Peripheral Bronchoscopy

Where have we been? Where are we going?

D. Kyle Hogarth, MD
Professor of Medicine
Director of Bronchoscopy
University of Chicago

Current Conflict of Interest (as of 9/27/22)

- **Stock Option holder/Stock holder:**
  - Body Vision, Broncus, Eolo, Eon, Gravitas, Imbio, Lanier, Magnisity, Noah Medical, LX-Medical, Med-Opsys, Monogram Orthopedics, Preora, Preview Med, Prothea-X, Ryme, Ruby Robotics, Spesana, VIDA
- **Individually Purchased Shares on open market (does NOT include mutual funds/retirement accounts):**
  - J&J, Exact Sciences
- **Consultant within last 3 years**:
  - Alpha Sights, Ambu, Atheneum, Auris, Body Vision, Boston Scientific, Broncus, Coleman, CSL, Deerfield, Eolo, Fluidda, Galvanize, Gilman Capital, GLG, Grand Rounds, Guidepoint Global, Imbio, Intuitive, J&J, Lanier, Level-Ex, Magnisity, MediFind, Morgan-Stanley, Mosaic, Noah Medical, NovaScan, Olympus (Spiration), Oncocyte, Patients Like Me, Preora, Preview Med, Prothea-X, PulmonX, Qure.ai, Ryme, Ruby Robotics, Serpex, Spesana, Takeda, TSC, Veracyte, Volv, Wave Life Sciences.
- **Research Dollars/Contracted Research (past 3 years and present):**
  - Ambu, Boston Scientific, Gala, Medtronic, Nuvaira, Olympus (Spiration), PulmonX, Shire
- **DSMB member (past and present)**
  - InhibRx (past)
- **Lectures Given (Honoraria received) within the last 3 years:**
  - Astra-Zeneca, Biodesix, B.I., Boston Scientific, Broncus, Genentech, Grifols, PulmonX, Spiration (Olympus), Takeda, Veracyte

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Incidental and Screen-Detected Nodule Management

DISTINCT POPULATIONS REQUIRE DIFFERENT CLINICAL APPROACHES

INCIDENTAL NODULES

>1.6 million
found annually in the US[1]


Symptoms


Chest X-ray & Other Imaging


Mayo Calculator (23%*) & VA Model (54%*)
*prevalence of cancer


Fleischner Guidelines & CHEST (ACCP) Guidelines

SCREEN-DETECTED

~125 thousand
detected annually in the US[2,3]


LDCT Screening Program

Only **~5.7%** of screen-eligible (**8M**) patients were screened in 2019[2]

Expanded USPSTF screen-eligible criteria


Brock Calculator (3-5%*)
*prevalence of cancer

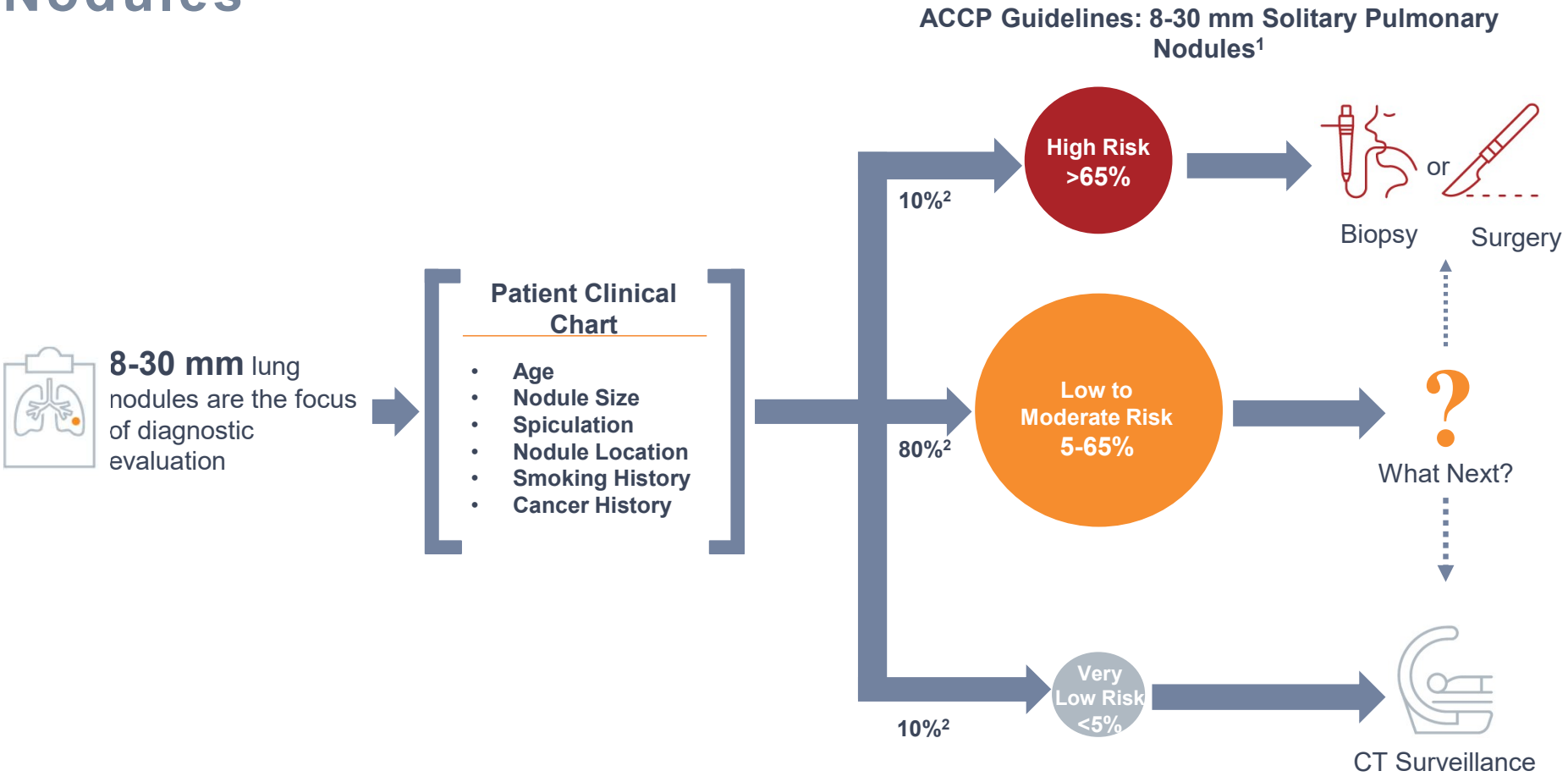

ACR guidelines (Lung-RADS) & NCCN screen-detected nodule guidelines

1. Gould et al. AJRCCM. 2015; 192(10).
2. American Lung Association. State of Lung Cancer 2020.
3. NLST Research Team. NEJM. 2011; 365: 395-409.

Nodule Risk Prediction Models

Model	Nodule Size, mm	Setting	Prevalence	AUC
VA (Gould)	4 - 30	Incidental	54%	0.73 - 0.79
Mayo (Swensen)	4 – 30 (CXR)	Incidental	23%	0.78 - 0.80
McWilliams model	1 – 70mm	Screening	5%	0.90

Most Patients Have Low to Moderate Risk Lung Nodules



1. Gould et al. *CHEST*. 2013; 143(Suppl 5): e93s-e120s.
2. Data calculated from Tanner et al. CHEST. 2015;148(6):1405-1414.

Risk of Cancer - Nodule Size

Nodule Size	Confirmed Lung Cancer		PPV (%)
	Yes	No	
4-7 mm	18 (7%)	3642 (53%)	0.5
7-10 mm	35 (13%)	2079 (30%)	1.7
11-20 mm	111 (41%)	821 (12%)	11.9
21-30 mm	58 (22%)	137 (2%)	29.7
> 30 mm	45 (17%)	64 (1%)	41.3

Table 1. Screens with lung cancer diagnosed within one year of the screening examination according to nodule*

Total screens	T0 screen (n = 26 309)		T1 and T2 screens (n = 48 817)	
Maximum nodule diameter	**No.**	**Lung cancer, No. (%)**	**No.**	**Lung cancer, No. (%)**
Negative screen				
No noncalcified nodule	14 673	14 (0.10)	27 181	17 (0.06)
<4 mm	4445	4 (0.09)	10 686	9 (0.08)
Positive screen				
4 mm	990	4 (0.40)	1775	2 (0.11)
5 mm	1475	3 (0.20)	2232	9 (0.40)
6 mm	1204	10 (0.83)	1831	7 (0.38)
7 mm	843	9 (1.11)	1248	19 (1.52)
8 mm	568	7 (1.23)	827	22 (2.67)
9 mm	371	5 (1.34)	544	15 (2.76)
10–14 mm	906	58 (6.40)	1319	91 (6.90)
15–19 mm	322	56 (17.39)	480	73 (15.21)
20–29 mm	218	58 (26.61)	274	48 (17.52)
≥ 30 mm	124	50 (40.32)	134	33 (24.63)
Nodule diameter not specified	21	0 (0.00)	30	2 (6.67)
Positive screen with no nodule ≥4 mm	149	3 (2.01)	249	14 (5.47)
Any positive screen	7191	263 (3.66)	10 950	335 (3.06)

74%

75%

Gierada et al. JNCI 2014;106(11)

Category	Description	Findings	Management
Lung-RADS 0		Incomplete scan	Additional screening or new scan
Lung-RADS 1	Negative	No lung nodules. Nodules with specific calcifications	Continue screening with LDCT in 12 months
Lung-RADS 2	Benign appearance or behavior	Solid Nodules: < 6 mm Part solid nodules < 6 mm Non solid nodules < 20 mm * Category 3 or 4 unchanged for ≥ 3 months	Continue annual screening with LDCT in 12 months
Lung-RADS 3	Probably benign	Solid nodules >6 to < 8 mm Part solid nodules > 6mm Non solid nodules	6 month LDCT
Lung-RADS 4A	Suspicious	Solid nodules ≥ 8 mm or < 15 mm OR growing < 8 mm or new 6 to < 8 mm	3 month LDCT. PET/CT if ≥ 8
Lung-RADS4B	Suspicious	Solid Nodules > 15 or new or growing and > 8 mm	PET/CT or tissue sampling

2017 Fleischner Society Guidelines for Management of Incidentally Detected Pulmonary Nodules

A: Solid Nodules*

Nodule Type	Nodules <6 mm (<100 mm^3)	Nodules 6–8 mm (100–250 mm^3)	Nodules >8 mm (>250 mm^3)	Comments
Single				
Low risk	No routine follow-up	CT at 6–12 mo, then consider CT at 18–24 mo	Consider CT at 3 mo, PET/CT, or tissue sampling	Nodules <6 mm do not require routine follow-up in low-risk patients (recommendation 1A)
High risk	Optional CT at 12 mo	CT at 6–12 mo, then at 18–24 mo	Consider CT at 3 mo, PET/CT, or tissue sampling	Certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-mo follow-up (recommendation 1A)
Multiple				
Low risk	No routine follow-up	CT at 3–6 mo, then consider CT at 18–24 mo	CT at 3–6 mo, then consider CT at 18–24 mo	Use most suspicious nodule as guide to management; follow-up intervals may vary according to size and risk (recommendation 2A)
High risk	Optional CT at 12 mo	CT at 3–6 mo, then at 18–24 mo	CT at 3–6 mo, then at 18–24 mo	Use most suspicious nodule as guide to management; follow-up intervals may vary according to size and risk (recommendation 2A)

B: Subsolid Nodules*

Nodule Type	Nodules <6 mm (<100 mm^3)	Nodules ≥6 mm (≥100 mm^3)	Comments
Single			
Ground glass	No routine follow-up	CT at 6–12 mo to confirm persistence, then CT every 2 y until 5 y	For certain suspicious nodules <6 mm, consider follow-up at 2 y and 4 y; if solid component(s) develops or growth occurs, consider resection (recommendations 3A and 4A)
Partly solid	No routine follow-up	CT at 3–6 mo to confirm persistence; if lesion is unchanged and solid component remains <6 mm, annual CT should be performed for 5 y	In practice, partly solid nodules cannot be defined as such until they are ≥6 mm, and nodules <6 mm usually do not require follow-up; persistent partly solid nodules with a solid component ≥6 mm should be considered highly suspicious (recommendations 4A–4C)
Multiple	CT at 3–6 mo; if lesion is stable, consider CT at 2 y and 4 y	CT at 3–6 mo; subsequent management based on the most suspicious nodule(s)	Multiple <6-mm pure GGNs† usually are benign, but consider follow-up at 2 y and 4 y in select patients at high risk (recommendation 5A)

Note.—Adapted and reprinted, with permission, from reference 4. These recommendations do not apply to lung cancer screening, patients with immunosuppression, or patients with a known primary cancer.

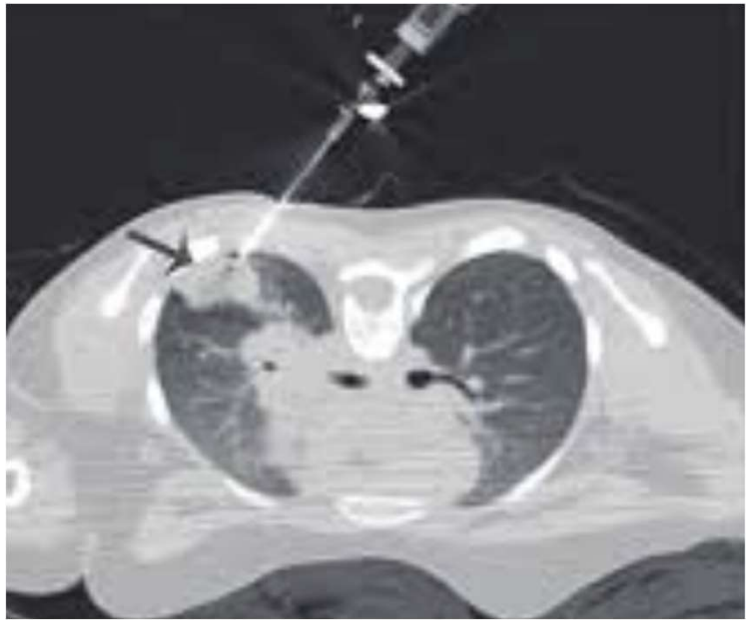
*Dimensions are the average of long and short axes, rounded to the nearest millimeter.

†GGNs = ground-glass nodules.

Time to Get Tissue

CT-TTNA
(BUT you've not staged the patient)

- Meta-analysis of 65 studies from 1985-2004
- Over 13,000 cases
- Sensitivity of 90% (individual study estimates ranged from 62% to 99%) for bronchogenic carcinoma
- PTX rate of 25%
- 15% required chest tube



Rivera. Chest. 2007 Sep;132(3 Suppl):131S-148S.

Standard Flexible Bronchoscopy Sensitivity (Generation Zero)

- Transbronchial biopsies: 57%, 21 studies
- Transbronchial brushes: 54%, 18 studies
- Lavage/washings: 43%, 14 studies

- Presence of +bronchus sign (60% vs 25%)
- Lesions <2cm: Sn 34%
- Lesion >2cm: Sn 63%

Gaeta et. Al. AJR Am J Roentgenol 1991 Dec;157(6):1181-5
Rivera et. al. Chest. 2013 May;143

Guided Bronchoscopy (1st Gen)

Technology	Studies, No.	Weighted Proportion, %	95% CI	Q Statistic	Q *P* Value
VB	10	72.0	(65.7-78.4)	21.0	.01
ENB	11	67.0	(62.6-71.4)	13.3	.21
GS	10	73.2	(64.4-81.9)	63.8	< .0001
U	11	70.0	(65.0-75.1)	15.2	.12
R-EBUS	20	71.1	(66.5-75.7)	84.2	< .0001
All	39	70.0	(67.1-72.9)	119.4	< .0001

- Meta-analysis of 3,052 lesions from 39 studies
- PTX rate of 1.5%

Wang et. al. Chest. 2012 Aug;142(2):385-393.

NAVIGATE TRIAL

ORIGINAL ARTICLE

Electromagnetic Navigation Bronchoscopy for Peripheral Pulmonary Lesions: One-Year Results of the Prospective, Multicenter NAVIGATE Study

Erik E. Folch, MD,[a,*] Michael A. Pritchett, DO,[b] Michael A. Nead, MD,[c] Mark R. Bowling, MD,[d] Septimiu D. Murgu, MD,[e] William S. Krimsky, MD,[f] Boris A. Murillo, MD,[g] Gregory P. LeMense, MD,[h] Douglas J. Minnich, MD,[i,j] Sandeep Bansal, MD,[k] Blesilda Q. Ellis, MD,[l] Amit K. Mahajan, MD,[m] Thomas R. Gildea, MD,[n] Rabih I. Bechara, MD,[o] Eric Sztejman, MD,[p] Javier Flandes, MD,[q] Otis B. Rickman, DO,[r] Sadia Benzaquen, MD,[s] D. Kyle Hogarth, MD,[t] Philip A. Linden, MD,[u] Momen M. Wahidi, MD,[v] Jennifer S. Mattingley, MD,[w,x] Kristin L. Hood, PhD,[x] Haiying Lin, MS,[x] Jennifer J. Wolvers, BSc,[x] Sandeep J. Khandhar, MD,[m] for the NAVIGATE Study Investigators

Journal of Thoracic Oncology Vol. 14 No. 3: 445-458

NAVIGATE TRIAL: Nodule Characteristics

Lesion properties	N = 1344 lesions in 1157 subjects undergoing lung lesion biopsy
Average lesion size < 20 mm	49.1% (660/1343)
Upper lobe lesion location	58.0% (780/1344)
Lesion in peripheral third of the lung	66.9% (899/1344)
Median distance from lesion to pleura (mm)	9.0 (1-20)
Ground glass lesions (Suzuki class 1 or 2)	6.3% (84/1338)
Spiculated lesion border	59.9% (804/1342)
Bronchus sign present on CT	48.5% (652/1344)
Multiple lesions sampled	13.7% (158/1157)
Pre-test probability of malignancy ≥65%[b]	59.0% (591/1002)[c]

Procedure characteristics	N = 1215 ENB procedures in 1215 subjects
General anesthesia	81.4% (989/1215)
Radial EBUS used during ENB	57.4% (698/1215)
Cone-beam CT used during ENB	4.9% (60/1215)
Fluoroscopy used during ENB	91.0% (1223/1344 lesions)
ROSE used	68.5% (748/1092 subjects)
Median total procedure time (bronchoscope in/out)	52.0 min (35-71)
Median ENB-specific procedure time (LG/EWC in/out)	25.0 min (14-40)
≥3 Biopsy tools used to sample lung lesions	72.7% (794/1092)

Journal of Thoracic Oncology Vol. 14 No. 3: 445-458

NAVIGATE TRIAL: Outcomes

- Tissue in 94% (6% unsuccessful navigation)
- 12-month diagnostic yield 72.9% (included unsuccessful nav cases)
- Deferred case analysis: 66.4% (all false neg) to 75.4% (all true neg)
- Sensitivity for malignancy 68.8%

Journal of Thoracic Oncology Vol. 14 No. 3: 445-458

NAVIGATE TRIAL: Subgroup Analysis

Variable	Dx Yield: n (%)
Average Lesion Size	
≥20 mm	446 (77.6)
<20 mm	321 (67.3)
Lesion Location	
Middle/Lower Lobe	294 (67.9)
Upper Lobe	474 (76.5)
Lung Zone	
Middle/Proximal	265 (73.8)
Peripheral Third	503 (72.5)
Bronchus Sign Present	
No	341 (67.1)
Yes	427 (78.3)
Distance to Pleura	
> 20 mm	182 (71.9)
11 - 20 mm	194 (73.5)
< 10 mm	384 (73.3)

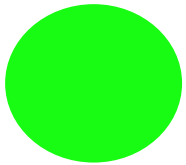
Journal of Thoracic Oncology Vol. 14 No. 3: 445-458

"With consecutive enrollment, NAVIGATE includes a significant portion of **traditionally difficult lesions**: 49% were less than 20mm, 58% were in the upper lobe, 51% without a reported bronchus sign, 67% in the peripheral third of the lung, 25% on the pleura"

- NAVIGATE Investigators

Challenges of any virtual navigation (and they are ALL virtual navigations)

- Is the green/yellow/blue ball *really* the lesion?
- CT-Body divergence occurs with Ion/Monarch/SuperDimension/Veran[illegible]icyte
- CBCT has better identified sources of error
  - Anatomic changes –respiratory motion, airway displacement, Insp/expir changes
  - Effects of atelectasis
  - Effects of local atelectasis/bleeding
  - Failure of tools



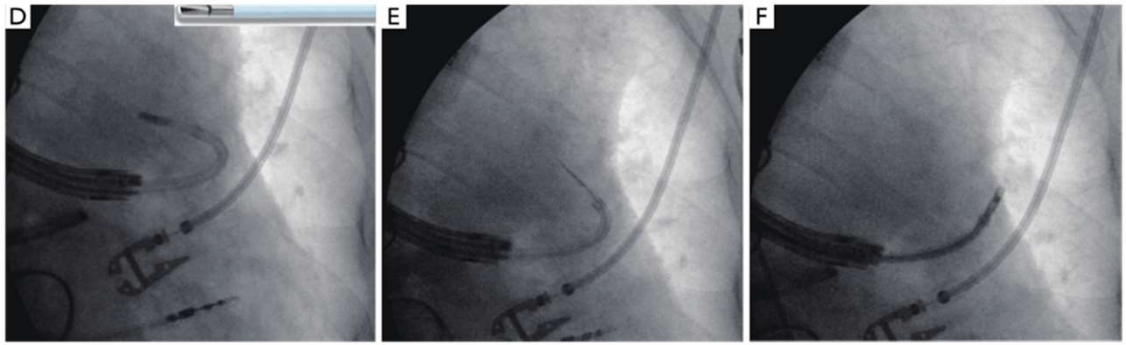
PLEASE EXPLAIN THE YIELD

Plastic Catheters

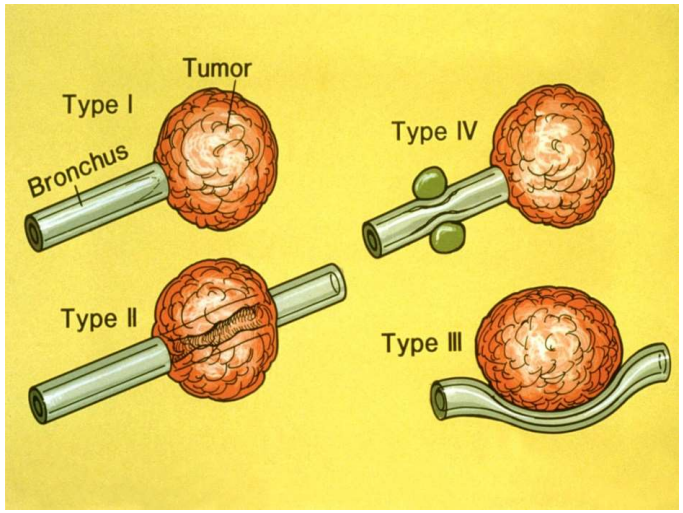
Edge EWC

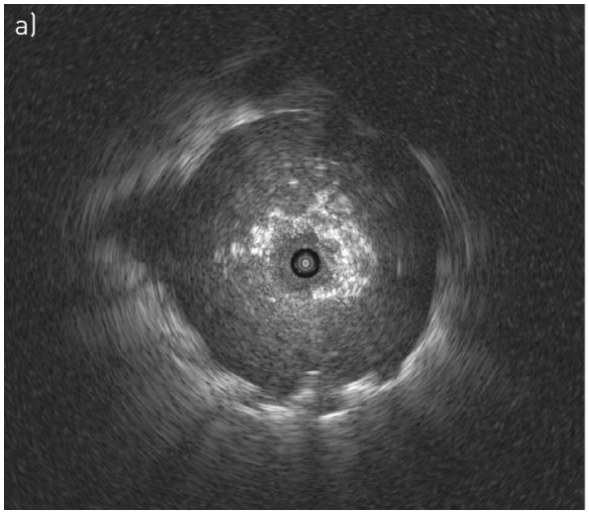
Tip Shapes 45, 90 and 180

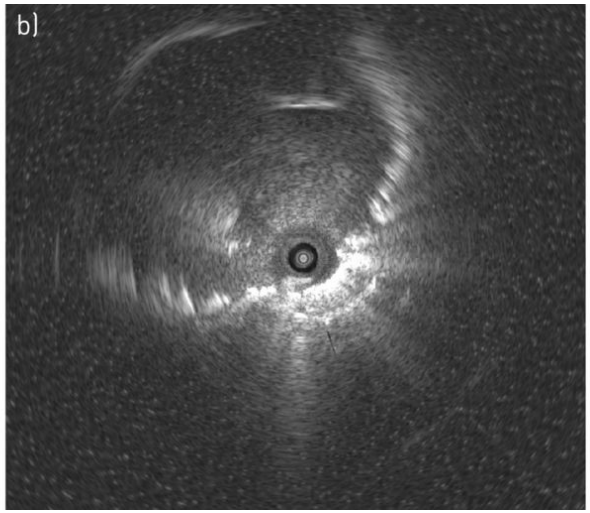
Tool Deflection



“Bronchus sign” and the Eccentric Nodule







Atelectasis

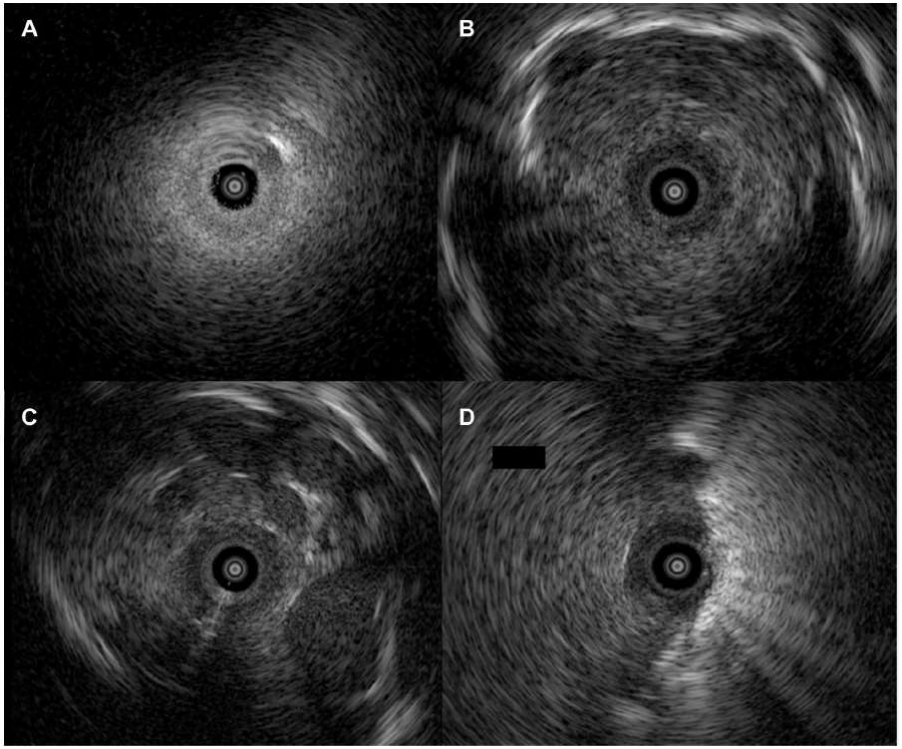


Figure 1 – *Radial-probe endobronchial ultrasound patterns. A, Aerated lung (snowstorm). B-D, Various patterns of nonaerated lung or atelectasis: concentric "tumor-like" with clear borders (B); concentric irregular with poorly demarcated borders (C); eccentric (D). (All images taken with 4-cm depth scanning).*

