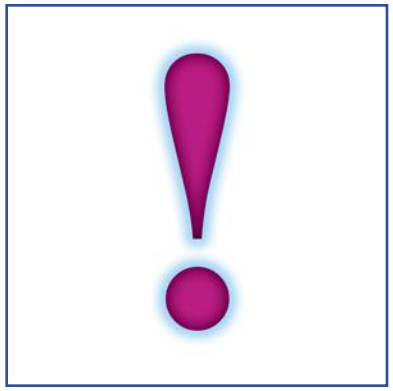
Pneumo Update Europe 2018

15 - 16 June, Budapest

Hot Topic: Pulmonary Imaging- What the scientific world is talking about



Hans-Ulrich Kauczor, Germany

What is new? What is important?

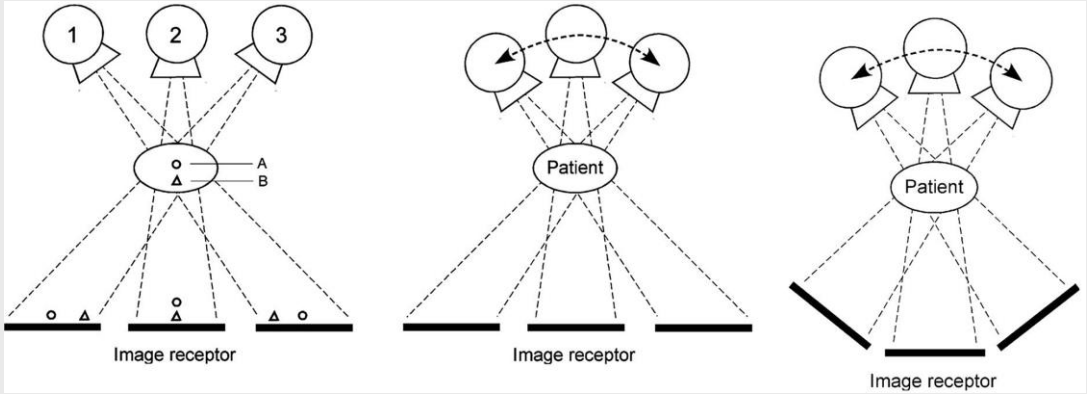
- **Technical Advances**
- **Airway diseases: COPD, CF**
- **Diffuse parenchymal lung disease**
- **Pulmonary nodules, lung cancer, radiomics**
- **Precision cancer therapy: pulmonary complications**

Technical advances

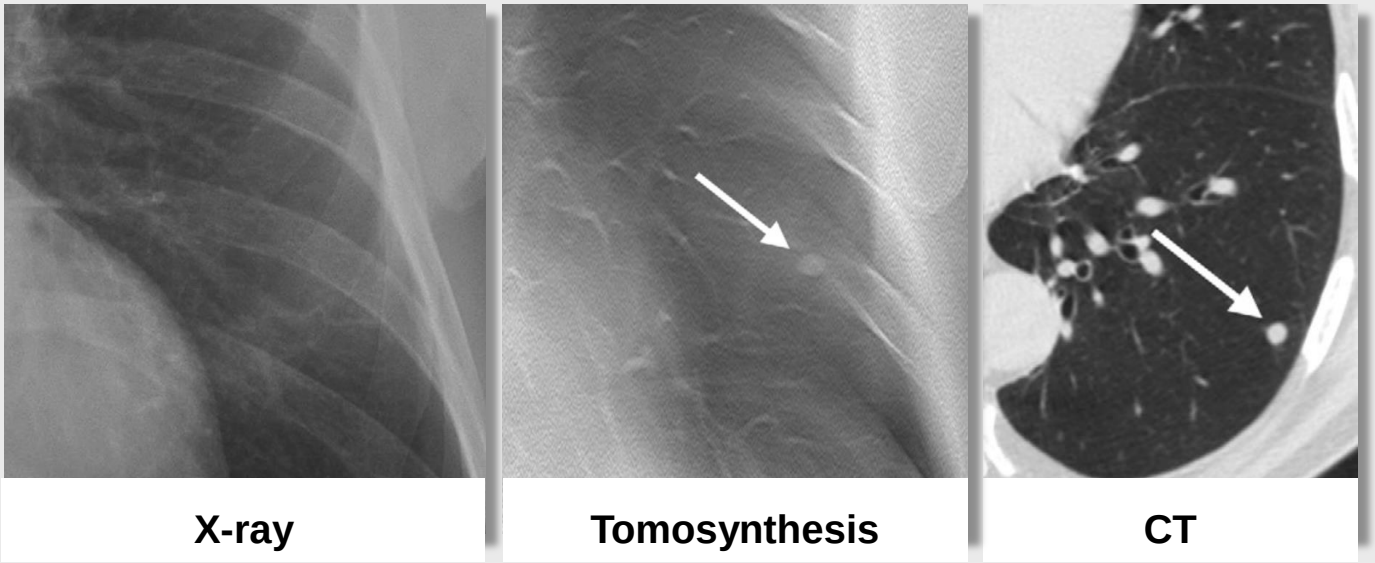
State-of-the Art: Technical Advances

- **Plain film, projection radiography**
- **CT: helical, dual energy, spectral**
- **MRI:**
  proton: ultrashort TE, contrast agent: Gd, oxygen
  non-proton: hyperpolarized gases: 3He, 129Xe

Digital Tomosynthesis



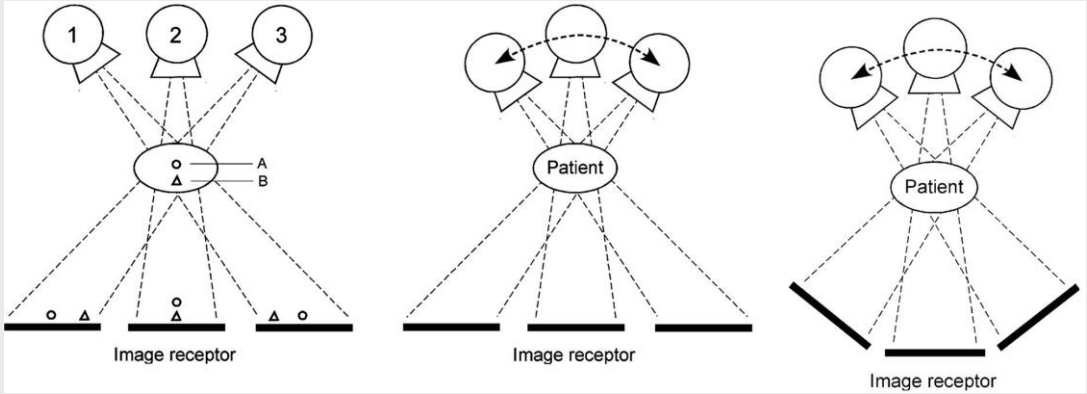
- **158 pulmonary nodules**
- **tomosynthesis: 120kVp, 60 images, 30º rotation, copper filter, dose 0.1 mSv**
  x-ray: two planes; 120kVp; dose 0.06 mSv



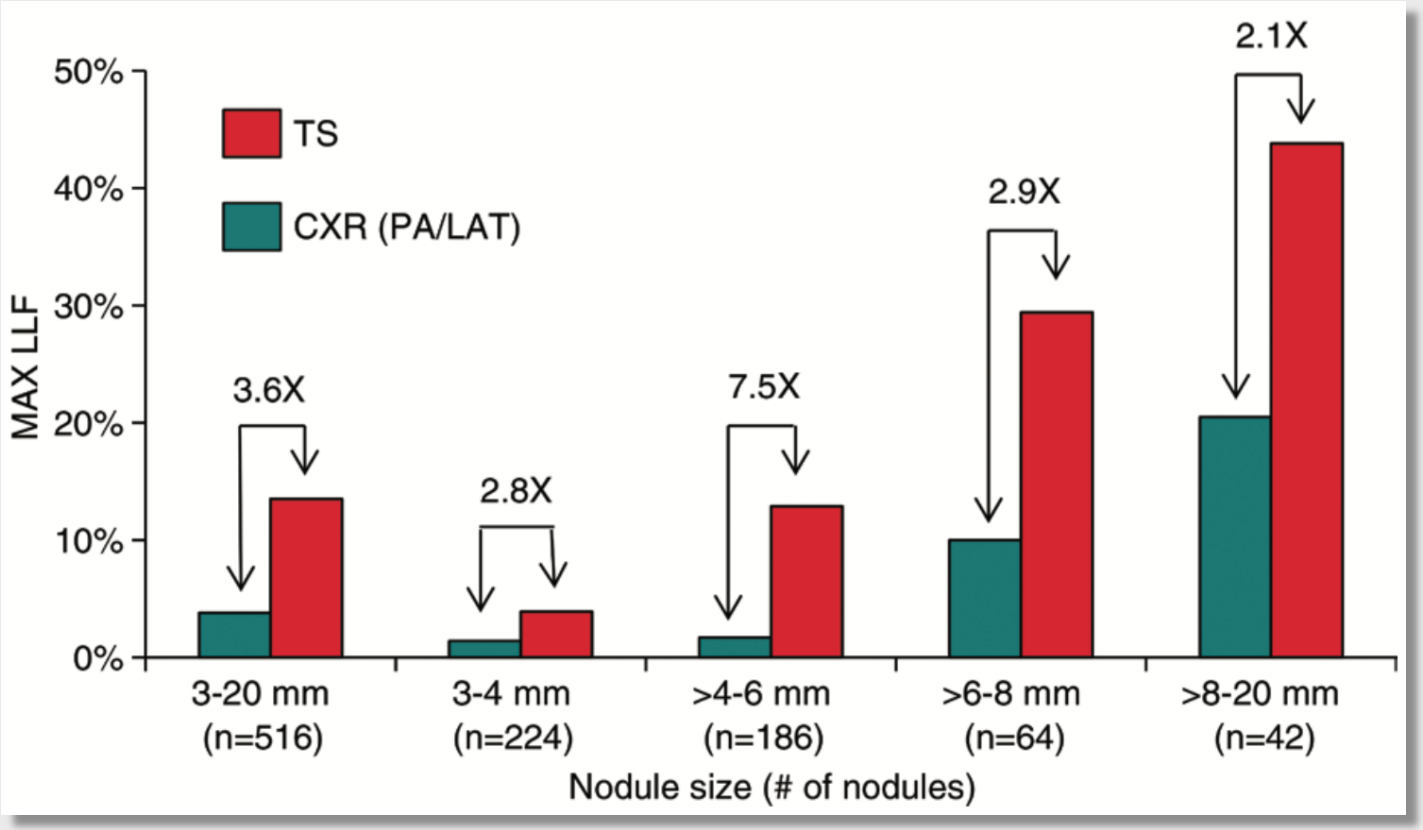
X-ray | **Tomosynthesis** | **CT**

Dobbins-JT et al. Radiology 2017; 282:236-250
Ferrari-A et al. Ann Transl Med 2018;6:91

Digital Tomosynthesis



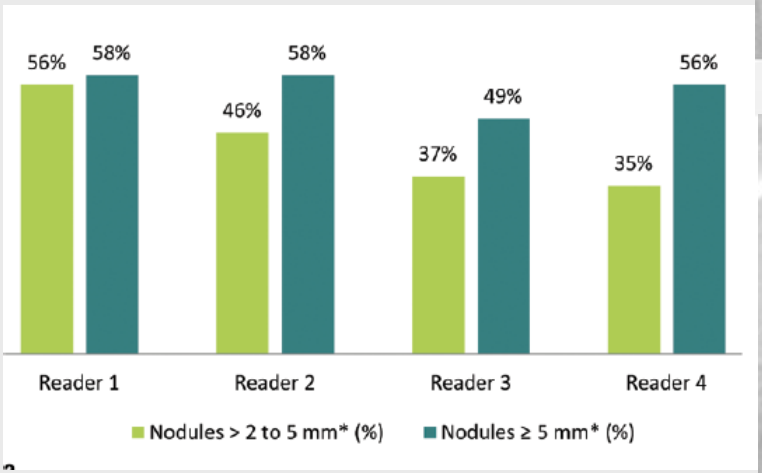
- **158 pulmonary nodules**



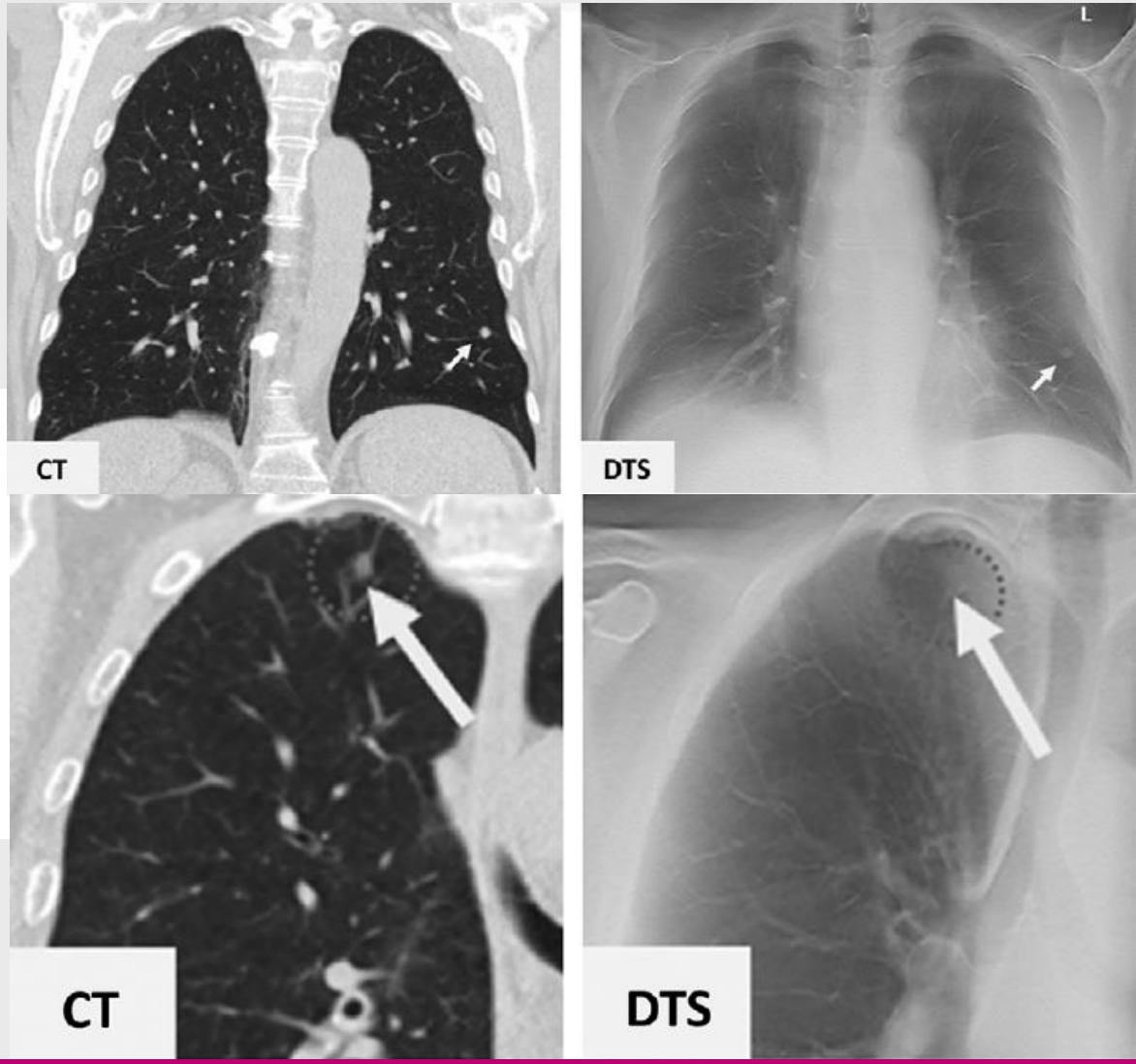
Dobbins et al. Radiology 2017; 282:236-250
Ferrari-A et al. Ann Transl Med 2018;6:91

Digital Tomosynthesis as good as CT?

1111 participants of Swedish cardiopulmonary Bioimage Study (SCAPIS)
125 with 252 nodules

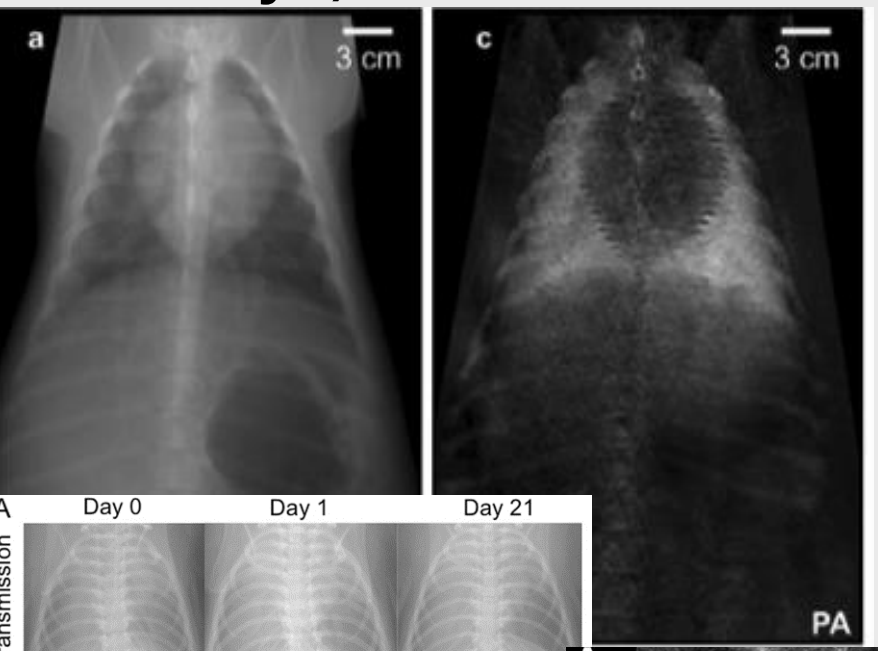


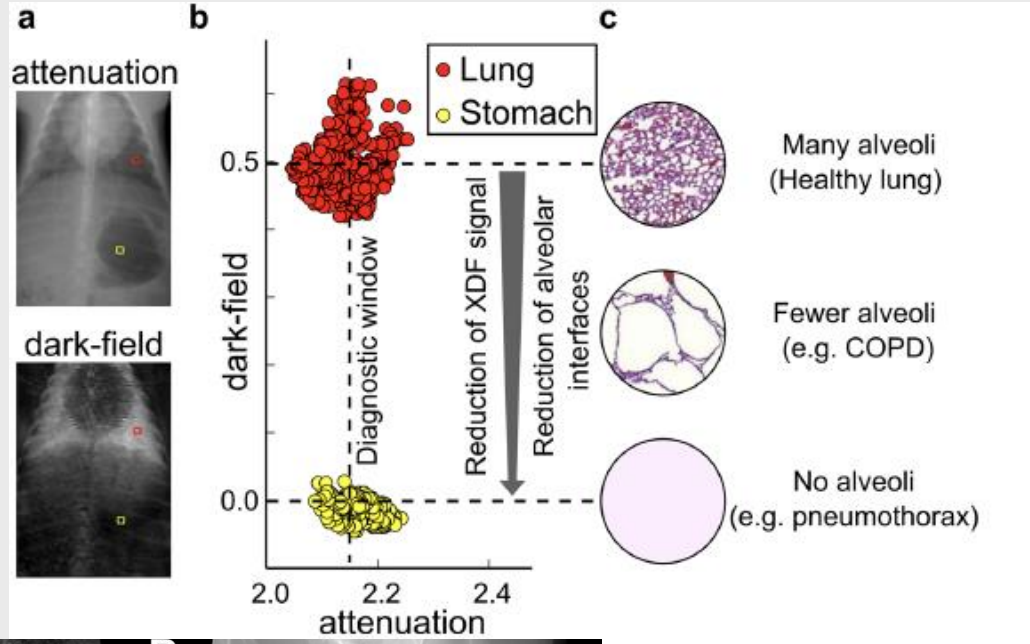
Meltzer-C et al. Radiology 2018; epub

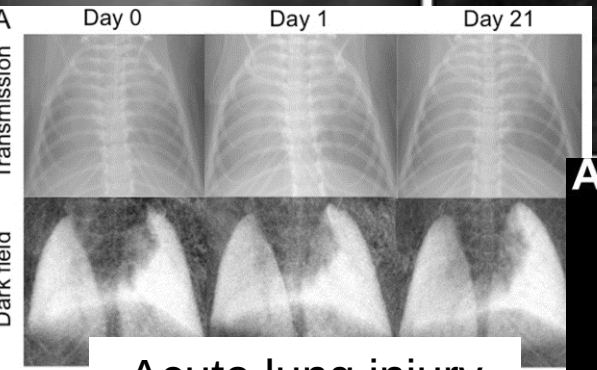


Darkfield Radiography

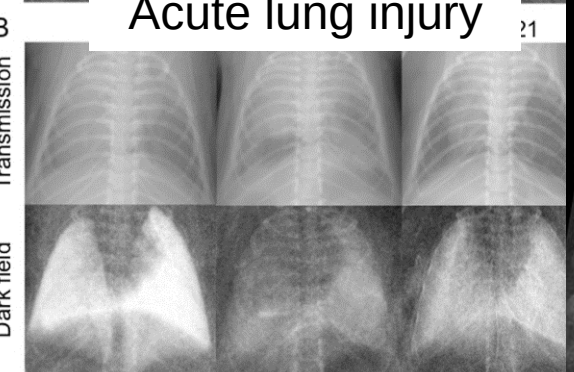
- **X-Rays, but scatter instead of attenuation; porcine model**

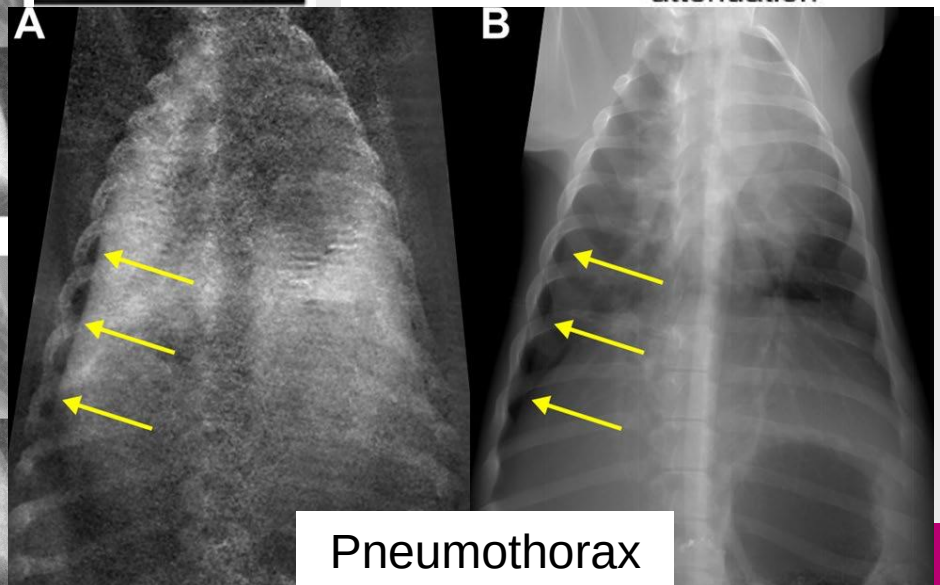






Acute lung injury



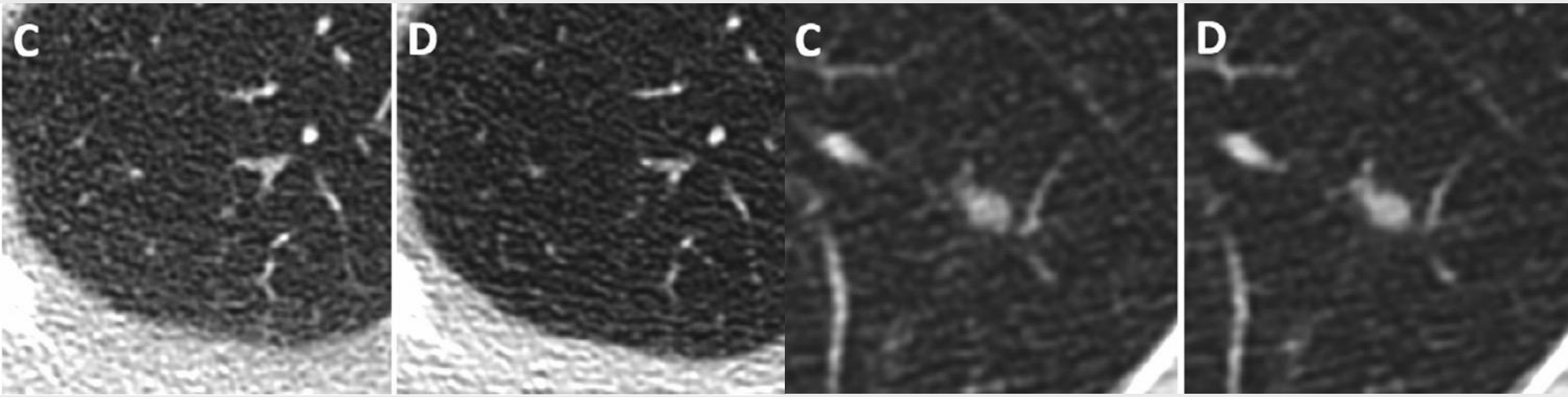


Pneumothorax

Gromann-LB et al. Sci Rep 2017;7:4807
Hellbach-K et al. Sci Rep 2018;8:2602
Hellbach-K et al. Sci Rep 2018;8:2096

