Full thoracoscopic segmentectomies for lung cancer: rational of a multiportal fissure-based approach

Dominique Gossot[1]^, Alessio Vincenzo Mariolo[1], Emmanuel Brian[1], Guillaume Boddaert[1], Agathe Seguin-Givelet[1,2]

[1]Thoracic Department, Curie-Montsouris Thorax Institute-Institut Mutualiste Montsouris, Paris, France; [2]Paris 13 University, Sorbonne Paris Cité, Faculty of Medicine SMBH, Bobigny, France

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Correspondence to: Dominique Gossot. Thoracic Department, Curie-Montsouris Thorax Institute - Institut Mutualiste Montsouris, 42 Bd Jourdan, F-75014 Paris, France. Email: dominique.gossot@imm.fr.

Abstract: Following the partial results of ongoing randomized trials, thoracoscopic anatomic sublobar resections (SLRs) may become the standard treatment of ground-glass opacities (GGO) and of some early-stage lung carcinomas. However, these procedures are challenging. The performance of closed-chest pulmonary segmentectomies, especially for complex ones, requires a meticulous dissection of bronchovascular elements. A thorough preparation facilitates the procedure. In this article, we review the different technical and technological aspects of the multiportal approach with fissure-first dissection. Prerequisites are (I) precise preoperative study of the anatomical variations, based on 3D reconstructions or 3D printing, (II) preoperative evaluation of safety margins, based on a virtual margin, (III) for small nodules, localization of the target using either preoperative or intraoperative marking, (IV) fissure-based approach to allow extensive dissection of bronchovascular elements, (V) intraoperative analysis of resection margins and intersegmental lymph nodes in order to extend resection in case on invaded margin or lymph node, (VI) accurate delineation and division of the intersegmental plane. Technical and technological helpful means are discussed in this article.

Although thoracoscopic lobectomies have been regarded for years as difficult procedures, they have finally been adopted and have almost become routine surgery in many centers.

Closed-chest sublobar resections (SLRs) are attracting a great deal of interest as evidenced by the increasing number of publications (1). However, unlike lobectomies, they prove to be a much more difficult technical challenge for thoracic surgeons. They do not just involve surgical skills but also new technologies. Some publications report a learning curve ranging between 30 and 80 cases (2-5). These publications are questionable because an analysis of the data shows that they include very few complex segmentectomies. After an experience of 750 thoracoscopic segmentectomies, we consider the cutoff for the learning curve, if any, to be at a much higher level. For our team, some complex segmentectomies still pose problems and, as Sato *et al.* we do regard some basilar resections as one of the most challenging procedures (6). There are several
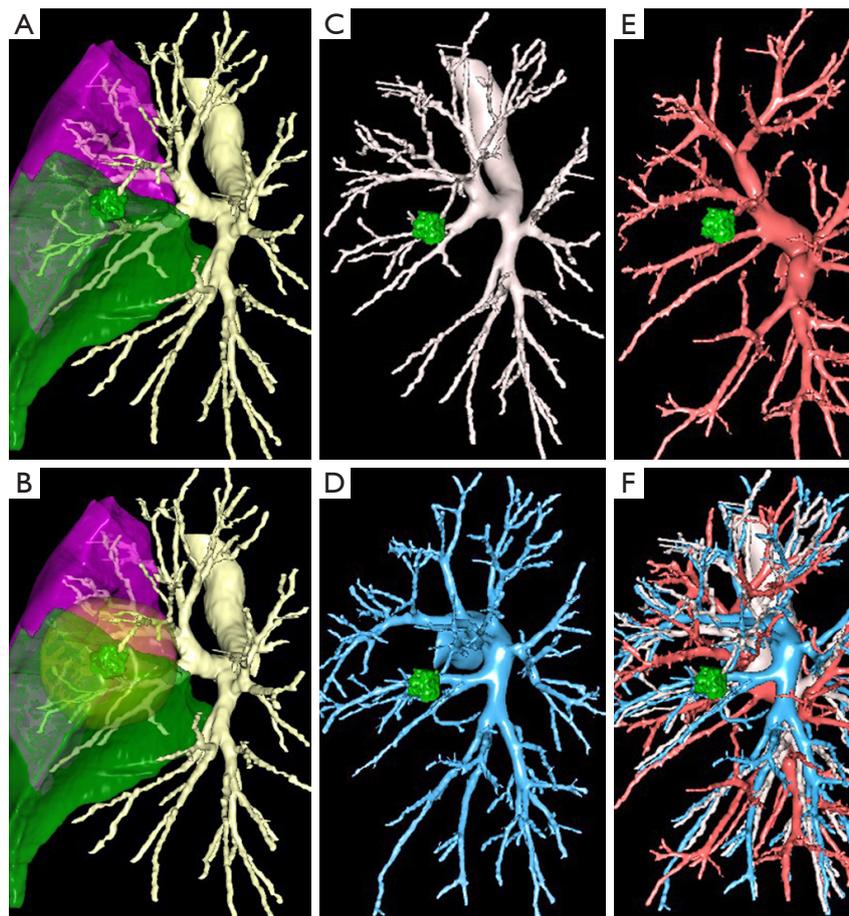
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^ ORCID: 0000-0002-7038-1924.

