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Bronchial branch tracing with cone-beam CT tool-in-lesion confirmation for peripheral pulmonary nodules

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Abstract

Background

Peripheral pulmonary nodules (PPNs) are increasingly detected through lung cancer screening. Conventional navigation techniques like bronchial branch tracing with radial endobronchial ultrasound (r-EBUS), lack 'tool-in-lesion' confirmation, limiting diagnostic yield. Cone-beam computed tomography (CBCT) addresses this gap. This study aimed to evaluate the feasibility of integrating CBCT into an established bronchial branch tracing and r-EBUS workflow as a targeted tool-in-lesion confirmation strategy

Method

This prospective, single-centre observational study compared standard bronchial branch tracing with r-EBUS against the same workflow with CBCT used for tool-in-lesion confirmation. Consecutive patients undergoing bronchoscopy for PPNs under general anaesthesia were enrolled with allocation determined by CBCT availability. Feasibility was determined by the primary endpoint of navigational yield. Secondary outcomes included diagnostic yield, procedural time, radiation exposure and safety.

Results

Forty patients were analysed (n=20 CBCT, n=20 standard of care). Demographic and nodule characteristics were similar between groups. In the CBCT arm, navigational yield with bronchial branch tracing alone was 75% increasing to 90% with CBCT guided re-navigation. Diagnostic yield was 80% in CBCT compared to 65% in standard of care(p=0.29). Procedure suite time was modestly increased (54.95 vs 49.65minutes, p=0.03) while anaesthesia and bronchoscopy times were similar. No complications occurred in the CBCT arm. Radiation exposure was higher with CBCT (mean total dose 3.9mSv vs 0.35mSv).

Conclusion:

Selective use of CBCT as a tool-in-lesion confirmation modality is feasible and can enhance navigational yield and diagnostic yield when added to a conventional bronchial branch tracing and r-EBUS workflow with minimal impact on procedural time. Despite an increase in radiation exposure, these findings support CBCT as a practical means of strengthening existing bronchoscopic workflows.

Main text

Peripheral pulmonary nodules (PPNs) are lung parenchymal opacities detected on cross-sectional imaging, not visible on bronchoscopic examination[1]. The American College of Chest Physicians (ACCP) recommends the least invasive diagnostic procedure that permits both diagnosis and staging in suspected lung cancer[2]. With the expansion of lung cancer screening programs and the resulting stage-shift toward smaller, early-stage cancers[3-6], optimising diagnostic yield becomes a priority.

Advances in bronchoscopic tools and navigational technologies have improved diagnostic performance. The introduction of radial endobronchial ultrasound (r-EBUS) represented a major step forward[7, 8]. However, diagnostic yield remains limited, attributable to the lack of definitive navigation confirmation of 'tool-in-lesion' and real-time visualization of nodule sampling. Various lesion characteristics can also impact diagnostic yield. Small lesions <2cm have lower diagnostic yield (11-42%), while larger lesions >3cm have a yield approaching 92%[1]. The presence of a bronchus sign on computed tomography (CT) is also a predictor of successful diagnosis correlating with concentric r-EBUS probe positioning within a nodule (yield 83-87%) compared to eccentric probe positioning adjacent to a nodule (yield 42%-61%)[9-11]. Alternatively, CT-guided transthoracic needle biopsy has diagnostic accuracy as high as 92.1%, but is associated with significant morbidity from pneumothorax (20.5-25.9%) and a 6.9% chest drain insertion rate causing hospitalisation and increasing costs[12]. This approach is also associated with malignant pleural seeding and rare systemic arterial air embolism[13, 14].

Advanced navigation platforms have been developed to improve access to peripheral targets, including electromagnetic navigation bronchoscopy (ENB), virtual navigation bronchoscopy (VNB), and robotic-assisted bronchoscopy (RAB)[15-23]. These have demonstrated non-inferiority to transthoracic needle biopsy[24]. However, centres without virtual navigation resourcing rely on bronchial branch tracing[25-27] or targeted sequential examination of airways with r-EBUS due to cost, equipment availability, and training requirements. Within this standard workflow, the remaining gap is tool-in-lesion **confirmation**, demonstrating the sampling tool positioned within the target lesion at the moment of tissue acquisition.