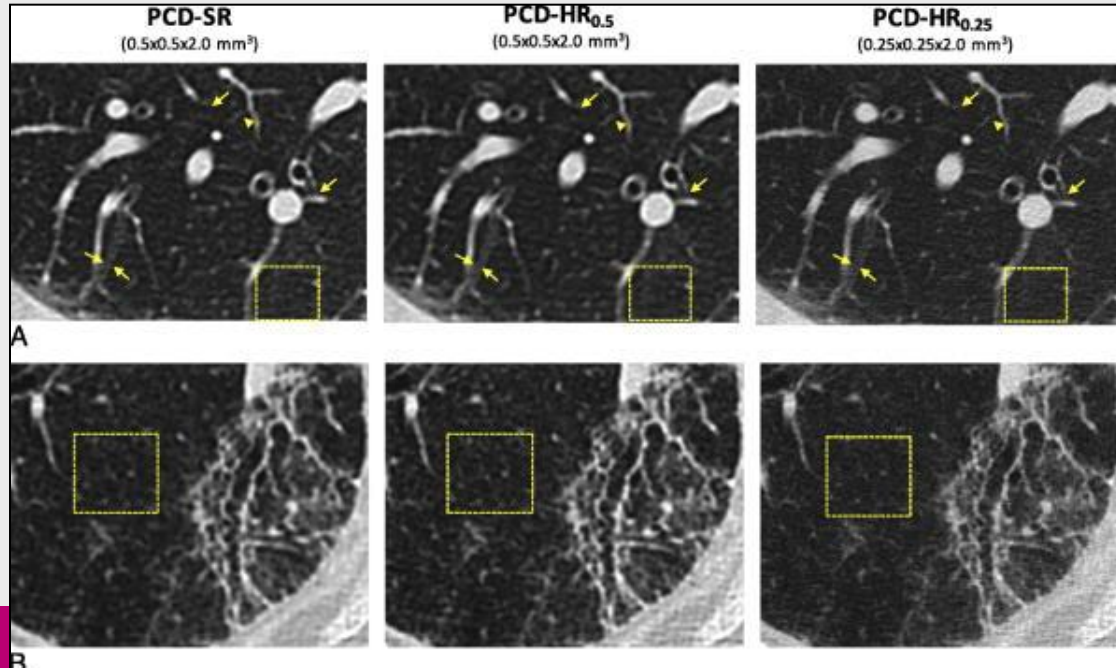
Photon Counting CT

- **Lower noise, higher resolution**



Current **Novel** **Current** **Novel**

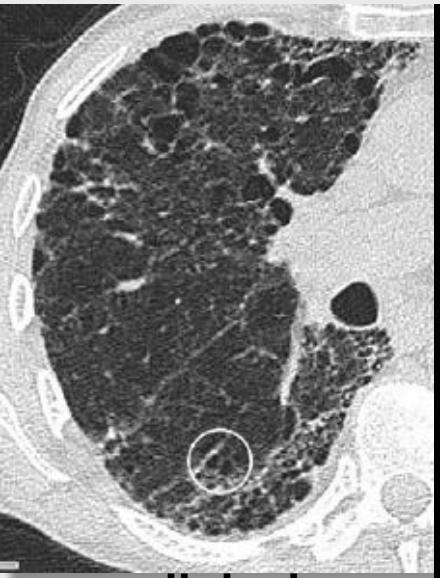
- **Improved further by high resolution matrix**



Symons-R et al. Radiology 2017;285:980-989
Pourmorteza-A et al Invest Radiol 2018; 53:365-372

µ-CT: Fibrosis

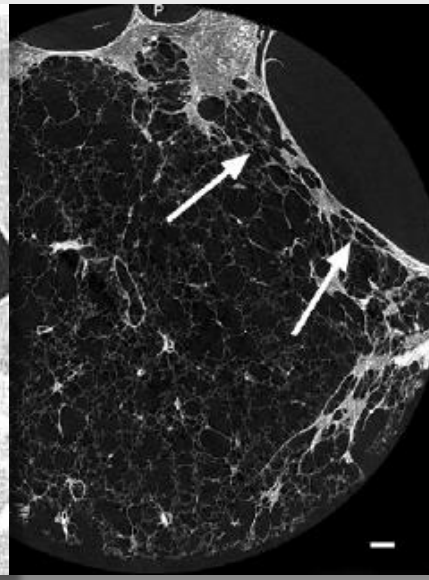
- Fibrosis starts peripherally and grows centrally in the lobule
- Alveolar collapse might be trigger of fibroproliferation



clinical

µ postmortem

clinical

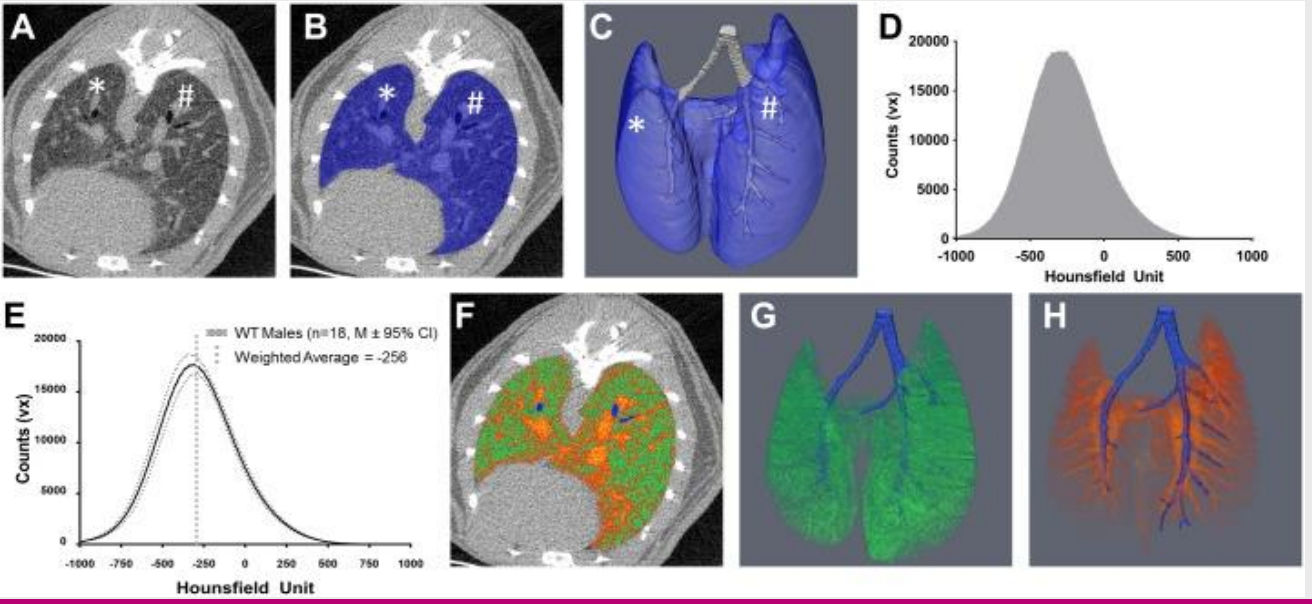


µ postmortem

Mai-C et al. Radiology 2017;283:252-263

µ-CT: Fibrosis

- **Separation of aerated volume, tissue volume, conducting airways**
- **TNF transgenic mice have higher tissue volume**



Bell-RD et al. PLoS One 2018;13:e0190678

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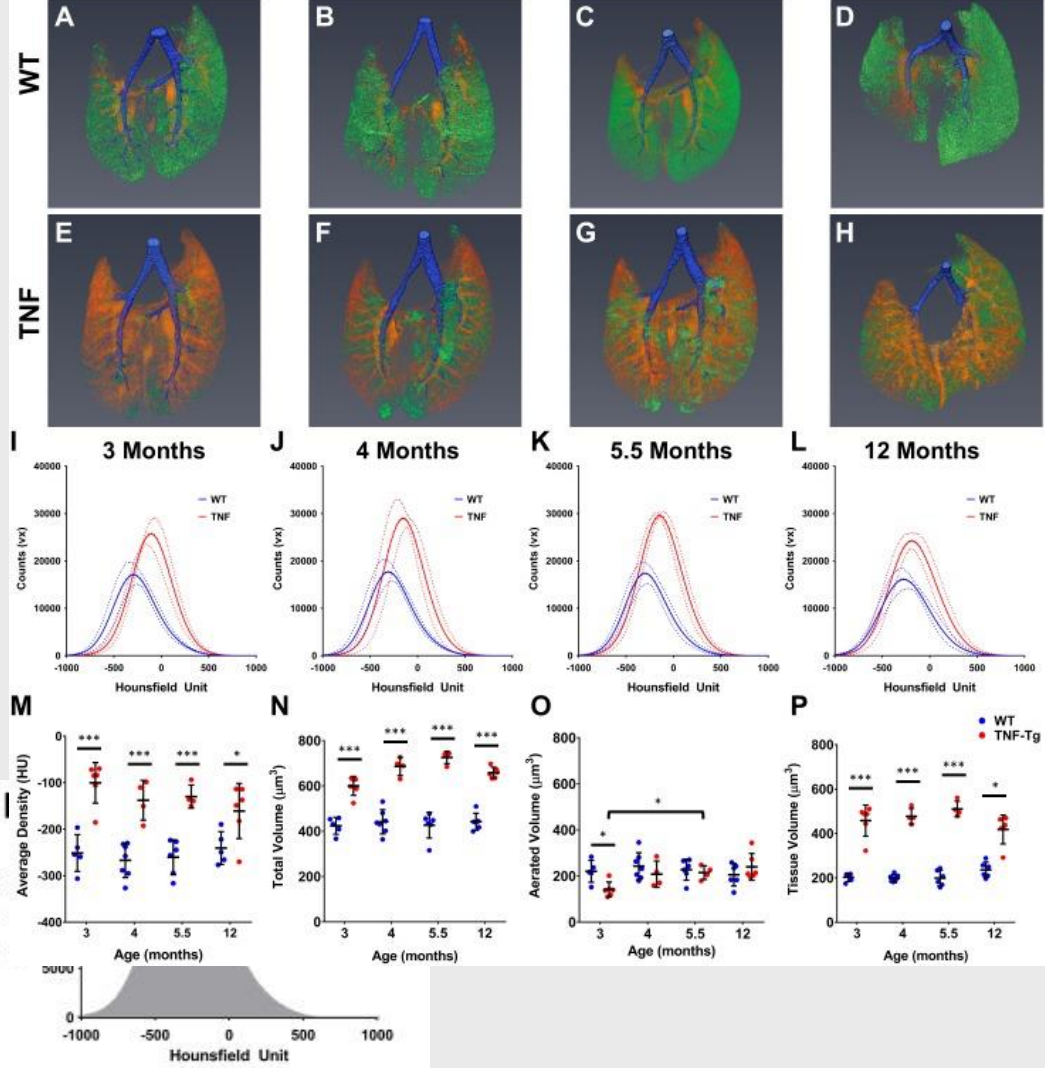
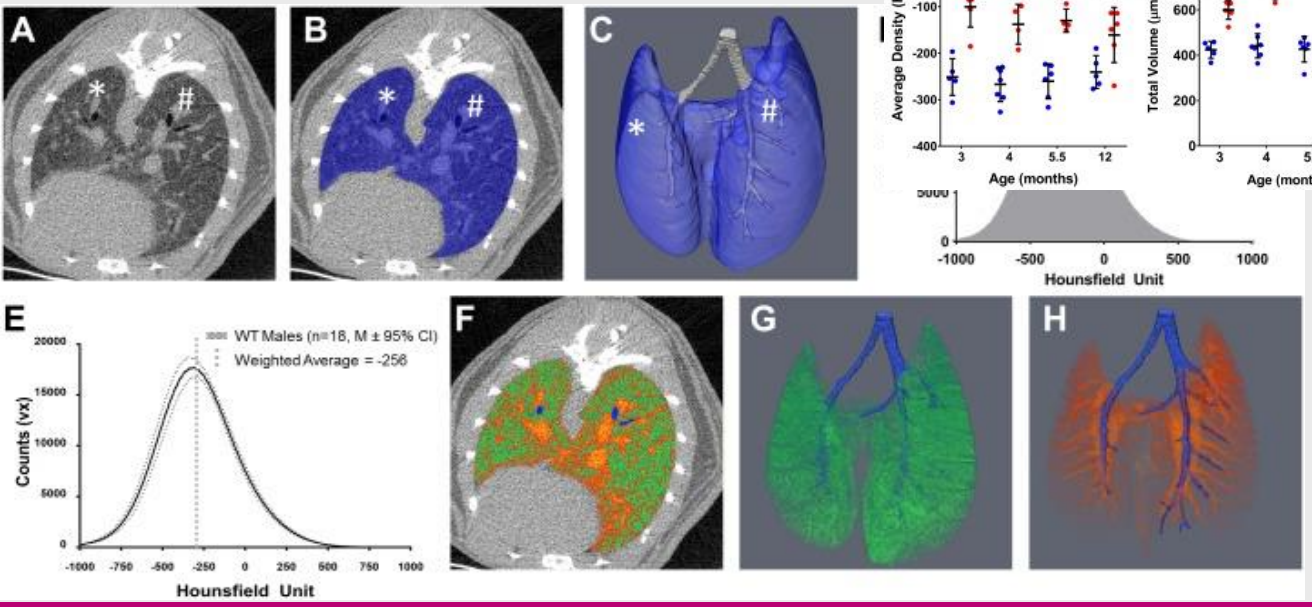




Bell-RD et al. PLoS One 2018;13:e0190678

Amid-proton transfer MRI

- 82 patients with pulmonary nodules, NH- groups of mobile proteins and peptides; comparison DWI; PET/CT

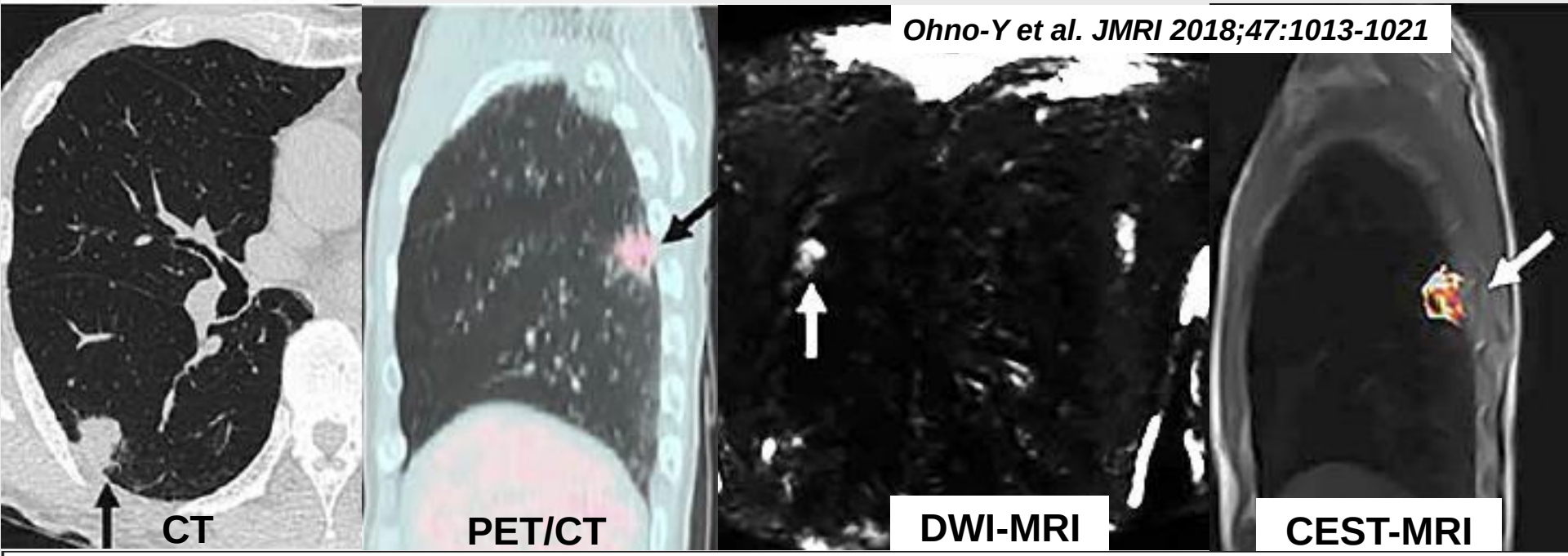
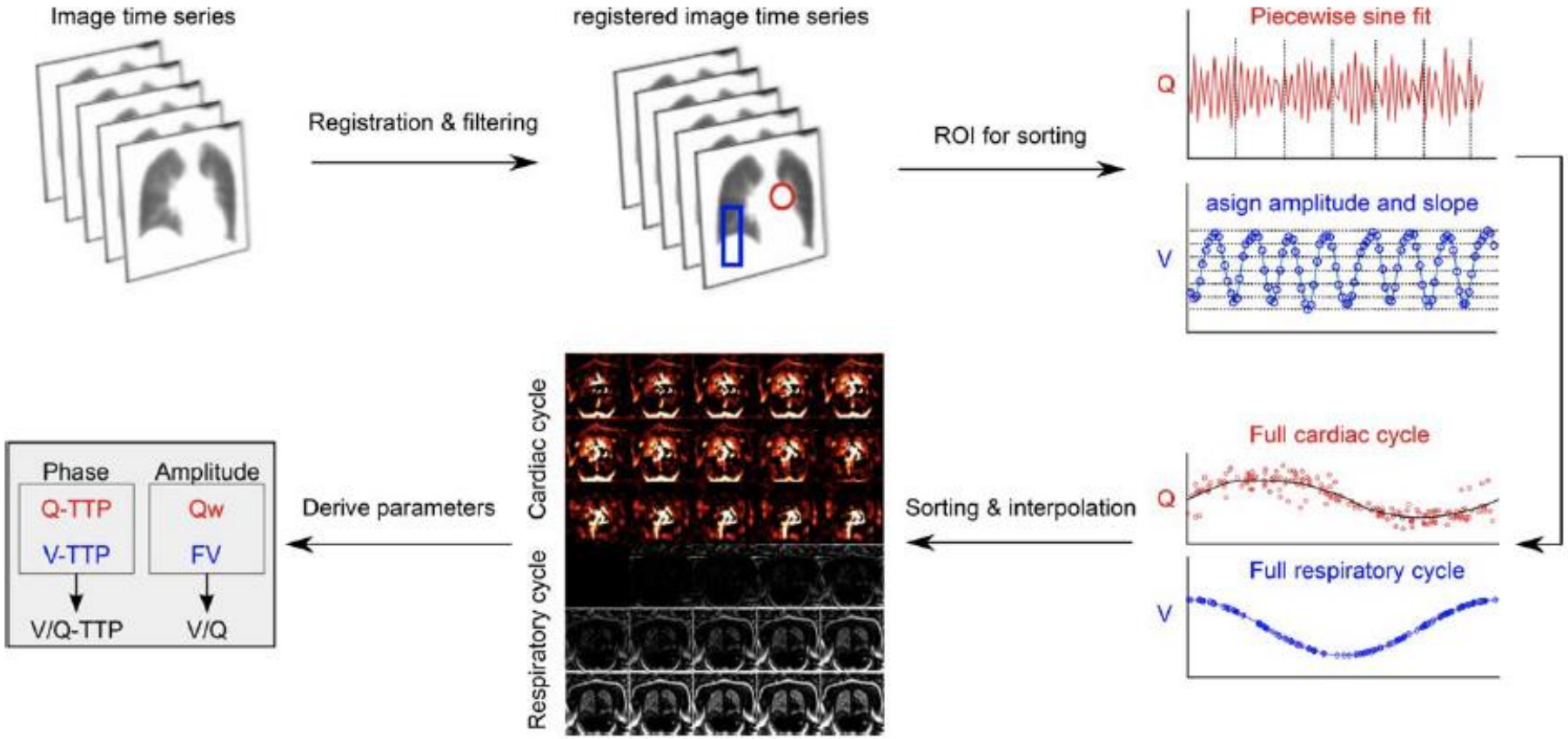


TABLE 1. Differences in Differentiation Between Malignant and Benign Nodules for Each Index

	Malignant nodules (Mean ± SD)	Benign nodules (Mean ± SD)	*P* value
Age	70.8 ± 6.8	69.7 ± 6.5	0.19
Long axis diameter*	18.5 ± 5.4	16.9 ± 5.9	0.29
MTR_{asym}(3.5 ppm) (%)	2.0 ± 6.4	−2.9 ± 4.9	0.0002
ADC ($\times 10^{-3} mm^2/s$)	1.2 ± 0.3	1.3 ± 0.2	0.0024
SUV	3.2 ± 1.6	2.3 ± 0.5	0.0008

Phase-resolved ventilation and perfusion MRI

- **Regional mapping, fourier decomposition**
- **Feasibility in volunteers COPD, CTEPH and CF patients**



Voskrebenzev-A et al. Magn Reson Med 2018;79:2306-2314

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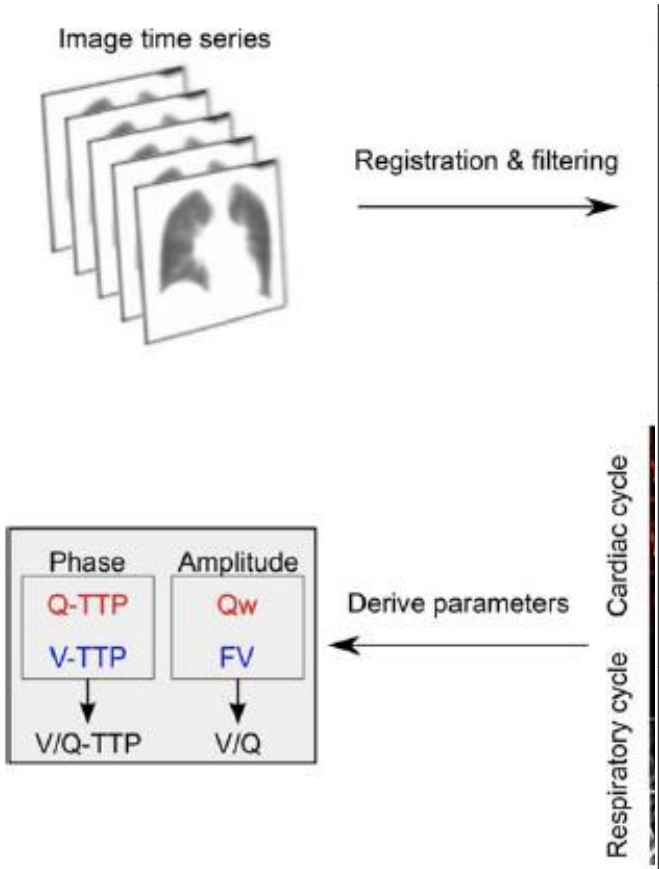
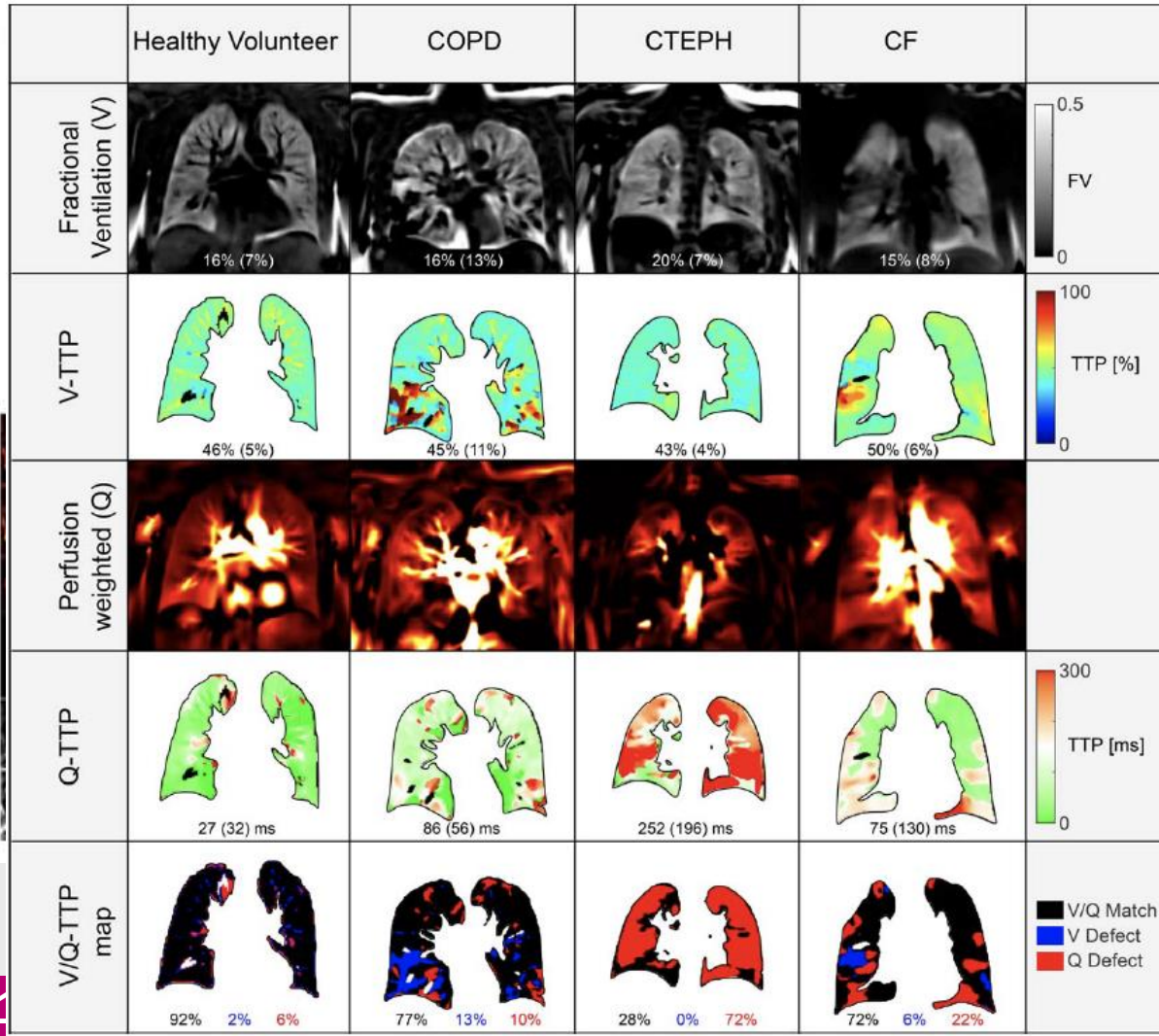




Voskrebenzev-A et al. Magn Reson Med 2018;79:2306-2314

Take Home: Technical Advances

- More innovations to be expexted
- Radiography => tomosynthesis
- Radiography => dark field
- CT => photon counting, dark field ?
- MRI => CEST, non-contrast, non-proton
  => functional, molecular

