

Essential Surgical Plan Modifications After Virtual Reality Planning in 50 Consecutive Segmentectomies

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ABSTRACT

BACKGROUND Lately, increased interest in pulmonary segmentectomy has been observed. Segmental border identification is extremely difficult on 2-dimensional computed tomography (CT). Preoperative application of virtual reality (VR) can provide better insight into patient-specific anatomy. The aim of this study was to investigate the added clinical value of 3-dimensional (3D) VR using PulmoVR for preoperative planning.

METHODS Patients with an indication for pulmonary segmentectomy were included between June 2020 and September 2021 at the Erasmus Medical Center, Rotterdam, The Netherlands. CT scans were (semi)automatically segmented to visualize lung segments, segmental arteries, veins, and bronchi. Three surgeons made a surgical plan on the basis of the conventional CT scan and subsequently analyzed the VR visualization. The primary outcome was the incidence of critical (ensuring radical resection) preoperative plan modifications. Secondly, data on observed anatomic variation and perioperative (oncologic) outcomes were collected.

RESULTS A total of 50 patients (median age at surgery, 65 years [interquartile range, 17.25 years]) with an indication for pulmonary segmentectomy were included. After supplemental VR visualization, the surgical plan was adjusted in 52%; the tumor was localized in a different segment in 14%, more lung-sparing resection was planned in 10%, and extended segmentectomy, including 1 lobectomy, was planned in 28%. Pathologic examination confirmed radical resection in 49 patients (98%).

CONCLUSIONS This 3D VR technology showed added clinical value in the first 50 VR-guided segmentectomies because a 52% change of plan with 98% radical resection was observed. Furthermore, 3D VR visualization of the bronchovasculture, including various anatomic variations, provided better insight into patient-specific anatomy and offered lung-sparing possibilities with more certainty.

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Stage I non-small cell lung cancer (NSCLC) is the most common type of lung cancer.¹ Traditionally, management of patients with stage I NSCLC consisted of lobectomy.²⁻⁴ Over the last few years, there has been an increasing interest, as well as a shift, toward lung-sparing sublobar anatomic resection techniques. An international consensus for segmentectomy in cases of benign pulmonary disease, carcinoid tumors, or pulmonary metastasis not suitable for wedge resection has been reached.^{5,6} Moreover, segmentectomy for small

(<2 cm) stage I NSCLC has been proposed by various groups.⁷⁻⁹ Preliminary results of a phase III randomized controlled trial (JCOG0802, comparing lobectomy vs segmentectomy) showed better 5-year overall survival but higher recurrence in the segmentectomy group without

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differences in recurrence-free survival, although the trial is currently under peer review for publication.¹⁰⁻¹² On the basis of existing literature, our hospital (Thoraxcenter, Erasmus University Medical Center, Rotterdam, The Netherlands) adopted pulmonary segmental resection in 2019 for resection of stage I NSCLC (<2 cm), small or deeply located carcinoid tumors, benign disease limited to lung segments, and intrapulmonary metastases from a primary extrathoracic malignant disease, not suitable for wedge resection.

Pulmonary segmentectomies are generally challenging for the surgeon because a thorough understanding of segmental anatomy is necessary for identification, isolation, and division of the segmental vessels and bronchi.^{7,8} Patient-specific bronchovascular variations increase complexity even further.^{13,14} Identifying intersegmental divisions and target branches of pulmonary arteries, veins, and bronchi on 2-dimensional (2D) computed tomography (CT) can be difficult. Virtual reality (VR) could allow for stereoscopic, immersive, and 3-dimensional (3D) visualization of the segmental borders and bronchovascular, thereby allowing better spatial insight into a patient's lung anatomy for preoperative planning.¹⁵ Our previously published prospective observational pilot study showed successful development and clinical application of an artificial intelligence (AI) and VR platform (PulmoVR) for segmentectomy planning.¹⁶

In this study, we performed a prospective single-center analysis of our first-year experience with surgical planning using PulmoVR, supplemented by virtual 3D-based images (Pulmo3D) for intraoperative guidance, for 50 consecutive patients undergoing pulmonary segmentectomy. The aim of our study was to investigate the added clinical value of PulmoVR by evaluating the incidence of critical changes in surgical plan

(compared with conventional CT-guided planning), the identification of anatomic variations, and subsequently, the perioperative (oncologic) outcomes to determine safety and clinical benefit.