Figure 1 Example of 3D modelization used for planification of a thoracoscopic segmentectomy for a lingular NSCLC. (A) Standard view (*lingula in green*, S^3 *in purple*), (B) standard view with virtual security margin (pale yellow sphere) indicating resection should be extended to S^3, (C) bronchi alone, (D) arteries alone, (E) veins alone, (F) global view with bronchi, arteries and veins. NSCLC, non-small cell lung cancer.

reasons for this: (I) anatomical variations are frequent (7,8) and require an extensive dissection within the fissure; (II) some segmentectomies are difficult to perform without preoperative mapping (9) and (III) management of the intersegmental plane can be tricky, especially for basilar segmentectomies (6).

The purpose of this article is to give some keys that we find useful, whatever the approach used. We will not detail the basic notions of patient positioning, trocars and the equipment used, that can be found elsewhere (10,11). We will only deal here with the principles that are applied in our department and that could apply to any other technique whatever the approach. Even more than for other procedures, preparation is of key importance.

Preoperative study of the anatomy

One of the difficulties of thoracoscopic anatomical segmentectomies (TAS) is the understanding of the anatomy of the bronchovascular pedicles. Some segments have an almost constant and an easily comprehensible anatomy, for example S^6 or S^{4+5} resections (lingulectomy). In other cases, there may be variations that are important to know, for example the presence of a mediastinal lingular artery during a left upper trisegmentectomy. A precise study of the preoperative CT can give indications. But only 3-dimensional (3D) reconstructions allow an accurate study of vessels and bronchi (9,12-14) (*Figure 1*). It shows precisely the number, size and direction of segmental bronchi, arteries and veins. For simple resections, the need
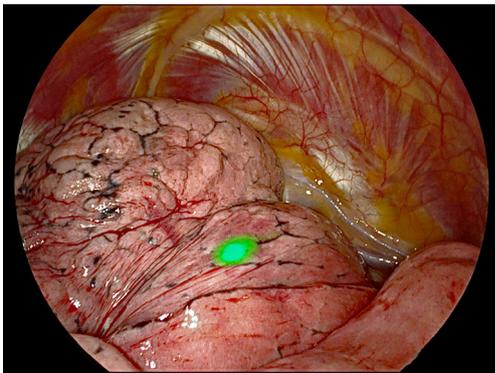
Figure 2 Localization of a target nodule of the right upper lobe by infrared imaging after transbronchial injection of indocyanine green.
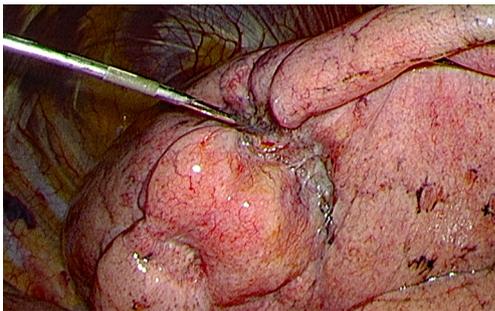

Figure 3 Intraoperative needle-biopsy of a cT1aN0 target nodule of the right upper lobe.

for preoperative 3D reconstruction may eventually decrease with growing experience (although it is still desirable), but 3D-modeling or 3D-printing is essential for complex segmentectomies, especially those of the lower lobe (6,15).