Cone-beam computed tomography (CBCT) integrates a compact CT system with a C-arm or O-arm providing near real-time cross-sectional images that track bronchoscope and biopsy tool position relative to a nodule, facilitating "tool-in-lesion" confirmation. Unlike conventional CT, which uses a fan-shaped x-ray beam to acquire individual axial slices one at a time, CBCT employs a cone-shaped beam capturing a larger volume of data in a single rotation[28]. CBCT can overcome false-positive findings such as intraprocedural atelectasis, a recognised limitation of r-EBUS navigation[29]. Although CBCT is often discussed as part of advanced navigation platforms, it can be applied more narrowly as a confirmation test layered onto conventional navigation (bronchial branch tracing and r-EBUS), rather than serving as the primary navigation modality[30, 31].

This study aimed to evaluate the feasibility of integrating CBCT into an established bronchial branch tracing and r-EBUS workflow as a targeted tool-in-lesion confirmation strategy. Feasibility was determined by navigational success (tool-in-lesion confirmation), with diagnostic yield, procedural time, radiation exposure and safety evaluated as secondary outcomes. We hypothesised that CBCT could be pragmatically implemented in a tertiary Australian setting and improve navigational and diagnostic performance by identifying suboptimal sampling despite apparently adequate r-EBUS positioning.

Methods

This was a prospective, observational, single-centre study with a control group conducted at a tertiary Australian hospital. The institutional standard-of-care for PPN biopsy is bronchial branch tracing combined with r-EBUS and fluoroscopy. Most procedures are performed under conscious sedation. One weekly general anaesthesia (GA) list is reserved for therapeutic bronchoscopy and complex diagnostic r-EBUS defined by nodule size, location or character as determined by interventional pulmonologists. A mobile O-arm CBCT (O-arm O2 imaging system, MedTronic, Minneapolis, United States of America) is shared between respiratory and surgical disciplines.

All diagnostic r-EBUS patients allocated to the more complex general anaesthesia procedure list were sequentially enrolled between July 1st 2023 and November 30th 2024. Eligible patients had a PPN (high or low pre-test probability of malignancy), requiring histological diagnosis with transbronchial biopsy. Excluded patients had a lung mass (>30mm in maximal diameter), were unable to consent, pregnant or age <18. All patients provided written consent. Patients on the GA list received standard-of-care (bronchial branch tracing navigation with r-EBUS and fluoroscopy) or CBCT-assisted bronchoscopy (standard workflow plus CBCT confirmation of tool-in-lesion), depending on CBCT availability on the day of the procedure dictated by priority use in orthopaedic and spinal operating theatres(figure 1).

Procedures were performed by an interventional pulmonologists and interventional pulmonology fellows, both of whom independently performed bronchial branch tracing[27]. In the CBCT arm, a P-190 flexible fibre-optic bronchoscope (BF-P190, Olympus, Tokyo, Japan) was inserted via an endotracheal tube. The O-arm was positioned around the patient. Lesion localisation was performed using bronchial branch tracing, r-EBUS probe (K-201/K-203, Olympus, Tokyo, Japan), guide-sheath and fluoroscopy from the O-arm. Two proceduralists required consensus of adequacy and accuracy of r-EBUS navigation documented as concentric, eccentric or unsuccessful and navigation videos were stored using a vendor neutral archive as proof of navigation effort. Once navigation was considered satisfactory, forceps were inserted through the guide-sheath into the lesion and the bronchoscope was placed in a scope holder. All staff left the operating room or stood behind acrylic lead shielding during the low-dose CT acquisition. Pre-CBCT navigational accuracy was determined by 'tool-in-lesion.' If unsuccessful re-navigation occurred with the EBUS probe and a second CBCT acquisition (post-CBCT navigational accuracy). If tool-in-lesion was confirmed, 2 brushings, 5-7 forceps biopsies and sterile saline washings were taken under fluoroscopy guidance. Transbronchial needle aspiration (PeriView FLEX NA-403D-2021, Olympus, Tokyo, Japan) was used at proceduralist discretion. Cryobiopsy was not used. If navigation was again unsuccessful, further navigation was not attempted. After sampling and assessing for complications, the team performed linear EBUS mediastinal lymph node staging if required. Biopsy samples were placed into formalin and saline for processing by pathology. The patient was then extubated. All standard-of-care control patients received bronchoscopy under GA, using the same bronchoscopic tools, performed by the same team in the same environment.

