



# How to improve the precision of closed chest sublobar resections

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**Abstract:** Despite carcinological results awaiting validation, sublobar resections (SLRs) are of increasing interest due to the progressive change in tumour profile and to their lower morbidity when compared to lobectomies. However, this morbidity remains too high in comparison to non-surgical alternatives. Decreasing the complication rate requires greater precision. We present here the different ways to improve the accuracy of the different steps of these interventions: (I) performing these procedures via a closed chest approach; (II) knowing as much as possible about segmental anatomy and studying mapping; (III) performing an intraoperative examination on the intersegmental lymph nodes and on resection margins; (IV) using a preoperative or intraoperative marking method to determine the intersegmental plane (ISP); (V) stapling ISP, an imperfect method but that currently represents the least bad compromise between accuracy and safety.

**Keywords:** Sublobar resection (SLR); segmentectomy; thoracoscopy; video-assisted thoracic surgery (VATS); modelization; infrared imaging

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The standard surgical treatment for non-small cell lung cancer (NSCLC) is pulmonary lobectomy, regardless of the stage of the cancer (1). However, trials are currently underway to compare survival between sublobar resection (SLR) and lobectomy for early stage-NSCLC. The results of these studies are expected within the next three years but, nevertheless, there is a growing interest in SLRs in the surgical community to treat some benign lesions, some metastases that cannot be removed by mere wedge resection, ground-glass opacities (GGOs) and even some early stage NSCLC. Reasons for this renewed interest are multiple: trying to improve patients' quality of life by better preserving respiratory function (2) and reducing the morbidity of major pulmonary resections. The morbidity of standard lobectomies is indeed 40% and mortality is more than 2% (3). In the 1990s, basing on the conclusions of the Lung Cancer Study Group, it was claimed that SLRs

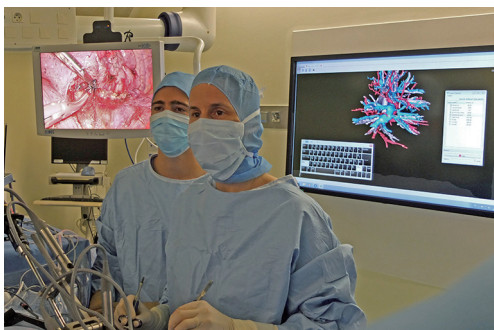
had a higher recurrence rate than lobectomies and had a lower survival rate (4). This had been confirmed by cohort studies (5). But until now, the question had not been asked whether these studies might not include a bias related to the fact that the surgical technique used in SLR did not always match oncological principles (6). In many studies, it is unclear whether SLR are true anatomical resections (wedges and segmentectomies are frequently mixed) and if an adequate lymph node dissection is performed. Comparative studies between anatomical segmentectomy associated to lymph node dissection and lobectomy from high-volume expert centers do not show any significant difference in survival (7-11).

In this hypothesis, segmentectomies become attractive, especially when they are performed by thoracoscopic surgery. It has indeed been shown by several studies, including one from our department (12), that post-operative

morbidity was significantly less by thoracoscopy than by thoracotomy. Nevertheless, the morbidity of thoracoscopic segmentectomies remains high, ranging from 15% to 30%, well above the morbidity of alternative techniques such as radiotherapy or radiofrequency, whose complication rate is <2% and whose mortality is null (13). Part of the morbidity of thoracoscopic segmentectomies can be explained by technical issues such as confusion in vascular anatomy and inappropriate management of the intersegmental plane (ISP). This is why one of our challenges is to drastically improve accuracy. The avenues for improvement are presented in this article.

