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**2022 World Conference
on Lung Cancer**

AUGUST 6-9, 2022 | VIENNA, AUSTRIA



Pulmonary – From Diagnostics to Therapeutics

Best of WCLC 2022

**Nicholas Stollenwerk, MD
University of California, Davis**



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Presenter Disclosures

I do not have any relevant financial relationships to disclose





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Overview

- 1) Lung Cancer Screening and Imaging
- 2) Bronchoscopy – diagnostics and therapeutics





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Lung Cancer Screening

Take home messages:

- There is no one-size-fits-all in LCS.
- Lung Cancer Screening rates are low, for many reasons.
- Non-radiographic screening tests are needed and will add to current image-based screening.
- Machine learning will likely help us screen in the future.





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Lung cancer screening patient experiences and satisfaction: Quantitative and qualitative findings from a survey study

Jaileene Pérez-Morales¹, Jarred Miller¹, Haley Tolbert¹, Rashmi Pathak¹, Monica Reyes¹, Jhanelle E. Gray¹,
Vani N. Simmons¹, Gwendolyn P. Quinn², and Matthew B. Schabath¹

¹H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, USA; ²New York University Grossman School of Medicine and Perlmutter Cancer Center, New York, NY, USA

Figure 5: Theme and subthemes of patient's response to open-ended questions

Positive Experiences	Negative Experiences
<ul style="list-style-type: none">• Always treated very well by radiation staff• I received a level of comfort to find out that I have probably no long-term issues as a result of my smoking• The medical staff and administrative staff consistently deliver the highest level of care and attention to myself and other family members at Moffitt's facilities• All went well as advertised. Appointment was met by hospital staff in timely manner and all were efficient at their jobs	<ul style="list-style-type: none">• Occasional difficulty in scheduling appointment• Distance from Sarasota and lack of 2-way communication with radiologists/screening doctors.• No return calls and no offer to review results.• Charges that continue after I pay my \$150 each year.• No follow up, lack of understanding of results• Billing issues

This all makes a lot of sense!



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The Correlation Between Exhaled Volatile Organic Compounds Using Breath Analyzer with Interleukin-23 (IL-23) in Lung Cancer

Raden Dicky Wirawan Listiandoko*, Ungky Agus Setyawan, Triwahju Astuti

Department of Pulmonology and Respiratory Medicine Medical Faculty of Universitas Brawijaya, Dr. Saiful Anwar General Hospital, Malang, Indonesia

- Why measure eVOCs? Non-invasive, repeatable over time, and possibly less expensive.
- IL23-producing human lung cancer cells promote tumor growth. Serum levels are associated with lung cancer.

Very interesting. Not sure how I would use this yet. Even eNO in asthma is not consistently helpful.



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Common MicroRNAs in Pre-diagnostic Serum Associated with Lung Cancer in Two Cohorts up to Eight Years Before Diagnosis: A HUNT Study

O.D. Røe^{1,2,3,4}, I. Fotopoulos⁵, O.T.D. Nguyen^{1,2}, T.H. Nøst^{6,7}, M. Markaki⁵, V. Lagani^{8,9}, R. Mjelle^{1,7}, T.M. Sandanger⁶, P. Sætrum^{1,7}, I. Tsamardinos⁵

¹Norwegian University of Science and Technology, Trondheim/NO, ²Levanger Hospital, Nord-Trøndelag Health Trust, Levanger/NO, ³Aalborg University Hospital, Aalborg/DK, ⁴Aalborg University Hospital, Aalborg/DK, ⁵FORTH, Heraklion/GR, ⁶UiT The Arctic University of Norway, Tromsø/NO, ⁷NTNU – Norwegian University of Science and Technology, Trondheim/NO, ⁸Ilia State University, Tbilisi/GE, ⁹King Abdullah University of Science and Technology KAUST, Tuwal/SA

Conclusions: There were a few significantly differential expressed microRNAs in serum up to eight years before diagnosis. These promising microRNAs alone, or in concert, may serve as early diagnostic or prognostic lung cancer biomarkers. These findings need to be validated in a larger prospective serum dataset.

Exciting, however, I agree, these findings will need to be validated in larger prospective serum data sets.



