Present & Future Pulmonary Diagnostics

07/28/25

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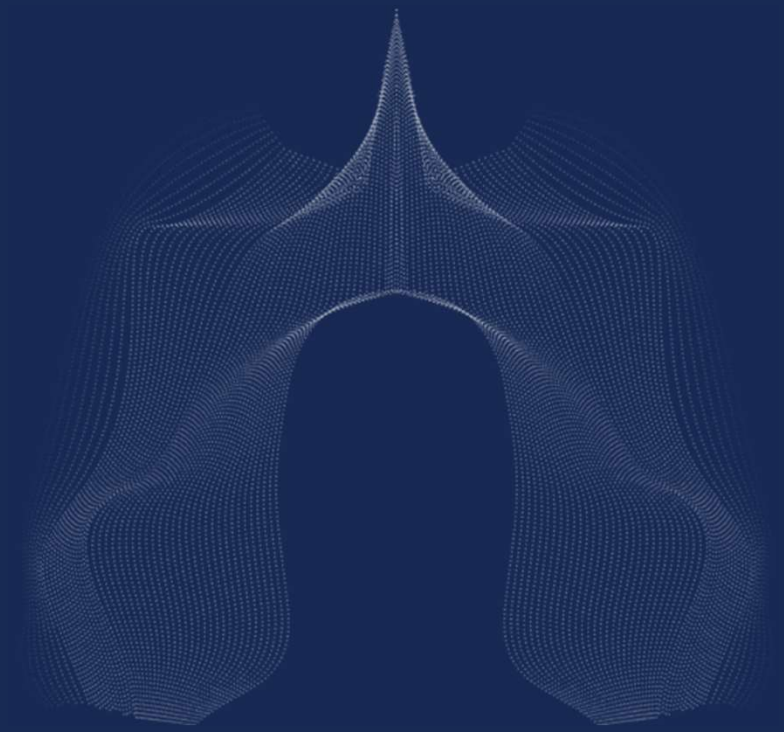

Present & Future Pulmonary Diagnostics

Objectives

- Understanding the current state of pulmonary diagnostics and the drawbacks for each separate modality
- Introduction to the incorporation of imaging modalities as a complementary pulmonary diagnostic tool
- Leveraging imaging modalities through the utilization of mathematical & AI-enhanced algorithms to gain further insights beyond current diagnostic capabilities

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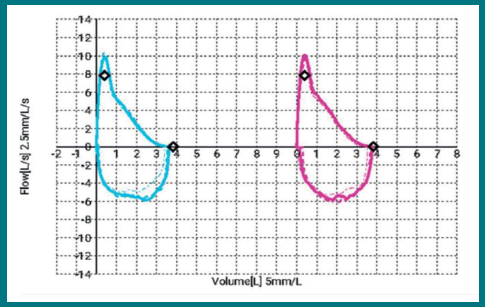
The Current State of Pulmonary Diagnostics

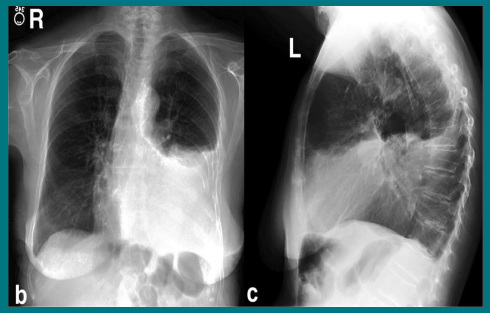
Spirometry & PFTs



✓ Lung Function

X Lung Structure

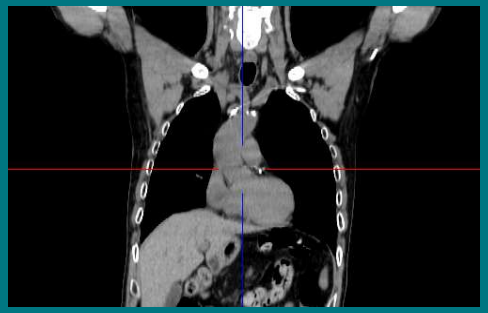
X-Ray Technology



X Lung Function

✓ Lung Structure

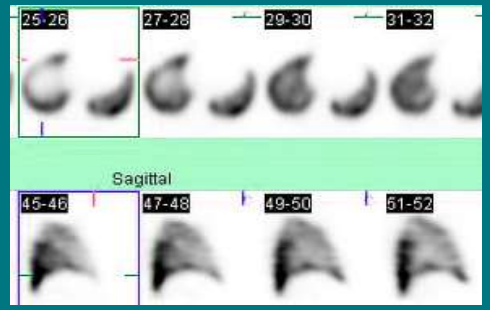
High-Resolution Chest CT



X Lung Function

✓ Lung Structure

Nuclear Medicine

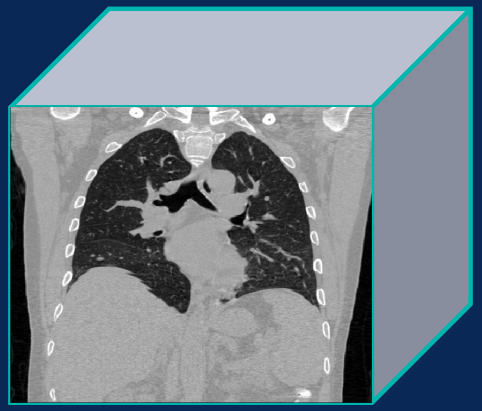


✓ Lung Function

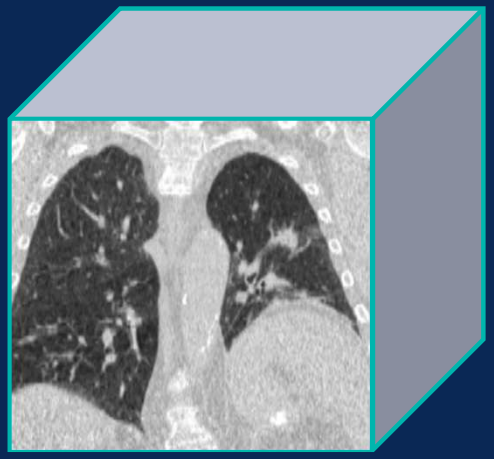
X Lung Structure

The above existing imaging modalities don't offer objective insight into lung function

Current Modalities



CT

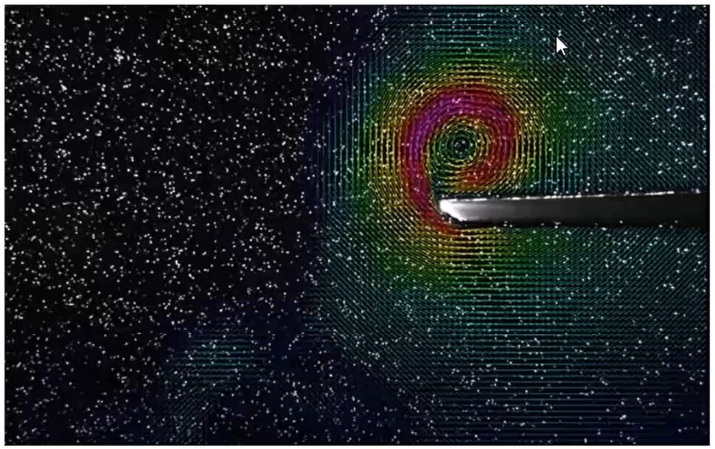


4DCT

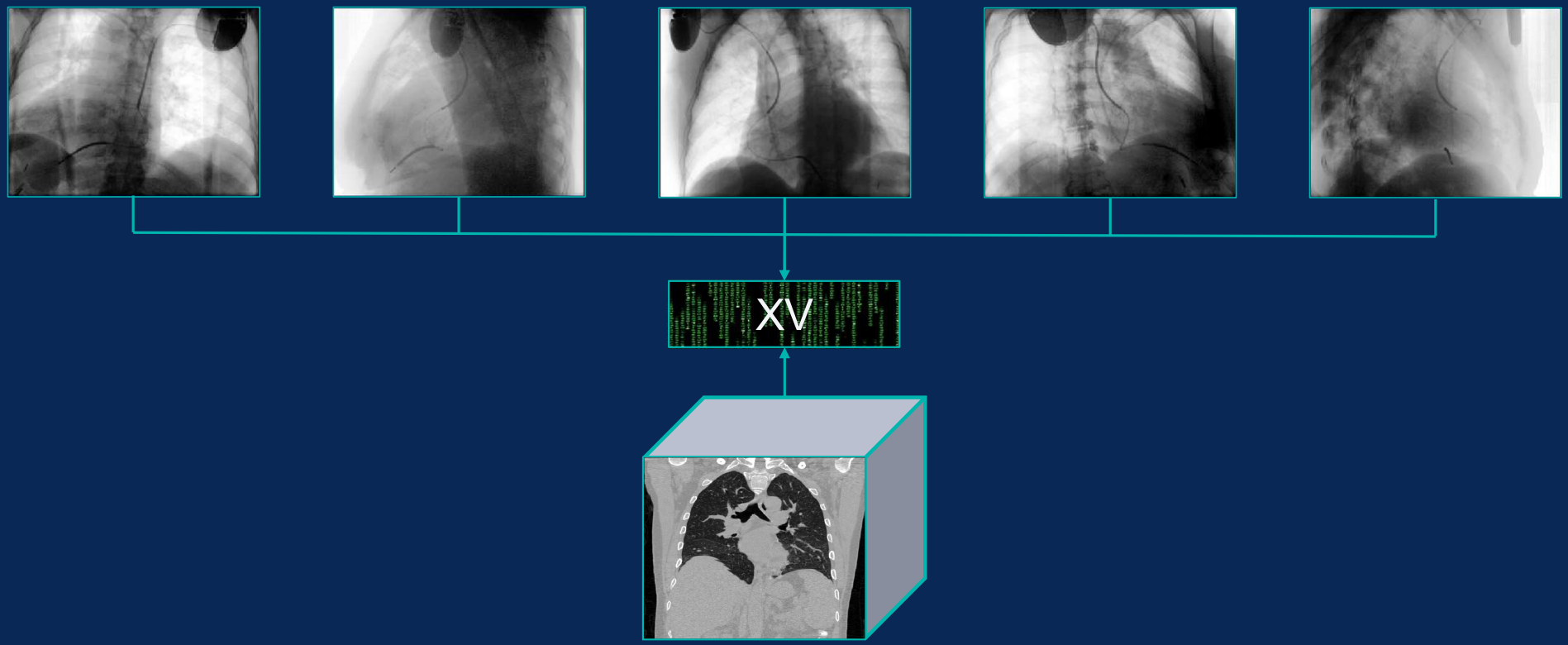
Spirometry

What is XV Technology?

- XV technology relies on a technique known as *computed tomographic x-ray velocimetry* (CTXV)
- CTXV combines *particle image velocimetry* (PIV) and *computed tomography* (CT)

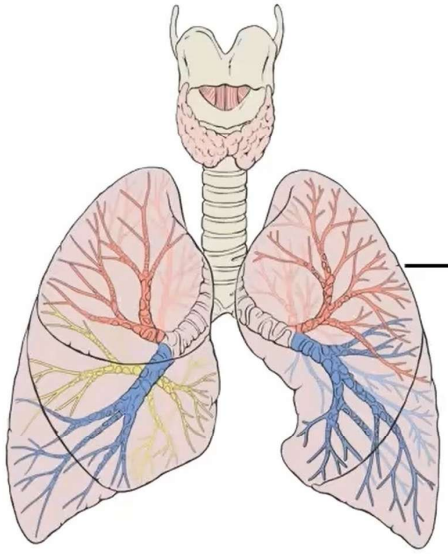


What is XV Technology?



Mathematical Modelling

- Mathematical modelling attempts to translate the real world into a mathematical language, which can then be solved and interpreted against the real life system



Model

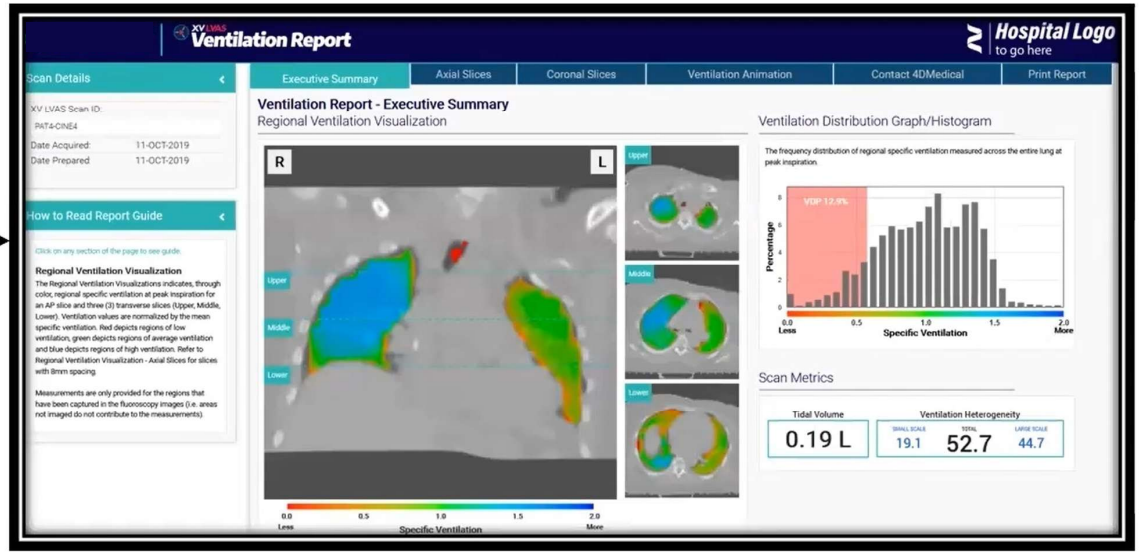
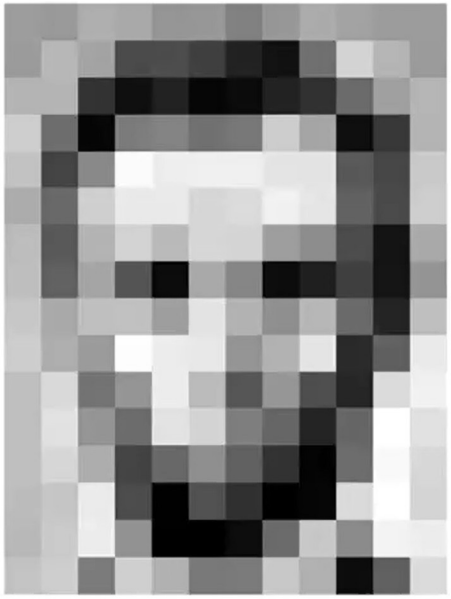


Image Processing

- Images allow us to data in the real world into pixels
- Each pixel consists of an intensity at a point in space



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155	182	163	74	75	62	33	17	110	210	180	154
180	180	50	14	34	6	10	33	48	106	159	181
206	109	5	124	131	111	120	204	166	15	56	180
194	68	137	251	237	239	239	228	227	87	71	201
172	105	207	233	233	214	220	239	228	98	74	206
188	88	179	209	185	215	211	158	139	75	20	169
189	97	165	84	10	168	134	11	31	62	22	148
199	168	191	193	158	227	178	143	182	106	36	190
205	174	155	252	236	231	149	178	228	43	95	234
190	216	116	149	236	187	86	150	79	38	218	241
190	224	147	108	227	210	127	102	36	101	255	224
190	214	173	66	103	143	96	50	2	109	249	215
187	196	235	75	1	81	47	0	6	217	255	211
183	202	237	145	0	0	12	108	200	138	243	236
195	206	123	207	177	121	123	200	175	13	96	218