Preoperative localization of the target

TAS are most often performed for early-stage tumors, i.e., small-sized, whose localization does not always give a preoperative pathological diagnosis, even using sophisticated techniques such as radial-EBUS or electromagnetic bronchial navigation (16). It is therefore important to be able to localize the target lesion. Until recently, the most common technique was preoperative CT-guided marking using a hook-wire or methylene blue or a combination of both methods (9). It has several disadvantages: discomfort or chest pain in some patients, pneumothorax, mobilization of the harpoon during patient transport, and even more
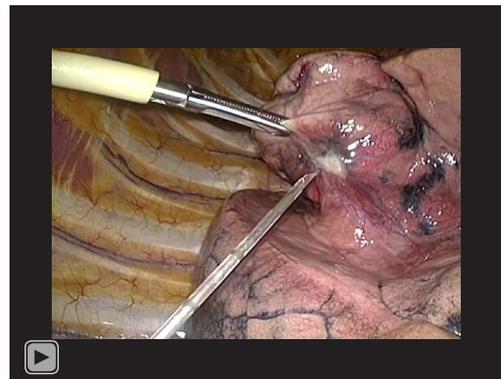
Video 1 Needle biopsy under thoracoscopic control of a small nodule in right segment 2.

serious accidents such as embolism. Placement of a coil has less morbidity but often interferes with the pathological examination. Preoperative marking by endobronchial approach under ENB after injection of methylene blue or indocyanine green (ICG) under infrared imaging is more precise, has no morbidity and can be done by the surgeon himself in the same operating time. It is now our routine technique. In our first 48 patients, the success rate of ENB-guided localization of lung nodules was 94% , this after an acceptable learning curve (17) (*Figure 2*).

Obtaining a pathological diagnosis

Anatomical segmentectomies are mostly indicated in stage I bronchial cancers, which means that the tumor is often small and not easily accessible to a percutaneous biopsy under CT. Some patients are therefore operated on without preoperative diagnosis. Wedge resection can distort the specimen and make the pathological study unreliable. When the lesion is localizable, it is therefore preferable to perform a needle biopsy (*Figure 3*; *Video 1*). The yield of these biopsies is as high as 90%. In case of failure, a resection using a vessel sealing device, with temporary or permanent closure of the pneumotomy by an absorbable running suture, is preferable to a resection by stapling. In some cases, especially in ground-glass lesions, intraoperative examination may not be possible and segmentectomy will therefore be both diagnostic and therapeutic.

Fissure-based approach

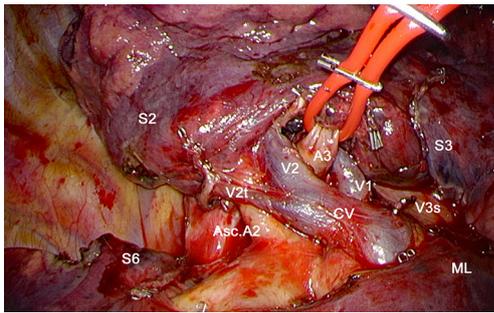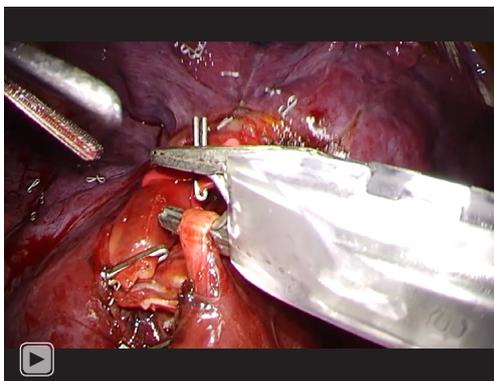So-called "fissure-last" techniques are not applicable

Figure 4 Example of an extensive venous dissection in the fissure, during a right S^3 segmentectomy.

Video 2 Arterial dissection (A8a and A8b) in the fissure during a right S8 thoracoscopic segmentectomy.

for TAS because vascular dissection within the fissure is essential to detect anatomical variations. Extensive dissection using a "fissure-first" approach provides the best exposure of the segmental pedicle elements (*Figure 4*) (18) (*Video 2*).

Access to the segmental branches of the pulmonary artery is more or less easy depending on whether the fissure is open or fused. The opening of a fused fissure can be a tedious part of the procedure and a source of oozing. It is always troublesome in thoracoscopy where the operating field must remain as "dry" as possible to maintain an optimal view. One of the keys to a non-hemorrhagic dissection in the fissure is to progress cautiously and step by step, from the periphery towards the hilum. Thin instruments, such as ultrasound scissors or electrother™mal bipolar sealer, are less cumbersome and just as effective as a stapler for sectioning the peripheral and thin part of a fissure. For its central and thicker part, a stapler remains necessary.