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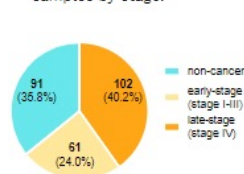


Sensitive Detection of Lung Cancer Using A Multiomic Plasma Cell-Free DNA (cfDNA) Sequencing Assay

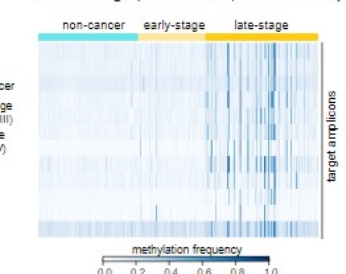
Jing Shan Lim¹, Jia Min Ho², Hao Chen², Aravind Madan Mohan², Yee Fang Hum², Ankit Das², Jin Wee Lee², Min-Han Tan¹, Yukti Choudhury²

¹Lucence Health Inc, Palo Alto, CA, USA, ²Lucence Diagnostics Pte Ltd, Singapore

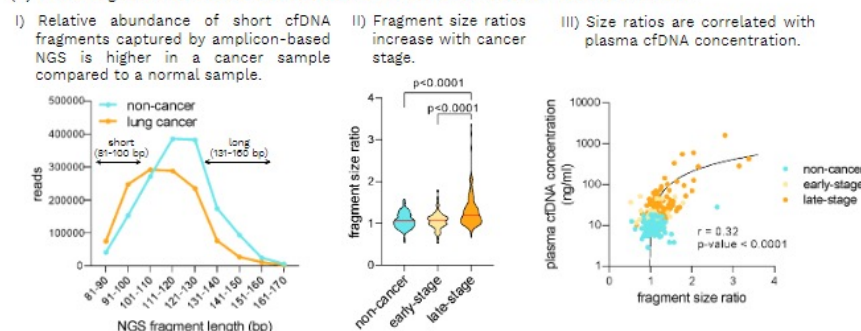
(A) Distribution of non-cancer and lung cancer samples by stage.



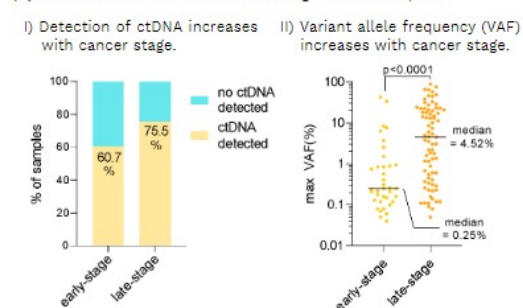
(B) Methylation frequencies increase with cancer stage (selected amplicons shown).



(C) cfDNA fragment size ratios are correlated with clinical and molecular features of cancer.

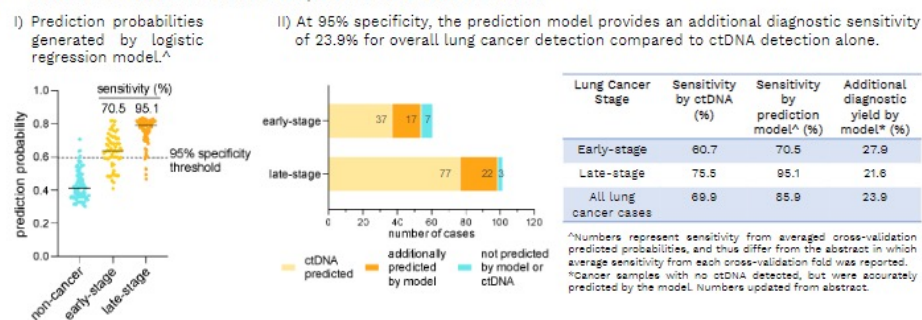


(D) ctDNA is more abundant in late-stage cancer samples.



CONCLUSION

(E) Prediction model incorporating plasma cfDNA concentration, cfDNA methylation, fragment size ratio and ctDNA detection detects more cancers compared to ctDNA detection alone.



Exciting, but there is still overlap in the groups. We will still need imaging and tissue.



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Abstract Title: Radiomics to Increase the Effectiveness of Lung Cancer Screening Programs. Radiolung Preliminary Results

A. Rosell¹, S. Baeza², S. Garcia-Reina², J. L. Mate², I. Guasch², I. Nogueira², I. Garcia-Olivé², G. Torres³, C. Sánchez-Ramos³, D. Gil³

¹Hospital Germans Trias i Pujol; UAB, BRN - Barcelona, ²Hospital Germans Trias i Pujol - Barcelona , ³Computer Vision Centre, UAB - Barcelona (Spain)

Conclusions

In our sample, the application of a hybrid radiomic system achieves high diagnostic accuracy (96.3%) to detect malignant nodules on chest CT. External validation in a lung cancer screening program is needed.

Funded by: ACMCiB, BRN, Fundació Ramon Pla, Lung Ambition Alliance

***Radiomics is the high-throughput mining of quantitative image features from standard-of-care medical imaging that enables data to be extracted and applied within clinical-decision support systems to improve diagnostic, prognostic, and predictive accuracy.