The primary endpoint was navigational yield. Pre-CBCT navigational yield, defined as the presence of tool-in-lesion on first CBCT spin, was recorded as a discrete variable. This was compared to the post-CBCT navigational yield, defined as tool-in-lesion in cases requiring re-navigation. Secondary outcomes included diagnostic yield defined as the number of patients in whom diagnostic samples were obtained divided by the total patients undergoing intervention. A strict diagnostic yield definition was used such that samples demonstrating histopathological evidence of malignancy were diagnostic. Samples demonstrating atypia were non-diagnostic. Benign diagnoses were considered diagnostic if they were positive for a specific benign condition. Non-specific diagnoses such as inflammation were only considered diagnostic if confirmed on transcutaneous CT biopsy and/or demonstrated interval resolution on serial imaging at a minimum of 6-months follow-up. Additional outcomes included time in procedure suite, anaesthesia time and bronchoscopy duration collated from anaesthetic records, and safety defined by mean radiation dose and complications. Significant bleeding was defined as grade 2 or above as stratified in the Delphi consensus statement[32]. Patient demographics, nodule characteristics, procedural data and diagnostic yield were compared to the standard-of-care control group.

Radiation data was collated directly from stored data within the fluoroscopy and CBCT devices. Procedural radiation doses were reported as a DAP (dose area product) for 2D-imaging and CTDI/DLP (Computed Tomography Dose Index/Dose Length Product) for CBCT. Retrospective computation of effective doses is unreliable in fluoroscopy due to continuously changing views and exposure settings. However, indicative radiation doses have been calculated to compare risk across modalities. For 2D-imaging on both systems effective doses have been calculated using typical views and the median screening DAP for each group using PCXMC (PCXMC Dose Calculations, Version 2.0 STUK 2008) and 3D doses are quoted from the manufacturer and scaled with DLP.

Continuous variables are reported as mean and standard deviation, and dichotomous variables as number and percentage. Baseline characteristics were compared with Student t-tests or Wilcoxon rank-sum tests for continuous variables as per distribution and chi square tests for dichotomous variables. Outcomes in both groups were compared with chi square tests. Analysis was completed with GraphPad Prism 9 (GraphPad, Boston, Massachusetts, USA).

Results

Fifty sequential patients underwent r-EBUS procedures on the GA procedural list. Ten were excluded due to lesion size >30mm. Twenty patients were enrolled in the CBCT group, dictated by CBCT availability and twenty underwent standard-of-care. Baseline characteristics were comparable between groups, although CBCT patients were older (mean 71 vs 60 years, p=0.004)(Table 1). Mean nodule size was similar (17.55mm (SD 6.74) versus 17.26mm (SD 6.78), p=0.44). In the CBCT arm, most nodules were solid (80%), upper-lobe predominant (70%) and associated with a bronchus sign (90%). There was no significant difference between groups in axial or cranio-caudal dimensions, pleural distance (17.1mm vs 22.5, p=0.14) or outer third location (15/20 vs 11/20, p=0.18). The mean bronchial branches traced were 6.4 vs 5.9 respectively (p=0.07).

In the CBCT arm, initial bronchial branch tracing with r-EBUS achieved a navigational yield with confirmed tool-in-lesion in 15/20 cases (75%), including 13 concentric and 2 eccentric r-EBUS views. Five cases demonstrated unsuccessful localisation (2 eccentric without tool-in-lesion and 3 unsuccessful(table 1). Following re-navigation guided by CBCT with bronchial branch tracing and r-EBUS, three additional nodules achieved concentric views with confirmed tool-in-lesion, increasing navigational yield to 18/20 (90%), a 15% absolute improvement. Nodules with persistent eccentric views could not be further optimised.

