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Role of post-mapping computed tomography in virtual-assisted lung mapping

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Abstract

Background: Virtual-assisted lung mapping is a novel bronchoscopic preoperative lung marking technique in which virtual bronchoscopy is used to predict the locations of multiple dye markings. Post-mapping computed tomography is performed to confirm the locations of the actual markings. This study aimed to examine the accuracy of marking locations predicted by virtual bronchoscopy and elucidate the role of post-mapping computed tomography.
Methods: Automated and manual virtual bronchoscopy was used to predict marking locations. After bronchoscopic dye marking under local anesthesia, computed tomography was performed to confirm the actual marking locations before surgery. Discrepancies between marking locations predicted by the different methods and the actual markings were examined on computed tomography images. Forty-three markings in 11 patients were analyzed.
Results: The average difference between the predicted and actual marking locations was 30 mm. There was no significant difference between the latest version of the automated virtual bronchoscopy system (30.7 ± 17.2 mm) and manual virtual bronchoscopy (29.8 ± 19.1 mm). The difference was significantly greater in the upper vs. lower lobes (37.1 ± 20.1 vs. 23.0 ± 6.8 mm, for automated virtual bronchoscopy; $p < 0.01$). Despite this discrepancy, all targeted lesions were successfully resected using 3-dimensional image guidance based on post-mapping computed tomography reflecting the actual marking locations.
Conclusions: Markings predicted by virtual bronchoscopy were dislocated from the actual markings by an average of 3 cm. However, surgery was accurately performed using post-mapping computed tomography guidance, demonstrating the indispensable role of post-mapping computed tomography in virtual-assisted lung mapping.

Keywords

Anatomic landmarks, Bronchoscopy, Lung neoplasms, Surgery, computer-assisted

Introduction

Virtual-assisted lung mapping (VAL-MAP) is a relatively novel preoperative lung marking technique in which multiple dye markings on the surface of the lung are used as a lung map.[1] Using this method, the rate of successful resection of small targeted lesions reportedly reaches 98% to 99%.[2–4] The technique has been utilized in wedge resection as well as segmentectomy, particularly in complex segmentectomies.[2,5,6] Moreover, the technique is free of serious complications, especially the potentially fatal air embolism observed in conventional percutaneous computed tomography (CT)-guided lung marking methods.[7–9] During VAL-MAP, virtual bronchoscopy (VB) is used to predict the locations of multiple dye markings on the lung surface. Blue dye (indigo carmine) is injected through a metal-tipped catheter to multiple target bronchi (3–6 per patient). Within 3 h, a post-mapping CT scan is taken to detect the water density

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of the injected dye to confirm the locations of the actual markings. This CT image is reconstructed into three-dimensional (3D) images to be used as a guide during subsequent surgery.[1,4] The necessity of including the post-mapping CT scan has often been questioned. Post-mapping CT may enhance the accuracy of VAL-MAP by adjusting the lung map after bronchoscopy;[4] however, it also necessitates additional time, cost, and radiation exposure to patients. An automated VB technique called "mapping mode" was developed and the algorism has been improved to predict the marking locations of VAL-MAP and reduce the workload of manually operated VB. This new system may enhance the accuracy of VB to predict the marking locations of VAL-MAP. The purpose of this study was to examine the accuracy of predicted markings and elucidate the role of the post-mapping CT scan. The marking locations predicted by VB were compared with the actual marking locations measured on the post-mapping CT scan.

Patients and methods

This study was retrospectively conducted using the patient data collected for VAL-MAP. The study was approved by the institutional review board, and informed consent was obtained from each patient before VAL-MAP. Patients were selected for preoperative VAL-MAP if the targeted lesion was expected to be hardly palpable and/or special attention was needed to determine the resection line. The patients who were included in the study underwent VAL-MAP and subsequent surgery in our institute after October 2015 when the Synapse Vincent version (ver.) 4.3 (Fujifilm Medical, Inc.) became available. Forty-three markings in 11 patients were analyzed in this study. The patient characteristics are shown in Table 1.

Table 1. Characteristics of 11 patients who underwent virtual-assisted lung mapping.