Currently, the field of radiomics lacks standardization. More data on clinical relevance and scientific integrity is needed.



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The National Lung Screening Trial (NLST) vs Nederlands–Leuvens Longkanker Screenings Onderzoek Trial (NELSON)

NLST:

- Ages 55-74.
- >30 pack years.
- Active smoker or quit within last 15 years.
- 3 annual scans
- 20.0% LC mortality reduction.
- Current Lung-RADS guidelines have adapted the diameter-based NLST protocol.

NELSON:

- Ages 50-74. Mostly men.
- >15 cigarettes a day for >25 years or >10 cigarettes a day for >30 years.
- Active smoker or quit within last 10 years.
- CT at 1, 2, and 2.5 years
- Semiautomated software determination of the nodule volume.
- 24.0% LC mortality reduction (men).
- BTS guidelines recommend a volume-based NELSON protocol.



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A COMPARISON OF STAGE- AND HISTOLOGY-SPECIFIC CT SENSITIVITY IN THE NELSON TRIAL AND THE NLST

Koen de Nijs¹, Kevin ten Haaf¹, Carlijn M. van der Aalst¹,
Matthijs Oudkerk², Harry J. de Koning¹,
on behalf of the NELSON study consortium

1: Erasmus University Medical Center, department of
Public Health – Rotterdam, the Netherlands

2: University Medical Center Groningen – Groningen, the
Netherlands

Take home messages from this group:

- Higher sensitivity in NELSON for early-stage adenocarcinoma and stage 2 squamous cell carcinoma.
- This higher CT sensitivity partially explains the favorable stage-shift and efficacy of the NELSON trial.
- Volume-based nodule management may improve the potential for lung cancer mortality reduction in population-based screening programs.



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Take home messages from this group:

Early Diagnosis of Lung Cancer Among Younger vs. Older Adults: Widening Differences in the Era of Lung Cancer Screening

Alexandra L. Potter
Massachusetts General Hospital
United States

- Younger adults (20-49 years) diagnosed with lung cancer are identified late in their disease course (>64%).
 - > 80% of age 20-29 presents with stage IV lung cancer.
 - Compared to 40% in patients older than 70.
- Early diagnosis stage shift has been demonstrated in patients over 50 (2018 compared to 2010), but not in younger patients.
- Different tumor biology, delays in diagnosis, and the absence of early detection methods, likely contribute to the high rate of stage IV disease among young adults.
- Although there was no improvement in early diagnosis among young adults. Median survival of young adults diagnosed with lung cancer increased by 14 months from 2010-2018, largely due to improvements in survival for patients with advanced disease.
- Identifying cancer in non-screening eligible groups poses a major challenge. Strategies to increase the early detection of lung cancer among patients currently ineligible for lung cancer screening (younger patients and older patients without sufficient risk factors) are urgently needed.



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The Granularity of Lung Cancer Screening Implementation

Anand Devaraj
Royal Brompton Hospital
Imperial College
London
UK

Take home messages from this group:

- Both NELSON and NLST have demonstrated that lung cancer screening reduced lung cancer mortality
- Comparison of CT sensitivity between NELSON and NLST using MISCAN model showed higher CT sensitivity for NELSON
- The computer program MISCAN is developed for use in evaluation of mass screening for disease

**The computer program MISCAN is developed for use in evaluation of mass screening for disease.



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US Preventative Services Task Force Recommendations 2021 vs 2013

- Ages 50-80
- >20 pack years.
- Active smoker or quit within last 15 years.
- 3 annual scans
- Additionally, clinicians can consider discontinuing screening when a person has either not smoked for 15 years or has developed a health problem that significantly limits life expectancy or the ability or willingness to undergo curative long surgery.



Bronchoscopy: Diagnosis and Therapeutics

Take home messages:

- The diagnostic accuracy of bronchoscopy has continued to improve over the past 20 years.
- With robotic-assisted bronchoscopy (RAB) and cone-beam CT (CBCT), diagnostic yield is similar to transthoracic needle aspiration.
- With this increased accuracy, therapeutics are becoming a more realistic possibility.

**The following 2 presentations from the 2022 WCLC from Desi ter Woerds and Daniela Gompelmann have excellent images. I am using this images for this presentation. These are not my personal images.

Navigation Bronchoscopy Mediated Sentinel Lymph Node Procedure: an Explorative Study in Ex-vivo Lung Cancer Specimens

Desi (K.M.) ter Woerds, Roel (L.J.) Verhoeven, Erik (H.F.M.) van der Heijden



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Take home messages:

- The pioneer plus catheter is an IVUS-guided catheter used in the treatment of chronic total occlusion of blood vessels.
- This group at Radboud UMC was able demonstrate (ex-vivo) that peripheral lymph nodes (or nodules) could be injected real-time. Isotope injection was verified using SPECT.
- This offers the possibility of real time guidance, hence verification of biopsy or injection.
- This is one of many possible tools. In-vivo feasibility to needs be determined.

