CHEST

Shape-Sensing Robotic-Assisted Bronchoscopy vs Digital Tomosynthesis-Corrected Electromagnetic Navigation Bronchoscopy

A Comparative Cohort Study of Diagnostic Performance

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BACKGROUND: Electromagnetic navigational bronchoscopy has been the dominant bronchoscopic technology for targeting small peripheral lesions and now includes digital tomosynthesis-electromagnetic navigational bronchoscopy (DT-ENB), allowing near-real-time intraprocedural nodule visualization. Shape-sensing robotic-assisted bronchoscopy (ssRAB), with improved catheter stability and articulation recently became available. Although the diagnostic performance of these two methods seems higher than that of legacy systems, data remain limited. We sought to compare the diagnostic yield of these two novel platforms after their introduction at our institution.

RESEARCH QUESTION: Does the diagnostic yield of ssRAB differ significantly from that of DT-ENB in patients undergoing biopsy of peripheral pulmonary lesions (PPLs)?

STUDY DESIGN AND METHODS: This retrospective comparative cohort study analyzed prospectively collected data on consecutive procedures performed with DT-ENB and ssRAB in their first 6 months of use at our institution. Biopsies were considered diagnostic if histopathologic analysis revealed malignancy or specific benign features that readily explained the presence of a PPL. Nonspecific inflammation, normal lung or airway, and atypia not diagnostic of malignancy were considered nondiagnostic.

RESULTS: SSRAB was used to biopsy 143 PPLs in 133 patients and DT-ENB was used to biopsy 197 PPLs in 170 patients. Diagnostic yield was 77% for ssRAB (110 of 143 PPLs) and 80% (158 of 197 PPLs) for DT-ENB (OR, 0.8; 95% CI, 0.5-1.4; $P = .4$). Median lesion diameters were 17 and 19 mm, respectively. No difference in diagnostic yield was found after adjustment for lesion size, bronchus sign, peripheral vs middle third location, and sex. Pneumothorax complicated 1.5% of ssRAB and 1.8% of DT-ENB procedures ($P = .86$).

INTERPRETATION: SSRAB and DT-ENB showed comparable diagnostic yields and safety profiles in this comparative cohort study. CHEST 2023; 163(4):977-984

KEY WORDS: digital tomosynthesis; electromagnetic navigational bronchoscopy; fluoroscopy; nodules; peripheral pulmonary lesion; robotic-assisted bronchoscopy

ABBREVIATIONS: DT = digital tomosynthesis; DT-ENB = digital tomosynthesis-electromagnetic navigation bronchoscopy; ENB = electromagnetic navigation bronchoscopy; PPL = peripheral pulmonary lesion; ssRAB = shape-sensing robotic-assisted bronchoscopy

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Take-home Points

Study Question: Does the diagnostic yield of shape-sensing robotic-assisted bronchoscopy (ssRAB) differ significantly from that of digital tomosynthesis-electromagnetic navigation bronchoscopy (DT-ENB) in patients undergoing biopsy of peripheral pulmonary lesions?

Results: The diagnostic yield was similar at 77% for ssRAB (110 of 143) and 80% (158 of 197) for DT-ENB (OR, 0.8; 95% CI, 0.5-1.4; $P = .4$). Adjustments for lesion size, bronchus sign, peripheral vs middle one-third location, and sex did not affect the diagnostic yield. Pneumothorax complicated 1.5% of ssRAB and 1.8% of DT-ENB procedures ($P = .86$).

Interpretation: Diagnostic performance and safety profiles were comparable for ssRAB and DT-ENB in this comparative cohort study using a uniform conservative definition of diagnostic yield.

Approximately 1.5 million indeterminate pulmonary nodules are identified annually in the United States by low-dose CT scan imaging.[1] In addition, the incidence of screen-detected nodules is projected to increase as lung cancer screening expands.[2-4] Because many nodules require biopsy for definitive diagnosis, an urgent need exists for minimally invasive diagnostic techniques with excellent performance and safety profiles.

