CENTRE FOR MEDICAL IMAGE COMPUTING
DEPARTMENT OF MEDICAL PHYSICS & BIOMEDICAL ENGINEERING

UCL

Image analysis for lung radiotherapy toxicity

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PART

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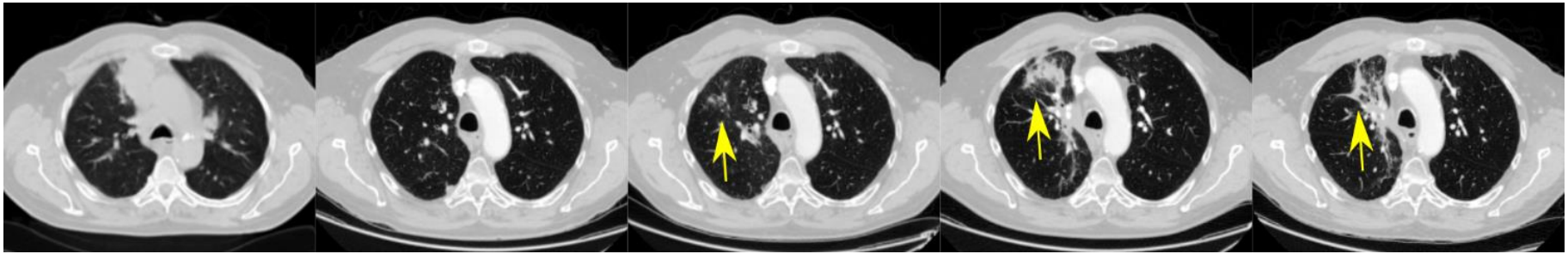
Background & Rationale

RILD is a common unwanted side effect of radical radiotherapy that leads to loss of quality of life in survivors [1]

- Acute (pneumonitis, <6 months) vs chronic (fibrosis >12months)
- Distinction between pneumonitis and fibrosis is often unclear clinically
- RILD is visible on CT imaging, bringing an opportunity for *quantification*

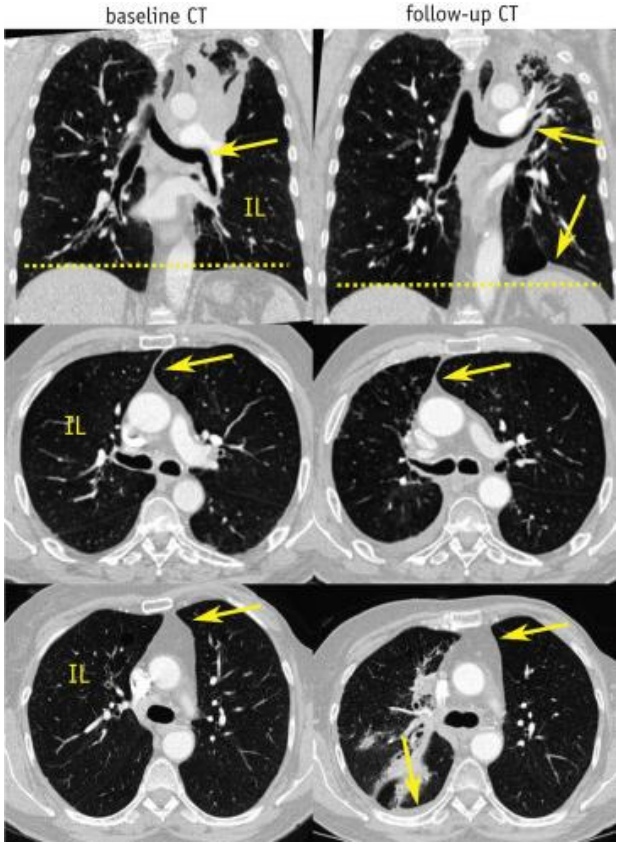


Pre-RT | 3-months | 6-months | 12-months | 24-months

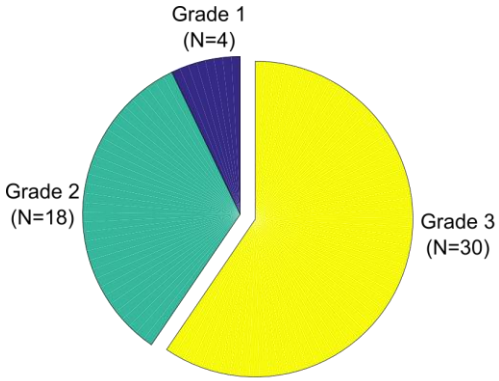
[1] Lopes Guerra et al, Int J Radiat Oncol Biol Phys 2012 83(4):e537-543