In some segmentectomies, it is not useful to open the fissures completely, thus limiting the mobility of the remaining segment(s) and preventing segmental torsion (19-21). If the fissure had to be completely opened, it may be necessary to secure a mobile segment, for example by anchoring S^6 to S^2 after a basilar segmentectomy or the lingula to S^8 after a left upper division segmentectomy. This is achieved thanks to a running suture, usually using V-Loc™.

Delineation of the intersegmental plane

One of the difficulties of thoracoscopic segmentectomies is the delineation and separation of the intersegmental plane. This step is particularly complex in basilar segmentectomies because of its three-dimensional pyramidal shape (6,15,22). By thoracotomy, this step is facilitated by palpation and by manual traction that can be exerted on the segment along the intersegmental vein. By thoracoscopy, the surgeon cannot use his/her hand and the limited space associated with the lack of distance do not allow perfect exposure of the anatomy. This is why, in almost all recent series, the intersegmental plane is stapled, despite certain disadvantages of stapling, in particular possible plication of the parenchyma (23). Stapling does not obviate the need for precise marking of the segmental boundaries.

Several methods have been described.

Method 1: the most commonly used technique is the creation of a delineation line between ventilated and non-ventilated lung, by re-ventilating the operated lung after the segmental bronchus has been stapled (10). Once the plane is found, it may be useful to mark the boundary between ventilated and nonventilated lung by cautery dots or by applying a clamp. This method has two disadvantages: (I) re-expansion of the lung interferes with vision; (II) the segment(s) to be resected may be partially re-ventilated by Kohn's pores and Lambert's ducts, which does not allow a clear demarcation (*Video 3*).

Method 2: for this reason, some authors have suggested a reverse technique: (I) place the stapler over the bronchus, without closing it; (II) reventilate the entire operated lung; (III) staple the bronchus; (IV) exclude the lung again. Thus, only the segment(s) to be resected remain expanded.

In practice, this method may also have disadvantages: before performing it, one must be sure that the resection is completed because the volume of the aerated segments can be troublesome and hamper dissection.
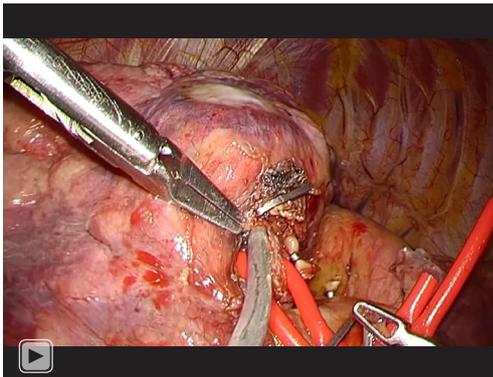
Method 3: the segmental bronchus is selectively catheterized through a fiberscope and jet ventilation is
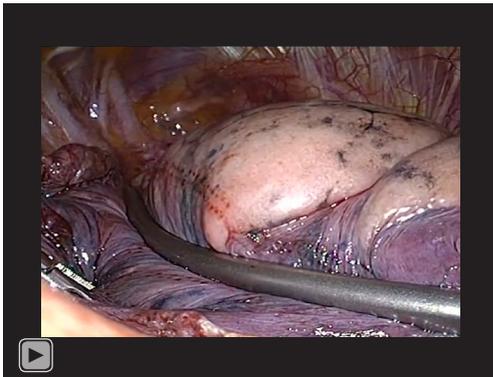
Video 3 Delineation of the intersegmental plane during a right S1+2 segmentectomy by a ventilation-deflation method.
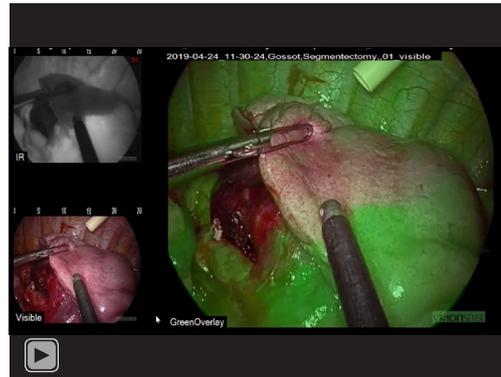
Video 5 Delineation of the intersegmental plane during a left S6 segmentectomy by infrared imaging.