PATIENTS AND METHODS

PATIENT SELECTION. This study was approved by the Medical Ethical Committee of the Erasmus Medical Center (MEC-2020-0702). A total of 50 consecutive patients, accepted and eligible for pulmonary segmentectomy between June 2020 and September 2021 at the Erasmus Medical Center, Rotterdam, The Netherlands, were enrolled in this study. Patients were included after setting of an indication by the multidisciplinary team, according to a previously described protocol.¹⁶

PREOPERATIVE PLANNING. VR-based planning supplemented the conventional 2D CT planning workflow. The surgeon documented the target segment or segments and surgical plan by evaluating the preoperative diagnostic 2D CT scans. Subsequently, the surgeon analyzed 3D VR visualization to document the target segment or segments by using PulmoVR. In oncologic cases or cases without pathologic diagnosis, after the target segment was determined, surgical margins were estimated by using a spherical virtual object (Figure 1), to estimate the feasibility of segmentectomy. If affected lung segment or segments or tumor resection margin remained uncertain, an automated AI-based, segmental anatomic segmentation, including visualization of segmental borders, was performed according to the previously published protocol.¹⁶

For cases with a challenging bronchovascular anatomy, intraoperative guidance using interactive virtual 3D model visualization was available on a monitor in the operating room (Video 1). These models were created by using Pulmo3D software, which was developed at our department together with MedicalVR and viewed on 3D Builder (Microsoft).

SURGICAL TECHNIQUE. The 3D video-assisted thoracoscopic surgery procedures were performed by 3 cardiothoracic surgeons and 1 senior resident, as previously described.¹⁶ If intraoperative frozen section of level 10 to 12 lymph nodes (which is routinely performed when segmentectomy for primary lung cancer is performed in our center) was positive for tumor cells, segmentectomy was converted to lobectomy for radical tumor excision according to international guidelines in case of N1 disease.¹⁷ If no preoperative conclusive pathologic diagnosis was available and wedge resection of the small tumor was possible, intraoperative frozen section analysis of the wedge was performed first, followed by segmentectomy

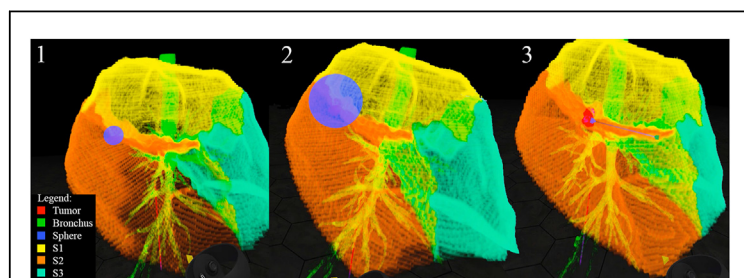


FIGURE 1 Target segment determination, measuring tumor size and resection margin. In oncologic cases, after the target segment was determined, surgical margins were estimated by using a spherical virtual object. (1) First, the tumor diameter is measured (13 mm), located in segment 2 but close to segment 1. (2) Tumor diameter is multiplied 3 times (39 mm), showing that the resection margin to segment 1 is insufficient. (3) Besides spherical measurement, linear resection margin can be measured as well, 55 mm to segment 3 in this case.

TABLE 1 Baseline Characteristics of Study Patients

Characteristic	Median [IQR] or n (%)
Age, y	65 [17.25]
Sex	
Male	28 (56)
Female	22 (44)
BMI, kg/m ²	25.5 [8]
Smoking history ^a	36 (72)
COPD	7 (14)
Asthma	3 (6)
Cardiovascular history	24 (48)
Pulmonary function, ^b %	
FEV ₁	90 [23]
FVC	102 [16.75]
Dlco	79 [29]

^aSmoking history includes former smokers and active smokers; ^bPulmonary function is shown as percentage to reference value on the basis of sex, length, and weight. BMI, body mass index; COPD, chronic obstructive pulmonary disease; Dlco, diffusing capacity of lung for carbon monoxide; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; IQR, interquartile range.

(or lobectomy in case of positive level 1 lymph nodes) in cases of primary lung carcinoma.

STUDY OUTCOMES. The primary outcome of this study was the incidence of critical changes in surgical plan after the addition of 3D VR planning compared with only conventional 2D CT planning. Critical changes in surgical planning were defined as changes that could potentially result in better outcomes (eg, radical resection [preferably with resection margins of at least 1 cm] and preservation of healthy lung tissue whenever possible). Changes in surgical plan were categorized as (1) different segment selection, (2) smaller segmentectomy, (3) extended segmentectomy (en bloc subsegmentectomy, or bi- or trisegmentectomy), or (4) lobectomy. Secondary

study outcomes included observed anatomic variation during 3D VR, perioperative outcome variables, and pathologic examination. Complications were subdivided into major complications (reoperation, readmission, conversion to thoracotomy, acute respiratory distress syndrome, massive hemorrhage (>1000 mL), empyema, tension pneumothorax) and minor complications (pneumonia, delirium, supraventricular arrhythmia, venous thromboembolism, chylothorax, prolonged air leak for more than 5 days, and atelectasis requiring bronchoscopy).

DATA EXTRACTION AND ANALYSIS. Documentation of the target segment or segments by using 2D CT and PulmoVR for preoperative planning was registered before surgery. All secondary outcomes were obtained from the patient's electronic file system. The data were analyzed using Microsoft Office Excel 2016.