Diagnostic yield in the CBCT arm was 16/20(80%)(table 2). Malignancy was diagnosed in 9 cases (six adenocarcinomas, two squamous cell carcinomas (SCC), one melanoma). Benign diagnoses included 3 tissue culture positive infections with post-treatment radiologic improvement, two anthracotic nodules (supported by exposure history, mediastinal sampling and stability on follow-up), one fibrotic nodule confirmed on CT-biopsy with stability at 12-months and one acute inflammatory nodule with interval resolution on follow-up. Four cases were initially non-diagnostic. Three were subsequently confirmed malignant on CT-guided biopsy and one was treated with SABR based on clinical and radiological suspicion. Among the five cases requiring CBCT-guided re-navigation, diagnostic tissue was obtained in three (SCC, anthracotic nodule, fungal infectious nodule with resolution on follow-up), indicating CBCT enhanced diagnostic yield by 15% (table 3).

In the control arm, the diagnostic yield was 13/20(65%). Malignancy accounted for eight cases (four adenocarcinoma, 1 primary lung SCC, one metastatic SCC from skin, 1 germ cell carcinoma and 1 metastatic cystic adenoid carcinoma). Benign diagnoses included 3 tissue culture positive infections responsive to treatment, one sarcoidosis (non-necrotising granulomas) and 1 inflammatory lesions (serial resolution on imaging). Seven cases (35%) were non-diagnostic including one inflammatory lesion, 4 bronchial wall, 1 benign alveolar parenchyma and 1 with non-diagnostic fragments.

No complications occurred in the CBCT arm. One moderate bleed occurred in the control arm. Three CBCT and four control patients underwent concurrent linear EBUS contributing to overall procedural time. Mean procedure suite time was longer for CBCT patients (54.95minutes vs 49.65minutes, p=0.03), while anaesthesia time (49.35 vs 45.15minutes, p=0.90) and bronchoscopy time (44.75 vs 41.25minutes, p=0.14) were similar(table 4).

The radiation dose was higher in CBCT patients. Although fluoroscopy time was lower in the CBCT arm (74.1 vs 136.5 seconds, p<0.001), the mean effective dose from fluoroscopy was higher (0.35mSv vs 2.7mSv in the CBCT arm). The mean 3D acquisition effective dose was 1.2mSv and hence patients received a mean total exposure of 3.9mSv in the CBCT arm (table 4).

All lung cancer cases were discussed at a lung cancer multidisciplinary meeting. In the CBCT arm, 6 (75%) patients had stage I cancer, treated with lobectomy (2/6) or SABR (4/6) based on performance status and comorbidities. Two stage II patients received systemic therapy. At the time of trial recruitment, neo-adjuvant chemo-immunotherapy was not standard-of-care in Australia. In the control arm, one patient had stage I, two stage II and two stage IV disease, one of which had a new nodule representing progression of a prior metastatic lung cancer diagnosis. Three patients underwent surgical resection and two received systemic treatment(table 5).

Discussion

In many global centres, bronchial branch tracing combined with r-EBUS remains the principal diagnostic approach for PPNs. This approach is supported by existing literature that bronchial branch tracing, even when used as a standalone navigation strategy, is **clinically effective for small peripheral lesions**, and that r-EBUS without advanced navigational technology remains relevant in the current practice paradigm, providing rapid and safe diagnosis[25, 26]. Within this context, this study demonstrates feasibility that integrating CBCT into a conventional r-EBUS workflow as a tool-in-lesion confirmation modality may enhance bronchial branch tracing navigation and diagnostic yield, rather than replacing an already effective technique.

Despite a technically challenging cohort characterised by small nodules (<2 cm), predominantly outer-third lung location (75%), and complex bronchial branch tracing (mean 6.4 branches), navigational yield and diagnostic yield in the CBCT group was high (90% and 80% respectively). The standard-of-care group had comparable lesion complexity and achieved a diagnostic yield consistent with published r-EBUS and bronchial branch tracing series for nodules <20 mm (65%). Although this difference did not reach statistical significance (p=0.29), the observed trend suggests a potentially meaningful reduction in false-negative sampling when CBCT is used to refine an established navigation method.