Percutaneous CT scan-guided biopsy long has been regarded as the gold standard to sample peripheral pulmonary lesions (PPLs) with a high reported diagnostic yield.[5] However, approximately 15% of cases are complicated by pneumothorax and many lesions are not technically amenable to percutaneous sampling, motivating interest in alternative methods.[6] Electromagnetic navigational bronchoscopy (ENB), in which an electromagnetic field is generated around the patient to guide the movement of catheters or tools in the airway, was introduced approximately 20 years ago.[7] ENB platforms have evolved over time, most recently to include digital tomosynthesis (DT) to correct for CT scan-body divergence (the difference in PPL position at the time of bronchoscopy vs its expected location based on a preprocedure CT scan). Digital tomosynthesis uses a standard C-arm fluoroscope to produce an intraprocedural three-dimensional image of the target lesion, allowing its location to be updated in the ENB targeting system. DT-ENB (superDimension; Medtronic) was introduced in February 2018 and has been reported to improve the diagnostic yield substantially over conventional ENB without DT.[8-10]

The Food and Drug Administration recently approved two robotic-assisted navigational bronchoscopy platforms. These systems, in which the bronchoscopist controls the insertion and articulation of a robotic bronchoscope with a controller or console near the patient, offer improved stability and visualization into more distal airways than standard bronchoscopes. One of these systems, the ION endoluminal platform (Intuitive Surgical, Inc.), uses a novel shape-sensing technology to track the position of its catheter, referred to as shape-sensing robotic-assisted bronchoscopy (ssRAB). Initial studies suggest ssRAB has a diagnostic yield of approximately 80%.[11,12] However, it currently does not offer near-real-time PPL localization for correction of CT scan-body divergence.

Data comparing ssRAB and DT-ENB are needed. Existing studies are noncomparative, use different diagnostic yield definitions, and include different patient populations, hindering comparisons across studies.[8-10,12-15] Specifically, as of June 2022, only four studies with > 30 patients reported on robotic-assisted bronchoscopy diagnostic yield, all using different yield definitions, limiting comparisons across studies.[12-15] Nonetheless, enthusiasm for these new technologies rapidly has outpaced available evidence, and these platforms increasingly are adopted in clinical practice. Comparative effectiveness data on the relative performance of these systems are needed urgently to provide crucial insight into optimal invasive sampling methods to inform patient care and hospital system capital investments. We hypothesized that the diagnostic yield of ssRAB and DT-ENB platforms for PPLs would be similar.

Study Design and Methods

Design and Participants

In this retrospective analysis of prospectively collected data from consecutive navigational bronchoscopies, we compared the diagnostic yield of ssRAB with that of DT-ENB after introduction of each platform at our institution (Vanderbilt University Medical Center, Nashville, TN). Data pertaining to consecutive navigational bronchoscopies at our institution have been collected prospectively since April 2018 (Research Electronic Data Capture tool; Vanderbilt University).[16,17] DT-ENB and

ssRAB were introduced in April 2018 and November 2021, respectively. Data from all navigational bronchoscopies performed in the 6 months after each technology was introduced were obtained from the database; these 6-month windows were chosen to minimize bias from operator experience. DT-ENB was used exclusively after its introduction because it was the only navigational platform available at our institution. Similarly, ssRAB was used exclusively after its introduction except for patients enrolled in an ongoing randomized trial requiring DT-ENB (Navigation Endoscopy to Reach Indeterminate Lung Nodules Versus Trans-Thoracic Needle Aspiration [VERITAS]; ClinicalTrials.gov Identifier: NCT04250194); these patients were excluded from this analysis. This study was approved by the institutional review board (Identifier: 212187).

Procedures

All navigational bronchoscopies were performed by board-certified interventional pulmonologists (F. M., O. B. R., or R. J. L.) or an interventional pulmonology fellow (S.-W.L., M. C. A., or J. K.) under the direct supervision of a board-certified interventional pulmonologist. All procedures were conducted in a dedicated bronchoscopy operating room under general anesthesia provided by a certified registered nurse anesthetist supervised by an anesthesiologist. Anesthetic care in all procedures consisted of total IV anesthesia with neuromuscular blockade, endotracheal intubation with an 8.5-mm endotracheal tube, a recruitment maneuver (40 cm H_2O pressure for 40 s) immediately after intubation followed by application of positive end-expiratory pressure of 15 cm H_2O throughout the procedure and minimization of the F_{IO_2} to limit atelectasis while maintaining oxygen saturation of at least 90%.

DT-ENB procedures were performed as described previously.[8,9] For ssRAB, planning based on a preprocedure CT scan of the chest was performed in PlanPoint (Intuitive Surgical). After an initial airway inspection and clearance of any secretions using a standard flexible bronchoscope (BF-Q190; Olympus), the ssRAB arm was docked to the endotracheal tube and the robotic catheter with a vision probe was inserted into the airway. Registration was performed by maneuvering through airways in all lobes. After navigation to the target PPL, the vision probe was removed to permit a biopsy.