157	153	174	168	150	152	129	151	172	161	155	156
155	182	163	74	75	62	33	17	110	210	180	154
180	180	50	14	34	6	10	33	48	106	159	181
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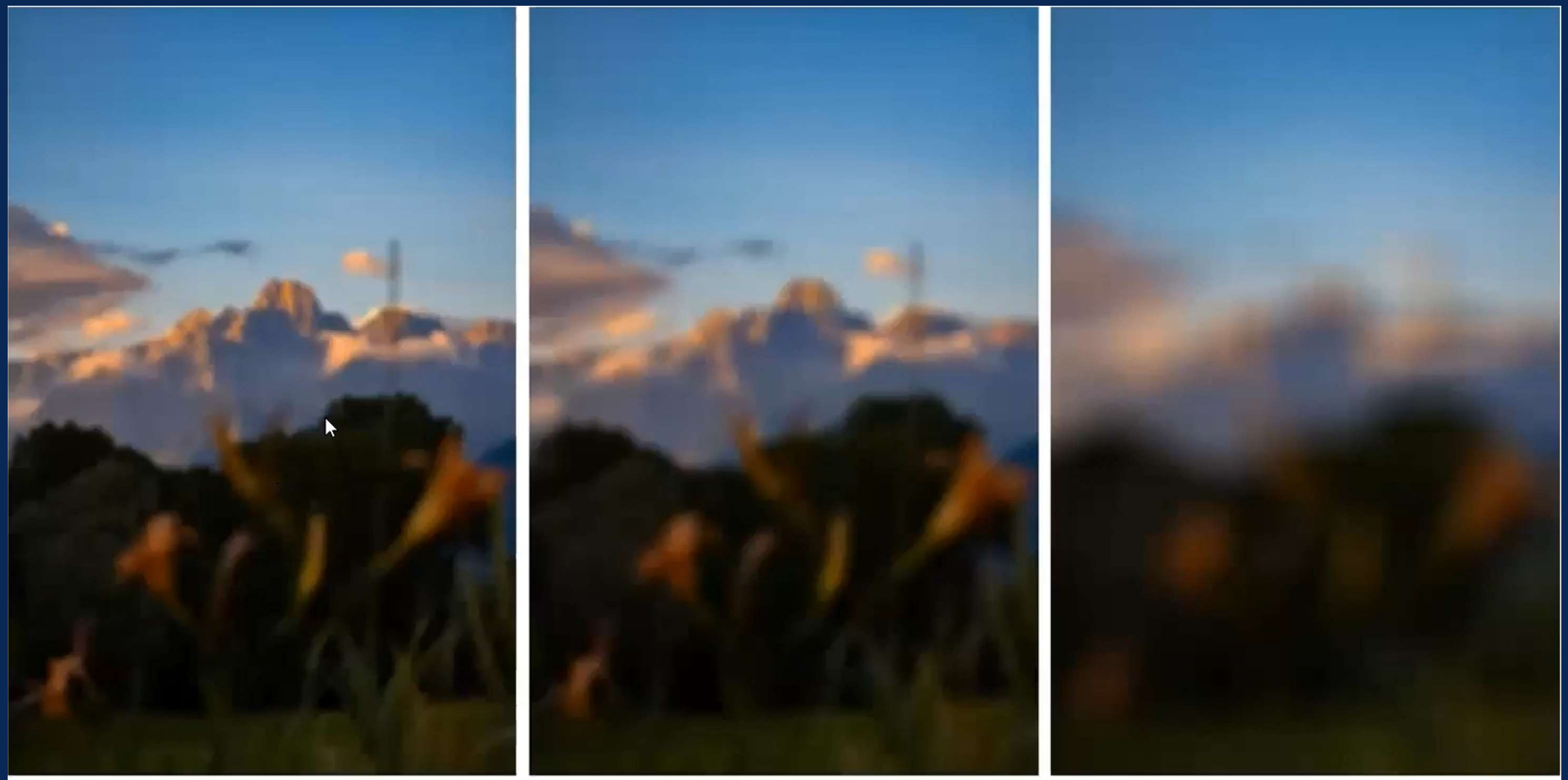
190	224	147	108	227	210	127	102	36	101	255	224
190	214	173	66	103	143	96	50	2	109	249	215
187	196	235	75	1	81	47	0	6	217	255	211
183	202	237	145	0	0	12	108	200	138	243	236
195	206	123	207	177	121	123	200	175	13	96	218

Image Processing

-64 brightness (left), +0 brightness (center) and +64 brightness (left)

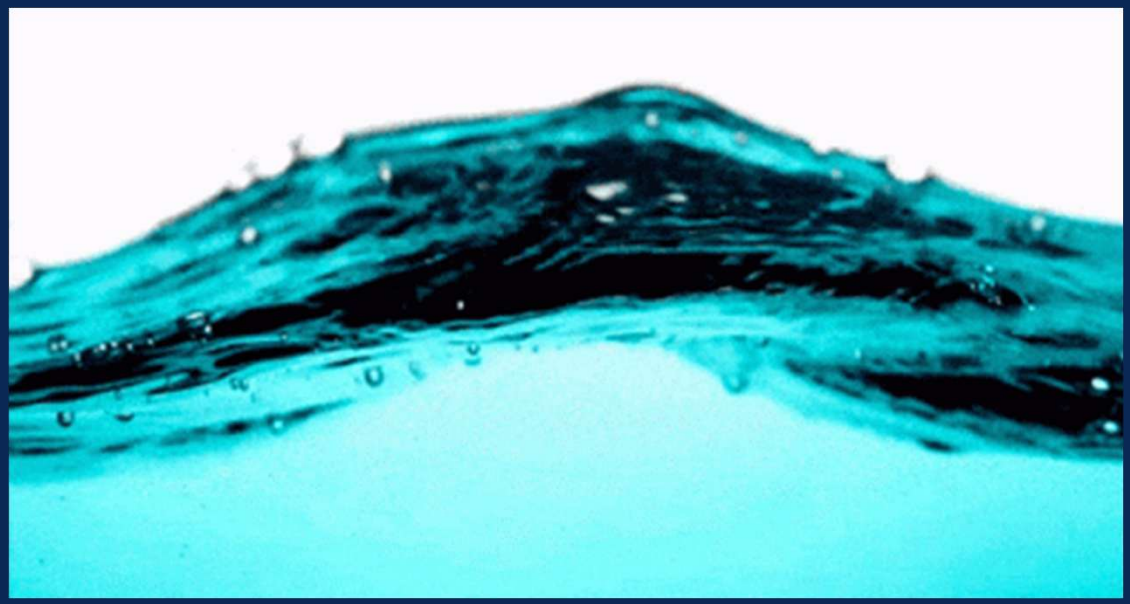
Image Processing



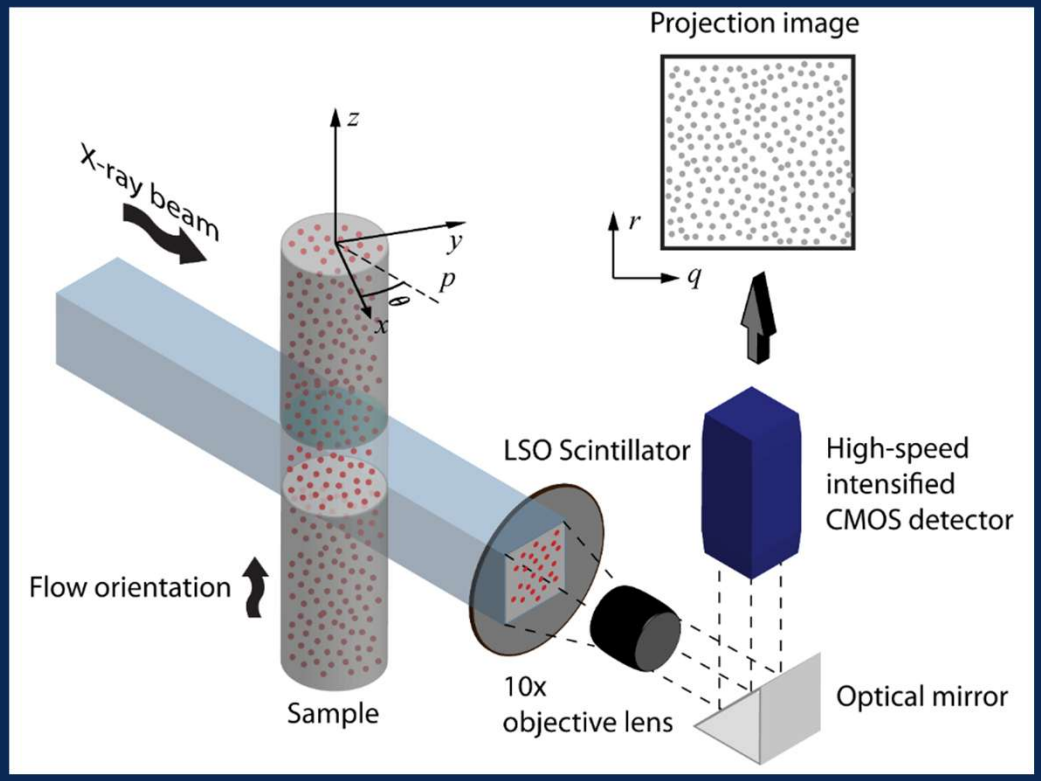
11 blur (left), 21 blur (middle), 71 blur (right)

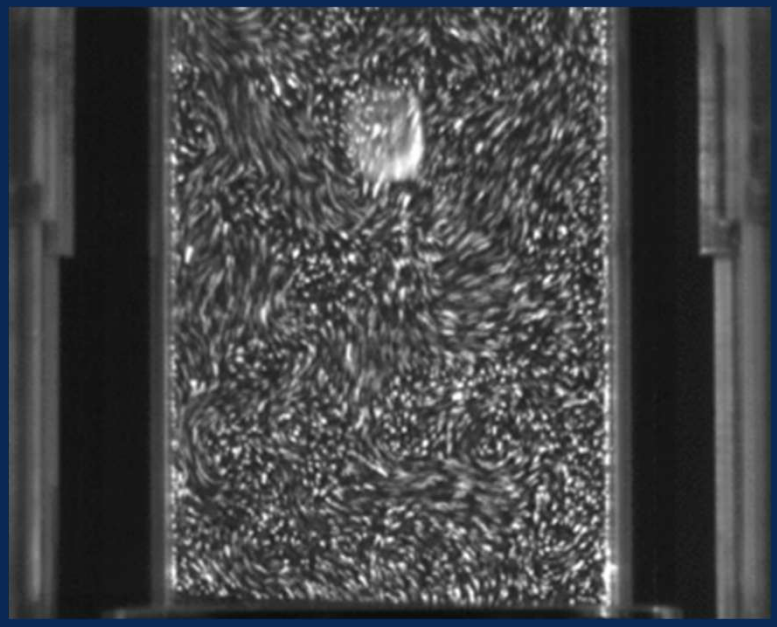
Particle Image Velocimetry

- *Particle Image Velocimetry* (PIV) is a technique used for modelling fluid motion

