Newer tools for peripheral pulmonary nodule (Archimedes, Cone Beam CT, Robotics, BodyVision)

DM seminar

04.03.2023

Outline

- Approach to SPN
- Archimedes system
- Cone Beam CT
- Robotics
- BodyVision
- Summary

Solitary pulmonary nodule

- A pulmonary nodule is defined on imaging as a small (≤30 mm), well-defined lesion surrounded by pulmonary parenchyma
- Morphologically, they are solid or subsolid (pure GGO or part solid) nodules
- Less than 5–10% of nodules were malignant as seen in NLST screened in over fifty thousand participants
- Among 57,496 participants with baseline LDCT scans in the International Early Lung Cancer Action Program, nonsolid (pure ground glass) and part-solid nodules were found in 4.2% and 5.0%, respectively- of which 0.7% and 0.8% were malignant

Henschke et al., International Early Lung Cancer Action Program. CT screening for lung cancer:. AJR. 2016 Dec;207(6):1176-84. National Lung Screening Trial Research Team. Reduced lung-cancer mortality with LDCT screening. NEJM. 2011 Aug 4;365(5):395-409.

Approach to SPN

- Assessing the risk of malignancy- Brock university model, clinical prediction model and Mayo clinic model
- PANOPTIC (Pulmonary nodule plasma proteomic classifier) trial- 5 clinical factors (Age, smoking status, nodule diameter, shape and location) and 2 plasma proteins (LG3BP and C163A)
- Clinical judgement
- Imaging characteristics

McWilliams et al. Probability of cancer in pulmonary nodules detected on first screening CT. NEJM. 2013 Sep 5;369(10):910-9. Gould Mk et al. A clinical model to estimate the pretest probability of lung cancer in patients with SPN. Chest. 2007 Feb 1;131(2):383-8. Silvestri GA et al. Proteomics biomarker's ability to characterise lung nodules: PANOPTIC trial. Chest. 2018 Sep 1;154(3):491-500.

- Nodule size- as the size of the solid component increases, there is increased risk of malignancy
- Nodule attenuation- (solid vs subsolid vs GGO)
- Growth size- No increase in size over >2 years or rapid increase in <20 days= lesion is likely benign
- Calcification and fat
- Border and location
- Enhancement with contrast

PET-CT

- Solid nodules- PET-CT is reliable
- PET demonstrates pooled sensitivity of 89 percent (95% CI, 86-91 percent) and specificity of 75 percent (95% CI, 71-79 percent) for detecting cancer
- Subsolid nodules- GGOs and part solid nodules are not well characterised by PET
- False positive nodules (pneumonia, mycobacterial diseases, sarcoidosis and rheumatoid nodules)
- False negative nodules (less metabolically active tumours)
- Morphologic-metabolic dissociation sign (Invasive mucinous adenocarcinoma)

Approach to SPN- INDIVIDUALISED



Gould Mk et al. Evaluation of individuals with pulmonary nodules: When is it lung cancer?: ACCP. Chest. 2013 May 1;143(5):e93S-120S.

Management options of SPN

- Non surgical biopsy
 - 1) Bronchoscopic techniques
 - 2) Transthoracic needle biopsy
- Surgical biopsy
- PET-CT

ARCHIMEDES SYSTEM







Archimedes system

Archimedes Lite

Lung Point

Bronchoscopic trans-parenchymal nodule access (BTPNA)

- Image Guidance for Bronchoscopy and Fused Fluoroscopy
- Real-time navigation
- Side-by-side navigation pairs real time and virtual images
- Navigation guides user to target with 3mm accuracy
- Airway path allows access to lesions without specialized, disposable instruments
- Standard 2 mm working channel compatible with bronchoscopic instruments
- Target is superimposed on virtual, actual bronchoscopic and live fluoroscopic views



Point of entry





Dilating the POE



Introducing the sheath

Sampling



3D View of the lesion





Real bronchoscopic images



Herth et al.(BTPNA): first in human trial for sampling SPN. Thorax. 2015 Apr 1;70(4):326-32.