Radial endobronchial ultrasonography (UM-S20-17S; Olympus) was used in all patients for both platforms, and all biopsies were performed under fluoroscopic guidance (GE 9800 or OEC 9900 Elite; GE Healthcare System). Transbronchial needle aspiration was the initial biopsy method in all patients using the 21-gauge Arcpoint pulmonary needle (Medtronic) in DT-ENB procedures and 19-gauge, 21-gauge, or 23-gauge Flexision needles (Ion; Intuitive Surgical, Inc.) in ssRAB procedures. Initial passes were submitted for rapid on-site cytologic examination (ROSE) in all cases. Additional sampling methods (forceps, cytology brush, focused peripheral wash) were performed after transbronchial needle aspiration at the operator's discretion.

Procedural data and complications were recorded prospectively. Final cytologic and surgical pathologic results and delayed complications were recorded 1 week after each procedure.

Outcomes

The primary outcome of interest was the difference in diagnostic yield between the two navigational platforms. Diagnostic yield was defined as the number of PPL biopsy samples obtaining lesional tissue divided by the total number of PPLs biopsied with a given technology. Biopsy samples were considered lesional or diagnostic if they yielded histopathologic findings that readily explained the presence of a nodule. Prespecified lesional findings were malignancy and specific benign histopathologic patterns, including granulomatous inflammation, organizing pneumonia, and robust neutrophilic inflammation or frank purulence. Other specific benign histopathologic findings were considered diagnostic only if the bronchoscopist and lung pathologist agreed that the findings readily explained the presence of a nodule (eg, necrosis with fungal forms present consistent with endemic fungal exposure, specific findings consistent with uncommon lesions such as hamartoma or amyloidoma). All other findings, including normal lung or airway, nonspecific inflammatory changes, and atypia not definitely diagnostic of malignancy, were considered nondiagnostic. Additional outcomes included factors associated with diagnostic yield and rate of complications based on definitions used in a national quality improvement project initiative for diagnostic bronchoscopy.[18]

Statistical Analysis

Descriptive statistics were calculated, including mean ± SD or median and interquartile range for continuous variables and percentages and frequencies for categorical variables. Comparisons between two navigational platforms were made using the Wilcoxon rank-sum and χ^2 tests for the continuous and categorical variables, respectively. Logistic regression was used to assess the association between diagnostic yield and two navigational platforms with the adjustment for nodule size, presence of bronchus sign, peripheral vs middle third location, and sex. Because some patients had > 1 lesion biopsied during the same procedure, a robust sandwich estimator was used to estimate the variance to account for the correlated PPL within the patient. We also performed a post hoc sensitivity analysis including only the initial PPL biopsied in patients in whom > 1 PPL was sampled. Statistical analysis was performed in R version 4.1.1 software (R Foundation for Statistical Computing.

Results

DT-ENB and ssRAB were introduced into clinical use on April 25, 2018, and November 3, 2021, respectively. A total of 197 PPLs were biopsied in 170 patients with DT-ENB and 143 PPLs were biopsied in 133 patients with ssRAB in the 6 months after each was introduced. An additional 22 nodules biopsied in the latter 6-month window using DT-ENB instead of ssRAB as part of a randomized controlled trial requiring DT-ENB (VERITAS; NCT04250194) were excluded.

DT-ENB and ssRAB groups were well balanced regarding most demographic and radiographic features (Table 1, 2). The median size of lesions biopsied in the DT-ENB and ssRAB cohorts were similar, at 19 mm (interquartile range, 14-28 mm) vs 17 mm (interquartile range, 12-27 mm), respectively. The size range of lesions biopsied via ssRAB was 0.5 to 7.9 cm (28 of 143 lesions were ≥ 3 cm) and 0.6 to 9.1 cm for DT-ENB (40 of 197 lesions were ≥ 3 cm). More women (59.4% vs 45.1%; $P = .013$) were in the DT-ENB group compared with the

ssRAB group and more nodules were located in the peripheral one-third of the lung in the DT-ENB group (67% [132 of 197]) compared with the ssRAB group (48% [69 of 143]; $P < .001$). Nodule densities and prevalence of bronchus signs were similar between groups (Table 2).