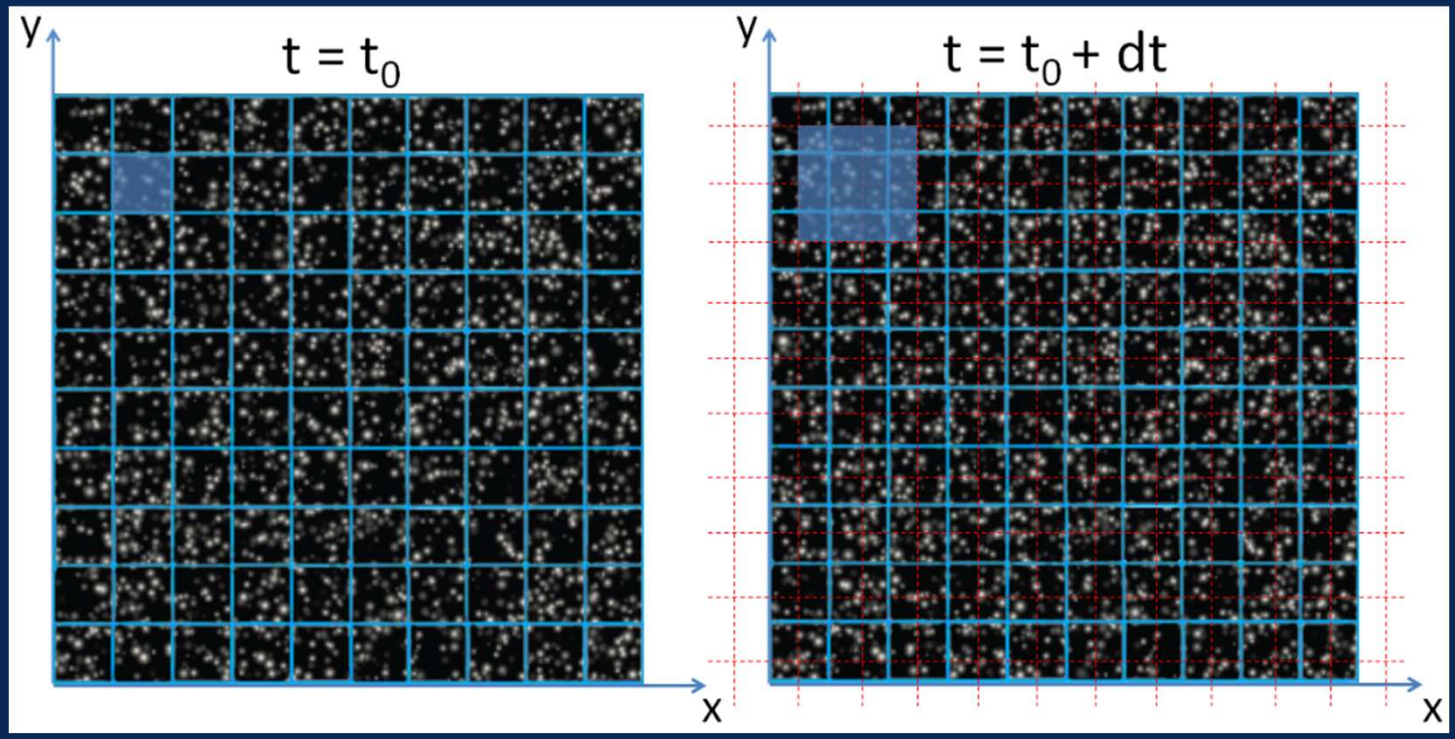


Particle Image Velocimetry





Particle Image Velocimetry



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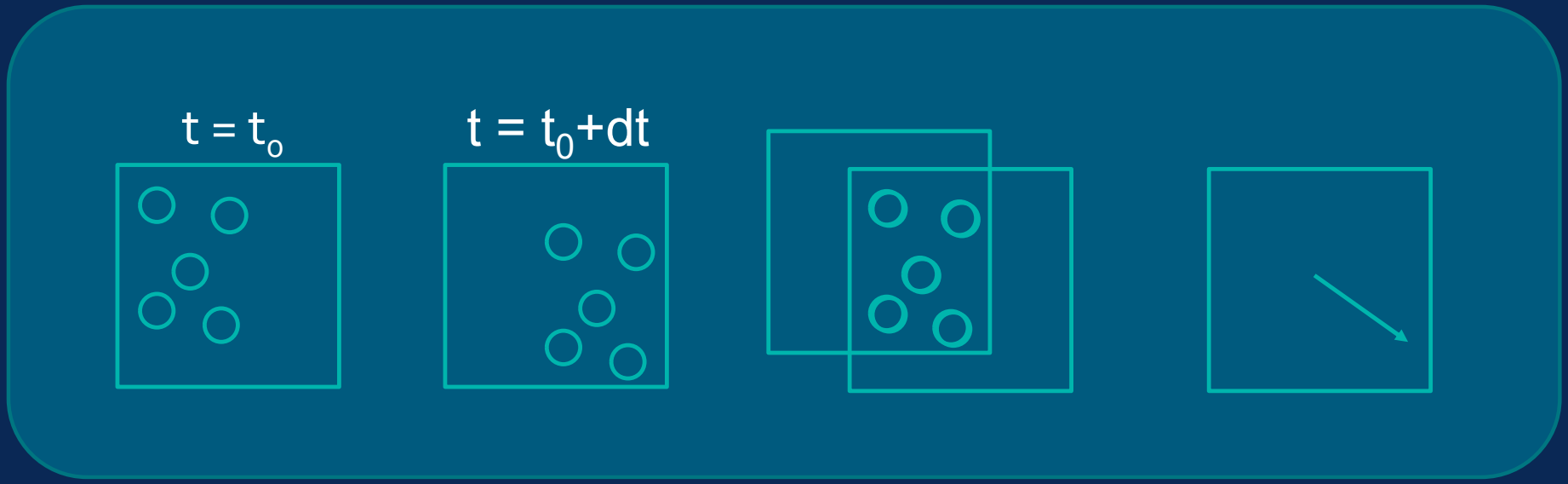
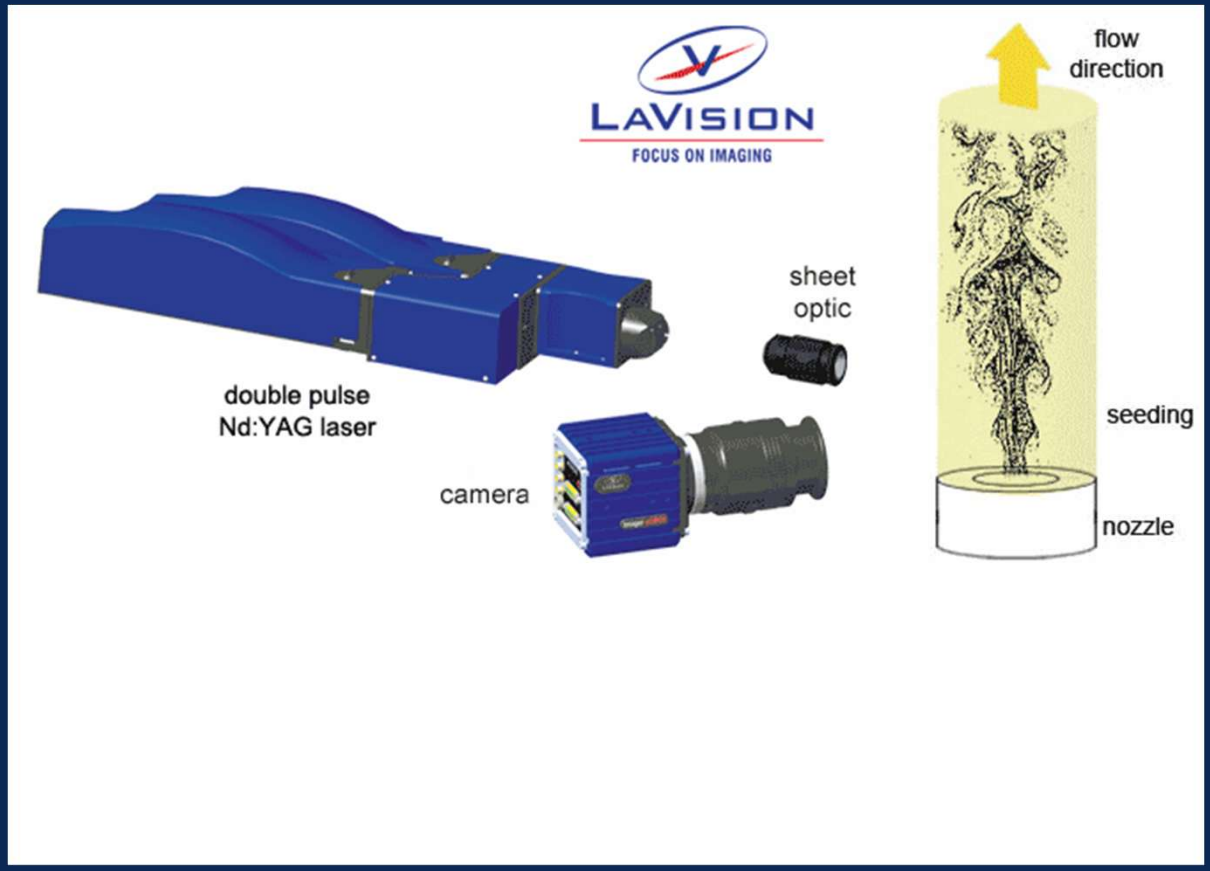
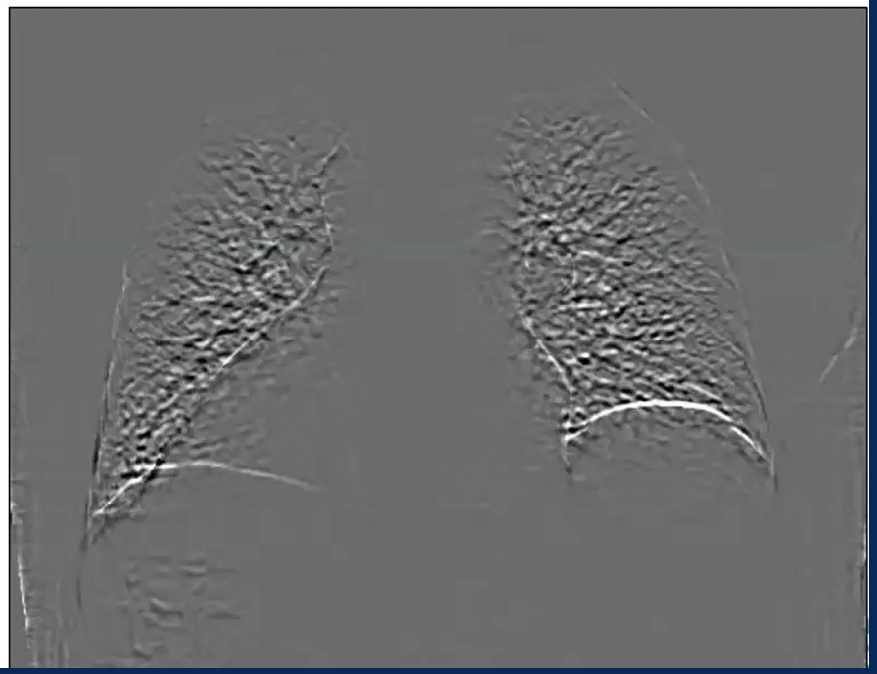


Particle Image Velocimetry



PIV with Lung Images

- Image processing techniques are used to enhance the lung tissue, which can be tracked using the same technique as for particles in a fluid



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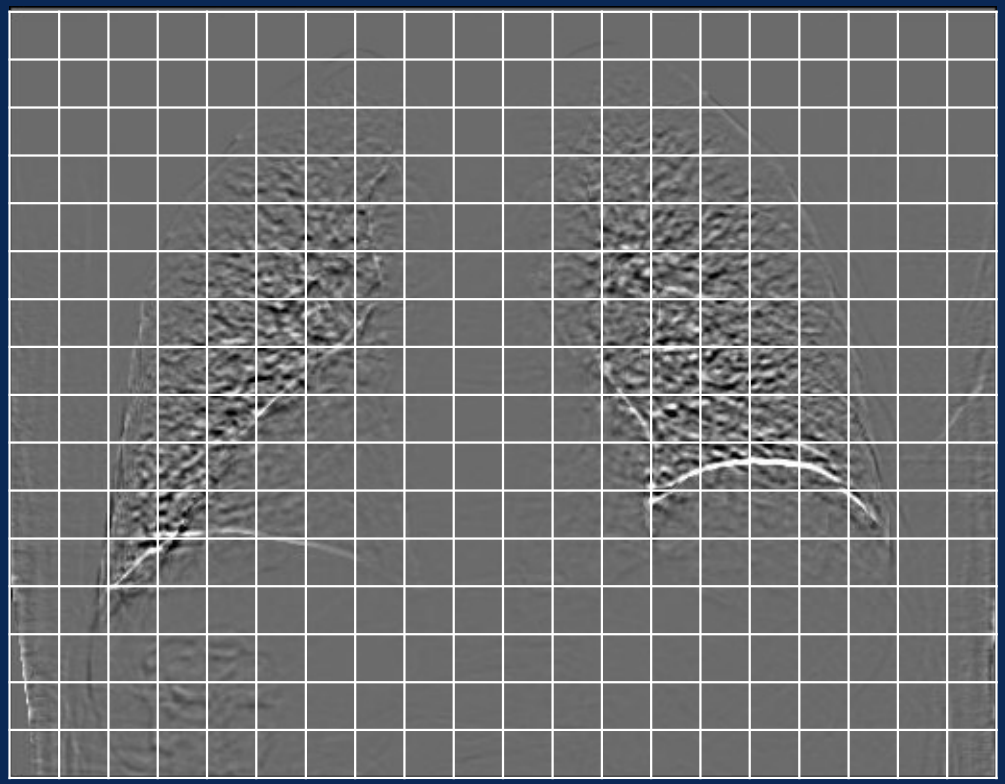
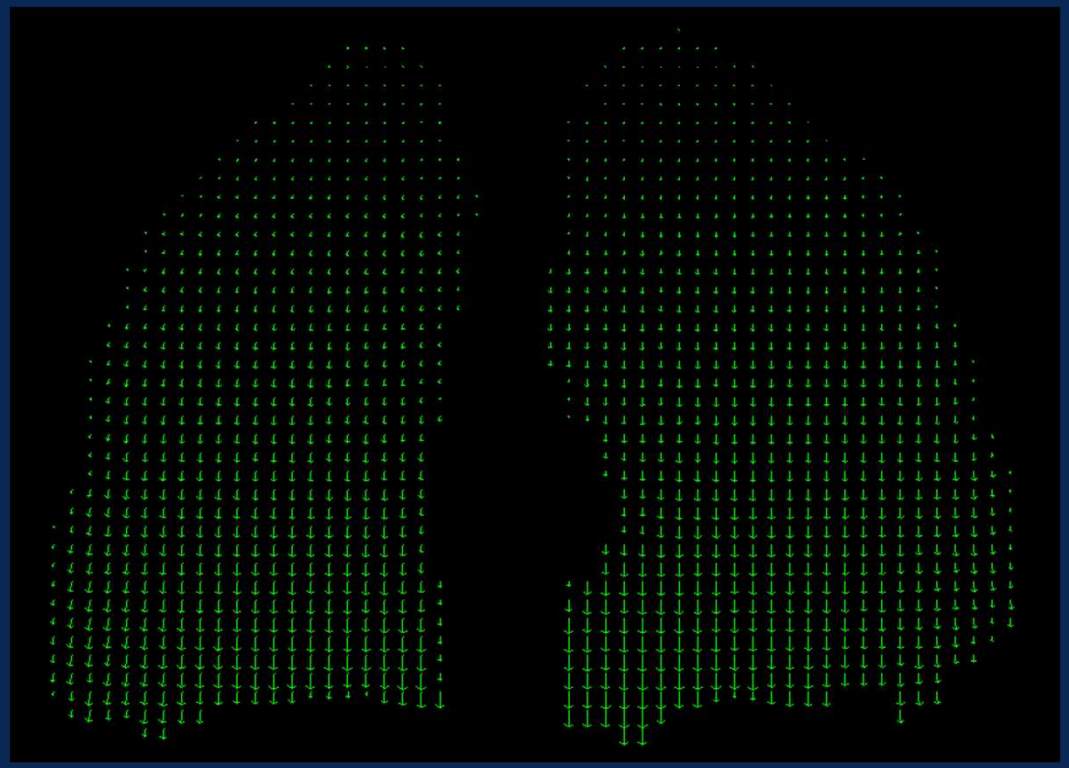
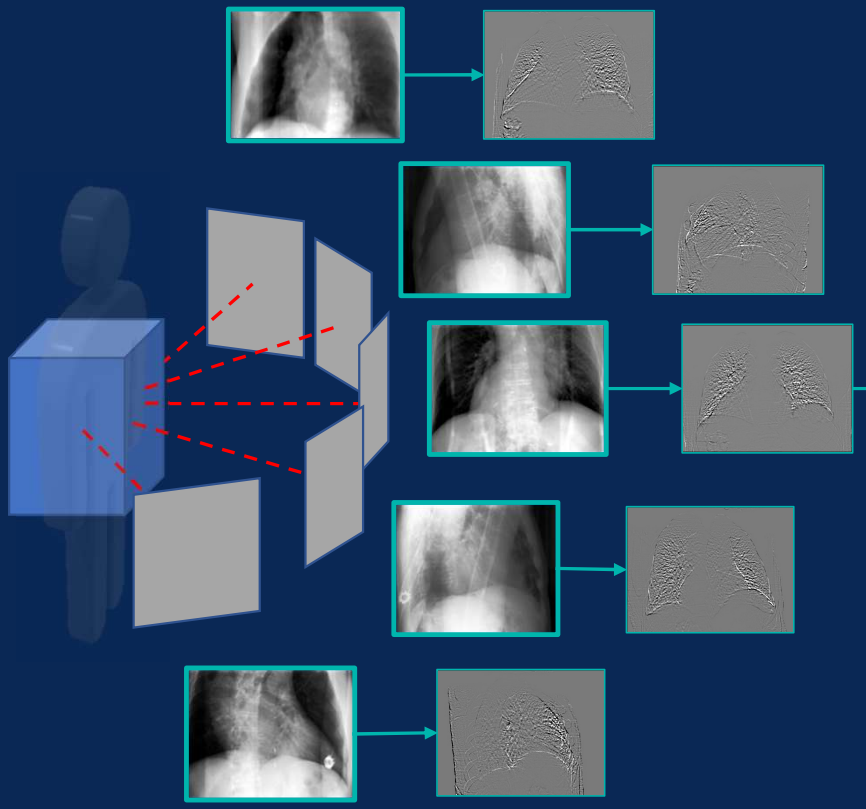
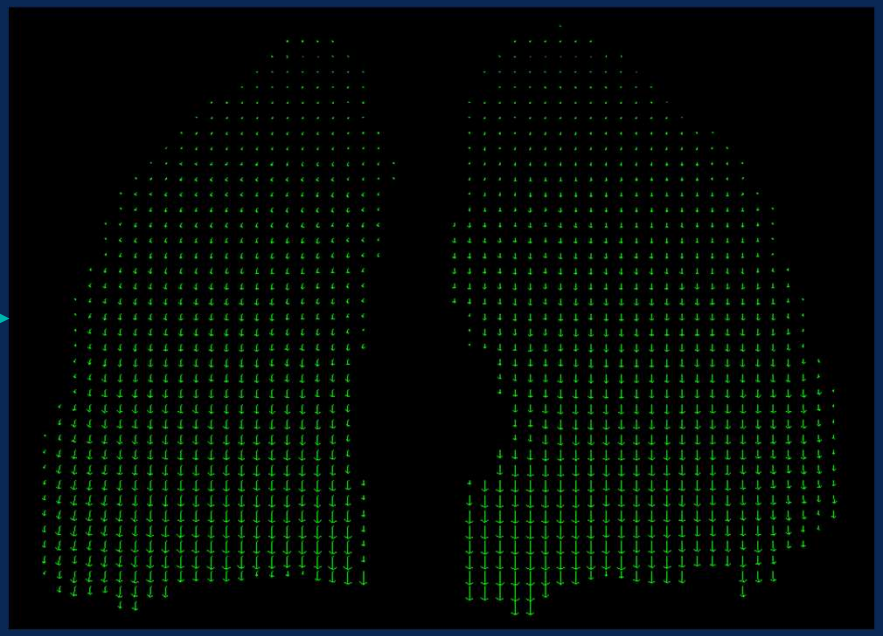