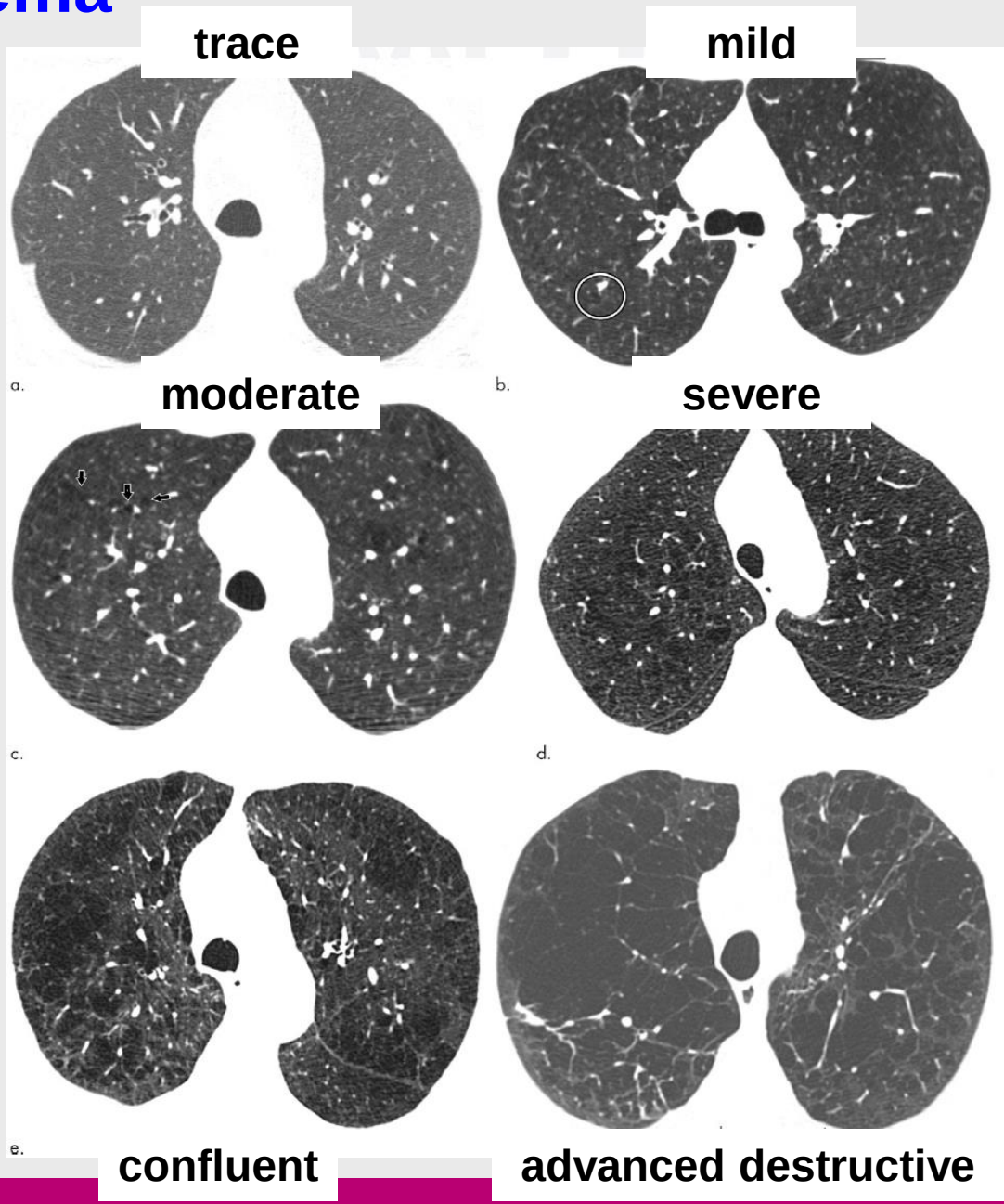
Airway diseases
COPD, CF

State-of-the Art: Airway disease

- CT => high resolution, low dose
- MRI => high resolution, low dose
- Quantification, imaging biomarkers
- Remodeling, exacerbation
- Surveillance

COPD: Visual Emphysema

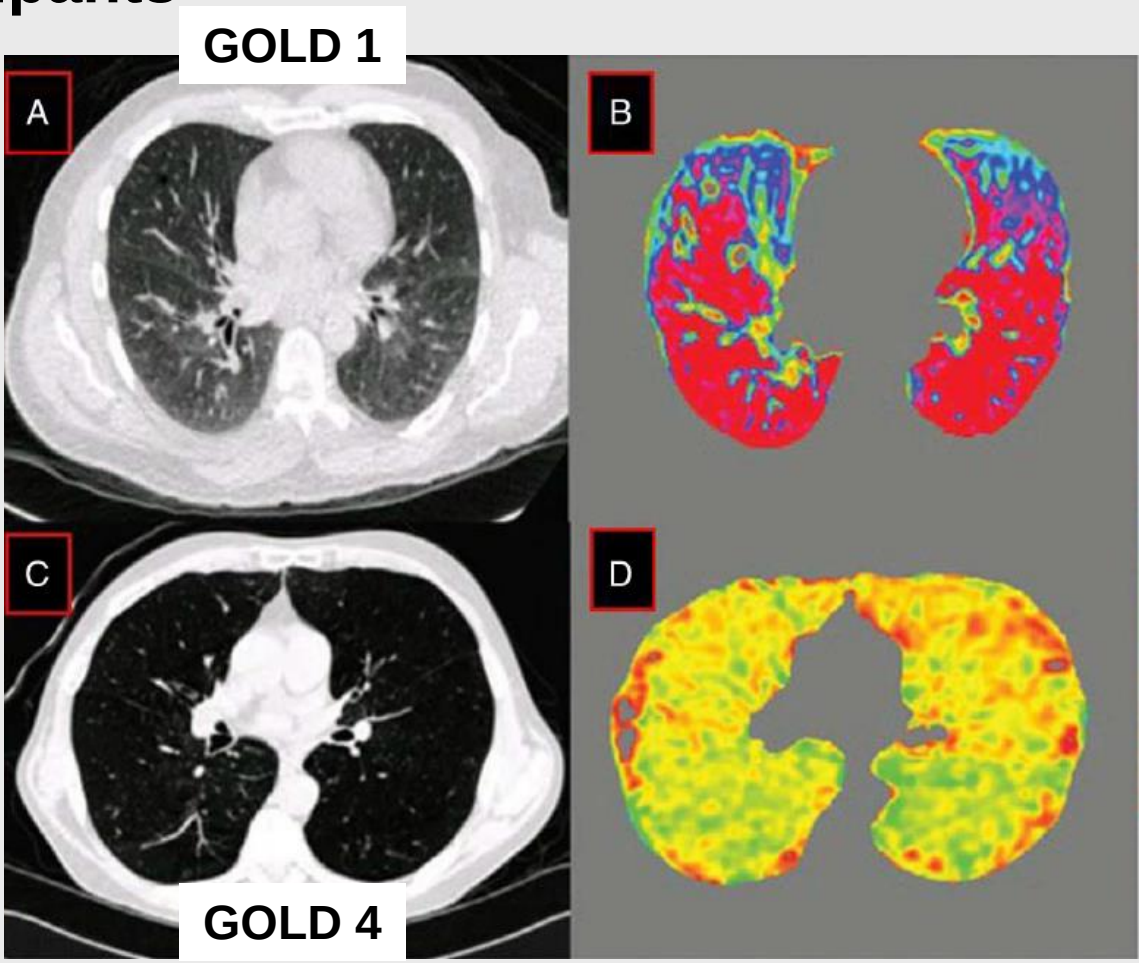
- 3171 COPDGene participants
  inspiratory CT
  obs agreement 0.7-0.85
  correlation with
  - increasing airflow
  - dyspnea
  - symptoms
  - GOLD stage
  - mortality



Lynch-DA et al. Radiology 2018 in press

COPD: CT Biomechanics

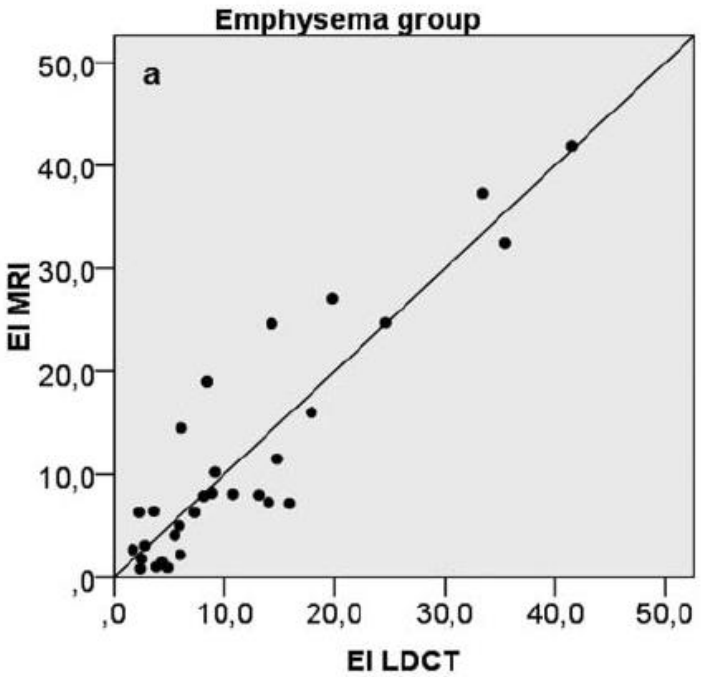
- **490 COPDGene participants**
  in-/expiratory CT registration deformation field
  better prediction of
  - resp. quality of life
  - BODE index
  - mortality

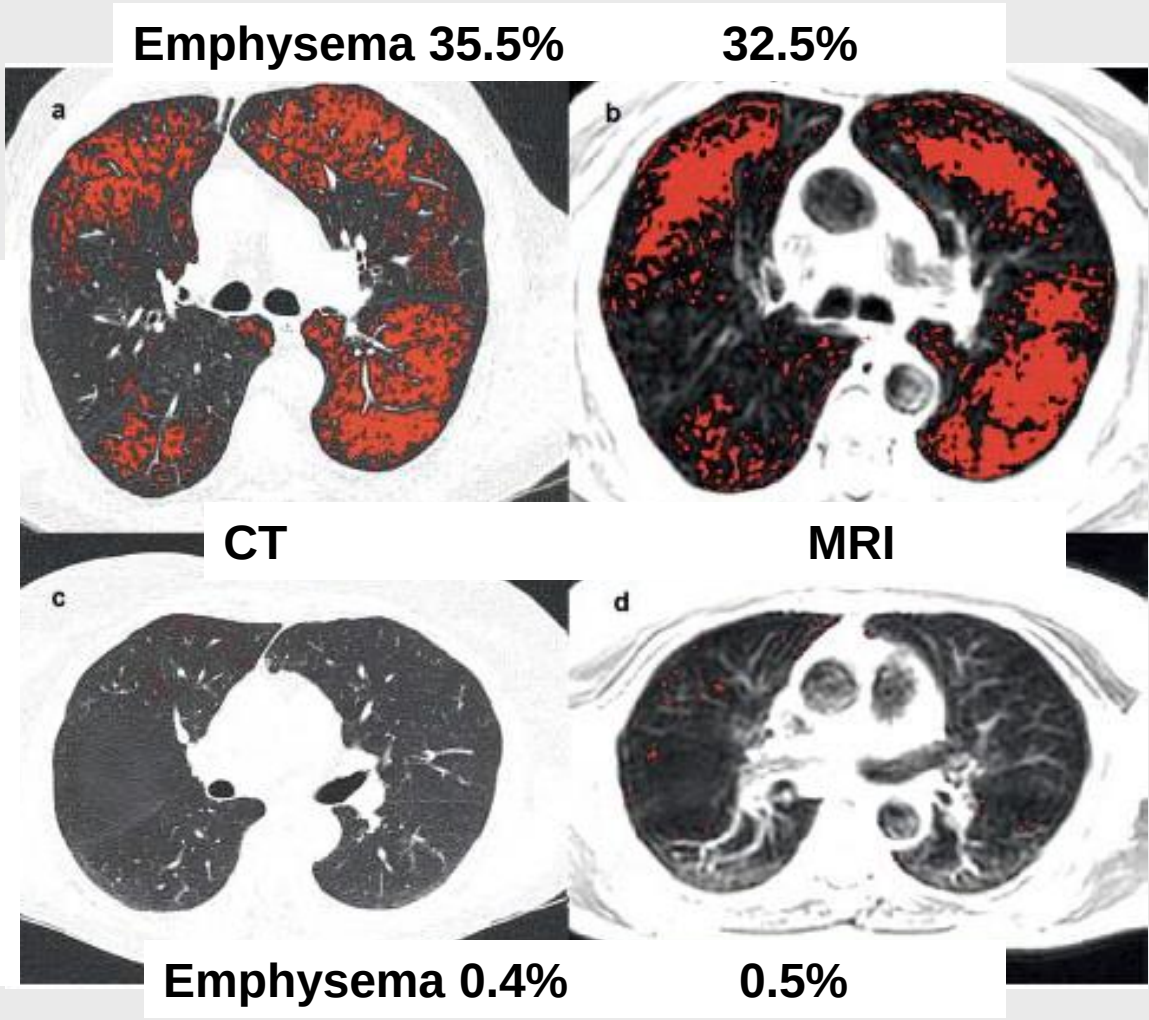


Bodduluri-S et al. Thorax 2017;72:409-414

COPD: CT vs MRI

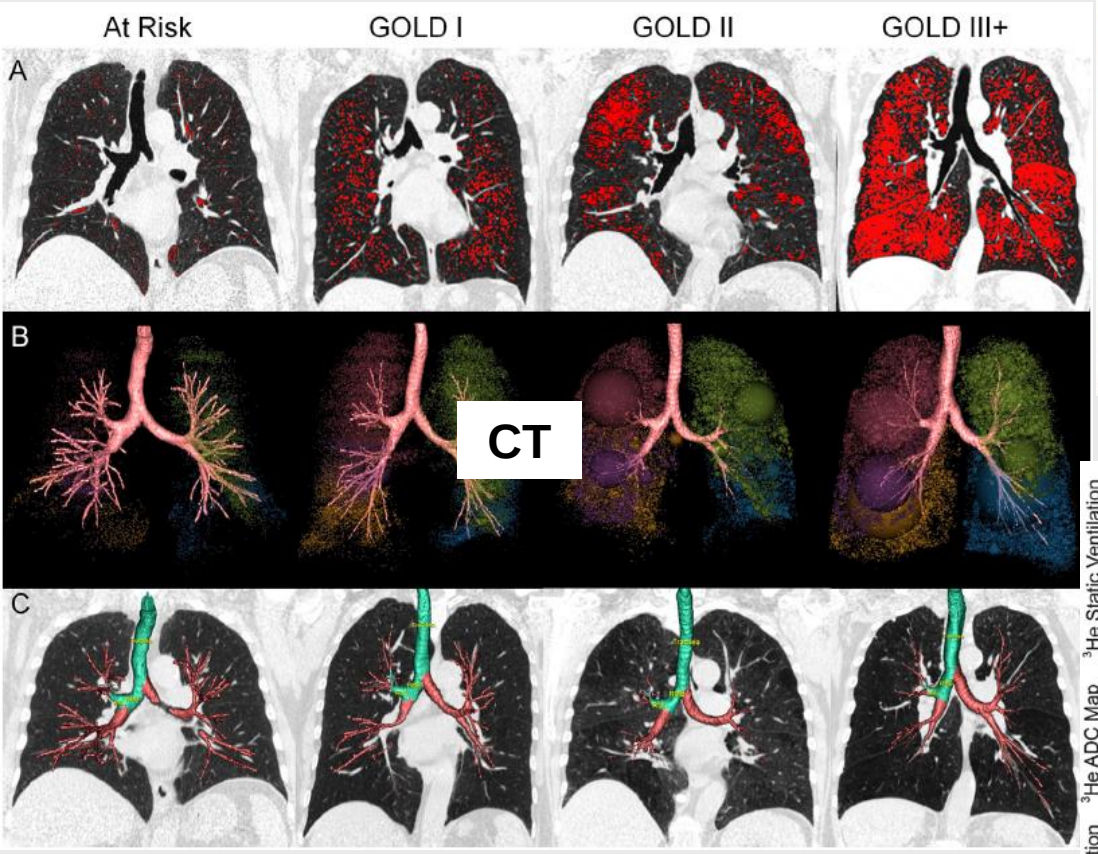
- 224 lung cancer screening participants
- Low dose CT
- Propeller T2W MRI

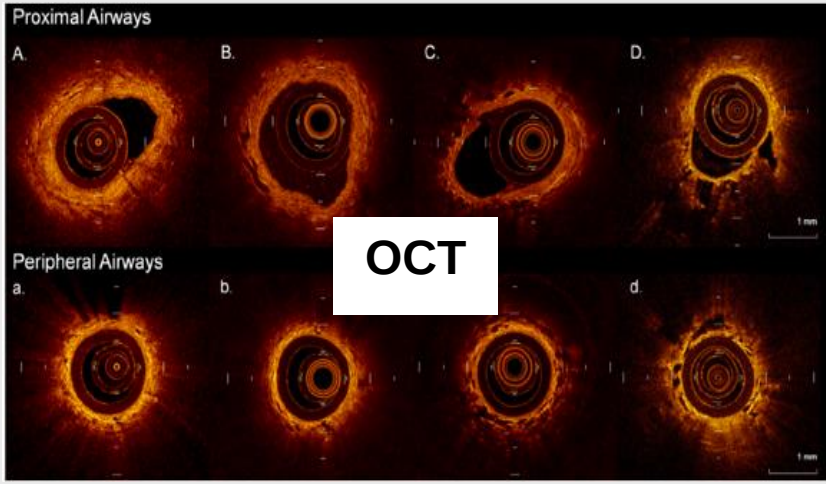


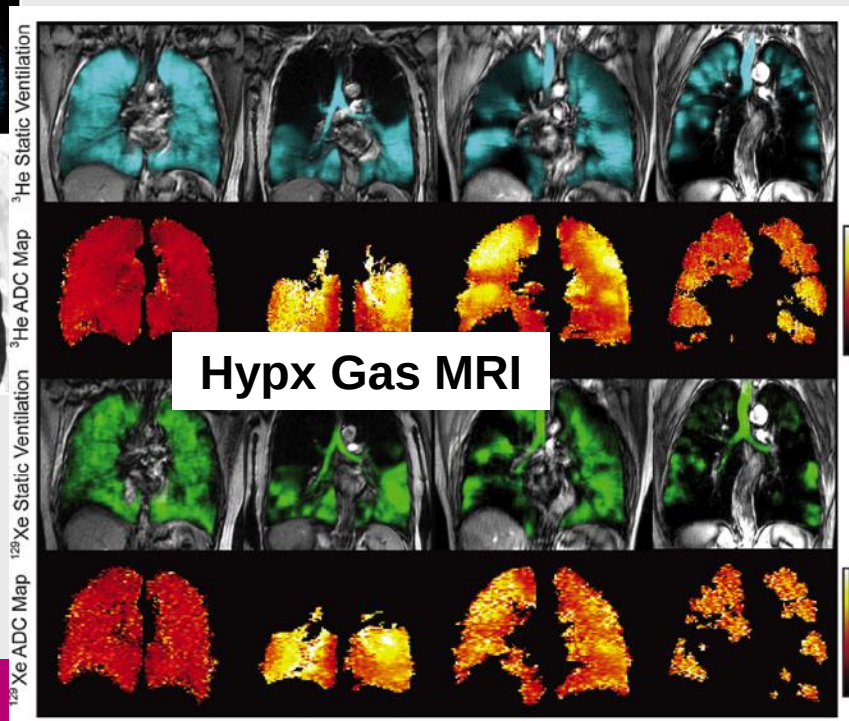


Meier-Schroers-M et al. Fortschr Röntgenstr 2018;epub

COPD: Imaging Biomarkers



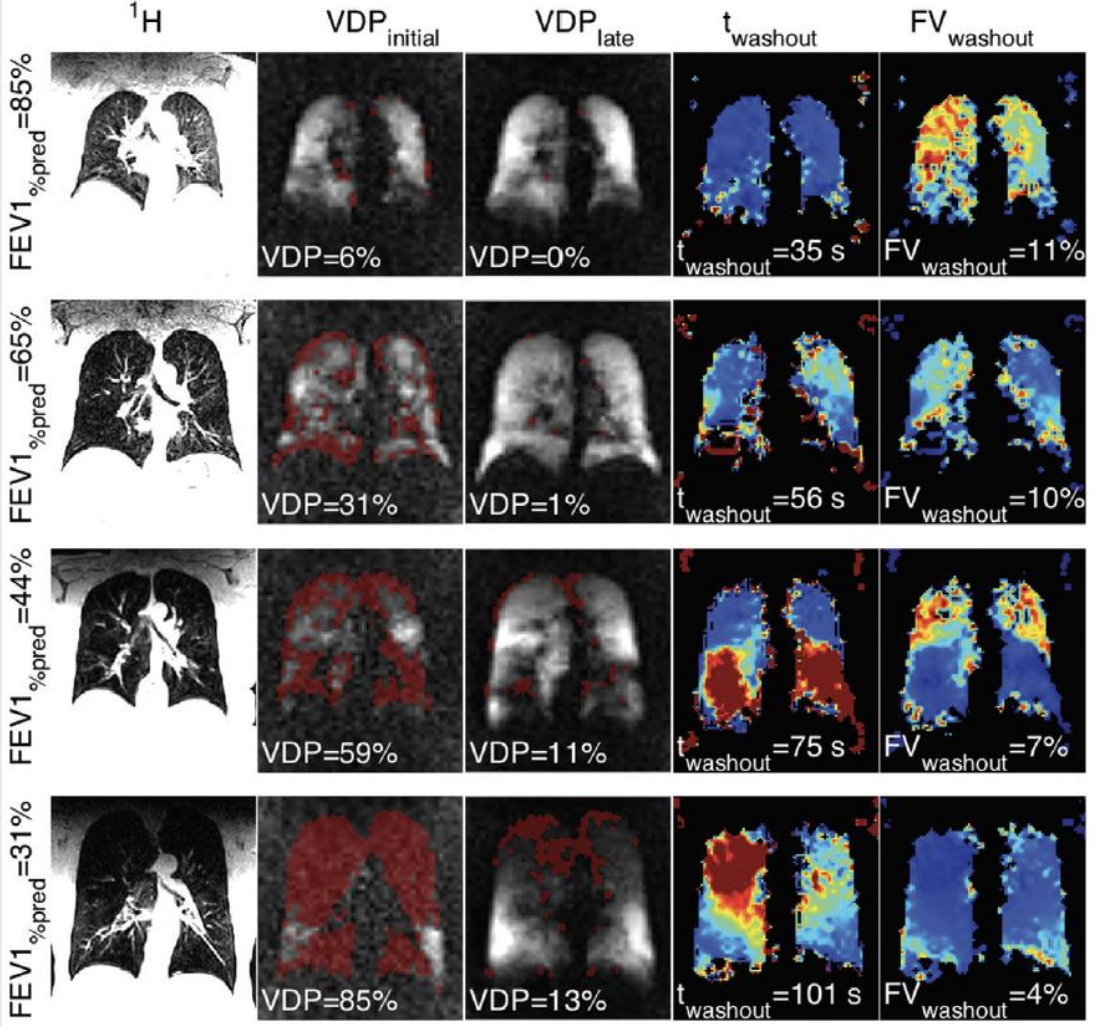


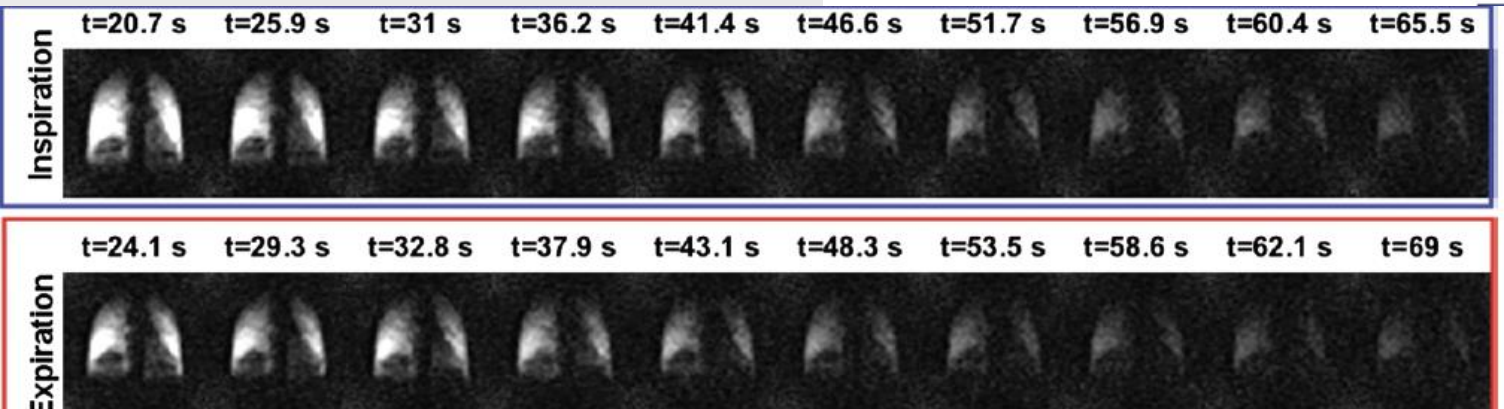


Kirby-M et al. Eur J Radiol 2017;86: 335-342

COPD: Ventilation MRI

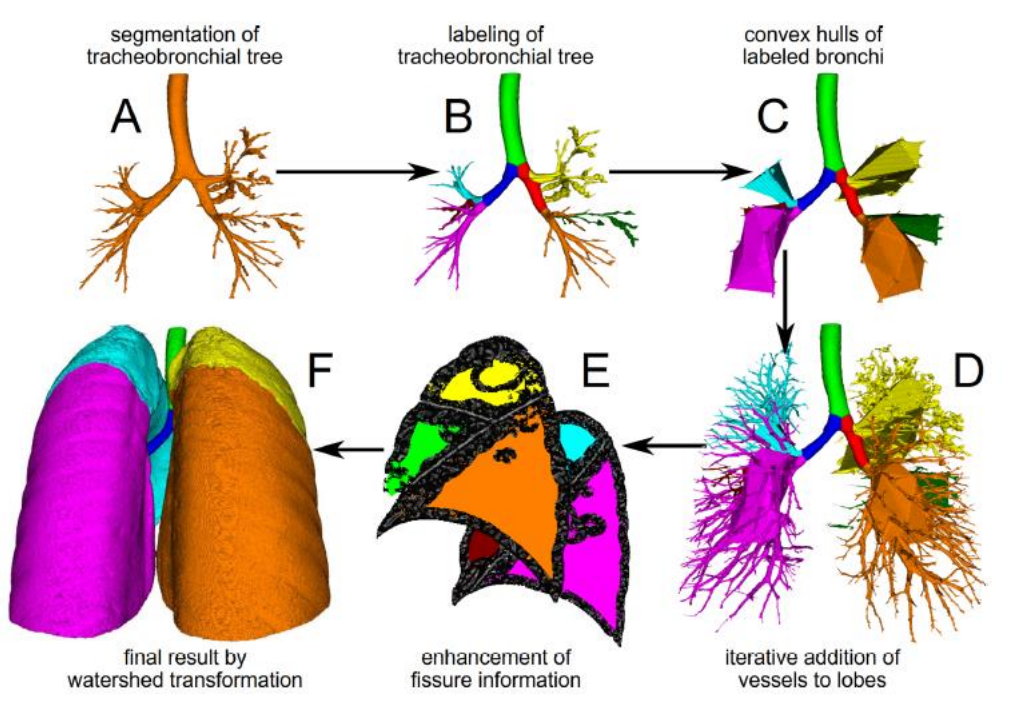
- 27 patients
- 19F MRI
- Free breathing
- Dynamic
- Defect volume
- Wash-out time
- Fractional ventilation





