

# Simulation and navigation techniques in segmentectomy for lung cancer

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Abstract: The diagnostic imaging technology for lung nodules has improved because of advances in computed tomography (CT) equipment. Therefore, surgical resections have increased for smallsized lung cancers or low-grade lung cancers with ground-glass opacity (GGO) that are not detected on chest radiographs. A recent Japanese prospective randomized study of segmentectomy versus standard lobectomy for small-sized lung cancer revealed better overall survival (OS) in the segmentectomy group, which supports segmentectomy for lung cancer patients. However, this prospective trial showed that postoperative recurrences were more frequent in the segmentectomy group than in the lobectomy group. In clinical practice, intentional segmentectomy for the lung has been indicated for lung cancer patients as several retrospective studies have shown favorable outcomes. The usefulness of a three-dimensional (3D) understanding of segmental anatomy has been reported, and new complex segmentectomies have been developed using 3D simulation. Advances in 3D-CT technology and simulation software provide precise preoperative simulation for surgical procedures that enable understanding of complex bronchovascular anatomy and 3D measurement of the surgical margin. A precise 3D simulation allows surgeons to perform safer complex segmentectomies. Hence, we can expect a better postoperative quality of life and improved survival by reducing the amount of resected parenchyma. We reviewed the expanding indications for lung segmentectomy and the growing demand for 3D simulation technology, including its advantages and limitations. We believe that this field will develop further as technology continues to advance.

**Keywords:** Three-dimensional computed tomography (3D-CT); lung cancer; segmentectomy; video-assisted thoracoscopic surgery (VATS); robot-assisted thoracoscopic surgery (RATS)

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# Introduction

Lung cancer is the leading cause of death worldwide, and lobectomy has been the standard surgical procedure for lung cancer since the results of a historical prospective clinical trial by the Lung Cancer Study Group (LCSG) in 1995 (1). However, the diagnostic imaging technology for lung cancer in the 1980s, which was used in this study conducted by the LCSG, is poor compared with modern technology, especially in terms of the resolution and accuracy of computed tomography (CT). With the subsequent worldwide spread of high-resolution (HR) CT, studies of well-differentiated lung adenocarcinoma exhibiting ground-glass opacity (GGO) on CT (2,3), studies of the relationship between the ratio of consolidation to the total tumor diameter (consolidation to tumor ratio; C/T

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ratio) in CT images and prognosis of lung cancer (4,5), and a single center study of sublobar resection for lung cancer as an intentional surgery (6,7), were reported and evidence has been accumulated. Due to such changes in the field of lung cancer, a large-scale prospective clinical trial was planned in Japan (JCOG0802/WJOG4607L) which matches the current level of lung cancer treatment. The results showed that intentional segmentectomy for small-sized lung cancer significantly improved overall survival (OS) compared with standard lobectomy (8).

From a technical perspective, new research on lung segmental anatomy has been reported since the 2010s with the advent of three-dimensional (3D) CT analysis software using HRCT (9,10). Additionally, with advances in thoracoscopic surgery, video-assisted thoracoscopic surgery (VATS) segmentectomy using preoperative 3D simulation has been reported (11-13), and is expected to become widespread. In this review article, we introduce the evolution of 3D-CT simulation and navigation with the demand for segmentectomy for lung cancer, and the latest 3D-CT simulation software specialized for lung segmentectomy that we use at Shinshu University. Furthermore, we describe other new 3D technologies such as virtual reality (VR) technology in the area of thoracic surgery.

# Development of lung cancer imaging by computed tomography

The historical prospective clinical trial reported by the LCSG in 1995 included radiographically detected lung cancers  $\leq$ 3 cm. Patient eligibility was described as "All patients had suspected lung cancer discovered on chest roentgenogram" (1). Since then, diagnostic imaging technology has improved drastically. Due to advances in CT equipment, surgical resections have increased for small-sized lung cancers and low-grade lung cancer with GGO that are undetected on chest radiographs.

In 2003, Ohde *et al.* have reported a study that investigated HRCT findings of lung cancer  $\leq 3$  cm in 101 lesions from 98 patients (4). They showed that non-invasive disease (tumor without lymph node involvement or vessel invasion) could be determined when the ratio of Cdmax (greatest diameter of consolidation found on all CT cuts) and Td (greatest diameter of tumor found on all CT cuts) was <0.5 (4). Based on this concept of consolidation to tumor ratio (C/T ratio), the results of the Japan Clinical Oncology Group (JCOG) 0201 study were reported in 2011. Suzuki

*et al.* have found that a lung adenocarcinoma  $\leq 2.0$  cm with a C/T ratio  $\leq 0.25$  was defined as the cutoff for radiological non-invasive lung cancer that predicts pathological noninvasive lung cancer (5). In this study, the provisional pathological definition of non-invasive lung cancer is lung adenocarcinoma without nodal involvement, vascular invasion, or lymphatic invasion. They concluded that widewedge resection, as a limited resection, could be adopted because these tumors have a limited potential for nodal involvement or lymphatic/vascular invasion (5).

