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Naman Garg
Texas Health Presbyterian Plano
Maria Haseem
Texas Health Presbyterian Plano
Sina Rahesh
Texas Health Presbyterian Plano
Kunal Jain
Texas Health Presbyterian Plano
Ross Charles Schumacher
ross.schumacher@icloud.com
Texas Health Presbyterian Plano

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Dual-Wield: An Observational Study of Utilization and Outcomes of Cryobiopsy and Intraoperative CT scan During Navigational Bronchoscopy

Naman Garg, DO[1]; Maria Haseem, MD[1]; Sina Rahesh, DO[1]; Kunal Jain, DO[1]; Ross Charles Schumacher, MD[2]

[1] Texas Health Presbyterian Plano, Department of Internal Medicine, Plano, Texas, USA
[2] Texas Health Presbyterian Plano, Department of Internal Medicine, Department of Pulmonology and Critical Care, Plano, Texas, USA

Author Information

Naman Garg, namang2016@gmail.com ORCID: 0009-0002-7568-1587

Maria Haseem, MariaHaseem@texashealth.org ORCID: 0000-0002-3505-6990

Sina Rahesh, SinaRahesh@texashealth.org ORCID: 0009-0005-3063-6952

Kunal Jain, KunalJain@texashealth.org ORCID: 0000-0003-4235-7676

Ross Charles Schumacher, ross.schumacher@icloud.com ORCID: 0000-0002-7577-3599

Corresponding author: Ross Charles Schumacher, MD, Texas Health Presbyterian Plano, Department of Internal Medicine, Department of Pulmonology and Critical Care, Plano, Texas, USA. Email: ross.schumacher@icloud.com

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Abstract

Background
Pulmonary nodules are common incidental imaging findings, and distinguishing malignant from benign etiologies frequently requires invasive sampling. CT-guided transthoracic needle biopsy offers high yield but carries pneumothorax rates of 15–45% and precludes concurrent mediastinal staging. Shape-sensing navigational bronchoscopy, intraprocedural cone-beam CT (CBCT), and transbronchial cryobiopsy have each independently improved bronchoscopy performance, but integration of all three into one workflow remains poorly characterized. We describe real-world utilization and outcomes of these modalities at a large volume community tertiary care center.

Research Question
What is the real-world utilization, diagnostic performance, and complication rate of navigational bronchoscopy for lung nodule sampling with the addition of CBCT and cryobiopsy?

Study Design and Methods
We conducted a retrospective cohort study of navigational bronchoscopy procedures performed at a single community tertiary care center between January 1, 2024, and January 1, 2026. Two physician investigators independently abstracted procedure reports, imaging, and pathology from the electronic health record, recording cryobiopsy use, CBCT use, target nodule size, pathology, and complications. Diagnostic yield was determined using the strict ATS/ACCP consensus definition.

Results
Among 199 navigational bronchoscopy procedures, 229 lesions were sampled. Mean nodule size was 22.4 ± 17.7 mm overall, smallest with cryobiopsy plus CBCT (17.4 ± 13.7 mm) and largest with no adjunctive modality (29.8 ± 20.3 mm). Overall diagnostic yield was 78.0%: 83.9% with cryobiopsy plus CBCT, 75.0% cryobiopsy alone, 70.4% CBCT alone, and 73.2% no adjunctive modality. The complication rate was 3.5% (7/199). Diagnostic yield trended higher in cases with both cryobiopsy and CBCT.

Conclusion
Integrating navigational bronchoscopy with CBCT and cryobiopsy achieved the highest diagnostic yield while sampling the smallest nodules with an acceptable safety profile. Prospective randomized studies are warranted to define the independent contribution of each adjunct and to detect any true incremental harm.

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Introduction:

Pulmonary nodules are among the most common incidental findings in thoracic imaging, with more than 1.5 million detected annually in the United States alone [1-2]. While approximately 95% of detected nodules are ultimately benign, distinguishing malignant from benign etiologies frequently requires invasive tissue sampling, placing a substantial procedural burden on patients and healthcare systems [1-2].