Harzheim D et al.BTPNA: feasibility and safety in an endoscopic unit. Respiration. 2016;91(4):302-6.

Evidence

Study	Methods	Results	Comments
 Strenman et al. CHEST 2015 Canine study 	 31 inorganic models of sub-centemetric pulmonary nodules were implanted beyond 7th generation of airways 	 The mean length of the 31 tunnels was 35 mm (20.5-50.3-mm range) Mean tunnel creation time was 16:52 min Diagnostic yield was 90.3% (28 of 31) 	 No pneumothorax Bleeding <2 ml in volume
 Herth et al. Thorax 2015 First human trial n=12 	 Nodule size- 10 to 40 mm Archimedes VBN systems POE→ coring needle→ negative suction→ atraumatic balloon dilator→ Tool in lesion confirmation→ Biopsy 	 BTPNA was successfully completed in 10 patients (83%) A positive biopsy was obtained in all 10 7/10 nodules were not visible on fluoroscopy 	 Done under GA No pneumothorax No bleeding Post-procedure surgical resection confirmed the accuracy of BTPNA

Study	Methods	Results	Comments
 Harzheim at al. Respiration 2016 n=6 	 Prospective, single arm interventional study 	 The mean length of the tunnels to the nodule was 29 mm (range 11–46) The size of the lesions ranged from 14 to 21 mm Diagnosis was achieved in 5/6 cases 	 Done under GA 2 pneumothoraces 1 required pigtail drainage
 Mezalek et al. ERS 2022 (N=13) 	 A HRCT scan was performed 1-5 days before Cytology brush, TBB and TPNA were performed using the C arm verification 	 median size of nodules was 21 mm (16-31 mm) Biopsy smears were positive in 100% of the positive cases 	 Done under GA Training with the Archimedes system is emphasised
 Yang et al Frontiers 2023 Pilot study in children 	 Retrospective analysis of 5 cases 	 Diagnosis was achieved in all 5 cases 	Done under GANo pneumothorax



Harzheim D et al. BTPNA: feasibility and safety in an endoscopic unit. Respiration. 2016;91(4):302-6

Cone Beam CT

- Cone beam CT (CBCT) is another imaging modality that may improve the diagnostic yield for bronchoscopic lung biopsy
- This modality has previously been widely adopted in many fields of interventional radiology, including intravascular and hepatobiliary interventions
- After image acquisition, the biopsy device location can be reviewed and adjusted to a new target location as needed with repeat scans



Mobile CBCT

Ceiling mounted CBCT

Floor mounted CBCT- compatible with Robotics

C-arm vs CBCT

Portable C arms	Mobile CBCT	Fixed CBCT
Inferior image quality	Superior quality images	Best image quality
Portable	Lower doses, portable	Central room
Digital tomosynthesis algorithms	True 3D imaging	True 3D imaging
	30 second image acquisition	5-8 second image acquisition
		CT augmented fluoroscopy
		Very expensive

WORKFLOW

- Isocentre (AP and lateral)
- Perform a test spin
- Breath hold
- 5-8 second spin
- Image acquisition

CT-to-body divergence

- CT-to-body divergence is the difference between the static pre-procedural CT and the dynamic breathing lung during bronchoscopic procedure
- How does any VBN platform work?
- Lung volume differences, atelectasis
- Pre-procedural scan timings and differences
- Anatomy alterations (pleural effusions)
- 16 to 18 mm variation is noted
- Hybrid operating rooms (CBCT plus fluoroscopy)

CT-to-body divergence

Green- VBN Guided pathway Purple- Actual intraoperative pathway

Pritchett MA et al. Divergence between preprocedural CT scans and lung anatomy during guided bronchoscopy. JOTD. 2020 Apr;12(4):1595.

CT-to-body divergence-atelectasis

Pritchett MA et al. Divergence between CT and lung anatomy during guided bronchoscopy. JOTD. 2020 Apr;12(4):1595.

CT-to-body divergence- how to overcome?