These results identified which lung cancer types could undergo limited resection, based on preoperative CT findings. However, even if the lesion meets these conditions, segmentectomy should be selected when a wide-wedge resection is not feasible because the lesion is deeply located in the lung parenchyma.

# Impact of segmentectomy for lung cancer

Since the report by LCSG (1), lobectomy has been the standard surgical procedure for lung cancer for over two decades. However, their study was based on medical standards from the 1980s. Since then, subsequent improvements in diagnostic imaging technology have resulted in small-sized lung cancers being detected on HRCT. Accordingly, results of intentional sublobar resection for stage I lung cancer was retrospectively analyzed, and several favorable results were reported. Kodama et al. have analyzed 46 patients who underwent intentional segmentectomy, and Koike et al. have evaluated 74 patients undergoing sublobar resection, including 14 wedge resections, and compared them with standard lobectomy and reported similar prognosis (6,7). Okada et al. have assessed 1,272 non-small cell lung cancer patients at a single institution and concluded that segmentectomy may be acceptable for patients with a tumor  $\leq 2$  cm in diameter without nodal involvement (14). Furthermore, their group reported a non-randomized trial conducted at 3 centers including 305 cases of segmentectomy without nodal involvement, lesions  $\leq 2$  cm, and lobectomy tolerance. Analysis showed that the recurrence rate and prognosis were not inferior to 262 patients who underwent lobectomy (15). Harada et al. have further evaluated the effect of segmentectomy on respiratory function and reported the functional advantage of segmentectomy over lobectomy. They found that a positive and significant correlation between the number of resected segments versus loss of forced vital capacity, loss of forced expiratory volume in 1 second at



**Figure 1** Surgical strategies for stage I lung cancer based on clinical trials. The results of the JCOG0804/WJOG4507L trial and JCOG0802/WJOG4607 trial have been published, and the patient's accrual of the JCOG1211 trial has been completed in November 2015. JCOG, Japan Clinical Oncology Group; WJOG, West Japan Oncology Group; RFS, relapse free survival; OS, overall survival.

2 and 6 months postoperatively, and the postoperative reduction of forced expiratory volume in 1 second was significantly less in the segmentectomy group (16).

In Japan, a prospective randomized study of segmentectomy versus lobectomy (JCOG0802/WJOG4607L) was started in 2008 (17), and the results were recently published (8). The benefit in respiratory function for the segmentectomy group was only 3.5% in the differences in proportion of median forced expiratory volume in 1 second at 12 months from surgery compared to lobectomy group, which was lower than the initial prediction. Surprisingly, the OS after segmentectomy was significantly better than that post lobectomy. However, the local relapse after segmentectomy was approximately twice as high (10.4% versus 5.4%), which underlines the importance of securing a sufficient surgical margin during segmentectomy.

A prospective phase 3 trial similar to JCOG0802// WJOG4607L was conducted by international group of Australia, Canada, and the USA (CALGB/Alliance 140503). Clinically T1aN0 (TNM7th,  $\leq 2$  cm) non-small-cell lung cancer patients were recruited for this study, and the primary endpoint is disease-free survival. This trial differs from JCOG trial in that it includes a wedge resection, and the equivalence of sublobar resection to lobectomy was presented at the 2022 World Congress of Lung Cancer, however, the final report is awaited.

Figure 1 shows the criteria for selecting surgical

procedures in patients with stage I lung cancer, based on Japanese clinical trials (8,18,19). As indicated by these published results and ongoing clinical trials, the importance and demand for segmentectomy may increase in the future, hence, all stage I lung cancer patients were candidate for lobectomy, previously. Furthermore, this indicates that the preoperative simulation based on 3D-CT will be an equally crucial factor as the surgical technique.

#### Segmental anatomy by 3D-CT of the lung

The development of HRCT has increased the detection of small-sized lung cancers and ground-glass nodules. Additionally, with the development of 3D-CT technology, a 3D construction of pulmonary vessels, especially pulmonary arteries (20), research on segmental anatomy including bronchi and pulmonary arteries and veins, and research on segmentectomy using these anatomical data have advanced (11,12).