For decades, CT-guided transthoracic needle biopsy (TTNB) has served as the primary modality for sampling peripheral pulmonary lesions, offering reported diagnostic yields of 85–95% and sensitivity for malignancy between 92% and 97% in experienced centers [3-4]. However, TTNB carries well-documented risks, with pneumothorax occurring in 15–45% of cases [3-5]. Additionally, TTNB does not permit concurrent mediastinal lymph node staging, often necessitating a second procedure for patients diagnosed with malignancy [6].

Bronchoscopic biopsy has recently undergone transformative advances in both intraoperative imaging and tissue acquisition. The VERITAS trial demonstrated that navigational bronchoscopy augmented with intraprocedural three-dimensional imaging was noninferior to TTNB in diagnostic accuracy while dramatically reducing pneumothorax rates [7]. The integration of cone-beam CT (CBCT) and digital tomosynthesis has been central to these improvements, providing real-time three-dimensional visualization that overcomes the longstanding challenge of CT-to-body divergence and enables precise tool-in-lesion confirmation [8-10]. Concurrently, the development of the cryoprobe has advanced tissue sampling, with the FROSTBITE-2 trial demonstrating a diagnostic yield of 88.6% for cryobiopsy versus 78.8% for conventional forceps biopsy across 500 patients, with no pneumothorax or significant bleeding in the cryobiopsy group [11]. Cryobiopsy retrieves larger, crush-free specimens that preserve histologic architecture, capabilities increasingly essential in the era of precision oncology [12-13].

While each of these technologies has been studied individually or in limited pairwise combinations, the integration of all three (navigational bronchoscopy, 3D C-arm imaging, and cryobiopsy) into a single procedural workflow has not been thoroughly evaluated. Emerging data suggest that multimodal approaches combining robotic bronchoscopy with CBCT and cryobiopsy achieve diagnostic yields exceeding 85% with minimal complications, however comparative data remains limited regarding how the additional modalities affect yield, average nodule size that can be sampled, and complication rates [13-15].

Here, we present a retrospective observational analysis of patients who underwent navigational bronchoscopy at a large-volume community tertiary care center equipped with both 3D C-arm guidance and transbronchial cryobiopsy. We examine individual and combined adjunctive modality usage rates, diagnostic yield, and complication rates.

Methods

Study Design and Patient Selection

We conducted a retrospective cohort study of navigational bronchoscopy procedures performed at Texas Health Presbyterian Hospital Plano between January 1, 2024, and January 1, 2026. A procedural database maintained by the institution's Pulmonary Nodule Program was used to identify all navigational bronchoscopy procedures performed during the study period. Multiple procedures performed on the same patient during the study timeframe were eligible for inclusion on an as-performed basis. Procedures that were scheduled but subsequently canceled or not performed were excluded from analysis.

This study was approved by the University of Texas Southwestern Medical Center Institutional Review Board with a waiver of informed consent given the retrospective nature of the study.

Data Collection

Two physician investigators (R.C.S. and N.G.) independently performed a structured review of the electronic health record (EHR) for each consecutive procedure performed at Texas Health Presbyterian Hospital Plano. For every case, procedural and clinical data were abstracted from pre-procedural imaging studies including CT chest ION protocol scans, bronchoscopy procedure reports, intraoperative fluoroscopic images, post-procedural chest radiographs, pathology reports, and other relevant peri-procedural physician documentation.

The following variables were collected: procedure date, operating physician, utilization of navigational bronchoscopy, use of transbronchial cryobiopsy, use of intraoperative cone-beam computed tomography (CBCT), size of the target nodule, and pathology reports. Utilization of navigational bronchoscopy, cryobiopsy, and CBCT was determined through review of procedure documentation and fluoroscopic images obtained intraoperatively.

Target pulmonary nodule size was determined through review of procedural documentation and radiographic imaging. When multiple nodules were present, procedural notes and fluoroscopic images were used to identify the sampled lesion, which was subsequently cross-referenced with pre-procedural CT imaging for measurement. In cases where lesion size was not explicitly documented, measurements were performed by the study investigators using available imaging.

All study data were entered into and managed using the REDCap electronic data capture platform.