From Desi (K.M.) ter Woerds, Roel (L.J.) Verhoeven, Erik (H.F.M.) van der Heijden



US-images

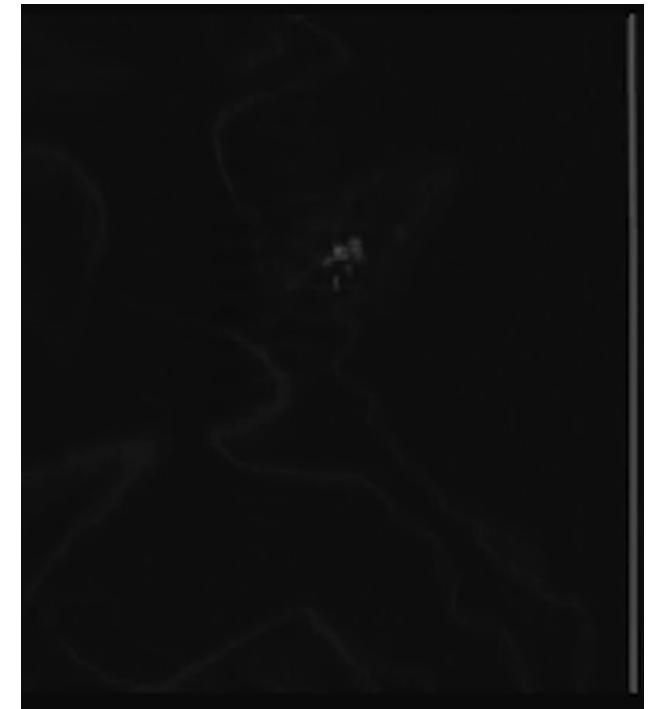
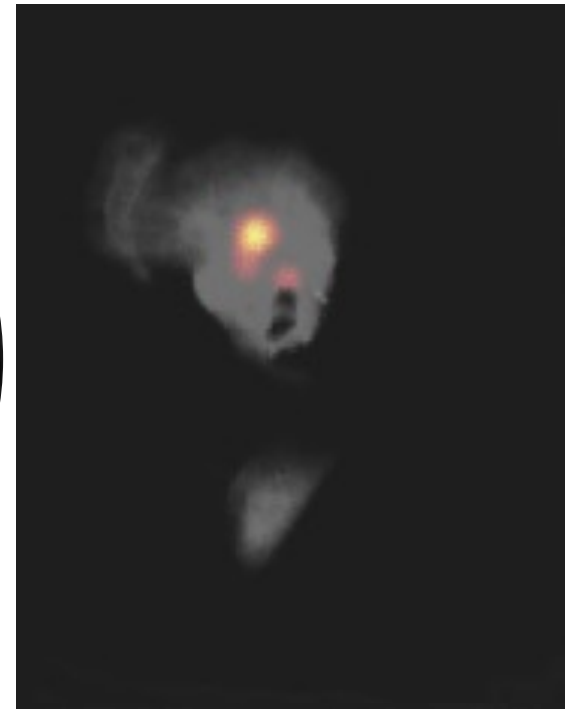
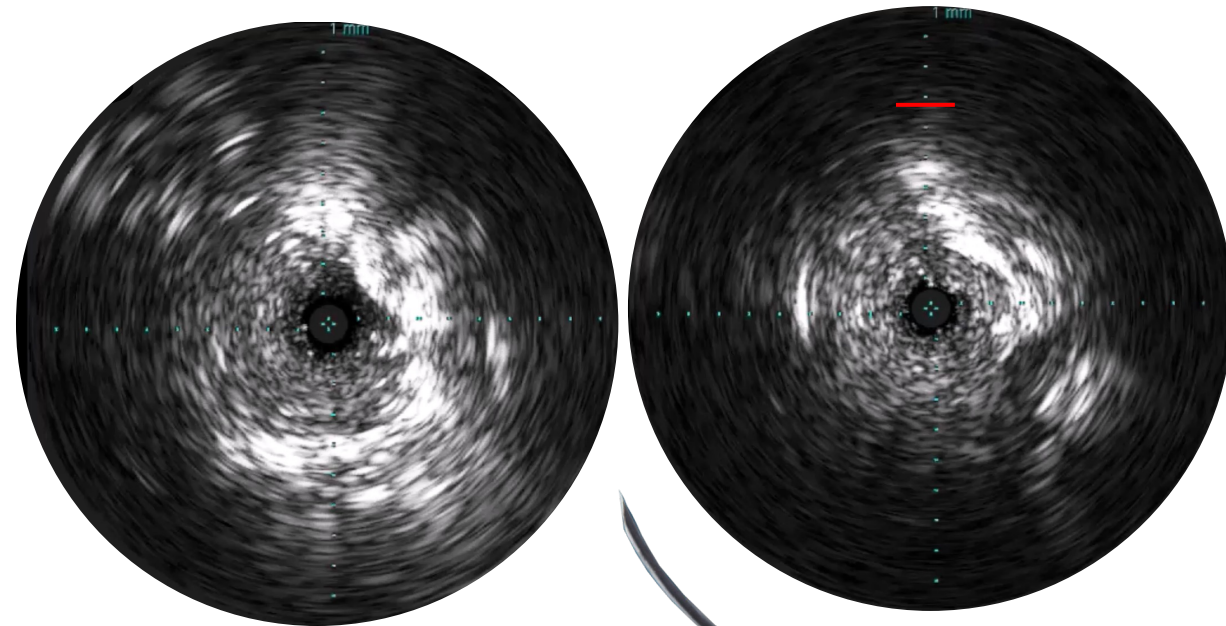
SPECT/CT-images