A key difference of this study compared to existing CBCT literature lies in the targeted application of CBCT, layered onto bronchial branch tracing navigation and r-EBUS rather than functioning as a primary navigation platform. Our methodology was similar to Casal et al's pilot study[33] which demonstrated improvement in navigational yield (80 to 95%) when CBCT was utilised, translating to an 80% diagnostic yield. Our methodology reflects real-world practice in centres without access to virtual navigational platforms, augmented fluoroscopy or robotic systems and highlights the strength of manual bronchial branch tracing approaches. The approach of bronchial branch tracing with r-EBUS has long formed the backbone of PPN navigation due to its relatively low-cost and minimal radiation exposure. Whilst r-EBUS improves nodule identification, it provides no real-time confirmation of target lesion sampling and is limited for lesions lacking a bronchus sign or in part-solid/non-solid nodules, which demonstrate increased ultrasound echogenicity[34, 35]. False-positives can occur in airway bleeding, caused by scope or tool trauma, endobronchial saline, and atelectasis, particularly in posterior lung fields[29]. In this study, CBCT identified suboptimal tool positioning despite apparently satisfactory r-EBUS views, prompting re-navigation in several cases, the majority of which subsequently yielded a diagnosis.

The modest increase in procedure suite time (54.95 vs 49.65mins, p=0.03) observed with CBCT was attributable to O-arm positioning and image acquisition, while bronchoscopy duration and anaesthesia time were not significantly different (44.75 vs 41.25mins). CBCT integration did not disrupt procedural workflow once familiarity was established. Safety outcomes were reassuring, with no complications observed in the CBCT group. The International Commission for Radiological Protection (ICRP) Publication 103 estimates a fatal cancer risk of approximately 5% per sievert for adults [30]. While radiation exposure was higher with CBCT than with standard fluoroscopy alone (3.9 mSv vs 0.35 mSv), this corresponds to an absolute risk increase from approximately 1 in 57,000 to 1 in 5,000. Notably, radiation doses in our cohort were lower than those reported in studies where CBCT was used as a primary navigation modality (5.8-14.3mSv) rather than as a targeted confirmation tool[36].

The literature supports an expanding role for navigational bronchoscopy. CBCT bronchoscopy achieves high diagnostic performance, with a pooled diagnostic yield of 78%[31]. When CBCT is combined with r-EBUS, navigation yields range from 75-93%[33, 37, 38] for a pooled diagnostic yield of 80% with acceptable pneumothorax (2.01%) and bleeding (1.08%) rates[30]. This compares favourably with r-EBUS alone which has diagnostic yields of 70%[39],

consistent with the historical yield of this technique in our centre, although large prospective registries report lower (57%)[19]. Across navigational platforms (ENB, VNB, RAB), high diagnostic yields are reported with yields similar to this study[24]. RAB currently represents the benchmark for navigation and sampling[40] with a pooled diagnostic yield of ~80%[23, 41]. However, recent randomized data suggests that navigation platform alone is not the primary determinant of diagnostic success, with non-inferior diagnostic yields demonstrated between RAB and ENB[42].

Diagnostic yields are reportedly highest, particularly for small lesions <2cm, when advanced navigation and CBCT are combined[43-45]. In this setting, CBCT overcomes CT-to-body divergence, defined as the difference between pre-procedure CT and nodule position in real-time under GA, by providing real-time tool-in-lesion imaging[46]. Augmented fluoroscopy can also overlay the CBCT image to outline the lesion and create navigation pathways intra-procedurally[29]. We did not have access to AF in our centre. Access to RAB and virtual navigation platforms remains limited in many centres, reinforcing the value of pragmatic workflows that enhance existing bronchoscopic techniques.

The major limitations of CBCT are the navigational learning curve particularly for small PPNs, and the radiation dose[36]. Tissue acquisition limitations continue to account for differences between successful tool-in-lesion navigation and diagnostic yield. Forceps and brushings sample predominantly endobronchially and TBNA can facilitate peri-bronchial nodule sampling, however these tools are difficult to manoeuvre in distal airways. Peripheral nodule cryobiopsy, particularly with the small 1.1mm cryoprobes, can facilitate greater tissue acquisition[47, 48]. Multi-modal sampling is critical to ensure adequacy of tissue for Programmed cell-death ligand 1 (PDL1) and molecular analysis, facilitating personalised lung cancer treatment[49].