Gutberlet-M et al. Radiology 2018;296:1040-1051

Cystic Fibrosis: Airway Remodeling (CT)



Konietzke.O et al. PLoS 2018; April-9
Weinheimer-O et al Proc SPIE Med Imag 2017

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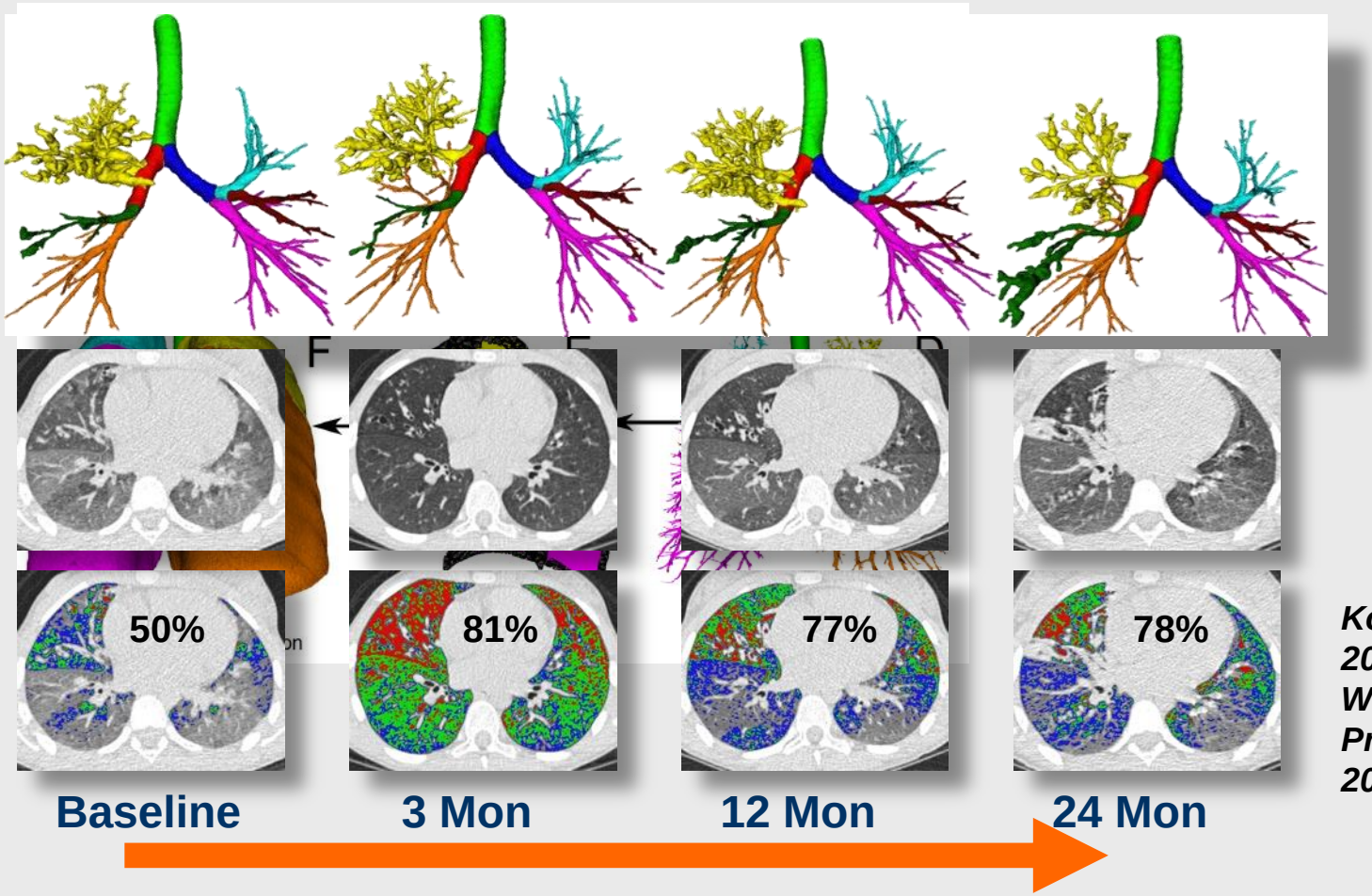

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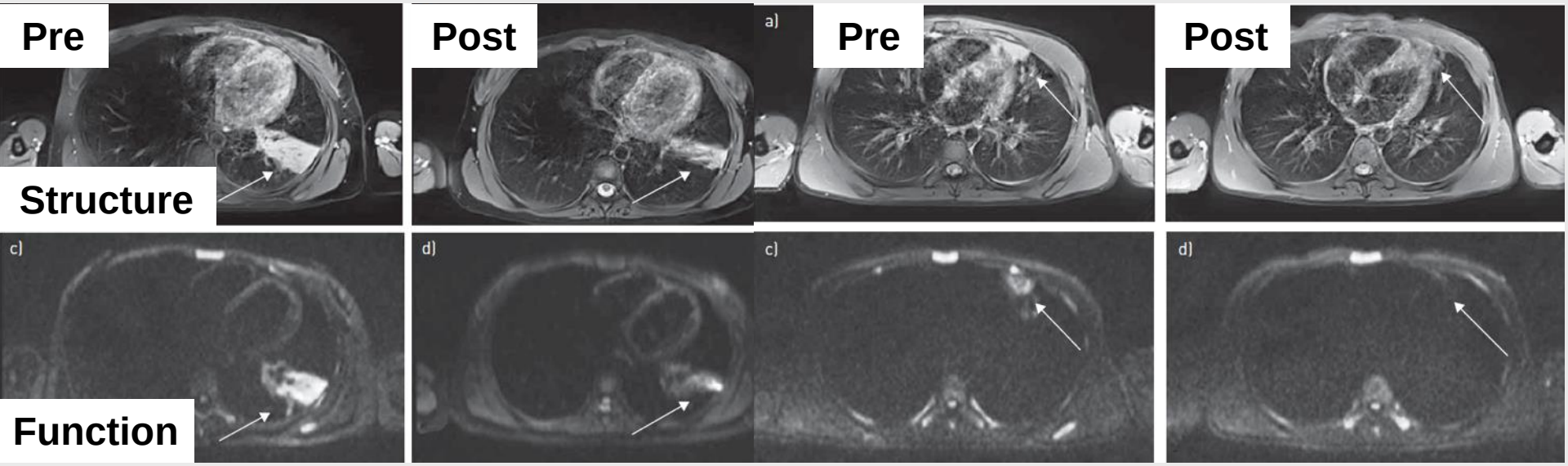
Cystic Fibrosis: Exacerbation (MRI)

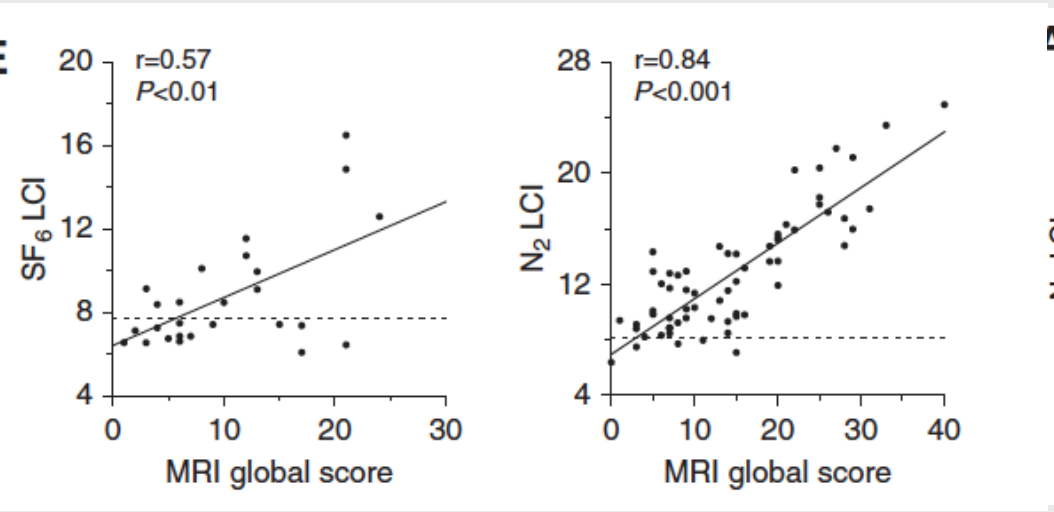
- 56 patients; 29 with exacerbations
- Discrepancies: T2 = structure, DWI = function (cellularity)

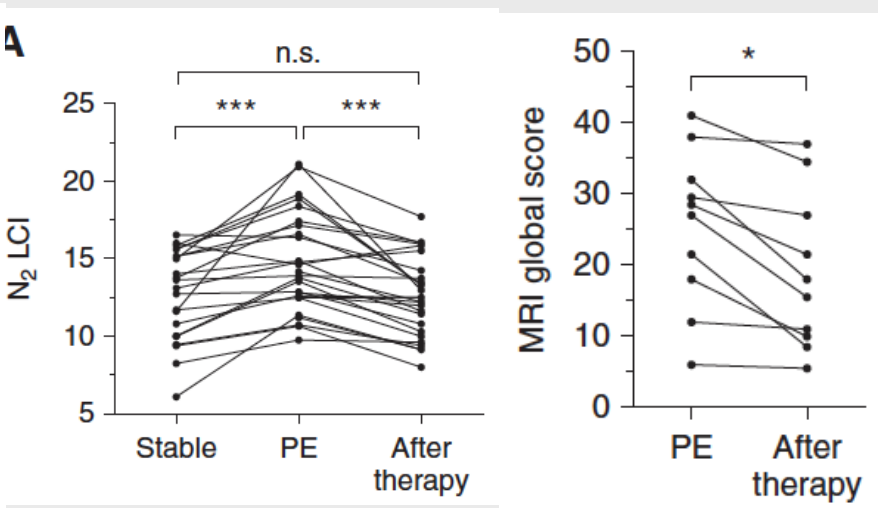


Ciet-P et al. Eur Resp J 2017;50:1601437

Cystic Fibrosis: Surveillance (MRI)

- **97 patients; MRI vs. LCI: complementary outcome measures**
- **MRI: regional perfusion and ventilation inhomogeneity**

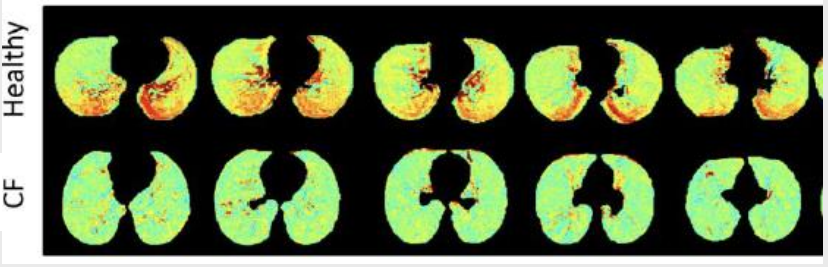


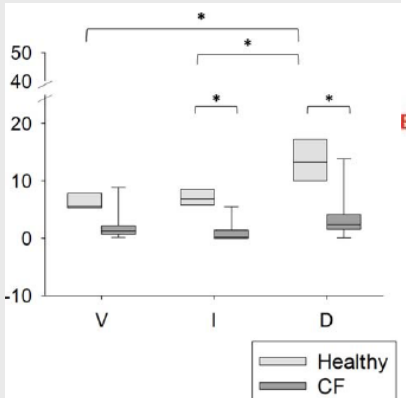


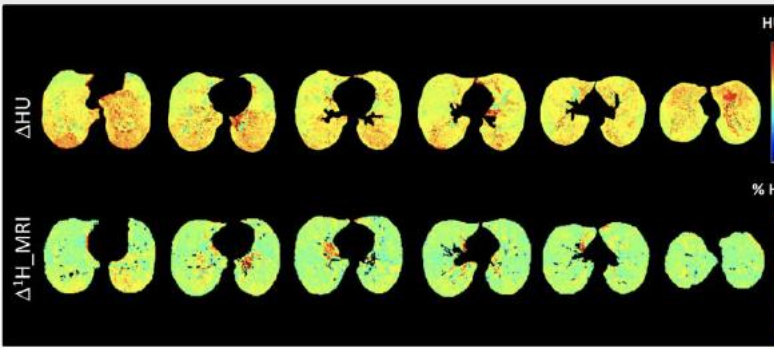
Stahl-M et al. Am J Respir Crit Care Med 2017;195:349-359

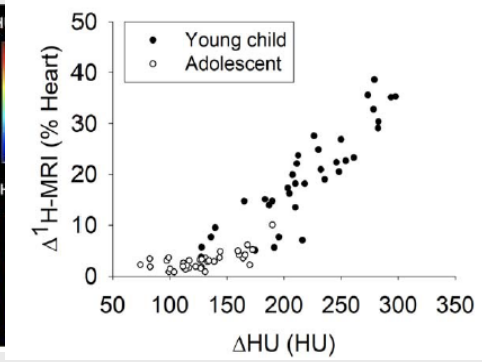
Cystic Fibrosis: Non-contrast MRI vs. CT

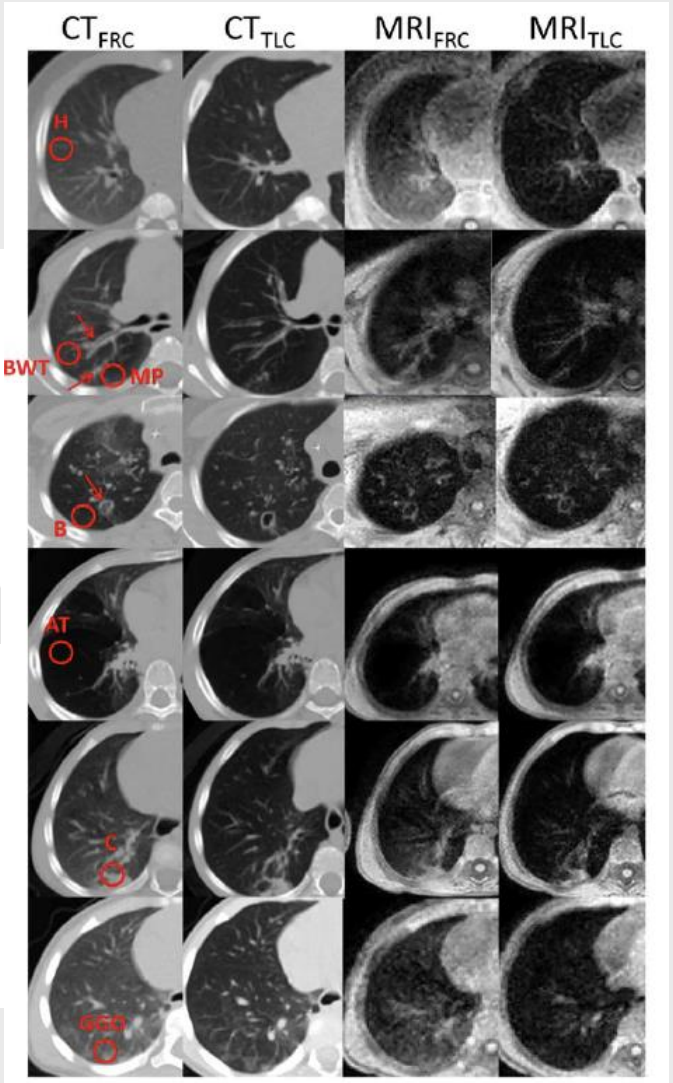
- **29 patients, in/ex CT and proton MRI**







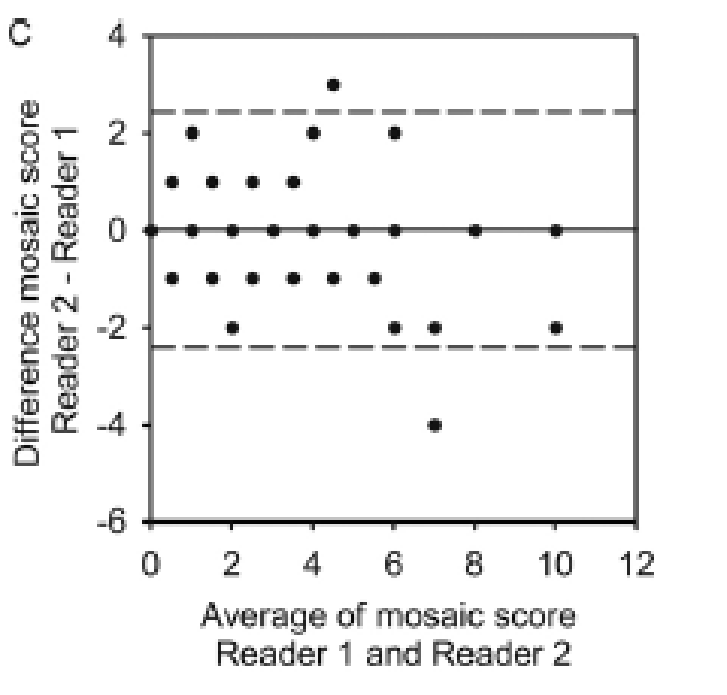


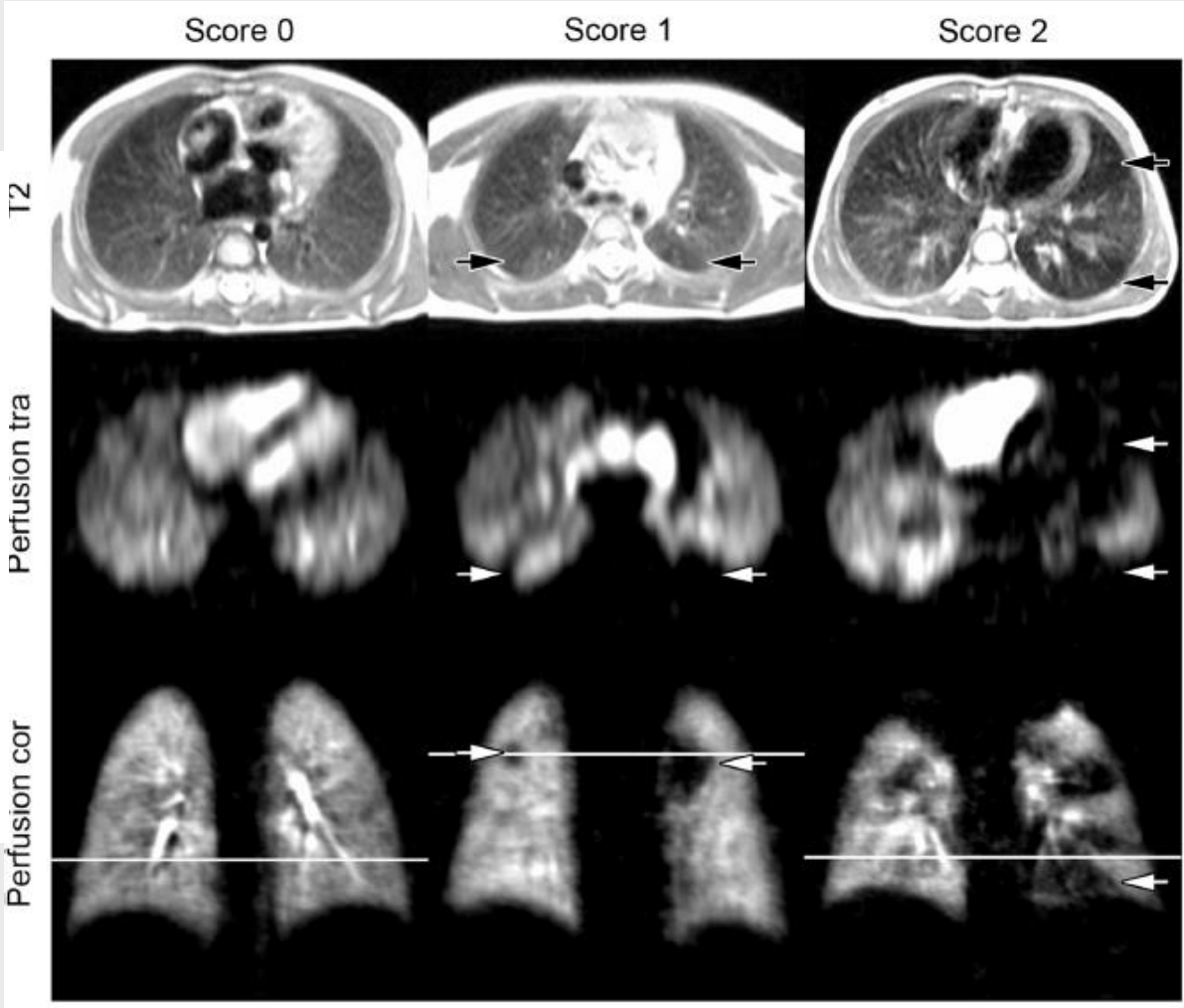


Pennati-F et al. J Magn Reson Imaging 2018;epub

Cystic Fibrosis: Non-contrast vs. CE-MRI

- **50 patients, T2w + contrast-enhanced T1w MRI**
- **Mosaic perf score**

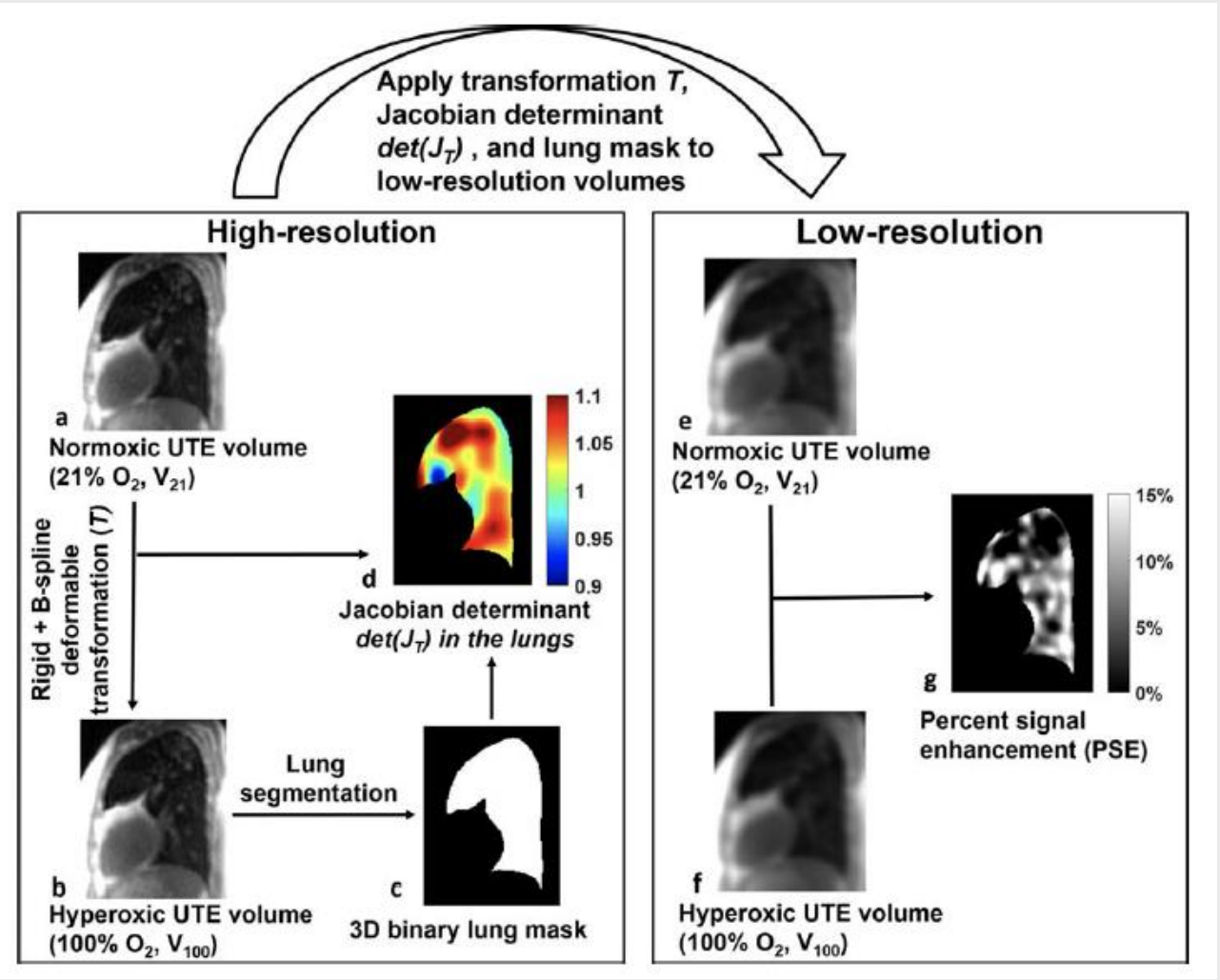




Leutz-Schmidt-P et al. Eur J Radiol 2018; 101:178-183

Cystic Fibrosis: Oxygen-enhanced UTE MRI

- **18 subjects, healthy, asthma, CF, repeatability**



Zha-W et al. J Magn Reson Imaging 2018;47:1287-1297

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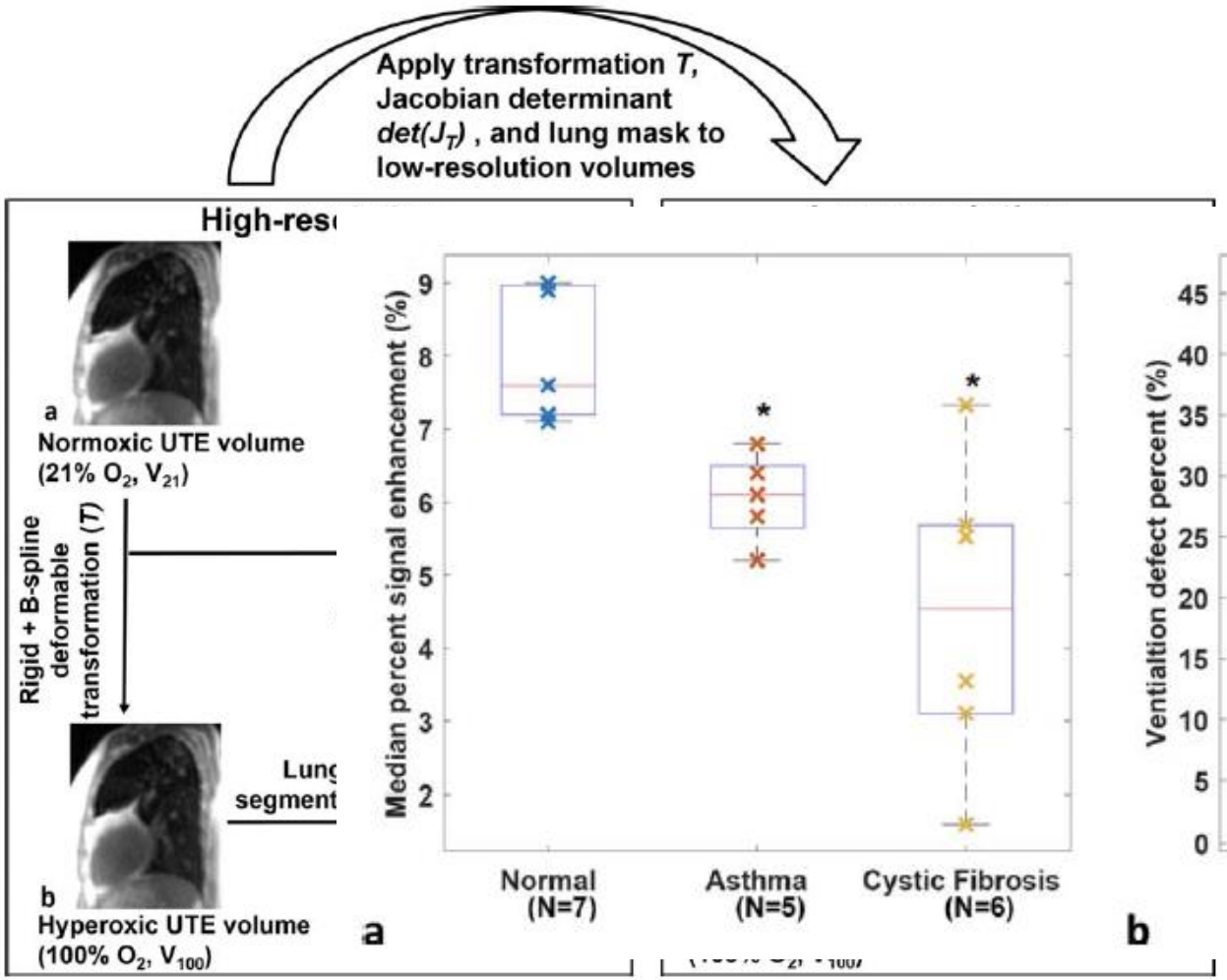