ORIGINAL INVESTIGATION

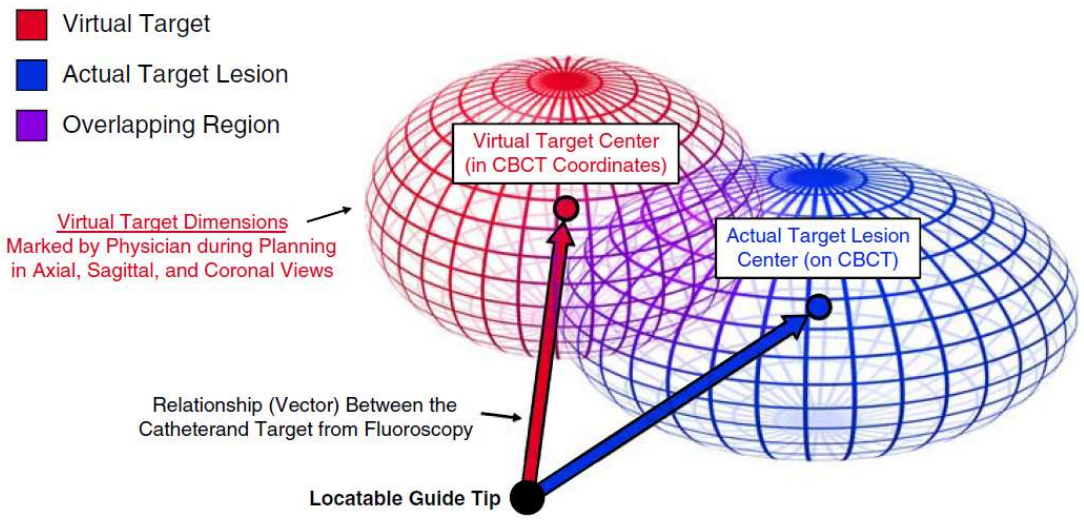
OPEN

Electromagnetic Navigation Bronchoscopy With Tomosynthesis-based Visualization and Positional Correction

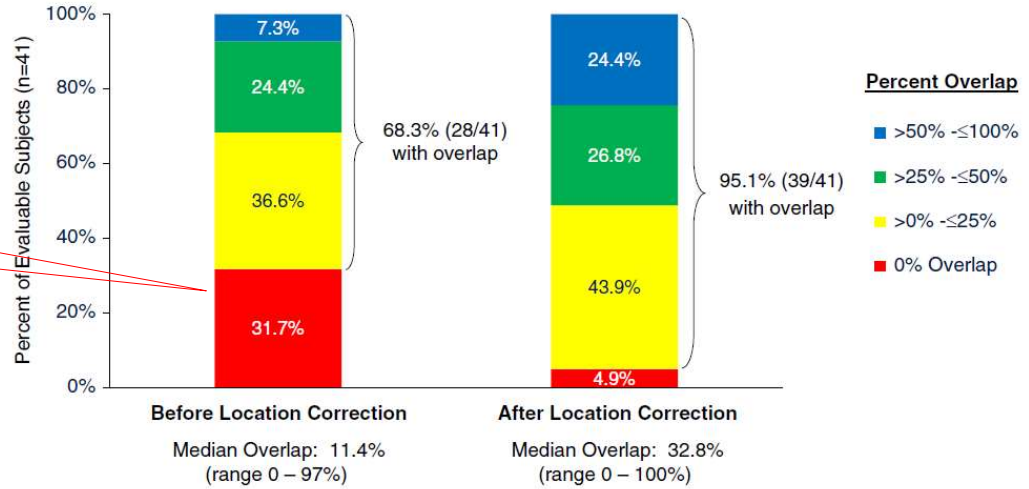
Three-dimensional Accuracy as Confirmed by Cone-Beam Computed Tomography

Michael A. Pritchett, DO, MPH, Krish Bhadra, MD,† and Jennifer S. Mattingley, MD‡*

J Bronchol Intervent Pulmonol • Volume 28, Number 1, January 2021


Virtual Target
Actual Target Lesion
Overlapping Region
Virtual Target Center
(in CBCT Coordinates)
Virtual Target Dimensions
Marked by Physician during Planning
in Axial, Sagittal, and Coronal Views
Actual Target Lesion
Center (on CBCT)
Relationship (Vector) Between the
Catheterand Target from Fluoroscopy
Locatable Guide Tip

!!!!


Percent of Evaluable Subjects (n=41)
100%
80%
60%
40%
20%
0%
7.3%
24.4%
36.6%
31.7%
68.3% (28/41)
with overlap
24.4%
26.8%
43.9%
4.9%
95.1% (39/41)
with overlap
Percent Overlap
>50% -≤100%
>25% -≤50%
>0% -≤25%
0% Overlap
Before Location Correction
Median Overlap: 11.4%
(range 0 – 97%)
After Location Correction
Median Overlap: 32.8%
(range 0 – 100%)

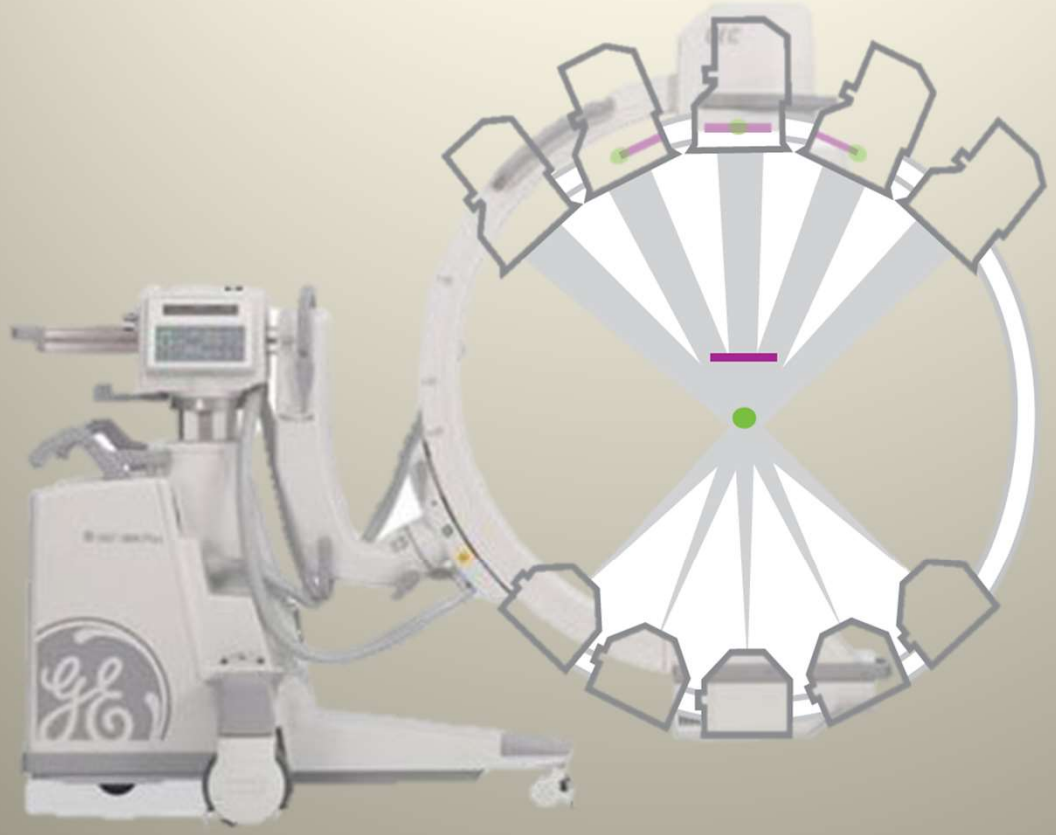
Overcoming Challenges of 1st Generation Navigation

- CT to body divergence
  - Improving ventilation strategies : The Pinehurst Protocol.
    - Better CT-procedural lung volume match
    - Prevention of atelectasis
  - Decreasing time of procedure
    - Prevention of atelectasis
  - Intra-procedural real time imaging (ie CBCT)
    - Fluoroscopic Navigation (Illumisite, LungVision)

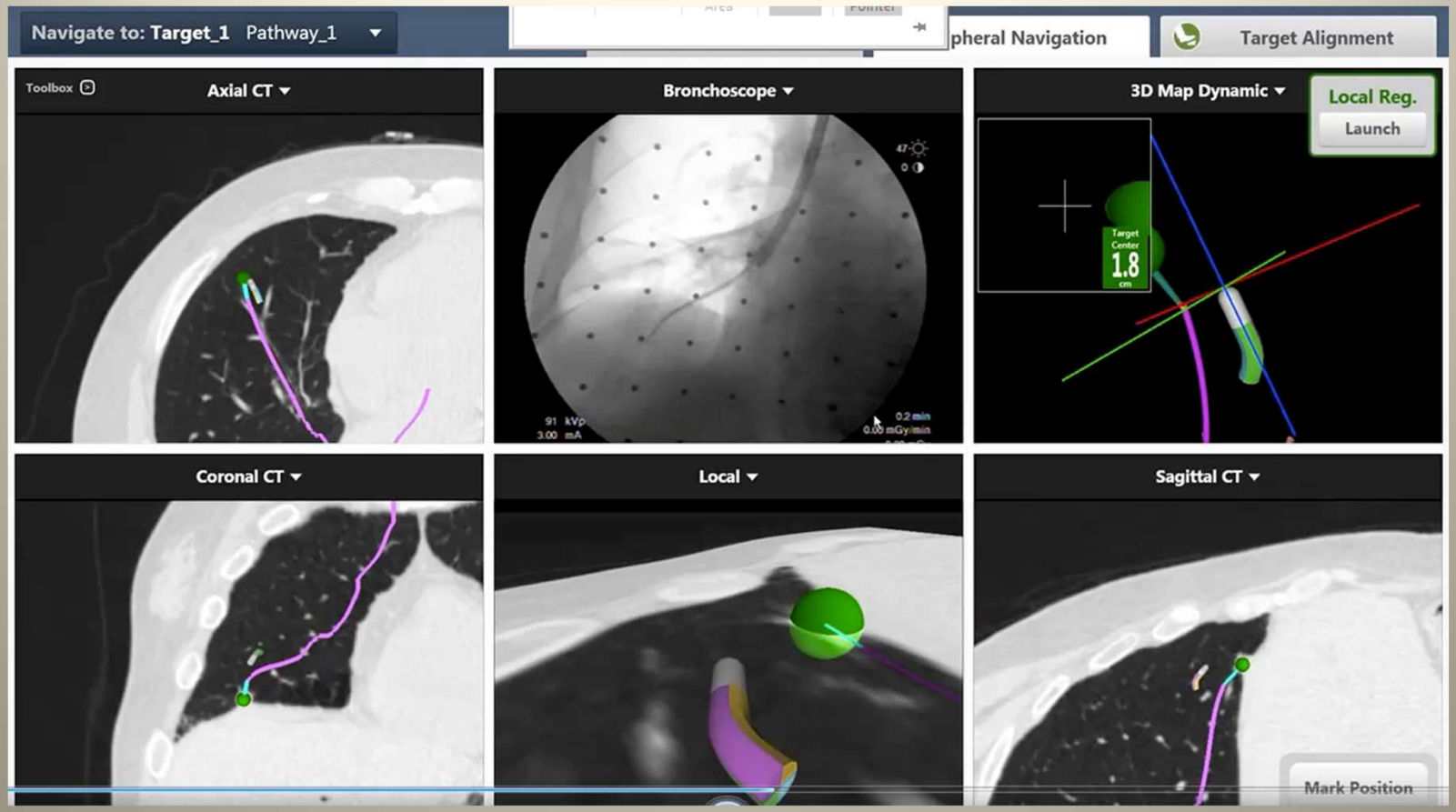
- Eccentric nodules
  - Replace plastic catheter with structural integrity
    - Robotic Bronchoscopy (Monarch Robot, Ion Robot)
  - Get structural integrity and find maneuverability at tip in distal lesions
    - Robotic Bronchoscopy (Monarch, Ion)

Illumisite: Next Generation superDimension

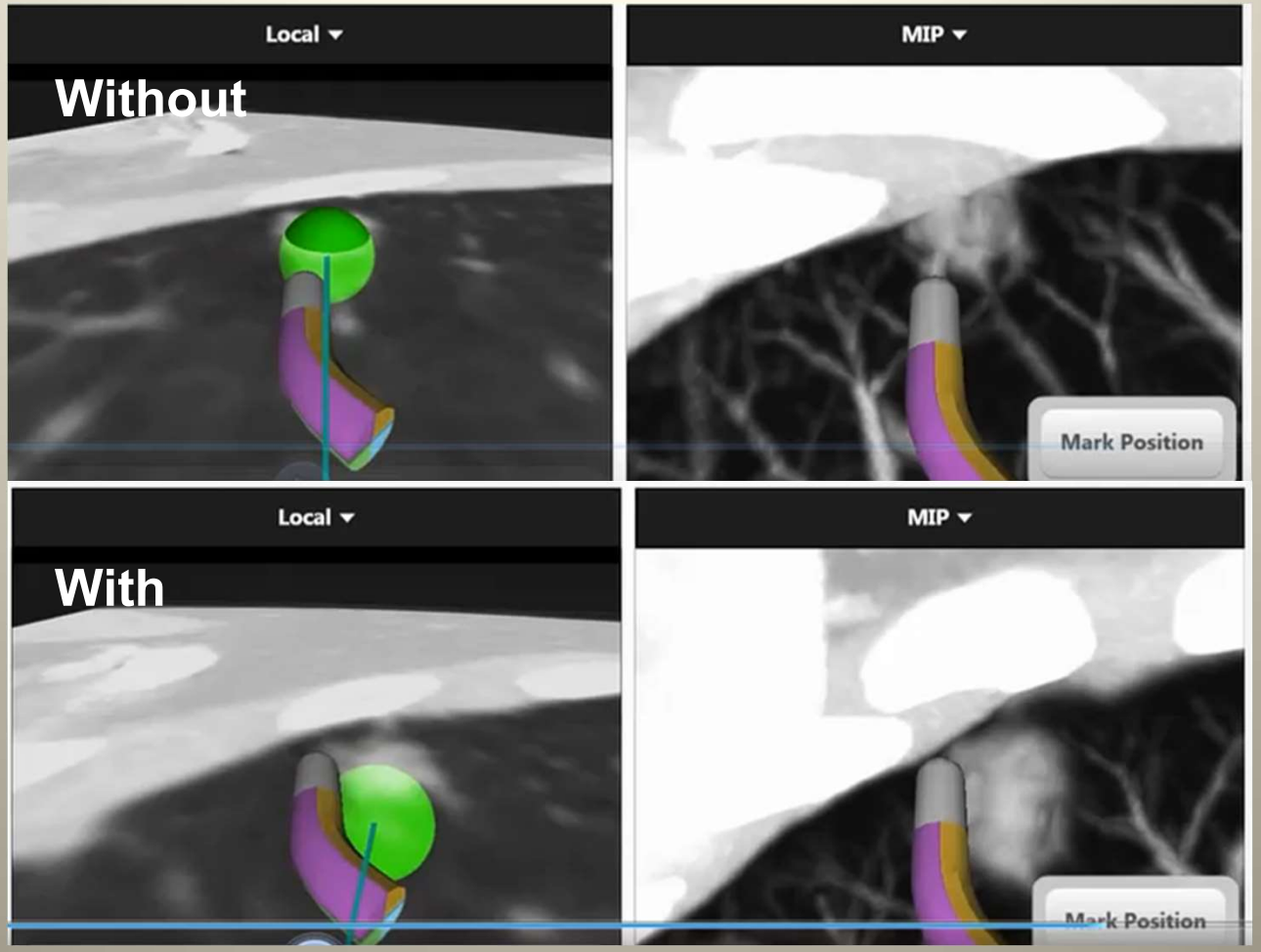
Fluoroscopic Navigation Technology: a way to fix CT to Body Divergence