Shimizu and colleagues conducted several segmental anatomical studies using 3D-CT and reported bronchovascular pattern variations of the right upper lobe, focusing on the pulmonary veins (9,10), and the variation patterns of the right middle and lower lobes (21). Additionally, they reported various new surgical procedures using 3D-CT such as the medial-basal segmentectomy (S7), subsuperior segmentectomy (S\*), right middle lobe segmentectomy, medial-basal segment

Author	Number of cases	Procedure	Approach	Feature	3D software	Year	Journal	Reference
Watanabe	14	Anatomic resection	Thoracotomy	3DCTA; pulmonary artery	Somatom Plus 4-VZ; Siemens Medical System, Germany	2003	Ann Thorac Surg	(20)
Oizumi	NA	Segmentectomy	Thoracoscopic	3DCTA; pulmonary artery and vein	64-channel multi-detector CT	2010	Ann Thorac Surg	(11)
Shimizu	42	Segmentectomy	27 hybrid VATS; 15 totally thoracoscopic	3DCTAB; pulmonary artery/ vein and bronchi	Ziostation, Ziosoft, Japan	2012	Interact Cardiovasc Thorac Surg	(12)
Nakazawa	34	RUL segmentectomy	Thoracoscopic	3DCTAB; pulmonary artery/ vein and bronchi	Ziostation, Ziosoft, Japan	2020	JTCVS Tech	(27)

#### Table 1 Clinical application of 3D-CT for segmentectomy

3D-CT, three-dimensional computed tomography; NA, not applicable; RUL, right upper lobe, VATS, video-assisted thoracoscopic surgery, 3DCTA, three-dimensional computed tomography angiography, 3DCTAB, three-dimensional computed tomography angiography and bronchography.

(S7)-sparing right basal segmentectomy, and superior lingular S4 segmentectomy (22-26).

Furthermore, Shimizu *et al.* have developed a simplified anatomical model for segmentectomy of the right upper lobe, focusing on the pulmonary vein variations (10), and reported the surgical outcomes of a model-based approach to the intersegmental vein (27). These studies focused on the relationship between bronchi and pulmonary veins because the branching pattern of veins is highly helpful for preoperative simulation and intraoperative navigation in right upper segmentectomy. *Table 1* summarizes the reports of 3D-CT simulation for segmentectomy or anatomical lung resection in clinical practice.

# Simulation and navigation techniques in thoracoscopic segmentectomy

Segmentectomy is a challenging surgical procedure attributed to the anatomical complexity of the lung. In segmentectomy, it is critical to perform preoperative simulation while ensuring an appropriate surgical margin based on the tumor size, tumor localization, and radiological findings such as solid or ground-glass nodules. Therefore, precise 3D-CT simulations are useful.

Recently, volume-rendering reconstruction software dedicated to lung segmentectomy was approved in Japan (REVORAS, 2020, Ziosoft, Inc., Tokyo, Japan). This software has new, advantageous functions with surgeon-oriented features as follows: semi-automated segmentectomy planning based on the location of the tumor and the dividing level of the bronchial or arterial branches (surgeons can determine any dividing level of the branches) and automated measurement of the margin distance. Specific 3D views for segmentectomy are useful in understanding the divided or preserved hilar structures and the shape of the lung parenchyma to be resected with the intersegmental plane (28). Although thin-slice enhanced CT is preferred for creating high-quality simulation images, even images created by plain CT are generally acceptable for clinical use. Another feature of REVORAS is that tracing the outer rim of the bronchi makes visualization clearer compared with the previous model Ziostation2 (2010, Ziosoft, Inc.). Figure 2 shows an image comparison between REVORAS, Ziostation2, and another widely used 3D software, Synapse Vincent (Ver.5.4, 2017, Fujifilm, Tokyo, Japan). The bronchial branches were more clearly and more distally recognized in REVORAS as compared with Ziostation2 and Synapse Vincent.