Lesion identification on CT

Real-time Al tomographic lesion reconstruction with CABT during dynamic registration

Dynamic registration and navigation along planned pathway towards the lesion

Real-time "tool in lesion" confirmation with CABT

Of course, image guided TTNA also overcomes CT-to-body divergence and hence has a superior yield

Pritchett MA et al. Divergence between CT and lung anatomy during guided bronchoscopy. JOTD. 2020 Apr;12(4):1595.

Study	Methods	Results	Comments
 CBCT plus augmented fluoroscopy plus ENB Pritchett et al. Journal of Bronchology and interventional pulmonology- 2018 	 Single centre retrospective analysis of 75 consecutive ENB procedures were analysed and 93 nodules were sampled Median size of the lesion was 16 mm (7- 55) Bronchus sign in 39% Visible on fluoroscopy- 49% 	 The overall DY by lesion was lesion of 83.7% [95% CI, 74.8%- 89.9%] Diagnostic accuracy was 93.5% (indeterminate lesions) 	 Done under GA Hybrid OR DY was similar in nodules of size <20 mm (83-84%) and >20 mm (96.3%) All procedures were done- BAL, brushing, TBLBx, needle aspiration
 Ultrathin bronchoscopy plus CBCT plus VBN- TBLBx 2019 Respirology Ali et al. N=40 	 Single centre prospectively collected data The median tumor size was 20 mm (range 9– 30) Solid and GGOs Ultrathin bronchoscope had an OD of 2.8 mm 	 The overall diagnostic yield was 90.0% 	 One case of pneumothorax and one case of lung abscess Done under GA

Study	Methods	Results	Comments
 CBCT plus ultrathin bronchoscope plus R-EBUS Casal et al. Journal of thoracic diseases 2018 n=20 	 Prospective single centre pilot study OD of bronchoscope was 4.2 mm Needle aspiration, biopsy, brushings and BAL were done Median size was 2.1 (range, 1.1–3) cm and median distance from pleura was 2.1 (0–2.8) cm 	 the mean effective dose (E) to patients from CBCT and fluoroscopy ranged from 11 to 29 mSv Diagnostic yield was 75% (lower due to atelectasis) 	 Median time of the procedure was 62.5 minutes (49-96) One case of pneumothorax Simultaneous staging EBUS was performed if ROSE demonstrated malignant cells
 RANB plus CBCT Benn et al Lung 2021 n=52 	 Single centre prospectively collected data Median nodule diameter was 17 mm in axial cuts and 14 mm in coronal cuts and 17 mm in sagittal cuts 	 Tissue diagnosis was obtained in 83% (49/59) of biopsied nodules 10 nodules were reported as inconclusive 	 Done under GA with special ventilation protocols to avoid atelectasis 3 times CBCT spins were done per procedure mean procedure time of 62 ± 24 min Pneumothorax- 2

Lung Navigation Ventilation Protocol to Optimize Biopsy of Peripheral Lung Lesions

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Background: Computed tomography-to-body divergence caused by respiratory motion, atelectasis, diaphragmatic motion and other factors is an obstacle to peripheral lung biopsies. We examined a conventional ventilation strategy versus a lung navigation ventilation protocol (LNVP) optimized for intraprocedural 3-dimensional image acquisition and bronchoscopic biopsy of peripheral lung nodules.

Methods: A retrospective, single center study was conducted in consecutive subjects with peripheral lung lesions measuring <30 mm. Effects of ventilation strategies including atelectasis and tool-in-lesion confirmation were assessed using cone beam computed tomography images. Diagnostic yield was also evaluated. Complications were assessed through 7 days. compared with conventional ventilation. Future prospective studies are necessary to understand the impact of protocolized ventilation strategies for bronchoscopic biopsy of peripheral lung lesions.