Tumor visibility

Injection visibility

Intratumoral injections

Peritumoral injections





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Diagnostic and Interventional Bronchoscopy: Updates and Futures

Daniela Gompelmann

**Medical University of Vienna
Austria**





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Take home messages:

- Standard bronchoscopy using fluoroscopic guidance does not perform well for small nodules.
 - ~60% sensitivity for nodules >2 cm diameter and <20% for nodules less than 2 cm diameter.
 - Peripheral location, ground glass density, and lack of an air-bronchogram decrease yield.
 - Yield depends significantly on bronchoscopist skill.
- In skilled operators using radial EBUS and/or electromagnetic navigation, bronchoscopy yield has been >70%.



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Take home messages:

- More recent studies using robotic-assisted bronchoscopy and cone-beam CT have show yields of ~90%.

Study	Number of patients/lesions	Mean diameter mm	Navigate and assistant techniques	Diagnostic yield %
Makris, 2007 (55)	40/40	23.5	ENB	62.5
Eberhardt, 2007 (18)	39/39	28.0	ENB	59.0
Bertoletti, 2009 (56)	54/54	31.2	ENB	61.1
Al-Jaghbeer, 2016 (15)	92/98	26.0	ENB	60.0
Eberhardt, 2007 (18)	40/40	24.0	ENB+RP-EBUS	87.5
Lamprecht, 2009 (57)	13/13	30.0	ENB+ROSE	76.9
Lamprecht, 2012 (58)	112/112	27.1	ENB+ROSE	83.9
Karnak, 2013 (25)	54/103	16.5	ENB+ROSE	83.3
Pritchett, 2018 (19)	75/93	16.0	ENB+CBCT	93.5
He, 2019 (22)	37/37	21.0	ENBCB	89.2

- This increased accuracy now makes the development of therapies using bronchoscopic guidance for treatment of early-stage lung cancer a possibility.