Variable	No. of patients
Age (years)	61.3 ± 9.4
Male	7
Female	4
No. of markings/patient	4.0 ± 1.3
Location of targeted lesion: no. of patients (markings)	
Right upper lobe	4 (11)
Right middle lobe	1 (1)*
Right lower lobe	3 (14)
Left upper lobe	3 (13)
Left lower lobe	1 (4)
Surgery	
Wedge resection	4
Segmentectomy	6
Lobectomy†	1
Primarily used virtual bronchoscopy	
Synapse Vincent version 4.3	5
Synapse Vincent version 4.4	6

*One marking in the middle lobe was excluded from the analysis. †The procedure was changed from segmentectomy to lobectomy after virtual-assisted lung mapping.

The VAL-MAP procedure was conducted in the steps indicated in Figure 1. First, thin-slice CT images (1.00- to 1.25-mm thickness) were reconstructed into 3D images. Depending on the operative plan, the ideal lung map was designed using VB. The route to reach each marking point was displayed on the VB monitor. Second, the mapping procedure was conducted preoperatively, usually on the day of surgery or the day before surgery. The details of the procedure have been described previously.[2,4] In short, with the patient under local anesthesia and mild sedation, a regular bronchoscope (BF-260; Olympus, Tokyo, Japan) was inserted orally. Once the target bronchus was identified, a blunt metal-tipped catheter (PW-6C-1; Olympus) preloaded with 1 mL of blue dye (indigo carmine; Daiichi Sankyo, Tokyo, Japan) was inserted through the working channel of the bronchoscope. Standard fluoroscopy was used to visualize the catheter tip reaching the visceral pleura. Finally, the dye was injected toward the visceral pleura by pushing the plunger connected to the catheter, followed by 20 mL of air. The injection procedure was repeated for each target bronchus. Third, within 2 h after the mapping procedure, a post-mapping CT scan was taken with the patient in the decubitus position with the marked side up to better inflate the marked lung.[2,4] The CT image was carefully read to identify the actual markings, which were usually seen as ground-glass opacities with or without bronchial dilation. Fourth, the post-mapping CT images were reconstructed into 3D images that included the tumor and each marking. Based on the actual lung map, the resection lines were adjusted to finalize the operation plan.

The mapping mode is based on the concept that all possible bronchoscopic marking locations should be predetermined by the bronchial anatomy of the patient. If all possible marking locations can be calculated from the CT images, a favorable set of markings can be selected among the candidate marking points. The computer program can provide the route to reach each selected marking on VB. This original mapping mode was integrated into the bronchoscopy simulator of the Synapse Vincent, a radiology workstation commercially available worldwide (Figure 2a). By January 2016, the algorithm had been improved to smooth the

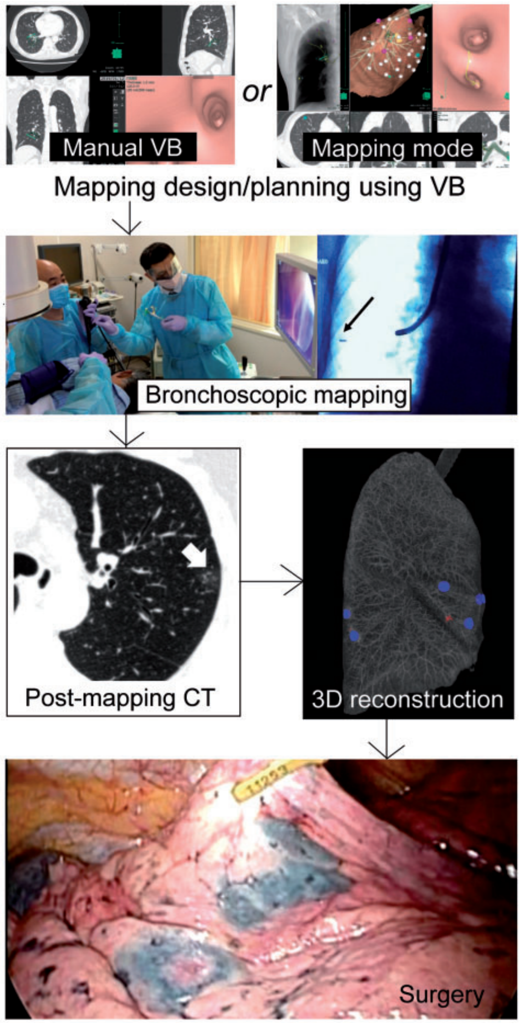

Figure 1. Steps in virtual-assisted lung mapping. A set of target bronchi can be selected using either manual virtual bronchoscopy or the mapping mode of the Synapse Vincent. According to the preoperative plan, bronchoscopic dye marking is conducted using standard fluoroscopy. Within 2 to 3 h of the procedure, post-mapping computed tomography is performed to confirm the locations of the markings and target tumor. The computed tomography images are reconstructed into 3-dimensional images. Finally, surgery is carried out using the 3-dimensional image as a guide. 3D: 3-dimensional; CT: computed tomography; VB: virtual bronchoscopy.