PIV with Lung Images

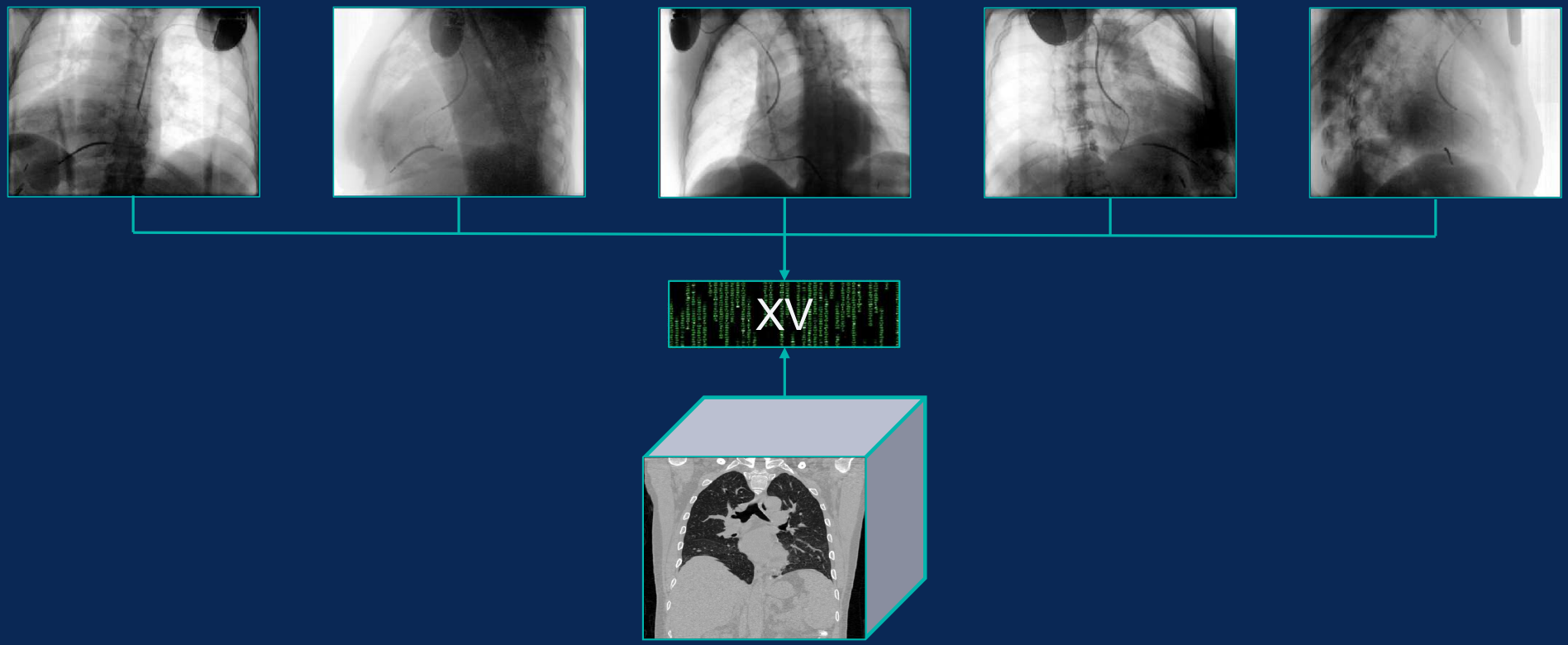


PIV in XV LVAS





XV Technology



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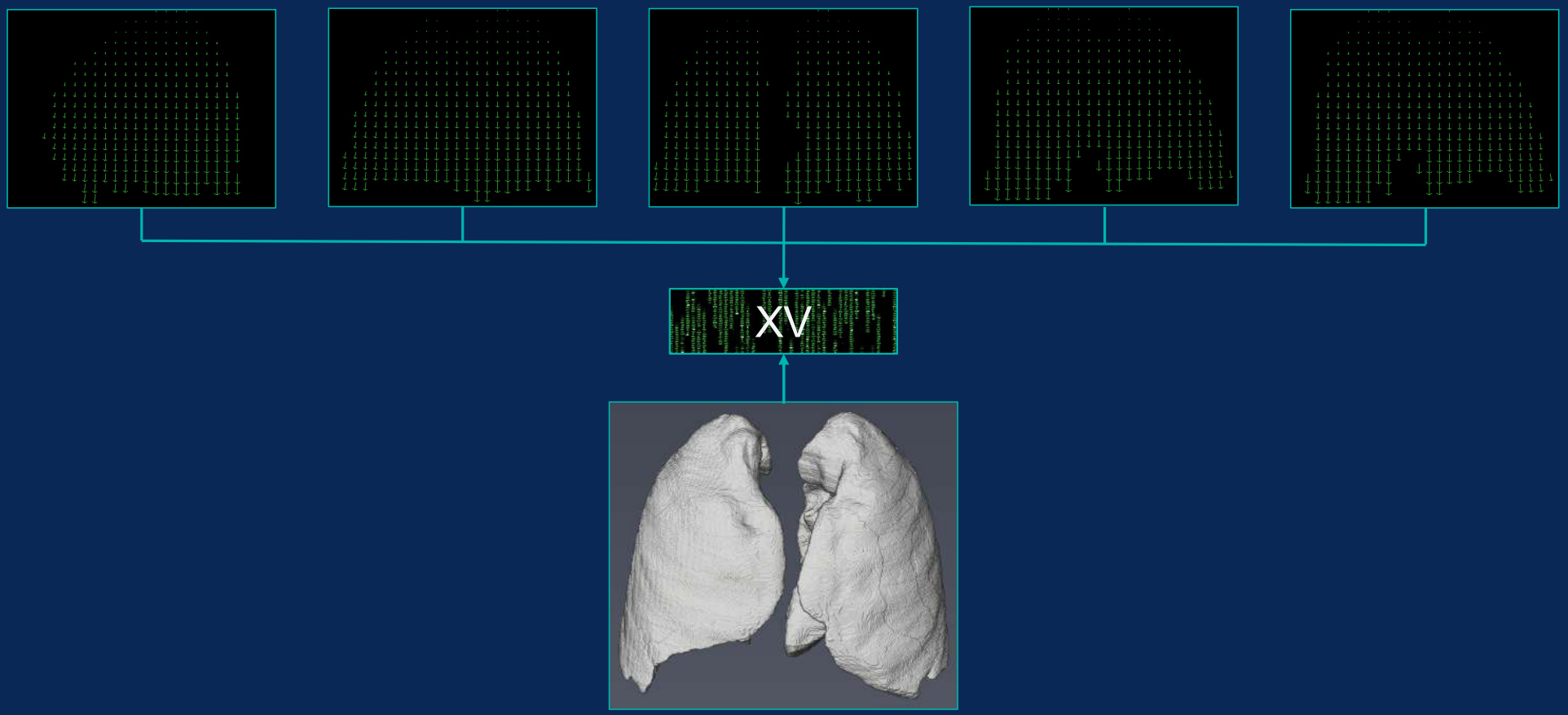

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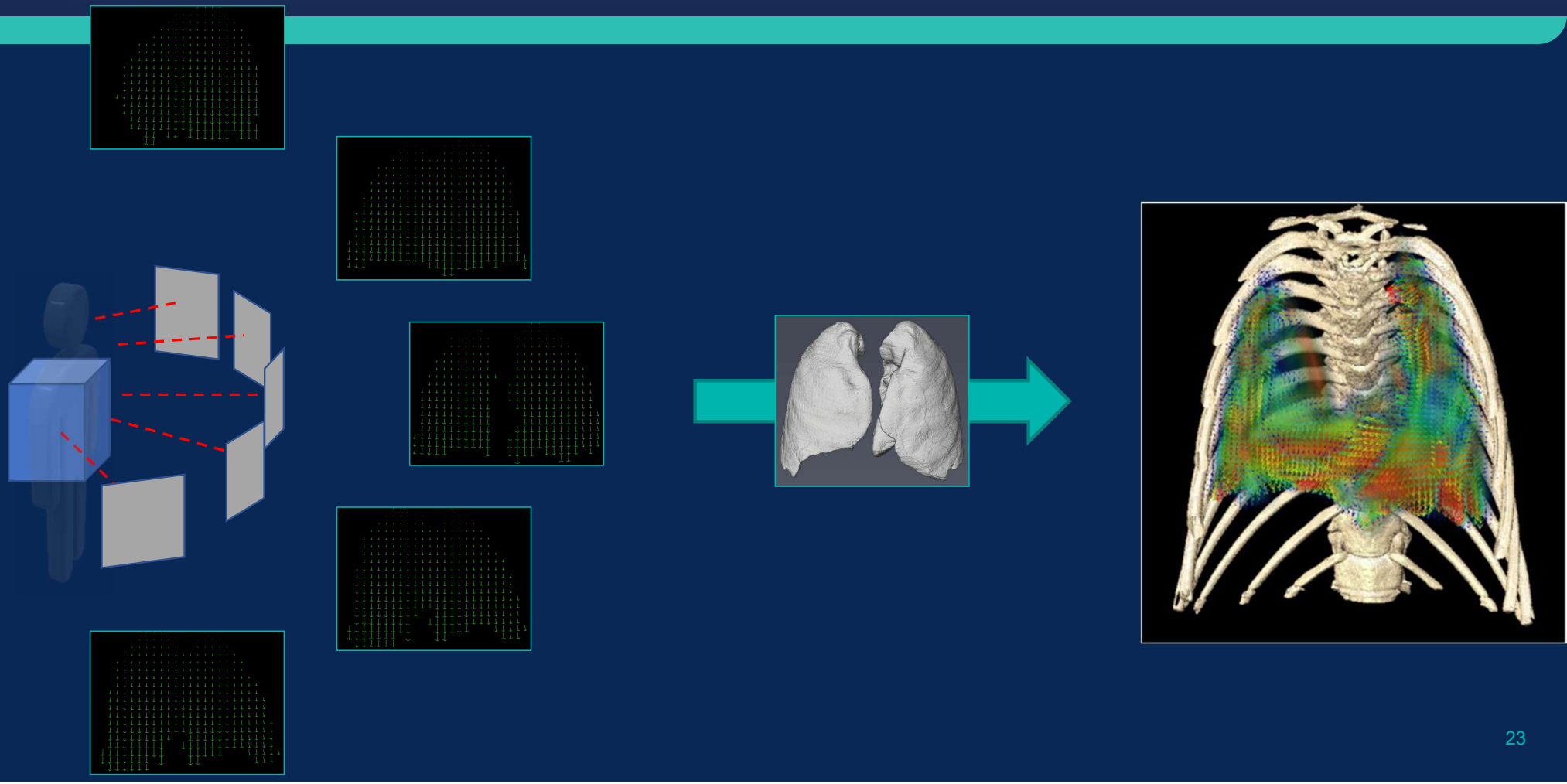
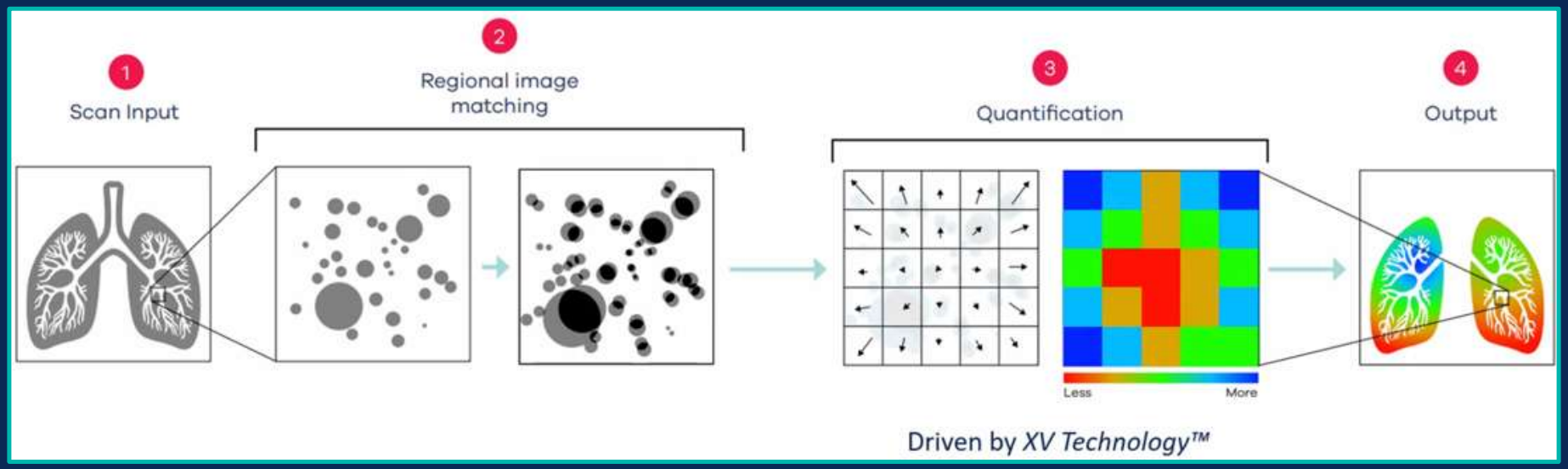


XV Technology



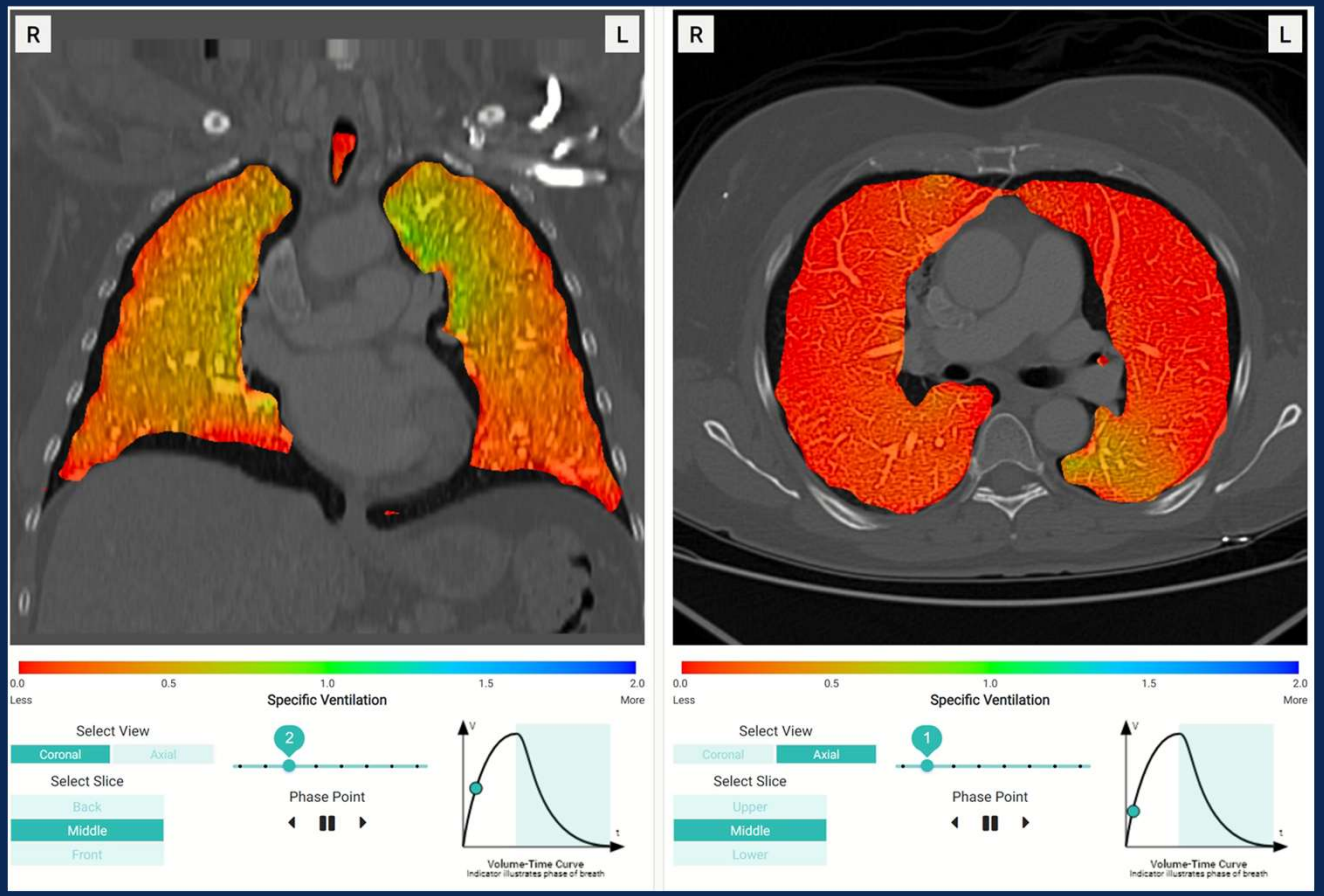
1 Inputs
Utilizes fluoroscopic X-ray at 5 angles during tidal breathing

2 Regional Image Matching
Lung segmentation, image voxel-wise registration

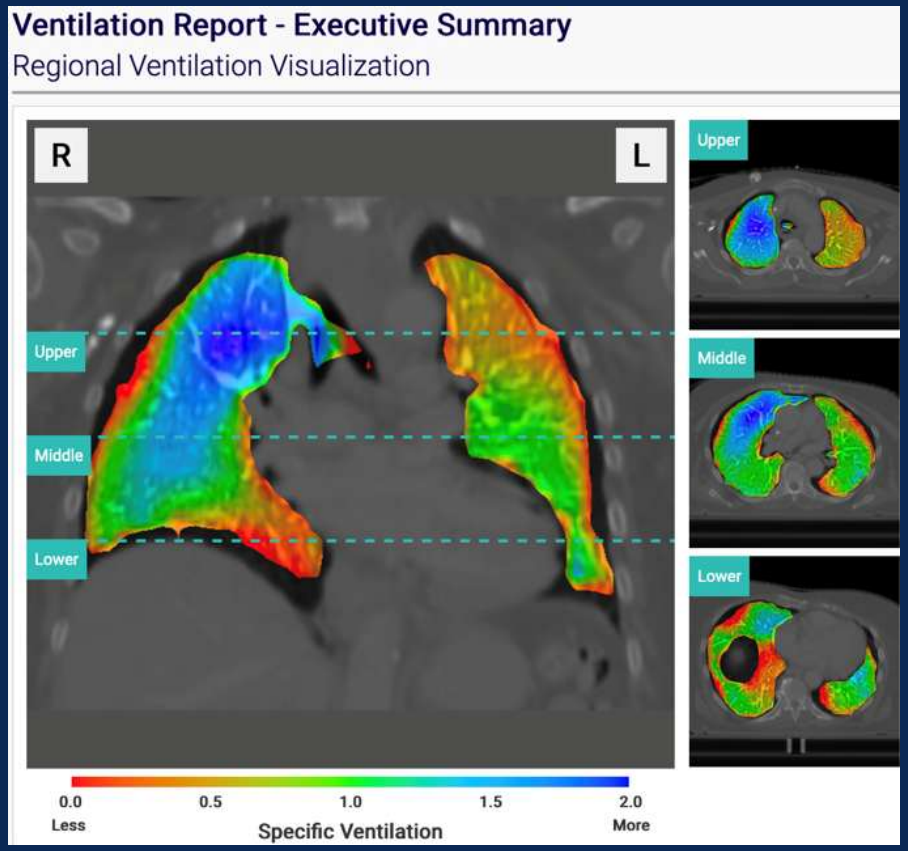
3 Quantification
X-ray velocimetry-based technique for motion field generation (XV Technology ™)

