

The STABLE Trial: Sustained Breath-Hold During Tissue Acquisition in Robotic Bronchoscopy—A Randomized Controlled Trial

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Abstract

Background: Respiratory motion and anesthesia-associated atelectasis may contribute to CT-to-body divergence and reduce the precision of peripheral pulmonary lesion sampling. Breath-hold ventilation has been proposed to stabilize the target and biopsy tool during robotic bronchoscopy, but prospective randomized evidence is limited. We evaluated whether sustained breath-hold during tissue acquisition improves diagnostic yield or tool-lesion positioning during imaging-integrated robotic bronchoscopy.

Methods: The STABLE (Study of Tool-lesion Alignment and Breath-hold Ventilation in Robotic Bronchoscopy for Peripheral Lung LEsions) Trial was a prospective randomized study of patients undergoing robotic bronchoscopy for peripheral pulmonary lesions using the Noah Galaxy system with integrated augmented fluoroscopy and C-arm-based tomosynthesis. Patients were randomized to standardized sustained breath-hold during tissue acquisition or conventional ventilation during tissue acquisition; both groups underwent brief breath-holds during AF/CABT image acquisition.

The primary endpoint was strict diagnostic yield according to ATS/ACCP definitions, independently adjudicated by a pulmonologist blinded to ventilation assignment. Secondary endpoints included successful lesion localization, tool-in-lesion (TIL), tool-touching-lesion (TTL), no tool in lesion (NTL), radiation exposure, and complications. Standardized mean differences (SMDs) assessed baseline balance.

Results: Among 117 randomized patients, 53 underwent breath-hold and 64 conventional ventilation. Mean age was 67.5 ± 10.0 versus 66.3 ± 10.4 years, and mean lesion diameter was 1.7 ± 0.7 versus 1.9 ± 0.8 cm, respectively. Most baseline characteristics were similar; the largest imbalances involved bronchus sign (34.0% vs 51.6%; absolute SMD 0.35) and left-upper-lobe location (28.3% vs 45.3%; SMD 0.35).

Overall strict adjudicated diagnostic yield was 89.7% (105/117). Diagnostic yield was 86.8% with breath-hold and 92.2% with conventional ventilation (OR 0.56, 95% CI 0.17–1.87, p-value 0.34). With greater than 1 year of ongoing follow-up, overall diagnostic accuracy was 97.4% (114/117).

Nearly all procedures achieved TIL or TTL (98.1% vs 96.9%). TIL occurred in 62.3% versus 64.1% (OR 0.93, 95% CI 0.44–1.97). Localization, tool-position distribution, sampling intensity, radiation exposure, and complications showed no clear between-group differences. Two pneumothoraces requiring chest-tube placement occurred (2/117; 1.7%), both in the conventional ventilation group. Across both groups, diagnostic yield increased from 0% with NTL to 85.0% with TTL and 95.9% with TIL.

Conclusions: Sustained breath-hold during tissue acquisition did not improve diagnostic yield or tool-lesion positioning during imaging-integrated robotic bronchoscopy. Diagnostic yield varied according to imaging-confirmed tool-lesion position, supporting procedural strategies that prioritize accurate real-time positioning rather than breath-hold alone.

Trial registration: International Standard Randomised Controlled Trial Number (ISRCTN) Registry, ISRCTN11802169; retrospectively registered (01/09/2026).

Introduction

Lung cancer screening and increasing use of cross-sectional imaging have expanded the number of peripheral pulmonary lesions requiring tissue diagnosis. Robotic bronchoscopy has emerged as a minimally invasive alternative to transthoracic biopsy and surgery; however, diagnostic performance remains limited by CT-to-body divergence resulting from respiratory motion, anesthesia-related atelectasis, and changes in intrathoracic anatomy after preprocedural CT acquisition. Contemporary robotic platforms integrate augmented fluoroscopy (AF) and C-arm-based tomosynthesis (CABT) to improve lesion localization and permit real-time correction of biopsy tool position.

Optimization of ventilation has become an important strategy to reduce CT-to-body divergence. The VESPA randomized trial demonstrated that lung-volume preservation reduced procedure-related atelectasis, while breath-hold and apneic oxygenation techniques have been proposed to further minimize respiratory motion and improve image registration during robotic bronchoscopy. Despite encouraging physiologic and observational data, prospective randomized evidence supporting routine breath-hold ventilation remains limited.

The **STABLE (Study of Tool-lesion Alignment and Breath-hold Ventilation in Robotic Bronchoscopy)** trial was designed to determine whether a standardized sustained breath-hold protocol improves strict diagnostic yield or the likelihood of achieving tool-in-lesion (TIL) positioning during robotic bronchoscopy performed with integrated AF and CABT. Secondary objectives included lesion localization, tool-lesion relationship (TIL, tool-touching-lesion [TTL], and no tool in lesion [NTL]), radiation exposure, procedural performance, complications, and the relationship between imaging-confirmed tool position and diagnostic success.

Methods

Study Design and Population

This prospective randomized clinical study included adult patients undergoing robotic bronchoscopy for biopsy of a peripheral pulmonary lesion at WVU Camden Clark Medical Center during 2025 to 2026. Patients were eligible when the target lung nodule was considered appropriate for bronchoscopic biopsy of peripheral pulmonary lesions using the Noah Galaxy robotic platform. Only solid and part-solid lung nodule lesions were represented in the analyzed cohort.