Key Words: electromagnetic navigation bronchoscopy, cone-beam computed tomography, tomosynthesis, fluoro-scopic navigation, ventilation, lung cancer

(J Bronchol Intervent Pulmonol 2022;29:7-17)

BACKGROUND

Despite the continual evolution of navigational bronchoscopy platforms, including endoluminal robotics, fluoroscopic-based electromagnetic navigation and shape sensing platforms, bronchoscopy for the

Lung navigation ventilation protocol

- Retrospective single centre trial
- Two groups of 25 consecutive patients with PLLs < 30mm was included
- In the first group, a conventional ventilation protocol was used between December 2017 and March 2018
- In the second group, a dedicated LNVP was used between February and March 2020

Lung navigation ventilation protocol

Upper and Middle Lobe	Lower Lobe lung
lung lesions	lesions
PEEP and APL valve set	PEEP and APL valve set
at 10-15 cmH20	at 15-20 cmH20

Lung navigation ventilation protocol

- Diagnostic yield was 70% for conventional ventilation and **92%** for LNVP (P=0.08)
- Sensitivity and specificity were 78% and 100%, respectively, for conventional group; 100% and 100%, respectively, for LNVP
- Positive predictive value was 100% for both patient groups
- Negative predictive value was 56% for conventional ventilation and 100% for LNVP
- Atelectasis was more prevalent in the conventional ventilation group, both for dependent atelectasis (R1: 64% and R2: 68% vs. R1: 36% and R2: 16%, *P*=0.00014) and sub-lobar/lobar atelectasis (R1: 48% and R2: 56% vs. R1: 20% and R2: 32%, *P*=0.01)

ROBOTICS

- Robotic bronchoscopy has better maneuverability, enabling navigation further into the periphery of the lung, and can remain static once a desired position is reached
- There are currently two companies in the market
- The Monarch (Auris), which was approved by the U.S. Food and Drug Administration in 2018
- Ion (Intuitive) was approved in 2019

MONARCH system

- The Monarch system robotic arms are operated with a small handheld controller similar to that for a videogame
- The controller guides an outer sheath that is wedged in a proximal position and then steers an inner scope to the biopsy site
- The robotic bronchoscope was able to be advanced farther into the lung periphery compared to a thin bronchoscope despite the scopes having the same outer diameter
- The outer sheath design provides support for the inner scope and allows for improved maneuverability

MONARCH system

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Robotic Endoscopic Airway Challenge: REACH Assessment

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Purpose. Bronchoscopy for peripheral pulmonary lesions continues to present challenges to clinicians. One potential limitation may be the inability to advance conventional bronchoscopes into close proximity of peripheral lesions before biopsy. This study was performed to assess the reach of a robotic endoscopic system within human cadaveric lungs compared with conventional thin bronchoscopes.

Description. All segmental bronchi (RB1 to 10, LB1 to 10) were accessed in two human cadavers using a conventional thin bronchoscope and robotic endoscope of identical outer diameter. Bronchus generation count and insertion depth measured by electromagnetic navigation and external fluoroscopy were recorded.

Evaluation. The robotic endoscope was advanced beyond the conventional thin bronchoscope in all segments, particularly in bronchi with increased angulation such as RB1 (mean generation count 8 versus 3.5, respectively) and LB1+2 (mean generation count 8 versus 4.5).

Conclusions. The robotic endoscopic system was advanced beyond a conventional thin bronchoscope with identical outer diameter into the periphery of human cadaveric lungs. Improved reach within the lung periphery may address some limitations with contemporary bronchoscopic approaches for peripheral lesion biopsy.

REACH assessment

- Cadavers-2
- Convectional thin bronchoscope (OD-4.2 mm and working channel of 2 mm)
- Robotic endoscopic system (Outer sheath of 5.9 mm, O.D-4.2 mm and working channel of 2 mm)

Segment	CTB Mean	RES Mean	Difference
Right upper lobe	1		
RB1	3.5	8	4.5
RB2	7.0	9.5	2.5
RB3	6.5	9.5	3.0
Right middle lob	e		
RB4	7.0	9.5	2.5
RB5	5.5	8.5	
Right lower lobe			
RB6	4.5	6.0	1.5
RB7	3.0	8.0	5.0
RB8	5.0	8.0	3.0
RB9	7.0	10.0	3.0
RB10	6.5	9.0	2.5
Left upper lobe			
LB1+2	4.5	8.0	3.5
LB3	5.0	7.0	
Lingula			
LB4	5.0	11.0	6.0
LB5	7.0	9.5	2.5
Left lower lobe			
LB6	4.5	7.5	3.0
LB7+8	5.0	8.5	3.5
LB9	8.0	11.0	3.0
LB10	7.0	8.0	1.0