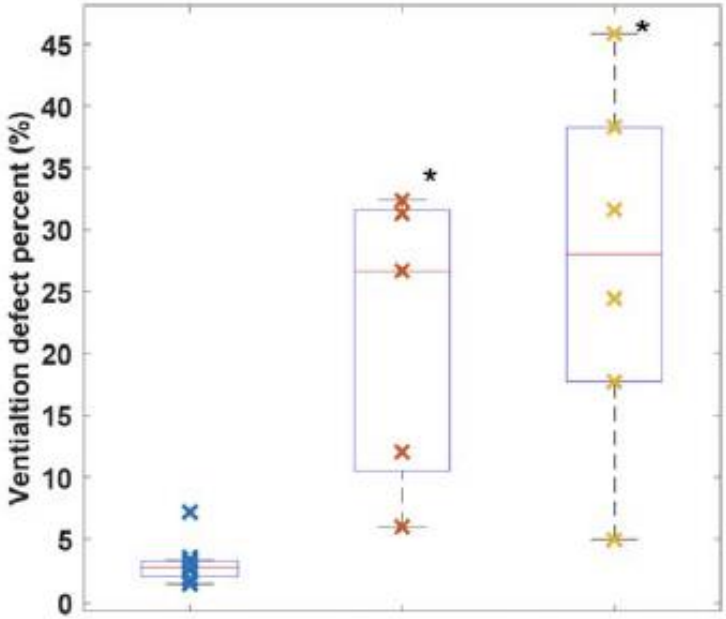

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Take Home: Airway Diseases

- CT => high resolution, low dose
- MRI => high resolution, no dose
- Quantification, imaging biomarkers
- Remodeling, exacerbation
- Surveillance

Diffuse Parenchymal Lung Disease

State-of-the Art:

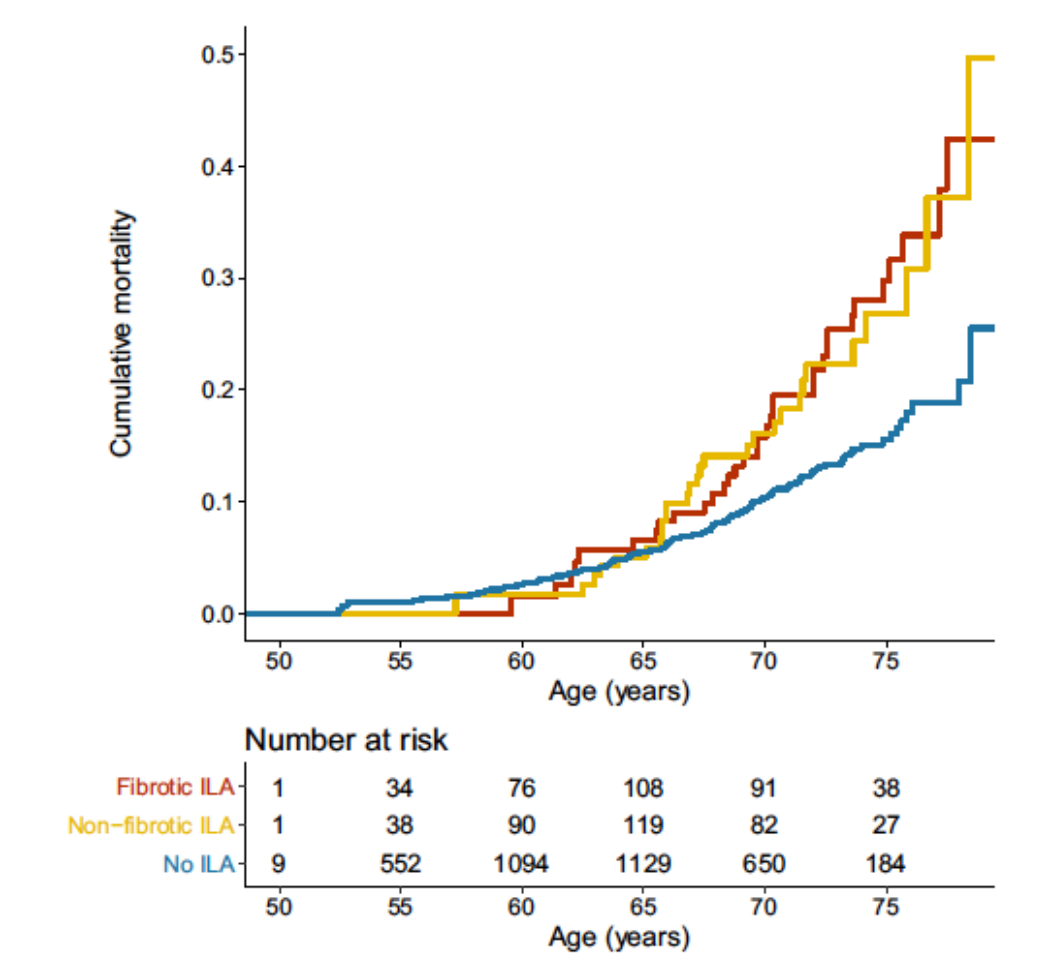
Diffuse Parenchymal Lung Disease

- **ATS/ERS guidelines**
- **Central role of CT**
- **MDT board diagnosis**
- **Recent white paper of the Fleischner Society**

Lynch-DA et al. Lancet Respir Med 2018;6:138-153

Interstitial Lung Abnormalities in Smokers

- Danish lung cancer screening trial
- Interstitial lung abnormalities in 332 (17%) participants
- Increased mortality regardless of fibrotic or non-fibrotic phenotype
- partly due to an association with lung cancer and non-pulmonary malignancies



Hoyer-N et al. Resp Med 2018;136:77-82

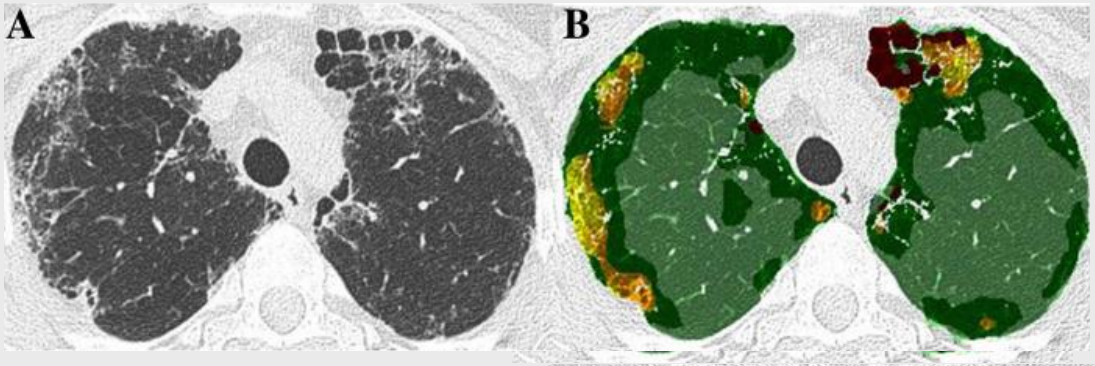
Interstitial Lung Abnormalities in Diabetics

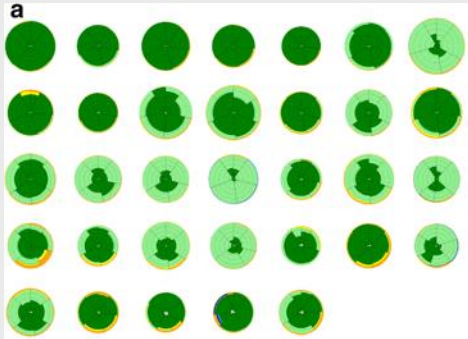
- 48 non-diabetics
  68 patients with pre-diabetes
  29 newly diagnosed
  110 patients with long-term T2D
- metabolic control
  diabetes-related complications
  breathlessness
  lung function
- T2D: increased breathlessness,
  higher prevalence of restrictive lung disease,
  CT evidence of interstitial disease
- => diabetic pneumopathy

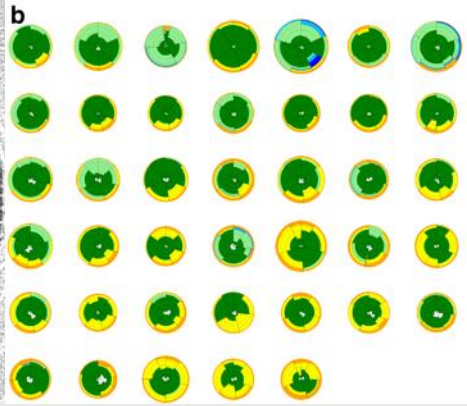
Kopf-S et al. Respiration 2018; accepted

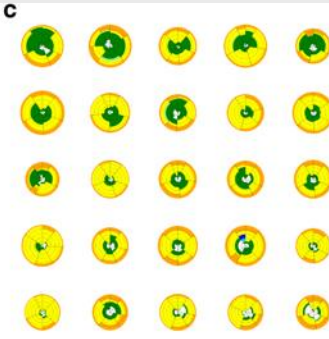
Idiopathic Pulmonary Fibrosis: CT

- **Pattern analysis and vascular volume**
- **“Severity”: more GGO, more reticulation => poor outcome**
- **Vessel-related structure predicts survival better FVC decline**





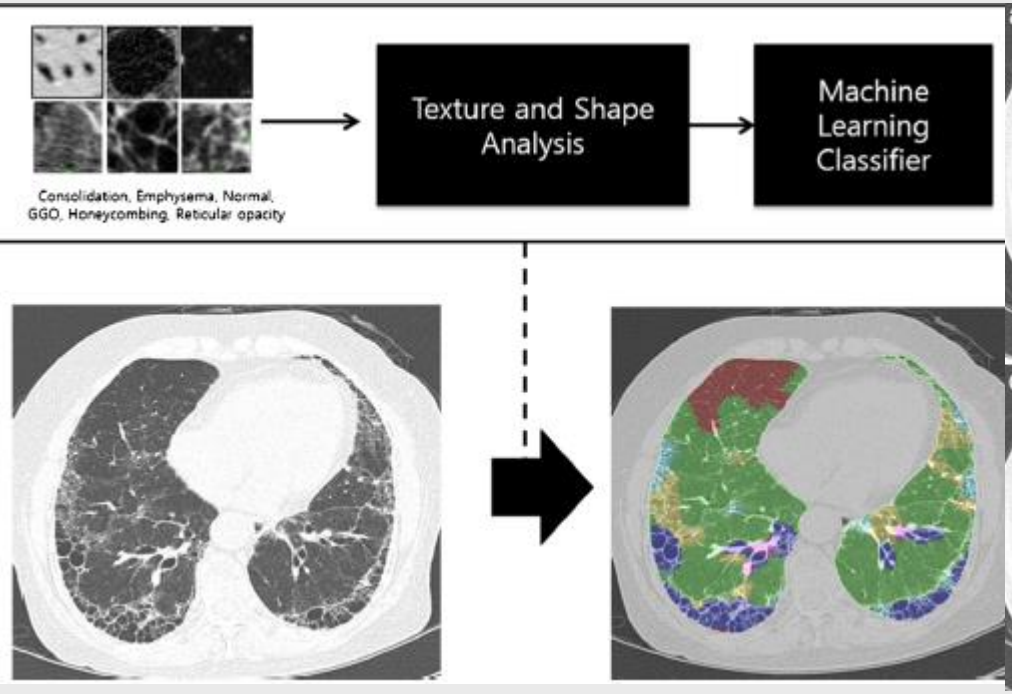


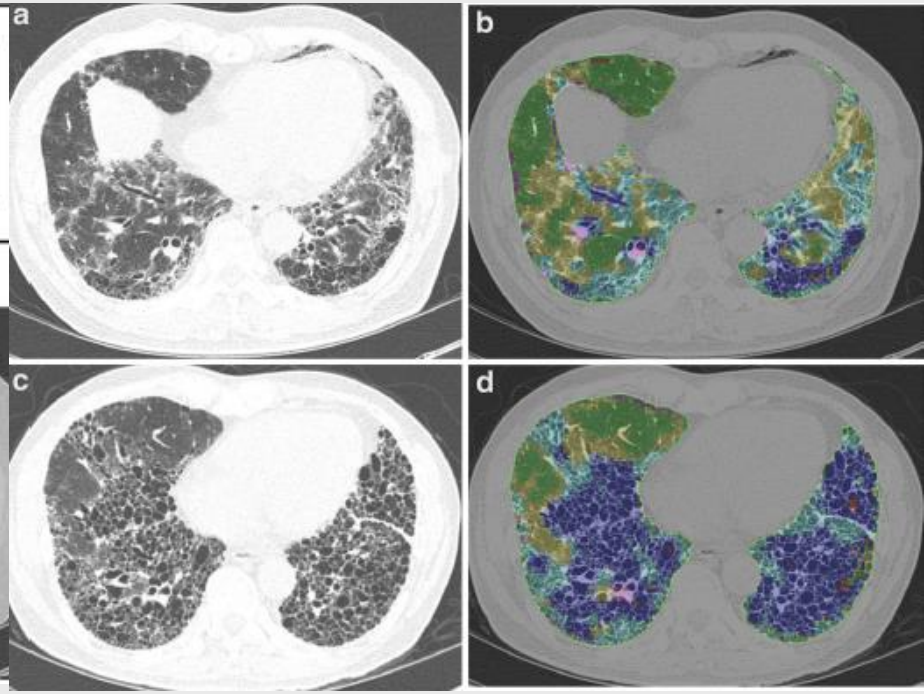


Jacob-J et al. BMC Pulm Med 2017;17:81
Jacob-J et al. Eur Radiol 2017; 27:3635-3646
Jacob-J et al AJRCCM 2018; epub

Idiopathic Pulmonary Fibrosis: CT

- **144 IPF patients**
- **Pattern analysis**
- **Fibrosis score independent predictor of survival => poor outcome**



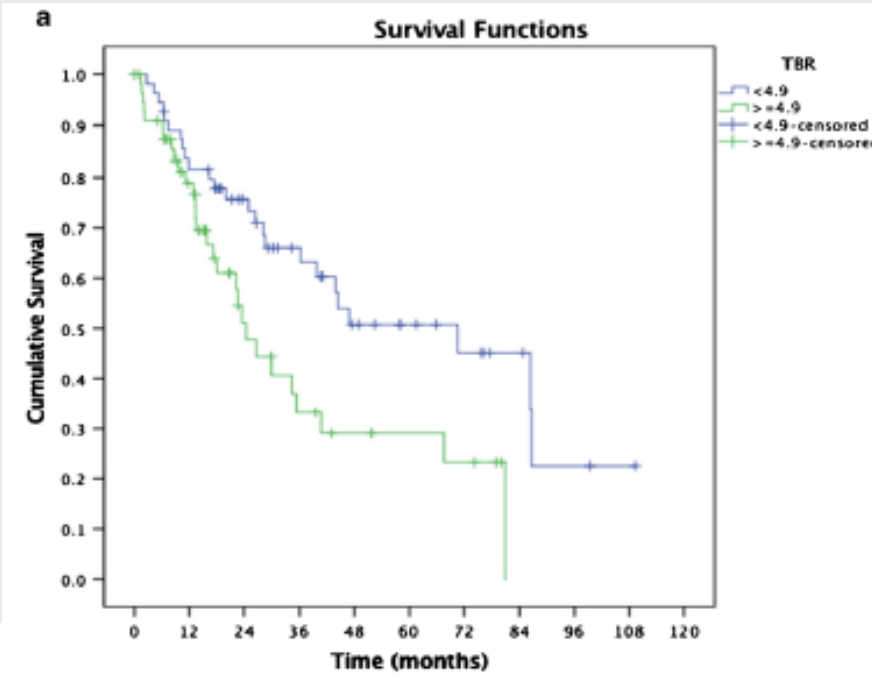


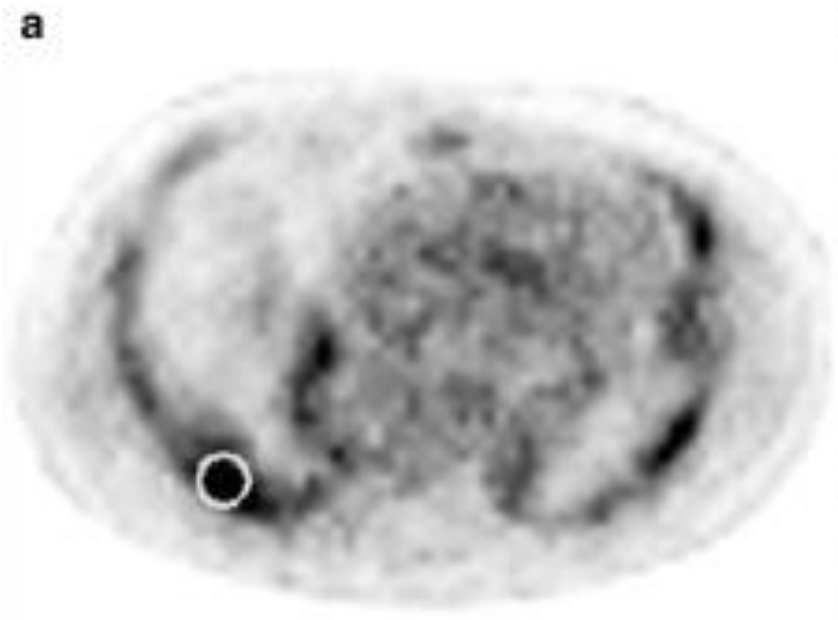
Lee-SM et al. Eur Radiol 2018;28:1293-1300

Idiopathic Pulmonary Fibrosis: PET/CT

- 113 IPF patients; FDG-PET/CT
- Target-to-background SUV
  < 4.9 med. survival 71 mo
  > 4.9 med. survival 24 mo

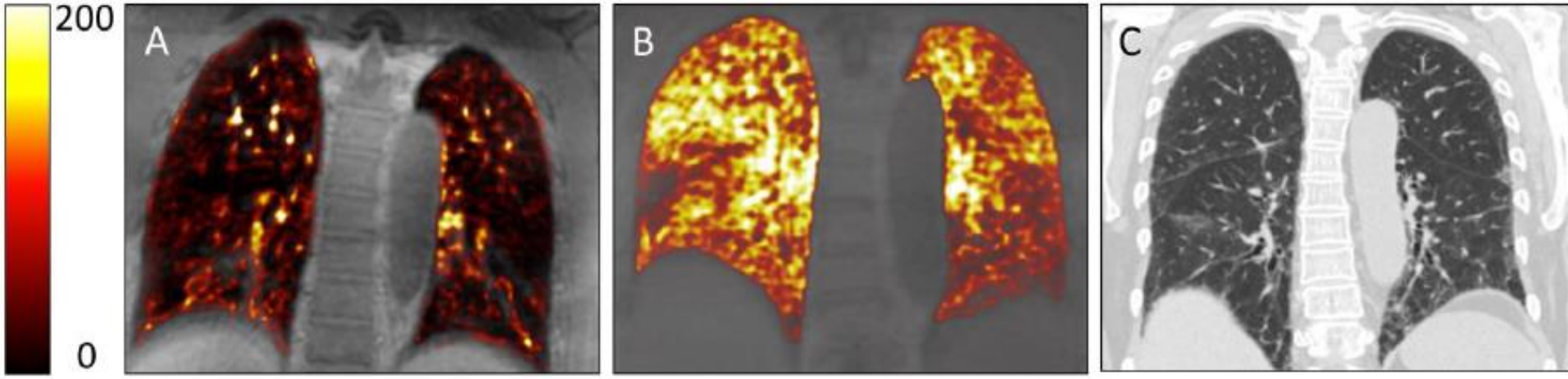
Win-T et al. Eur J Nuc Med Mol Imag 2018;45:806-815





Pulmonary Fibrosis: Gadofosveset-enhanced MRI

- Vascular leakage
- Gadofosveset is a FDA-approved albumin-binding contrast agent
- Detects vascular permeability, used for vascular MRI
- 6 pulmonary fibrosis patients; FDG-PET/CT
- Vascular leak increased vs. health controls

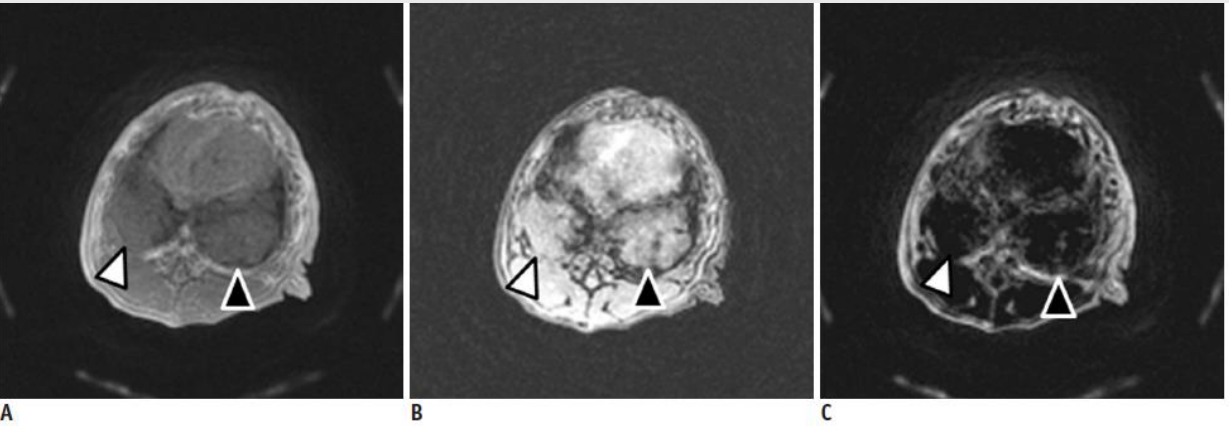


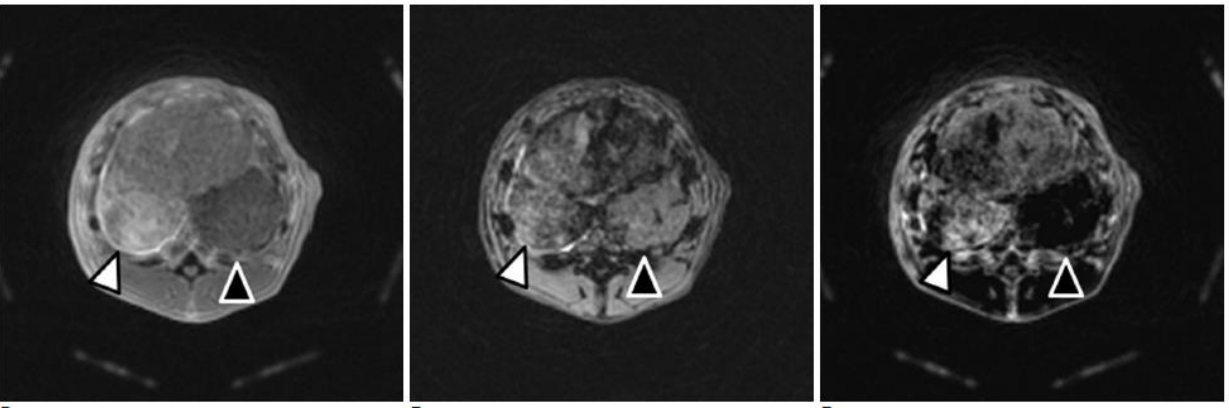
Healthy IPF IPF CT

Montesi-S et al. ERJ 2018; epub

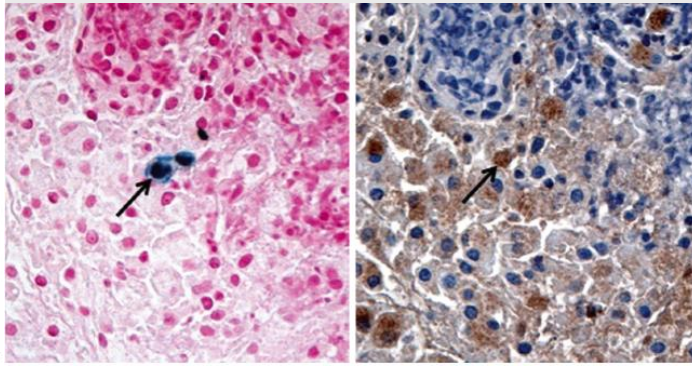
Pulmonary Fibrosis: Iron-oxid-enhanced MRI