Slide courtesy of Fabian Maldonado, MD



Slide courtesy of Fabian Maldonado, MD



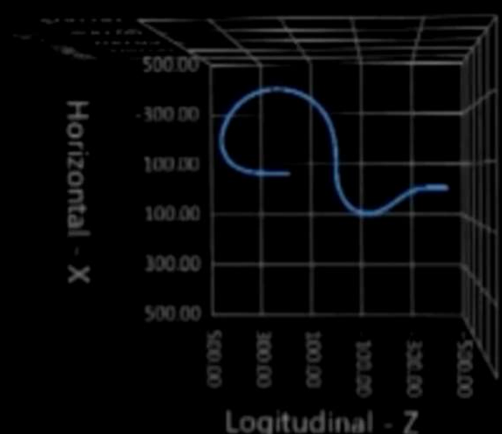
Slide courtesy of Fabian Maldonado, MD

Next Generation EMN with SuperD

Robotics

Ion System

- Single scope design
- 2.0 working channel
- Uses shape sensing coil
- Optics are removed during biopsy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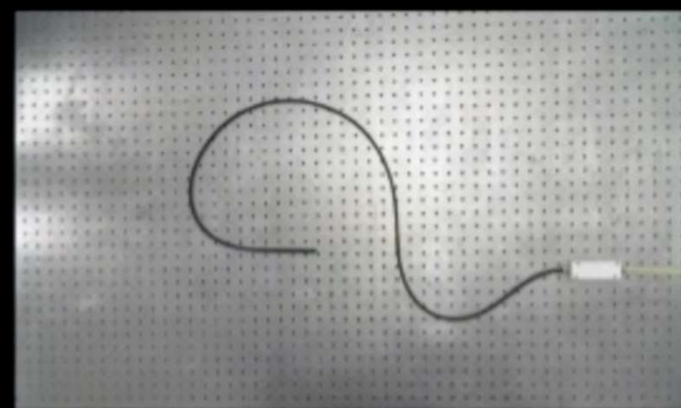
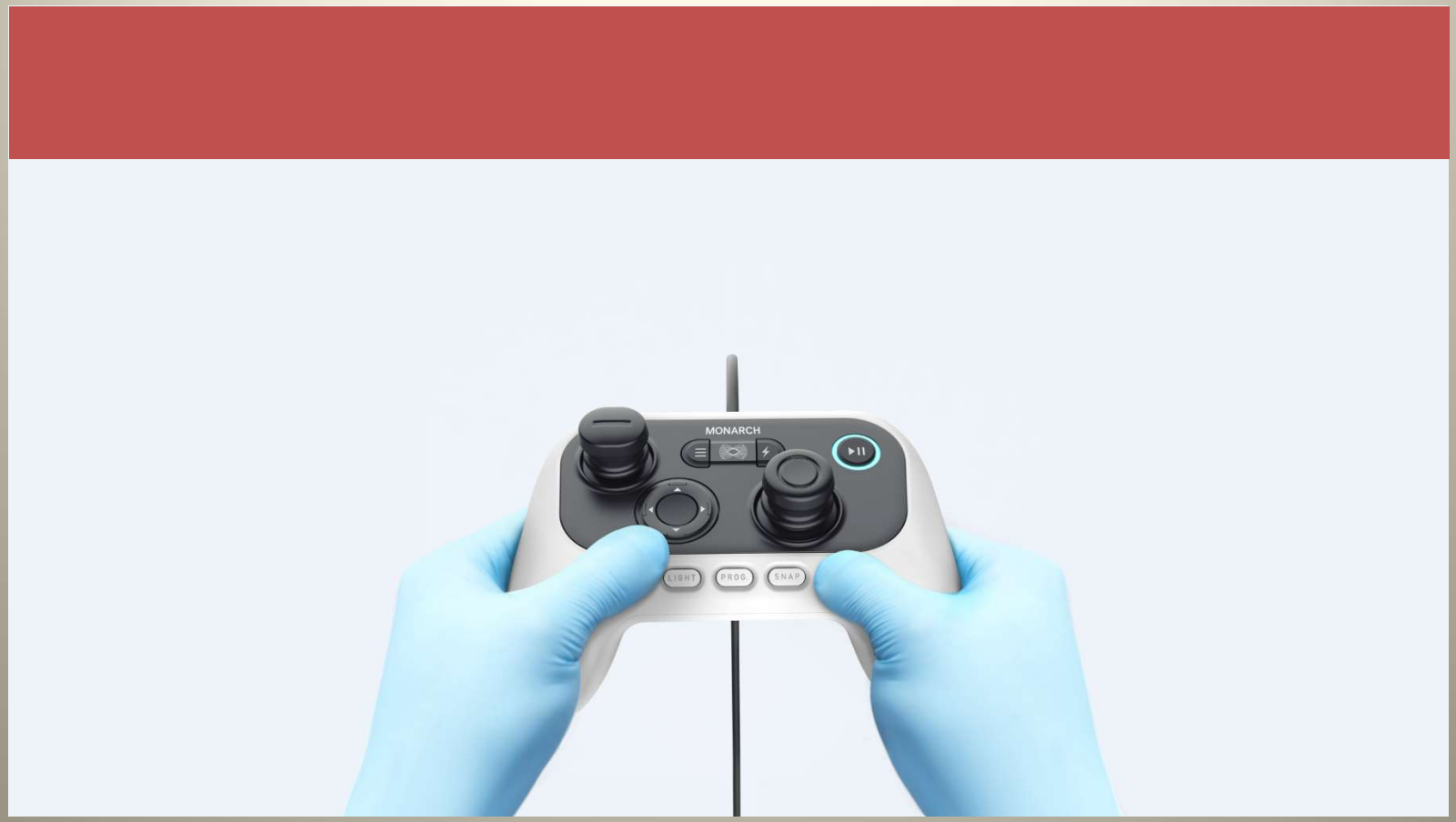
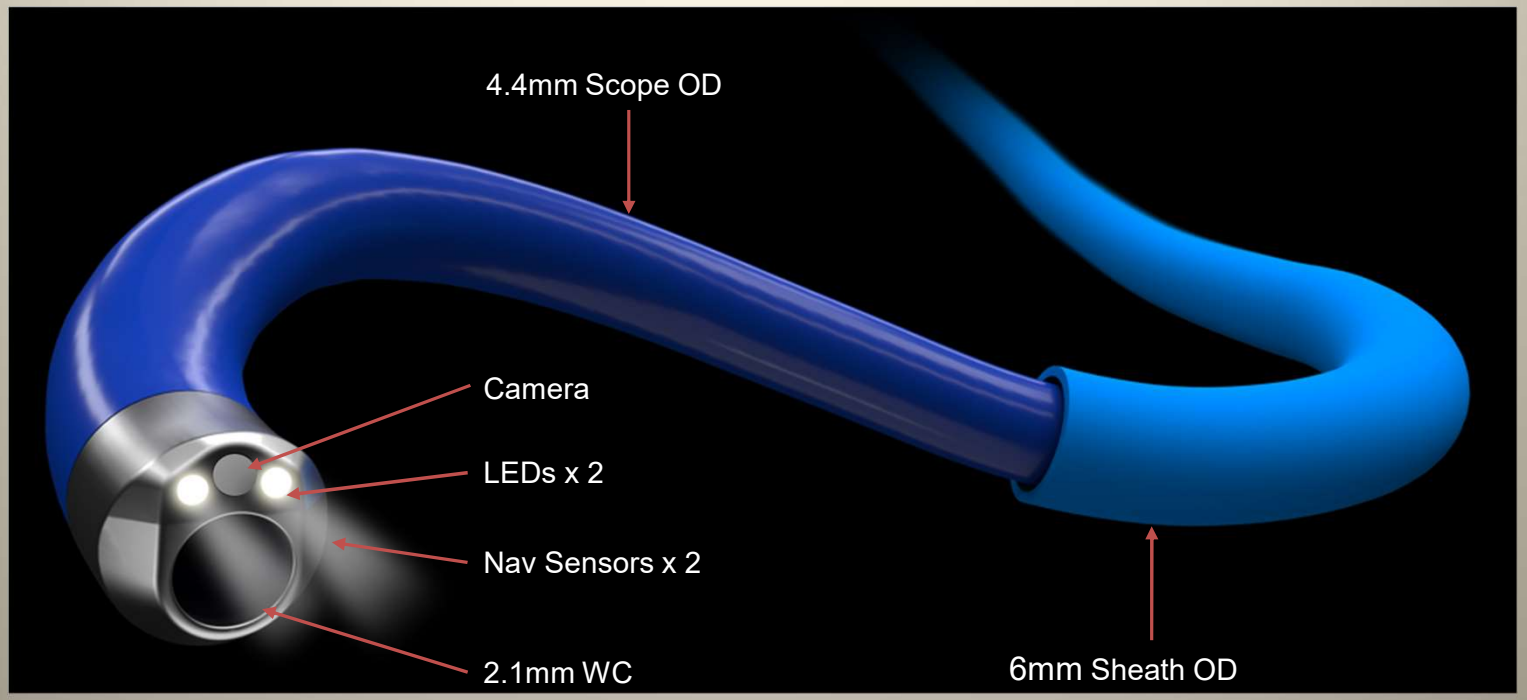
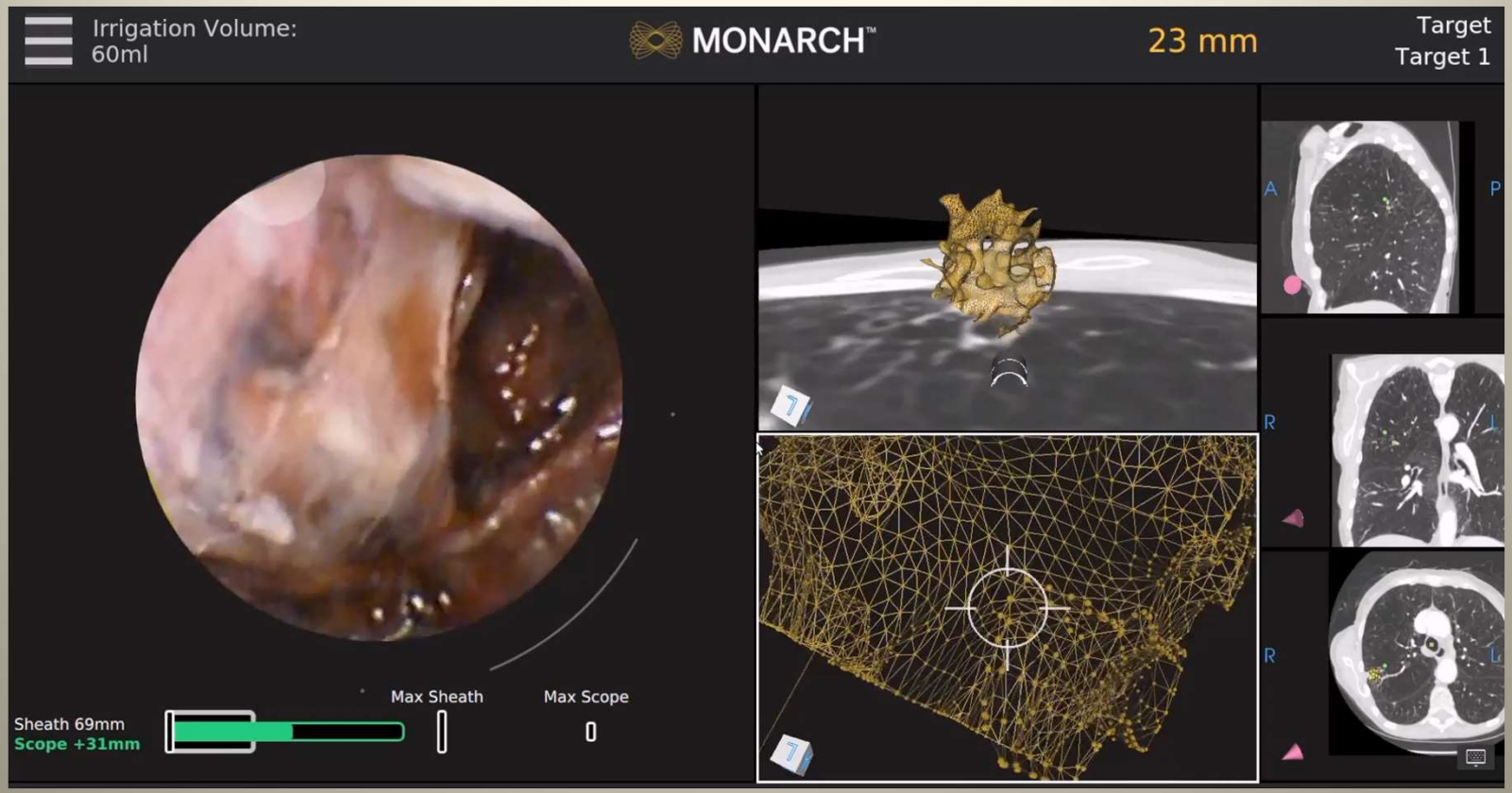
Logitudinal - Z

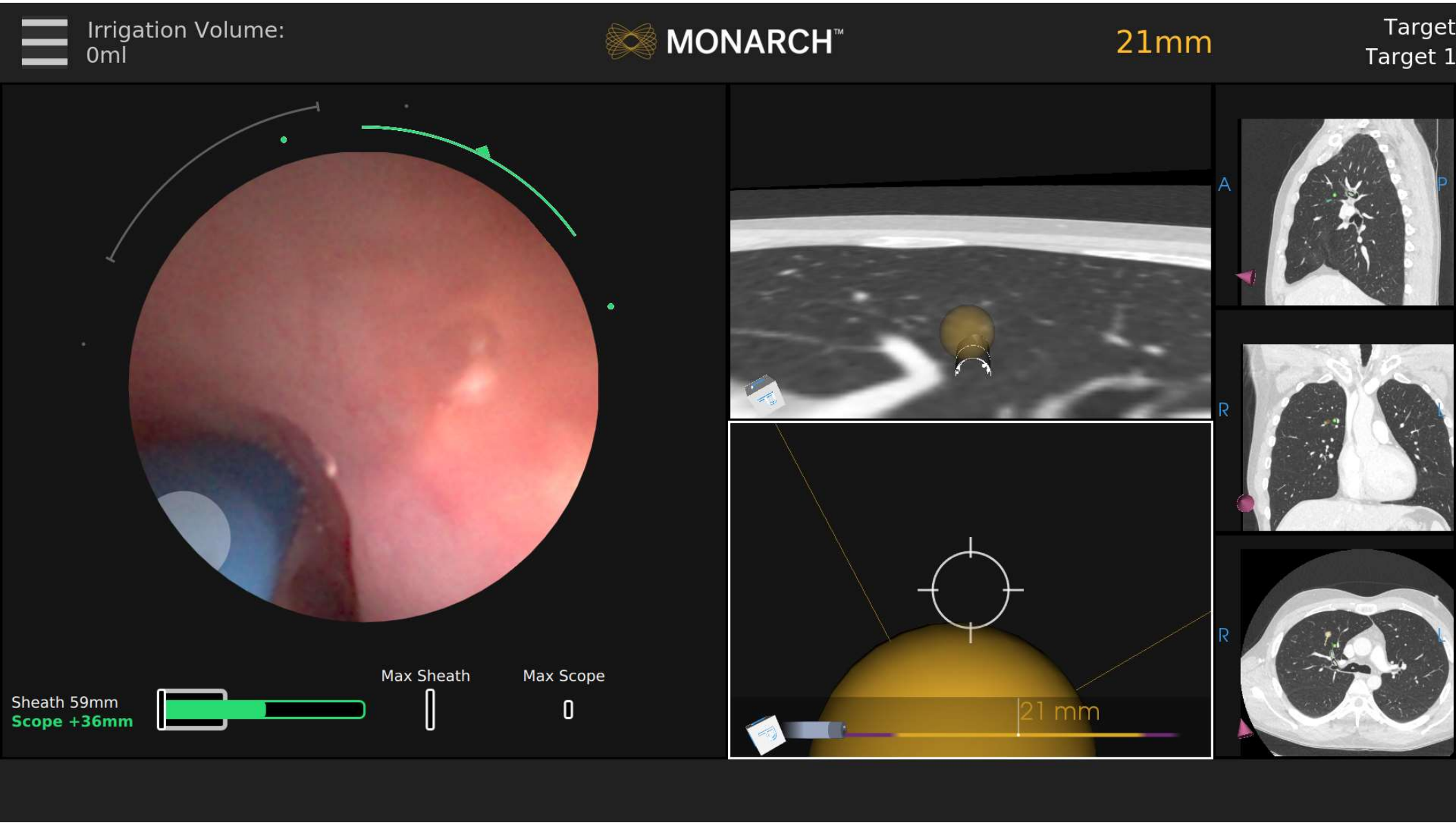


The Monarch




4.4mm Scope OD
Camera
LEDs x 2
Nav Sensors x 2
2.1mm WC
6mm Sheath OD


Irrigation Volume:
60ml
MONARCH™
23 mm
Target
Target 1
A
P
R
L
R
Max Sheath
Max Scope
0
Sheath 69mm
Scope +31mm


Irrigation Volume:
0ml
MONARCH™
21mm
Target
Target 1
Max Sheath
Max Scope
Sheath 59mm
Scope +36mm
21 mm
A
P
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R
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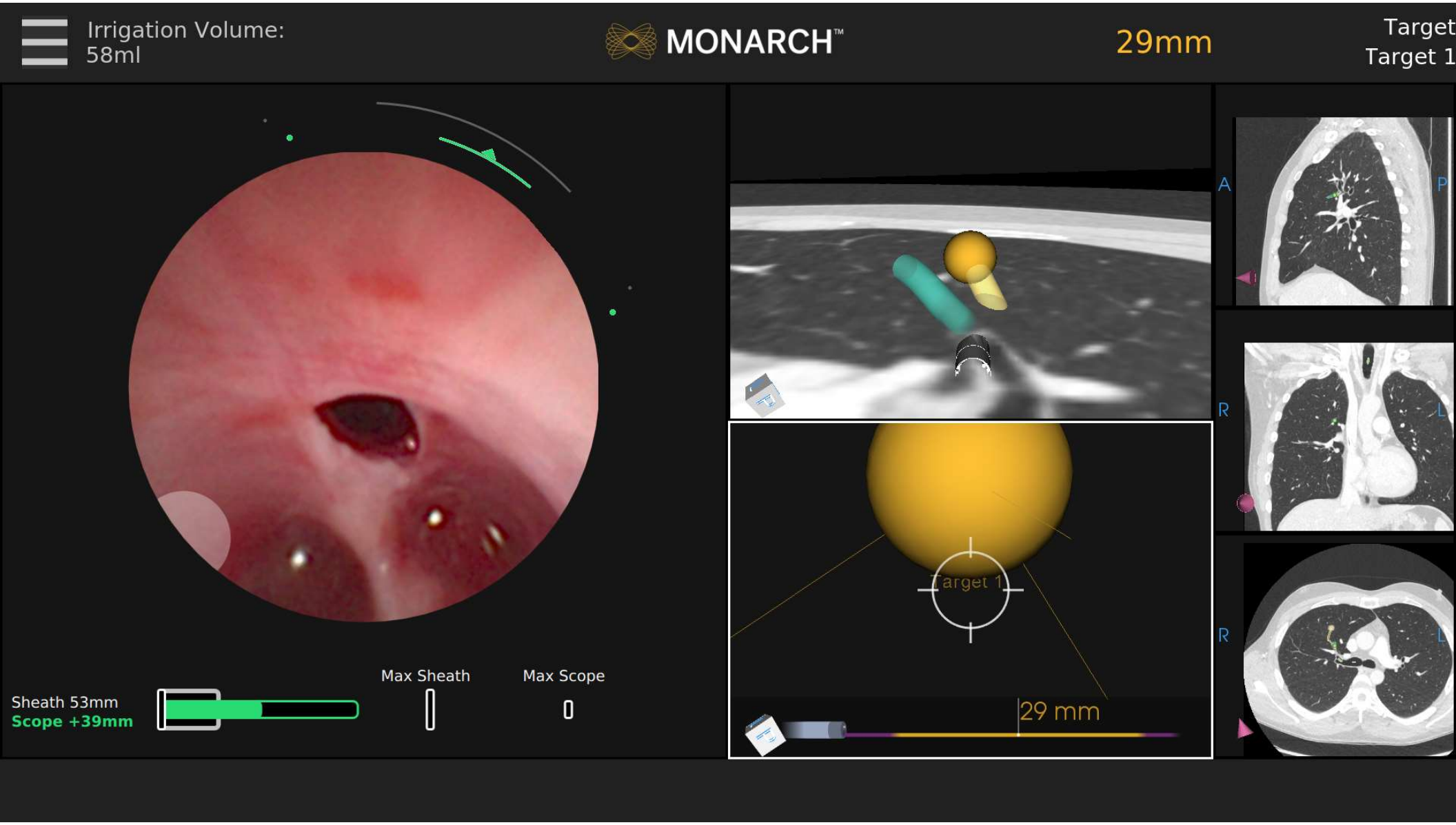

Irrigation Volume:
58ml
MONARCH™
29mm
Target
Target 1
A
P
R
L
R
L
Target 1
29 mm
Max Sheath
Max Scope
Sheath 53mm
Scope +39mm

Biopsy Results

- TTNA: squamous cell, but not a lot of tissue to run testing

- TBBx Forceps (through the hole I made): plenty of tissue for molecular analysis and ICH.
- Proof it was metastatic head/neck cancer.

Robotic Bronchoscopy: Value Proposition

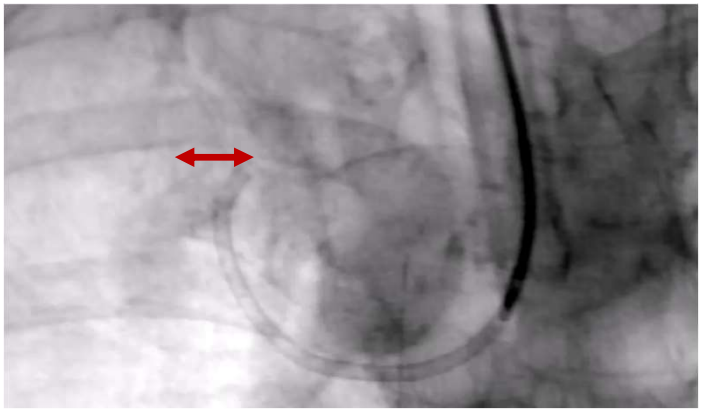
- **Better tip integrity**
- **Greater reach to periphery**
- **Direct Visualization of Lesion**

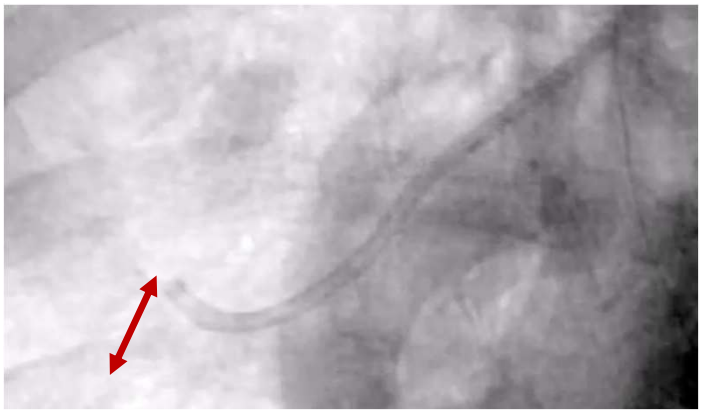
↓

Better Overall Yield

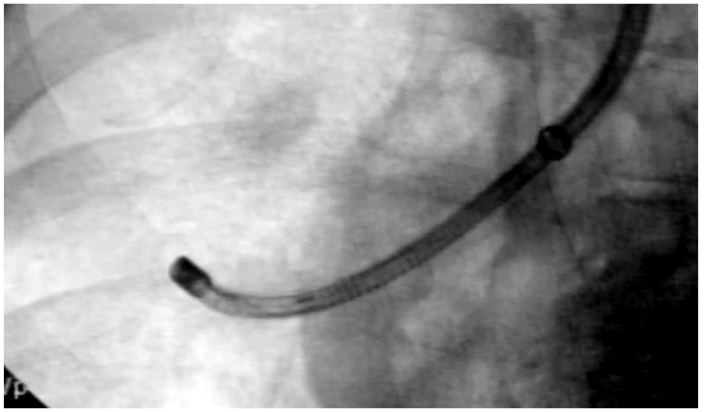
ROBOTIC STABILITY

EWC FIRM TIP 180°



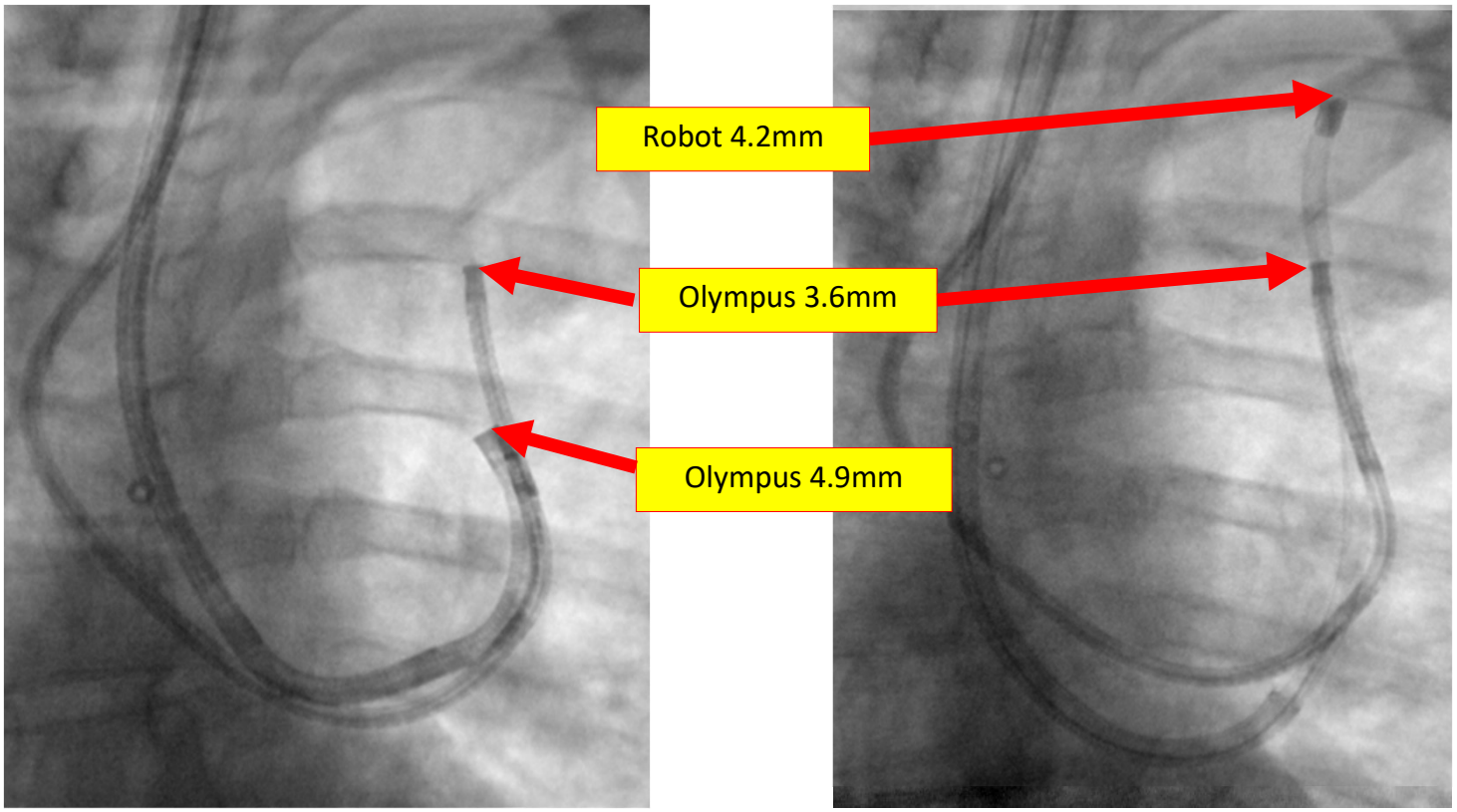


ROBOT PLATFORM



*videos captured in a cadaver, at the same target location

ROBOTIC BRONCHOSCOPY: FURTHER REACH



Study	Platform/ No of pts/follow up	Navigation success/confir-mation	Bronchus sign	Diagnostic yield definition	Tools/sampling technique	Adjuvant imaging	Reported Diagnostic yield
Chaddha 2019 BMC Pulm Med	Monarch/165 6 months	88.6%/REBUS	63%	+	Needle, Forceps % NA	REBUS, 2D fluoro	69-77%
Chen 2020 Chest	Monarch/55 1 year	96.2%/REBUS	60%	++	Needle 100%, Forceps x3 (IfN)	REBUS, 2D fluoro	74.1%
Benn 2021 Lung	Ion/52 5-16 months	85% virtual 100% CBCT	46%	– –	Needle 100% Forceps 76%	Cone beam CT	86%
Fielding 2019 Respiration	Ion/29 6 months	96.5%/virtual 93%/ REBUS	59%	– –	Needle, Forceps, Brush	REBUS, 2D fluoro	79%
Dekel 2021 Chest	Ion/131 1 year	98.7%/EBUS + 2D/3D fluoro (91% rEBUS)	63%	++	Needle 97% Forceps 32%	REBUS, 2D, 3D fluoro	81.7%

Chaddha *et al. BMC Pulmonary Medicine* (2019) 19:243
https://doi.org/10.1186/s12890-019-1010-8

BMC Pulmonary Medicine

RESEARCH ARTICLE Open Access

Robot-assisted bronchoscopy for pulmonary lesion diagnosis: results from the initial multicenter experience

Udit Chaddha[1*†], Stephen P. Kovacs[2†], Christopher Manley[3], D. Kyle Hogarth[4], Gustavo Cumbo-Nacheli[5], Sivasubramanium V. Bhavani[6], Rohit Kumar[7], Manisha Shende[8], John P. Egan III[9] and Septimiu Murgu[6]

165 procedures, 167 nodules
- Includes first Monarch procedures at 4 initial sites
- Majority of cases completed with Monarch 1st gen software

Diagnostic yield definition
- Defined as the percentage of procedures yielding a diagnosis based on final pathology
- If f/u tests demonstrated alternate dx, lesion growth, or new LAD or mets, then procedure considered non-diagnostic
- Average follow-up was 185 days (+/- 55)

Nodule properties →

Table 2 Lesion characteristics

Size, mm	25.0 ± 15.0
< 10	11/167 (6.6)
10–30	108/167 (64.7)
> 30	48/167 (28.7)
Location	
Right Upper Lobe	46/167 (27.5)
Right Middle Lobe	21/167 (12.6)
Right Lower Lobe	32/167 (19.2)
Left Upper Division	40/167 (24.0)
Lingula	1/167 (0.6)
Left Lower Lobe	27/167 (16.2)
Peripheral lesion[a]	118/167 (70.7)
Lesion appearance	
Solid	125/167 (74.9)
Ground Glass	17/167 (10.2)
Mixed	15/167 (9.0)
Cavity	10/167 (6.0)
Bronchus sign	106/167 (63.4)

35.4%

Chaddha et al. BMC Pulmonary Medicine (2019) 19:243

Table 3 Diagnostic yield based on lesion characteristics

	Diagnostic yield	*P*-value
Location		0.72
Right Upper Lobe	35/46 (76.1)	
Right Middle Lobe	14/21 (66.7)	
Right Lower Lobe	20/32 (62.5)	
Left Upper Division	26/40 (65.0)	
Lingula	1/1 (100)	
Left Lower Lobe	20/27 (74.1)	
Peripheral lesion	80/118 (67.8)	0.47
Bronchus sign	83/106 (78.3)	0.001
r-EBUS view		< 0.001
No view	7/26 (26.9)	
Eccentric view	43/60 (71.7)	
Concentric view	66/81 (81.5)	
Lesion endobronchial visibility	40/50 (80.0)	0.053
Lesion appearance		0.74
Solid	86/125 (68.8)	
Ground Glass	12/17 (70.6)	
Mixed	12/15 (80.0)	
Cavity	6/10 (60.0)	
Size		0.11
< 10	5/11 (45.5)	
10–30	74/108 (68.5)	
> 30	37/48 (77.1)	

No difference in yield with regard to nodule location
- Size, bronchus sign not used as variables

78% yield with bronchus sign
- Did they have direct view?