This study has multiple additional limitations. Patient placement on the GA list was not controlled, as there were no strict criteria defining a challenging nodule (e.g. <2cm, subsolid, no bronchus sign). This was designed to provide real-world evidence of the types of cases CBCT might be used for in our centre. A standard-of-care control arm determined by CBCT availability helped to control for selection bias. Numbers were also small in this feasibility study, reducing the generalisability of results. From a technical perspective, at the time of enrolment our institution did not have access to the MP190 bronchoscope which could have aided in reach. We also did not implement cryobiopsy into the sampling workflow. These two factors could have improved further the already respectable diagnostic yield in both groups. Lastly, formal cost-effectiveness analysis was not conducted, although prior modelling suggests that improving bronchoscopic sensitivity and selective use of advanced imaging may confer downstream economic value[50].

Conclusion

In centres where bronchial branch tracing with r-EBUS remains standard practice for peripheral pulmonary nodule diagnosis, CBCT feasibly enhanced navigation by confirming tool-in-lesion and identifying suboptimal positioning not apparent on r-EBUS alone. Used pragmatically for tool-in-lesion confirmation, CBCT enabled targeted re-navigation and was associated with improved navigational and diagnostic yield in a technically challenging cohort, with minimal impact on procedural time. Despite an increase in radiation exposure, these findings support CBCT as a practical means of strengthening existing bronchoscopic workflows.

Abbreviations

Abbreviation	*Expansion*
PPN	*Peripheral pulmonary nodule*
CBCT	*Cone Beam Computed Tomography*
r-EBUS	*Radial endobronchial ultrasound*
ACCP	*American College of Chest Physicians*
ENB	*Electromagnetic navigation bronchoscopy*
RAB	*Robotic-assisted bronchoscopy*
VNB	*Virtual Navigation Bronchoscopy*
GA	*General Anaesthesia*
CTDI/DLP	Computed Tomography Dose Index/Dose Length Product
DAP	*Dose area product*
SCC	*Squamous cell carcinoma*
SABR	*Stereotactic ablative body radiotherapy*
TBNA	*Transbronchial needle aspiration*

Declarations

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Statement of ethics

*The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study obtained Ethics and Governance approval from the Central Adelaide Local Health Network Human Research and Ethics c*ommittee (2023/HRE00015*). Informed consent was obtained from all individual participants for the procedures performed.*

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Tables

Characteristics	CBCT	Control	p value
Age (years)	71.30±10.21	60.10±12.42	p=0.004
Gender			
Male	10 (50%)	9 (45%)	p=0.75
Female	10 (50%)	11 (55%)	p=0.75
ASA			
Mean	2.80	2.75	p=0.75
Median	3	3	
Nodule Location			
RUL	7 (35%)	6 (30%)	p=0.74
RML	1 (5%)	0	NS
RLL	3 (15%)	5 (25%)	p=0.43
LUL	7 (35%)	7 (35%)	p=1
LLL	2 (10%)	2 (10%)	p=1
Nodule diameter			
Mean (mm)	17.55±6.74	17.26±6.78	p=0.44
Median (mm)	15.50	14.67	
Nodule size by dimension*			
Long axis (mm)	19.26±7.90	19.05±7.88	p=0.26
Short axis (mm)	16.40±6.51	14.53±6.12	p=0.18
Cranio-caudal (mm)	15.60±7.01	18.20±8.43	p=0.15
Bronchus sign			
Yes	18 (90%)	18 (90%)	p=1
No	2 (10%)	2 (10%)	p=1
Nodule Character			
Solid	16 (80%)	18 (90%)	p=0.38
Part-solid	2 (10%)	0	NS
Ground glass	2 (10%)	1 (5%)	p=0.55
Cavitating	0	1 (5%)	NS
Distance from pleura (mm)^	17.10±15.67	22.50±16.42	p=0.14
Location in the outer third			
Yes	15 (75%)	11 (55%)	p=0.18
No	5 (25%)	9 (45%)	p=0.18
Bronchial branches traced#	6.38±1.00	5.94±0.86	p=0.07
Pre-CBCT navigational accuracy			
Concentric with tool in lesion	13 (65%)		
Eccentric with tool in lesion	2 (10%)		
Eccentric without tool in lesion	2 (10%)		
Unsuccessful	3 (15%)		
Post-CBCT navigation			
Concentric with tool in lesion	16 (80%)		
Eccentric with tool in lesion	2 (5%)		
Eccentric without tool in lesion	2 (10%)		

Unsuccessful	0 (0%)