extension of a bronchial branch toward the visceral pleura, and integrated into the updated version of the Synapse Vincent (ver. 4.4; Figure 2b). Thus in our patient cohort, ver. 4.3 of the Synapse Vincent was primarily used from October 2015 to December 2015, and ver. 4.4 was primarily used from January 2016 to March 2016.

In addition to using the primary version of the mapping mode in Synapse Vincent (either ver. 4.3 or 4.4), the other version of the mapping mode as well as the manually operated VB system were used to predict the marking locations in a retrospective manner. With the data obtained from the primarily used mapping mode, the same target bronchus was tracked by the other version of the mapping mode to predict the marking locations on the lung surface. Similarly, the manually operated VB system in the 3D viewer of the Synapse Vincent was used to track the same target bronchus until the final branching had been identified with the mapping mode. If the bronchial root was still visible by VB, it was tracked; otherwise, the VB scope progressed along a straight route to predict the marking locations on the visceral pleura. The marking location predicted by each method was recorded separately as 3D coordinates (i.e., X, Y, and Z).

The post-mapping CT images were reviewed to determine the actual marking locations. The center of each marking was plotted on the pre-mapping CT images based on the geometrical characteristics of the lung, such as the vasculature. The plot was also recorded as 3D coordinates. The distance between each predicted and actual marking point was calculated as:

$$\text{Distance (mm)} = \sqrt{\begin{array}{l}\{(X1 - X2)Kx\}^2 + \{(Y1 - Y2)Ky\}^2 \\ \quad + \{(Z1 - Z2)Kz\}^2\end{array}}$$

The 3D coordinates of a marking location are expressed as (Xn, Yn, Zn). The distance for each axis was calibrated depending on the imported Digital Imaging and Communications in Medicine data, and the calibrating coefficient for each axis was expressed as Kx, Ky, and Kz, respectively. The distances between predicted marking locations was calculated in the same way. Comparison of the distances among different prediction methods and/or actual markings was performed using paired *t* tests. Comparison of the predicted and actual marking locations among different lobes was performed using unpaired *t* tests.

Results

A representative case of lung resection assisted by VAL-MAP is shown in Figure 3. The predicted maps created by different methods appeared similar; however, the 3D image reflecting the locations of the actual markings based on the post-mapping CT images appeared different from those predicted by VB (Figure 3d). In this example, 3 of 4 markings were placed relatively close to the planned markings, but one of the markings was largely displaced by 6 cm (Figure 3e). The planned resection line for S3 segmentectomy was adjusted on the 3D image of the