### Optimal understanding of anatomy

The bronchovascular anatomy of the pulmonary segments is complex and includes multiple variations (14-16). It can even be asserted there is no standard segmental anatomy. The concern related to the thoracoscopic approach is the



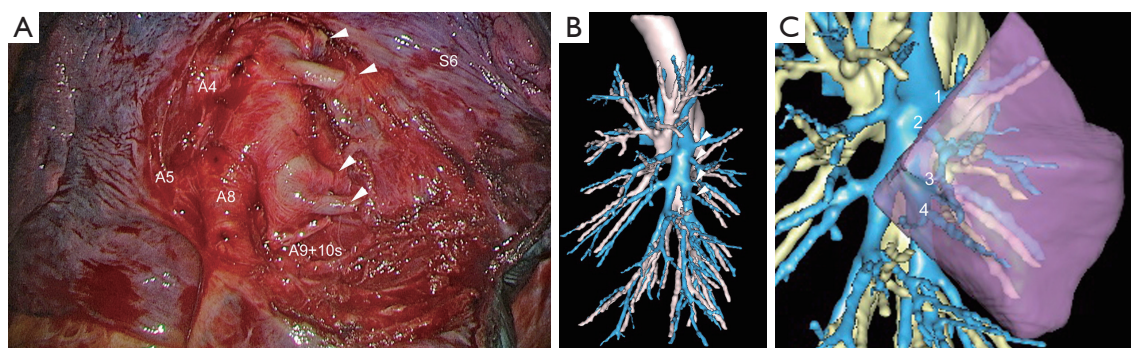
**Figure 1** Display of 3D reconstruction on a large touch-screen during a thoracoscopic segmentectomy.

difficulty to properly expose anatomical structures and the lack of global vision of the lung. The distribution and direction of arteries and veins is therefore often difficult to apprehend. For example, the opening of the fissure and extensive dissection of the vessels only allows them to be exposed over a limited length, so it is often problematic to state that a particular vessel is intended for a particular segment. This is why it is essential backing on mapping during the procedure but also beforehand to study anatomical variations in the preoperative period. This mapping is based on a three-dimensional (3D) reconstruction from an injected computed tomography (CT)-scanner. Most patients whose renal function is compatible with an injected CT can have a preoperative modelization.

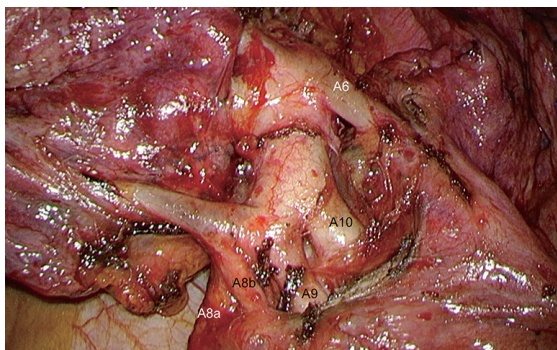
Currently, several software programs allow navigation through the anatomy, layer by layer and superimposing elements, for example bronchi and arteries or bronchi and veins. In our department, we have found that when the surgeon has a cartography, it is used during surgery in more than 75% of cases, even if he/she has studied the reconstruction before the operation (*Figures 1,2*).

Several teams have demonstrated the study of preoperative computed tomography 3D reconstruction helps asserting the number and direction of arteries with good correlation. Oizumi *et al.* reported a correlation rate between 3D model and intraoperative findings of 98% (17). Eguchi *et al.* demonstrated in 14 consecutive patients the usefulness of manipulating the 3D CT navigation using a tablet interactively during the thoracoscopic procedure, helping them to perform the procedure safely and offering a valuable learning with regard to pulmonary vessel anatomy (18).

With the vascular pattern in mind the surgeon can



**Figure 2** Example of an arterial variation of left segment 6, as observed during a  $S^{9+10}$  segmentectomy. (A) The surgeon discovers 4 arteries distributing to  $S^6$  (arrows); (B,C) 3D modelization confirm these arteries are indeed vascularizing  $S^6$ . The numbers 1, 2, 3 and 4 in (C) indicate the 4 arteries for segment 6.