Table 1: Patient demographics, baseline nodule characteristics and navigational yield. Data are presented as n(%), mean±SD
ASA (American Society of Anaesthesiologists), RUL (Right upper lobe), RML (Right middle lobe), RLL (Right lower lobe), LUL (Left upper lobe), LLL (left lower lobe), SD (Standard Deviation), CBCT (Cone-Beam Computed Tomography), NS (Not significant).
*Nodule size as measured in radiology report
^Shortest distance to pleura from nodule
#Agreement between two proceduralists

Diagnostic yield	Subtype	CBCT arm: n(%)	Control arm: n(%)	p value
Cancer	**Total Cancers**	**9 (45%)**	**8 (40%)**	**p=0.75**
	Adenocarcinoma	6 (30%)	4 (20%)	
	SCC	2 (10%)	1 (5%)	
	Metastatic SCC (Skin)	0	1 (5%)	
	Metastatic Melanoma	1 (5%)	0	
	Metastatic Germ cell tumour	0	1 (5%)	
	Metastatic Cystic adenoid carcinoma	0	1 (5%)	
Benign	**Total benign**	**7 (35%)**	**5 (25%)**	**p=0.49**
	Infection with positive tissue culture	3 (15%)	3 (15%)	
	Sarcoidosis	0	1 (5%)	
	Fibrotic nodule^	1 (5%)	0	
	Inflammatory nodule*	1 (5%)	1 (5%)	
	Anthracotic nodule	2 (10%)	0	
Non-diagnostic		**4 (20%)**	**7 (35%)**	**p=0.29**
Total diagnostic yield		**16/20 (80%)**	**13/20 (65%)**	**p=0.29**

Table 2: Diagnostic yield. CBCT (Cone beam Computed Tomography), SCC (Squamous Cell carcinoma)
*Only if confirmed on alternate biopsy method and/or interval resolution on follow-up imaging.
^confirmed on CT guided biopsy

Mean nodule size (mm)	Bronchus sign	Nodule Character	Distance from pleura (mm)	Pre-CBCT Navigational yield	Bronchoscopy Ad
16	Yes	Solid	12	Not Seen	Re-navigation
11	Yes	Solid	0	Not Seen	Re-navigation
19.3	Yes	Solid	11	Not Seen	Re-navigation
11	No	Solid	2	Eccentric (unsuccessful tool-in-lesion)	Re-navigation
15	Yes	Solid	53	Eccentric (unsuccessful tool-in-lesion)	Re-navigation

Table 3: Patients with a negative pre-CBCT navigational yield outcomes. CBCT (Cone Beam Computed Tomography), SABR (stereotactic ablative radiotherapy)
^interval follow up CT stability, a history of occupational dust exposure and positive anthracotic mediastinal lymph nodes sampled with linear EBUS

Procedural outcomes	Subtype	CBCT arm	Standard of care (C Arm fluoroscopy)	p value
Radiation	Fluoroscopy time (s)(mean)	74.13	136.50	p=0.0001
	Indicative effective dose from 2D (mSv)(mean)	2.70	0.35	
	Effective dose from 1 3D acquisition (mSv)(mean)	1.20	-	
	Total (mSv)(mean)	3.90	0.35	
Procedural time	Time in procedure suite (mins)	54.95	49.65	p=0.03
	Time under anaesthesia (mins)	49.35	45.15	p=0.90
	Procedural time (mins)	44.75	41.25	p=0.14
Complications	Bleeding (n)(%)	0	1 (5%)	
	Pneumothorax (n)	0	0	
	Other (n)	0	0	

Table 4: Procedural characteristics. CBCT (Cone Beam Computed Tomography), mSv (millisieverts)

Lung cancer outcomes	Subtype	CBCT n=8 (%)	Control n=5 (%)
Adenocarcinoma	IA2	2(25%)	1(20%)
	IA3	1(13%)	0
	IB	2(25%)	0
	IIA	0	1(20%)
	IIB	1(13%)	0
	IVA	0	2(40%)
Squamous cell carcinoma	IA2	1(13%)	0
	IIB	1(13%)	1(20%)
Management	Surgical	2(25%)	3(60%)
	SABR	4(50%)	0
	Systemic treatment	2(25%)	2(40%)