Localization Success:
-Overall, 77% localization using rEBUS
- 88.6% "navigation success" – combo of rEBUS and diagnostic tissue

Yield:
- 72% yield eccentric - ? higher than expected
- 81% yield concentric
- 27% yield with no rEBUS image

? Tool failure ?

Attenuated yield even with larger nodules

Overall Yield: 69% to 77% depending on how f/u was managed in "inflammation"

Chaddha et al. BMC Pulmonary Medicine (2019) 19:243

[Thoracic Oncology Original Research]

CHEST

Robotic Bronchoscopy for Peripheral Pulmonary Lesions

A Multicenter Pilot and Feasibility Study (BENEFIT)

Alexander C. Chen, MD; Nicholas J. Pastis Jr, MD; Amit K. Mahajan, MD; Sandeep J. Khandhar, MD; Michael J. Simoff, MD; Michael S. Machuzak, MD; Joseph Cicenia, MD; Thomas R. Gildea, MD; and Gerard A. Silvestri, MD

CHEST 2021; 159(2):845-852

54 procedures, 54 nodules

- Learning curve: Study population initial 15 procedures per site
- Majority of cases completed with Monarch 1st gen software
- Primary outcome lesion localization with rEBUS (along with safety outcomes)

Diagnostic yield

- Defined as a “biopsy that resulted in a specific malignant process or a specific diagnosis of a non-malignant process that explained the presence of the lesion (granuloma, fungal elements)”
  - “Inflammation” was considered diagnostic only if there was improvement or resolution on f/u or if confirmed by surgical biopsy
  - If follow-up imaging was unavailable, a finding of “inflammation” was considered non-diagnostic.
  - “Atypical cells” were considered non-diagnostic
  - Biopsy specimens that showed normal pulmonary elements were also considered non-diagnostic, regardless of improvement on follow-up imaging

* All follow up was for at least one year

Nodule properties: →

TABLE 1] Baseline Characteristics

Characteristic	Value
Patient	
Total,[a] No.	54
Female, No. (%)	29 (53.7)
Age, mean (SD), y	67.1 (8.5)
BMI, mean (SD), kg/m^2	28.8 (6.3)
Lesion	
Nodule size, mean (SD),[b] mm	23.2 (10.8)
≤20	23 (42.6)
21-30	19 (35.2)
>30	12 (22.2)
Bronchus sign, No. (%)	32 (59.3)
Nodule location, No. (%)	
Right upper lobe	19 (35.2)
Left upper lobe	12 (22.2)
Right middle lobe	6 (11.1)
Right lower lobe	8 (14.8)
Left lower lobe	9 (16.7)

30.5

CHEST 2021; 159(2):845-852

TABLE 3] Results

Result	No./No. (%)	*P* Value
Lesion localization[a]		
Overall	51/53 (96.2)	
Concentric	31/51 (60.8)	
Eccentric	20/51 (39.2)	
Diagnostic yield		
Overall radial endobronchial ultrasound view	40/54 (74.1)	
Concentric	25/31 (80.6)	.502
Eccentric	14/20 (70.0)	
Bronchus sign		
Present	24/32 (75.0)	>.999
Absent	16/22 (72.7)	
Lesion size, mm		
≤30	30/42 (71.4)	.710
>31	10/12 (83.3)	

Significant drop between localization and yield

Categorization based on definition of lung nodule (<3cm)

CHEST 2021; 159(2):845-852

› Ann Thorac Surg. 2022 Jan 17;S0003-4975(22)00042-X. doi: 10.1016/j.athoracsur.2021.12.041. Online ahead of print.

Factors Associated with Diagnostic Accuracy of Robotic Bronchoscopy with 12-month Follow-up

Abhinav Agrawal [1], Elliot Ho [2], Udit Chaddha [3], Baris Demirkol [4], Sivasubramanium V Bhavani [5], D Kyle Hogarth [2], Septimiu Murgu [2]

Affiliations + expand

PMID: 35051388 DOI: 10.1016/j.athoracsur.2021.12.041

annalsthoracicsurgery.org

THE ANNALS OF THORACIC SURGERY

- 124 consecutive patients
- Fairly conservative definition of yield: (1) a specific malignant process or 2) a specific non-malignant process that explained the lesion
- At least 12 month follow up
- Navigation to lesion in 94% based on system imaging; 82% by rEBUS
- Overall accuracy 77%
- Accuracy contingent on rEBUS view (concentric or eccentric)
  - 85% concentric vs 84% eccentric vs 38% for no rEBUS view
  - Bronchus sign NS
- Multivariate analysis: rEBUS view and nodule >20mm significant

FULL TEXT ARTICLE

Shape-Sensing Robotic-Assisted Bronchoscopy in the Diagnosis of Pulmonary Parenchymal Lesions

Article in Press: Accepted Manuscript

Or Kalchiem-Dekel MD, James G. Connolly MD, I-Hsin Lin PhD, Bryan C. Husta MD, FCCP, Prasad S. Adusumilli MD, FACS, Jason A. Beattie MD, Darren J. Buonocore MD, Joseph Dycoco BS, Paige Fuentes MS, David R. Jones MD, FACS, Robert P. Lee MD, FCCP, Bernard J. Park MD, FACS, FCCP, Gaetano Rocco MD, FRCSEd, Mohit Chawla MD, FCCP and Matthew J. Bott MD, FACS

Chest. 2021 Aug 9;S0012-3692(21)03625-4. doi: 10.1016/j.chest.2021.07.2169. Online ahead of print.

FULL TEXT ARTICLE

Shape-Sensing Robotic-Assisted Bronchoscopy in the Diagnosis of Pulmonary Parenchymal Lesions

Chest. 2021 Aug 9;S0012-3692(21)03625-4. doi: 10.1016/j.chest.2021.07.2169. Online ahead of print.

- 159 lesions, 130 patients (retrospective observational)
- Median lesion size: 18mm
- Bronchus sign: 63%
- 85% localization rate
- Diagnostic yield 82%
  - 100% for lesions $\geq$ 3cm
  - 69% for lesions <2cm
- Pneumothorax: 1.5%

Dekel, et al. Chest 2021

131 procedures, 159 nodules

- Includes Ion procedures at one site
- Primary outcome diagnostic yield per lesion (plus primary safety outcome)

Diagnostic yield

- Defined differently based on outcome
  - Malignant considered diagnostic, unless proven FP at time of surgery
  - Non-malignant (inflammation, infection, etc) considered diagnostic if:
  - a nonmalignant cause was confirmed by an alternative sampling method, such as transthoracic or surgical biopsy;
  - follow-up imaging demonstrated regression or resolution of the lesion
  - the lesion was shown to remain unchanged on follow-up imaging for >1 year
  - All follow up was for at least one year

Note: Atypical cells considered ND

Nodule properties: ⟶

Variable	Value
Lesion size, cm, median (IQR)	1.8 (1.3-2.7)
Lesion lobar location, N (%)	
RUL	53 (33.3)
RML	11 (6.9)
RLL	20 (12.6)
LUL	41 (25.8)
LLL	34 (21.4)
Lung centrality, N (%)	
Inner 2/3	97 (61.0)
Outer 1/3	62 (39.0)
“Bronchus sign”, N (%)	
Positive	100 (62.9)
Negative	59 (37.1)

34%

Chest. 2021 Aug 9:S0012-3692(21)03625-4. doi: 10.1016/j.chest.2021.07.2169

Intraoperative imaging	Value
Radial probe EBUS, N (%)	**136 (85.5)**
Radial probe EBUS view, N (%)	
Concentric	72 (53.0)
Eccentric	52 (38.2)
No view	12 (8.8)
2D fluoroscopy, N (%)	127 (79.9)
2D/3D fluoroscopy, N (%)	32 (20.1)
Diagnostic Yield, N (%)	
Overall	**130/159 (81.7)**
<1cm	12/18 (66.6)
1-2cm	50/71 (70.4)
2-3cm	39/42 (92.9)
>3cm	28/28 (100)

15% cases no rEBUS use

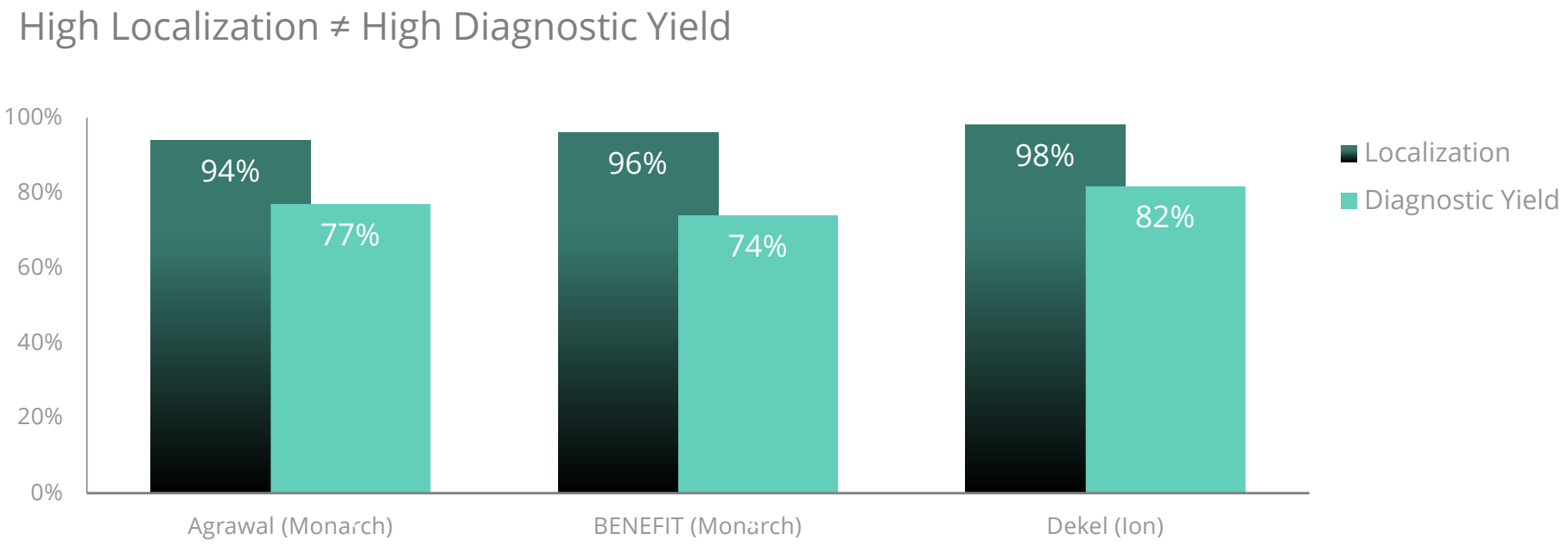
Stated overall localization 98%, but unclear if imaging guided adjustments were made

81.7% yield

Drop-off once <2cm

Chest. 2021 Aug 9:S0012-3692(21)03625-4. doi: 10.1016/j.chest.2021.07.2169

Robotic Navigation Platforms: No Correlation Between Localization and Yield



So what have we learned?

Value Proposition: Have We Achieved It?

Proposed Advantages

- Better tip integrity
- Greater reach to periphery
- Direct Visualization of Lesion
- Better Overall Yield

Literature Observations

- Yield has only increased modestly
- Localization seems improved*
- Some mention of visualization, but still not 100% even when occurred
- Yield seems not connected to rEBUS confirmation, may be tied to image guidance (CBCT/3D fluoro)

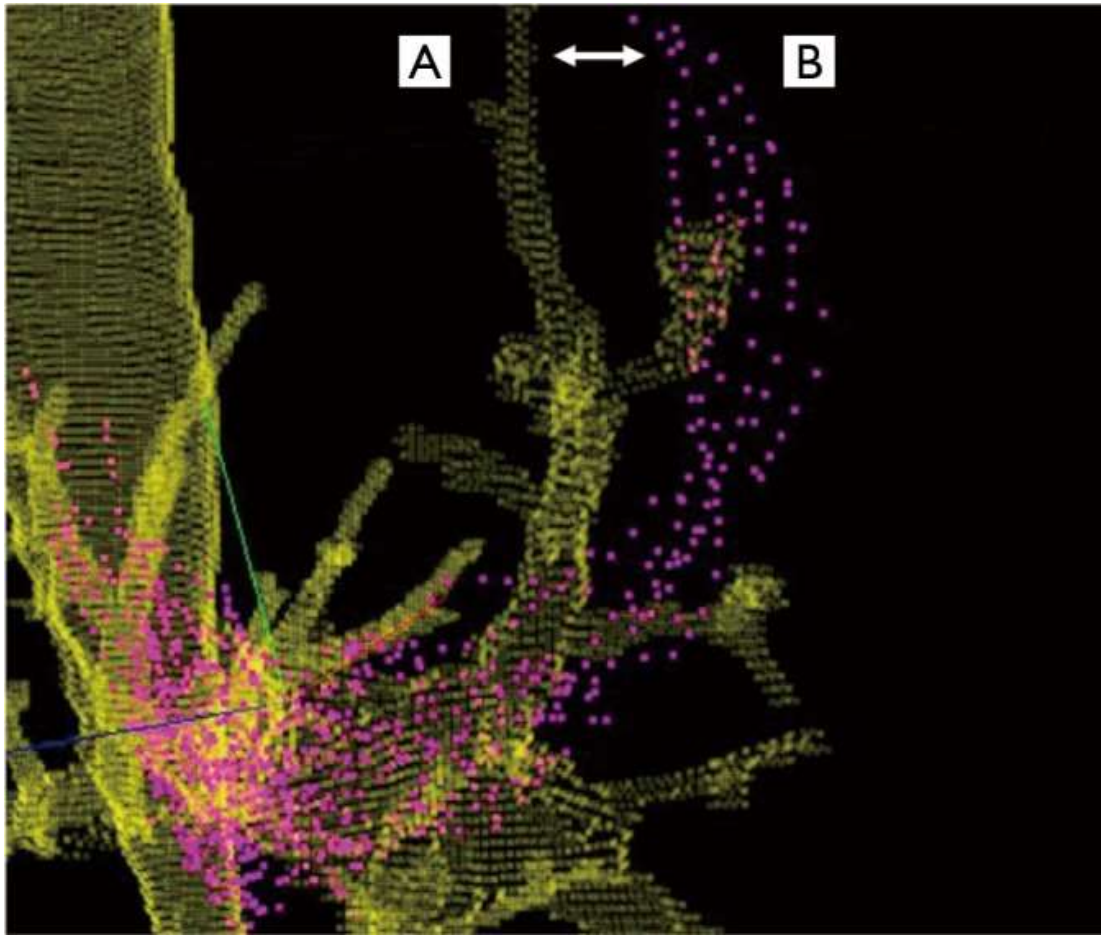
Realization?

Gaps Still Remain in Lung Navigation and Biopsy

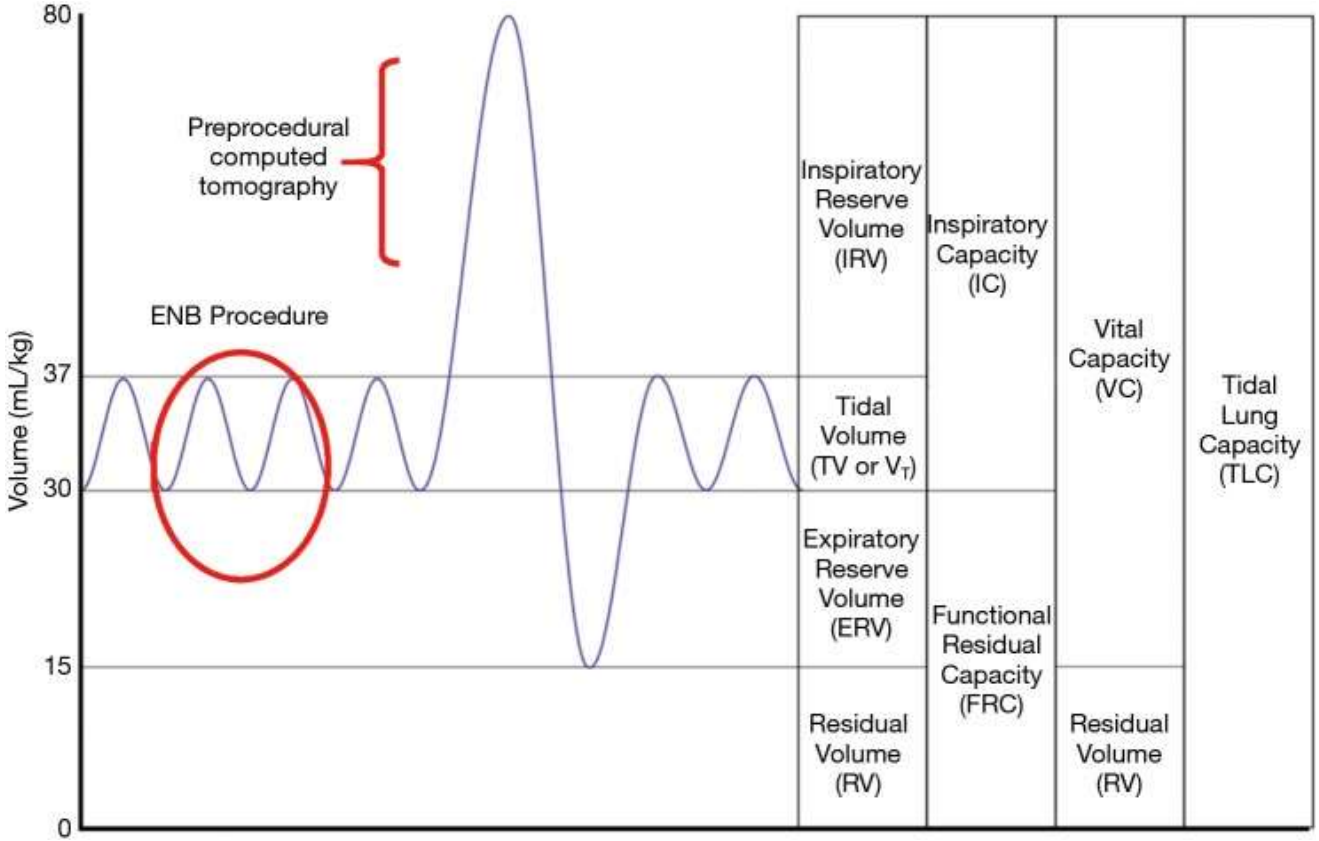
Gaps Still Remain in Current Robotic Platforms

Lesion localization

- Virtual Navigation bronchoscopy – the “electronic target” is not the actual target
- Problem is CT2BD

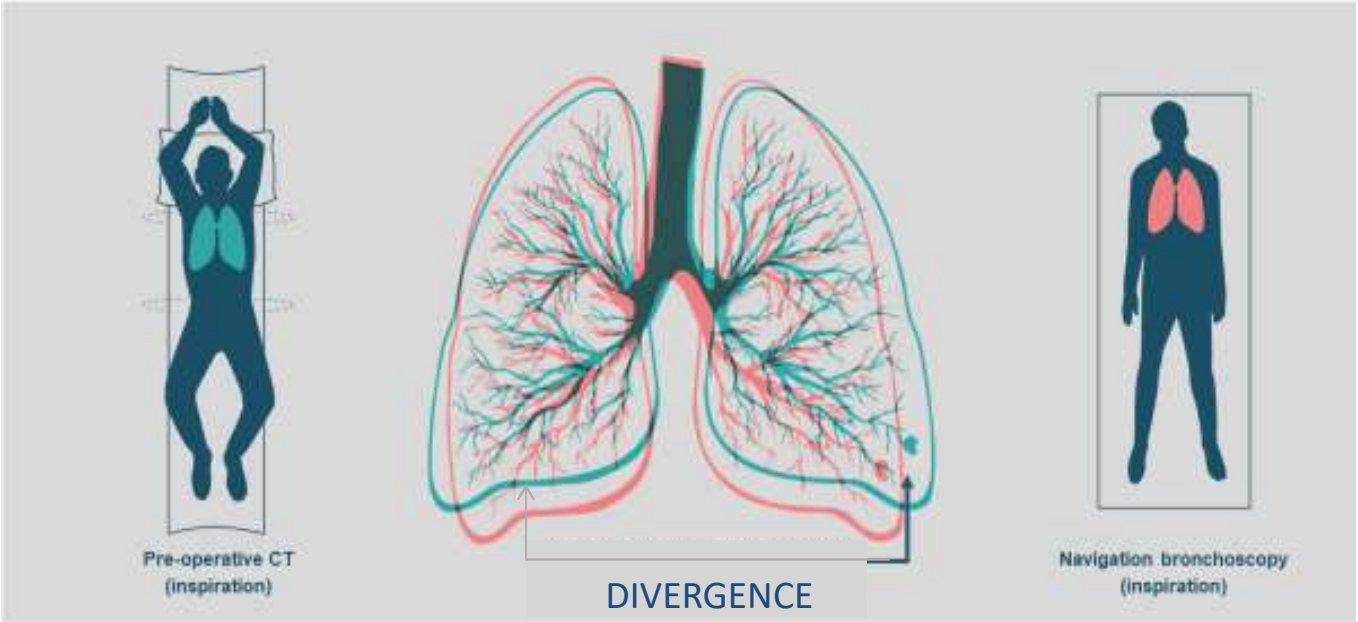


Pritchett MA, Bhadra K, Calcutt M, Folch E. Virtual or reality: divergence between preprocedural computed tomography scans and lung anatomy during guided bronchoscopy. J Thorac Dis. 2020 Apr;12(4):1595-1611. doi: 10.21037/jtd.2020.01.35. Erratum in: J Thorac Dis. 2020 Aug;12(8):4593-4595. PMID: 32395297; PMCID: PMC7212155.