4 Output
Dynamic lung expansion maps are generated, and regional lung ventilation metrics reported

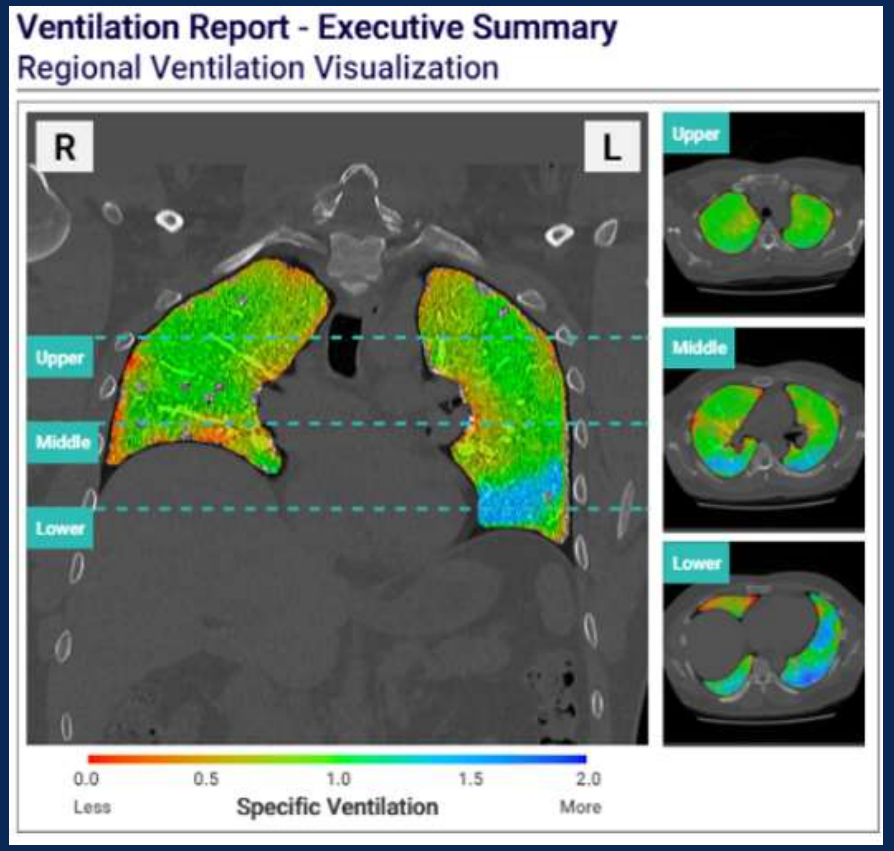
XV Technology in Motion



XV LVAS



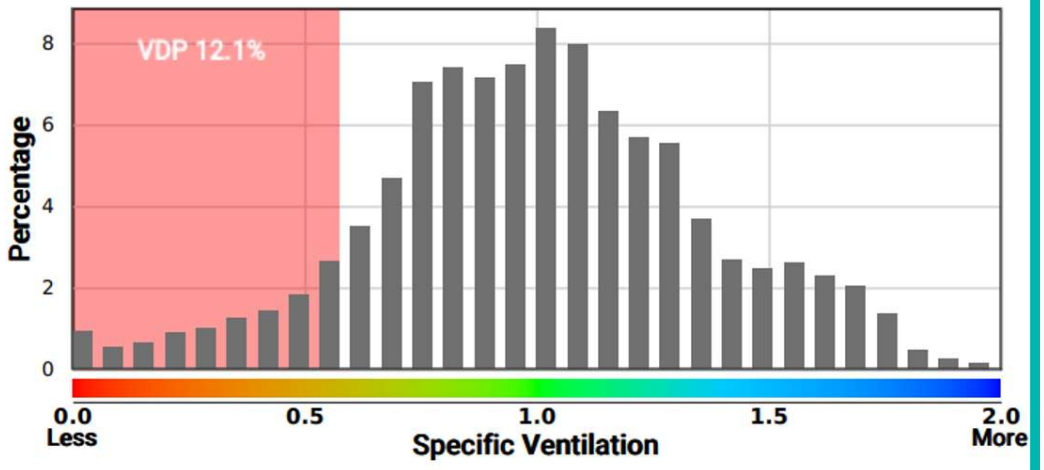
CT LVAS



XV LVAS

Ventilation Distribution Graph/Histogram

The frequency distribution of regional specific ventilation measured across the entire lung at peak inspiration.



CT LVAS

Ventilation Histogram

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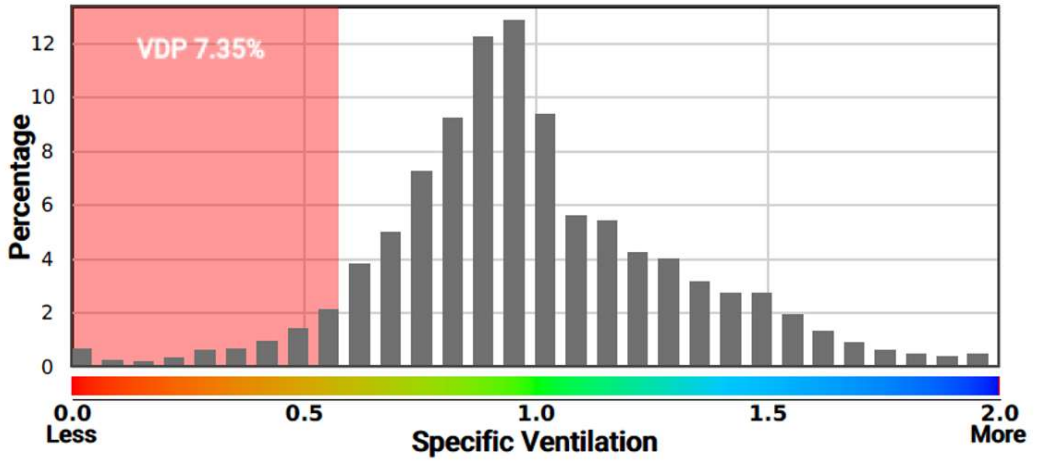
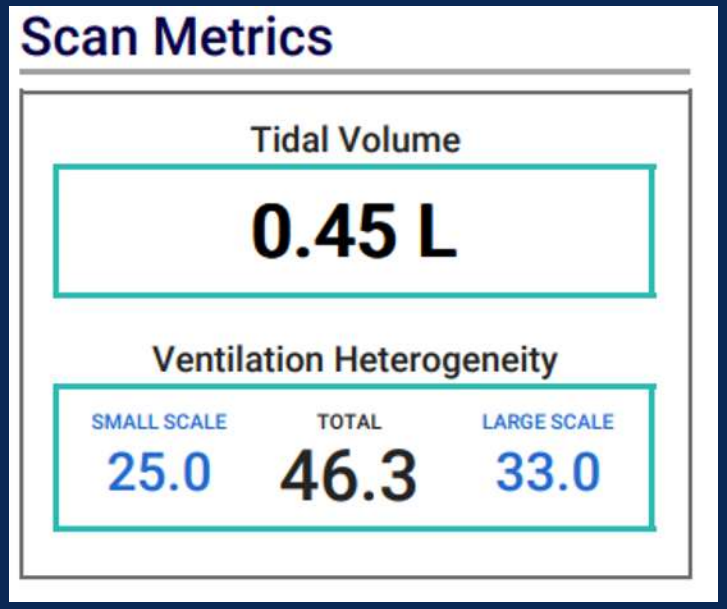
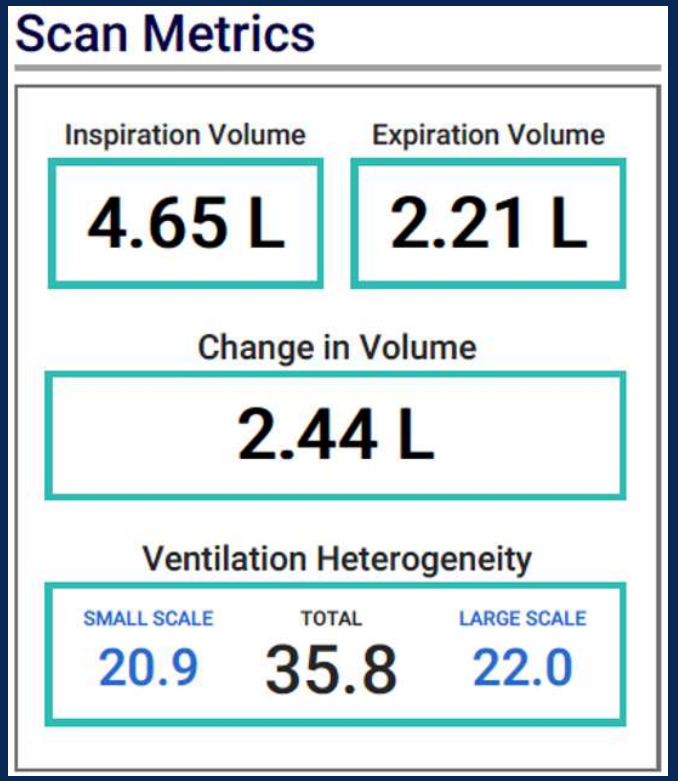


XV LVAS



CT LVAS

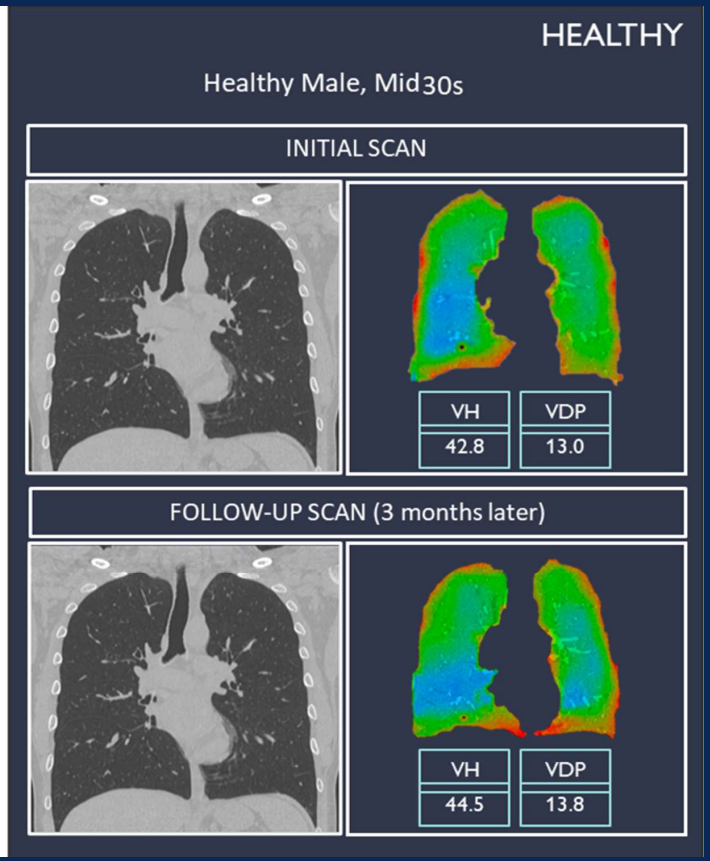


Clinical Utility

1. Validated assessment of regional lung function

2. Reliable repeatability of findings

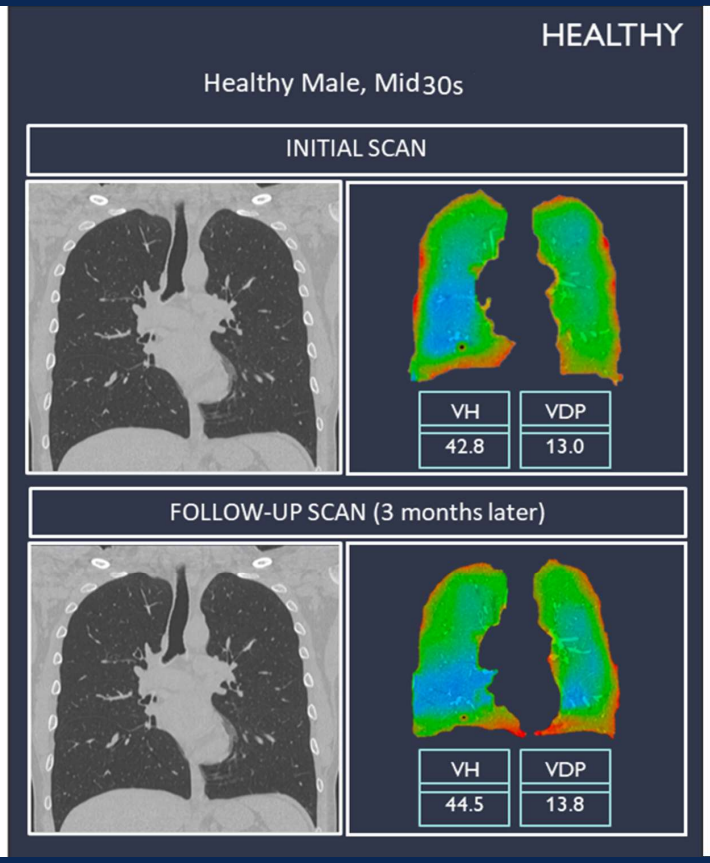
VH: Ventilation Heterogeneity
VDP: Ventilation Defect Percentage