Table 5: Eventual staging and management of lung cancer diagnoses. CBCT (Cone Beam Computed tomography, SABR (Stereotactic ablative radiotherapy)

Figures

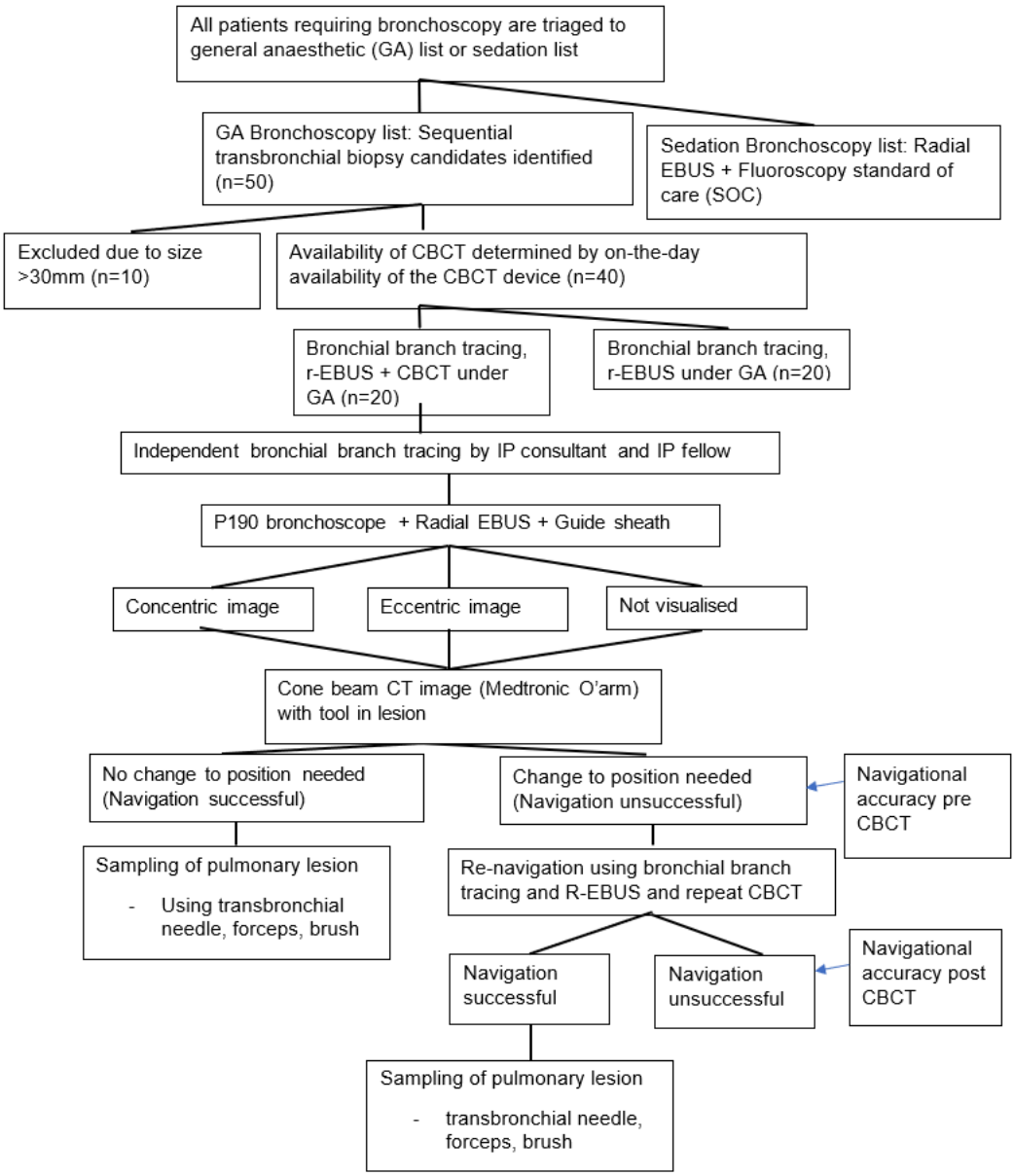


Figure 1

Study design. CBCT (Cone Beam Computed Tomography), R-EBUS (Radial Endobronchial Ultrasound), SOC (standard of Care), GA (General Anaesthetic)