Outcomes

Pathology reports were reviewed for all sampled lesions, and strict diagnostic yield was assessed according to the American Thoracic Society/American College of Chest Physicians (ATS/ACCP) statement on diagnostic yield reporting for guided bronchoscopy [16]. Diagnostic yield was evaluated at both the individual nodule level, when multiple nodules were sampled, and the whole-procedure level based on the aggregate results of all lesions sampled during the incident procedure. For each nodule, investigators determined whether the biopsy result met ATS/ACCP criteria for a diagnostic or non-diagnostic result. Cases in which the ATS/ACCP criteria was insufficient for classification were individually reviewed, with final determination reached through negotiated consensus involving a senior advanced bronchoscopist (R.C.S.). Final pathology results were additionally categorized as malignant or non-malignant.

Procedure-related complications were recorded and included pneumothorax requiring intervention, bleeding requiring medical intervention, and post-procedural respiratory failure.

Data Quality Assurance

To establish abstraction reliability, both physician investigators independently reviewed an initial subset of procedures and compared abstracted data. Inter-reviewer concordance was >95%.

Statistical Analysis

Descriptive statistics were used to summarize study population, procedural, and outcome data. Given the unequal sample sizes across modality groups and the retrospective, unmatched study design, no formal statistical comparisons between groups were performed; results are presented descriptively.

Results

Study Population

A total of 276 procedures were assessed for eligibility from the procedural database maintained by the institution's Pulmonary Nodule Program. 50 procedures were excluded: 11 fell outside the predefined study period (January 1, 2024, to January 1, 2026), and 39 were scheduled but subsequently cancelled. Of the remaining 226 records that underwent manual chart abstraction, 27 were further excluded: 20 lacked a distinct nodule that was biopsied, 3 underwent flexible bronchoscopy rather than navigational bronchoscopy, 2 had no actual procedure performed, 1 could not be located in the electronic medical record, and 1 had no pathology report available. The final analytic cohort comprised 199 procedures on 193 distinct patients. Of these, 119 were female and 74 were male. Some patients underwent multiple procedures [Figure 1].

Procedural details

All procedures were performed using the Ion™ navigational bronchoscopy platform and were further categorized by specific modality [Table 1]: transbronchial cryobiopsy and CBCT (n = 87; 43.7%), transbronchial cryobiopsy alone (n = 44; 22.1%), CBCT alone (n = 27; 13.6%), and no adjunctive modality (n = 41; 20.6%). All transbronchial cryobiopsies were performed using a 1.1-mm cryoprobe.

Lesion Characteristics

A total of 229 pulmonary lesions were sampled across 199 procedures [Figure 2]. The mean nodule size was 22.4 ± 17.7 mm overall. Mean nodule size varied by procedural modality: 17.4 ± 13.7 mm in the transbronchial cryobiopsy plus CBCT group, 26.5 ± 20.8 mm in the transbronchial cryobiopsy–alone group, 20.4 ± 13.5 mm in the CBCT-alone group, and 29.8 ± 20.3 mm in the no adjunctive modality group [Figure 3].

Diagnostic Outcomes

The overall diagnostic yield, using strict criteria defined according to the ATS/ACCP consensus definition, was 78.0% (155 /199). The highest diagnostic yield was observed in the transbronchial cryobiopsy plus CBCT group at 83.9% (73/87), followed by the transbronchial cryobiopsy–alone group at 75.0% (33/44), the no adjunctive modality group at 73.2% (30/41) and the CBCT-alone group at 70.4% (19/27) [Figure 4].

Safety Outcomes

Procedural complications are summarized in Table 2. The overall complication rate was 3.5% (7/199 procedures). Complications included six pneumothoraxes and one episode of post-procedural hypoxia without pneumothorax. Five of the seven complications occurred in the transbronchial cryobiopsy plus CBCT group (5/87; 5.7%), with one complication each in the transbronchial cryobiopsy–alone group (1/44; 2.3%) and the no adjunctive modality group (1/41; 2.4%). No complications were observed in the CBCT-alone group (0/27; 0.0%).