After enrollment and before the procedure, patients were individually randomized to sustained breath-hold or conventional ventilation using computer-based simple randomization with equal probability of assignment. Assignment was generated at the time of randomization, with no pre-generated allocation sequence available to the procedural team. Of 117 patients, 53 were assigned to breath-hold and 64 to conventional ventilation (Fig. 1).

This study was retrospectively registered with the ISRCTN registry (ISRCTN11802169) under the title “Breath-hold during robotic bronchoscopy for lung nodule biopsy.” The study was conducted in accordance with applicable institutional requirements and the principles of the Declaration of Helsinki. The study was conducted and reported in accordance with the CONSORT guidelines for randomized controlled trials, and a completed CONSORT checklist is provided as an additional file.

Preprocedural Planning and Anesthesia

Preprocedural chest CT images were imported into the Noah Galaxy planning software, and a virtual pathway to the target lesion was constructed. All procedures were performed under general anesthesia with endotracheal intubation, typically using an 8.5-mm internal-diameter tube. A standardized ventilatory strategy was used in both groups to minimize CT-to-body divergence and dependent atelectasis, including an FiO_2 <50%, tidal volumes of 8–10 mL/kg ideal body weight, and positive end-expiratory pressure (PEEP) of 10 cm H_2O .

In both groups, augmented fluoroscopy (AF), C-arm-based tomosynthesis (CABT), and final tool-position confirmation were performed during brief end-inspiratory breath-holds to minimize respiratory motion during target lesion image acquisition.

Patients randomized to the breath-hold group additionally underwent a standardized sustained breath-hold protocol during tissue acquisition using a tidal volume of 800 mL, PEEP of 10 cm H_2O , an adjustable pressure-limiting (APL) valve setting of 20 cm H_2O , and a FiO_2 of 50%. Breath-holds were initiated immediately after final AF/CABT confirmation of tool position and maintained only for the time required to complete tissue acquisition, with duration individualized according to procedural conditions and patient physiology.

Whenever feasible, multiple transbronchial needle aspiration (TBNA) passes were obtained during a single breath-hold, followed by a second breath-hold for multiple transbronchial forceps biopsies. Additional breath-holds were performed only when further sampling was required. Mechanical ventilation was resumed between breath-holds until adequate oxygenation and ventilation were achieved.

In the conventional ventilation group, tissue sampling was performed during ongoing mechanical ventilation following AF/CABT confirmation of tool position, without a protocolized sustained breath-hold.

Robotic Bronchoscopy and Integrated Imaging Workflow

All procedures were performed using the Noah Galaxy Robotic Bronchoscopy System with electromagnetic navigation, integrated augmented fluoroscopy (AF), and C-arm-based tomosynthesis (CABT) using a standard GE OEC 9900 C-arm. Following registration, the robotic bronchoscope was

advanced along the planned pathway. Radial-probe endobronchial ultrasound was used to characterize the lesion as concentric, eccentric, or no view.

AF was performed in multiple fluoroscopic projections to identify the target lesion and assess alignment of the robotic bronchoscope and biopsy tool. CABT was obtained through rotational C-arm acquisition and three-dimensional reconstruction to confirm the tool-lesion relationship. When suboptimal alignment was identified, the bronchoscope trajectory or tool position was adjusted, followed by repeat imaging as needed.

Successful lesion localization was defined as intraprocedural identification of the target lesion using AF and/or CABT. Following localization, the tool-lesion relationship was classified according to biopsy tool position. Tool-in-lesion (TIL) was defined as the biopsy instrument positioned within the lesion. Tool-touching-lesion (TTL) was defined as the biopsy instrument contacting or abutting the lesion without definite intralesional positioning. No tool in lesion (NTL) was defined as the biopsy instrument positioned outside the lesion without direct tool-lesion contact. (Fig. 2)

Tissue Acquisition and Pathologic Classification

Tissue acquisition followed a standardized multimodality workflow. At least four transbronchial needle aspiration (TBNA) passes were generally performed first, followed by at least five transbronchial forceps biopsies. The number of TBNA passes and forceps biopsy specimens obtained was recorded. Rapid on-site cytologic evaluation (ROSE) was available to assess specimen adequacy. Bronchoalveolar lavage and mediastinal staging with convex-probe EBUS were performed when clinically indicated. BAL microbiology was incorporated into the diagnostic classification when a specific infectious organism was identified in the appropriate clinical and pathologic context.

The primary outcome was strict diagnostic yield at the index procedure according to the ATS/ACCP research statement. A procedure was considered diagnostic when it produced either a specific malignant (SM) or specific benign (SB) diagnosis. Nonspecific inflammation, normal lung tissue, and findings not meeting strict diagnostic criteria were classified as nondiagnostic (ND). All cases were independently reviewed by a second pulmonologist (S.C.) who did not participate in the procedures and was blinded to ventilation assignment and tool-lesion position. Inter-rater agreement was assessed using Cohen's κ , with disagreements resolved by consensus. Discordant classifications were prespecified to undergo consensus review, with third-reviewer adjudication if consensus could not be reached.

Secondary endpoints included lesion localization, tool-lesion relationship (tool-in-lesion [TIL], tool-touching-lesion [TTL], and no tool in lesion [NTL]), radiation exposure, diagnostic yield according to tool position, and clinically significant complications. The prespecified clinically significant complication was pneumothorax requiring chest-tube placement.