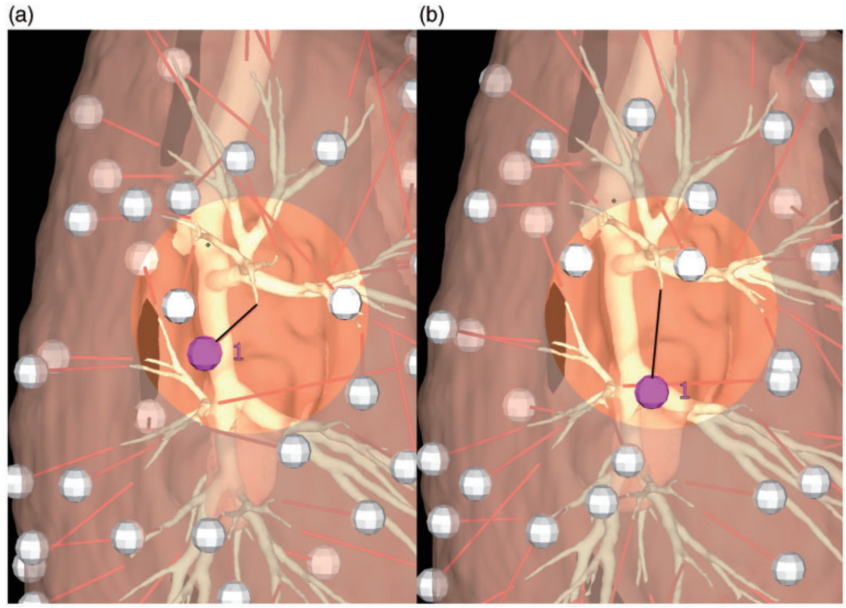

Figure 2. Different versions of the Synapse Vincent mapping mode. (a) Mapping mode version 4.3. (b) Mapping mode version 4.4. Each branch of the bronchial tree depicted on thin-slice computed tomography is extended according to the algorithm of the program to the visceral pleura, where the point is displayed as a white ball (candidate marking). The extended bronchial roots are displayed as red lines. Once a predicted marking point is selected, the color of the ball changes to purple. Note the different locations of the predicted markings between version 4.3 and version 4.4. The circle in the figures highlights the difference in the two mapping mode versions.

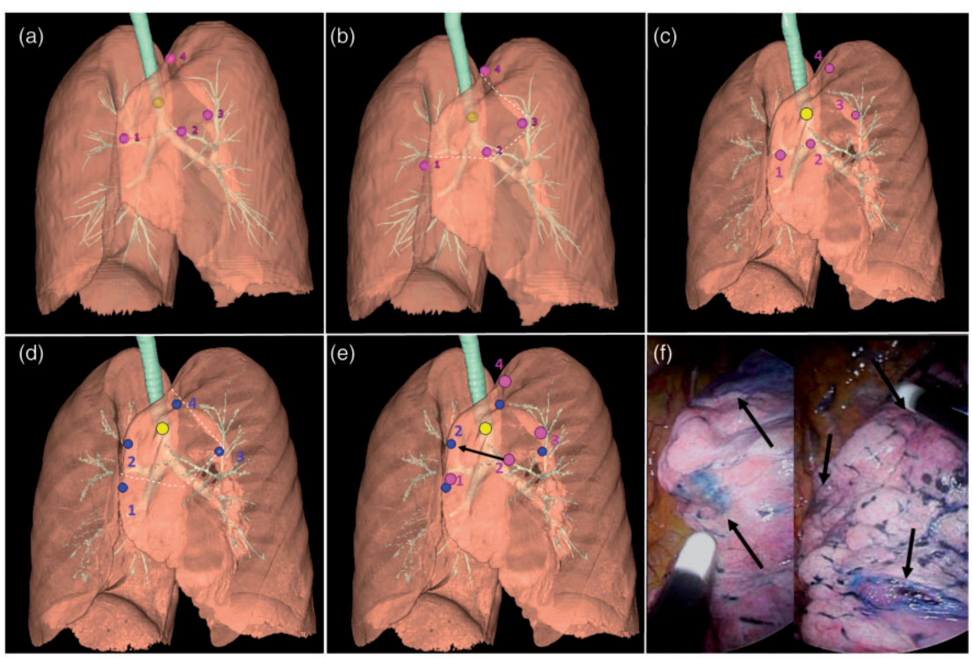

Figure 3. Representative case of virtual-assisted lung mapping. Marking points predicted by different preparation methods (a) Synapse Vincent version 4.3, (b) Synapse Vincent version 4.4, and (c) manual virtual bronchoscopy. (d) Actual marking points based on post-mapping computed tomography are shown. The numbered purple dots are the predicted marking points in a to c, and the numbered blue dots in d are the actual marking points. The resection lines were planned on the 3-dimensional image predicted by the version 4.4 mapping mode, the version primarily used in this case (interrupted lines in b). (e) A merged image of b and d, showing dislocation between the predicted and actual markings. (f) Intraoperative views indicating each marking (arrows), showing essentially identical localization of each mark indicated by post-mapping computed tomography. Surgery (left S3 segmentectomy) was completed without any problem using a 3-dimensional image made from the post-mapping computed tomography image as a guide.