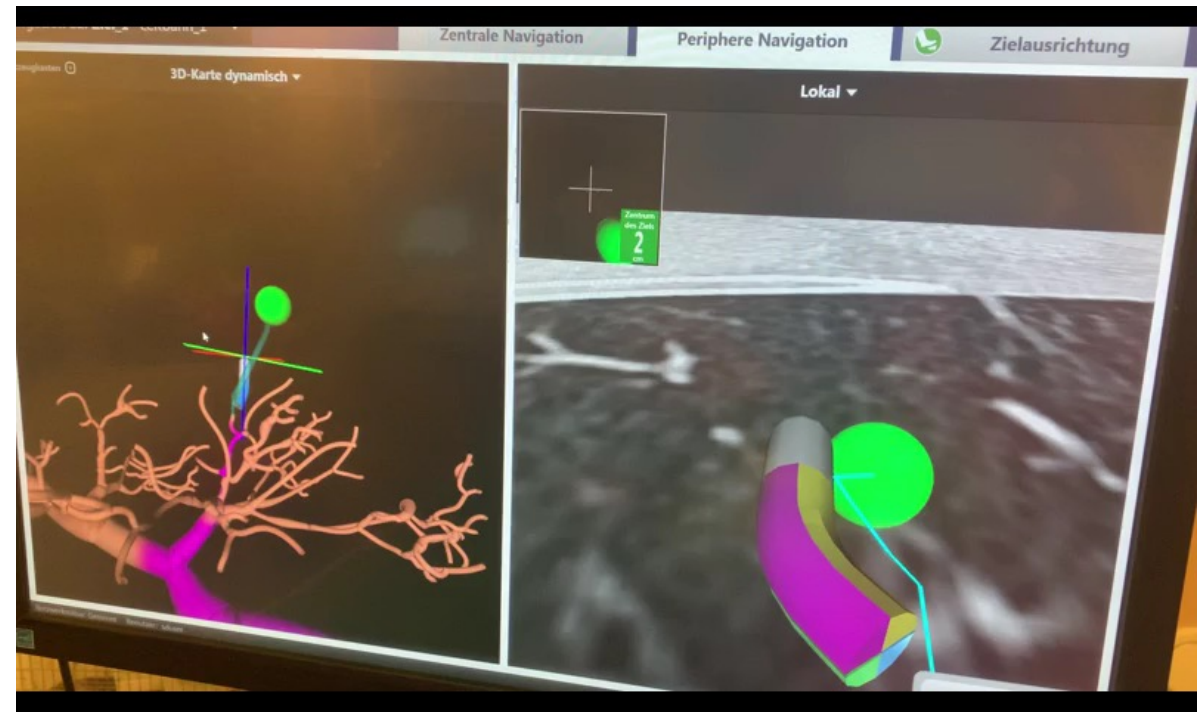


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From Daniela Gompelmann
(Electromagnetic Navigation Bronchoscopy)



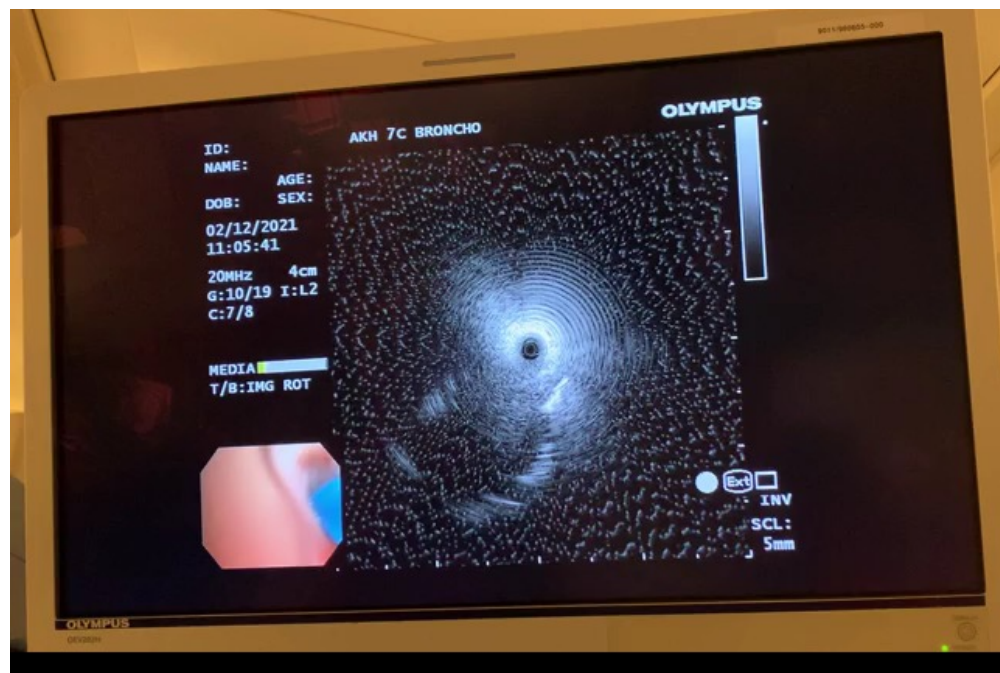


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From Daniela Gompelmann
(Radial EBUS)