At Shinshu University Hospital, we adopted custommade precision segmentectomy with preoperative simulation and intraoperative navigation using REVORAS in daily clinical practice. This includes both thoracotomy or thoracoscopic and VATS and robot-assisted thoracoscopic surgery (RATS) segmentectomy. For all patients undergoing segmentectomy, we create 3D-CT images to plan segmentectomy. Based on the planning with expected



**Figure 2** Comparison of simulated images of 3D software. 3D image of right upper lobe bronchi created by REVORAS (A) Ziostation2 (B), and Synapse Vincent (C). Combined images of pulmonary artery/vein and bronchi of REVORAS (D), Ziostation2 (E), and Synapse Vincent (F). (A,B,D,E) are images obtained from the same CT image from a patient. 3D, three-dimensional; CT, computed tomography.

volume loss and margin distance, we determine which segment(s) and/or subsegment(s) should be removed and which segmental/subsegmental branches should be divided or preserved with adequate margins (28). The actual time required for deliberated simulation of segmentectomy for each case is about 10–20 minutes. *Figure 3* shows an actual 3D simulation by REVORAS and an intraoperative view of VATS left S<sup>3</sup>b subsegmentectomy for a patient with a 4-mm metastatic lung tumor. In this case, the automatically simulated margin distance was 4.5 mm; hence, subsegmentectomy was performed by dissecting the V<sup>3</sup>c and extended into S<sup>3</sup>c and the pathological margin was negative.

Preoperative simulation and intraoperative navigation by displaying the resected bronchi and pulmonary vessels using REVORAS can facilitate segmentectomy or complex subsegmentectomy with an appropriate dissection of the pulmonary vessels, bronchi, and lung parenchyma, which leads to an appropriate surgical margin.

A limitation of various 3D simulation software currently

in use is that it does not reflect the collapsed lung during surgery because the simulation was performed using preoperative CT by fully inspirated state that is similar to a fully ventilated lung. Another limitation is the cost of the software. Commercially available 3D simulation software such as REVORAS, Ziostation, and Synapse Vincent are considerably expensive, and each institute must install them to use.

#### Other new 3D technologies in thoracic surgery

VR devices and software have become popular and are being tested for application in the field of thoracic surgery (29). Ujiie *et al.* have reported preoperative planning and simulation using VR technology by 3D polygon data derived from preoperative CT data and head-mount displays and applied their initial experience of lingula-sparing left upper segmentectomy (30). Li *et al.* have applied augmented reality (AR) and 3D-print models to 55 thoracoscopic lung segmentectomy or subsegmentectomy that revealed favorable



**Figure 3** 3D simulation and surgical view of VATS left S<sup>3</sup>b subsegmentectomy. Yellow arrowhead indicates 4 mm-diameter metastatic lung tumor in left S<sup>3</sup>b (A). Surgical margin distance automatically displayed (B). Simulation of pulmonary artery and bronchus dissection by REVORAS and yellow arrows indicate vessels and bronchi to be dissected (C-E). Actual intraoperative view of VATS S<sup>3</sup>b subsegmentectomy, and yellow arrows indicate vessels and bronchi to be dissected as in the simulation by REVORAS (F-H). 3D, three-dimensional; VATS, video-assisted thoracoscopic surgery.

outcomes such as shorter operating time, less intraoperative blood loss, and shorter length of hospital stay (31).

VR technology has further been applied to VATS training in the field of thoracic surgery. Jensen *et al.* have reported a simulation-based test of VATS lobectomy of a

right upper lobe using a VR simulator and established valid evidence for a VR simulator test (32,33). Furthermore, Haidari *et al.* have described five VATS lobectomy simulations using a VR simulator (34,35).

Arjomandi Rad et al. have reviewed extended reality

(XR), encompassing both VR and AR, and described three areas: (I) the application of XR in thoracic surgery training; (II) preoperative planning of thoracic procedures; and (III) intraoperative assistance from articles that explored the use of VR and/or AR (36). They emphasized the benefits of XR for surgical training, particularly in junior trainees, by allowing them to operate in a realistic, but ethically riskfree setting, as well as enhancing preoperative planning and intraoperative guidance (36).

Yoon *et al.* have reported another clinical application of 3D technology other than preoperative simulation or training. They improved the quality of informed consent using personalized 3D-printed lung models for lung cancer patients. This method helped obtain preoperative informed consent and improved patient comprehension (37).

Tokuno *et al.* have reported an original software called resection process map (RPM) that can create dynamic virtual images (deformable images) that enable more accurate intraoperative simulation (38,39).

Several of these technologies are still under development, however, we expect further progress in this field.

# Conclusions

In the field of thoracic surgery, the demand for segmentectomy, which requires more complex and precise planning and procedures, will inevitably increase. Rapidly advancing 3D-based simulations will enable more precise and accurate surgical planning, navigation, and surgical training. These are expected to contribute to safe surgery, which will lead to improved surgical outcomes.

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