RESULTS

PATIENT CHARACTERISTICS. A total of 50 patients (median age, 65 years; 56% male) were referred for elective segmentectomy (Table 1). Patients had a clinical diagnosis of NSCLC stage I (50%), metastases (18%), benign disease (8%), or carcinoid tumor (8%), or they had no preoperative pathologic diagnosis (16%) (Table 2). In patients with NSCLC, the median tumor diameter was 13.5 mm, and most were clinically staged as cT1b N0 M0 (56%). Three patients with cT1c N0 M0 were included for segmentectomy as well: 1 patient with poor lung function (diffusing capacity of lung for carbon monoxide of 63%), 1 patient with another primary lung tumor in the contralateral lung who required adjuvant chemotherapy, and 1 patient with a 22-mm NSCLC tumor who eventually underwent lobectomy. One patient with cT1b N2 M1c stage IV

TABLE 2 Clinical Diagnosis or Staging and Tumor or Lesion Diameter^a

Clinical Diagnosis	Count, n (%)	Tumor or Lesion Diameter, mm,		TNM Classification			
		Median [IQR]	n (%)	Clinical TNM ^b	n (%)	Pathological TNM ^b	n (%)
NSCLC	25 (50)	13.5 [6.7]	32 (63)	cT1a N0 M0	7 (28)	pT1a N0 M0	7 (14)
				cT1b N0 M0	14 (56)	pT1b N0 M0	15 (30)
				cT1c N0 M0	3 (12)	pT1b N1 M0	1 (2)
				cT1b N2 M1c	1 (4)	pT1b N2 M0	1 (2)
						pT1c N0 M0	5 (10)
				pT2a N0 M0	3 (6)		
Metastasis	9 (18)	11.5 [15.0]	9 (18)
Benign	4 (8)	31 [12.5]	4 (8)
Carcinoid	4 (8)	10.9 [10.9]	3 (6)
No diagnosis	8 (16)	14 [4.4]
No tumor	0 (0)	-	2 (4)

^aClinical diagnosis of all patients, showing tumor or lesion diameter per group. For primary lung carcinoma, the clinical tumor stage is reported; ^bStaging according to the eighth edition of the TNM classification for NSCLC. IQR, interquartile range; NSCLC, non-small cell lung carcinoma.

TABLE 3 Change of Surgical Plan After Addition of 3-Dimensional Virtual Reality to 2-Dimensional Computed Tomography for Preoperative Planning

Change of Surgical Plan	Yes n (%)	No n (%)
Change of plan	26 (52)	24 (48)
Type of change		
Different segment selection	7 (14)	...
More lung sparing segmentectomy	5 (10)	...
Extended segmentectomy	13 (26)	...
Lobectomy	1 (2)	...

NSCLC, was referred for segmentectomy because of oligoprogression of a lesion in the lingula (not suitable for wedge resection) during targeted therapy.

CHANGE OF PREOPERATIVE SURGICAL PLAN. Change of the preoperative surgical plan with the addition of 3D VR to conventional 2D CT preoperative planning was

observed in 26 (52%) patients (Table 3). A different tumor segment location was documented for 7 (14%) patients (Figure 2A). A total of 5 (10%) patients were planned for a more lung-sparing (limited) segmentectomy (Figure 2B) and 14 (28%) patients for an extended segmentectomy (Figure 3A), including 1 lobectomy. Lobectomy needed to be performed on the basis of tumor location in 3D VR. On the basis of 2D CT, segment 1 and segment 2 resection of the right upper lobe was planned; however, 3D VR showed localization within all 3 segments of the upper lobe, thus resulting in lobectomy (Figure 3B).

ANATOMIC VARIATION. During PulmoVR analysis, various anatomic variations of the bronchovasculture were observed that were not seen during 2D CT analysis, nor were they documented by the radiologist. Anatomic variations consisted of arterial and venous abnormalities (eg, additional segmental vasculature) (Figure 4) or the presence of an extra lung segment (segment X) (Figure 5A, Video 2).