The primary outcome of diagnostic yield was similar with ssRAB (77% [110 of 143]) and DT-ENB (80% [158 of 197]; OR, 0.8; 95% CI, 0.5-1.4; $P = .4$) (Table 3). Among patients undergoing DT-ENB, 54% of PPLs (107 of 197) were malignant and 26% of PPLs (51 of 197) showed specific benign histopathologic features. Among patients undergoing ssRAB, 55% of PPLs (78 of 143) were malignant and 22% of PPLs (32 of 143) showed specific benign histopathologic features (Table 3). A multivariate logistic regression analysis of the primary outcome adjusting for nodule size, presence of bronchus sign, peripheral one-third vs middle one-third location, and sex did not differ from the unadjusted analysis (OR, 0.87; 95% CI, 0.49-1.6; $P = .6$). In a post hoc sensitivity analysis including only the first nodule biopsied per patient, the diagnostic yield was similar with ssRAB (80% [106 of 133]) and DT-ENB (81% [138 of 170]; OR, 0.9; 95% CI, 0.5–1.6; $P = .7$); multivariate logistic regression adjusting for the same factors listed above did not differ from the unadjusted sensitivity analysis (OR, 1.0; 95% CI, 0.5-1.8; $P = .9$).

The overall diagnostic yield (including PPLs biopsied by both platforms) was affected positively by nodule size, concentric radial endobronchial ultrasonography image acquisition, and solid nodule density (Table 4). When each platform was analyzed separately for factors affecting diagnostic yield, solid nodule density was associated with diagnostic biopsies using DT-ENB (OR, 4.4; 95% CI, 1.9-9.9; $P = .001$). Bronchus sign and concentric radial endobronchial ultrasonography image were associated with diagnostic biopsies using ssRAB (OR, 3.1 [95% CI, 1.2-7.7; $P = .015$] and OR, 3.5 [95% CI, 1.4-8.4; $P = .004$], respectively).

The most common complication was pneumothorax, occurring in 1.5% of patients (2 of 133) and 1.8% of patients (3 of 170) in the ssRAB and DT-ENB groups, respectively ($P = .86$). One patient (0.6%) in the DT-ENB group and 2 patients (1.5%) in the ssRAB group required tube thoracostomy. No patients required additional intervention because of bleeding in either cohort.

Discussion

In this comparative cohort study of prospectively collected data, no difference was found in diagnostic yield between ssRAB and DT-ENB. This is the first study that permitted a meaningful comparison of the diagnostic performance of these two novel platforms given similar cohorts drawn from the same patient population with the same operators performing procedures within the same 6-month window from platform introduction using the same conservative definition of diagnostic yield. No significant difference remained between platforms after adjustment for possible confounders, including PPL size, presence of a bronchus sign, location in the peripheral one-third of the lung, and sex.

Existing literature suggests that the diagnostic yield of ENB ranges from 47% to 94%, whereas studies to date on robotic-assisted bronchoscopy have reported diagnostic yields ranging from 69% to 86%.[8-10,12-15,19–21] Despite these and many additional studies reporting on the diagnostic performance of various technologies to biopsy PPLs, no unifying definition of diagnostic yield

TABLE 1] Demographic Data

Variable	DT-ENB (n = 170)	ssRAB (n = 133)	*P* Value
Sex			.013
Male	69 (40.6)	73 (54.9)	
Female	101 (59.4)	60 (45.1)	
Age, y	63 ± 11.7	64 ± 12.5	
Smoking status			.94
Cigarette use	122 (71.8)	96 (72.2)	
Never	48 (28.2)	37 (27.8)	
Outpatient status	154 (90.6)	124 (93.2)	.41

Data are presented as No. (%) or mean ± SD, unless otherwise indicated. DT-ENB = digital tomosynthesis-electromagnetic navigation bronchoscopy; ssRAB = shape-sensing robotic-assisted bronchoscopy.

TABLE 2] Comparison Between DT-ENB and ssRAB Procedure Characteristics

Variable	DT-ENB (n = 197)	ssRAB (n = 143)	*P* Value
Nodule size			
Overall size, mm	19 (14-28)	17 (12-27)	.4
Presence of bronchus sign	64 (32)	57 (40)	.16
Nodule density			.97
Solid	165 (83.8)	119 (83.2)	
Subsolid	26 (13.2)	19 (13.3)	
Ground-glass opacity	6 (3)	5 (3.5)	
Location			
Peripheral one-third	159 (80.7)	68 (48)	< .001
Specific lobes			
Right upper lobe	65 (33)	39 (27.3)	
Right middle lobe	17 (8.6)	20 (14)	
Right lower lobe	39 (19.8)	30 (21)	
Left upper lobe	53 (26.9)	23 (16.1)	
Lingula	1 (0.5)	10 (7)	
Left lower lobe	22 (11.2)	21 (14.6)	
Radial ultrasound image			.34
Concentric	74 (37.6)	66 (46.2)	
Eccentric	88 (44.7)	61 (42.7)	
No view	24 (12.2)	13 (9.1)	
Missing data	11 (5.5)	3 (2.0)	