Discussion

In this observational study, 199 navigational bronchoscopy procedures sampling 229 lesions were performed by seven operators at a single large-volume community tertiary care center over 24 months, with a high overall diagnostic yield and a low complication rate. Notably, there appears to be an increase in diagnostic yield, paired with a paradoxical decrease in nodule size, as operators utilize both cryobiopsy and cone-beam CT concurrently [Table 1]. Yield was highest when cryobiopsy and CBCT were combined (83.9%), a group that also sampled the smallest average lesions in the cohort (mean, 17.4 ± 13.7 mm), with several lesions <8mm. By contrast, the groups sampling

larger nodules had lower yields: 73.2% with no adjunctive modality (mean, 29.8 mm) and 75.0% with cryobiopsy alone (mean, 26.5 mm). We surmise that the combined approach using cryobiopsy and CBCT was preferentially applied to the most challenging peripheral targets, with the full multimodal toolkit reserved for smaller and more difficult lesions. Because modality selection was not randomized and was left to operator discretion, this likely reflects at least some confounding by indication. Thus, the observed increase in diagnostic yield among the smallest nodules should not be interpreted as evidence of head-to-head superiority, but rather as suggesting that the incremental value of combining cryobiopsy and CBCT may be greatest for smaller, difficult-to-access lesions (where real-time three-dimensional confirmation and larger tissue specimens would be most beneficial).

The advanced diagnostic bronchoscopy literature reports a wide range of diagnostic yields, in part because yield is variably defined and calculated across studies. Lentz et al., in the VERITAS trial, demonstrated that navigational bronchoscopy augmented with intraprocedural three-dimensional imaging was noninferior to CT-guided transthoracic needle biopsy while substantially reducing pneumothorax [7]. Thiboutot et al., in the FROSTBITE-2 trial, reported a diagnostic yield of 88.6% for transbronchial cryobiopsy compared with 78.8% for conventional forceps biopsy, with no pneumothorax or significant bleeding in the cryobiopsy group [11]. Multimodal series combining navigational bronchoscopy with CBCT and cryobiopsy have described yields exceeding 85%, however their definitions of diagnostic yield vs diagnostic accuracy have varied [13-15]. Our overall diagnostic yield across all navigational bronchoscopies was 78.0% using the strict ATS/ACCP consensus definition, which is within the range reported in previous trials. However, yield still varied considerably depending on the use of cryobiopsy and/or CBCT. Several features of our cohort likely account for these findings, namely that our study reflects unselected, consecutive procedures at a community center rather than a curated referral population, and modality integration was heterogeneous and left to operator discretion.

The complication rate compares favorably with historical experience. CT-guided transthoracic needle biopsy carries a reported pneumothorax rate of 15–45% [3-5], whereas our overall rate was 3.5%, comprising of six pneumothoraxes and one episode of post-procedural hypoxia without pneumothorax. Within the cohort, five of the seven events occurred in the cryobiopsy-plus-CBCT group (5.7%), and none occurred in the CBCT-alone group [Table 2]. Because the combined group also included the smallest and potentially most peripheral nodules, in which cryobiopsy in proximity to the visceral pleura may carry incremental risk, a modest increase in pneumothorax risk is bioplausible; however, the small number of events precludes firm conclusions. The larger, crush-free specimens obtained by cryobiopsy preserve histologic architecture and may be increasingly relevant in the era of precision oncology, in which adequate tissue for molecular and immunohistochemical characterization is essential [12-13].

Limitations

Our study has several limitations related to its single-center, retrospective, and observational design. Generalizability may be limited by institution-specific factors, including procedural volume, operator training, familiarity with the workflow, and the availability of advanced imaging. Modality was assigned at operator discretion rather than by randomization, and the groups were unequal, unmatched, and not subjected to significance testing, which precludes comparative-effectiveness inference. Diagnostic yield was defined at the level of the index procedure, but nondiagnostic and nonspecific benign results were not systematically adjudicated through longitudinal radiographic or clinical follow-up, which may underestimate our true yield. Finally, although we observed variation in diagnostic yield across proceduralists, we did not formally assess outcomes by individual provider, as the primary aim was to characterize outcomes at the institutional level, and the use of CBCT and cryobiopsy varied by operator over the study period.