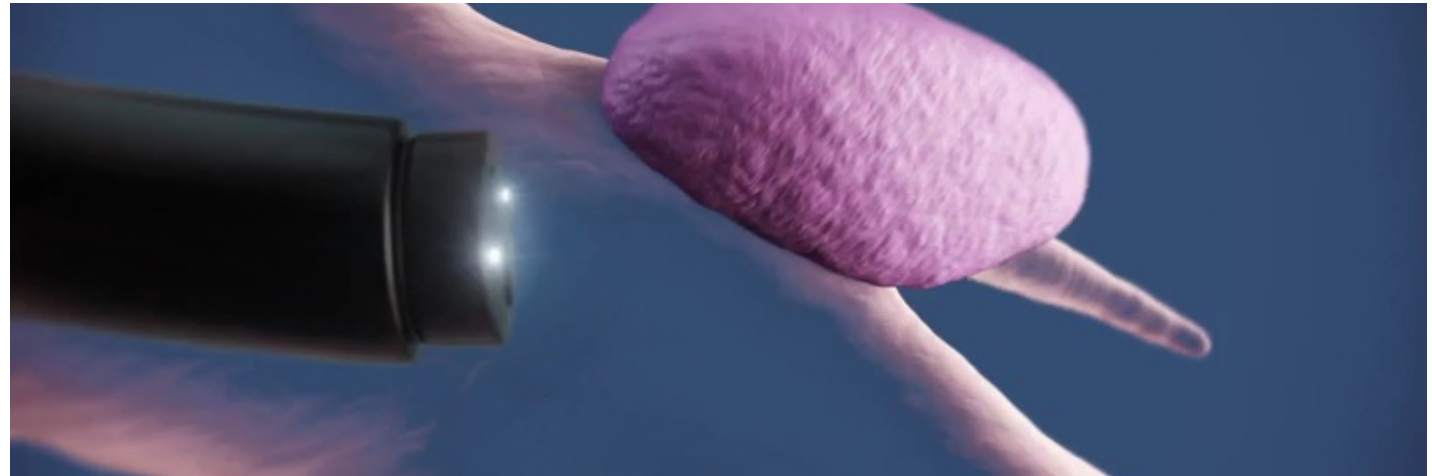
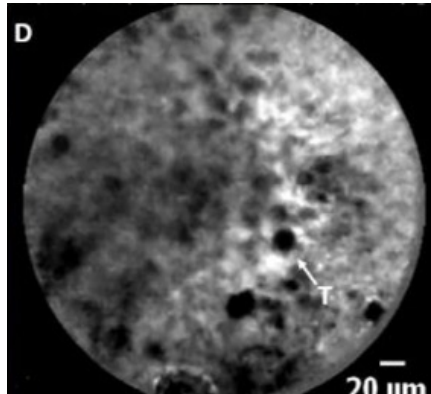
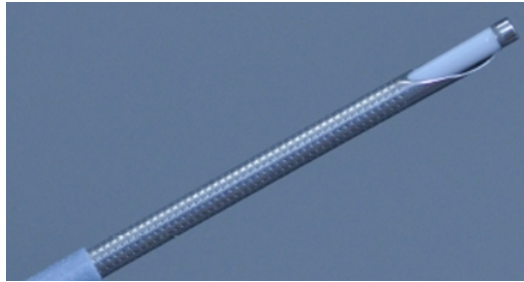


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From Daniela Gompelmann (Needle-based confocal laser endomicroscopy - nCLE)





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Robotic-assisted bronchoscopy (RAB)

2 systems currently available

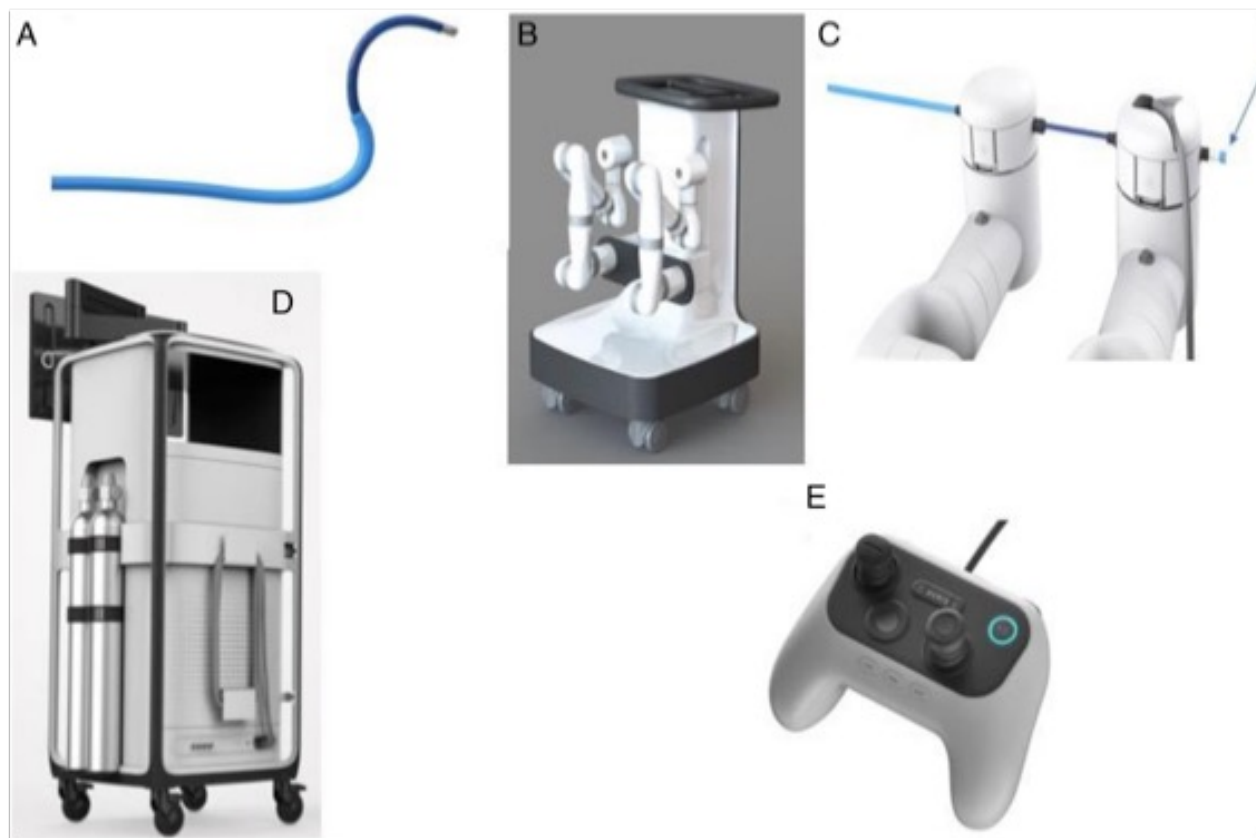
- One system uses virtual bronchoscopy, electromagnetic navigation, and robotic bronchoscopy.
- Visualization all the way to the biopsy site.
- The other system combines visual and virtual bronchoscopy with shape-sensor technology to determine location relative to the airways.
- Avoids the problems of electromagnetic navigation.