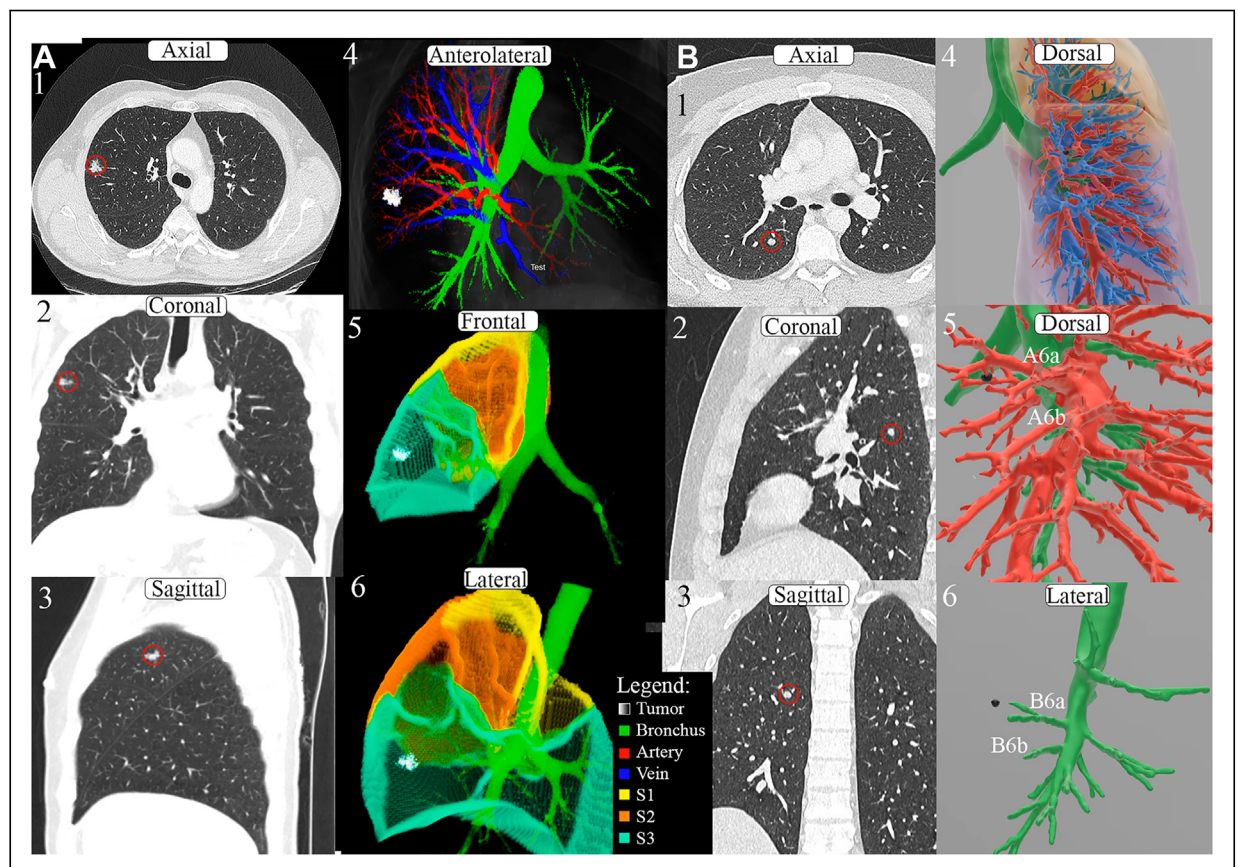


FIGURE 2 Change of plan with different target segment and limited planned resection. (A) (1), (2), and (3) 2-dimensional computed tomographic views showing tumor (red circle) in the right upper lobe. On the basis of 2-dimensional computed tomography, tumor was localized in segment (S) 2. (4) Anterolateral view of the bronchovasculture. On the basis of this visualization, tumor segment localization remained unclear. (5) and (6) 3-dimensional virtual reality visualization including segment borders. Tumor is clearly located in S3. (B) (1), (2), and (3) 2-dimensional computed tomography showing a tumor in the right lower lobe, planned for S6 resection. (4), (5), and (6) Pulmo3D renders showing a small tumor in S6 with 2 arterial branches and 2 bronchi, thus making subsegmentectomy of S6a possible.