**Figure 3** Example of common anatomical variation: lingular artery arising from a basilar artery. Without large opening of the fissure, this variation can be overlooked.

perform a safer dissection of the pulmonary artery branches, especially when the fissure is fused and/or when lymph nodes are present. We use an online service that provides patient's 3D modeling from medical DICOM images (Visible Patient™, Strasbourg, France). The images are anonymized and then uploaded on a secured web portal. A 3D reconstruction from these images is created according to the surgeon's request. The 3D model can be used via a planning software and manipulated from any direction, either on a laptop, on a tablet or smartphone. All members of the surgical team have a direct access to the images on their own phone or tablet so that strategy and technical issues can be discussed within the group at any time. The software not only allows studying the main anatomical landmarks, in total or separately, but provides the following helpful functions: (I) display of virtual segmentectomy by clicking on a selected bronchus; (II) calculation of the volume of the resected segment; (III) calculation and simulation of a safety margin. This helps visualizing if the planned segmentectomy will have a safe margin, or if a more extended resection must be chosen for carcinological safety.

With growing surgical experience and with an extensive vascular dissection, it is possible to operate without reconstruction in some relatively simple segmentectomies. But in complex ones, 3D visualization is almost mandatory and will become part of the thoracic surgeon's arsenal in a near future, just like any imaging system or equipment. Not only will the surgeon save time, but the patient will also gain in safety and overall the precision of the procedure will be improved. In this respect, it is interesting to note that in France, insurance companies are in the process of reimbursing these reconstructions.

Although 3D modeling is an insight, it is not yet the ideal tool and does not solve all orientation and comprehension problems during the procedure. The perfect system would be the use of augmented reality with overlaying on the screen of real and virtual anatomy. Unfortunately, it seems we have to wait several years for such a system. The technological challenge is indeed major because of the movements of the anatomical structures related to heartbeats and especially the fact that the models are made from a CT on a ventilated lung while the surgeon operates on a non-ventilated lung.

3D printing of the modelization can be an improvement as it can be manipulated manually and is more intuitive (19). The technology is still in its infancy and the costs are high, but progresses and cost cutting are expected.

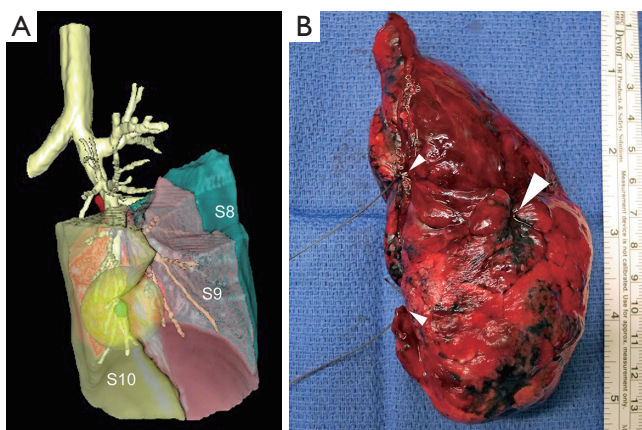
### Optimal approach

It is important to have a representation of the anatomical landmarks before and during the procedure. But this would be useless if the surgeon does not have an optimal exposure of anatomical structures. For thoracoscopic lobectomies, a “fissure first” approach is usually compared to a “fissure last” approach, which is theoretically faster and easier. For this reason, the latter technique—up to now—appeals most surgeons. However, for anatomical SLR, a large fissure opening is necessary to dissect segmental arteries and veins and detect the many anatomical variations (*Figure 3*). In the case of a fused fissure, the tunnel technique with opening of parenchyma by stapling along the arterial plane can help (20).

Appropriate exposure of anatomical structures, use of high-definition imaging combined or not with 3D display, use of dedicated instrumentation whose size is adapted to the diameter of bronchovascular elements, use of adequate hemostatic tools, are key elements to optimize the understanding and preservation of segmental anatomy as well as the quality of dissection (21).