Video 4 Delineation of the intersegmental plane during a left S2 segmentectomy by selective bronchial insufflation.

Figure 5 Example of delineation of the intersegmental plane lobe by infrared imaging after systemic injection of indocyanine green, during a right basilar segmentectomy.

applied (24). This is a cumbersome method because it requires intraoperative fibroscopy on a patient having a double-lumen tube and being placed in lateral decubitus.

Method 4: an alternate technique consists in stapling the bronchus and then puncturing its distal stump with a needle. The needle is connected to a catheter linked to a syringe and air is injected. This technique has given rise to gas embolisms which should make one very wary (25). In addition, the needle may actually be introduced not into a segmental bronchus, but into a subsegmental bronchus (*Video 4*).

Method 5: once the segmental vessels have been severed, the entire lung is ventilated with pure oxygen for 5 minutes. Then the segmental bronchus is stapled. The segment that is no longer vascularized retains oxygen since there is no more gas exchange and remains pink and aerated while the

remaining parenchyma turns purple (26).

Method 6: intrabronchial injection of a dye. The aim is to mark with a dye (indigo carmine or methylene blue) either the target segment or the adjacent segments. To do this, the sub-segmental bronchi of the segment are catheterized, either by fibroscopy or by ENB, injecting the dye and air to ease its diffusion. While this method effectively marks the segment(s), it delineates the margins very poorly and is therefore not very accurate.

Method 7: systemic indocyanine injection (*Video 5*). The technique is based on the fact that ICG, when it binds to plasma proteins and when stimulated by a laser, emits a near-infrared light. This light is detected by an infrared camera, which gives a green coloration to all vascularized tissues (*Figure 5*). Only the segment that has been devascularized keeps its natural color. Depending on
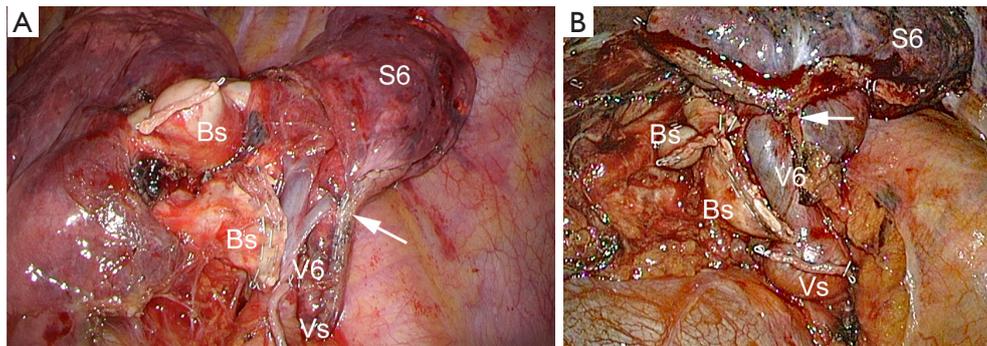
Figure 6 V^6 vein at completion of a left basilar segmentectomy. (A) Preservation of the vein (arrow), (B) doubt on a squeeze of the V^6 vein by the staple line (arrow). Bs, stump of the basilar bronchus, As, stump of the basilar arterial trunk; Vs, stump of the basal veins.

the sensitivity of the system used, the green color appears more or less quickly, between 30 seconds and 2 minutes. It generally diffuses quite quickly, so that the marking of the intersegmental plane must be done rapidly, for example using cautery dots. The reliability of the method varies between 85% and 100% (27-30). The method can fail in patients with chronic obstructive bronchitis (COPD).

Division of the intersegmental plane

At the time of open surgery, surgeons favored opening the plane with electrocautery along the intersegmental vein, once the bronchus and arteries had been controlled. Hemostasis and aerostasis were controlled by HF-cautery, sutures and/or clips, possibly reinforced for some authors by application of biological glue or a fibrinogen patch (31,32). The plane was left open.