Table 1. Generation Count

 $CTB = conventional \ thin \ bronchoscope; \qquad RES = robotic \ endoscopic \\ system.$

A- convectional thin bronchoscope

B- Robotic endoscopic system

- The Ion platform uses an ultrathin robotic catheter with a 3.5-mm outer diameter
- EMN is not required because the catheter is fitted with **shape-sensing technology** to provide accurate positional information
- The catheter is advanced with a trackball and wheel controller
- In order to have such a small outer diameter, the optic is removed once the target is reached, and the catheter (with shape-sensing technology) is used as a guide sheath through which various sampling instruments are introduced

- Plan your procedure with app (PlanPoint software)
- Integration with PACS
- Navigate to the lung (shape sensing technology)
- Confirm the target
- Biopsy

Study	Methods	Results	Comments
 ACCESS study 8 cadavers 67 nodules Chen et al. Respiration 2019 	 Artificial tumour targets of size 10- 30mm were implanted into 8 cadavers R-EBUS, fluoroscopy and EMN were used simultaneously MONARCH system was used 	• The overall DY was 97% (65/67)	 The mean nodule size was 20.4 mm
 Felding et al. Respiration 2019 N=29 First human trial to assess feasibility 	 ION system mean lesion size of 12.2 ± 4.2, 12.3 ± 3.3, and 11.7 ± 4.1 mm in the axial, coronal, and sagittal planes R-EBUS, fluoroscopy and VNB were allowed 	 TBNA, brushings, BAL and biopsy were allowed Nodule was reached in 28/29 cases RUL nodule of size 11.1 mm was not accessible 	 Done under GA Prior suctioning and clearance of airways was done prior No pneumothorax No bleeding DY was 79.3% (95% CI: 60.3–92.0%)

Study	Methods	Results	Comments
 RANB plus CBCT Benn et al Lung 2021 n=52 	 Single centre prospectively collected data Median nodule diameter was 17 mm in axial cuts and 14 mm in coronal cuts and 17 mm in sagittal cuts ION system 	 Tissue diagnosis was obtained in 83% (49/59) of biopsied nodules 10 nodules were reported as inconclusive 	 Done under GA with special ventilation protocols to avoid atelectasis 3 times CBCT spins were done per procedure mean procedure time of 62 ± 24 min Pneumothorax- 2
 PRECISE STUDY Abstract Preliminary data Nashville, CHEST 2022 N=129 Multicentre study 	 median nodule diameter was 16 mm median generation location of 7 CT Bronchus sign was present in 25% of cases ION system SSRAB plus R-EBUS 	 Diagnostic yield was 104/129 (81%, 95% CI: 73-87%) Subjects with vs. without a CT bronchus sign was 26/32 (81%) and 78/97 (80%) Sensitivity for malignancy was 84/97 (87%, 95% CI: 78-93%) 	 Median procedure time was 52 min Pneumothorax- 4% Bleeding- 3%

BodyVision

- Augmented fluoroscopic navigation enhances nodule as well as airway visualization in an attempt to improve sensitivity of navigation-guided bronchoscopy using AI technology
- Chest tomosynthesis
- Augmented fluoroscopic navigation is designed to minimize CT to body divergence
- There are three available augmented fluoroscopic platforms currently available
- 1) Fluoroscopic navigation
- 2) BodyVision
- 3) SONIALVISION

Chest tomosynthesis

- Chest tomosynthesis is a radiographic technique that offers some of the tomographic benefits of CT at a lower radiation dose
- The average effective dose of chest tomosynthesis is 0.15 mSv
- The technology for performing chest tomosynthesis is not widely available
- The technique involves acquiring multiple angular radiographic projections of the chest using a conventional x-ray tube and detector and a special computer-controlled tube mover
- Reconstruction algorithms are then applied to create the image.
- For nodule detection, tomosynthesis is more sensitive than chest radiography but less sensitive than CT
- Approximately one-half of nodules measuring ≥6 mm on CT are detected with tomosynthesis
- Tomosynthesis cannot be used as the primary modality for nodule detection
- However, it may be useful to longitudinally follow known nodules in combination with CT