### Optimizing safety margins

Compared to lobectomies, SLR comprise an increased risk of local recurrence as resection margins tend being closer to the tumor. Schuchert *et al.* have clearly demonstrated that segmentectomies outcome compares favorably with lobectomy for stage I NSCLC but that margin/tumor ratios of less than 1 are associated with a higher rate of recurrence (22). In this study, a margin/tumor diameter ratio exceeding 1, was associated with a significant reduction rates



**Figure 4** Determination of the safety margin (A) by preoperative modelization (nodule in green, margin in pale yellow) and (B) by intraoperative examination of nodule (large arrow) and the staple line between 2 stiches (small arrows)

compared with ratios of less than 1 (25.0% versus 6.2%;  $P=0.0014$ ). The rate of local recurrence was 7.7% and was correlated in most cases with a tumor margin less than 2 cm. Preoperative modeling can help making decision and plan the adequate SLR. On the software we are using, we have added an automatic calculation and representation of the safety margin. A similar concept has been developed by other teams (23) (Figure 4A). During the procedure, an intraoperative examination of the margins should be performed whenever the lesion is not very far from the staple line. As the pathologist cannot examine the entire staple line, we place 2 stitches on the area to be examined (Figure 4B). In our series, the margin was insufficient in 5 patients leading to extend the segmentectomy to the adjacent segment or to the lobe. It should be noticed that a borderline margin sometimes came as a surprise to the surgeon who thought section was widely distant from the tumor (24). Failing to examine intraoperative margins exposes the patient to a significant risk of local recurrence and may partly explain the poorer results of SLR in some multicentric series.

### Performing an adequate lymph node dissection

Several studies suggest intersegmental lymph node clearance to play a major role in the results of segmentectomies. Wolf *et al.* have demonstrated that in early stage NSCLC, lobectomy was associated with longer overall and recurrence-free survival. SLRs were associated with an increased rate

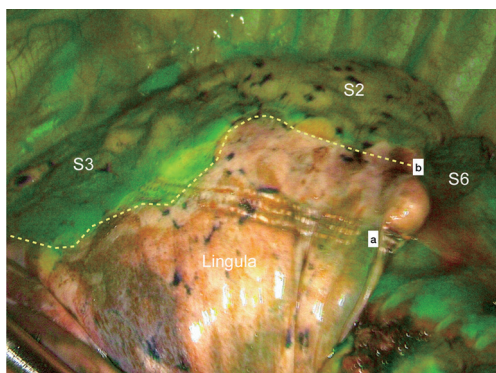
of local recurrence (16% versus 8%,  $P=0.1117$ ). However, when lymph nodes were sampled during segmentectomy, local recurrence rate and overall and recurrence-free survival distributions were similar to those of lobectomy (25). Similar conclusions have been reported in a more recent paper by Cox *et al.* (26). In the beginning of our experience, we were clearing all intersegmental lymph nodes but asked for frozen section only when these looked suspicious. However, with a larger experience, we have been confused by benign looking intersegmental LN which were actually invaded so that we are now asking for an intraoperative pathological analysis even for a normal looking node (24).

### Enhancing the precision of identification of the ISP

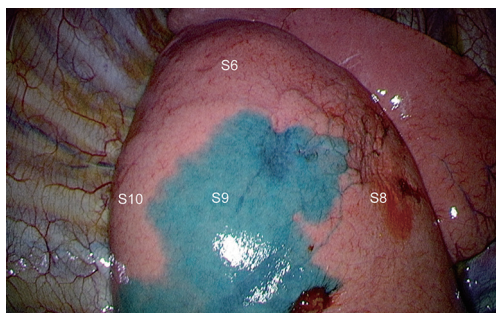
Inadequate determination and division of the ISP can determinate unsatisfactory oncological and surgical results, being the main cause of locoregional recurrence and impaired long-term survival following segmentectomy.