Pritchett MA, Bhadra K, Calcutt M, Folch E. Virtual or reality: divergence between preprocedural computed tomography scans and lung anatomy during guided bronchoscopy. J Thorac Dis. 2020 Apr;12(4):1595-1611. doi: 10.21037/jtd.2020.01.35. Erratum in: J Thorac Dis. 2020 Aug;12(8):4593-4595. PMID: 32395297; PMCID: PMC7212155.

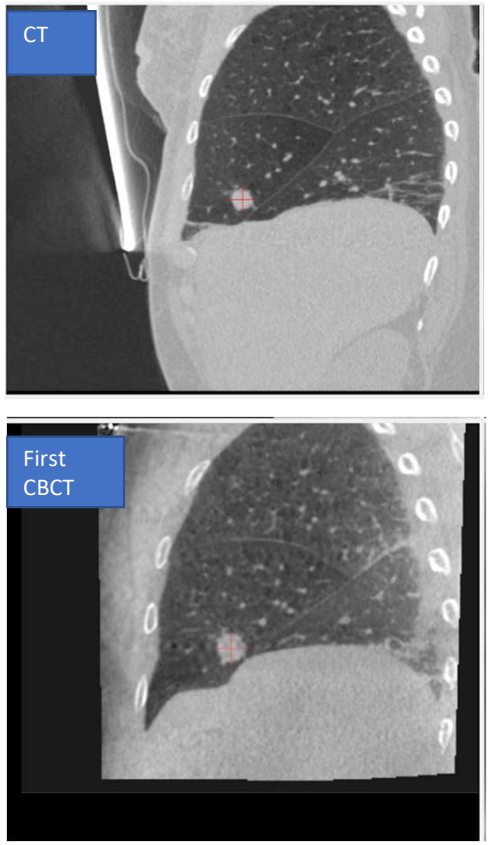
CT to Body divergence

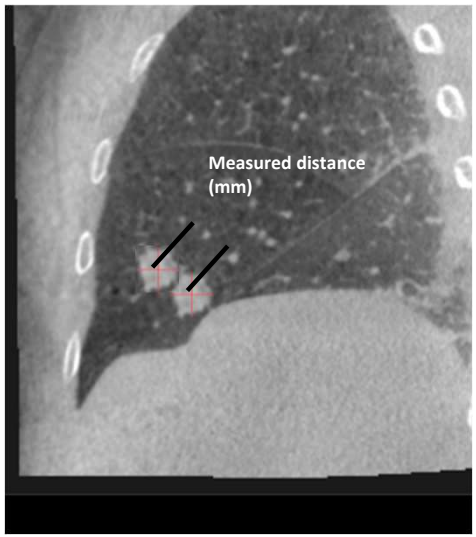


Note: airways and nodules both show mismatch

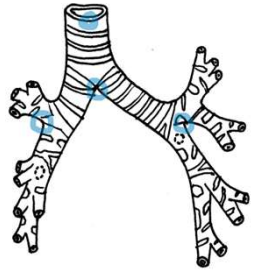
Pritchett, M. JTO 2018; Suppl (Oct):S403

Nodule Movement Measurements





CT to CT comparison
Planning CT vs CBCT
Registration based on central airway landmarks



Lobes	Divergence (mm) Avg (Max)
Upper lobes	12.6 (35.9)
Non upper lobes	18.4 (28.89)

Pritchett, M. JTO 2018; Suppl (Oct):S403

Why does CT2BD divergence occur?

- Atelectasis
- Tissue distortion from the catheter system
- Hemorrhage
- Myriad of other potential factors (pleural effusions, perturbations in anatomy, etc)

Bhadra K, Setser RM, Condra W, Pritchett MA. Lung Navigation Ventilation Protocol to Optimize Biopsy of Peripheral Lung Lesions. J Bronchology Interv Pulmonol. 2022 Jan 1;29(1):7-17. doi: 10.1097/LBR.0000000000000756. PMID: 33734150.

Pritchett MA, Bhadra K, Calcutt M, Folch E. Virtual or reality: divergence between preprocedural computed tomography scans and lung anatomy during guided bronchoscopy. J Thorac Dis. 2020 Apr;12(4):1595-1611. doi: 10.21037/jtd.2020.01.35. Erratum in: J Thorac Dis. 2020 Aug;12(8):4593-4595. PMID: 32395297; PMCID: PMC7212155.

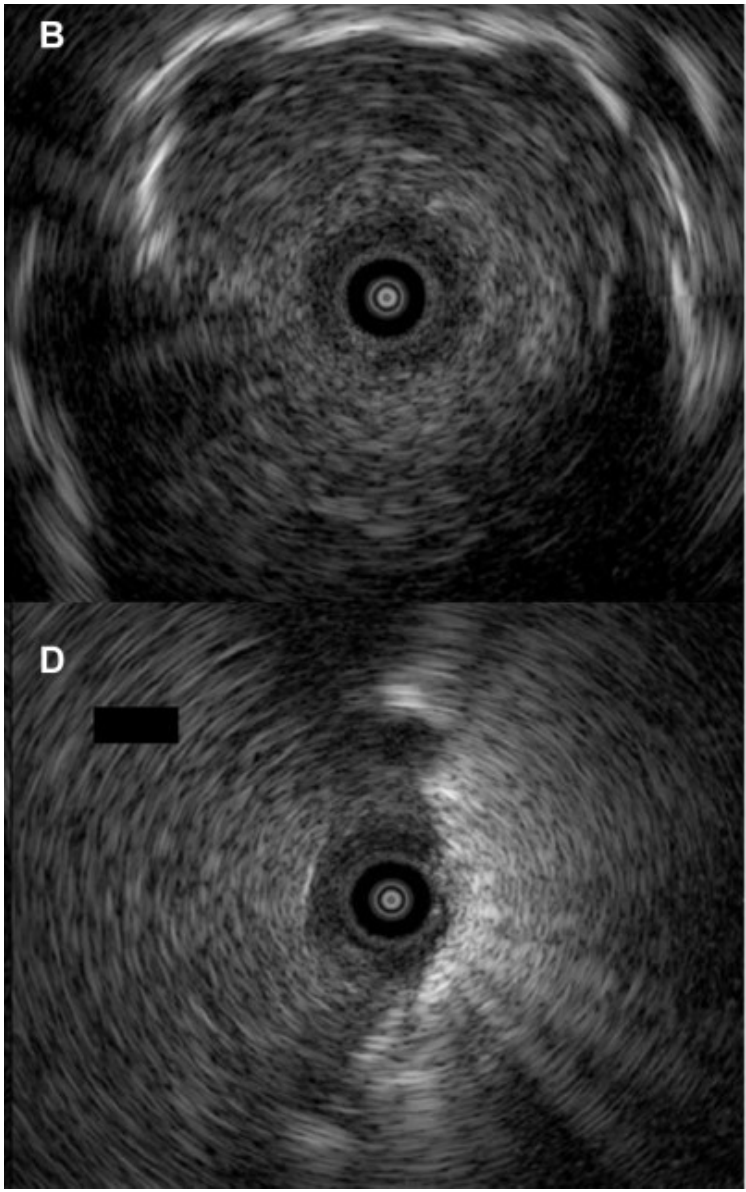
Radial probe localization

- REBUS is only lateral looking
- Images lack directionality making it difficult to obtain optimal target alignment
- Non-aerated lung or atelectatic lung and hemorrhage may produce a concentric pattern with sharply demarcated or irregular borders that mimic lung nodules.
- These false positives images can result in inappropriate provider confidence and biopsy of normal lung tissue.

1. Bhadra K, Setser RM, Condra W, Pritchett MA. Lung Navigation Ventilation Protocol to Optimize Biopsy of Peripheral Lung Lesions. J Bronchology Interv Pulmonol. 2022 Jan 1;29(1):7-17. doi: 10.1097/LBR.0000000000000756. PMID: 33734150.
2. Sagar AS, Sabath BF, Eapen GA, Song J, Marcoux M, Sarkiss M, Arain MH, Grosu HB, Ost DE, Jimenez CA, Casal RF. Incidence and Location of Atelectasis Developed During Bronchoscopy Under General Anesthesia: The I-LOCATE Trial. Chest. 2020 Dec;158(6):2658-2666. doi: 10.1016/j.chest.2020.05.565. Epub 2020 Jun 17. PMID: 32561439; PMCID: PMC8173777.

Radial probe localization

REBUS studies with high sensitivity are likely due to publication bias and should be interpreted with caution.



1. Sainz Zuñiga PV, Vakil E, Molina S, Bassett RL Jr, Ost DE. Sensitivity of Radial Endobronchial Ultrasound-Guided Bronchoscopy for Lung Cancer in Patients With Peripheral Pulmonary Lesions: An Updated Meta-analysis. Chest. 2020 Apr;157(4):994-1011. doi: 10.1016/j.chest.2019.10.042. Epub 2019 Nov 15. PMID: 31738928.
2. Sagar AS, Sabath BF, Eapen GA, Song J, Marcoux M, Sarkiss M, Arain MH, Grosu HB, Ost DE, Jimenez CA, Casal RF. Incidence and Location of Atelectasis Developed During Bronchoscopy Under General Anesthesia: The I-LOCATE Trial. Chest. 2020 Dec;158(6):2658-2666. doi: 10.1016/j.chest.2020.05.565. Epub 2020 Jun 17. PMID: 32561439; PMCID: PMC8173777.

We need to correct for CT-to-Body Divergence

- LungVision and Illumisite as well as CBCT– Corrects for CT2BD
- Current commercially available robotics do not have the ability to correct CT2BD.

Tool in lesion confirmation

- Tool in lesion gives the provider the highest level of confidence
- If you are not in it, you can adjust
- If you are in the lesion, you can utilize your biopsy tools (FNA, brush, TBBX, TBCB, BAL)
- Current robotics platforms cannot accomplish this on their own

Navigational Platforms Use a Virtual Target and Virtual Image Guidance

NOT REAL!

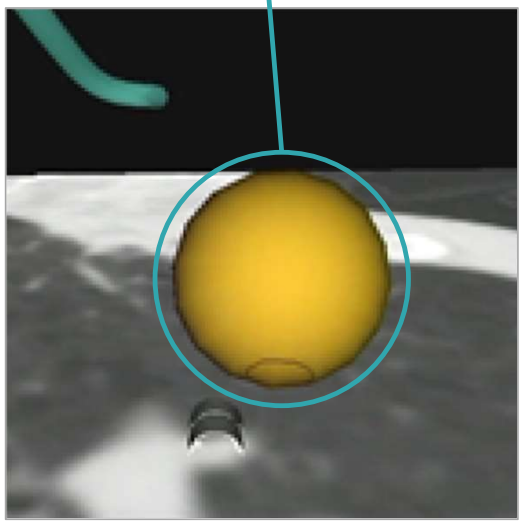


Image from Robotic Bronchoscope

Virtual Target

CT-to-Body Divergence

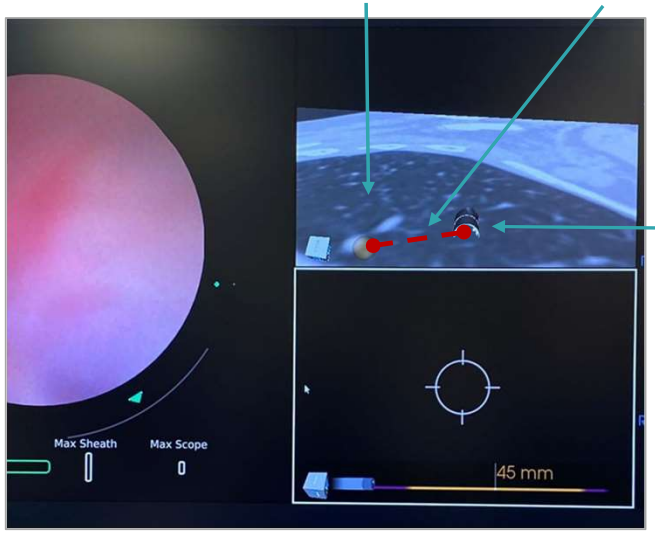
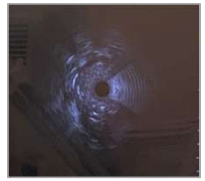


Image from Robotic Bronchoscope

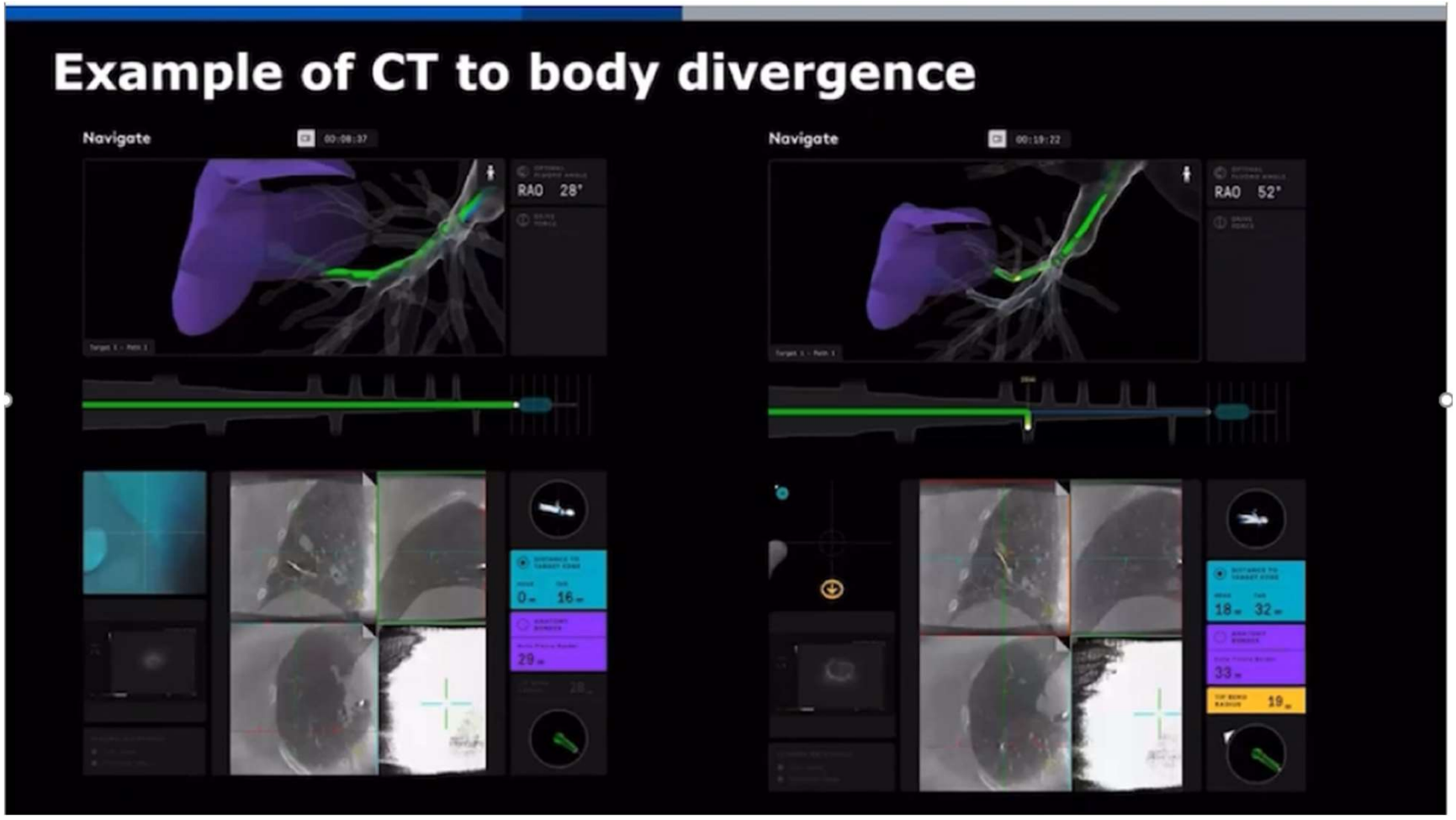
Actual Target Verified by r-EBUS



r-EBUS image

[1] Image courtesy of Ekeke CN, Vercauteren M, Istvaniczdravkovic S, Semaan R, Dhupar R. Lung Nodule Evaluation Using Robotic-Assisted Bronchoscopy at a Veteran's Affairs Hospital. Journal of Clinical Medicine. 2021; 10(16):3671.
[2] Images courtesy of Dr. D. Kyle Hogarth at the University of Chicago Medical Center.

CT to Body Divergence: NOT just an EMN thing…Shape Sensing Too



INTEGRATION OF SHAPE-SENSING ROBOTIC-ASSISTED BRONCHOSCOPY AND CONE-BEAM CT FOR THE BIOPSY OF PULMONARY NODULES

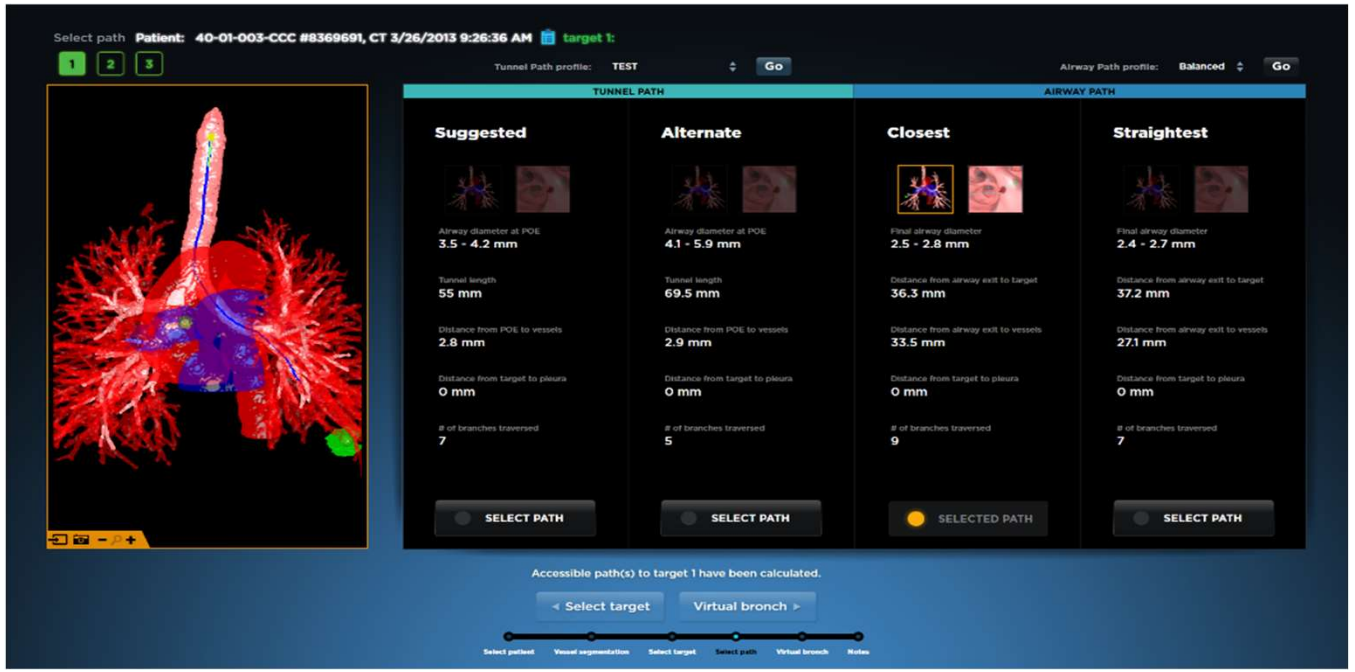
MICHAEL PRITCHETT LEAH MULLER DAVID OST JANANI REISENAUER ADNAN MAJID MICHAEL SIMOFF COLLEEN KEYES ROBERTO CASAL MIHIR PARIKH JAVIER DIAZ-MENDOZA SEBASTIAN FERNANDEZ-BUSSY AND ERIK FOLCH

- Nodule movement displayed random pattern in distance, amplitude or direction, and no trends seen relative to distance, location and diagnostic outcome
- 52% of nodules' centers were <10 mm from their pre-procedural centers
- 48% were displaced 10–35 mm; median nodule displacement was 9.6 (6.4, 16.0) mm.
- The direction of the CT-BD vector by lobe was not significantly different than zero.

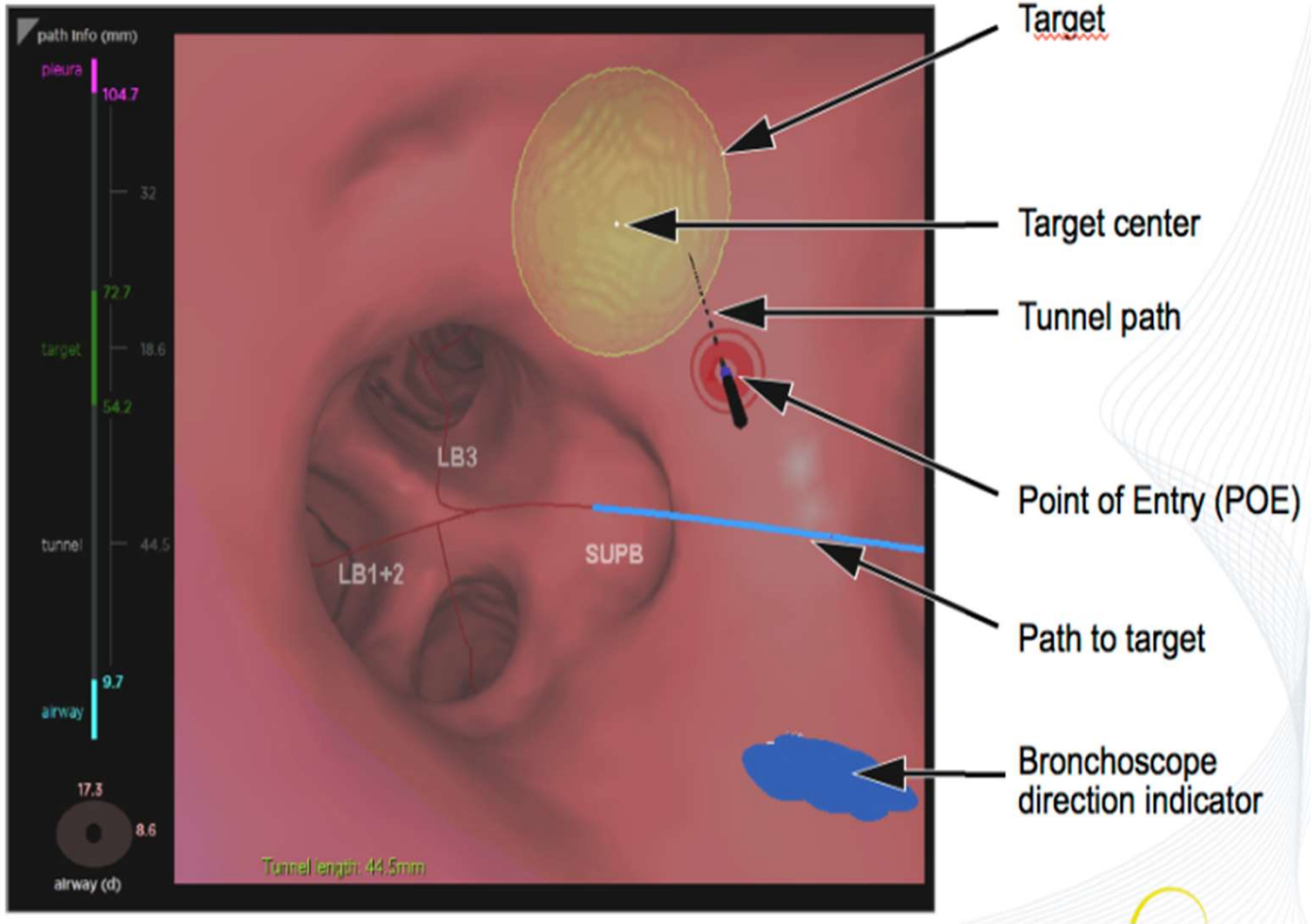
Maybe combining old and new?