Fluoroscopic navigation

- The first and most established is Fluoroscopic Navigation (SuperDimension-Medtronic), which utilizes digital tomosynthesis by conventional fluoroscopy to visualize and reregister the target nodule location
- Improves positional accuracy of the navigation catheter due to real-time changes
- Assists with path correction if the nodule has changed locations during the procedure

Catheter

Fiducial marker

BodyVision

- Another augmented fluoroscopy platform, LungVision (BodyVision), enables enhanced fluoroscopic visualization of airways with predetermined pathways as well as target lesions
- These enhanced views are obtained by utilizing preoperative CT planning software along with fluoroscopic registration

SONIALVISION

- SONIALVISION (Shimadzu) was studied in 40 patients with radial EBUS with sheath guide combined with preprocedural chest tomosynthesis to serve as a map
- 4th generation of C-arm
- Armed with tomosynthesis
- Focussed on orthopaedic and dental speciality
- R and D into interventional pulmonology is very sparse

Workflow

Study	Methods	Results	Comments
 Aboudara et al. 2019 Respirology S-ENB (n=101) F-ENB (n=67) 	 Retrospective review of all ENB (SuperDimension MedTronic) C-arm LAO and RAO 25° Done for 8-30 seconds 	 The primary outcome of diagnostic yield was significantly higher in the F-ENB group (79%, 53/67) than the S-ENB group (54%, 55/101) (P = 0.0019) 	 Done under GA R-EBUS was allowed TBLBx, brushing, BAL and needle aspirations were done
 Cicenia et al. Journal of bronchology and interventional pulmonology 2020 N=57 	 Prospective multicentre study in the US LungVision system Median and mean nodule size was 20.0 and 27.6 mm 	 Of the 57 nodules targeted, 53 nodules (93%) were successfully localized and verified by REBUS The overall diagnostic yield of nodules sampled in the study was 75.4% 	 Done under moderate sedation
Pertzov et al.CHEST 2017N=27	 Single centre retrospective study LungVision system 	 Median lesion size was 25 mm (range 13-50) The overall diagnostic yield was 74% (20/27) 	 Done under moderate sedation No pneumothorax No bleeding

Study	Methods	Results	Comments
 Pritchett et al. Journal of bronchology and interventional pulmonology 2018 n=60 	 Single centre prospective study CBCT to confirm the location The average distance between lesion location as shown by LungVision augmented fluoroscopy and actual location measured by CBCT was 5.9mm (range: 2.1 to 10.0 mm) 	 The median lesion diameter was 18.0 mm (range: 7.0 to 48.0 mm) Localization success was 96.1% Diagnostic yield at the index procedure was 78.4% 	 Average CT-to-body divergence was 14.5mm (range: 2.6 to 33.0 mm) from preprocedure CT to intraprocedural CBCT images Done under GA
 Pertzov at al. Thoracic cancer 2021 LungVision navigational platform plus cryobiopsy N=63 	 Single centre prospective study LungVision followed by brushings, BAL and biopsy (3-5 forceps and 2 cryobiopsy) 	 Median nodule size (IQR) was 25.0 mm (18–28) Diagnosis was achieved in 77.8% (49/63) overall 	 Diagnosis was achieved in 81.8% (27/33) with the second-generation system, 73.3% (22/30) with the first generation system

How do we approach any case?

- CT bronchus sign- bronchoscopy
- EBUS-TBNA is simultaneously planned- bronchoscopy
- Pleural or subpleural nodules- TTNA
- Beyond this, it falls into centre experience and available tools
- These systems have a huge learning curve and are still far from perfect
- Patient preferences

Available armamentarium- our setup

- Ultrathin bronchoscope
- R-EBUS
- VBN
- Fluoroscopy
- Lung cryobiopsy (eccentric lesion on r-EBUS)
- CBCT?