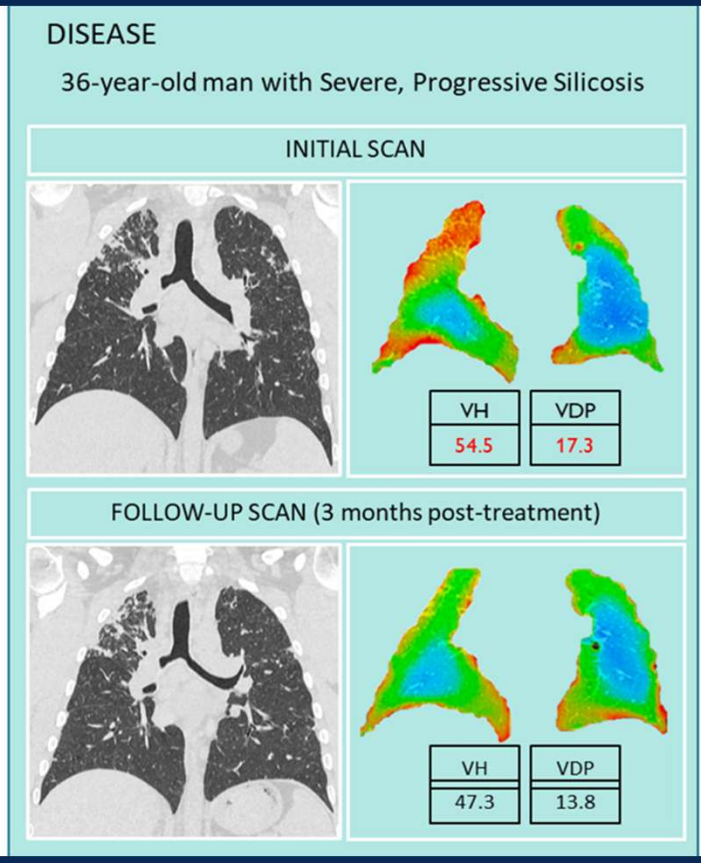


Clinical Utility

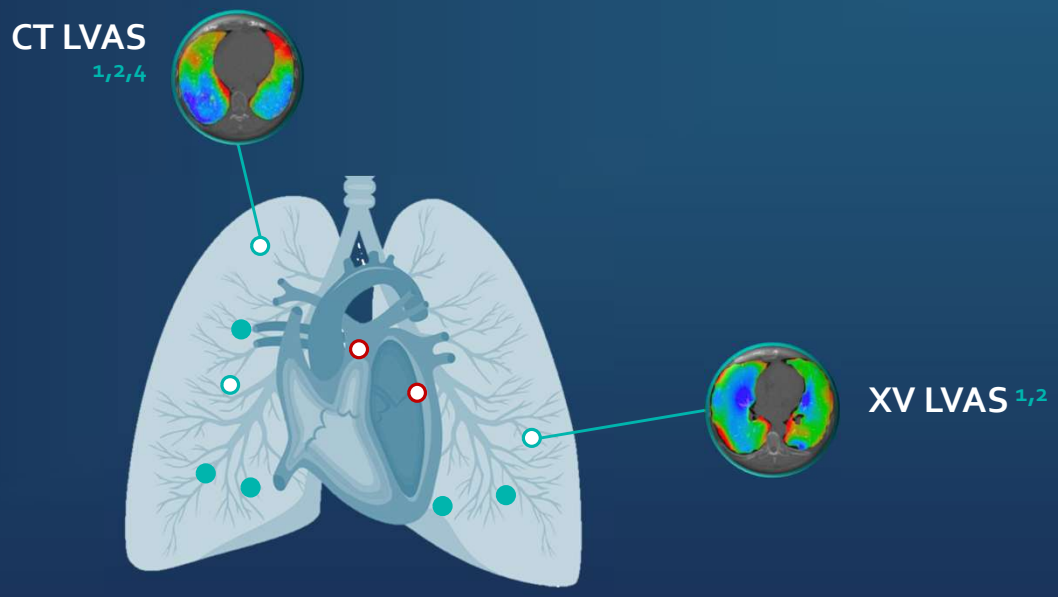
1. Validated assessment of regional lung function
2. Reliable repeatability of findings
3. Quantification of regional ventilation defects
4. Effective monitoring of disease and treatment effects

VH: Ventilation Heterogeneity
VDP: Ventilation Defect Percentage



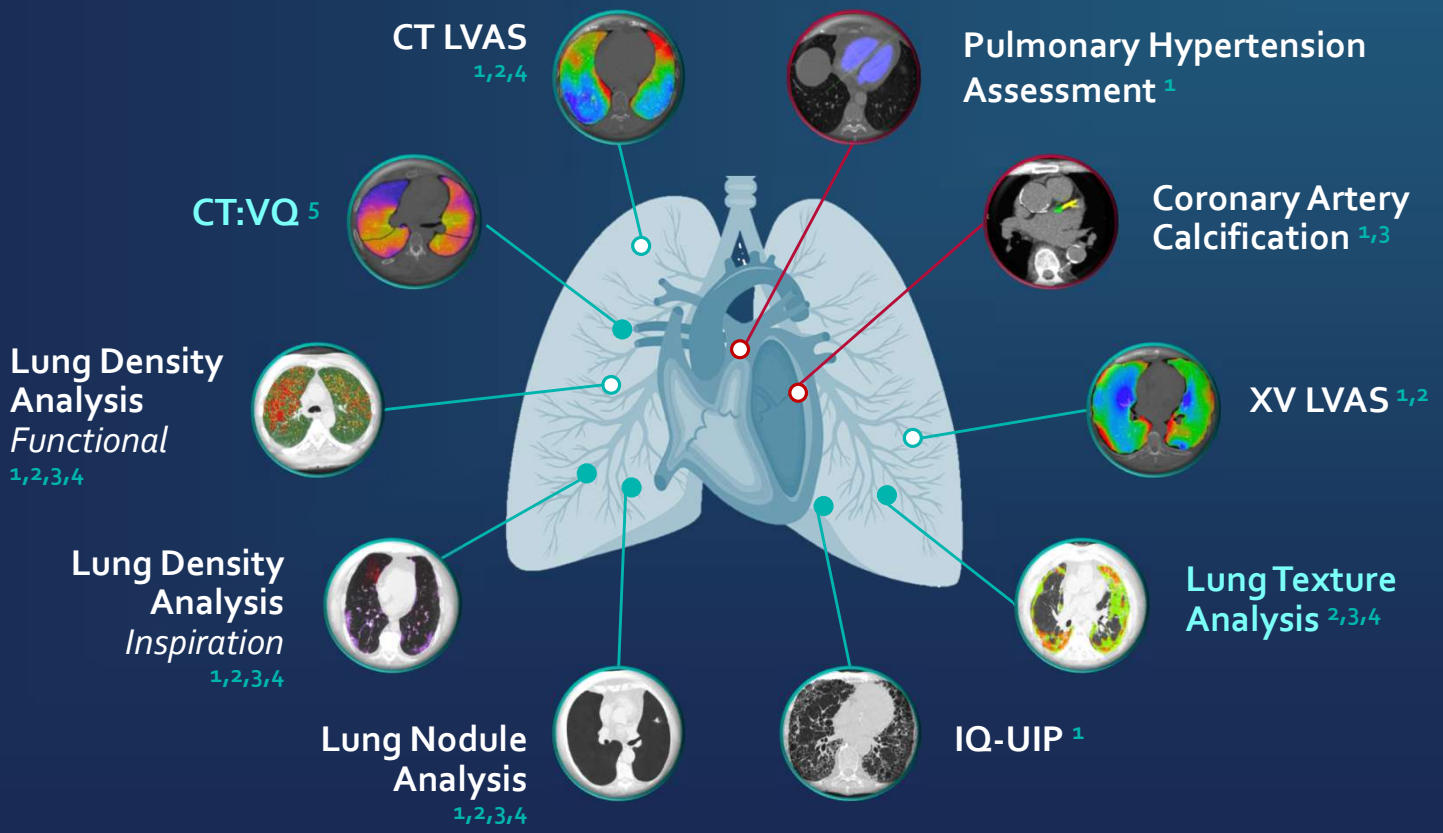


Functional Lung Analysis



1. FDA cleared
2. TGA approved
3. CE Approved
4. CMDR Canada
5. FDA clearance pending

Functional & **Structural** Lung Analysis



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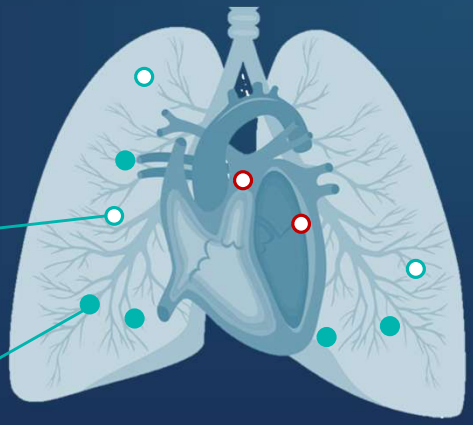
Structural Lung Analysis

Lung Density Analysis
Functional
1,2,3,4

Lung Density Analysis
Inspiration
1,2,3,4



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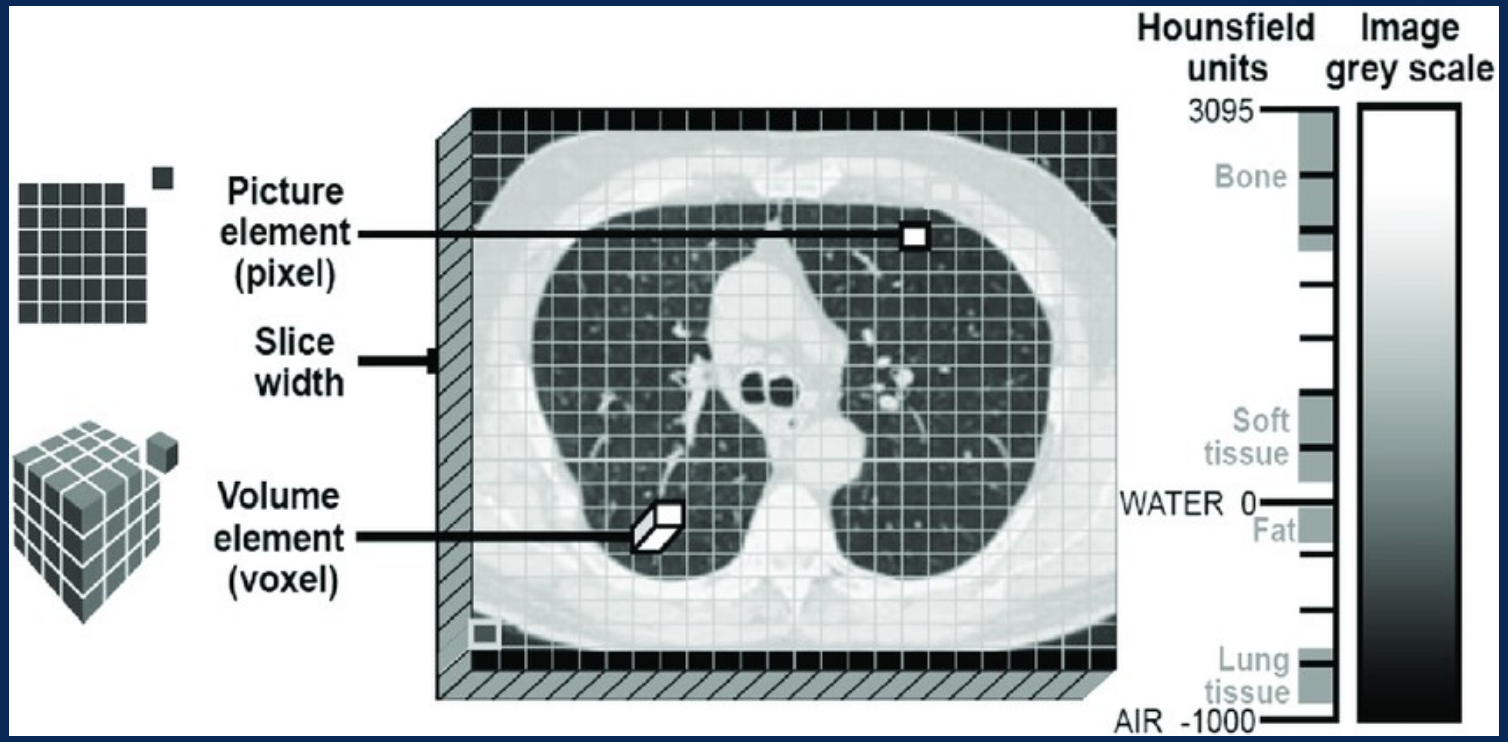
5. FDA clearance pending

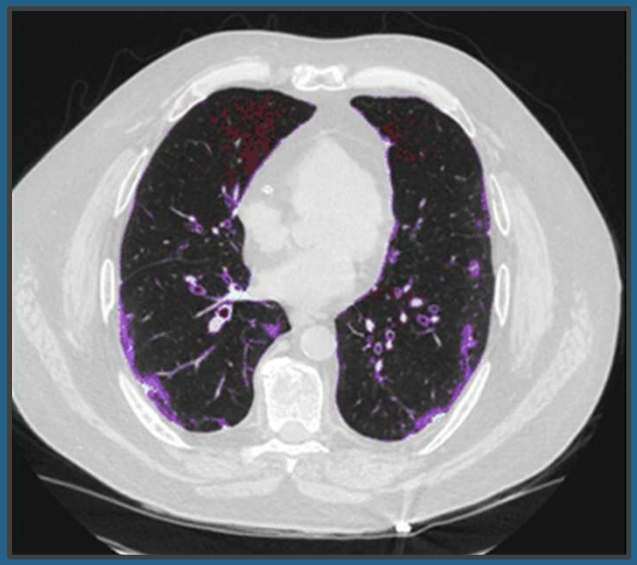
Hounsfield Thresholding



Lung Density Analysis – Inspiration (LDAi)

Fully-automated detection and quantification of EMPHYSEMA and High Attenuation (HAA)

Original CT Series



LDAi Analysis Series

LAA (emphysema) < -950 HU
HAA (GGO & Reticulation) -700 to -200 HU
VHA (consolidation) > -200 HU

LDAi Gaining Additional Insights

% of NLST participants with major smoking-related conditions

2.5%
Lung Cancer[1]
> 70% detected stage I or II

30.7%
Emphysema[2]
> 82% with no prior diagnosis of COPD

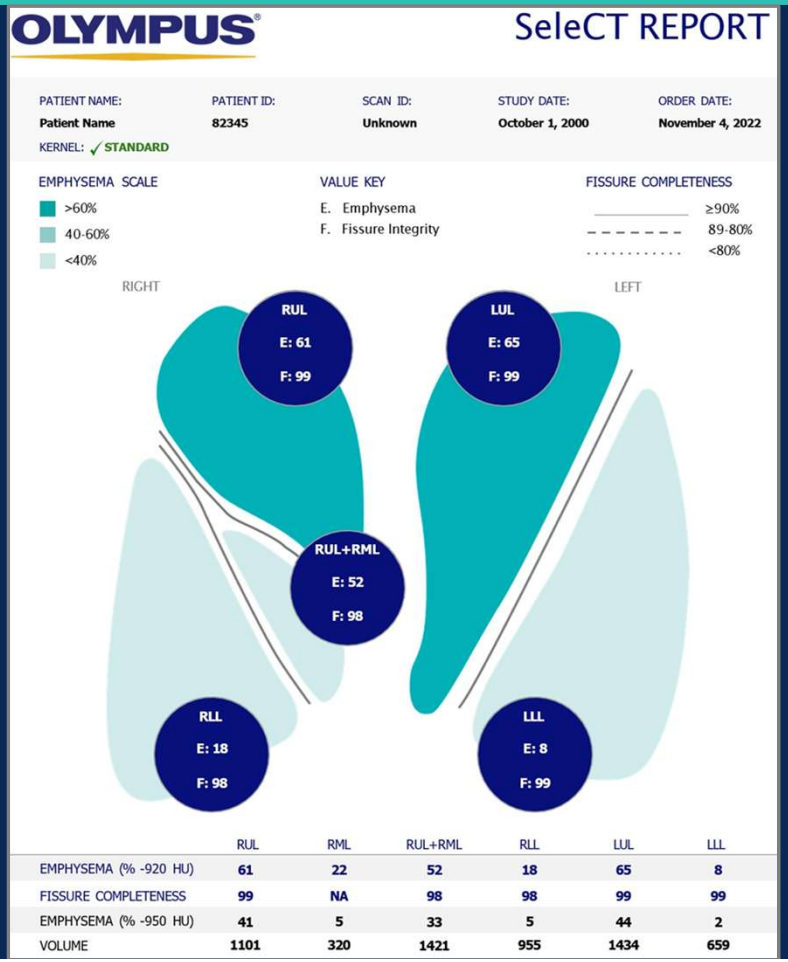
6.7%
CAC[3]
Majority with no prior diagnosis

1. The National Lung Screening Trial Research Team. N Engl J Med 2011;365:395-409
2. Mulshine JL et al. Ann Am Thorac Soc. 2023 Apr;20(4):499-503.
3. Gareen et al. JAMA Intern Med. 2023;183(7):677-684.