- Superparamagnetic iron-oxide nanoparticles (ferumoxytol)
- Iron uptake in macrophages
- UTE MRI (CODE)
- Enhancement in granulomatosis disease, not cancer



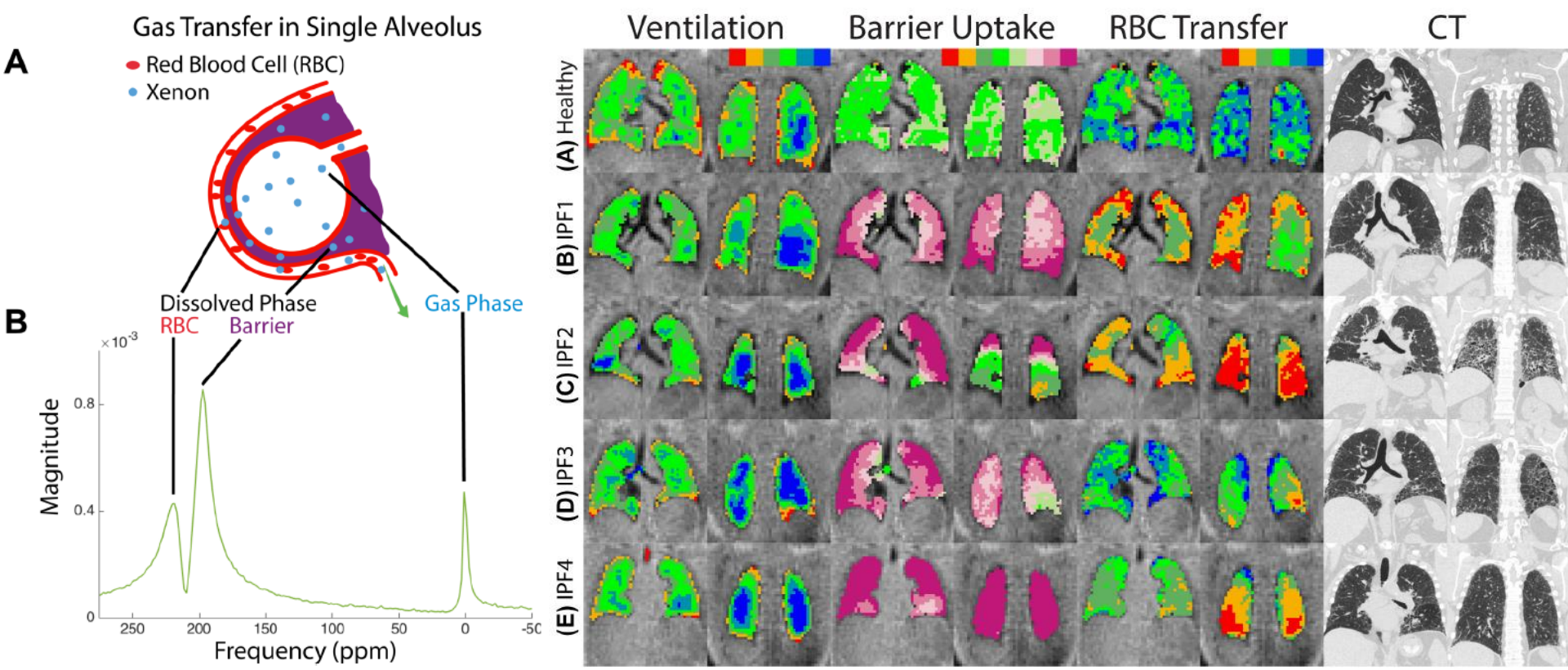


Yoon-SH et al. KRJ 2018;19:153-157



Pulmonary Fibrosis: Hypx 129Xe Gas Exchange MRI

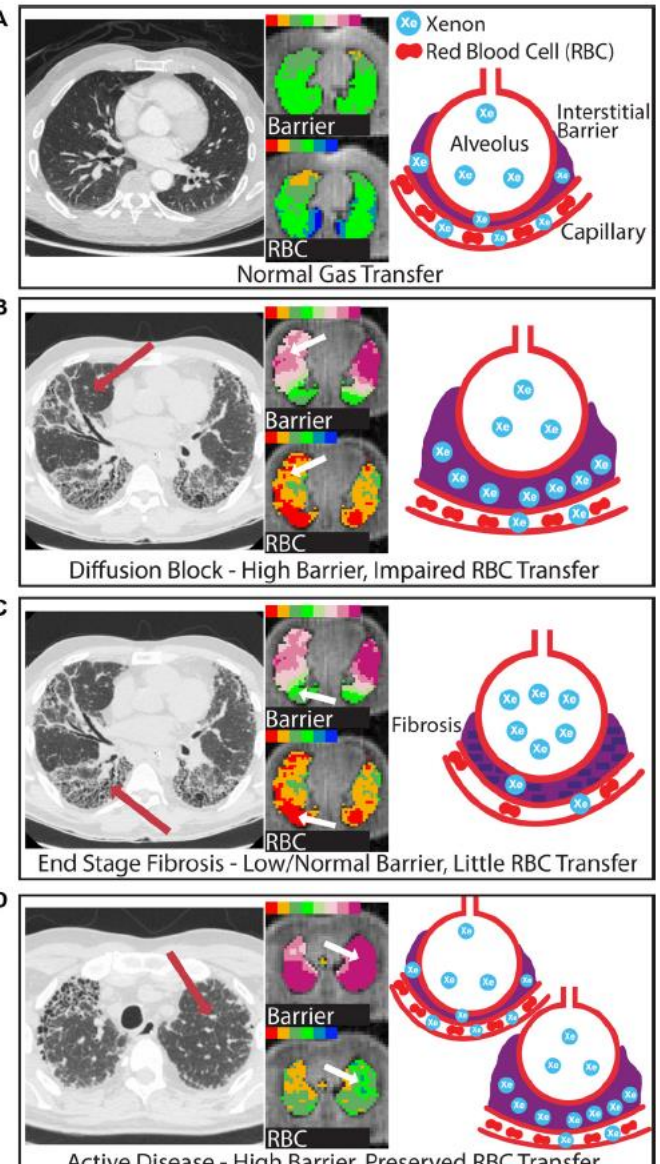
- **13 healthy, 12 IPF patients**

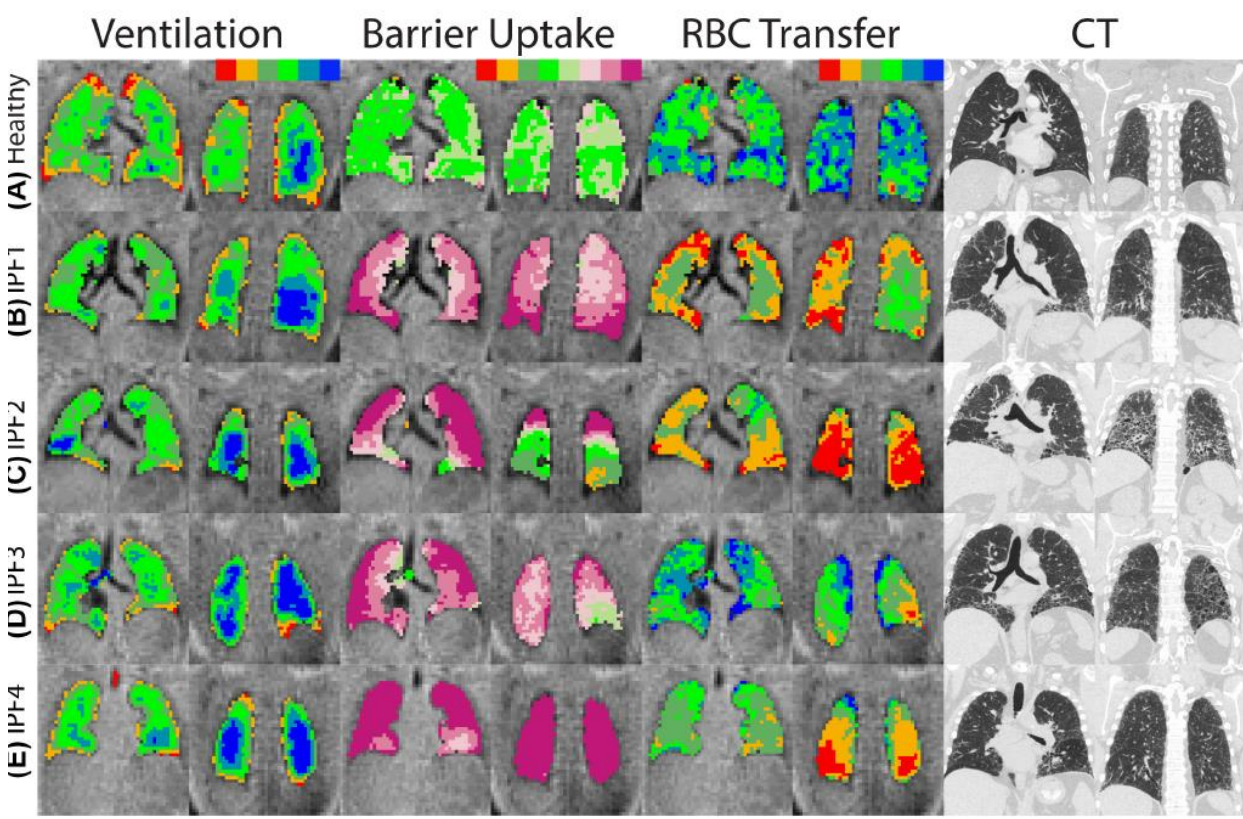


Wang-JM et al. Thorax 2018;73:21-28

Pulmonary Fibrosis: Hypx 129Xe Gas Exchange MRI

- **13 healthy, 12 IPF patients**





Wang-JM et al. Thorax 2018;73:21-28

Take Home: Diffuse Parenchymal Lung Disease

- **Comorbidities**
- **Quantification, imaging biomarkers**
- **Activity, remodeling: metabolism**
  vascular permeabilility
  inflammation (macrophage)

Pulmonary Nodules
Lung Cancer
Radiomics

State-of-the-Art: Pulmonary Nodules, Lung Cancer

- **Fleischner Guidelines 2.0**

A: Solid Nodules*

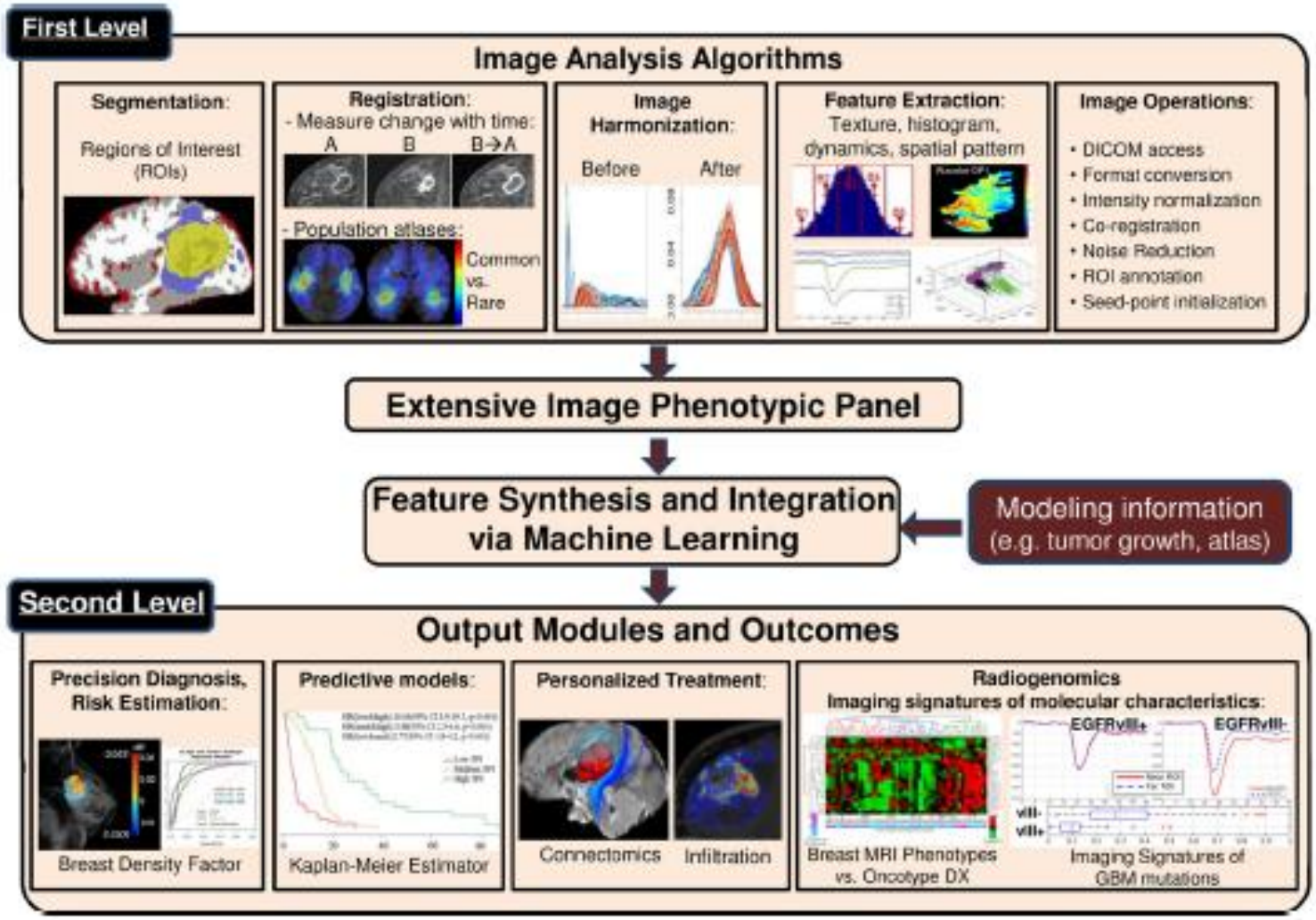
Nodule Type	Size		
	<6 mm (<100 mm³)	6–8 mm (100–250 mm³)	>8 mm (>250 mm³)
Single			
Low risk†	No routine follow-up	CT at 6–12 months, then consider CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling
High risk†	Optional CT at 12 months	CT at 6–12 months, then CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling

MacMahon-H et al. Radiology 2017;284:228-243

- **Lung Rads**
- **Lung cancer staging 8th edition**

State-of-the Art: Radiomics

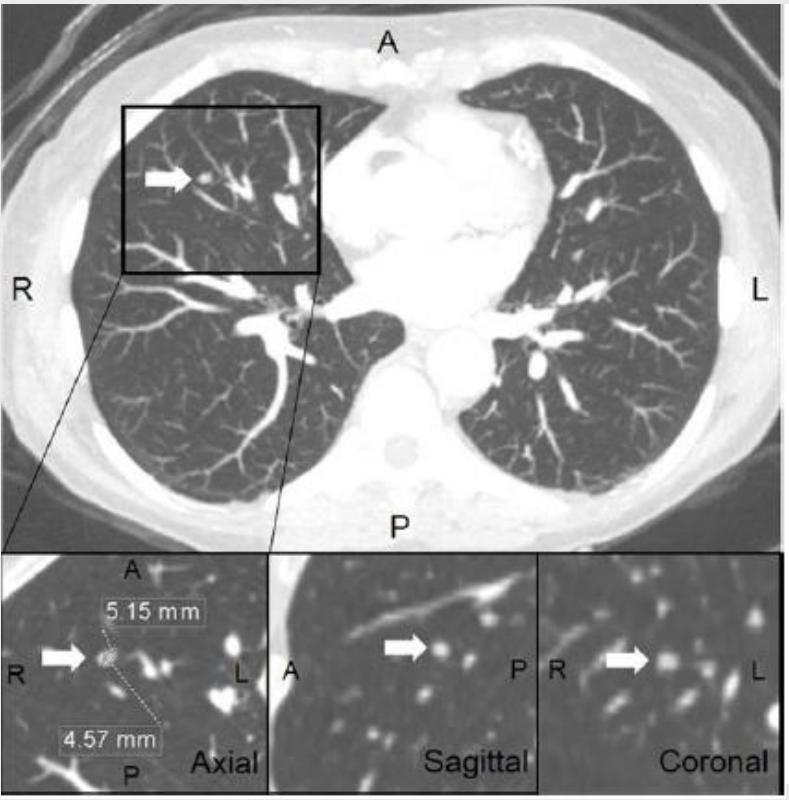
- **Quantitative imaging analytics**
- **Precision diagnostics, predictive modeling of outcome**

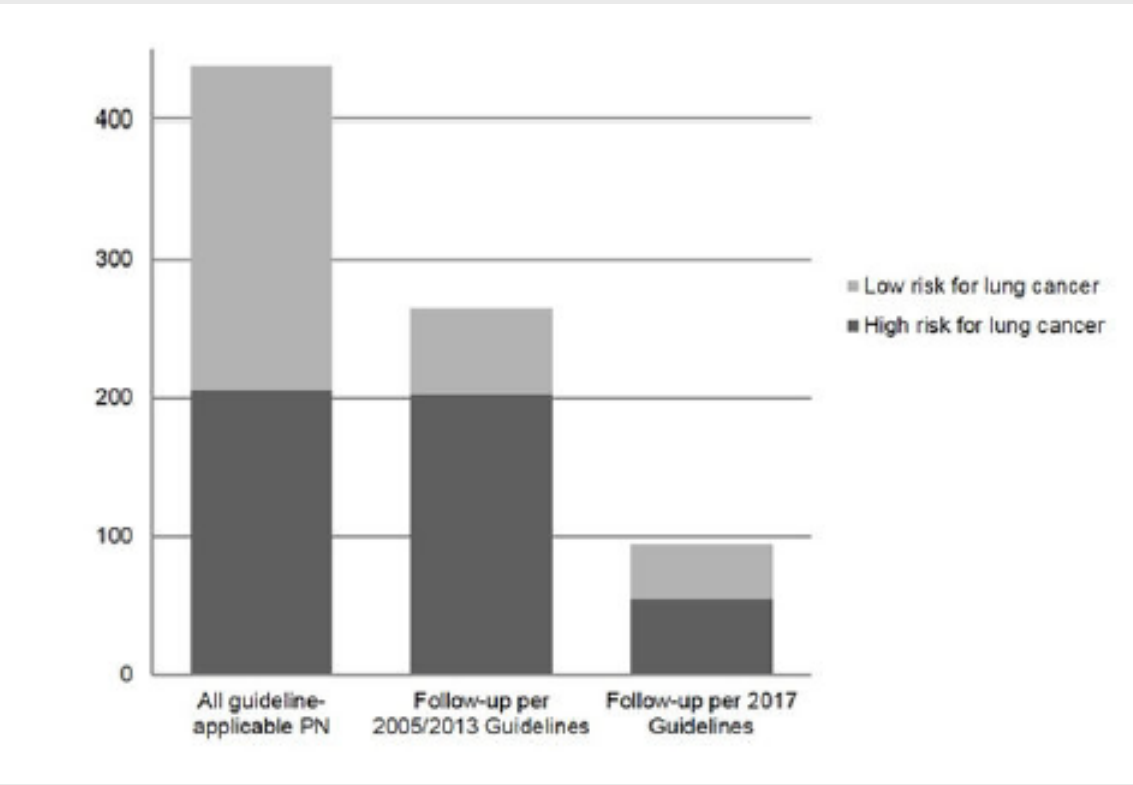


Davatzikos-C et al. J Med Imag 2018;5:011018

Pulmonary Nodules: Fleischner Guidelines 2.0

- 2066 patients with coronary CTA, 578 pulmonary nodules
- Patients required follow-up reduced by 65%

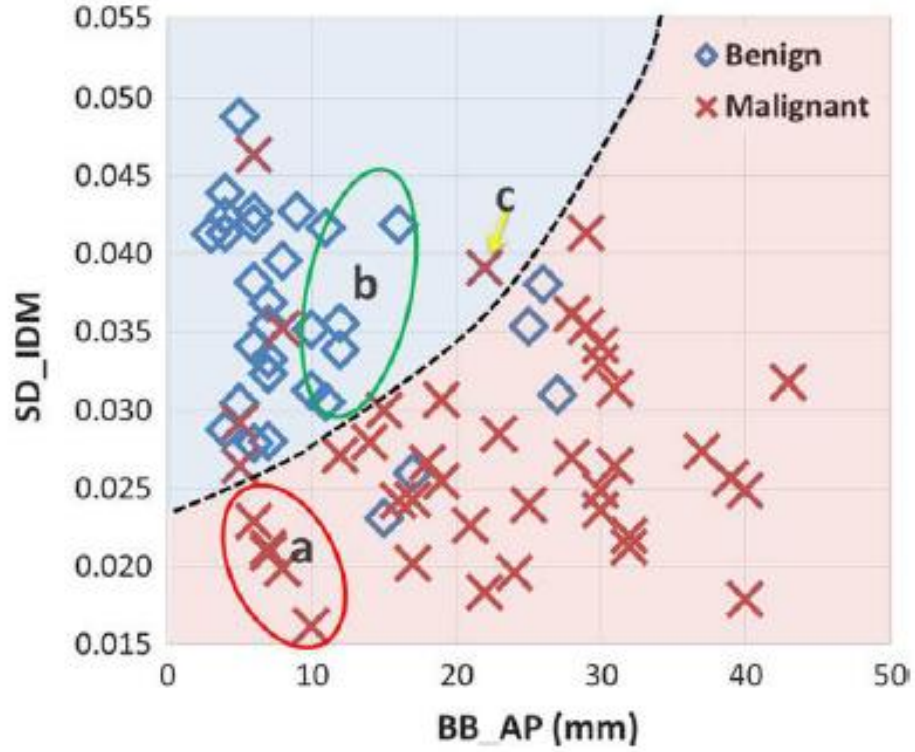


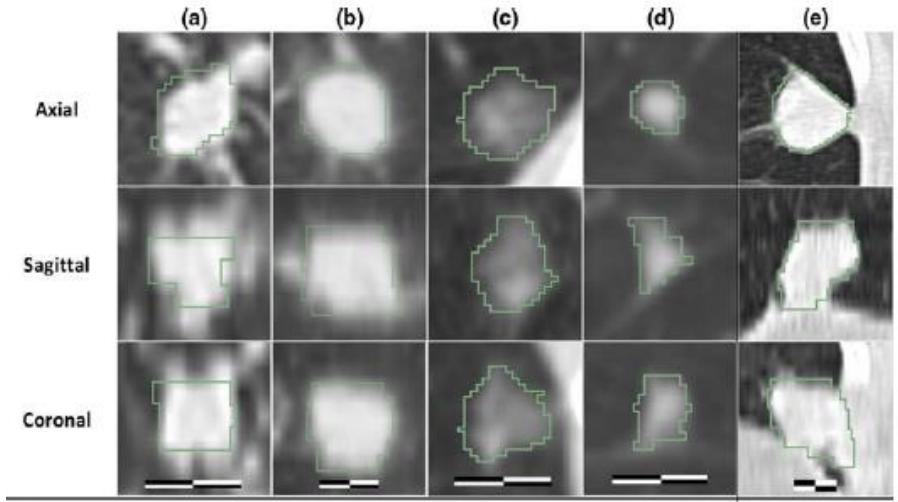


Scholtz-JE et al. J Cardiovasc Comput Tomogr 2018;12:28-33

Pulmonary Nodules: Radiomics Prediction Model

- 72 pulmonary nodules (31 benign, 41 malignant)
- Lung Image Database Consortium image collection
- Accuracy 85%, better than Lung Rads 72%