Data are presented as No. (%) or median (interquartile range), unless otherwise indicated. DT-ENB = digital tomosynthesis-electromagnetic navigation bronchoscopy; ssRAB = shape-sensing robotic-assisted bronchoscopy.

exists, which greatly hinders the comparison of results across studies.[22] Variations in this definition have been shown to skew yield figures drawn from identical datasets by more than 20%, yielding vastly different estimates of diagnostic performance.[22] The definition used in the ACCP Quality Improvement Registry, Evaluation, and Education (AQuIRE) registry is among the more conservative examples in the literature, in which bronchoscopy was considered diagnostic only if a malignant or specific benign diagnosis was established at the index bronchoscopy, with nonspecific findings considered nondiagnostic.[18] We used a similar definition in the current study. However, many studies have not required specific findings to be present to declare a biopsy diagnostic. NAVIGATE, for example, considered any biopsy results not diagnostic of malignancy (including a finding of normal lung tissue, clearly indicating an inadequate sampling of a PPL) to be diagnostic (true negative) if the lesion regressed over time.[19] The definitions used in Robotic Bronchoscopy for Peripheral Pulmonary Lesions: A Multicenter Pilot and Feasibility Study (BENEFIT)[15] and the study by Kalchiem-Dekel[12] of ssRAB considered nonspecific inflammation with subsequent regression (BENEFIT) or regression or stability for 12 months (the latter study) to be diagnostic, whereas biopsy results of only normal lung or airway were not, representing a middle ground between the AQuIRE and Clinical Evaluation of superDimension Navigation System for Electromagnetic Navigation Bronchoscopy (NAVIGATE) definitions. Overall, these divergent definitions result in incommensurable study results.

Additional factors beyond diagnostic yield definitions, including varying cancer prevalence and biases inherent in retrospective single-center investigations, also introduce variability and limit generalizability and comparisons across studies. Such concerns motivated the current study, in which the same conservative diagnostic yield definition is used across all procedures performed. Other sources of interstudy variation, including variable operator experience with a given platform and institutional difference, were minimized by the design of the current work. Although this limits the generalizability of the diagnostic yield estimates presented, it also controls for these other relevant

TABLE 3] Diagnostic Findings for DT-ENB and ssRAB Cohorts

Diagnostic Finding	DT-ENB (n = 197)	ssRAB (n = 143)
Diagnostic or lesional biopsy	158 (80)	110 (77)
Malignant	107 (54.3)	78 (54.5)
Specific benign diagnosis	51 (25.9)[a]	32 (22.4)
Nonspecific diagnosis	39 (19.8)	33 (23.1)
Malignant		
NSCLC adenocarcinoma	52 (48.6)	40 (51.3)
NSCLC squamous	18 (16.8)	10 (12.8)
NSCLC NOS	9 (8.4)	4 (5.1)
Small cell carcinoma	5 (4.7)	1 (1.3)
Carcinoid	3 (2.8)	4 (5.1)
Metastasis	13 (12.2)	18 (23.1)
Lymphoma	3 (2.8)	1 (1.3)
Poorly differentiated	3 (2.8)	. . .
Unable to specify	1 (0.9)	. . .
Specific benign diagnosis		
Frank purulent/neutrophilic/culture positive	22 (43.1)	7 (21.9)
Granulomatous	14 (27.5)	12 (37.5)
Organizing pneumonia	8 (15.7)	9 (28.1)
Others that explain the presence of a nodule[b]	7 (13.7)	4 (12.5)

Data are presented as No. (%). DT-ENB = digital tomosynthesis-electromagnetic navigation bronchoscopy; NOS = not otherwise specified; NSCLC = non-small cell lung cancer; ssRAB = shape-sensing robotic-assisted bronchoscopy.
[a]One of 51 of specific benign nodules (1.9%) in the DT-ENB group was malignant (false negative) after 2 years of follow-up (available for all DT-ENB cases). The false negative case was organizing pneumonia, which was later found to be lymphoma.
[b]Additional specific benign diagnoses established by DT-ENB: respiratory bronchiolitis (n = 1), fibroelastotic scar (n = 3), organizing fibrin with atypical stromal cells consistent with radiation effect (n = 1), and hamartoma (n = 2). Additional specific benign diagnoses established by ssRAB: pericardial cyst (n = 1), organizing fibrin with atypical stromal cells consistent with radiation effect (n = 1) and hamartoma (n = 2).