The conventional and most common maneuver used for delineation of the ISP consists of inflating the whole lung after occlusion of the target segmental bronchus inducing collapse of the segment to be resected and inflation of the remaining lung. However, because of the collateral ventilation through the pores of Kohn and because the inflated segments limits working space during thoracoscopic procedures, this method is unreliable. Some authors reported a method based on the use of near-infrared imaging system with indocyanine green (ICG) systemic injection after the division of the segmental vessels and bronchi by endostapler or clips, so that the fluorescence covered all structures except the isolated segment to be resected. The reported success rate ranges from 85% (27) to 100% (28). We are using systemic injection of ICG routinely in all our segmentectomy cases for 2 years and in our experience, the success rate is closer to 90% (Figure 5). It seems that poor vascularization of the parenchyma, as observed in patients presenting with chronic obstructive pulmonary disease (COPD), can be a cause of failure. According to Pischik and Kovalenko who had a 5% failure rate, COPD only reduces the duration of staining, but they observed bad results in patients with severe emphysema (29).

Endobronchial dye injection has also been reported (30). Sekine *et al.* demonstrated an accurate detection of ISP by maintaining the targeted colored segment when ICG injection into the associated bronchus followed by ligation of the segmental vein, was performed (31). Zhang *et al.*



**Figure 5** Dividing the intersegmental plane during a thoracoscopic lingulectomy. The plane demarcation line is very different between standard thoracoscopy [b] and near-infrared imaging [a].



**Figure 6** Determination of the intersegmental plane by endobronchial instillation of methylene blue through electromagnetic navigation. Note the inaccurate border between segments.

described a new technique consisting of methylene blue 0.1% (20 mL) injection into the bronchus of the target pulmonary segments through an intravenous needle after division of the vessels and bronchus of the segments to be resected (32).

Sato *et al.* described a virtual assisted pulmonary mapping (VAL-MAP), consisting of simultaneous marking of the pulmonary lesion to be removed and ISP on 3D images combining virtual bronchoscopy and endobronchial dye injection, achieving a success rate of 92.6% (33). Preoperative dye-injection can also be achieved via Electromagnetic Navigation Bronchoscopy (ENB) (30) (Figure 6).

### Optimal method for dividing the ISP

Once identified, severing the ISP is another challenge. It

was performed by electrocautery for a longtime. Because of the increasing number of anatomic SLR performed by thoracoscopy or video-assisted thoracic surgery (VATS), most surgeons are now using stapling. This method has been longtime criticized. Some authors reported that the stapling technique, may lead to plication of the parenchyma, impairing pulmonary re-expansion (34) while others demonstrated that stapling does not lead to less preserved function than electrocautery (35). The possible appearance of consolidation along the surgical stump has also been described as a complication after stapling the ISP. This finding could be related to the lesion of the intersegmental vein which has a role in the venous drainage of half of the preserved segment and which may be trapped in the staple line. According to these authors, the impaired venous drainage, could be the cause of chronic ischemia and subsequent parenchymal destruction (36). The clinical and radiologic support to these critics has not been investigated and has pushed us performing a CT study after segmentectomy. Our results are submitted to publication and under review. In summary, we have evaluated the presence of atelectasis, defined as an area of parenchymal consolidation larger than 5 mm in horizontal section view on CT scan, along the staple line, 3 to 4 months after the operation. We found only few atelectasis along the staple line. All of them were minor and the adjacent remaining segments were always well perfused with no sign of chronic ischemia. None of the atelectasis required surgery.

The development of the ISP by electrocautery, has been linked to prolonged air leak (PAL) (37) so that some authors described the use of various type of sealant and/or mesh. Matsumura *et al.* described better results with polyglycolic acid, an absorbable material that is able to closely adhere to irregular sections of the lung, effectively sealing air leakage and allowing a fast chest drain removal and excellent lung expansion (38). In a study from our department, there were only 8% patients who developed a PAL (39). These results are consistent with those reported in our previous series of 228 anatomic pulmonary segmentectomies (12) and lower than those reported by others who use to cut the ISP by electrocautery (40,41).