Statistical Analysis

The study used a pragmatic sample size based on consecutive enrollment during the prespecified study period; no formal a priori sample-size calculation was performed. Statistical analyses were performed using IBM SPSS Statistics (IBM Corp., Armonk, NY, USA). A two-sided P value < 0.05 was considered statistically significant. Continuous variables are presented as mean $\pm$ SD or median, as appropriate, and categorical variables as counts and percentages. Baseline balance between randomized groups was assessed using absolute standardized mean differences (SMDs), without significance testing. Procedural and radiation variables were compared using the Mann-Whitney U test, and categorical outcomes using Fisher's exact or Pearson χ^2 tests, as appropriate. Binary treatment effects are reported as odds ratios (ORs) with 95% confidence intervals (CIs). Missing data were not imputed; analyses used available observations. All analyses were two-sided.

Generative artificial intelligence tools (OpenAI ChatGPT and Grammarly) were used to assist with language editing, manuscript organization, figure and table preparation, and data verification. All analyses, interpretations, and final manuscript content were independently reviewed and approved by the authors, who take full responsibility for the work.

Results

Study Cohort and Baseline Characteristics

Of 121 patients assessed for eligibility for bronchoscopic biopsy of a peripheral pulmonary lesion, four were excluded before randomization: one elected CT-guided percutaneous biopsy and three elected imaging surveillance. The remaining 117 patients were randomized to breath-hold ventilation (n = 53) or conventional ventilation (n = 64), and all were included in the primary analysis. A CONSORT diagram Fig. 1 is provided to depict this.

Mean age was 67.5 ± 10.0 years in the breath-hold group and 66.3 ± 10.4 years in the conventional group (SMD 0.11). Mean BMI was identical at 27.3 kg/m^2 (SMD 0.00), and male sex accounted for 43.4% and 35.9%, respectively (SMD 0.15). Mean lesion diameter was 1.7 ± 0.7 cm with breath-hold and 1.9 ± 0.8 cm with conventional ventilation (SMD 0.23). One breath-hold participant had two target lesions recorded in the left and right upper lobes.

Most measured characteristics were acceptably balanced (Table 1), although bronchus sign was less common in the breath-hold group (34.0% vs 51.6%; SMD 0.35), and left-upper-lobe targets were less frequent (28.3% vs 45.3%; SMD 0.35). Solid lesion appearance (67.9% vs 64.1%; SMD 0.08) and mean maximum SUV (8.8 ± 6.5 vs 9.4 ± 7.5 ; SMD 0.08) were similar.

Primary Outcome

Overall strict adjudicated diagnostic yield was 89.7% (105/117). Diagnostic yield was 86.8% (46/53) in the breath-hold group and 92.2% (59/64) in the conventional ventilation group (OR 0.56; 95% CI, 0.17–1.87, p-value 0.34). The randomized comparison did not demonstrate improved diagnostic yield with breath-hold ventilation. Clinically acceptable tool-lesion contact (TIL or TTL) was achieved in 52/53 (98.1%) breath-hold procedures and 62/64 (96.9%) conventional procedures, with only three procedures overall classified as NTL.

Independent blinded review demonstrated complete agreement with the initial diagnostic classification (117/117; Cohen's κ = 1.00); therefore, no consensus or third-reviewer adjudication was required. Overall, 74 cases had a specific malignant diagnosis, 31 had a specific benign diagnosis, and 12 were nondiagnostic. The distribution of final pathologic and microbiologic diagnoses according to tool-lesion relationship is provided in Supplementary Table S1.

With greater than 1 year of ongoing follow-up, overall diagnostic accuracy was 97.4% (114/117). Among the 12 initially nondiagnostic cases, three were subsequently diagnosed with malignancy at surgical resection, while nine had benign outcomes on longitudinal imaging follow-up. (Supplementary Table S2)

Lesion Localization and Tool Position

Successful lesion localization was achieved in 98.1% of breath-hold cases and 95.3% of conventional cases. Concentric radial EBUS views occurred less frequently with breath-hold (24.5% vs 42.2%) and eccentric views more frequently (64.2% vs 46.9%). Because radial EBUS view is obtained after randomization, this difference is a procedural observation rather than baseline imbalance.

Tool-position distributions were similar between groups. TIL was achieved in 33/53 breath-hold procedures (62.3%) and 41/64 conventional procedures (64.1%; OR 0.93; 95% CI, 0.44–1.97). TTL occurred in 35.8% versus 32.8%, and NTL in 1.9% versus 3.1%. Figure 3 illustrates diagnostic yield and tool-position distributions between the two study groups.

Breath-hold ventilation did not increase TIL frequency (62.3% vs 64.1%). Across both randomized groups, diagnostic yield was highest with TIL (95.9%), followed by TTL (85.0%) and NTL (0%).

Diagnostic Yield According to Tool-Lesion Relationship

Imaging-confirmed TIL or TTL was achieved in 114/117 procedures (97.4%). Independent of ventilation strategy, diagnostic yield demonstrated a graded relationship with tool position, increasing from 0% with NTL to 85.0% with TTL and 95.9% with TIL. TIL yield exceeded TTL yield, although the estimate was imprecise (OR, 4.18; 95% CI, 0.98–17.7). Both TIL and TTL also had higher diagnostic yield than NTL. Because tool position was assessed after randomization, these analyses are exploratory and should not be interpreted causally.

Procedural, Radiation, and Safety Outcomes

Procedural complexity was similar between groups. Mean C-arm spins were 2.1 ± 0.85 with breath-hold and 2.03 ± 0.62 with conventional ventilation. Mean TBNA passes were 4.70 ± 0.70 and 4.67 ± 0.71 , and mean transbronchial biopsy samples were 5.72 ± 1.03 and 5.73 ± 1.20 , respectively. Patients in the breath-hold group required a mean of 3.0 ± 0.4 sustained breath-holds per procedure (median, 3; range, 2–4).