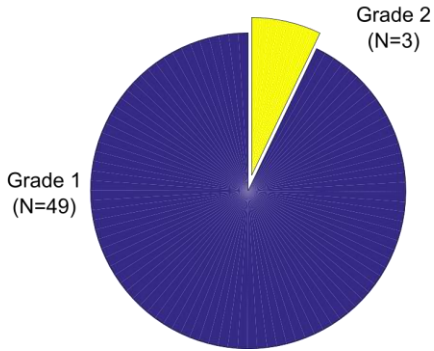
Lung toxicity is reported using RTOG/EORTC and CTCAE scoring systems

- Radiological component focused on subjective assessment of parenchymal change
- At 12-months parenchymal, volume reduction and pleural changes are common [2]
- Variability in reporting according to system used [3]
- Need for detailed and objective scoring systems



[2] Veiga et al, Radiother Oncol 2018 126(2):300-306
[3] Simone II, Semin Radiat Oncol 2017 27(4):370-377





RTOG/EORTC Late Radiation Morbidity Scoring Schema			
	Grade 1	Grade 2	Grade 3
Lung radiographic appearances	Slight	Patchy	Dense

Common Terminology Criteria for Adverse Events (CTCAE) v4.0				
	Grade 1	Grade 2	Grade 3	Grade 4
Radiographic pulmonary fibrosis volume	<25%	25 - 50%	>50 - 75%	>75% + severe honeycombing

[4] Veiga et al, ASTRO 2018 Annual Meeting

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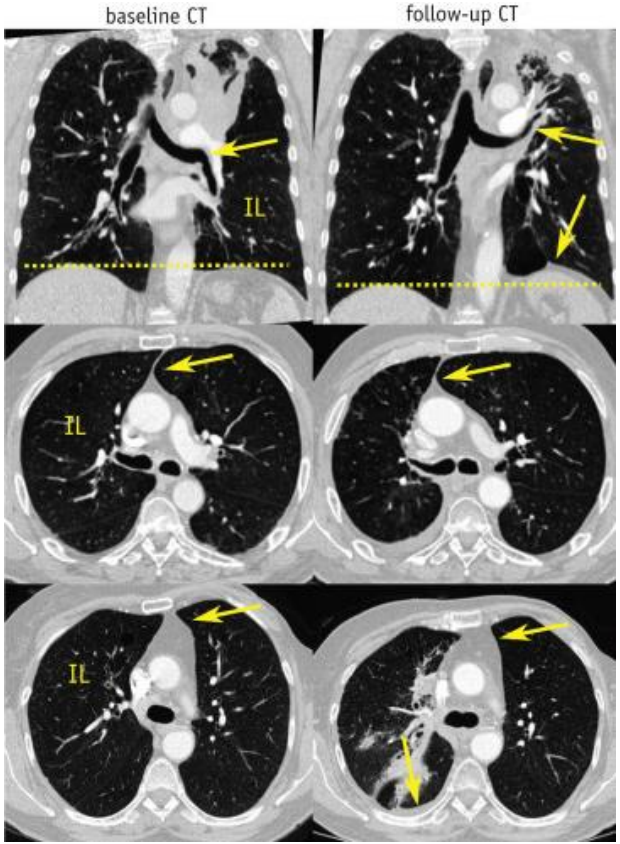

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[3] Simone II, Semin Radiat Oncol 2017 27(4):370-377

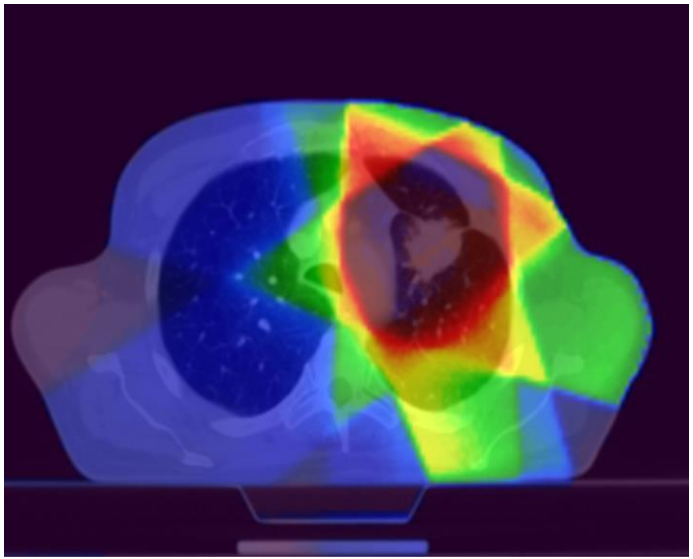
Research Questions

- What are the common radiological findings of RILD?
- Can we use serial CT imaging to quantify RILD?
- How does radiological RILD evolve post-RT?
- Can we link radiological RILD to dosimetry and clinical endpoints?