Conclusion

This report describes both our institutional outcomes with CBCT and transbronchial cryobiopsy employed during navigational bronchoscopy and shows observational data that implies an additive benefit of both technologies used in tandem as opposed to individually. For all-comers, we achieved a diagnostic yield (using the strict ATS/ACCP definition) of 78.0% and a complication rate of 3.5% in a real-world community setting, while also demonstrating how the addition of multiple intraprocedural tools can increase diagnostic yield, despite those multiple tools being used more frequently to sample smaller lesions.

Prospective, adequately powered studies with standardized lesion characterization and systematic follow-up will be needed to define the independent contribution of each modality and to identify the lesions most likely to benefit from a combined (CBCT + cryobiopsy) approach. Our study shows a signal toward improved diagnostic yield with the addition of cryobiopsy and CBCT, and for more consistent sampling of small nodules, including those <8mm. We would contend that a modern bronchoscopy suite would benefit from having access to both CBCT and cryobiopsy, and believe our above data supports that thesis. The signal for increased complications noted in the combined modality arm warrants further evaluation in larger community-based prospective studies.

Figures and Graphs

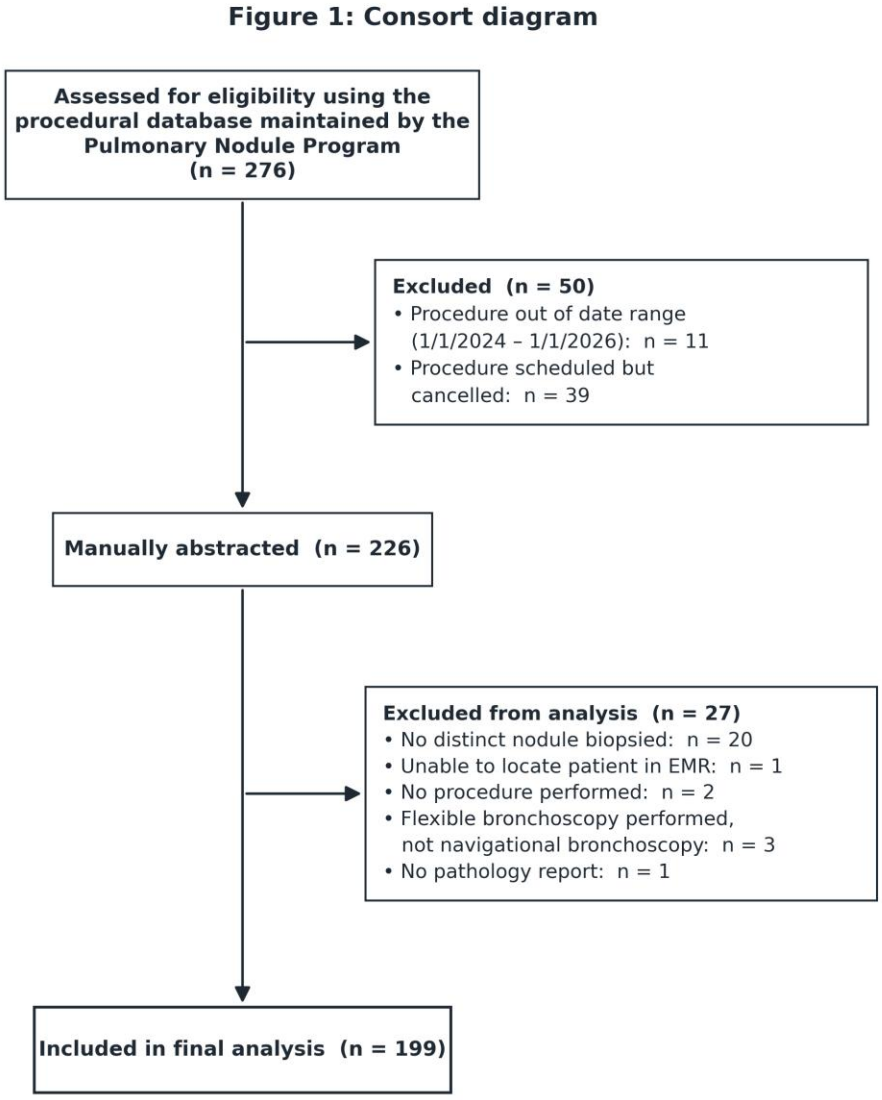


Figure 1: Consort diagram showing cohort selection for final analysis

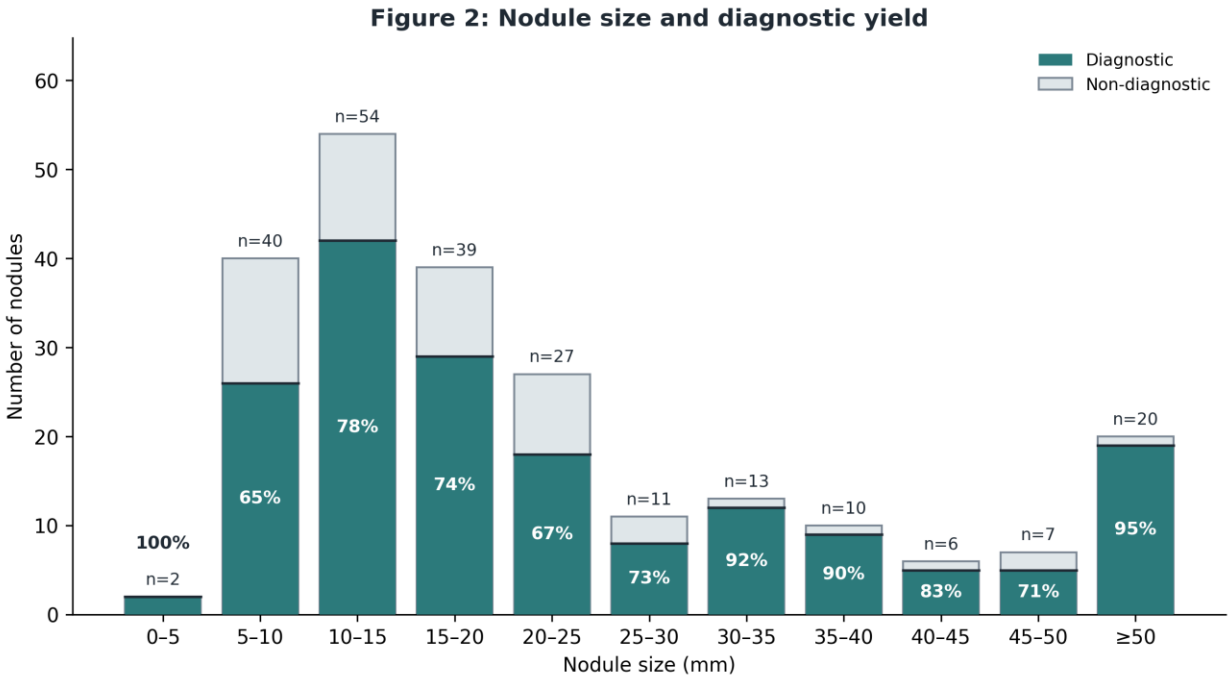


Figure 2. Distribution of sampled pulmonary nodules by size, with per-bin diagnostic yield. n = 229 nodules from 199 procedures.