Radiation exposure showed no clear between-group differences. Fluoroscopy time was 5.8 ± 4.4 minutes with breath-hold versus 6.1 ± 3.7 minutes with conventional ventilation. Air kerma was 35.5 ± 26.3 versus 39.0 ± 21.6 mGy, and dose-area product was 22.2 ± 16.4 versus 24.4 ± 13.5 Gy·cm², respectively. Two pneumothoraces requiring chest-tube placement occurred, both in the conventional ventilation group (0/53 vs 2/64). No clinically significant bleeding requiring intervention was observed in either group.

An exploratory lesion-level subgroup analysis included 118 lesions from 117 patients because one patient underwent biopsy of synchronous RUL and LUL lesions. Overall strict diagnostic yield increased with lesion size, from 70.0% (7/10) for lesions < 1 cm to 86.4% (51/59) for lesions 1 to < 2 cm and 98.0% (48/49) for lesions $\geq$ 2 cm. Within these size categories, diagnostic yield with breath-hold versus conventional ventilation was 80.0% (4/5) versus 60.0% (3/5) for lesions < 1 cm, 80.0% (24/30) versus 93.1% (27/29) for lesions 1 to < 2 cm, and 100% (19/19) versus 96.7% (29/30) for lesions $\geq$ 2 cm. These exploratory subgroup comparisons were small and showed no consistent pattern favoring either ventilation strategy (Supplementary Table S3).

Discussion

To our knowledge, this is the first prospective randomized study evaluating standardized sustained breath-hold during tissue acquisition in imaging-integrated robotic bronchoscopy. Despite a strong physiologic rationale and encouraging observational data [3,4,9], STABLE did not demonstrate improved biopsy performance with sustained breath-hold. Strict diagnostic yield was 86.8% with breath-hold and 92.2% with conventional ventilation (OR, 0.56; 95% CI, 0.17–1.87). TIL positioning, lesion localization, sampling intensity, radiation exposure, and complication rates showed no clear between-group differences. Diagnostic yield instead varied according to imaging-confirmed tool-lesion position.

Respiratory motion and anesthesia-related atelectasis contribute to CT-to-body divergence during guided bronchoscopy. Sustained breath-hold and apneic oxygenation techniques have therefore been proposed to improve image registration and tool-lesion stability during robotic bronchoscopy [3,4,9–11]. However, the available evidence has largely consisted of physiologic reviews, technical descriptions, and retrospective observational studies, with limited prospective randomized evidence demonstrating improved diagnostic performance.

STABLE tested a focused mechanistic hypothesis: whether sustained breath-hold during biopsy would improve TIL and diagnostic yield by reducing respiratory motion. Breath-hold did not improve TIL frequency, lesion localization, or diagnostic yield, possibly because integrated augmented fluoroscopy (AF), C-arm-based tomosynthesis (CABT), and active tool correction already provide effective real-time

compensation for CT-to-body divergence. Imaging-confirmed TIL or TTL was achieved in 97.4% of procedures and exceeded 96% in both groups. Diagnostic yield was 95.9% with TIL versus 85.0% with TTL (OR, 4.18; 95% CI, 0.98–17.7), suggesting that once lesion access is achieved, optimizing intralesional tool position may be more important than respiratory stabilization alone.

These findings should be distinguished from broader ventilation strategies intended to prevent anesthesia-related atelectasis. The VESPA randomized trial demonstrated that recruitment maneuvers, lower inspired oxygen concentrations, and positive end-expiratory pressure substantially reduced intraoperative atelectasis [1]. In contrast, STABLE evaluated whether adding a sustained breath-hold during biopsy, provided incremental benefit after an optimized ventilation strategy had already been established. Accordingly, the absence of benefit from breath-hold should not be interpreted as evidence against established lung-volume preservation strategies [1,11].

Patient positioning may provide an additional means of reducing atelectasis not corrected by ventilation alone. In selected patients with dependent lung lesions, lateral decubitus positioning improved target visualization, TIL positioning, and diagnostic yield compared with a VESPA-based strategy [13]. STABLE did not randomize patient positioning or directly quantify atelectasis and therefore cannot exclude a role for positioning in selected patients. Similarly, Goudra et al. reported acceptable navigation success despite variable adherence to formal ventilation protocols, suggesting that overall procedural workflow may influence success more than any single ventilatory maneuver [14]. In the recent real-world comparative VITAL study, CT-to-body and tool-tissue divergence were addressed through integrated imaging and direct visual confirmation of tool deployment, allowing real-time lesion localization and tool adjustment; suggesting favorable tool-lesion alignment was strongly associated with diagnostic success [19].

Although sustained breath-hold did not increase TIL, STABLE reinforces the importance of imaging-confirmed tool-lesion alignment. Navigation to a virtual target or fluoroscopic lesion localization does not ensure that the biopsy instrument remains within the lesion after anatomic divergence, atelectasis, or catheter deflection. AF and CABT permit assessment and correction of this final spatial relationship. The high yield observed with TTL also suggests that tangential lesion contact may remain diagnostically productive when adequate sampling is obtained with dynamic tool adjustment with AF in fluoroscopic orthogonal planes [14, 16]. Although this post-randomization analysis was exploratory and operator-reported, the graded relationship between tool position and diagnostic yield supports tool-lesion alignment as an important procedural marker of successful tissue acquisition.