actual markings (interrupted lines in Figure 3d). During surgery, each marking was identifiable at the same location as shown on the 3D image of the actual markings (Figure 3f), and the lung resection was completed based on the adjusted resection lines without any problem. In some cases, the actual marking locations were largely displaced from the predicted ones, as shown in Figure 4. Even in such cases, the intraoperative findings were consistent with the 3D view developed from the post-mapping CT (Figure 4f), and the planned resection was conducted without any problem. The difference between the two versions of the mapping mode, ver. 4.3 and ver. 4.4, was significantly smaller than the differences between ver. 4.4 and manual VB and between ver. 4.3 and manual VB (Figure 5), suggesting that prediction by ver. 4.4 is closer to that by manual VB. The distances between predicted and actual marking locations showed significantly larger dislocations in ver. 4.3 compared to ver. 4.4 or manual VB (Figure 6). The amount of dislocation from the predicted marking locations to the actual marking locations was further examined according to the lung lobe (Figure 7). One marking in the middle lobe was excluded from the analysis. Markings in the upper lobes showed larger dislocations than those in the lower lobes, regardless of prediction methods. In all cases, 3D images were constructed from the post-mapping CT scan, and these images were displayed in the operating room to navigate surgery. In one patient, the targeted nodule suspected to be a metastatic lung tumor was unexpectedly enlarged on the post-mapping CT scan, and the procedure was therefore changed from segmentectomy to lobectomy. The locations of the actual markings observed during the operation appeared identical to those observed on the post-mapping CT images. The remaining 5 wedge resections and 5 segmentectomies were conducted as planned, with sufficient margins (i.e., resection margin larger than the tumor diameter or 2 cm).

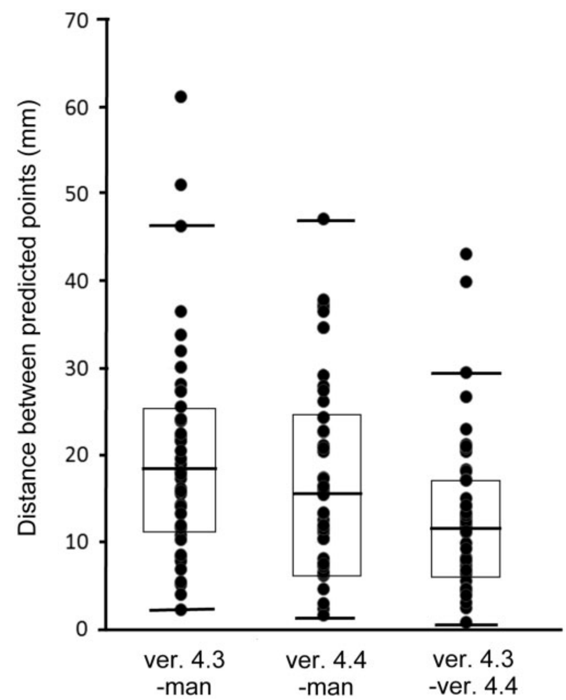

Figure 5. Distance between marking points predicted by different methods. The difference between the two versions of the mapping mode (ver. 4.3 and ver. 4.4) was significantly smaller than the difference between ver. 4.4 and manual virtual bronchoscopy and between ver. 4.3 and manual virtual bronchoscopy, which tended to be largest ($p < 0.01$ in paired t test). man: manual; ver: version.

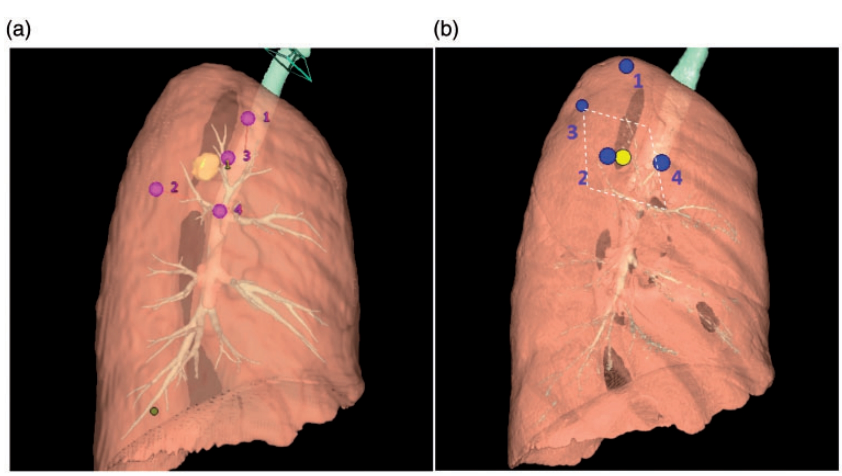

Figure 4. A case of virtual-assisted lung mapping with significant dislocation. (a) Predicted marking points made by mapping mode version 4.3. (b) Actual marking points based on post-mapping computed tomography. Note the dislocation between the predicted and actual markings. The interrupted lines indicate planned resection lines.