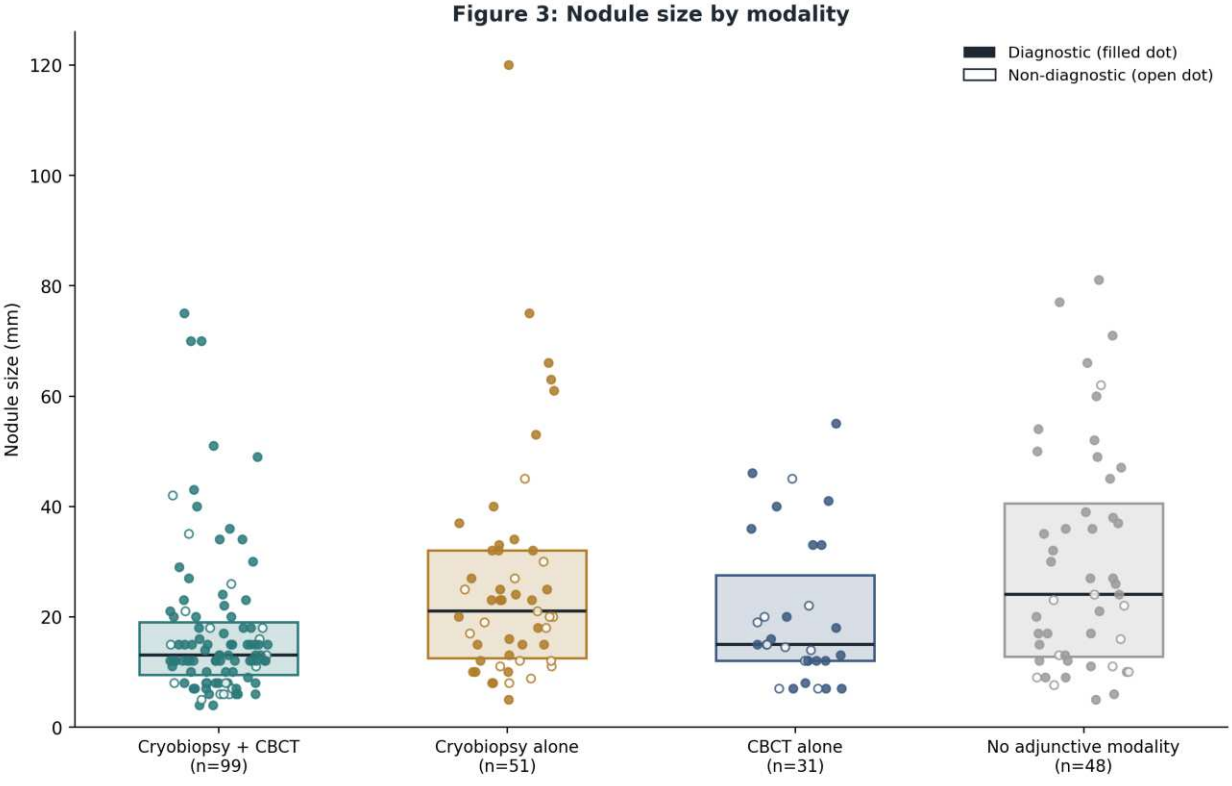


Figure 3. Nodule size distribution by procedural modality. Box = interquartile range, line = median; each dot is one nodule (filled = diagnostic, open = non-diagnostic). n = 229 nodules from 199 procedures.