The absence of a measurable radiation benefit is also relevant. Sustained breath-hold did not reduce the number of C-arm spins, fluoroscopy time, air kerma, or dose-area product, suggesting that respiratory stabilization alone did not eliminate the need for iterative imaging or tool adjustment. Radiation exposure in STABLE was within the range previously reported with AF/CABT [17], within a growing literature characterizing radiation exposure during imaging-integrated bronchoscopy using these technologies [17,18]. It remains possible that breath-hold improved individual image acquisitions or

reduced motion artifact in ways not captured by cumulative radiation measures. Future studies should directly evaluate respiratory excursion, registration error, image quality, breath-hold duration and frequency, the interval from imaging confirmation to tissue acquisition, and tool displacement after ventilation resumes.

The safety profile of intermittent sustained breath-hold ventilation was favorable. Two pneumothoraces requiring chest-tube placement occurred in the conventional ventilation group and none in the breath-hold group; however, the study was not powered to detect differences in uncommon adverse events. Prolonged apneic techniques have been associated with predictable hypercapnia and increased vasopressor requirements during substantially longer periods of apnea than those used in STABLE [4,12]. Individual breath-hold duration, serial carbon dioxide measurements, oxygenation, and vasopressor exposure were not systematically recorded and should be incorporated into future comparative studies.

Breath-hold ventilation may still be useful in selected situations with substantial respiratory motion or persistent CT-to-body divergence, particularly highly mobile lower-lobe or juxtadiaphragmatic lesions. In exploratory lesion-level analysis, no consistent benefit of breath-hold was observed across lesion-size categories or lobar locations. However, diagnostic yield increased progressively with lesion size, from 70.0% for lesions < 1 cm to 86.4% for lesions 1 to < 2 cm and 98.0% for lesions $\geq$ 2 cm. This finding suggests that lesion size remains an important determinant of diagnostic performance even within an imaging-integrated robotic workflow with high rates of tool-lesion confirmation. These subgroup analyses were exploratory and involved small numbers, particularly for subcentimeter lesions, and should therefore be interpreted cautiously.

Collectively, these findings suggest that success during robotic bronchoscopy is multifactorial and depends on ventilation strategy, imaging guidance, tool-lesion alignment, and tissue acquisition. This is consistent with CONFIRM, which reported an 89.0% strict diagnostic yield despite very high CBCT-confirmed TIL rates [15], and also with MATCH-2, which demonstrated high concordance between integrated digital tomosynthesis/augmented fluoroscopy and CBCT for TIL confirmation [16]. In STABLE, tool position was similarly assessed spatially using CABT reconstruction in three orthogonal planes, while the more granular TIL/TTL/NTL classification distinguished intralesional positioning from tangential contact. Despite imaging-confirmed TIL or TTL in 97.4% of procedures, diagnostic yield varied according to final tool position.

This study has several limitations. First, it was conducted at a single center using a single robotic bronchoscopy platform within a highly standardized imaging-integrated workflow, which may limit generalizability to centers without AF or CABT, other robotic platforms, or operators with different levels of experience. All procedures were performed by a single bronchoscopist, which minimized inter-operator variability and strengthened internal consistency but may limit external validity.

Second, neither the bronchoscopist nor the anesthesia team could be blinded to ventilation assignment, introducing the potential for performance bias. Although the sampling sequence, ventilatory protocol,

and imaging workflow were standardized, C-arm image acquisition and reconstruction also depended on radiologic technologists. Small differences in patient positioning, image acquisition timing, or reconstruction could have introduced procedural variability, although use of a consistent institutional workflow and experienced personnel likely minimized this effect.

Third, simple randomization resulted in unequal group sizes and minimal baseline imbalances, including bronchus-sign prevalence and lobar distribution. The relatively small sample size and low number of nondiagnostic and safety events also limited statistical precision and precluded robust assessment of uncommon complications or small treatment differences. The modest sample size could also limit statistical precision and the ability to detect small between-group differences; therefore, the observed results should not be interpreted as establishing equivalence between ventilation strategies.

Fourth, although a standardized sustained breath-hold protocol was used, individual breath-hold durations and physiologic responses were not prospectively recorded because breath-holds were individualized according to procedural conditions and patient physiology. Consequently, cumulative breath-hold exposure, physiologic tolerance, and their relationships with procedural or diagnostic outcomes could not be systematically evaluated. Pure ground-glass nodules were not represented in this cohort, limiting applicability to that lesion subtype. Patient positioning was also not randomized or systematically recorded relative to lesion location.

Finally, the analysis of tool-lesion position was performed after randomization and should be considered exploratory. Although pathology assessment was blinded to ventilation assignment and strict ATS/ACCP diagnostic-yield definitions were applied to minimize classification bias [2], tool-position assessment was operator-reported and therefore subject to some degree of observer bias. Nevertheless, the consistent association between more favorable tool position and higher diagnostic yield supports accurate tool-lesion alignment as an important procedural marker of successful tissue acquisition.

An additional strength was independent blinded adjudication of the primary diagnostic endpoint, which demonstrated complete agreement with the initial classification ($\kappa = 1.00$), supporting the robustness of the strict diagnostic yield assessment.

Despite these limitations, STABLE provides prospective randomized evidence that routine sustained breath-hold does not improve diagnostic yield within a contemporary workflow incorporating integrated imaging and active tool correction. Procedural attention should instead focus on lung-volume preservation, real-time lesion confirmation, optimal tool-lesion alignment, and adequate tissue acquisition. Future multicenter studies incorporating objective physiologic and imaging endpoints should determine whether selected high-motion lesions or specific patient subgroups may benefit from targeted breath-hold strategies.