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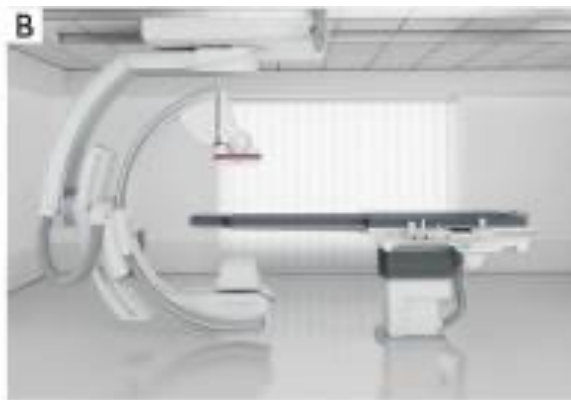


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Cone-beam CT systems



floor mounted (A); ceiling (B); biplane (C); CBCT-enabled mobile (D); robotic (E).



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Bronchoscopy directed
therapeutics for early stage
lung cancer.

From Daniela Gompelmann

- Radiofrequency ablation
- Microwave ablation
- Photodynamic therapy
- Brachytherapy
- Cryotherapy
- Vapor ablation

Trials		Tumour	Technique	Outcome
Tanabe et al. Chest 2010	n=10	NSCLC T1N0M0	Endoscopic RFA under CT-guidance	safe and feasible
Koizumi et al Respiration 2015	n=20	NSCLC T1-2N0M0	Endoscopic RFA under CT-guidance	local control in 82.6%
Xie F et al. Respiration 2017	n=3	NSCLC stage IA	Endoscopic RFA under CT-guidance	partial response (n=2) complete response (n=1)

Trial		Tumour	Technique	Outcome
Lau et al. Abstract. J Thorac Oncol 2018	n=3	metastases	MWA under EMN and CT-guidance	Safe and feasible
Pritchett et al. Abstract. Chest 2020.	n=10	Tumour < 2 cm	MWA under EMN and CT-guidance	Complete tumor ablation in 100%
Chan et al. Trans Lung Cancer res. 2021	n=25	30 pulmonary nodules < 3 cm	MWA under EMN and CT-guidance	1-Year-FU: stable disease in 100%
Lau et al. Abstract. ERS 2021.	n=30	39 pulmonary nodules < 3 cm	MWA under EMN and CT-guidance	Successful ablation in 100%; successful outcome after 1 month in 100%



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Take Home Messages

- ✓ Lung Cancer Screening has room for improvement.
- ✓ There is no one-size-fits-all in LCS.
- ✓ Technology (Artificial Intelligence/Machine Learning) may help.
- ✓ Lung cancer screening and radiographic imaging have not replaced the need for diagnostic procedures and tissue.
- ✓ The diagnostic accuracy of bronchoscopy continues to improve.
- ✓ With this increased accuracy, therapeutics are becoming a more realistic possibility.