How Archimedes Works

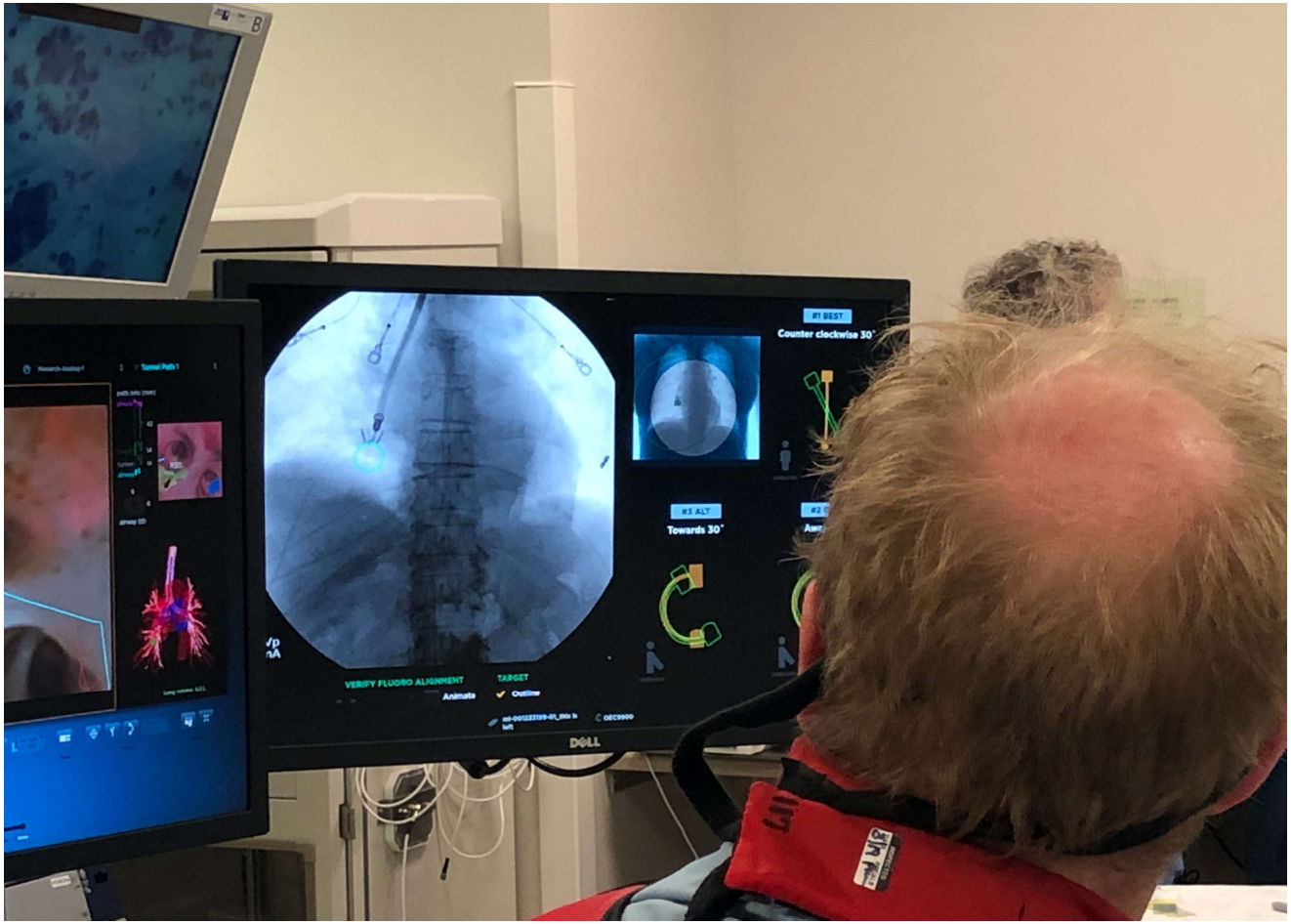
- Step 1: Import patient CT into Archimedes
- Step 2: Identify Vessels
- Step 3: Define target(s)
- Step 4: Calculate - software outlines vessels and multiple paths for safe approach to peripheral nodule: both airway and tunneling options provided



- Step 6: Review selected path in Virtual Bronchoscopy
- Step 7: Ready for procedure



The Core technology



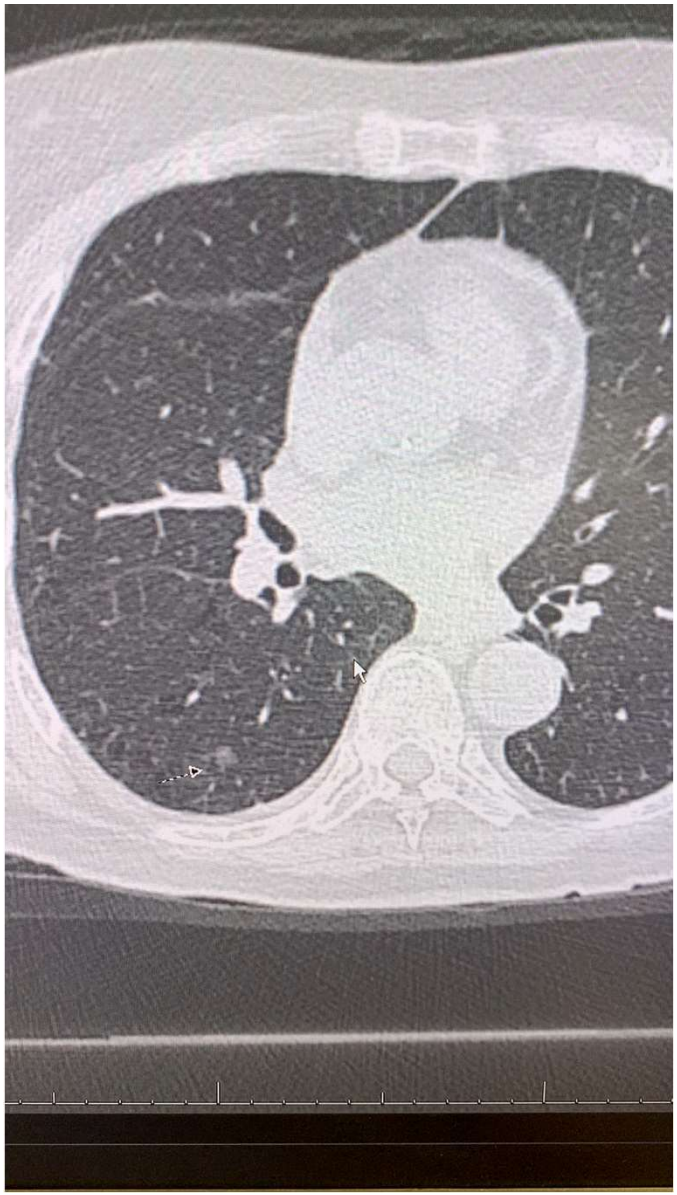
The Core technology

- Fused Fluoroscopy – integrates C-arm into video bronchoscope for live time, 3 dimensional view during procedure
- Able to superimpose nodule from CT scan onto fluoro view
- Allows both Guided TBNA or tunneling BTPNA procedure (Bronchoscopic TransParenchymal Nodule Access)
- Guiderails to ensure an avascular path if tunneling

The Core technology

Case

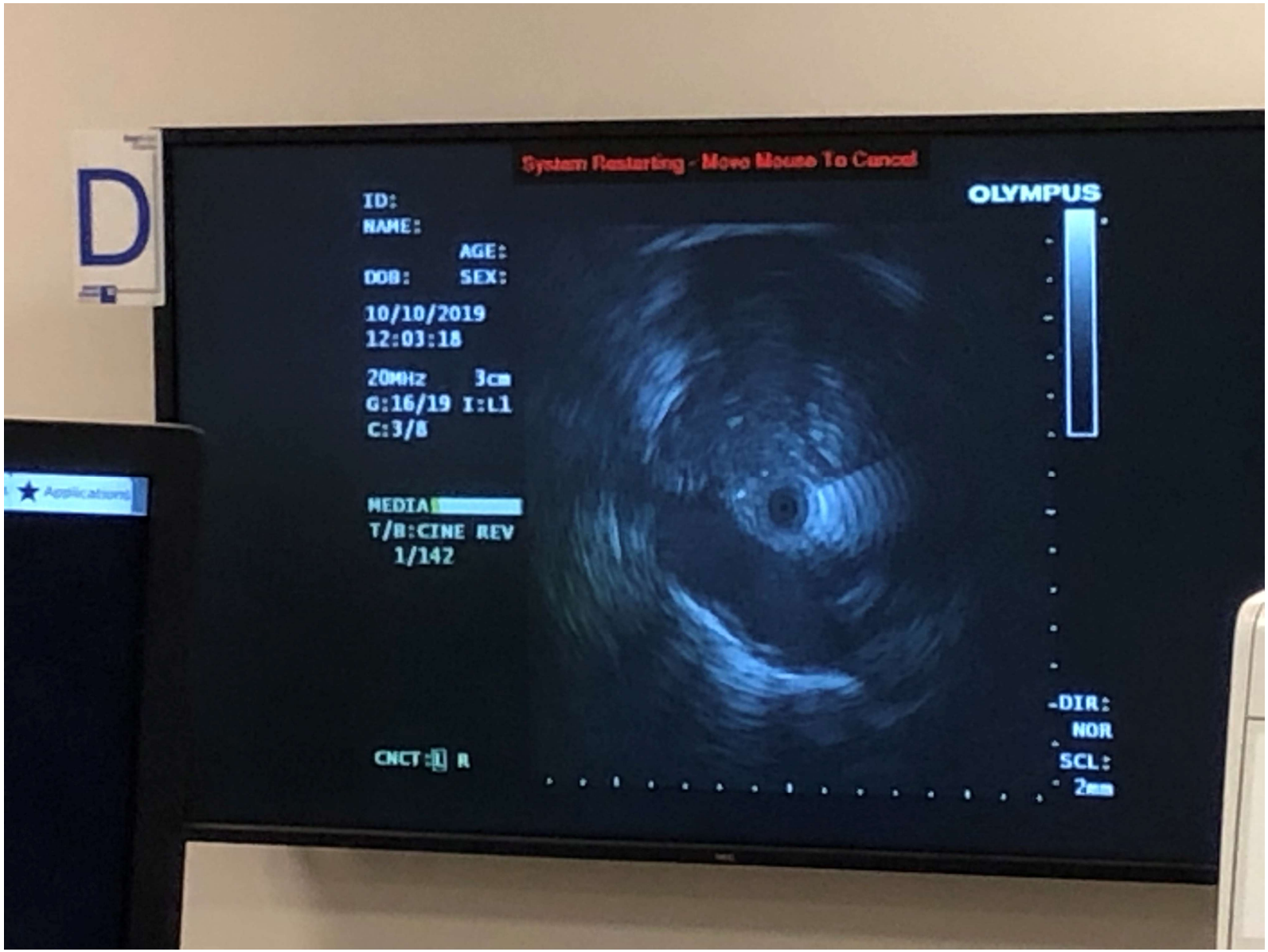
- 85 y.o. with lymphoma history (NED). Multiple GGOs in the lung
- f/u imaging show RML nodule that is 1.3cm in size and is PET positive (nothing else lights up). Along the minor fissure



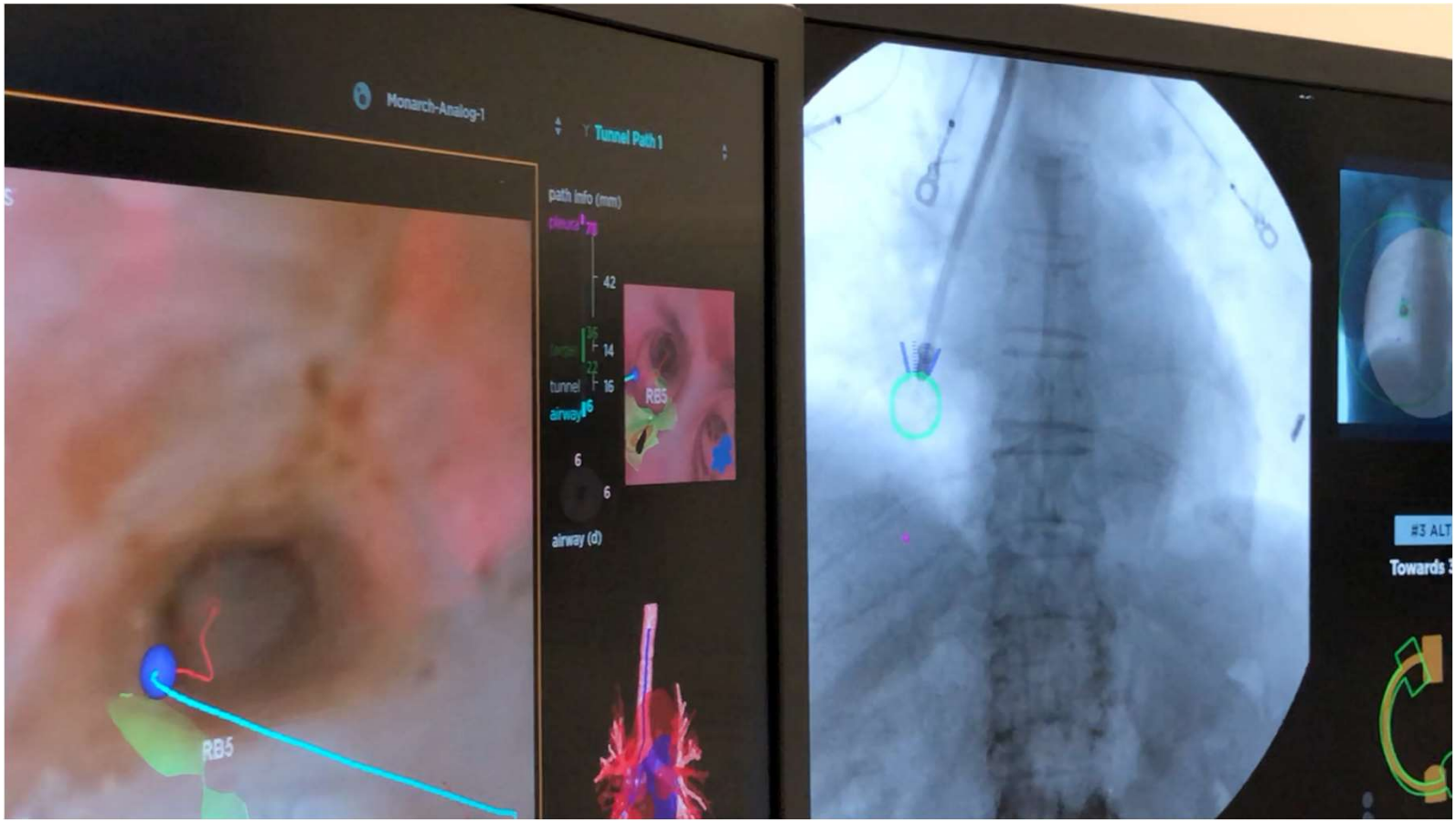

Archimedes
OLYMPUS
MONARCH

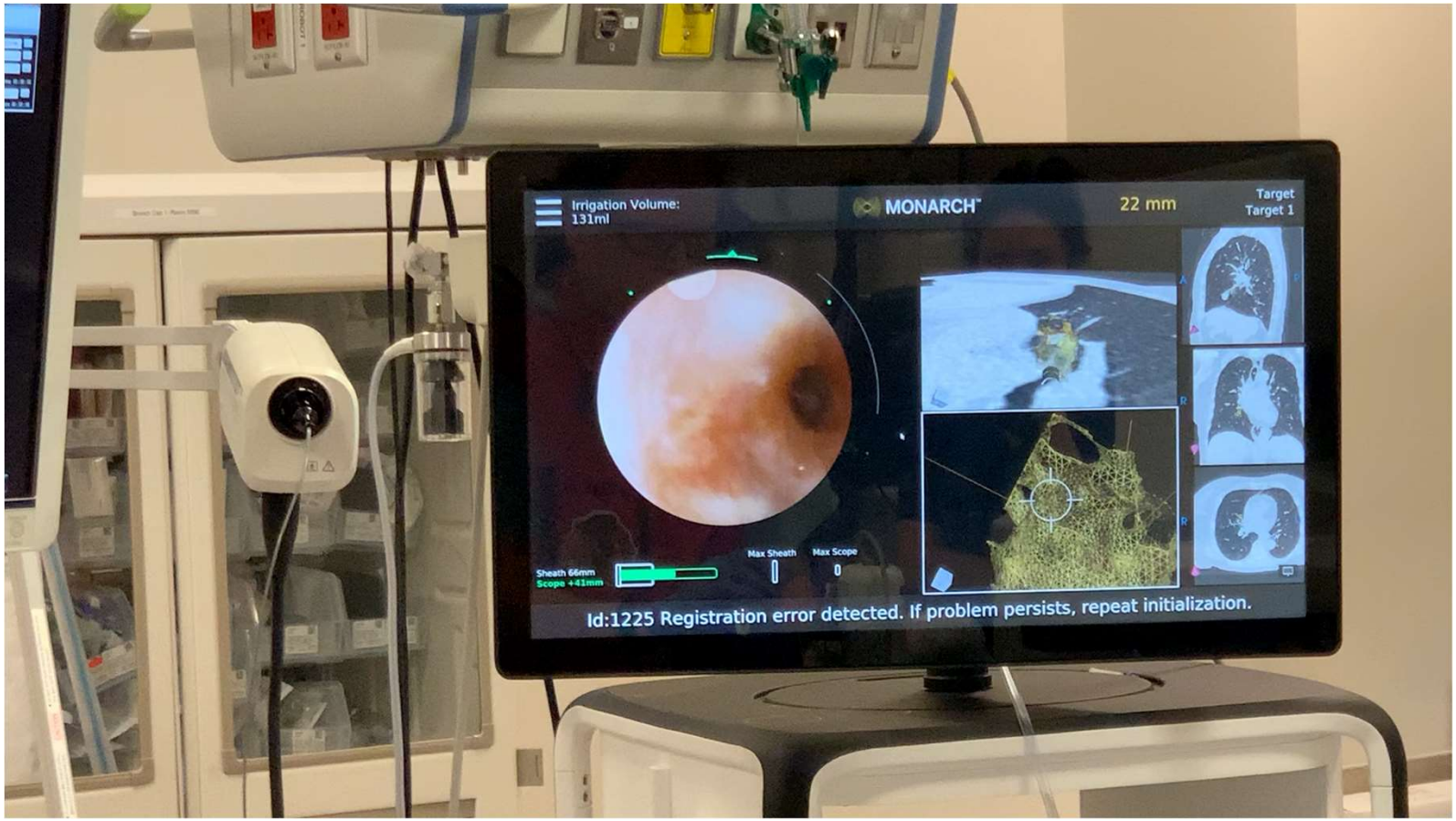

STERIS
Archimedes

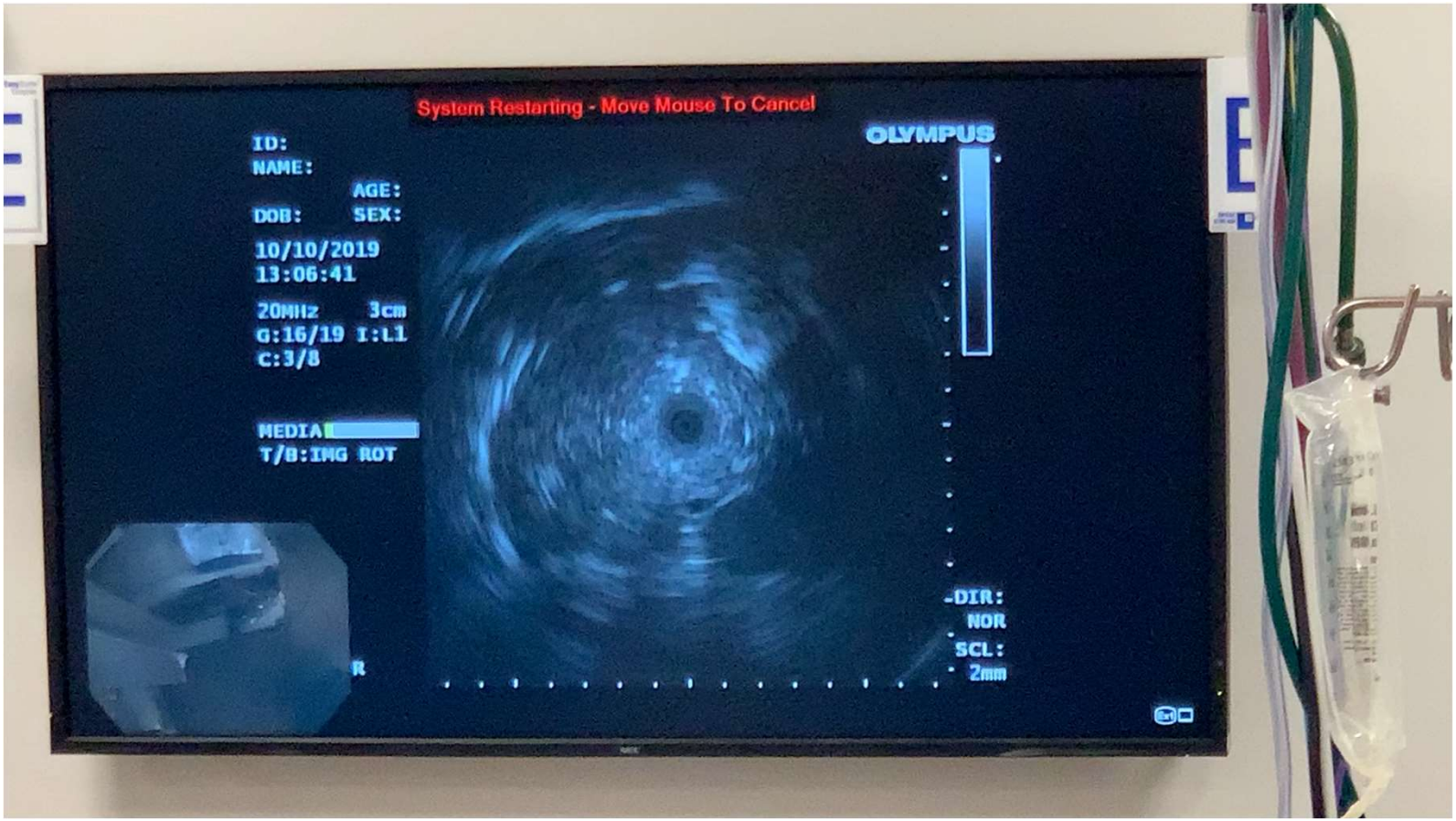

STERIS
OLYMPUS

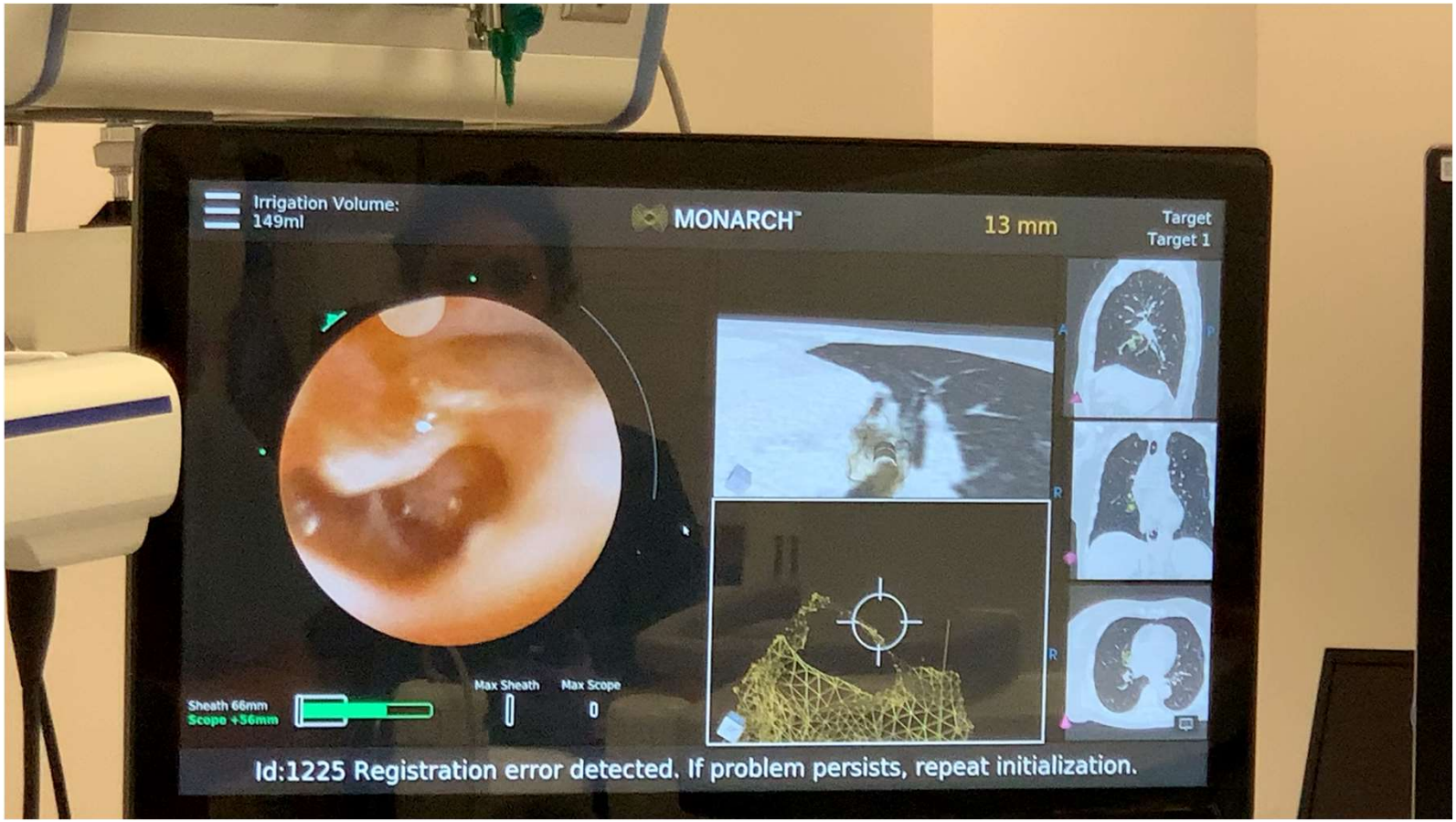

System Restarting - Move Mouse To Cancel
OLYMPUS
ID:
NAME:
AGE:
DOB:
SEX:
10/10/2019
12:03:18
20MHz
3cm
G:16/19
I:L1
C:3/8
MEDIA
T/R:CINE REV
1/142
DIR:
NOR
SCL:
2mm
CNCT:
R


Irrigation Volume:
131ml
MONARCH
26 mm
Target
Target 1
Id:1225 Registration error detected. If problem persists, repeat initialization.