Conclusion

In the STABLE randomized trial, sustained breath-hold during tissue acquisition did not improve strict diagnostic yield, lesion localization, or tool-in-lesion positioning during robotic bronchoscopy with integrated AF and CABT. Diagnostic yield demonstrated a graded relationship with imaging-confirmed tool-lesion position. These results support prioritizing real-time lesion confirmation and precise tool positioning, while reserving breath-hold as a selective adjunct pending further multicenter evidence.

Abbreviations

AF	augmented fluoroscopy
APL	adjustable pressure-limiting
ATS	American Thoracic Society
ACCP	American College of Chest Physicians
BAL	bronchoalveolar lavage
BMI	body mass index
CABT	C-arm-based tomosynthesis
CI	confidence interval
CT	computed tomography
DAP	dose-area product
EBUS	endobronchial ultrasound
FiO ₂	fraction of inspired oxygen
FNA	fine-needle aspiration
ND	nondiagnostic
NSCLC	non-small cell lung carcinoma
NTL	no tool in lesion

OR
odds ratio
PEEP
positive end-expiratory pressure
ROSE
rapid on-site cytologic evaluation
SB
specific benign
SM
specific malignant
SMD
standardized mean difference
SUV
standardized uptake value
TBBx
transbronchial biopsy
TBNA
transbronchial needle aspiration
TIL
tool-in-lesion
TTL
tool-touching-lesion.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the West Virginia University Institutional Review Board (protocol number STUDY00000720). Written informed consent to participate was obtained from all participants. The study was conducted in accordance with applicable institutional requirements and the principles of the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request, subject to institutional requirements and protection of participant confidentiality.

Competing interests

The other authors declare that they have no competing interests.

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Authors' contributions

RM contributed to study conception and design, statistical analysis and interpretation of the data, and drafting and critical revision of the manuscript. NM contributed to study design, interpretation of the findings, manuscript development, and critical revision of the manuscript. OD contributed to interpretation of the findings, manuscript development, and critical revision of the manuscript. SC contributed to study conceptualization, data acquisition and organization, preparation of tables, interpretation of the data, and critical revision of the manuscript. All authors contributed substantially to the work, reviewed and approved the final manuscript, and agree to be accountable for the accuracy and integrity of the work.

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Tables

Table 1
Baseline Characteristics According to Ventilation Strategy

Characteristic	Breath-hold (n = 53)	Conventional ventilation (n = 64)	Absolute SMD
Age, years	67.5 ± 10.0	66.3 ± 10.4	0.11
BMI, kg/m²	27.3 ± 6.9	27.3 ± 9.7	0.00
Male sex	23 (43.4)	23 (35.9)	0.15
Lesion diameter, cm	1.7 ± 0.7	1.9 ± 0.8	0.23
Right upper lobe	16 (30.2)	18 (28.1)	0.05
Right middle lobe	3 (5.7)	3 (4.7)	0.04
Right lower lobe	10 (18.9)	7 (10.9)	0.23
Left upper lobe	15 (28.3)	29 (45.3)	0.35
Left lower lobe	8 (15.1)	7 (10.9)	0.12
Multilobar (LUL/RUL)	1 (1.9)	0 (0.0)	0.20
Bronchus sign present	18 (34.0)	33 (51.6)	0.35
Solid lesion	36 (67.9)	41 (64.1)	0.08
Part-solid lesion	17 (32.1)	23 (35.9)	0.08
Maximum SUV	8.8 ± 6.5	9.4 ± 7.5	0.08

Table 2
Primary, Procedural, Radiation, and Safety Outcomes

Outcome	Breath-hold (n = 53)	Conventional (n = 64)	Effect estimate (95% CI)
Diagnostic yield	46/53 (86.8)	59/64 (92.2)	OR 0.56 (0.17–1.87)
Lesion successfully localized	52/53 (98.1)	61/64 (95.3)	OR 2.56 (0.26–25.34)
TIL	33 (62.3)	41 (64.1)	OR 0.93 (0.44–1.97)
TTL	19 (35.8)	21 (32.8)	
NTL	1 (1.9)	2 (3.1)	
C-arm spins	2.11 ± 0.85	2.03 ± 0.62	
TBNA passes	4.70 ± 0.70	4.67 ± 0.71	
Transbronchial biopsy samples	5.72 ± 1.03	5.73 ± 1.20	
Fluoroscopy time, min	5.8 ± 4.4	6.1 ± 3.7	
Air kerma, mGy	35.5 ± 26.3	39.0 ± 21.6	
Dose-area product, Gy·cm ²	22.2 ± 16.4	24.4 ± 13.5	
Pneumothorax requiring chest tube	0/53 (0.0)	2/64 (3.1)	

Table 3
Diagnostic Yield According to Tool-Lesion Relationship

Tool position	Diagnostic	Nondiagnostic	Overall diagnostic yield	Breath-hold yield	Conventional yield
TIL	71	3	95.9%	90.9%	100%
TTL	34	6	85.0%	84.2%	85.7%
NTL	0	3	0%	0%	0%
Overall	105	12	89.7%	86.8%	92.2%

