasing the available delay between labelling and operation.

Pneumothorax, hemothorax and chest pain related to the above stated procedures variously occurred in all series. In our experience only six patients (16%) developed an asymptomatic pneumothorax, but neither hemothorax nor chest pain have been reported. The low incidence of complications in our series is probably due to the absence of foreign bodies at the end of the procedure and to the little volume of contrast injected, altogether 0.3 cm³, without the necessity to prolong the injection during the withdrawal of the needle for labelling of visceral and parietal pleura.

A few authors experienced endotheracic echography during thoracoscopy [6,9,13,14]. The technique may be really useful, but it is limited by the presence of the air in the lung parenchyma, producing reverberating artefacts [15]. A complete deflation of the lung and the filling of the chest cavity with saline solution, which improves the surface contact of the transducer, seem to overcome the problem. By these tricks some authors describe the possibility to detect the nodule and to assess its borders.

We obtained the same goal with our technique. During the procedure, we always searched for residual radioactivity, scanning with the probe over and below the stapler line, in order to modify depth and direction of the resection and obtain an oncologically adequate exeresis.

In conclusion, radiolocalization by gamma-probe, during thoracoscopy, seems to be an effective procedure with less complications and failures than other techniques.

Future and predictable developments of our technique are connected to the utilization of radiolabelled tumour-associated monoclonal antibodies which will allow the intra-operative tumour localization by means of the same endoscopic gamma-detecting probe, that is what is already happening for colorectal cancer [16]. A second, more reliable, opportunity to improve radioguided thoracoscopic surgery seems to be the ongoing engineering research, which is developing an endoscopic beta-detector probe able to localize with great accuracy a tumour previously labelled with a positron emitting isotope [17,18]. Patients with undetermined nodules, which accumulate the 18F-labeled-fluoro-2-deoxy-o-glucose (FDG) at a PET examination, might undergo a thoracoscopic resection with intraoperatively localization of the nodules by an endoscopic beta-detecting probe.

It is predictable that such improvements in radioguided surgery may extend, in a near future, the indications for thoracoscopic resections in oncology.

References