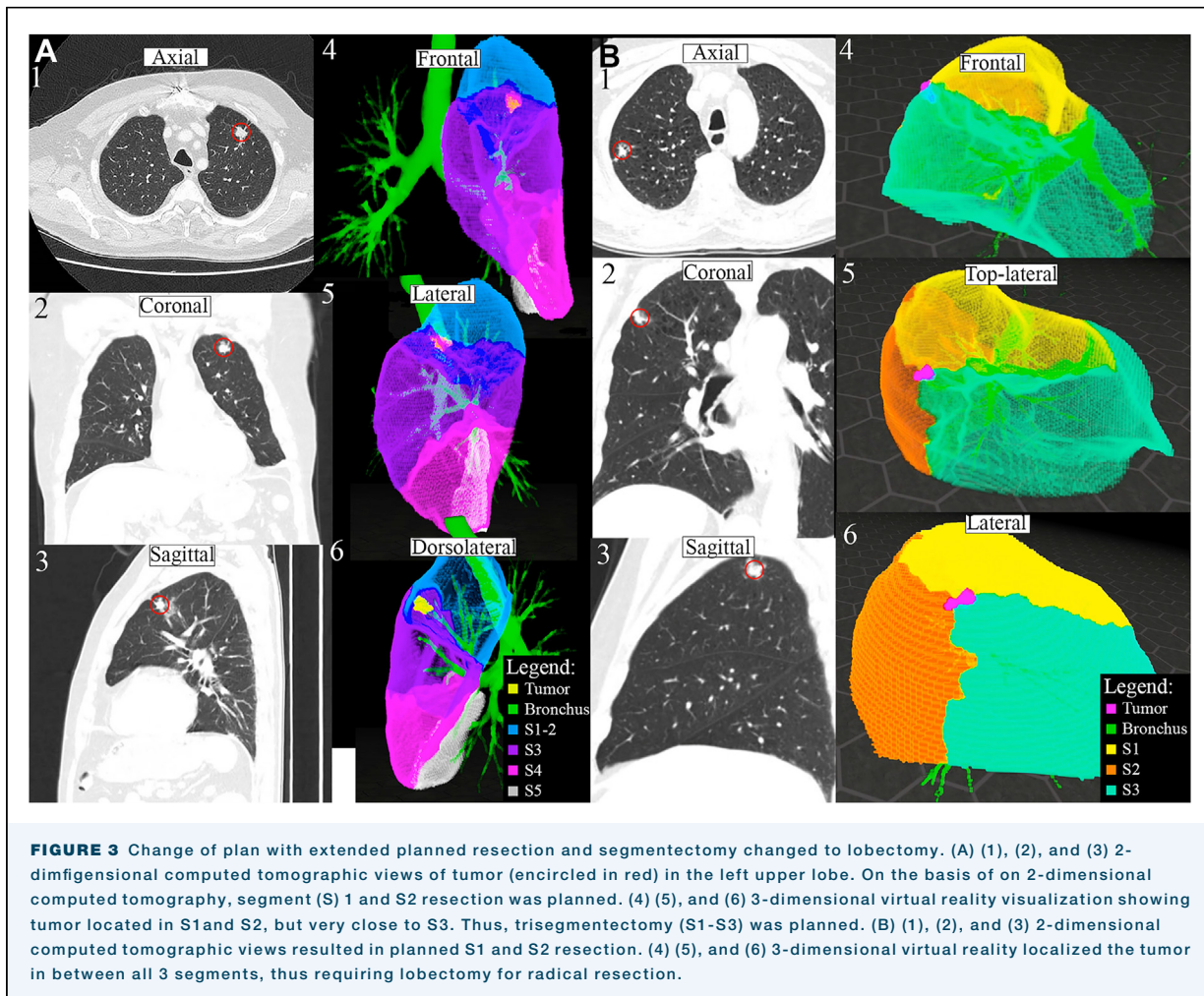
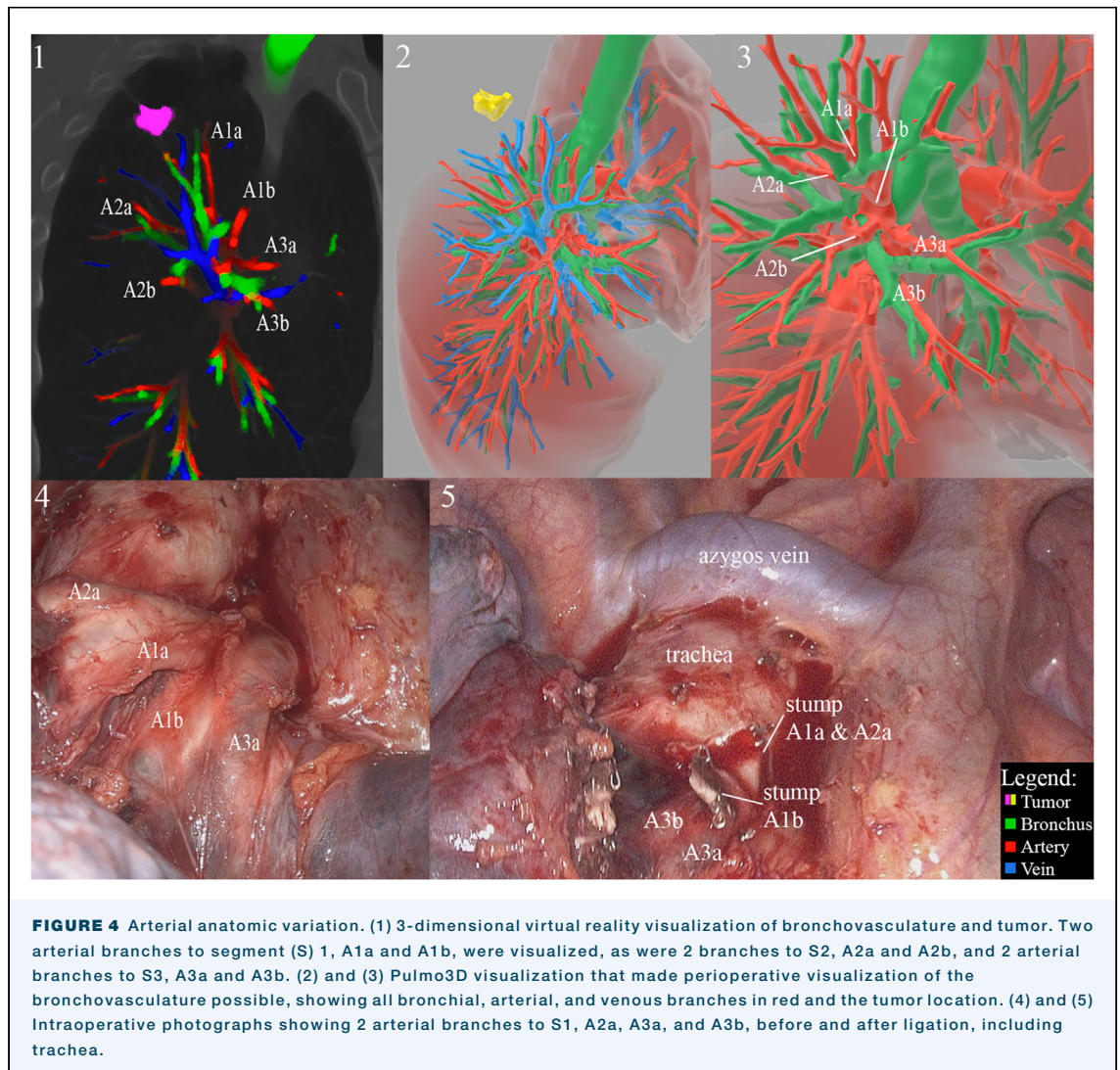