LDAi Adding Quantifiable Analysis to CT Scans & Reports

Custom Designed

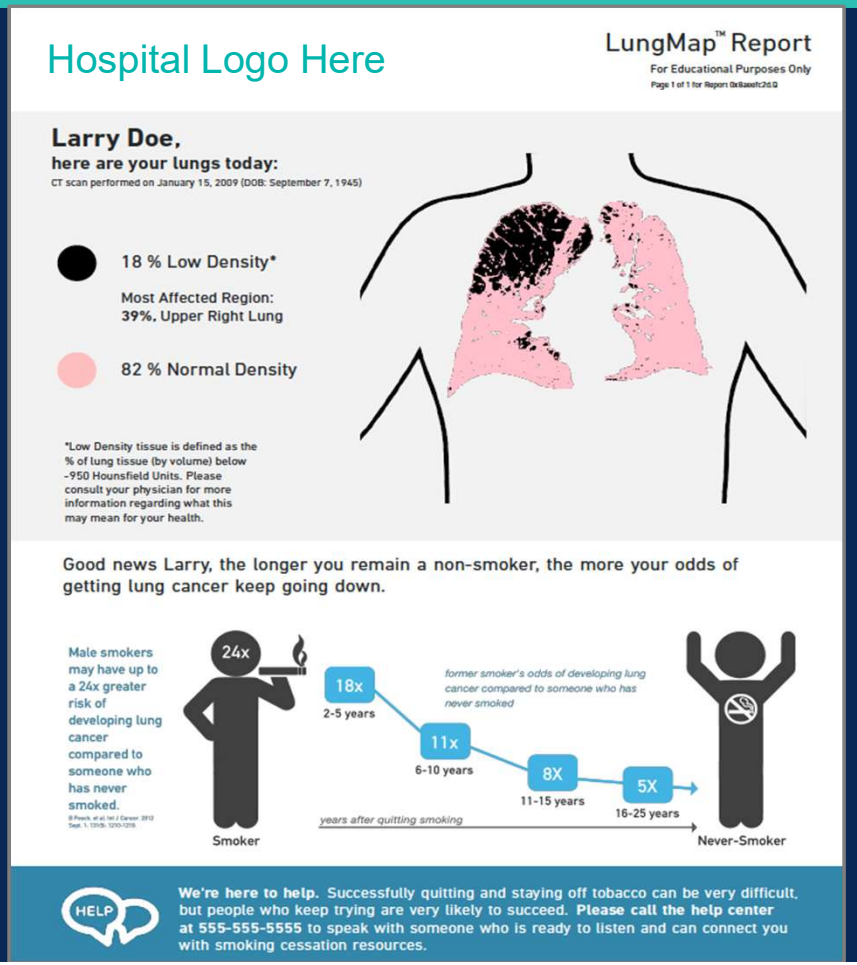
A custom algorithm designed for Olympus Spiration valve system including a customized and branded report and overall branded SeleCT QA service



LDAi Customized Reports for Patients

Patient LungMap™ for Smoking Cessation Counseling

- Simple yet powerful visual
- Quantification for easy comparison on future screenings
- Emphasizes the benefits of quitting smoking
- Provides help-line information
- Customizable logo and help line number



Development and Impact of a Patient-Centered, CT Image Data-Enhanced Lung Cancer Screening CT Report on Smoking Cessation Behaviors

Charlene McEvoy [1], Elizabeth Lando-King [2], Lauren Keith [3], Charles Hatt [3], Douglas Arenberg [4], Ella Kazerooni [4], Harry Lando [2]
[1] HealthPartners, Minneapolis, MN; [2] University of Minnesota, Minneapolis, MN; [3] Imbio, Inc, Minneapolis, MN; [4] Michigan Medicine, Ann Arbor, MI

NASHVILLE CHEST 2022 OCTOBER 16-19

Purpose

To develop a patient-centered lung cancer screening (LCS) CT report (Report) using data from each individual patient's specific screening CT exam to describe the impact of smoking cessation on current and future smoking-related disease risks, short and long-term health outcomes, and evaluate the report's impact on smoking cessation behaviors.

Methods

Study Details

Patients scheduled for Lung Cancer Screening at HealthPartners (Minneapolis, MN) and Michigan Medicine (Ann Arbor, MI) were approached for participation in this study.

Inclusion Criteria	Exclusion Criteria
• Age 55-74 • Smoking history ≥ 30-pack years • Currently actively smoking cigarettes • Ability to read, write and communicate in English • Screening CT scheduled at either HealthPartners or Michigan Medicine • Available by telephone for counseling and/or follow-up communications	• Clinically significant health problems that make projected lifespan ≤ 2 years • LungRads Category 3 or 4 resulted out on screening CT

Patients who provided informed consent were randomized to one

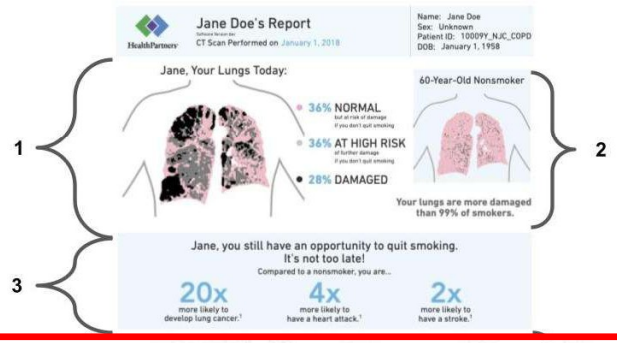
	Arm 1	Arm 2	Arm 3
Usual Care*	✔	✔	✔
Personalized Report		✔	
Counseling**			✔

* Usual Care: Receiving a screening results letter in the mail notifying them of
number for regional Quitline.
** Counseling: 45 minute telephone smoking cessation counseling session wit
developed at Mayo Clinic. In the event that the participant is in Arm 4 and recie
personalized report, the counseling protocols were updated to incorporate revi
Tobacco Treatment Specialists.

Primary outcomes included
- Follow-up calls at 3 weeks
- 3 months and 6 months to assess self-reported calls to the Quitline
- Readiness to quit among those who had not stopped smoking
- Quit attempts
- Use of cessation aids (programs and medications)
- Self-reported current tobacco use status.

Secondary outcomes included:
- Use of cessation services at 3 weeks, 3 months and 6 months.

Thinking about quitting was analyzed using logistic regression analysis, and readiness to quit (5-point Likert scale) was analyzed using a two-sample t-test.



Conclusions and Clinical Implications

A novel, patient-centered, automatically generated Lung Cancer Screening CT informed report was equivalent to a 45-minute tobacco cessation treatment visit at increasing thinking about quitting, and increased readiness to quit up to 3-months later. This report may enhance Lung Cancer Screening health outcomes by providing both screening results and other smoking-related health risks to promote cessation behaviors.

Report's development
- Multiple rounds of interviews and focus group discussions with individuals eligible for LCS.

The final Report reflects the constructs of the Health Belief Model
1. Image Section, visual feedback and quantitative results,
2. Comparative Section, mapping of the patient's lung status to a corresponding cohort of participants,
3. Health Outcomes Section, information about the long-term health outcomes for the associated participant cohort,
4. Quit Now Section, benefits of making a quit attempt, and
5. Outreach Section, contact information for smoking cessation support

Results

Cohort

Arm	Total Number	Sex *F/M*	Age *Mean (STD)*
1	79	38/41	67 (6)
2	80	38/42	65 (6)
3	82	52/30	65 (5.45)
4	90	38/42	54 (6)

Outcomes Details
CTQUIT: "Are you thinking about quitting cigarettes permanently?" Yes/No. *Haldane-Anscombe correction used
Readiness: "How ready are you to quit smoking?"4-level Likert scale. 4 = Very Ready
Likely to get CA: "In your opinion, how likely are you to get lung cancer in the next 10 years if you continue smoking?" 4-level Likert scale. 4 = Very Likely

Outcomes

	Call Response Rate			CT QUIT *Odds Ratio*			Readiness *Average Score*			Likely to get CA *Average Score*		
Arm	3 W	3 M	6 M	3 W	3 M	6 M	3 W	3 M	6 M	3 W	3 M	6 M
								75	2.85	2.85	2.94	2.95
								08	3.0	3.27	3.19	3.14
								61	2.80	3.24	3.06	3.09
								07	3.07	3.22	3.34	3.08

quitting" for participants who
iving counseling was 4.5

regarding readiness to quit

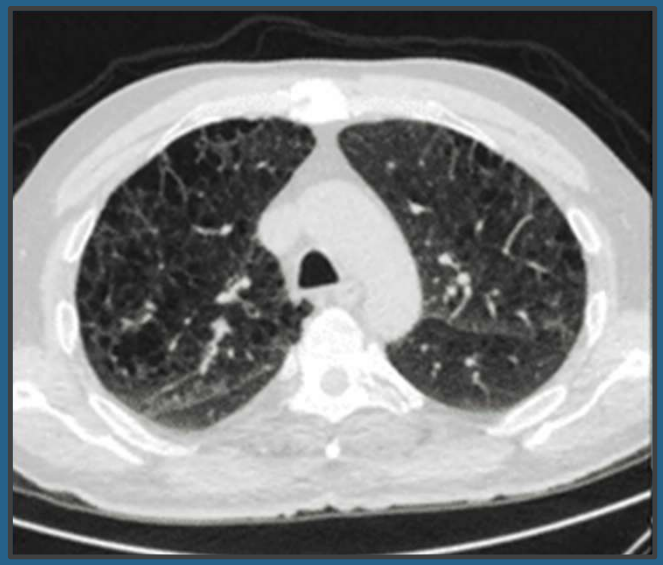
were more likely to get lung
cancer in the next 10 years than participants who did not ($p<0.05$).

Conclusions and Clinical Implications

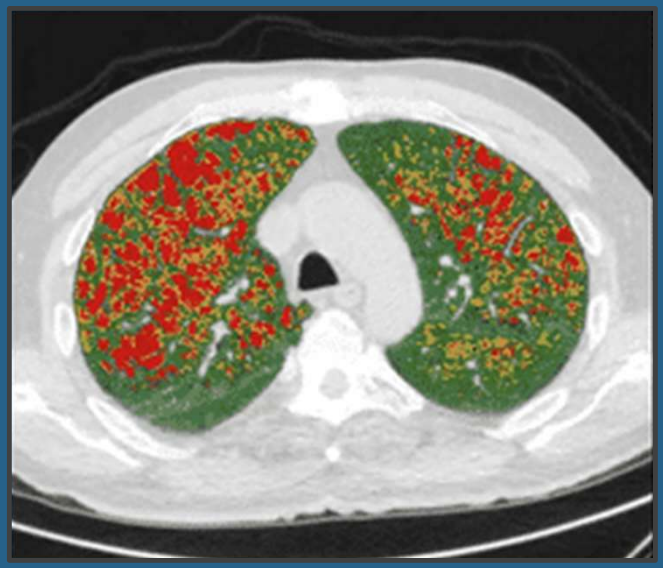
A novel, patient-centered, automatically generated Lung Cancer Screening CT informed report was equivalent to a 45-minute tobacco cessation treatment visit at increasing thinking about quitting, and increased readiness to quit up to 3-months later. This report may enhance Lung Cancer Screening health outcomes by providing both screening results and other smoking-related health risks to promote cessation behaviors.

Lung Density Analysis – Functional (LDAf)

Advanced COPD analysis of early-stage AIR TRAPPING and late-stage EMPHYSEMA



Original CT Series



LDAf Analysis Series

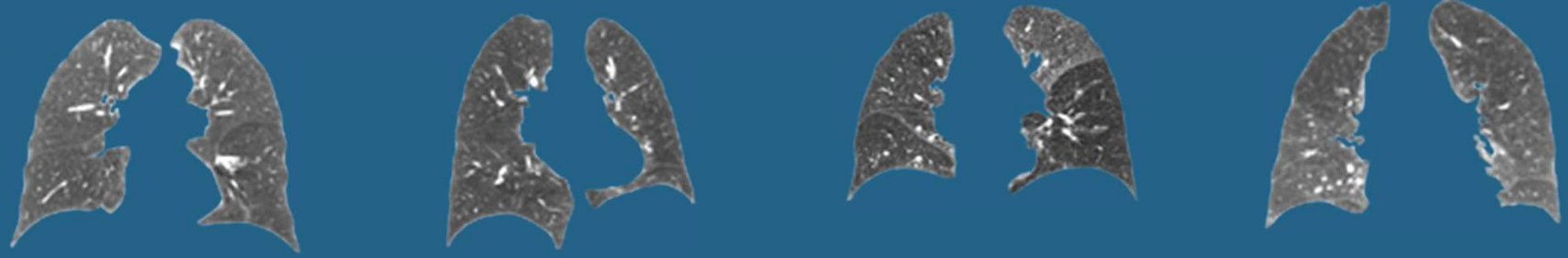
Normal
Early Disease
Advanced Disease

Standard Clinical Assessment

	Subject A	Subject B	Subject C	Subject D
GOLD	2	2	2	2
$FEV1_{pp}$	61%	62%	61%	62%

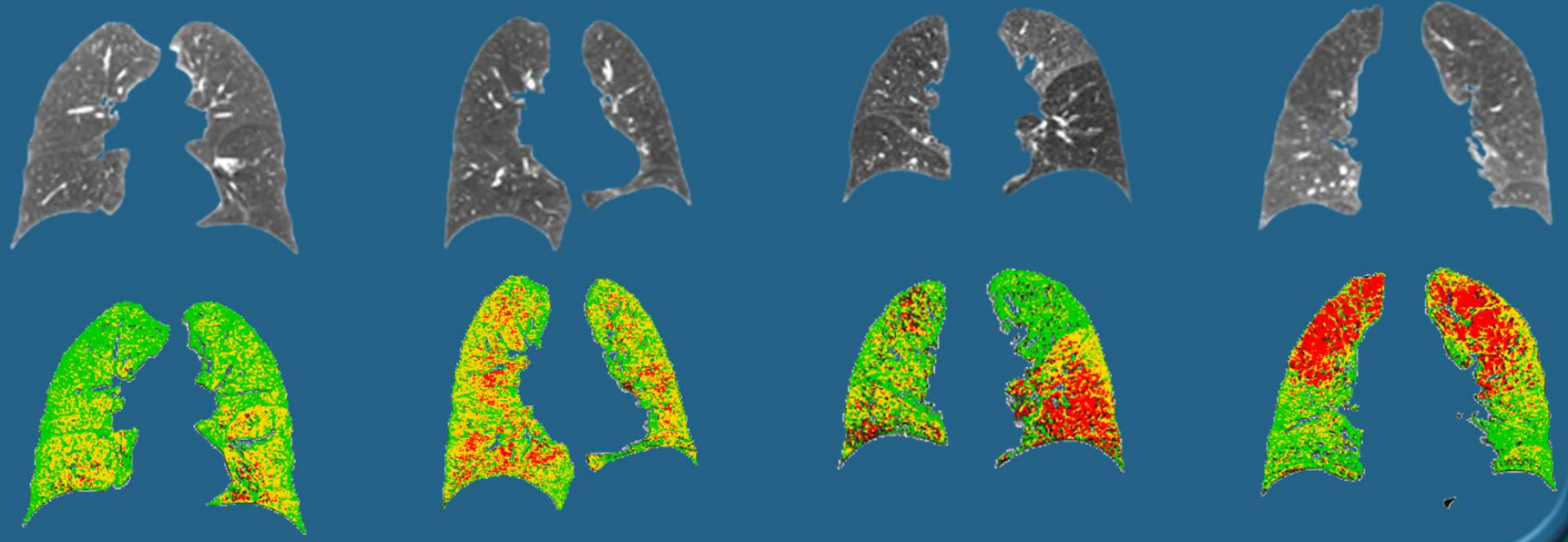
Standard Clinical Assessment

	Subject A	Subject B	Subject C	Subject D
GOLD	2	2	2	2
$FEV1_{pp}$	61%	62%	61%	62%



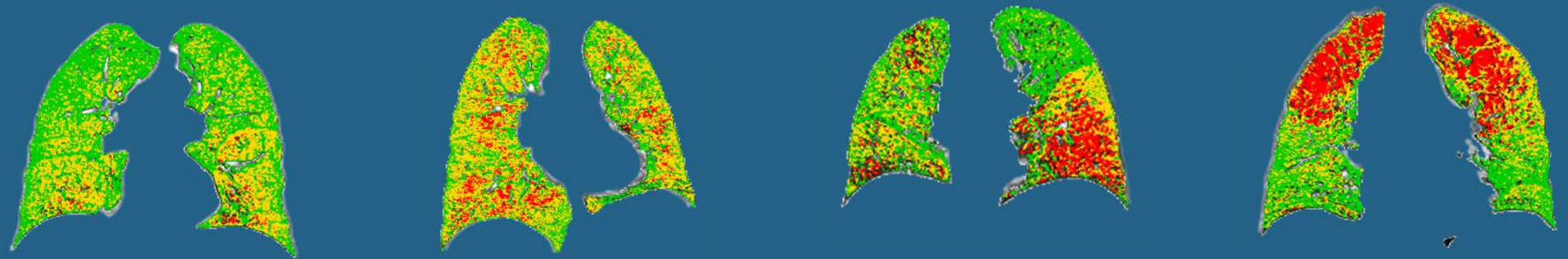
LDAf Analysis

	Subject A	Subject B	Subject C	Subject D
GOLD	2	2	2	2
$FEV1_{pp}$	61%	62%	61%	62%

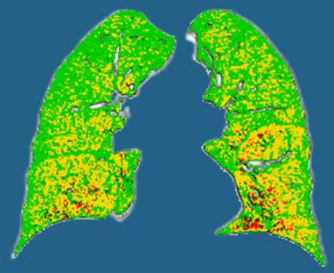
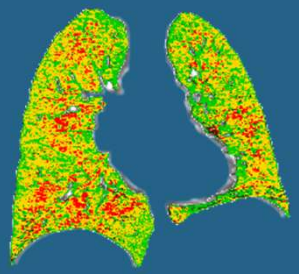
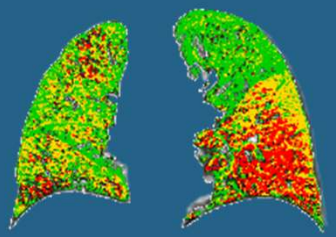
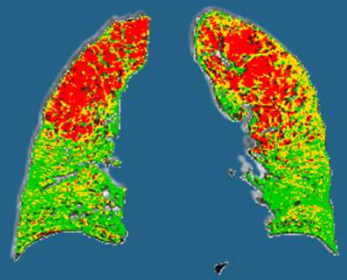