Figure 4: Diagnostic yield and complication rate by modality

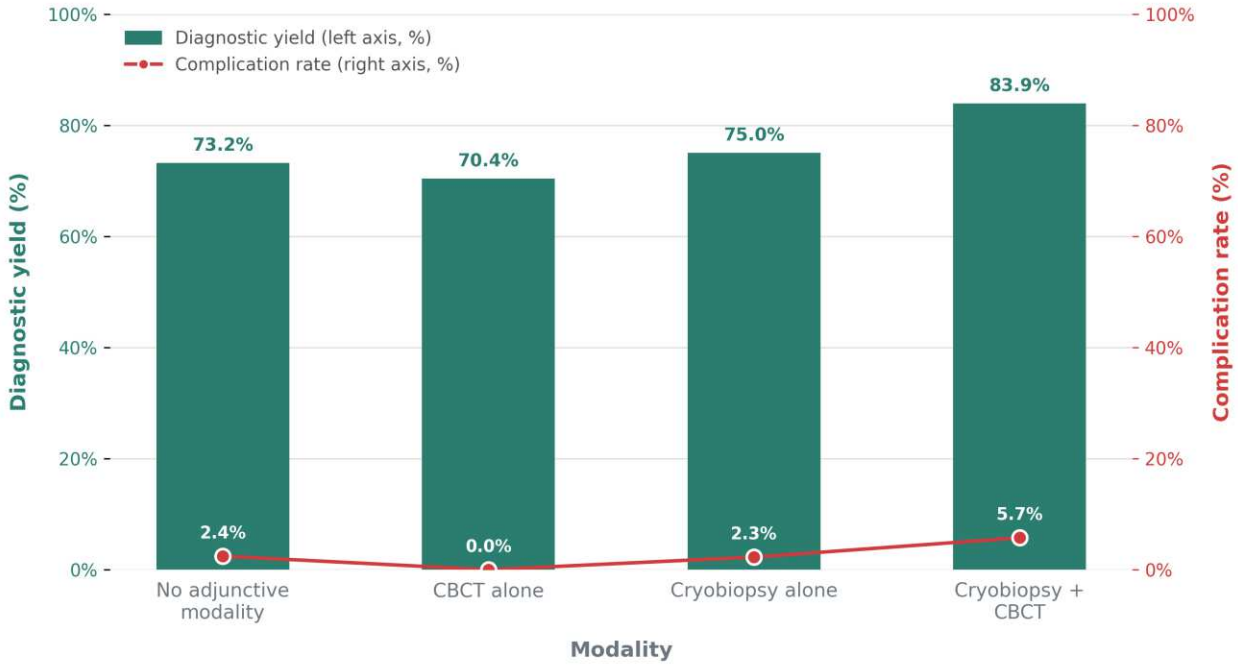


Figure 4. Diagnostic yield and complication rate by bronchoscopy modality.

Table 1. Procedural outcomes.

Modality	Procedures (n)	Diagnostic yield (%)	Complications (%)	Nodule size, mm mean ± SD
Cryobiopsy + CBCT	87	73/87 (84%)	5/87 (5.7%)	17.4 ± 13.7
Cryobiopsy alone	44	33/44 (75%)	1/44 (2.3%)	26.5 ± 20.8
CBCT alone	27	19/27 (70%)	0/27 (0.0%)	20.4 ± 13.5
No adjunctive modality	41	30/41 (73%)	1/41 (2.4%)	29.8 ± 20.3
All procedures	**199**	**155/199 (78%)**	**7/199 (3.5%)**	**22.4 ± 17.7**

Table 1. Procedural outcomes by navigational bronchoscopy modality. Some procedures had more than one nodule sampled. Mean nodule size was calculated from the total number of nodules sampled with each modality: 229 nodules in total (Cryobiopsy + CBCT, 99; Cryobiopsy alone, 51; CBCT alone, 31; no adjunctive modality, 48). Diagnostic yield and complications are per procedure.

Table 2. Complications.

Complication	Cryobiopsy + CBCT (N = 87)	CBCT alone (N = 27)	Cryobiopsy alone (N = 44)	No adjunctive modality (N = 41)	All procedures (N = 199)
Any complication — no. (%)	**5 (5.7)**	**0 (0.0)**	**1 (2.3)**	**1 (2.4)**	**7 (3.5)**
Pneumothorax — no. (%)	4 (4.6)	0 (0.0)	1 (2.3)	1 (2.4)	**6 (3.0)**
Post-procedural hypoxia — no. (%)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	**1 (0.5)**

Table 2. Complications by navigational bronchoscopy modality.

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Statements & Declarations

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

N.G. collected, processed, and analyzed the data and prepared the tables and figures. N.G. (Methods), S.R. (Introduction), M.H. (Results), K.J. (Discussion), and R.C.S. (Conclusion) wrote the manuscript. All authors reviewed and approved the final manuscript.

Ethics Approval

This study was approved by the University of Texas Southwestern Medical Center Institutional Review Board. Given the retrospective nature of the study, a waiver of informed consent was granted. All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Declaration of Helsinki and its later amendments.

Data availability

The data that support the findings of this study are available from the authors upon reasonable request.

Consent to Participate

Informed consent was waived by the University of Texas Southwestern Medical Center Institutional Review Board given the retrospective design of this study.

Consent to Publish

Not applicable. This manuscript does not contain any individual person’s identifiable data in any form.