FIGURE 3 Change of plan with extended planned resection and segmentectomy changed to lobectomy. (A) (1), (2), and (3) 2-dimensional computed tomographic views of tumor (encircled in red) in the left upper lobe. On the basis of on 2-dimensional computed tomography, segment (S) 1 and S2 resection was planned. (4) (5), and (6) 3-dimensional virtual reality visualization showing tumor located in S1 and S2, but very close to S3. Thus, trisegmentectomy (S1-S3) was planned. (B) (1), (2), and (3) 2-dimensional computed tomographic views resulted in planned S1 and S2 resection. (4) (5), and (6) 3-dimensional virtual reality localized the tumor in between all 3 segments, thus requiring lobectomy for radical resection.

PERIOPERATIVE OUTCOMES. All procedures were performed through video-assisted thoracoscopic surgery without conversion to thoracotomy (Supplemental Table 1). Median operation duration (from skin incision to skin closure) was 200 minutes. Median blood loss was 45 mL, and median hospital stay after surgery was 4 days. No perioperative death occurred. Two reoperations were necessary because, in 1 patient, no tumor was observed in the pathologic specimen (although no tumor was found in the completion lobectomy), and in 1 patient, definitive pathologic examination showed malignant disease, even though frozen section analysis of the wedge resection did not show a tumor during the index operation, thus requiring completion segmentectomy in a second operation. A minor complication (9 in total) occurred in 8 (16%) patients, including pneumonia ($n = 2$), supraventricular arrhythmia ($n = 2$), and prolonged air leak ($n = 5$).

In relation to the 3D VR preoperative plans, a total of 41 (82%) surgical procedures were performed according

to plan, whereas a more extended resection than initially planned was performed in 9 (18%) cases (Supplemental Table 2). None of these unplanned extended resections were suggested on the basis of conventional CT planning. In 1 patient, an additional resection of part of segment 10 was performed in addition to resection of segments 7 to 9 because no tumor was observed macroscopically (in this patient, reoperation was necessary because no tumor was found). Given positive lymph nodes in intraoperative lymph node frozen sections, 2 resections (4% of total or 7.6% of NSCLC cases) needed to be converted to lobectomy. In 1 patient, a right upper lobectomy was performed instead of a planned segment 3 resection as a result of intraoperative uncertainty of surgical margins. In the fourth patient, venous drainage of segments 1 and 2 of the right upper lobe would have been compromised after segment 3 resection, thereby resulting in lobectomy (Figure 5B). Four additional segmentectomies were extended to lobectomy during surgery: (1) satellite lesions were macroscopically



suggested in the remaining lobe of the target segment (although not seen on 2D CT or 3D VR, neither found in pathologic examination); (2) a benign lesion in basal segments where a basilar segmentectomy was planned; however, intraoperatively, segment 6 was affected by extreme adhesions, resulting in lobectomy; (3) micropapillary adenocarcinoma in frozen section of segment 7, which caused us to convert segmentectomy to lobectomy because of the aggressive nature of this micropapillary subtype; and (4) conversion to lobectomy after bleeding during segment 2 resection.

PATHOLOGIC EXAMINATION. All specimens were sent to a dedicated pathologist for examination (Table 2). None of the negative intraoperative lymph node frozen sections showed tumor cells during definitive pathologic examination. In 2 cases, there was no histologic match with the clinical diagnosis. In the patient with a diagnosis of carcinoid tumor who underwent

reoperation, no tumor was found (either in the segment or in the lobe), and in the patient with cT1b N2 M1c, a granuloma was found instead of a satellite metastatic nodule. Pathologic examination confirmed radical resection in 49 patients (98%). In 1 patient, R1 resection of a carcinoid tumor was seen, but no remaining tumor tissue was observed during a follow-up positron emission tomography CT dotatate scan. In the case of NSCLC, the resection margin was larger than 1 cm in 23 cases (72%), of which the resection margin (to the bronchial staple line) was equal to or greater than tumor size in 13 (41%) cases. In the remaining 9 cases, the resection margin was less than 1 cm.