Discussion

This study was conducted to examine the accuracy of marking locations predicted by different methods of VB. We found a relatively small difference in predictions of the marking locations among the different methods, while the actual markings depicted by post-mapping CT were dislocated by an average of 3 cm from the predicted marking points. Most importantly, surgery was conducted as planned using the dislocated lung map based on the post-mapping CT images as guidance without any major problems. These results suggest that post-mapping CT with subsequent 3D reconstruction is indispensable for accurate performance of surgery using VAL-MAP.

In the original description of VAL-MAP, manual VB was used to select target bronchi and then predict marking locations.[1] However, this initial step of VAL-MAP (Figure 1) was somewhat time-consuming because it involved repeated trial and error to locate a suitable target bronchus. It took 10 to 20 min per mark and 1 to 2 h in total. Because all possible marking locations are theoretically predicted from the bronchial anatomy of the patient, the mapping mode was eventually developed in the bronchoscopy simulator module of the Synapse Vincent in 2015. In our experience, this mapping mode indeed dramatically decreased the preparation time from 1 to 2 h to 20 to 30 min per case. Because the program automatically displays the array of possible marking locations (white balls in Figure 2), ideal marking candidates can be simply selected depending on the operation plan. The route to reach the point is then automatically generated on VB. The improvement in the program's algorithm further smoothed the route to reach a predicted marking location (Figure 2). Despite the improvement in the mapping mode, this study revealed that the current VAL-MAP technique results in dislocation of markings by an average of 3 cm regardless of the method used. The surprisingly large discrepancy can be explained by technical limitations of VAL-MAP rather than individual bronchoscopists' experience. First, VB cannot

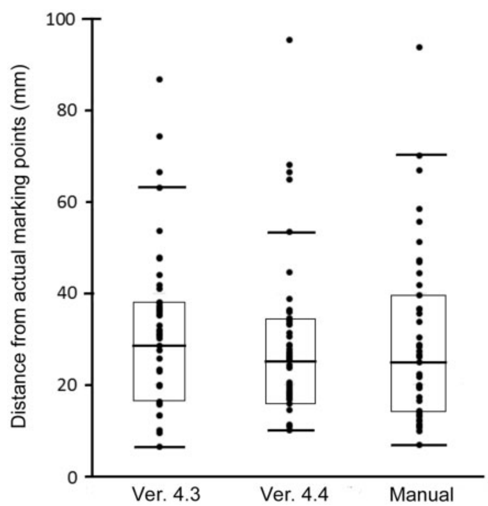

Figure 6. Distance between predicted and actual marking points. Version 4.3 showed significantly larger dislocation from the actual markings compared with manually operated virtual bronchoscopy ($p = 0.038$) or ver. 4.4 ($p = 0.042$) in the paired *t* test. ver: version.