Figures

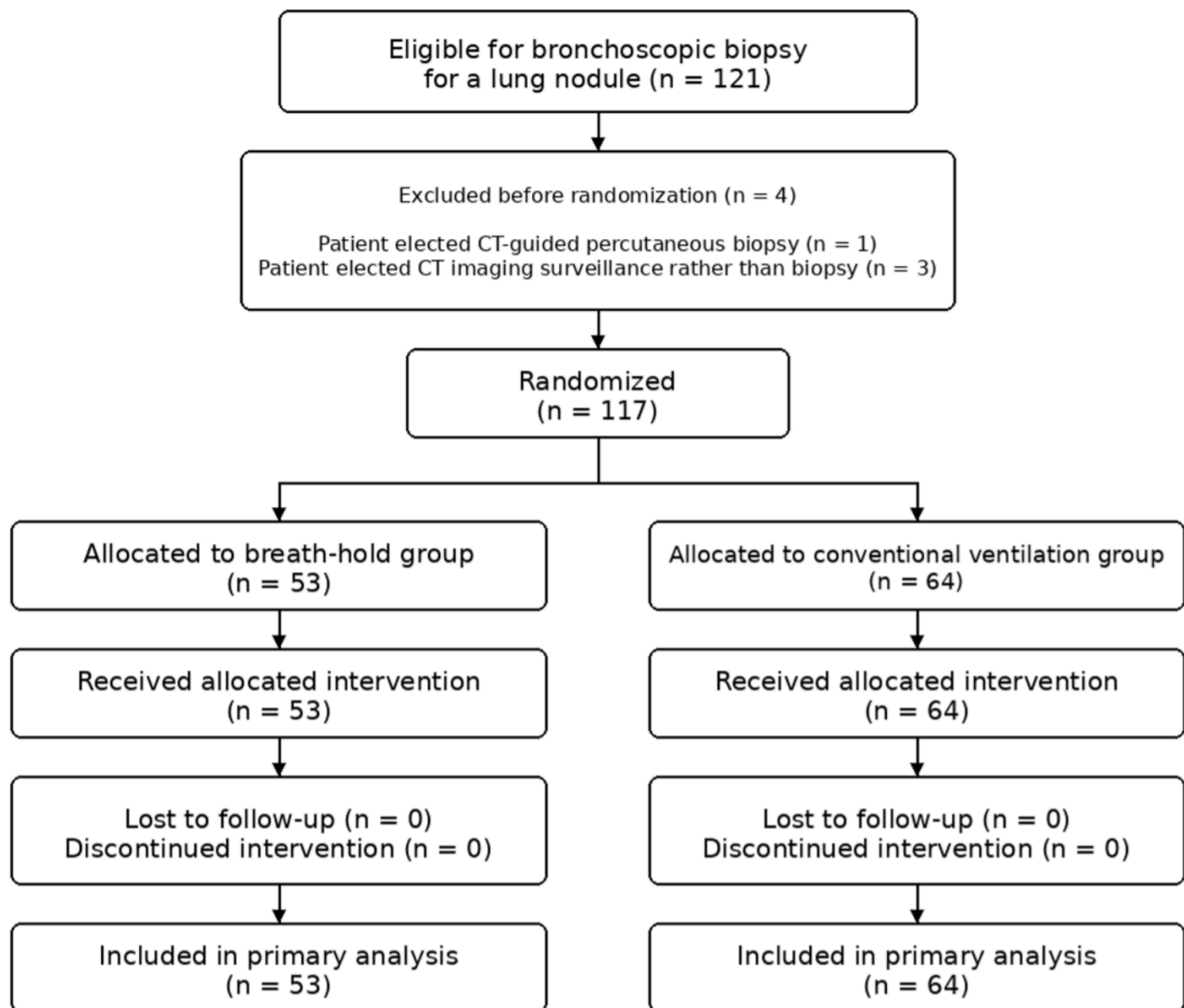


Figure 1

CONSORT flow diagram of patient enrollment, randomization, allocation, follow-up, and analysis in the STABLE trial.