COMMENT

Challenges for pulmonary segmentectomies have been identified as understanding of the segmental anatomy

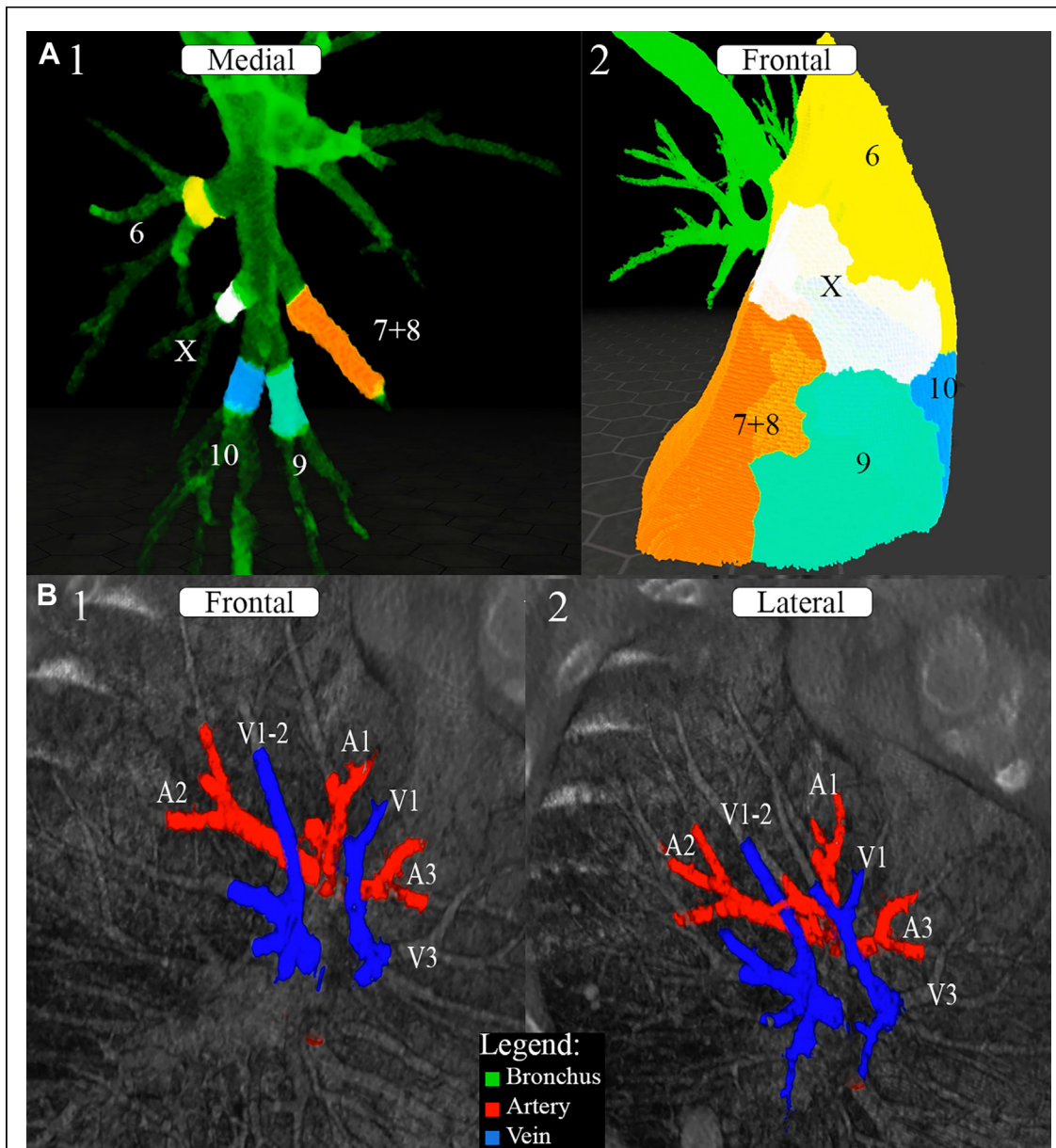


FIGURE 5 Anatomic variation visualization in 3-dimensional virtual reality with (A) the extra segment and (B) aberrant venous drainage. (A) (1) and (2) 3-dimensional virtual reality visualization of bronchi branches of the left lower lobe, showing segment (S) 6, S7 to S8, S9, S10, and extra segment X. (B) (1) and (2) 3-dimensional virtual reality visualization of vasculature of the right upper lobe of a patient planned for S1 and S2 resection. 3-dimensional virtual reality showed that venous drainage of S1 (V1) passes through S3 and crosses the artery A3 before drainage into the right upper pulmonary vein. Given this anatomic variation, lobectomy was required.

and existence of many pulmonary vascular variations and abnormalities. For the preoperative planning, 2D CT is still the current standard. PulmoVR was developed to allow 3D VR visualization of the pulmonary anatomy for preoperative planning. Our study investigated the change of preoperative plan when supplementing conventional 2D CT with 3D VR, a change observed in 52% of the patients. We hypothesized that 3D VR visualization allowed better discernment of the bronchi, veins, and

arteries, thereby providing an overall better preoperative anatomic view of the patient's anatomy and resulting in the 52% change of plan. Pulmo3D was used as perioperative guidance for the surgeon. Furthermore, various anatomic variations were observed in 3D VR.