This method has two advantages: the section is anatomical and the remaining parenchyma is functional. There are however shortcomings: the technique is difficult to apply via thoracoscopy, due to the lack of manual palpation. Oozing and/or true hemorrhage from the divided plane can be difficult to control thoracoscopically. If the section is perfectly anatomical, air leakage can be minimal. However, prolonged air leaks (33) are observed. Ohtsuka *et al.* showed that the use of cautery alone resulted in significantly more prolonged air leaks than when a combined method of electrocautery and stapling was used (34).

Separation by stapling is now the most commonly used technique during thoracoscopy. Once the line of demarcation is determined, a dedicated clamp is applied to the parenchyma (11). The clamp is closed to compress the parenchyma. This compression creates a mark on the squeezed parenchyma and then facilitates the application

of the staple. The lung can be re-ventilated and the clamp possibly moved depending on the delineation line between ventilated and non-ventilated areas.

With few exceptions, the thickest staples are used. The availability of thick tissue staples (5 mm) and tri-staple technology has largely reduced staple line dehiscence that was sometimes observed with previous generations.

Advantages are the relative simplicity and speed of the procedure, the perfect hemostasis and satisfactory aerostasis, allowing rapid removal of chest tube and thus early discharge of the patient.

Disadvantages are the cost, the limited opening of the staplers, sometimes making it difficult to load thick parenchyma, the difficulty in maneuvering the stapler if the chest cavity is narrow, less precise and less anatomical division, risk of biting on the intersegmental vein if it has not been clearly identified (*Figure 6*).

Partial plication of the remaining segment(s), which would therefore be less functional, has been seen as a concern. This plication by compression of the parenchyma on the staple line is a reality but does not seem to have any clinical consequence, as demonstrated by our team (23). In an experimental study on sheep lung parenchyma, Asakura *et al.* showed that the volume of remaining parenchyma was indeed reduced if the entire section was done by stapling. But if the thin part of the fissure was sectioned with a scissor and the thick part stapled, there was no significant difference (31). Clinically, Miyasaka *et al.* showed no significant difference in respiratory function between these two methods (35).

Despite the drawbacks mentioned above, stapling is the most used method in recent series of thoracoscopic segmentectomies. But it is a delicate step of the operation, sometimes long and tedious, during which one should not
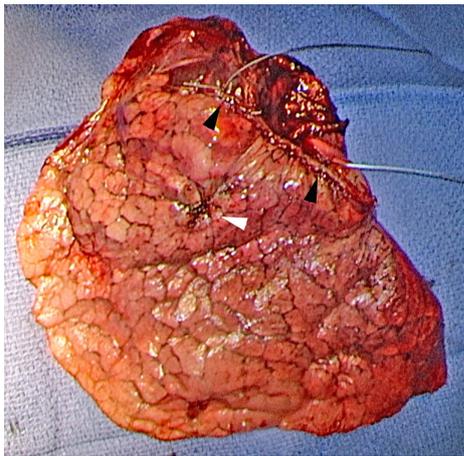
Figure 7 Example of intraoperative examination of the resection margins of a left S^3 segmentectomy for a CT1a NSCLC. White arrow indicates nodule, black arrows indicate portion of the staple line to be examined by frozen section. NSCLC, non-small cell lung cancer.

hesitate to reposition the stapler several times to make sure it is in the appropriate direction. For basilar partial segmentectomies, using short reloads instead of 60 mm ones allows one to progress step by step and is safer.

Intraoperative analysis of resection margins

In oncological surgery, a segmentectomy is valid only if resection margins are sufficient. The rate of local recurrence is indeed correlated to the distance of these margins to the target tumor. Schuchert *et al.* have shown that segmentectomies have equivalent survival to lobectomies except when the margin/tumor diameter ratio is <1 with, in these cases, an increased risk of local recurrence (36). When this ratio is >1, the recurrence rate is significantly lower (25.0% versus 6.2%; P=0.0014). In this study, the local recurrence rate was 7.7% and was observed in patients with a resection margin of less than 2 cm. In our study of 284 TAS for cancer (19), resection margins were insufficient on intraoperative examination in 7 patients, leading to extend resection to another segment or even to the lobe. The study of resection margins by frozen section is essential because macroscopic examination is insufficient. Thus, the invasion of the resection margins was sometimes unexpected by the surgeon, who thought he was far away from the lesion (19). According to the recommendations (37), the resection margin should be at least equal to the largest diameter

of the nodule and should be 2 cm for lesions whose largest diameter is >2 cm. Therefore, an intraoperative examination should be performed after removal of the staple line. Resection should be extended to lobectomy in case of doubtful margin. Since it is difficult to consider an examination of the entire resection margin, it is preferable to mark the limits of the area to be examined with 2 stay-stiches (19) (*Figure 7*).