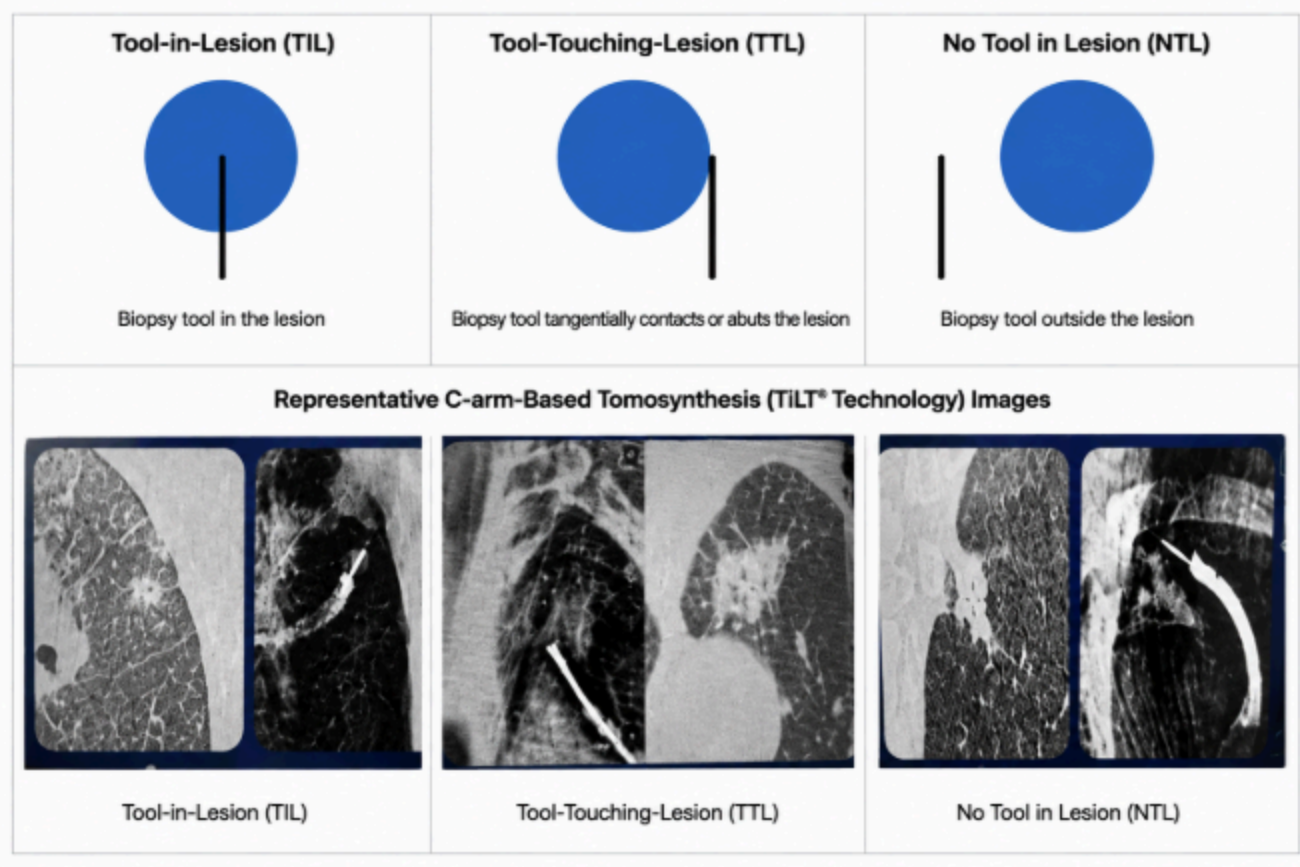


Figure 2

Representative schematic illustrations and corresponding C-arm–based tomosynthesis images demonstrating the predefined tool–lesion relationship classifications: tool-in-lesion (TIL), tool-touching-lesion (TTL), and no tool in lesion (NTL).

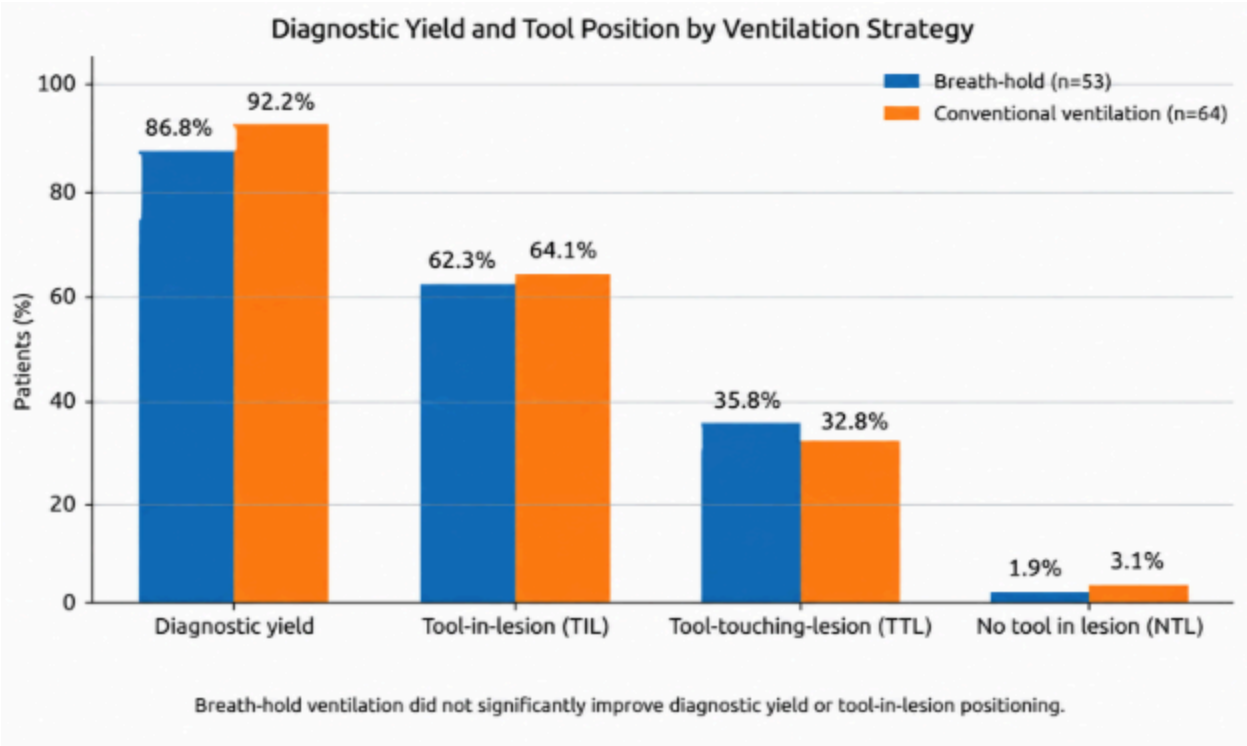


Figure 3

Diagnostic yield and tool-position distribution according to randomized ventilation strategy. Breath-hold ventilation did not improve diagnostic yield or TIL positioning. TTL denotes tool-touching-lesion; NTL denotes no tool in lesion.

Supplementary Files

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- [STABLEBMCSupplementaryTables.docx](#)