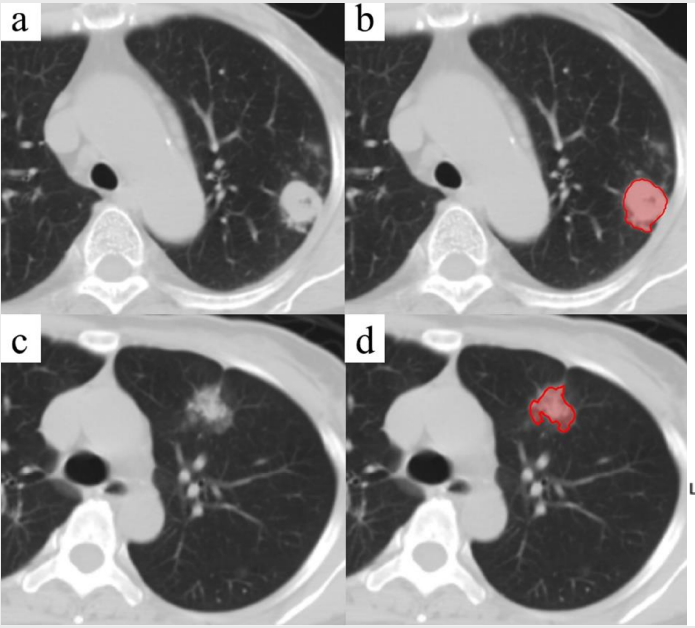


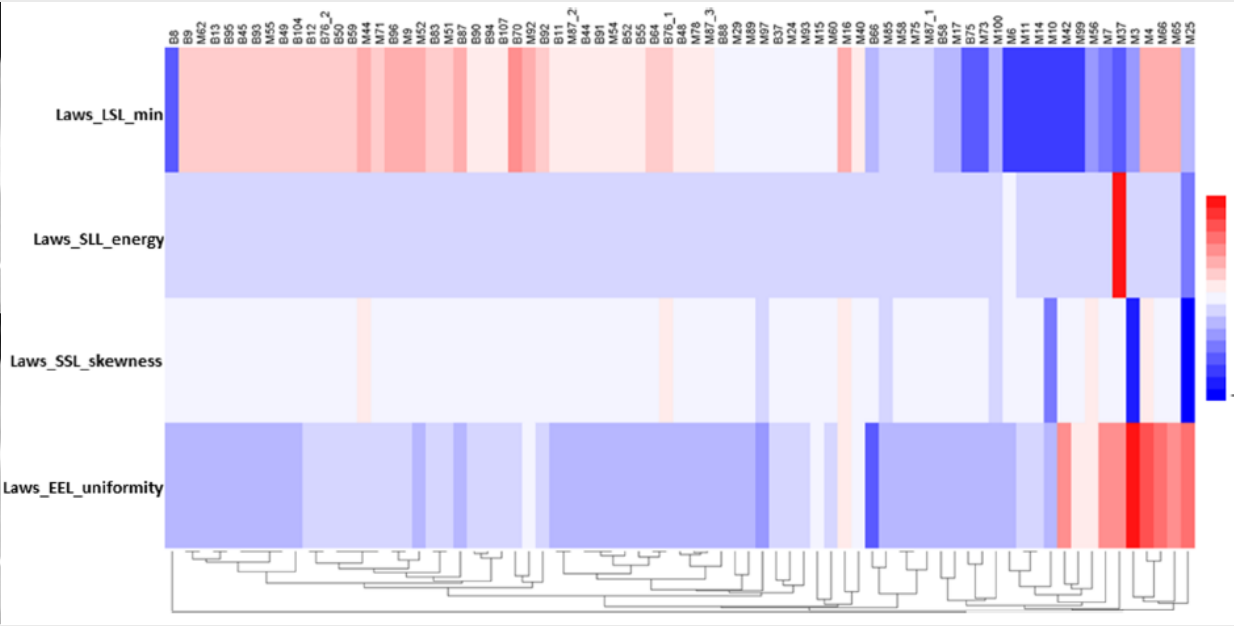
rue Status	Benign	Benign	Malignant	Malignant	Malignant
VM-LASSO	Benign	Benign	Malignant	Malignant	Benign
B_AP (mm)	10	16	10	7	22
D_IDM	0.035	0.042	0.014	0.021	0.039
ung-RADS	4X: Malignant	4A: Malignant	3: Benign	2: Benign	4B: Malignant
ize (mm)	10	16	9 (4)	7	20
ype	Solid	Solid	Part Solid	Solid	Solid
alcification	Absent	Absent	Absent	Absent	Absent
piculation	3	1	1	1	1

Choi-W et al. Med Phys 2018;45:1537-1549

Pulmonary Nodules: Radiomics Prediction Model

- 72 pulmonary nodules (33 benign, 42 malignant)
- Retrospective analysis of clinical routine CT
- Accuracy 84%, sensitivity 93%, specificity 73%

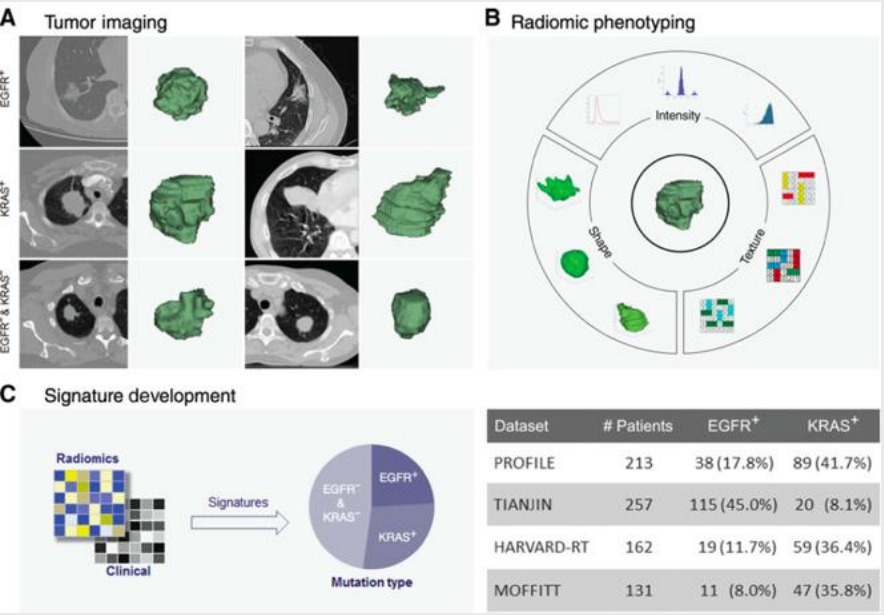




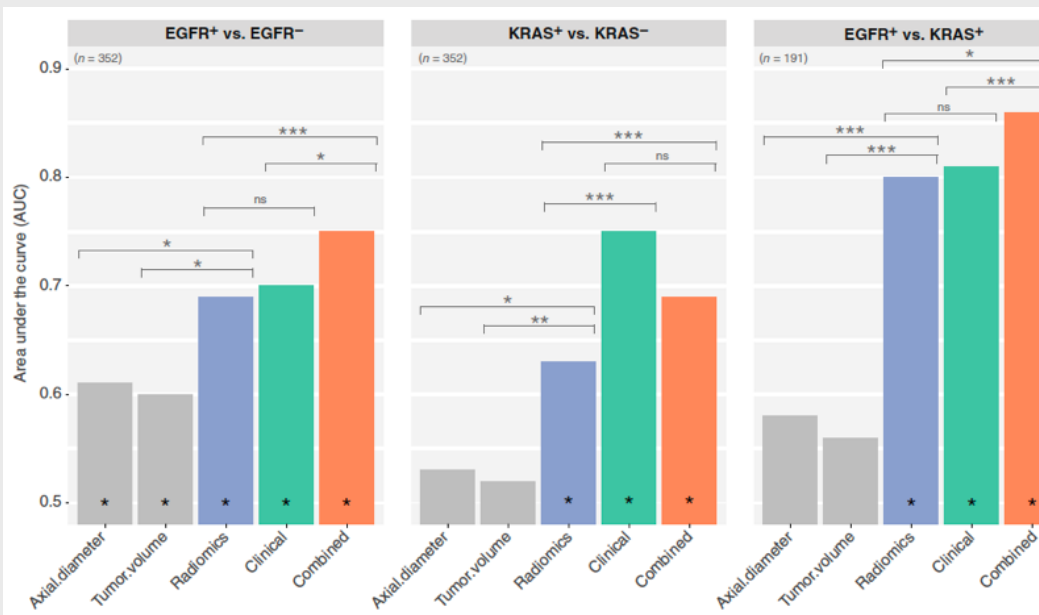
Chen-CH et al. PLoS One 2018 Feb-5

Lung Adenocarcinoma Heterogeneity: Radiomics

- **763 patients: radiomics + genomics**
- **EGFR, KRAS mutations**



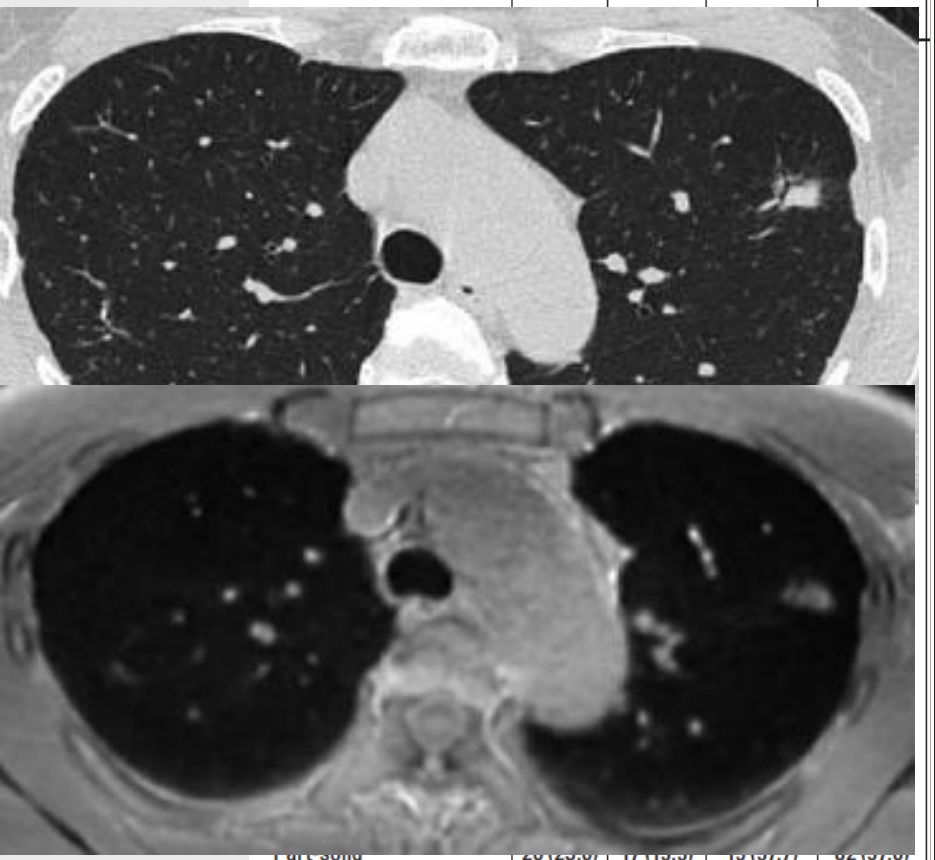
Dataset	# Patients	EGFR+	KRAS+
PROFILE	213	38 (17.8%)	89 (41.7%)
TIANJIN	257	115 (45.0%)	20 (8.1%)
HARVARD-RT	162	19 (11.7%)	59 (36.4%)
MOFFITT	131	11 (8.0%)	47 (35.8%)



Rios Velazquez-E et al. Cancer Res 2017;77:3922-3930

Pulmonary Nodules: MRI

- 51 patients
- 119 pulmonary nodules
- CT and UTE MRI



Pure ground-glass opacity	11 (10.0)	12 (10.9)	10 (90.9)	97 (98.0)

Wielpütz-MO et al. AJR 2018;210:1-10
Ohno-Y et al. JMRI 2018 epub

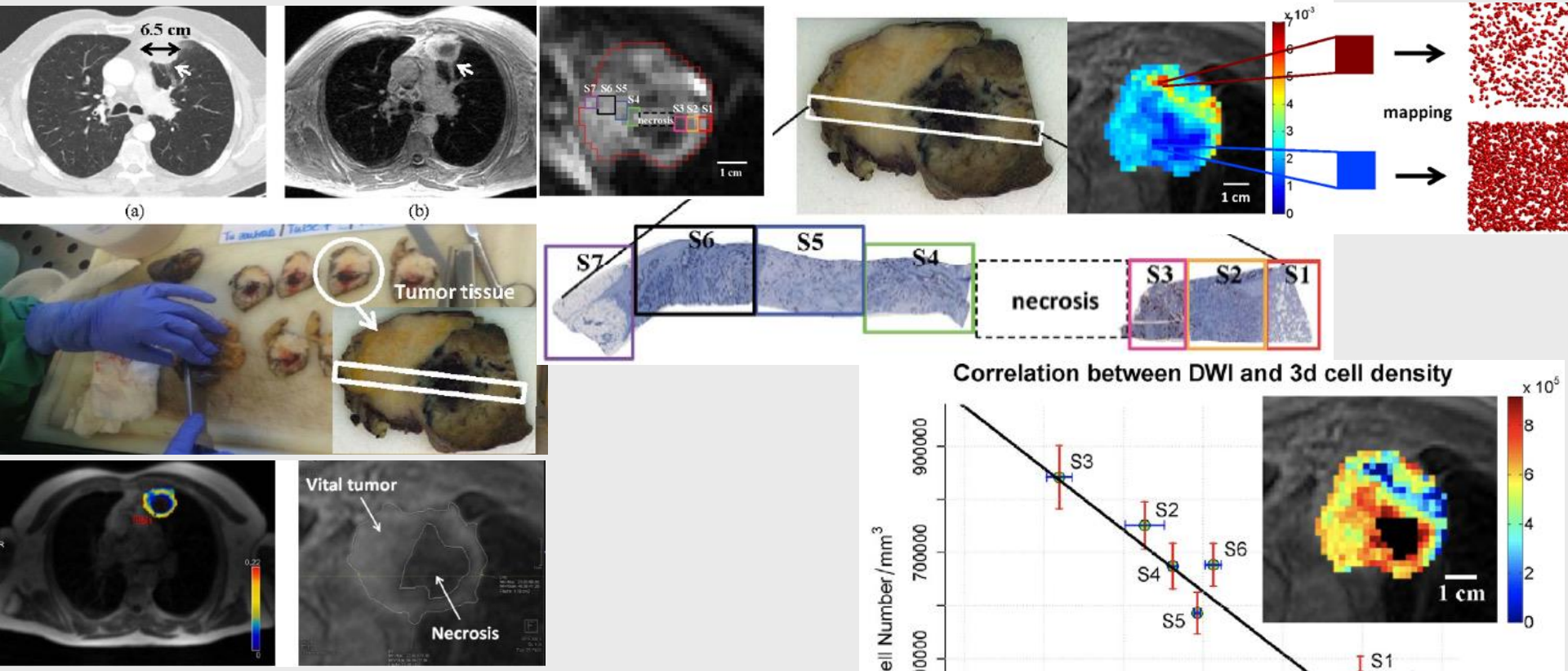
TABLE 4. Currently Recommended MR Protocols for Nodule Detection and Evaluation

		MR technique	Additional comments
Nodule detection		STIR turbo SE or HASTE imaging	Black-blood technique would be better to be applied. Respiratory gating would be better to be applied rather than breath holding, if possible.
		Pulmonary thin-section MRI with ultra-short TE	Ultra-short TE would be better to be shorten at ≤192 μs. Respiratory gating would be better to be applied rather than breath holding, if possible.
Nodule evaluation	Nondynamic technique	T1-weighted turbo SE or HASTE imaging	Black-blood technique would be better to be applied. Respiratory gating would be better to be applied rather than breath holding, if possible.
		3D T1-weighted radiofrequency-spoiled GRE imaging with interpolation and/or partial Fourier techniques as well as fat suppression method	VIBE (Siemens Healthcare), LAVA (GE Healthcare), THRIVE (Philips Medical Systems), Quick 3D (Canon < previously Toshiba > Medical Systems)
		T2-weighted turbo SE or HASTE imaging	Black-blood technique would be better to be applied. Respiratory gating would be better to be applied rather than breath holding, if possible.
		STIR turbo SE or HASTE imaging	Black-blood technique would be better to be applied. Respiratory gating would be better to be applied rather than breath holding, if possible. Moreover, contrast ratio between lesion to muscle would be better to be evaluated for quantitative assessment.
		Diffusion-weighted imaging	Apparent diffusion coefficient as well as lesion-to-spinal cord ratio evaluations would be better to be applied.
		Contrast-enhanced T1-weighted turbo SE or HASTE imaging	Black-blood technique would be better to be applied. Respiratory gating would be better to be applied rather than breath holding, if possible.
		Contrast-enhanced 3D T1-weighted radiofrequency-spoiled GRE imaging with interpolation and/or partial Fourier techniques as well as fat suppression method	VIBE (Siemens Healthcare), LAVA (GE Healthcare), THRIVE (Philips Medical Systems), Quick 3D (Canon < previously Toshiba > Medical Systems)
	Dynamic contrast-enhanced technique	Dynamic first-pass contrast-enhanced T1-weighted GRE imaging with ultra-fast TE	Ultra-short TE would be better to be shorten at ≤0.2 msec. Temporal resolution would be better to be set at ≤1.5 sec with and without applying parallel imaging technique. Bolus injection protocol would be better to be considered with field strength.

VIBE: volumetric interpolated breath-hold examination, LAVA: liver acquisition with volume acceleration, THRIVE: T1 high resolution isotropic volume excitation, Quick 3D: fast and segmented 3D T1-weighted spoiled-gradient-echo.

Lung Cancer Heterogeneity: DWI Cell Count

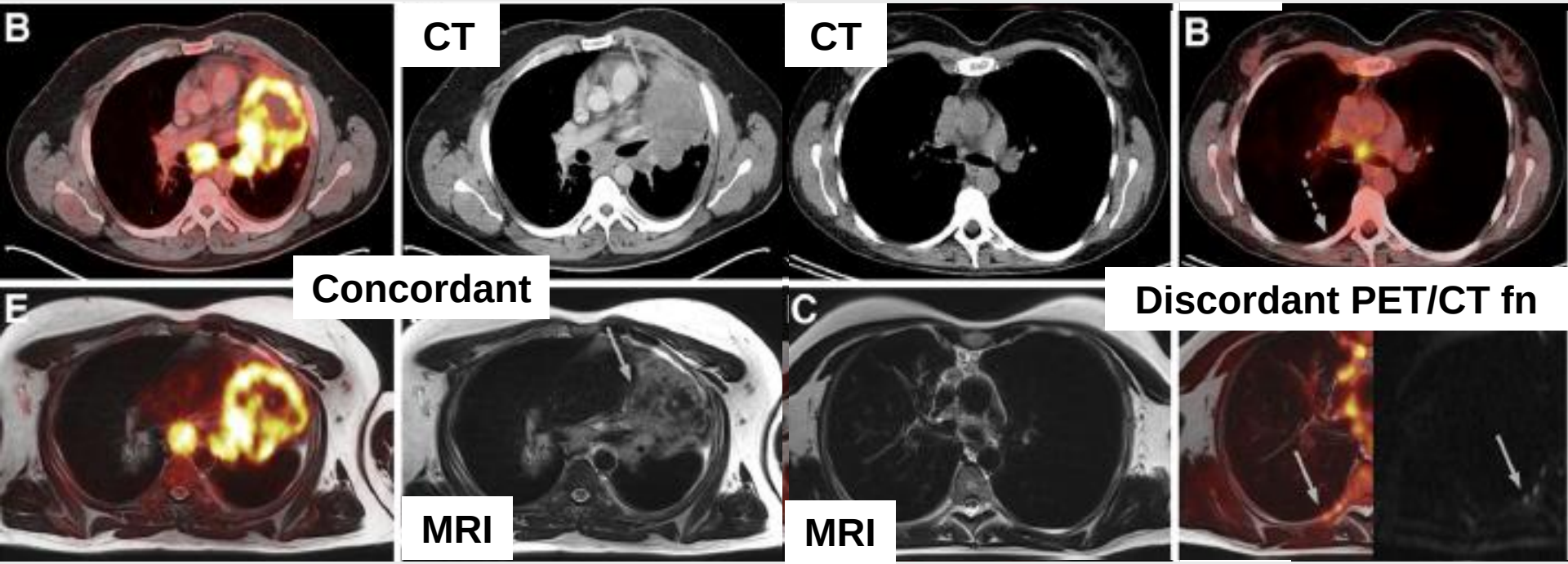
- **Feasibility, imaging histology pipeline, validation**



Yin-Y et al. IEEE Transactions Med Imag 2018;37:35-46

Lung Cancer Staging: PET/MRI vs. PET/CT

- **77 patients: comparable staging results, therapeutic decisions**



Schaarschmidt-BM et al. Eur Radiol 2017;27:681-688

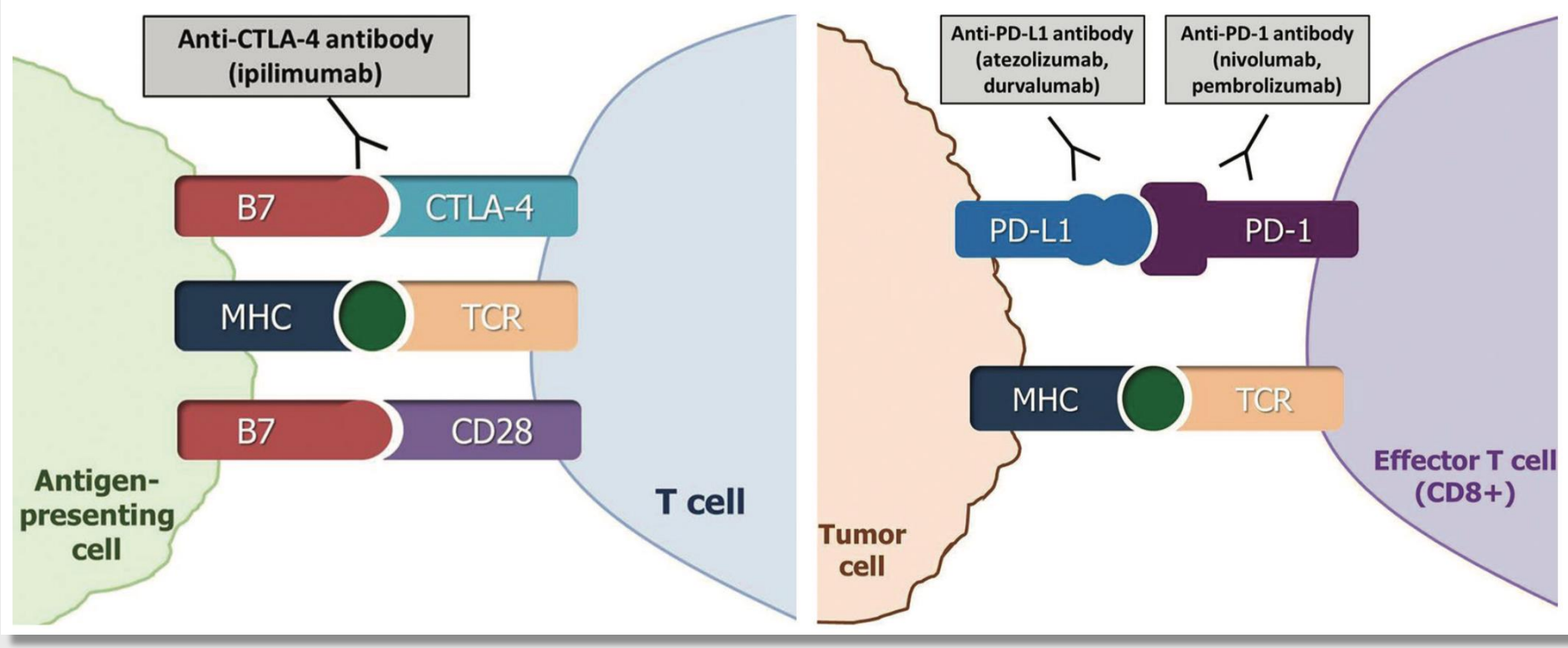
Take Home: Nodules, Lung Cancer, Radiomics

- **Tumor characterization**
- **Tumor heterogeneity**
- **Therapy response** **early detection**
  quantification
  prediction

Precision Cancer Therapy: Pulmonary Complications

State-of-the-Art: Pulmonary Complications

- **Immunotherapy**
- **Checkpoint inhibitors: PD-1, PD-L1, CTLA-4**

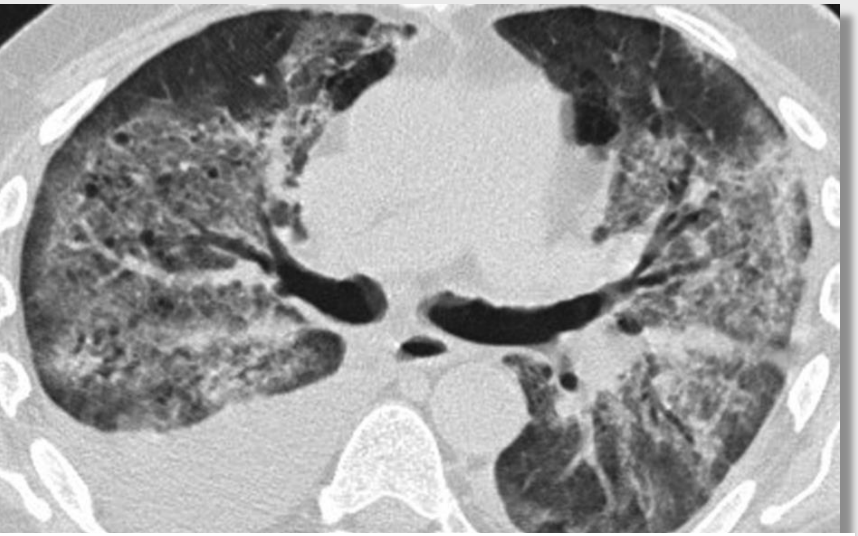


- **Immune-related adverse events (irAEs): pneumonitis, hypophysitis, thyroiditis, hepatitis, pancreatitis, colitis**

*Nishino-M et al. Radiographics 2017;**37:1371-1387***

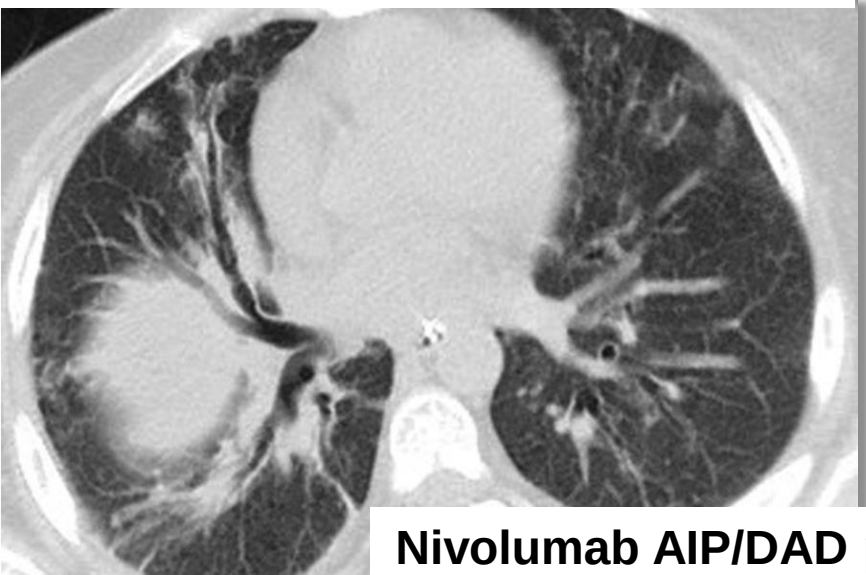
Pulmonary Complications of Immunotherapy