Virtual reality provides the user with an immersive environment with the patient-specific CT scan.¹⁸ Given this immersive and secluded experience, the surgeon will have full attention on the bronchovascular

anatomy of the patient. Furthermore, by using the interactive features, such as (de)activating various segmented structures or slicing or rotating the patient, various steps of the surgery can be simulated. Contrast injection for CT is not necessarily needed for PulmoVR's AI-based analysis to segment various structures, a feature that makes this preoperative planning technique possible for patients with allergies to contrast media.¹⁶ The VR setup requires an initial investment for the hardware (approximately €2000-€4000) and software, which then results in unlimited review possibilities of CT scans and thus lowers the threshold to use the system after purchase. Regarding hardware, off-the-shelf computers and VR headsets can be used. The software (MedicalVR) can be purchased for a research or education-only license fee or for clinical purposes after CE certification and approval by the US Food and Drug Administration, both of which are expected late 2022 and late 2023 to early 2024, respectively. The rendering of CT scans for a specific procedure takes approximately 30 seconds and requires that the surgeon exports the CT scan data from their local picture archiving and communication system (PACS). Additional segmentations or analyses can be performed according to surgeon's preference and the complexity of the cases. The system's interface is designed by us (surgeons) together with MedicalVR, so our colleagues can use it at their desk without the need for extra technical assistance from any other department.

To understate the difficulty of pulmonary segmentectomy planning, a center with surgeons highly experienced in pulmonary segmentectomy had unplanned outcomes in 8% of the procedures (including 3% unplanned additional resections in cases of NSCLC).¹⁹ Various explanations can be given for this high number of unplanned outcomes and our high number of 52% change of plan. First, the 3D perspective, including colored structures of interest, aids the user in segment selection. Second, having surgeons as the study population in this study can be part of the explanation for the high percentage of change of plan. It may be hypothesized that surgeons (in general, and in this study) find it difficult to localize tumors or lesions in a specific lung segment on conventional 2D CT. It could be interesting to compare the outcomes between 2D CT and 3D VR for a different study population, such as cardiothoracic radiologists, to see whether their target location determinations are more similar.

The change in operative plan is driven by 2 factors: (1) being as lung sparing as possible, but (2) without comprising oncologic radicality. Oncologic radicality can be achieved by removal of the lung segment with the tumor, including sufficient resection margin, without positive lymph nodes that require conversion to

lobectomy. Sufficient resection margin is a term that is under debate worldwide because no consensus has been reached on what margin should be maintained. On the basis of the literature, a parenchymal resection margin larger than 1 cm should be pursued because of the longest recurrence-free survival in this patient group.^{20,21} Our pathology department was used to defining bronchial resection margins rather than parenchymal resection margins, but we incorporated this measurement in the pathologic examination workflow for segmentectomy. Because segmental borders can be determined by AI and the distance from the tumor to the segmental border can be measured in PulmoVR, the resection margin can be precisely determined preoperatively. From now on, we can compare VR-calculated resection margins and margins that are based on pathologic examination.

Three patients with NSCLC stage cT1c N0 M0 were included for segmentectomy on the basis of the multidisciplinary team decision. According to the literature, it is debatable whether a tumor larger than 2 cm is oncologically resected safely with segmentectomy or whether recurrence risk is too high in these patients. Furthermore, intraoperative frozen section of the tumor for staging and resection margin could be an interesting feature, if possible logistically and in terms of time. Our histologic diagnosis showed upstaging to pT1c or pT2a in 4 cases. If this information is known perioperatively, lobectomy could be considered in these patients. Furthermore, if parenchymal resection margin could be determined intraoperatively, it can be determined whether resection margin is adequate or whether additional resection is necessary.

Although augmented reality or VR could be used for preoperative planning or training, it would be interesting to investigate the use of augmented reality or extended reality for intraoperative guidance.^{18,22,23} A major challenge in intraoperative guidance using extended reality is the shape change of the lung during the surgery (collapsed) compared with fully inflated (thus, during CT imaging). On the basis of the results of this study, we are preparing a multicenter study to investigate the added clinical value of 3D VR over 2D CT in several hospitals in The Netherlands and that will also provide more information on interobserver variability.

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DISCLOSURES

Amir H. Sadeghi and Edris A. F. Mahtab are coinventors of the virtual reality-based technology (PulmoVR) presented in this article. All other authors declare that they have no conflicts of interest.

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