TABLE 4] Factors Associated With Diagnostic Yield Combining Both Platform

Variable	Diagnostic Biopsy (n = 268)	Nondiagnostic Biopsy (n = 72)	Combined (n = 340)	*P* Value
Biopsy platform				.46
DT-ENB	158 (59)	39 (54)	197 (58)	
ssRAB	110 (41)	33 (46)	143 (42)	
Radial ultrasound				< .001
Concentric	121 (46.9)	19 (27.9)	140 (42.9)	
Eccentric	116 (45)	33 (48.5)	149 (45.7)	
No view	21 (8.1)	16 (23.5)	37 (11.3)	
Size, mm	19 (14-29)	15 (12-21)	18 (13-27)	.001
Peripheral one-third location	158 (59)	43 (60)	201 (59)	.91
Bronchus sign	102 (38)	19 (26)	121 (36)	.066
Nodule density				< .001
Solid	234 (87.3)	50 (69.4)	284 (83.5)	
Subsolid	26 (9.7)	19 (26.4)	45 (13.2)	
Ground-glass opacity	8 (3)	3 (4.2)	11 (3.2)	

Data are presented as No. (%) or median (interquartile range), unless otherwise indicated. DT-ENB = digital tomosynthesis-electromagnetic navigation bronchoscopy; ssRAB = shape-sensing robotic-assisted bronchoscopy.

variables associated with yield: in the hands of the same experienced operators, targeting similar lesions with a consistent prevalence of malignant disease and similar patient populations, the diagnostic yield of ssRAB and DT-ENB seem comparable.

It is noteworthy that this first-generation ssRAB platform without integrated digital tomosynthesis or other near-real-time imaging correction for CT scan-body divergence produced a nearly identical yield as a mature DT-ENB platform. This high yield despite the lack of integrated three-dimensional intraprocedural imaging might be the result of enhanced stability, visual-based navigation through the peripheral airways guided by accurate shape-sensing navigational technology, and the ability to adjust catheter articulation finely during target lesion biopsy. Digital tomosynthesis integration with ENB was shown in prior work to increase the diagnostic yield from 54% to 79%,[8] and preliminary data on the combination of ssRAB with other real-time intraprocedural 3D imaging methods report higher diagnostic yields of 86% to 93% (using cone-beam CT scan imaging and three-dimensional fluoroscopy, respectively), suggesting that digital tomosynthesis integration with ssRAB may improve yields further.[13,23] Conversely, DT-ENB diagnostic yields may improve further with articulating catheters instead of current catheters with fixed distal curvatures.

This study has several limitations. It is derived from a single high-volume center where navigational bronchoscopy is performed or supervised by experienced interventional pulmonologists, which may limit the generalizability of our findings. However, as discussed previously, this design also allows for a more reliable comparison of the technical aspects of ssRAB and DT-ENB. As in all nonrandomized studies, unbalanced unmeasured confounders between groups may have biased the results presented, although logistic regression was used to adjust for known confounders and prospective collection of all data reduced the risk of bias during data abstraction. Some baseline differences were found between study groups (sex, proportion of PPLs in the peripheral one-third of the lung), adjustments for which did not change the primary outcome. It is possible some of the difference in PPL proportion in the outer one-third of the lung was the result of inconsistent classification in the absence of formal radiologic segmentation. Finally, we report diagnostic performance using diagnostic yield, rather than diagnostic accuracy, the latter of which requires a prolonged follow-up period to ensure that specific benign findings in fact were true-negative (benign) nodules. In the DT-ENB cohort for which complete 2-year follow-up is available, only 1 of 51 nodules (1.9%) with specific benign pathologic features ultimately was determined to be malignant, suggesting that this conservative definition of yield used in both cohorts is unlikely to deviate significantly from diagnostic accuracy.

Interpretation

We conclude that ssRAB and DT-ENB platforms seem equivalent for the diagnosis of PPLs with similar complication profiles. Future randomized trials should confirm these findings and may help to delineate further whether particular patient or PPL features predict a higher likelihood of diagnosis with one platform vs the other.

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