Monarch-Analog-1
Tunnel Path 1
path info (mm)
42
14
16
tunnel
airway
6
6
airway (d)
RB5
RB5
#3 ALT
Towards


Irrigation Volume:
131ml
MONARCH™
22 mm
Target
Target 1
Max Sheath
Max Scope
0
Sheath 66mm
Scopa +41mm
Id:1225 Registration error detected. If problem persists, repeat initialization.


System Restarting - Move Mouse To Cancel
ID:
NAME:
AGE:
DOB:
SEX:
10/10/2019
13:06:41
20MHz
3cm
G:16/19 I:L1
C:3/8
MEDIA
T/B:IMG ROT
R
OLYMPUS
DIR:
NOR
SCL:
2mm


Irrigation Volume:
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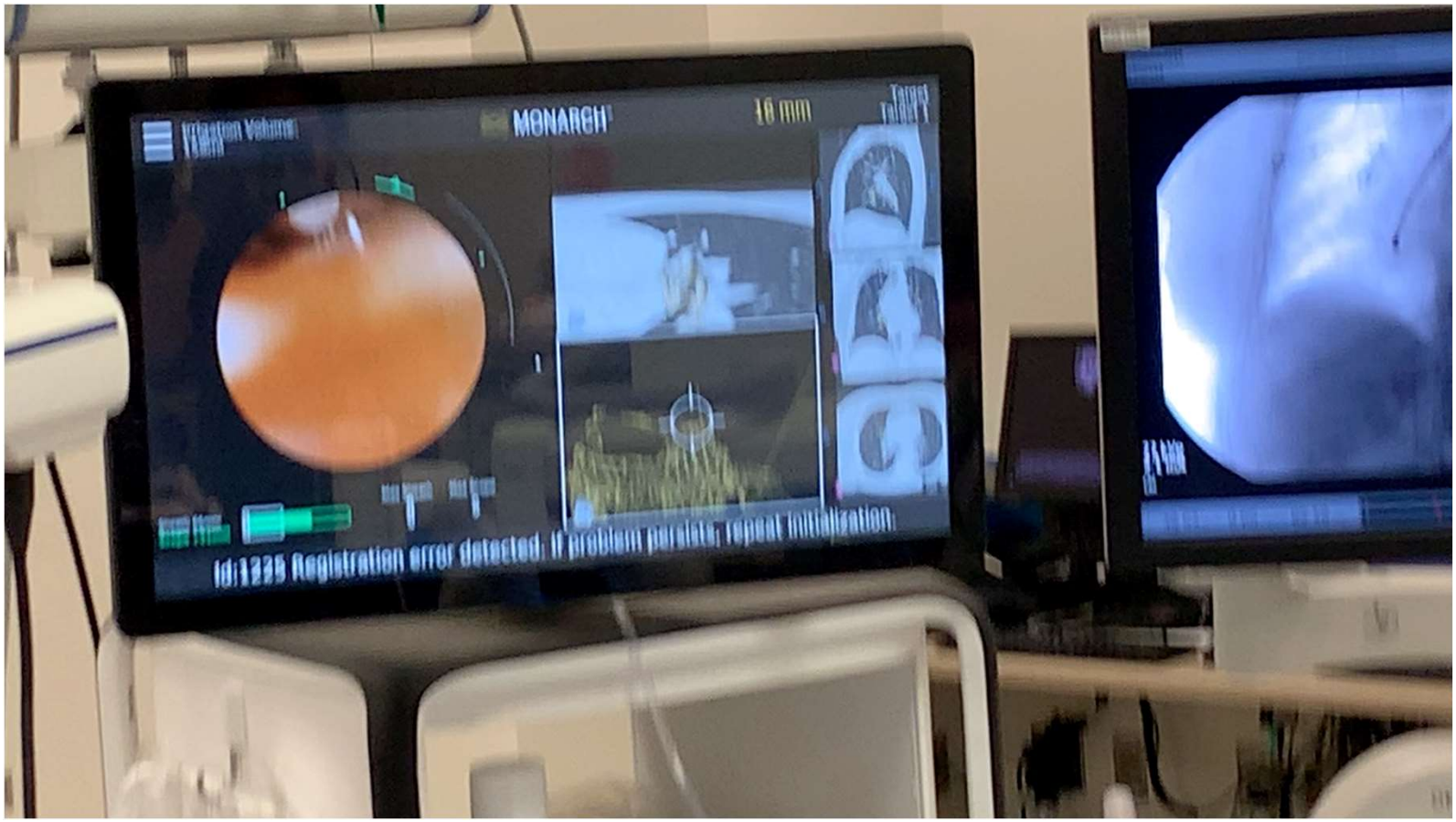
MONARCH™
13 mm
Target
Target 1
Max Sheath
Max Scope
Sheath 66mm
Scope +56mm
Id:1225 Registration error detected. If problem persists, repeat initialization.

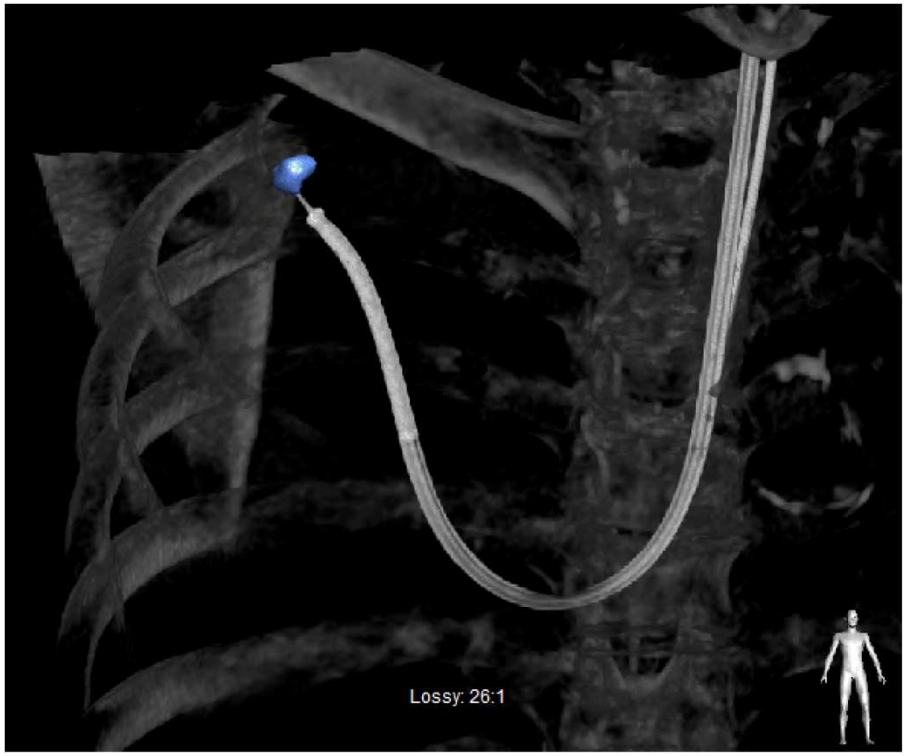

MONARCH
16 mm
Id:1225 Registration error detected. If problem persists, repeat initialization.

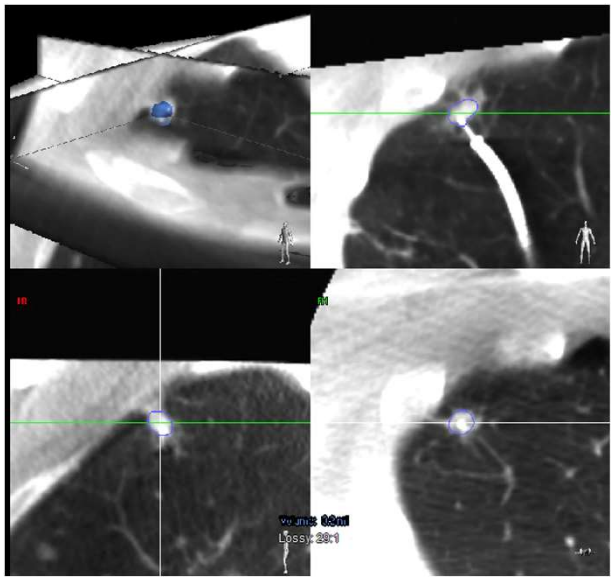

System Restarting - Move Mouse To Cancel
IMAGE STREAM
Easy
INPUT
MENU
SCROLL
PIP

How Are We Addressing the Gaps That Exist in Robotics with CT to Body Divergence?

- The bigger gaps (CT to body divergence, no real-time lesion updates) that exist still require additional adjunct technologies.
- CBCT and Body Vision are two examples which could be used to solve these problems

Cone Beam CT: great, but $$$$$$$

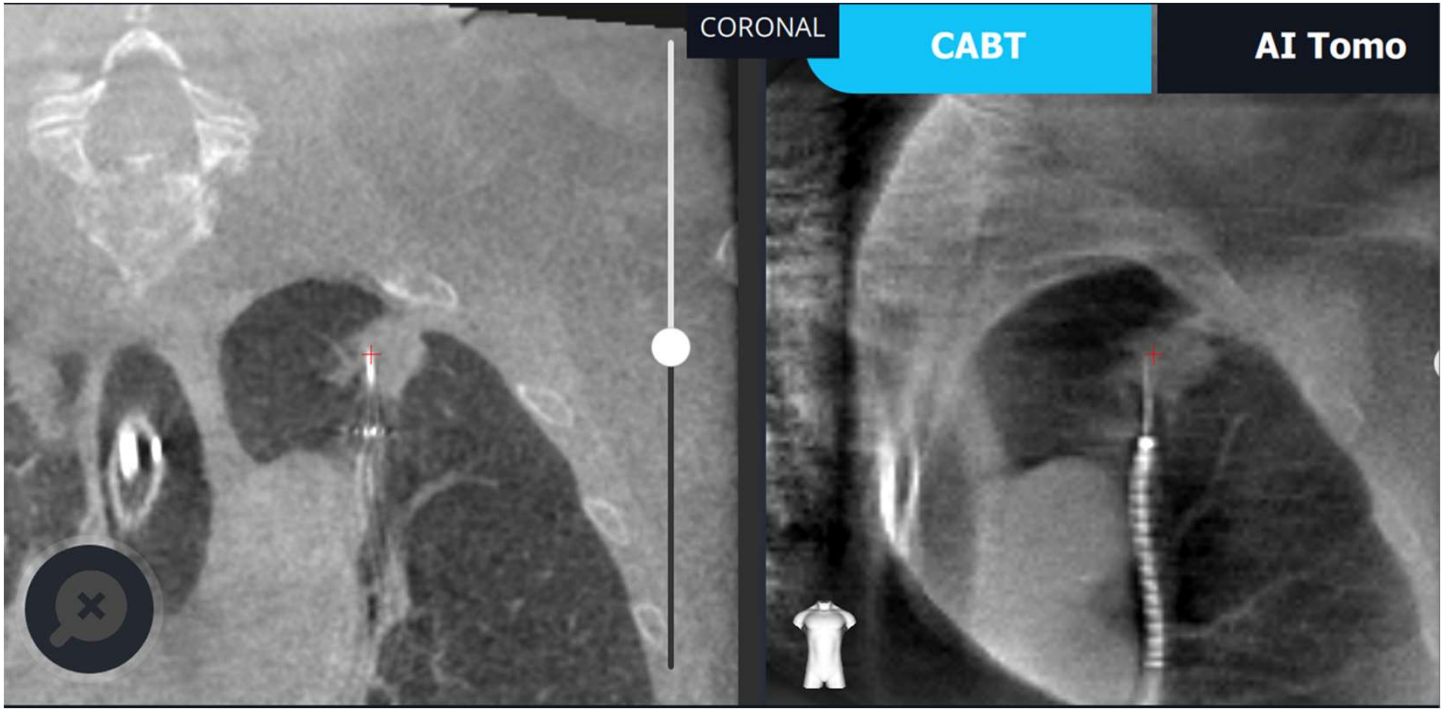




Providing a ‘CBCT like’ imaging

Phillips CBCT

Body Vision Intraoperative CT Imaging
(real time, from GE 9900 c-arm)

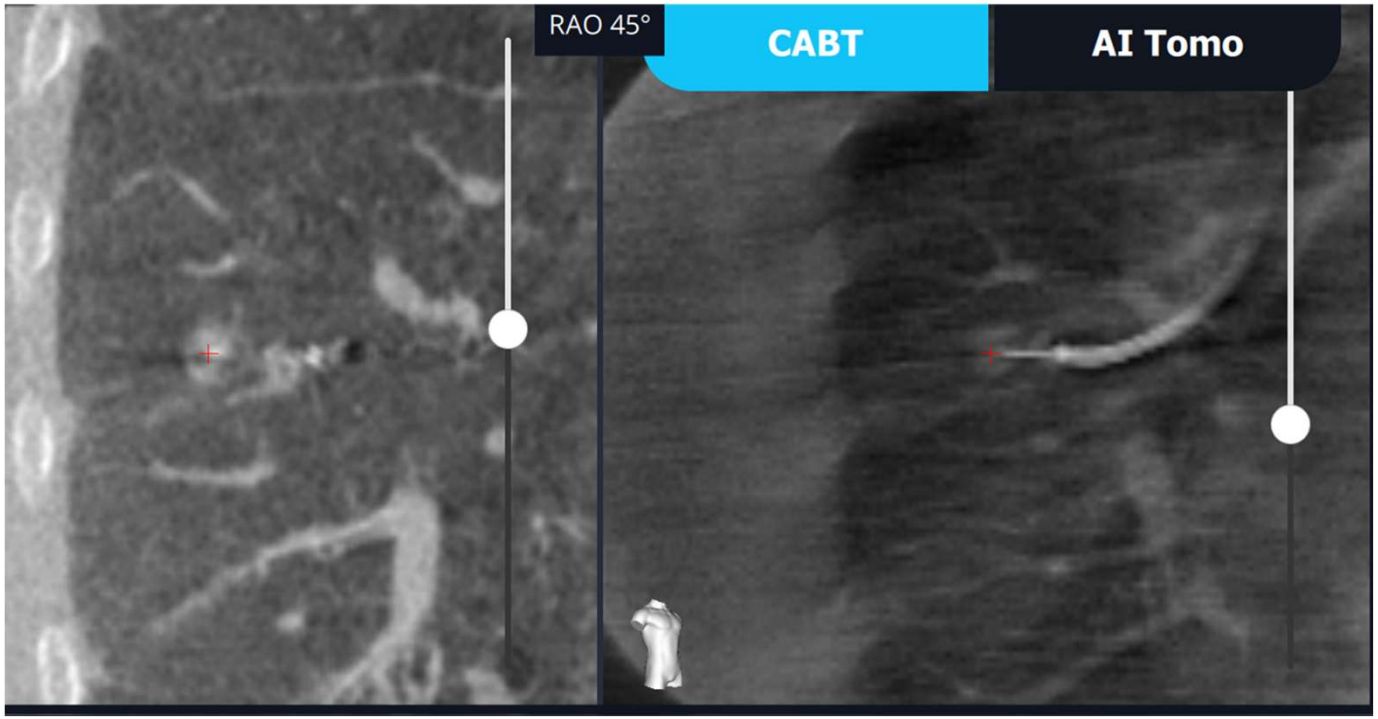


22mm solid LUL

Providing a ‘CBCT like’ imaging

Phillips CBCT

Body Vision Intraoperative CT Imaging
(real time, from GE 9900 c-arm)



9mm solid RLL

LungVision
and
The Monarch:

Real time Tomosynthesis but
without direct integration

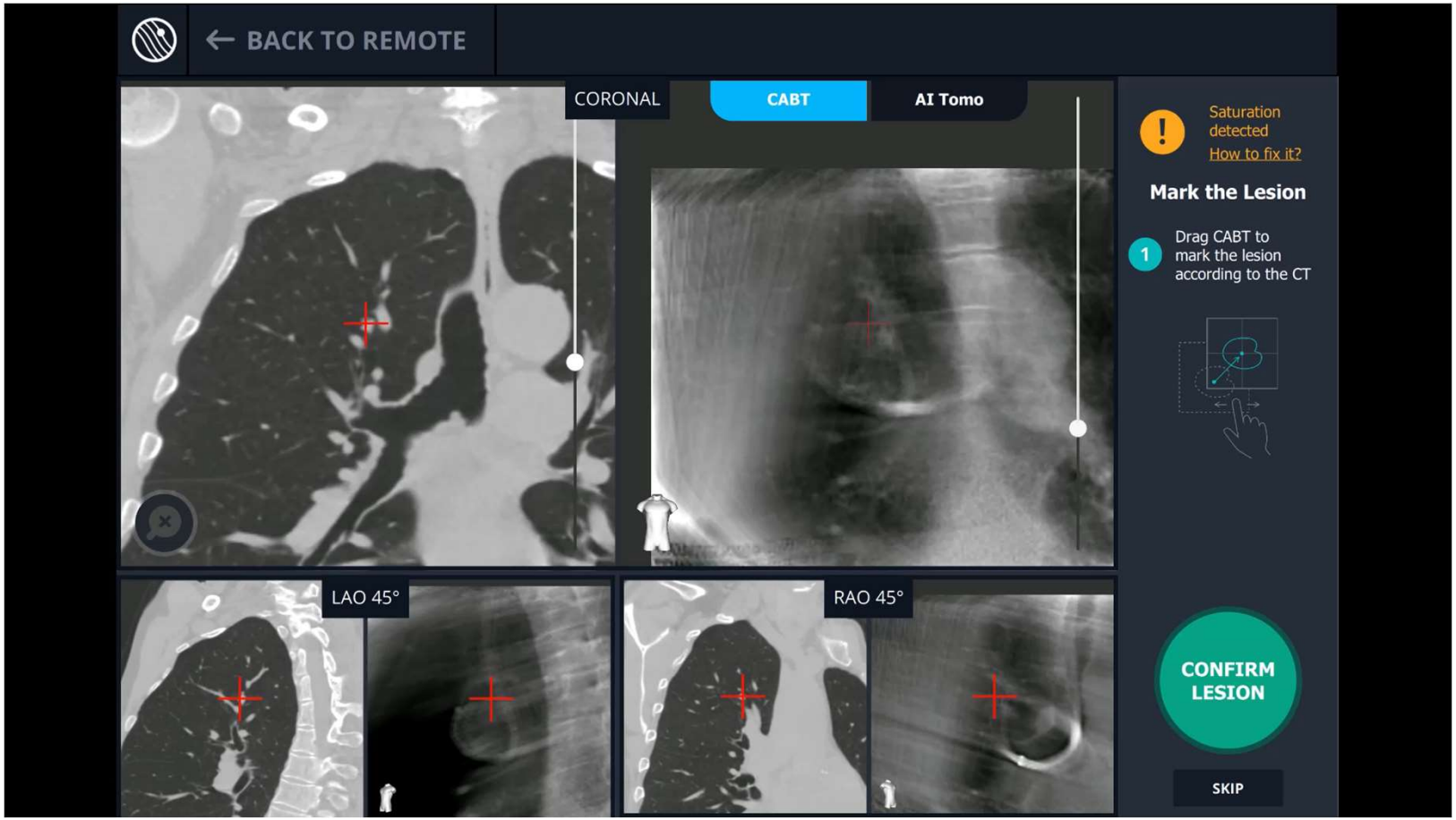
Case

- 64 y.o. smoker with history of colon cancer (resected and cured) and complex renal cyst (work-up pending for malignancy). During workup, found to have a nodule
- 8 mm lesion in the RUL
- PET positive. Also has activity in the area of prior colon resection (was negative on recent colonoscopy). Possible activity in the renal lesion.

Navigation with Monarch

- Usual plan developed.
- 8mm lesion in the RUL without a direct airway into it.
- Bracketed by 2 blood vessels

CABT- Tool in lesion



Navigation and Biopsies

Metastatic Renal cell

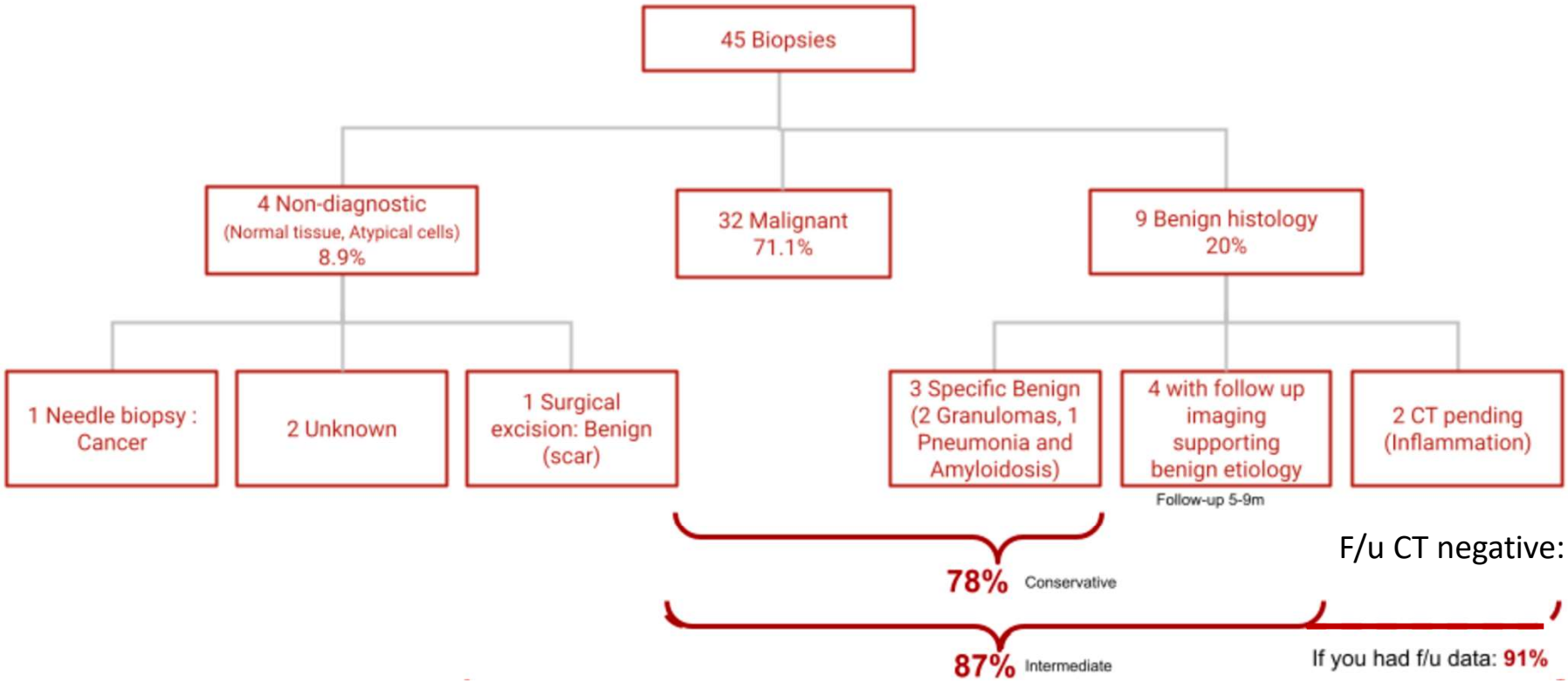
- (1st needle pass)

Single Center – Single User data to Date

Not peer reviewed.