Miyasaka *et al.* compared electrocautery and the use of staplers for dividing the ISP during 49 segmentectomies (37). PALs were observed in 4 patients (8.2%). Three of these 4 patients underwent a chemical pleurodesis and one of them was reoperated for closing the air leak. None of these complications occurred in the stapler group ( $P=0.005$ ). In a series of 102 hybrid VATS segmentectomy, electrocautery alone, i.e., without stapler, was used to divide the ISP and

**Table 1** Summary of technical means to improve precision of sublobar resections

To be optimized	Mean	Benefit	Limitation	Expected progress
Anatomy understanding	3D modelization	Precise mapping	Cost Time consuming	Augmented reality?
	Exposure	Clear display of anatomical structures	Time consuming Can be difficult if fused fissure	
Determination of safety margins (with IOE)	3D modelization	Preoperative determination of segments to be resected	Cost Time consuming	
	Intraoperative examination	Allows immediate extension if invasion	Time consuming Not 100% reliable	On site examination?
Intersegmental LN clearance (with IOE)	Extensive intersegmental dissection	Allows immediate extension if invasion	Time consuming	Sentinel LN?
Precise determination of intersegmental plane	Intrabronchial dye marking	Easy Cheap	Inaccurate demarcation line	
	Systemic ICG with NIRI	Very accurate	10% failure rate Dedicated system Toxicity if hepatic insufficiency	
Precise division of intersegmental plane	Stapling	Safe	Difficult handling	Sealing device?
			Bulky	
			May injure IS vein	
			Cost	

3D, 3-dimensional; IOE, intraoperative examination; LN, lymph nodes; ICG, indocyanine green; NIRI, near-infrared imaging; IS, intersegmental.

a fibrin sealant was applied along the raw surface of the remaining lung to prevent air leakage. PALs were observed in 4 patients (3.9%). Ohtsuka *et al.* compared 2 groups of patients having the ISP divided by electrocautery alone and electrocautery combined with stapling (42). The incidence of PAL was higher in the group electrocautery alone than in the group combination of electrocautery and staplers [14% (3/22) *vs.* 4% (1/25),  $P=0.025$ ]. Thus, as mentioned by Miyasaka *et al.*, dividing the ISP by electrocautery may result in more PALs (37).

Stapling the ISP is not yet the perfect method. Its handling is not that easy, especially in patients with small chest cavity. Loading thick tissues can be tedious, as their opening is limited, and disruption of the staple line can occur (43). Stapling the ISP seems to be a safe procedure. Our study showed that the rate of adjacent parenchyma atelectasis after intersegmental stapling during

thoracoscopic anatomic segmentectomies is low (12.9%) and small in size with an average diameter of 8 mm. In view of these results, questions about the deleterious effect of stapling, on the viability of the adjacent parenchyma, do not seem justified. These findings do not prevent stapling from being carried out in the most precise and least traumatic way possible. This implies that all available technical means allowing for an accurate delineation of the ISP should be used, i.e., 3D modelization and intraoperative marking, whatever the method.

In total, it is possible to improve the precision of the SLRs. We have attempted summarizing the various means on *Table 1*. This is necessary to further reduce the morbidity of these procedures, which is already lower than that of lobectomies but still too high compared to non-surgical techniques. This requires (I) performing these procedures via a closed chest approach; (II) knowing as much as possible

about segmental anatomy and studying mapping before and during the procedure; (III) performing an intraoperative examination on the intersegmental lymph nodes and on resection margins to expand resection if necessary; (IV) using a preoperative or intraoperative marking method to determine the ISP as accurately as possible; (V) stapling ISP, an imperfect method but that currently represents the least bad compromise between accuracy and safety.

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