Preoperative 3D modeling can help thanks to the virtual safety margin which shows if resection should be extended to an adjacent segment (9,38) or if lobectomy should be considered.

Intersegmental lymph node dissection

The quality of thoracoscopic hilar, interlobar and intersegmental lymph node dissection to be done during thoracoscopic SLR is debated.

In our experience based on the previously cited study (19), the rate of correction from clinical TNM stage to higher pathological stage was 10.4%. Concerning only the change of lymph node status from cN0 to pN1 or pN2, it is estimated in our series at 5.7%. This rate is lower than that observed after lobectomy, which was 11.6% in the series by Boffa *et al.* (39), but is explained by the predominance of clinical stage IA. In a very large study of 11,531 patients, Boffa *et al.* showed that the rate of upstaging from N0 to N2 was not significantly different between thoracotomy and thoracoscopy but that there was a clear difference in favor of thoracotomy for the rate of upstaging from N0 to N1. This difference decreased with the experience of the operator. With experience, it is indeed possible to make a more extensive dissection of the bronchovascular pedicles, to sample the lymph nodes and thus to make an intraoperative examination at the slightest doubt if an intersegmental lymph node seems suspicious (19) (*Video 6*).

Studies have emphasized the importance of intersegmental lymph node dissection during thoracoscopic segmentectomies. Two studies have shown that in early-stage non-small cell lung cancer (NSCLC), lobectomies had better overall and recurrence-free survival than segmentectomies except when the latter were associated with lymph node dissection (40,41). In the study of Xiao *et al.*, the probability of finding positive isolated and remote LN (iLNs) was 40% when an adjacent node (aLN) was invaded (42) (*Figure 8*). The authors concluded that when an aLN was metastatic at frozen section, segmentectomy should not be recommended and resection should be extended to lobectomy, a rule now adopted by many teams (15,19,42,43).
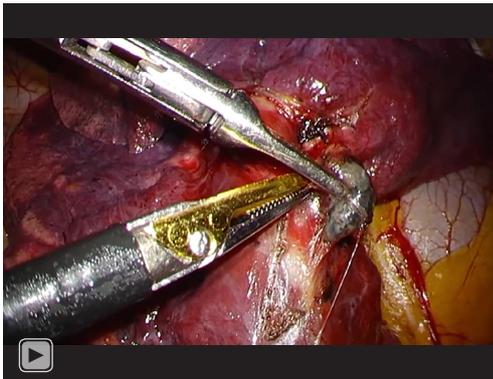
Video 6 Dissection and intraoperative examination of an intersegmental lymph node during a right S8 thoracoscopic segmentectomy.
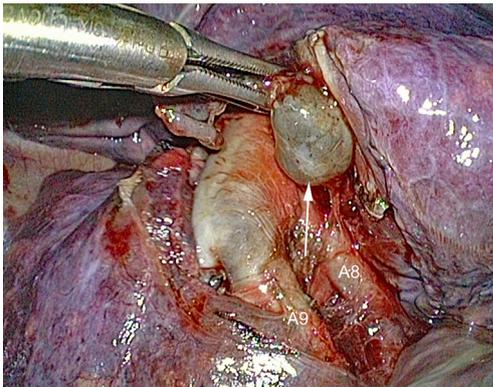

Figure 8 Example of an intersegmental lymph node to be examined by frozen section, during a right S^8 segmentectomy. In this case: node (white arrow) station 12 is located between A^8 and A^9 arteries.

In summary, the performance of closed-chest SLR requires a rigorous technique based on an optimal comprehension and visualization of the anatomy. The preparation of the procedure is an essential step that comprises several aspects: (I) visualization of the target nodule in relation to the segment(s) to be resected with an analysis and planning of the safety margins; (II) modelization of the anatomy; (III) if necessary, labeling of the target. The procedure itself requires a fissure-based approach to avoid missing anatomical variations. The fissure must be widely open for an optimal vision of the vessels. Intraoperative analysis of the intersegmental lymph nodes and resection margins is essential to extend the resection to a lobectomy at the slightest doubt and to respect the criteria of oncological surgery.

Footnote

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