- **Toxic pneumonitis, different patterns**



Rituximab-CHOP AIP/DAD pattern

Nivolumab NSIP pattern



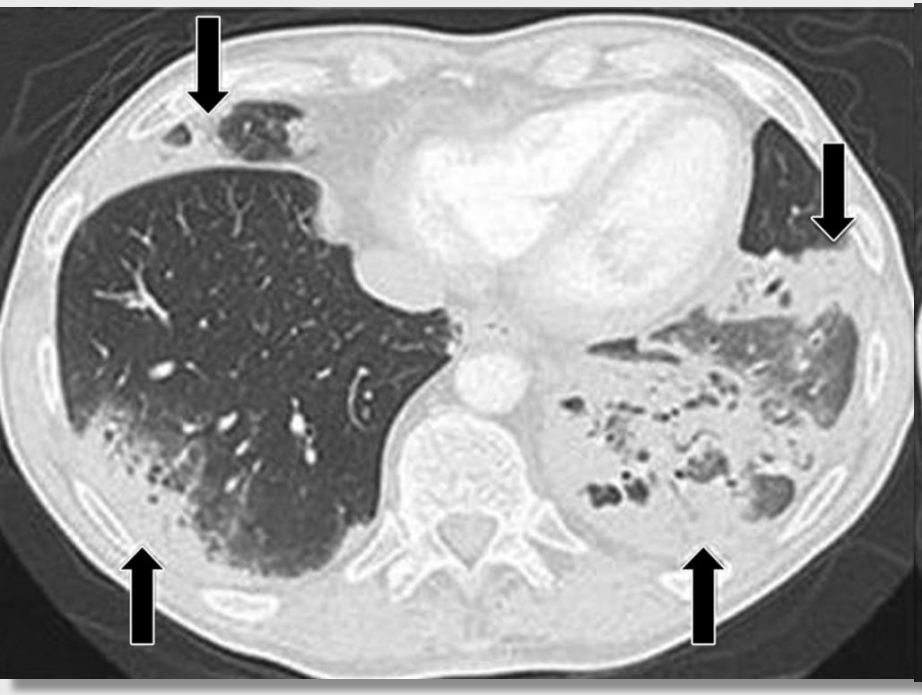
Nivolumab AIP/DAD pattern

Nivolumab HP pattern

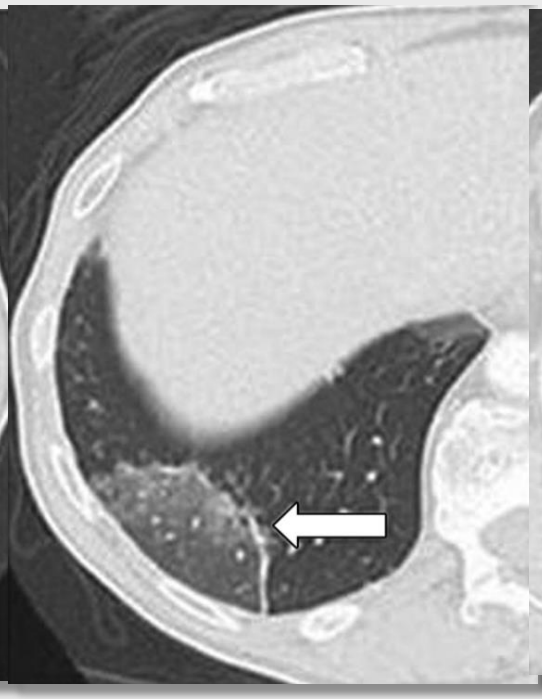
Nishino-M et al. Radiographics 2017;37:1371-1387

Pulmonary Complications of Immunotherapy

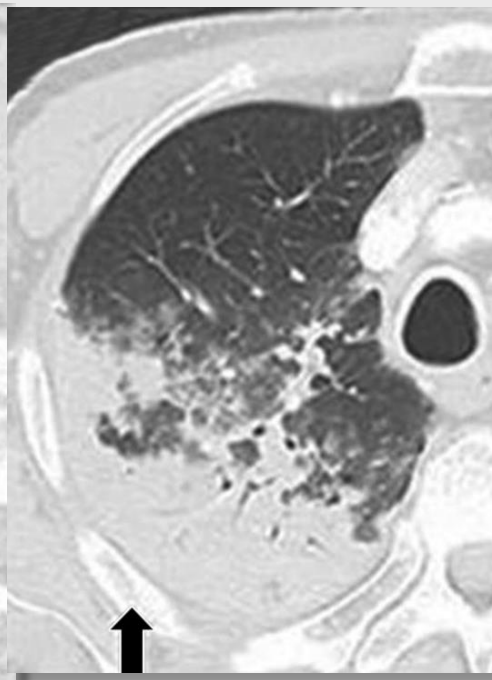
- **Toxic pneumonitis, COP pattern**



Nivolumab



Nivo off, steroids on

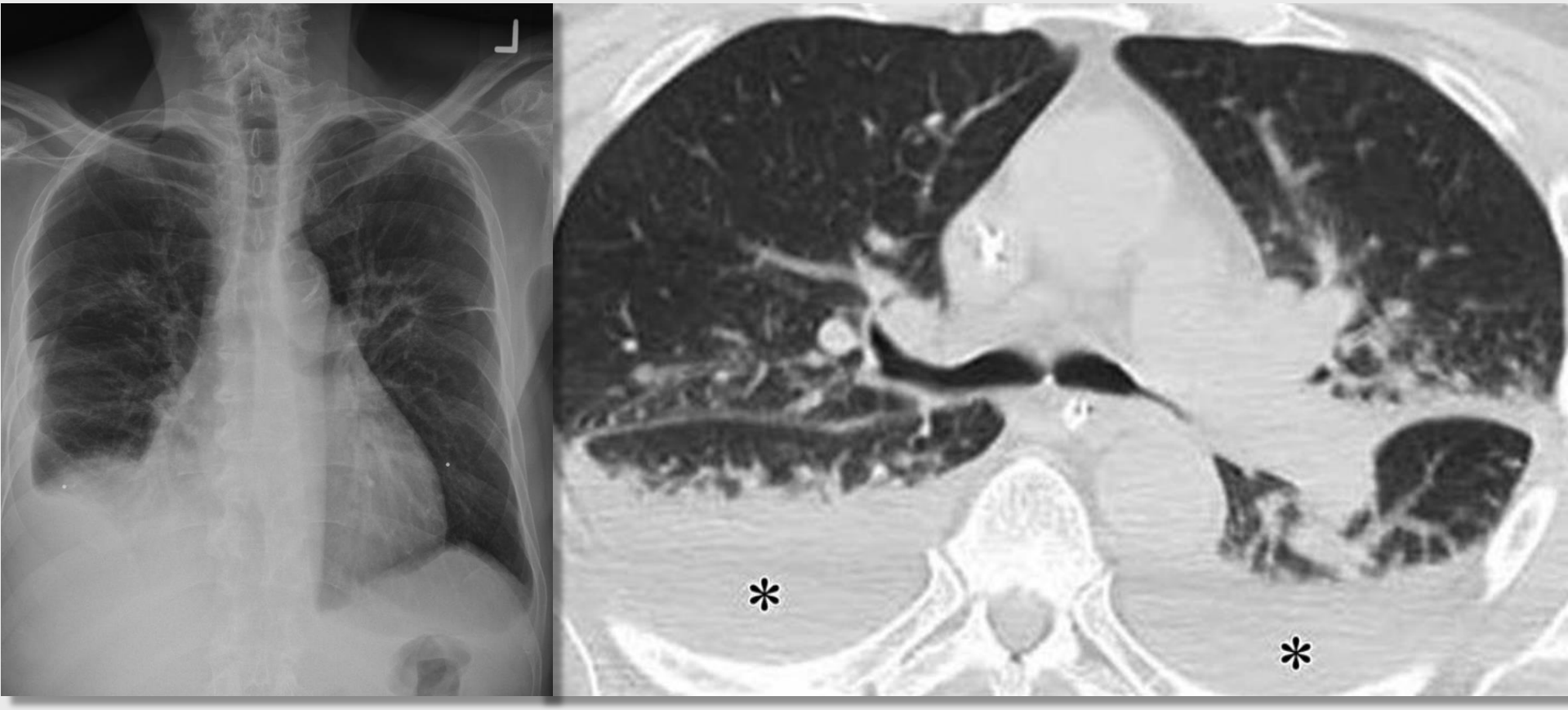


Steroids off

*Nishino-M et al. Radiographics 2017;**37:1371-1387***

Pulmonary Complications of Immunotherapy

- Toxic pulmonary edema
- Toxic pleural effusion



Nilotinib

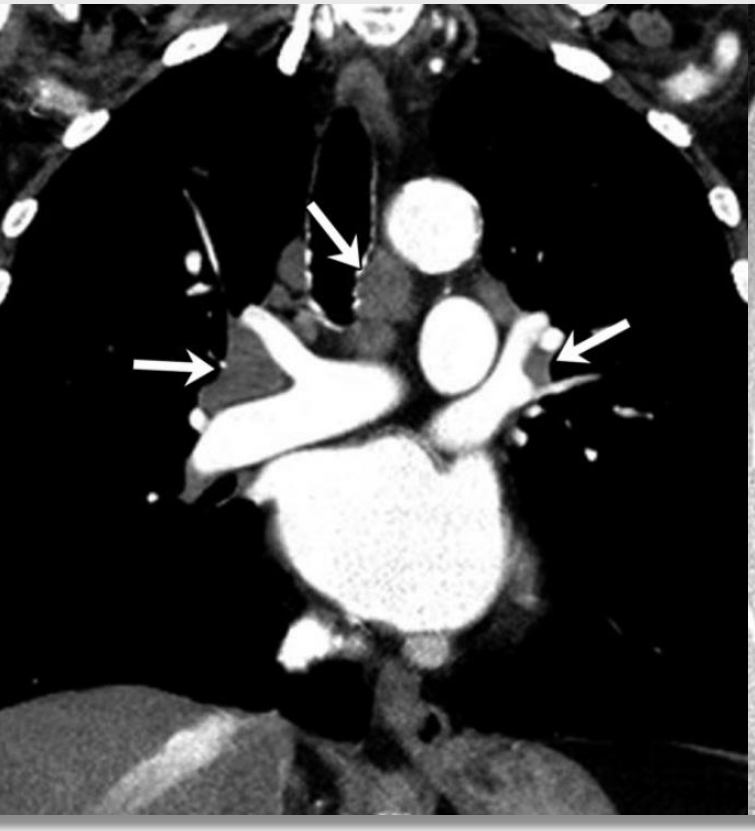
Nivolumab + Ipilimumab

*Nishino-M et al. Radiographics 2017;**37:1371-1387***

Pulmonary Complications of Immunotherapy

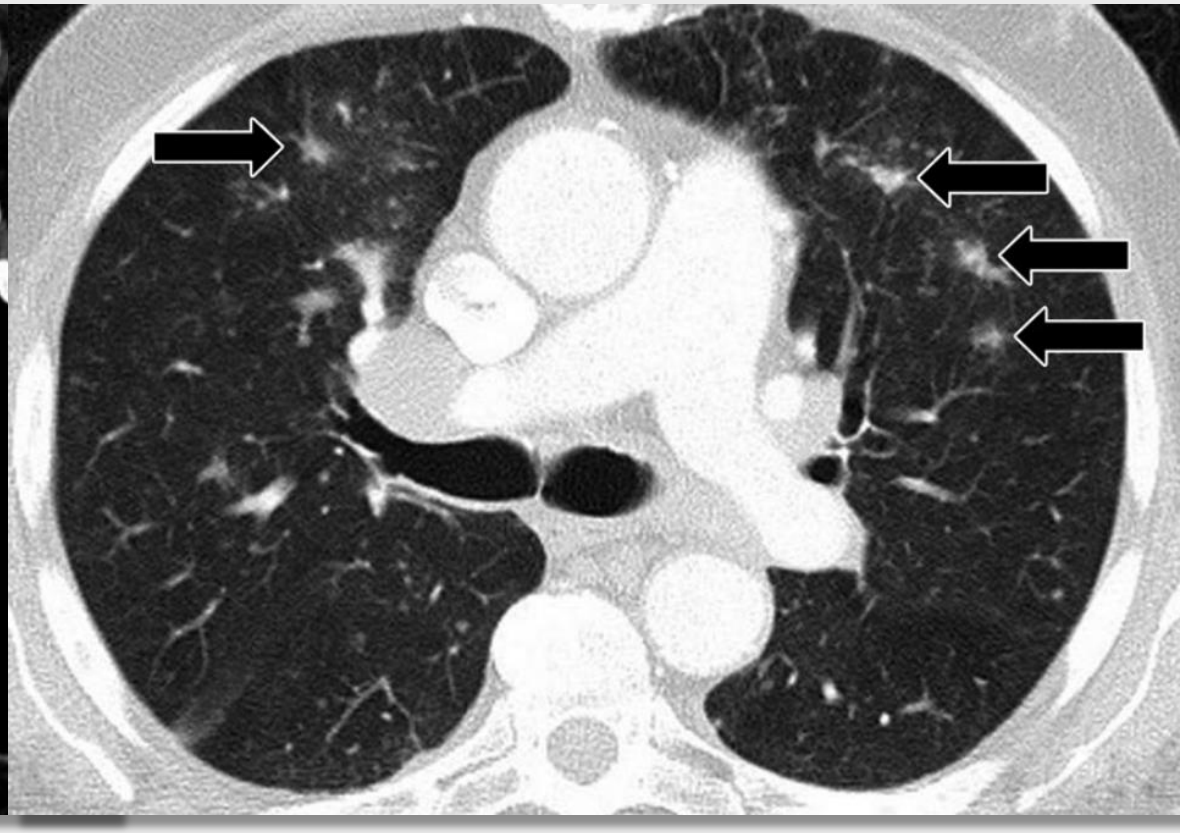
- **Sarcoid mimikry**

Lymphadenopathy



Ipilimumab

Perilymphatic nodules



Ipilimumab

*Nishino-M et al. Radiographics 2017;**37:1371-1387***

NSCLC Treatment: PD1-Inhibitors ir RECIST

- **Immune-related RECIST > RECIST 1.1, e.g. longer TTP**
  RR = 18 %; pseudoprogression rare

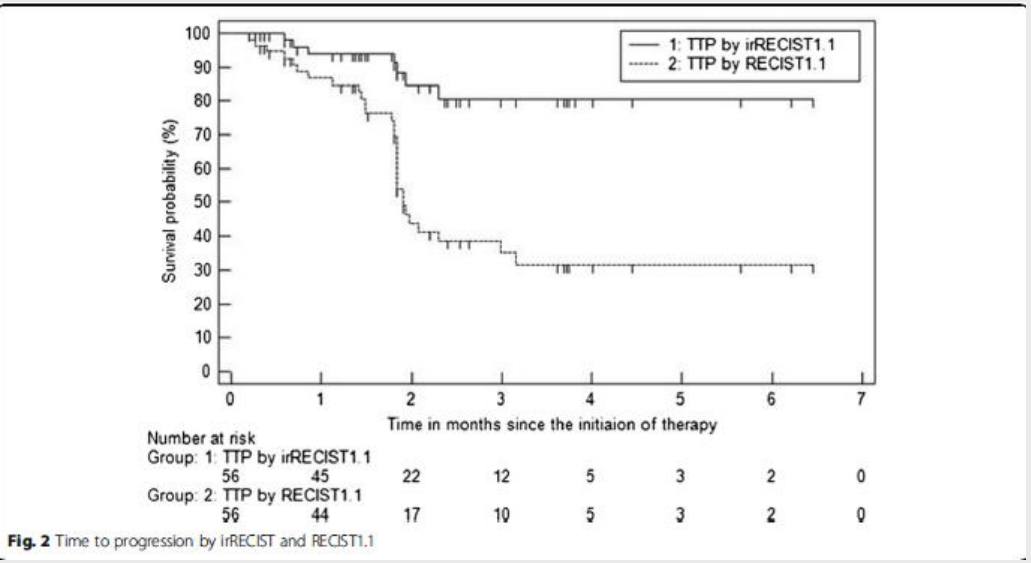
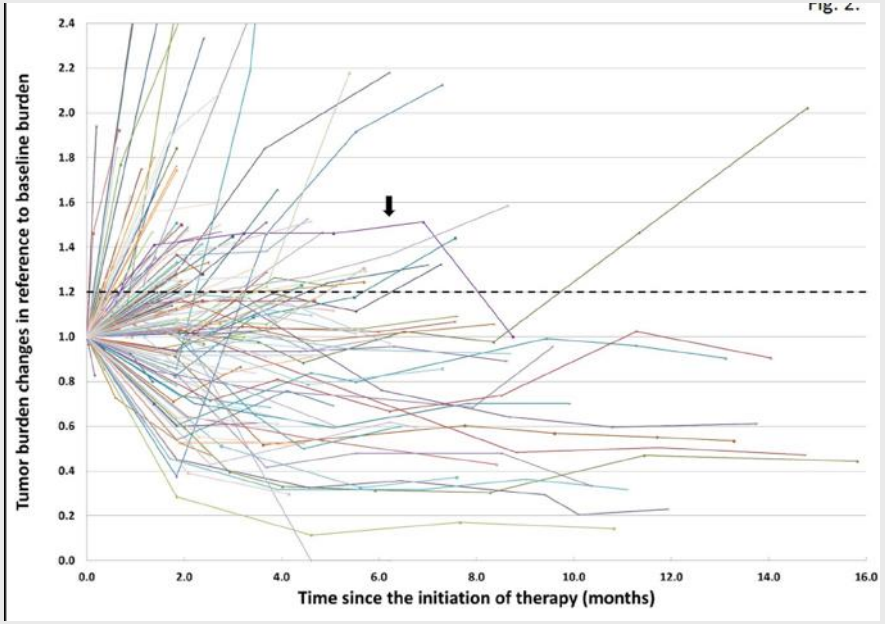


Fig. 2 Time to progression by irRECIST and RECIST1.1



Nishino-M et al. J Immunotherapy Cancer 2016;4:84;
Nishino-M et al. Clin Cancer Res 2017;23:5737-5744

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- **Immune-related RECIST > RECIST 1.1, e.g. longer TTP**
  RR = 18 %; pseudoprogression rare

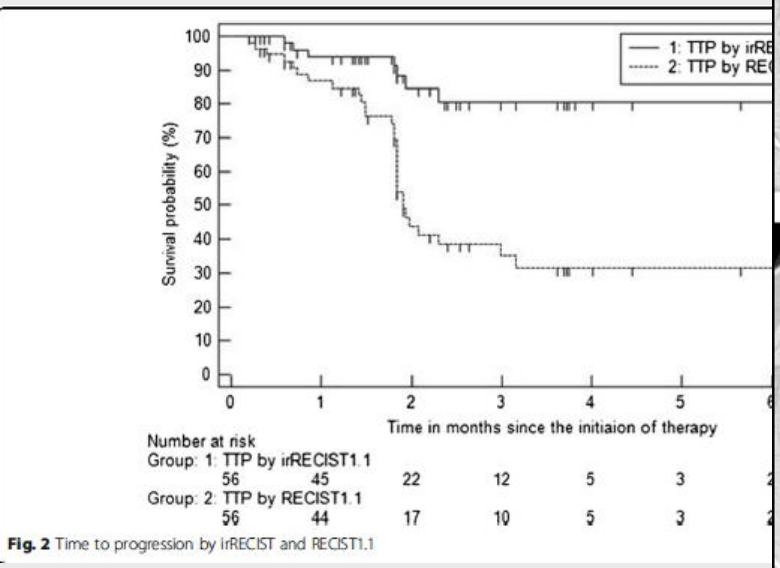
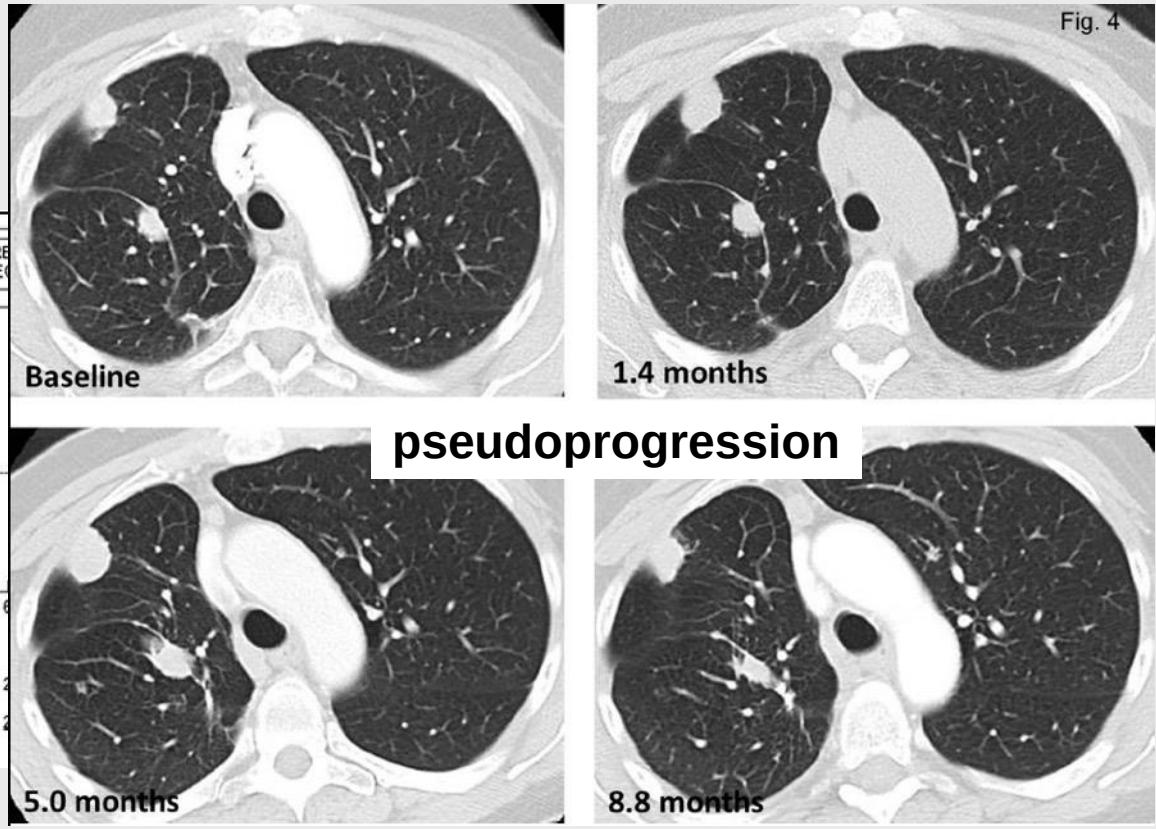


Fig. 2 Time to progression by irRECIST and RECIST1.1



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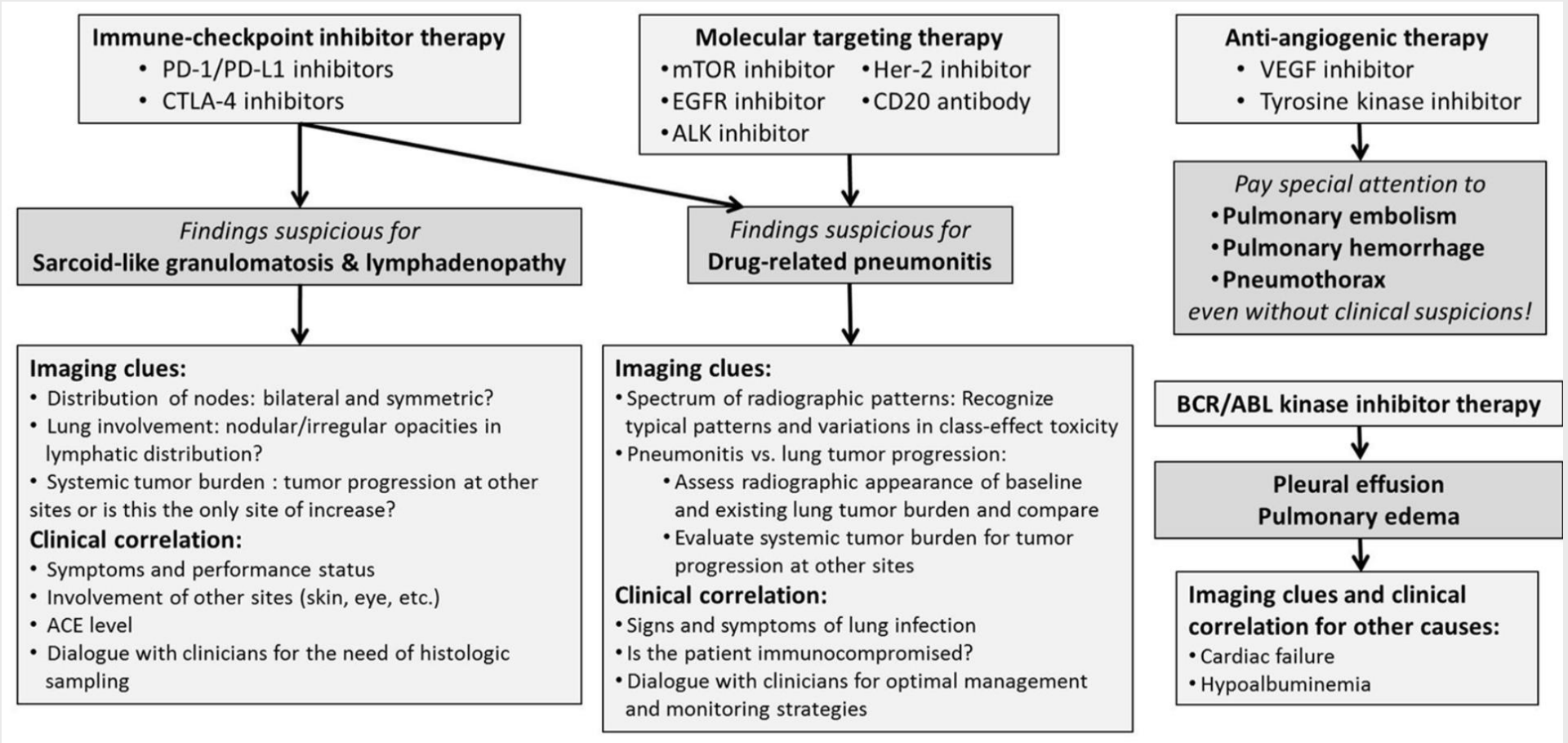
Take Home: Pulmonary Complications



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