LDAf Analysis

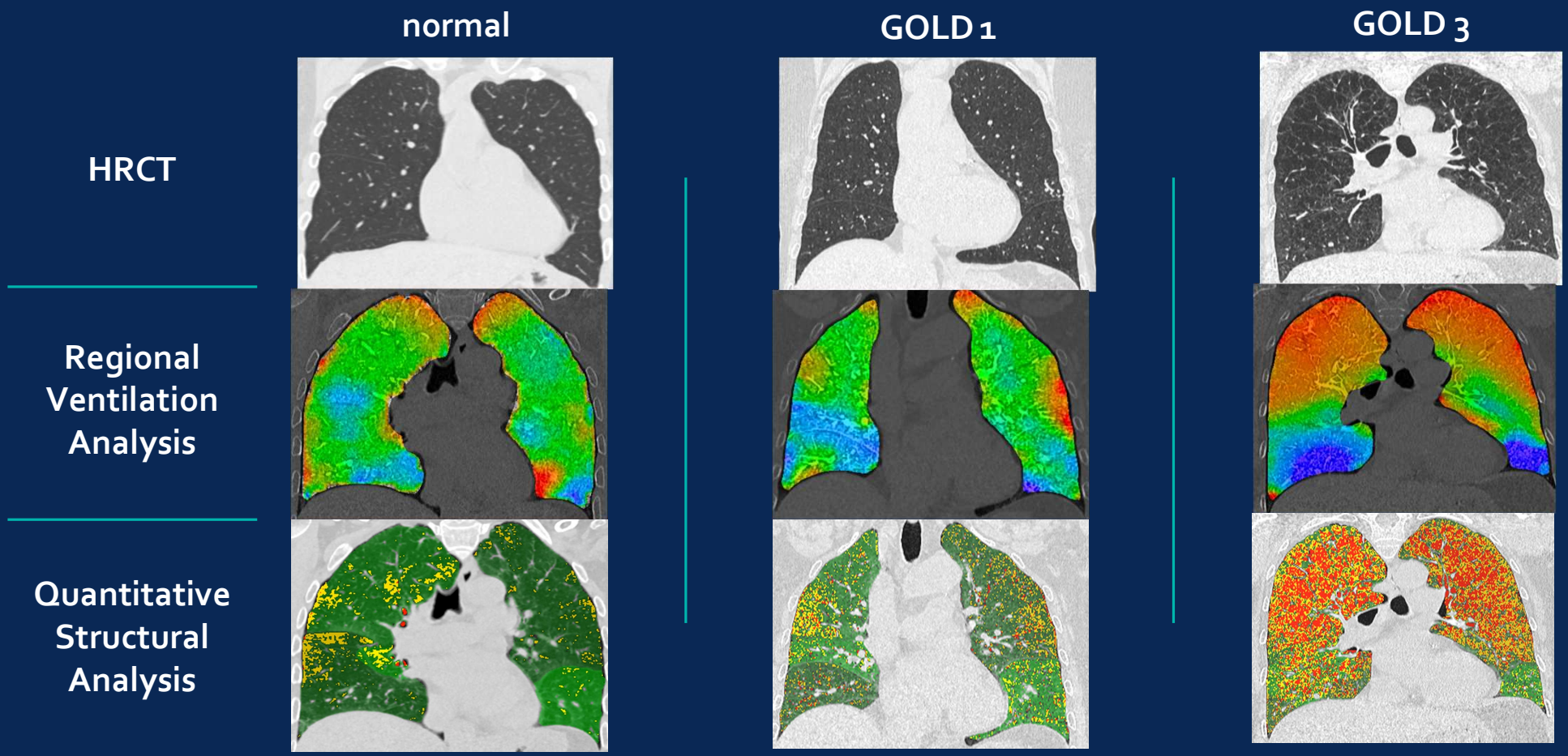
	Subject A	Subject B	Subject C	Subject D
GOLD	2	2	2	2
$FEV1_{pp}$	61%	62%	61%	62%



LDAf Adding Quantifiable Analysis to CT Scans & Reports

	Subject A	Subject B	Subject C	Subject D
GOLD	2	2	2	2
$FEV1_{pp}$	61%	62%	61%	62%
				
Normal	56%	42%	48%	43%
Functional *(air-trapping)*	41%	49%	32%	26%
Persistent *(indic. of emphysema)*	3%	9%	13%	25%

Combining Lung Function & Structure



Solving the Clinical Conundrum

The Conundrum in Lung Assessment

A mismatch between clinical tests and imaging often occurs, whereby anatomic findings can overlap, lag, or precede clinical symptoms.

Need **structural** and **functional** to make a better, informed clinical decision.

Not solved by historical standard of care testing (Spirometry, X-ray, CT scans)

Clinical Tools Needed to Solve the Conundrum

Functional lung analysis providing visual qualitative and quantitative assessment of **ventilation**

+

Structural lung analysis providing visual qualitative and quantitative assessment of lung **anatomy**

Applications for Technologies in Clinical Practice

Breathlessness

A complex clinical presentation

- Is it Lung related?
- Is it Cardiac related?
- Is it other causes or psychosomatic?

Restrictive diseases

DRRD / CB *Deployment-related respiratory disease/ Constrictive bronchiolitis |* ***ILD*** *Interstitial Lung Disease |* ***IPF*** *Idiopathic pulmonary fibrosis |* ***Dust Exposures*** *— Silicosis, asbestosis, pneumoconiosis*

Obstructive diseases

COPD *Chronic Obstructive Pulmonary Disease— Emphysema, Chronic Bronchitis |* ***Asthma*** *|* ***CF*** *Cystic Fibrosis*

Intervention and pharmaceutical

Lung Reduction therapies | Disease progression / regression | Compliance

Potential Use Cases

- Acute Bronchitis
- Alpha-1 Antitrypsin Deficiency (AATD)
- ARDS
- Asthma
- Asthma/COPD Overlap
- Bronchopulmonary Dysplasia
- Bronchoscopic Lung Volume Reduction
- COPD
- COVID-19
- Cystic Fibrosis
- Emergency Room
- General anaesthesia
- HIV-related Lung Diseases
- Hospital 30 day readmission
- Implantable cardioverter-defibrillator (ICD)
- Inability to comply with PFT requirements
- IPF
- Lung Transplant
- Medical Devices
- Neuromuscular Lung Disease
- Occupational Lung Disease
- Other lung cancer treatment options
- Pneumonia
- Pulmonary edema
- Pulmonary Hypertension
- Pulmonary Rehabilitation
- Radiation for Lung cancer
- Radiation Therapy
- Sarcoidosis
- Sepsis
- Surgical Planning
- Thoracic Surgery
- Tuberculosis (TB)

Thank You!

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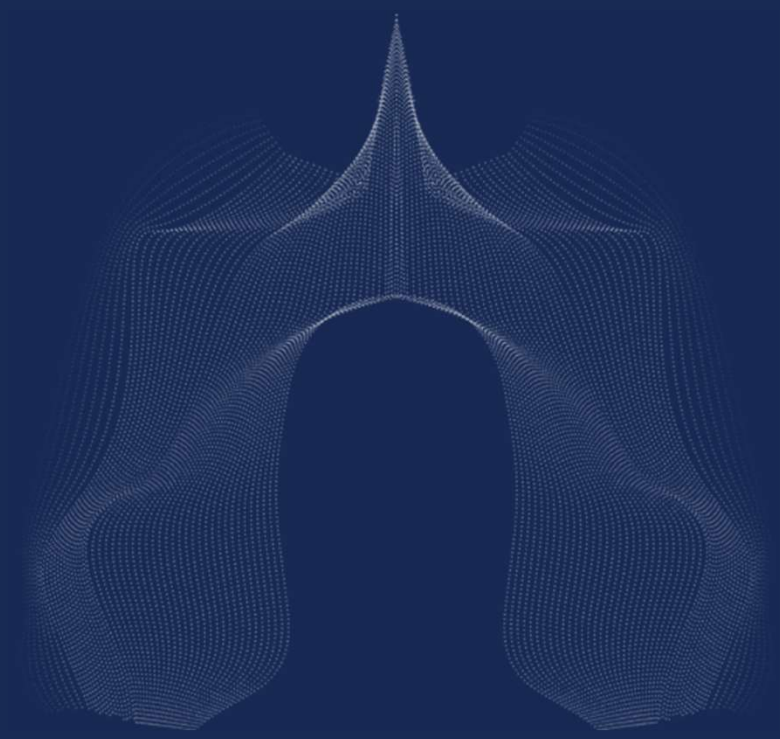
David G. Westenkirchner, BS, RRT

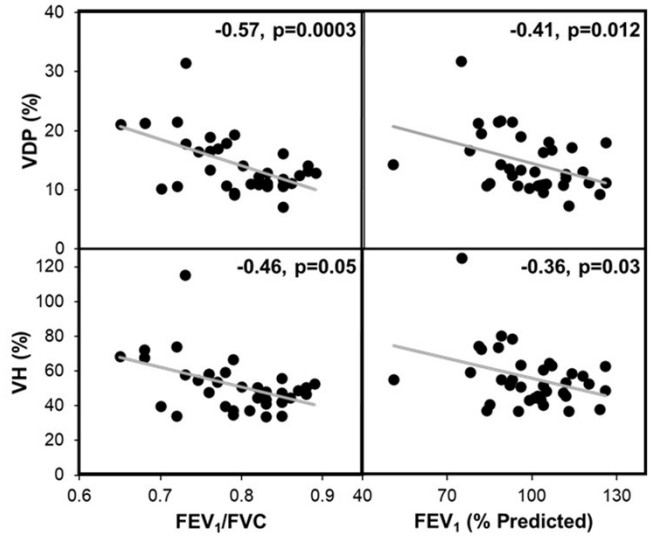


Appendix

Clinical Trial Results: Cedars Sinai (FDA Validation study)

Ventilation Heterogeneity as a biomarker of disease

- Patients undergoing thoracic radiotherapy for non-lung cancer malignancies were assessed using PFTs and functional lung imaging before treatment and at 4- and 12-months post treatment.
- Results revealed correlation between VDP and VH—and spirometry (FEV_1 and FEV_1/FVC).*



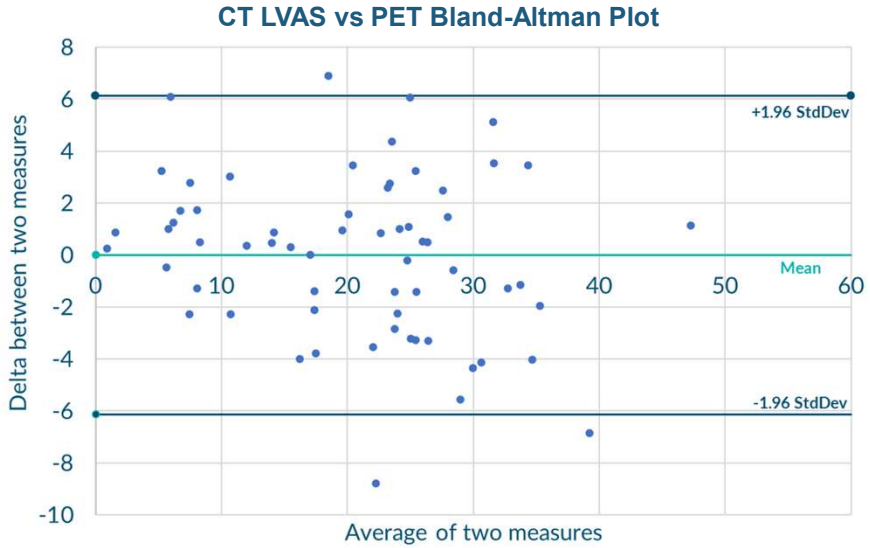
Case Study

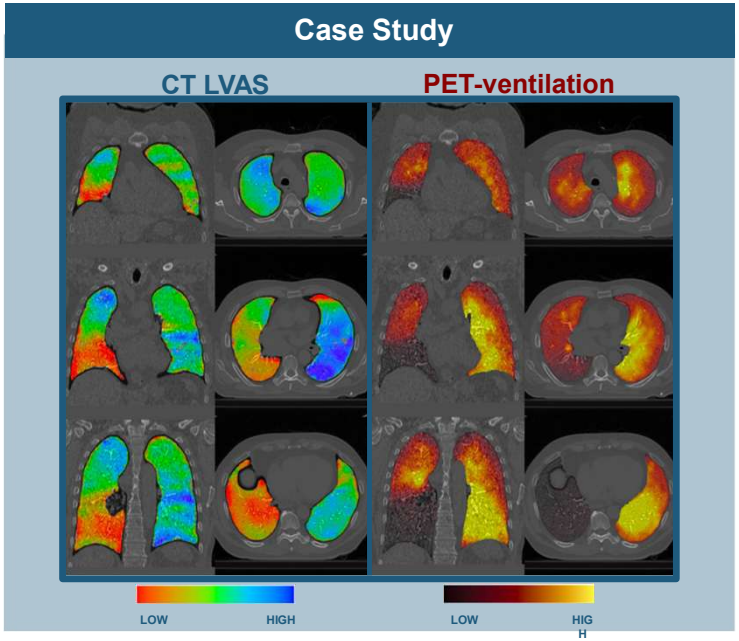
This case study demonstrates the capability of functional lung imaging to detect subtle changes in lung function which are otherwise undetectable or delayed using PFTs. A decline in lung function assessed by VDP and VH was observed at 4-months post-treatment, whereas PFT outputs remained largely unchanged until 12-months post radiotherapy treatment.

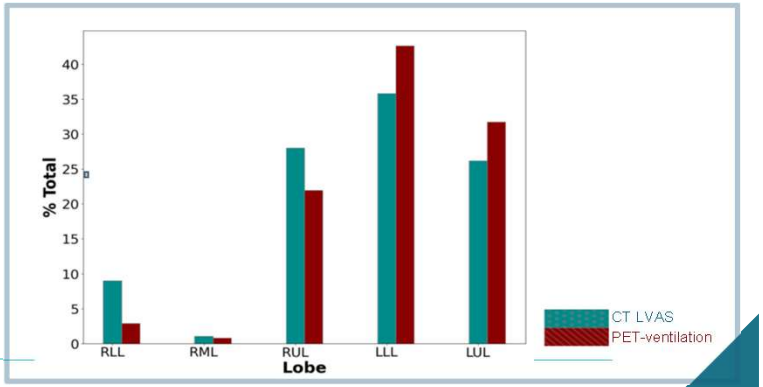
*Presented data is from HFFLI study (ClinicalTrials.gov Identifier: NCT02735746) using XV LVAS (FDA cleared, ARTG listing number: 344948).

Clinical Validation of CT LVAS

- Lung cancer patients underwent ventilation imaging using PET-ventilation and CT LVAS* scans.
- CT LVAS demonstrated good agreement with PET-ventilation in the assessment of ventilation at a lobar level.
- CT LVAS offers benefits of improved spatial resolution, avoidance of exogenous contrasts and wide availability making it a powerful imaging tool for a range of applications, including surgical or targeted treatment planning, disease characterization, and general lung health assessment.







4DMedical Partnership Presentation

*CT LVAS ARTG listing number: 344948

*Results accepted for presentation at ATS meeting (May 19-24, 2023, Washington, DC)

4DMedical™