45 consecutive cases using Monarch with Lung Vision are presented here
Data is retrospective
Single Center
One user’s data

Location (N=45) LLL LUL RLL RML RUL	**N (%)** 3 (6.7) 11 (24.4) 9 (20.0) 7 (15.6) 15 (33.3)
Size (mm)	**Mean±SD** 16.1±7.8
Robot time (Min)	**Mean±SD** 56.4±19.6
Procedure time (Min)	**Mean±SD** 75.4±22.6



F/u CT negative: yield is 91%


BACK TO REMOTE
100%
CORONAL
CABT
AI Tomo
LAO 45°
RAO 45°
Mark the Lesion
1
Drag CABT to mark the lesion according to the CT
CONFIRM LESION
SKIP

Robot 2.0 is coming…perhaps will solve?

- A system that can incorporate multiple technologies (reach, stability, vision at all times but finally adds real-time lesion updates to the navigation AND augmented fluoroscopy

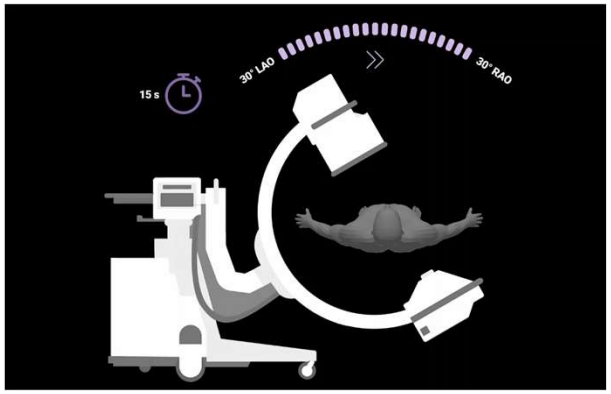
- Take your current Robot, but add the capabilities of FluroNav (target updating) and LungVision (augmented fluro and 3D views) BUILT INTO THE SYSTEM

- The Galaxy System

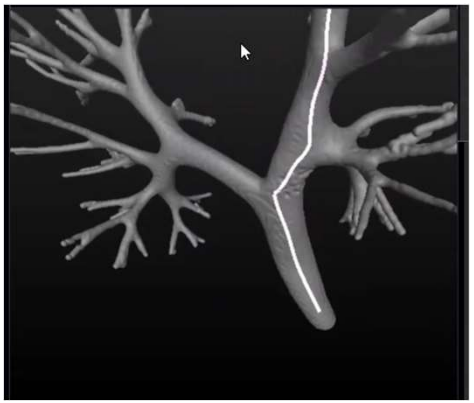
Noah's platform is being designed with the intent to improve surgery. All information in this presentation represents the design goals of Noah Medical. The product has not been cleared by the FDA and is not for commercial sale in the United States

Addressing Gaps in Robotics – TiLT+ Technology™

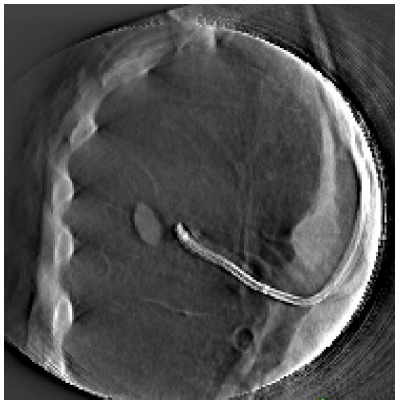
- **TiLT+ Technology** incorporates tomosynthesis directly into the Galaxy System
- By utilizing the fluoro equipment that is already available and routinely used, an intraoperative update of the lesion location can be provided

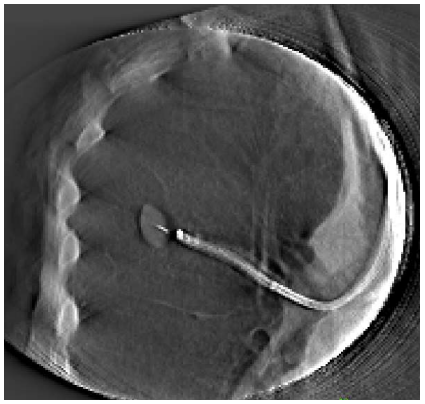


C-Arm Spin



Lesion Location is Updated in Real-Time





Tool-In-Lesion Confirmed

TiLT = Tool in Lesion Tomography

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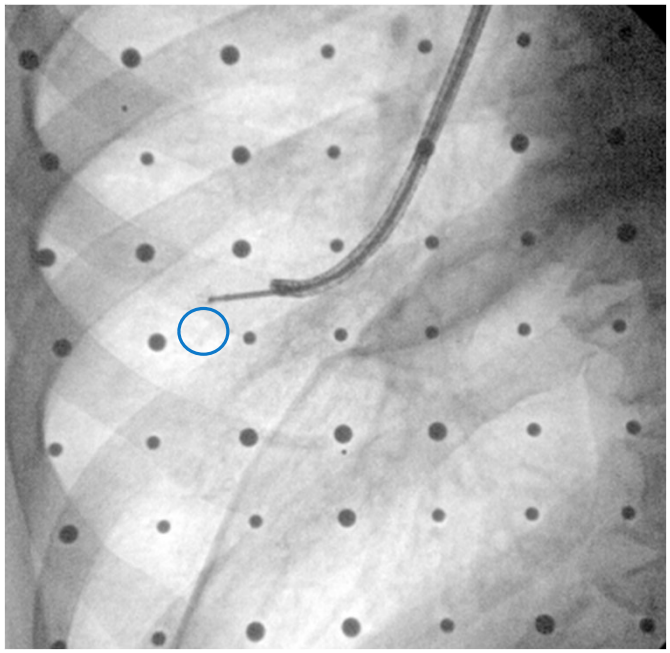
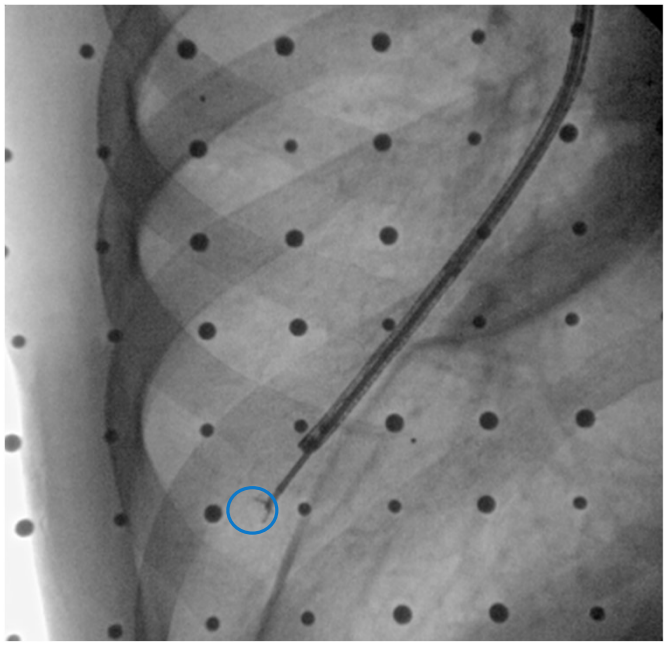
TiLT+ Technology™ & Augmented Fluoroscopy

- TiLT+ Technology integrates augmented fluoroscopy to provide a graphic overlay for real-time, simultaneous visualization of both tool and lesion



Visualize lesion in relation to tools



Orient and readjust in real-time for accurate deployment

Single Use Bronchoscope Technology

- Galaxy's single use disposable bronchoscope is built for performance and efficiency
- The always-on-camera scope provides direct visual confirmation as physicians navigate to the lesion
- The single use feature allows for improved efficiency, workflow and could potentially reduce the risk of cross contamination

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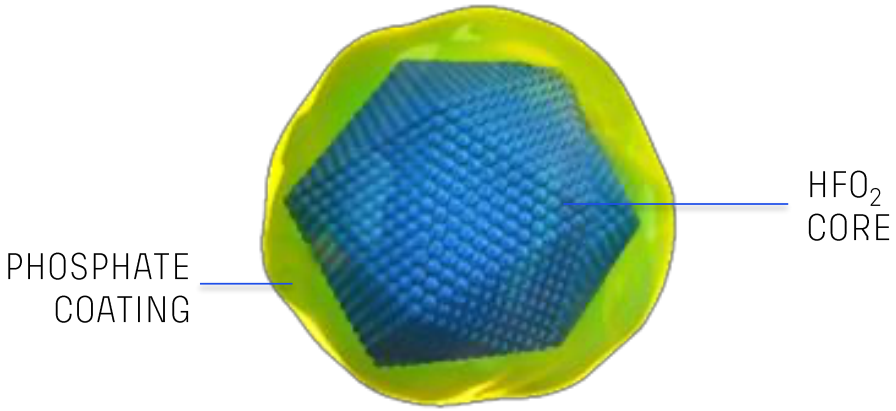
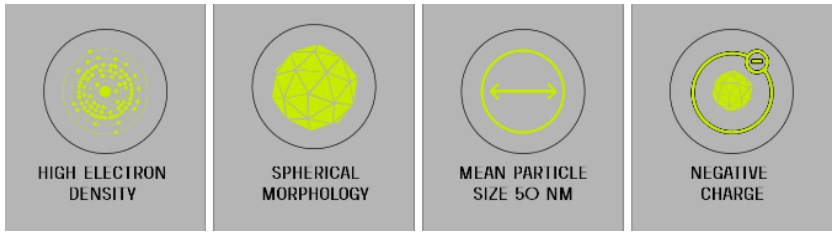
Therapy

NBTXR3 is a first-in-class radioenhancer

- Designed at the nanoscale to increase the energy dose deposition of radiotherapy within the tumor
- Administered by a direct and single intratumoral injection as a percentage of baseline tumor volume
- Activated by radiotherapy to trigger local physical cell death and activate the immune system to yield a systemic effect

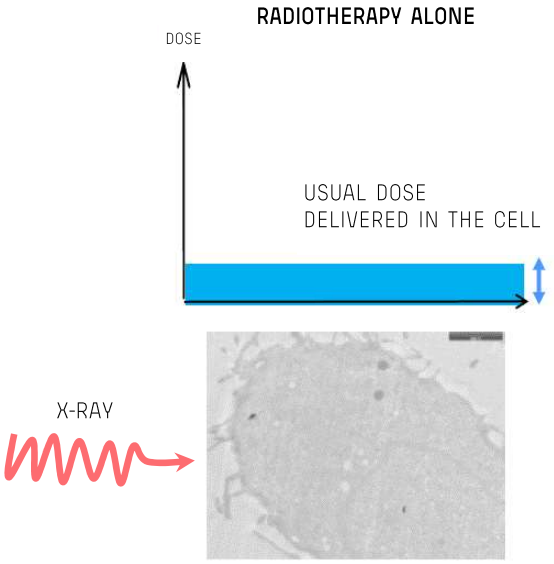


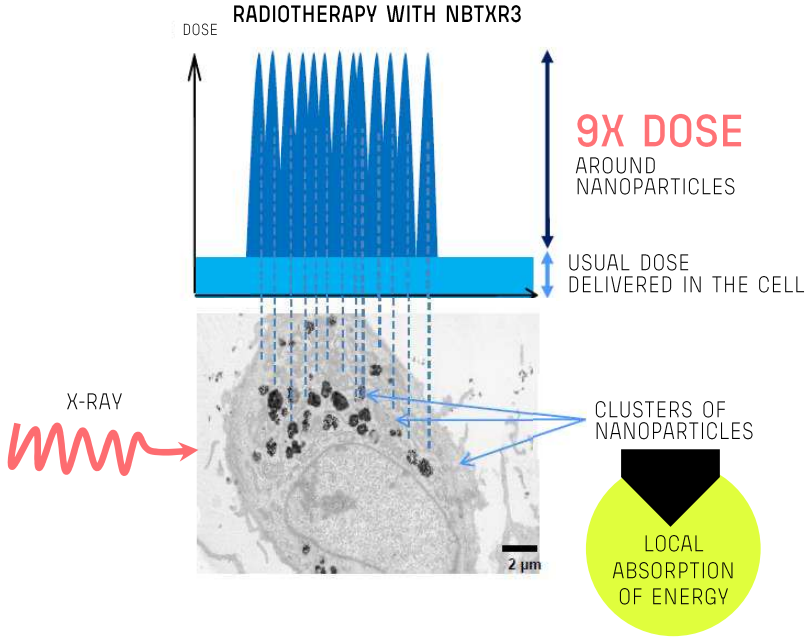
NBTXR3 IS A SUSPENSION OF NANO-SIZED PARTICLES COMPOSED OF A CORE OF HAFNIUM OXIDE FUNCTIONALIZED WITH PHOSPHATE GROUPS ON THE SURFACE



NANOBIOTIX

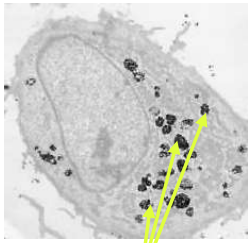
NBTXR3 has a universal physical mechanism of action





NANOBIOTIX

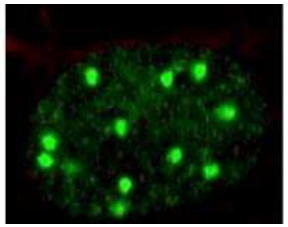
NBTXR3 triggers cellular destruction and activates an adaptive immune response



CLUSTERED NANOPARTICLES
IN CYTOPLASM

NBTXR3 + RT

LARGE ENERGY DEPOSITION IN
A NANO-VOLUME
 PHYSICAL DAMAGE



- STRUCTURAL DAMAGE
- DNA DAMAGE
- STRESS
- IMMUNOGENIC CELL DEATH
- CGAS-STING PATHWAY ACTIVATION

DENDRITIC CELL ACTIVATION

CD4 & CD8 ACTIVATION

TUMOR INFILTRATION
AND CELL KILLING

DIRECT CELL DEATH
(APOPTOSIS, NECROSIS...)

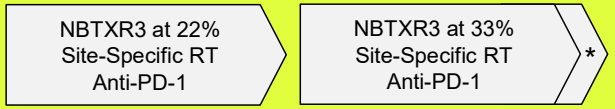
NANOBIOTIX

NANORAY-1100:
A Phase I Study of NBTXR3 Activated by RT for Patients with Advanced Cancers Treated with an Anti-PD-1 Therapy

3 cohorts that are anti-PD-1 naïve or non-responsive:

1. LRR or R/M HNSCC amenable to re-irradiation
2. Lung metastases from any primary eligible for PD-1
3. Liver metastases from any primary eligible for PD-1*

Standard 3+3 Dose Escalation



***Cohort 3 will escalate to 42% NBTXR3 dose level in the absence of excessive DLTs**

Key Inclusion Criteria:

- ECOG PS 0-2
- Life expectancy >12 weeks
- Has at least one measurable and injectable tumor
- PD-1 non-responders: SD or PD between 8 and 12 weeks after initiating anti-PD-1 therapy

Key Exclusion Criteria:

- History of severe IR-AEs related to anti-PD-1
- Extensive metastatic disease unamenable for RT
- More than one prior line of immunotherapy
- Not recovered from AEs due to prior therapies

Primary Endpoints

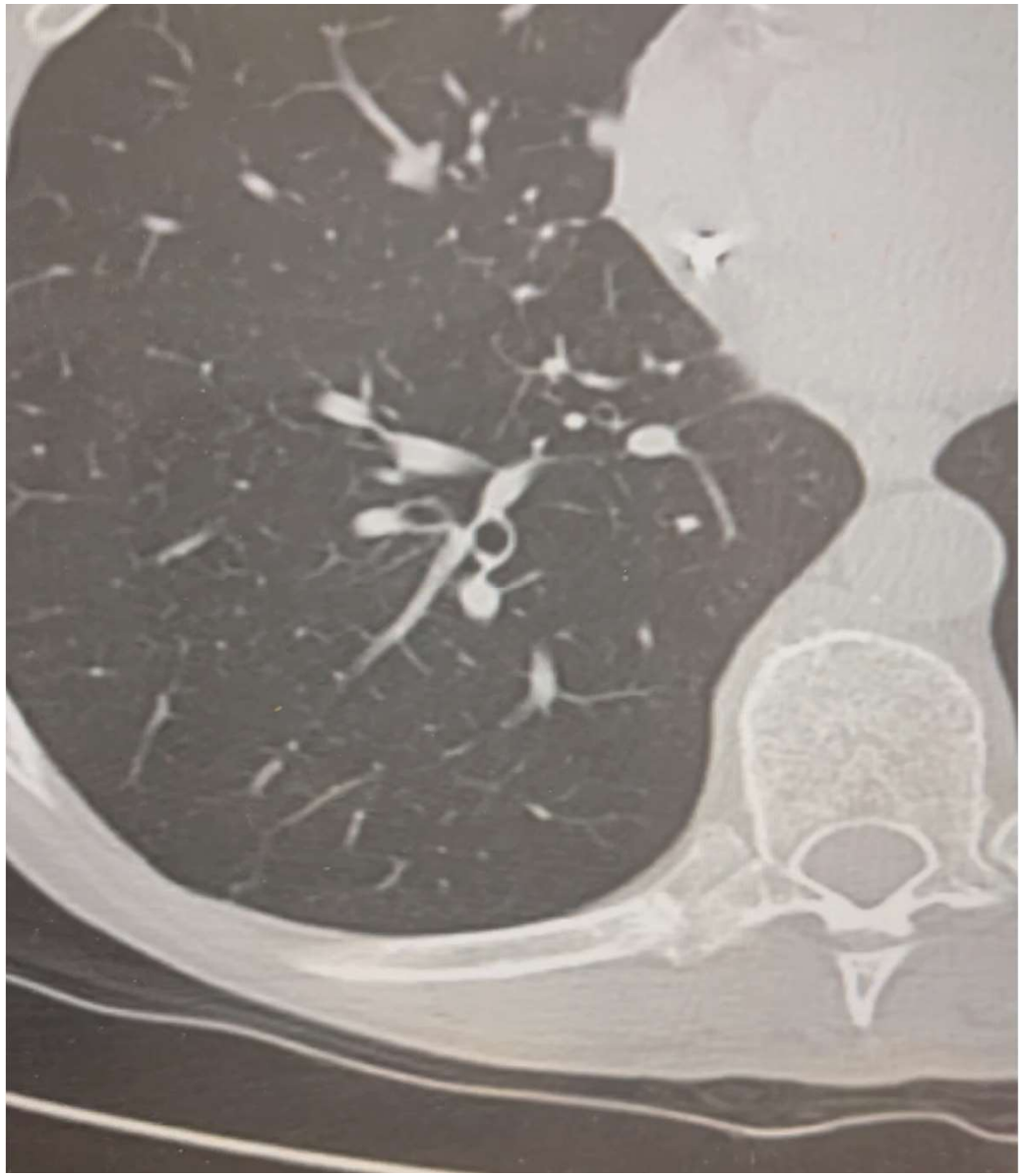
- DLTs, MTDs, RP2D

Secondary Endpoints

- Objective Response Rate
- Safety and Feasibility
- Body Kinetic Profile

Sample Size = 60

RT: radiotherapy; LRR: locoregional recurrent; R/M: recurrent and metastatic; ECOG: eastern cooperative oncology group; PS: performance status; SD: stable disease; PD: progressive disease; IR: immune-related; AEs: adverse events; DLT: dose limiting toxicity; MTD: maximum tolerated dose; RP2D: recommended phase 2 dose



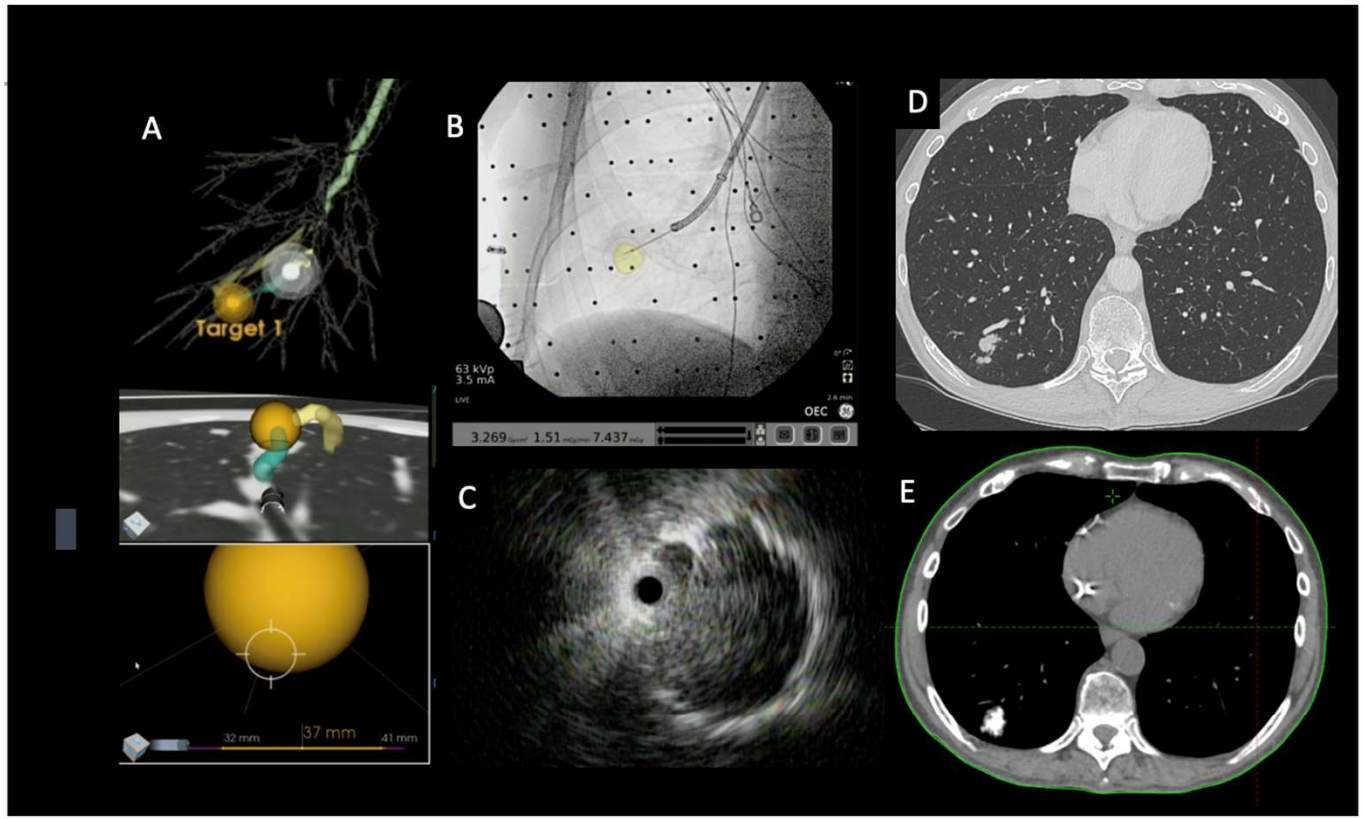


Figure 1: Case 1. Pathway, augmented fluoroscopy, radial EBUS and CT scanning pre and post injection. A – Monarch platform planning software image showing the scope aligned and positioned at 3 cm from the target. B – BodyVision confirmation of needle in target. C – Radial EBUS showing an eccentric lesion. D- CT before NBTXR3 injection; E- CT scan after NBTXR3 injection, performed for radiotherapy planning, showing the hyperdense radiopaque material

Go Hawks!!!

Thank You

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773-991-5812