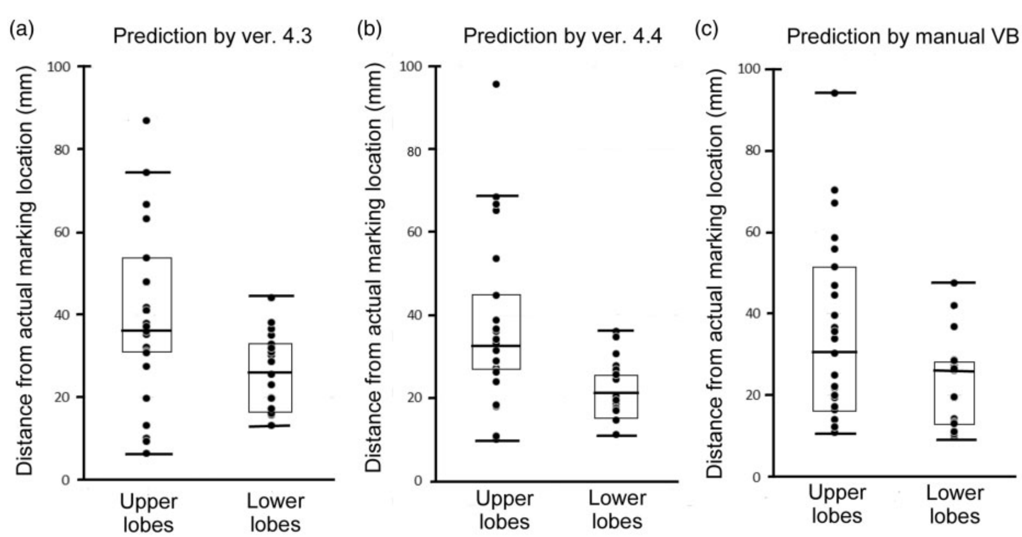

Figure 7. Distance between predicted and actual marking points according to lung lobe. Markings in the upper lobes showed a greater distance between the predicted and actual marking points in each prediction method, including (a) version 4.3 ($p = 0.023$), (b) version 4.4 ($p < 0.01$), and (c) manually operated virtual bronchoscopy ($p = 0.031$). Upper lobes, $n = 24$; lower lobes, $n = 18$; one marking in the middle lobe was excluded from the analysis. VB: virtual bronchoscopy; ver: version.

sufficiently depict peripheral bronchi. The VB in the Synapse Vincent usually detects 8 to 12 branchings, while a bronchus generally branches more than 20 times. Considering the thickness of CT images and the noise caused by respiratory movement, depiction of bronchial branching by computer software is inherently limited. Second, the diameter of the fiberoptic bronchoscope to be used in the current VAL-MAP technique (external diameter 4.5–5.5 mm) limits the bronchial size to be reached. Utilization of an ultrathin bronchoscope is a potential option,[10] although the standard metal-tipped catheter we use requires a working channel with a 2-mm diameter. Real-time electromagnetic navigation bronchoscopy is another realistic option with which to improve the accuracy of marking.[11]

Most importantly, despite the discrepancies stemming from the limitations of the current VAL-MAP technique, we had little trouble performing lung resection with VAL-MAP. Previous studies have demonstrated striking accuracy rates (as high as 99%) in the detection and resection of targeted lesions.[1–3] The success of the operation is closely associated with the post-mapping CT scan, by which we identify the actual markings and their relationship to the targeted tumor.[4] The primary role of VAL-MAP is to provide geometric information regarding the lung surface. Thus even if the markings are dislocated from the original plan, the information provided by the actual markings appear sufficient to navigate surgery. If necessary, techniques such as the use of auxiliary lines and anatomical landmarks on 3D images may further facilitate accurate resection of targeted lesions.[5] As such, post-mapping CT and subsequent 3D reconstruction are indispensable in the current VAL-MAP technique. Given that markings do dislocate from predicted markings and that adjustment by post-mapping CT images allows us to conduct accurate surgery, the next question would be how meticulously we need to design and prepare VAL-MAP using VB. Although further investigation is necessary to address this question, we still consider that mapping design and preparation are important to create an effective lung map that successfully guides surgery. For example, in wedge resection of a ground-glass nodule, a common VAL-MAP design is a triangle that surrounds the tumor, indicating appropriate resection lines. Even if each of the markings is dislocated to some extent, the triangular shape of the map is maintained, still providing useful geometric information, indicating appropriate resection lines and tumor locations. In this regard, the present study was designed to examine the dislocation of each single mark; the relationships among multiple markings was not evaluated. Further investigation is necessary to examine the role of the mapping design in successful conduction of VAL-MAP-assisted surgery.

We acknowledge that there are multiple limitations in this study. First, we retrospectively predicted the marking locations using manual VB or the version of automated VB that had not been used before surgery; thus the order in which VB was conducted could have biased the results. Second, this was a single-center study using only the Synapse Vincent workstation. The accuracy of predicting marking locations using other workstations remains unknown, although detection of peripheral bronchi is expected to be similarly limited. Third, as discussed above, we only measured the distance between the predicted and actual marking locations for each mark; we did not take the relationship among multiple markings into account. In conclusion, prediction of the marking location using VB alone is limited whether using a manual or automated system. Post-mapping CT enables adjustment of the lung map that reflects the actual locations of the markings, allowing for successful lung resection.

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Declaration of conflicting interests

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