Data

IDEAL CRT trial cohort [5]

- Stage I/II multicenter trial of stage II-III non-small cell lung cancer (NSCLC)
- N = 120
- Isotoxic chemoradiation
- Most plans conventional (88%)
- 63-73Gy RT, 30 fractions, over 5 or 6 weeks
- Lung EQD2 mean dose of 18.2Gy
- OS = 36.9months (6-week protocol)
- CT images and clinical tests collected
  - 3, 6, 12 and 24-months post-RT

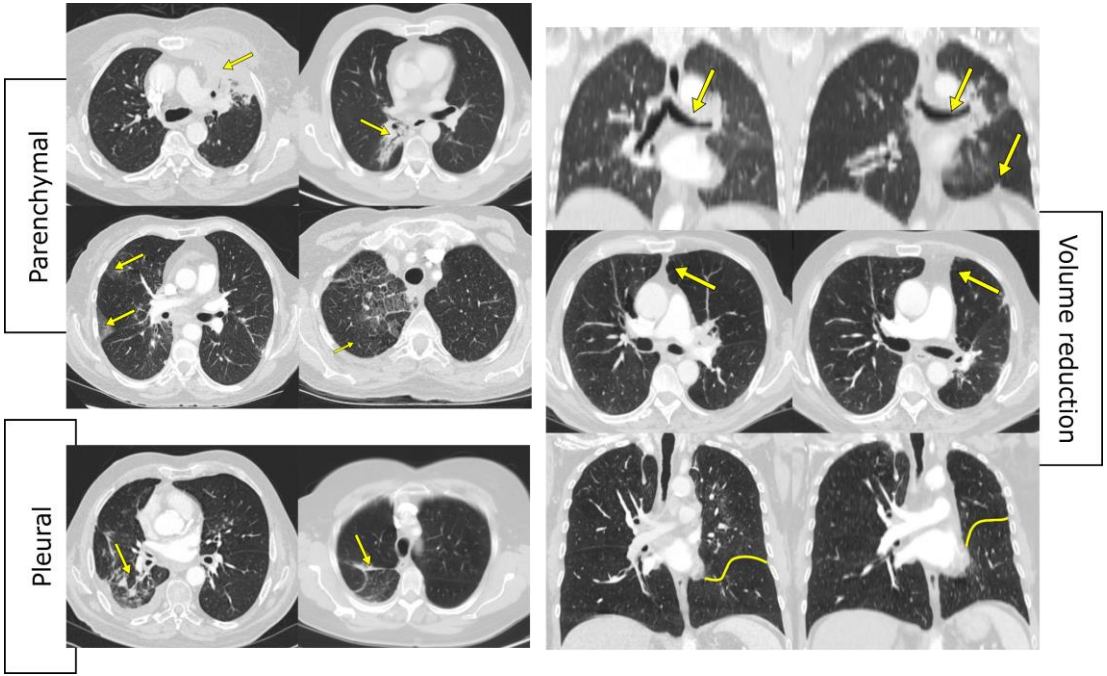


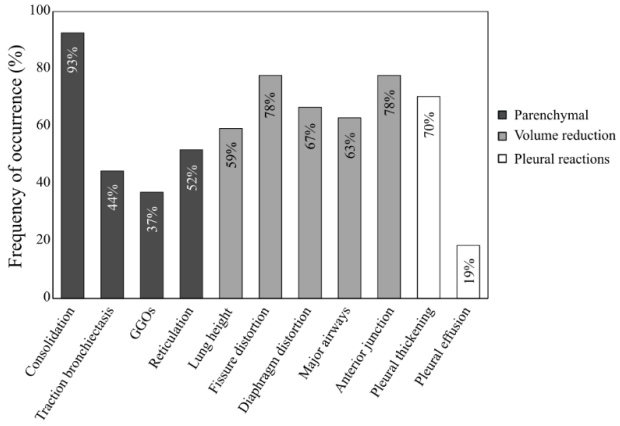
[5] Landau et al, Int J Radiat Oncol Biol Phys 2016 95(5):1367-1377

Radiological findings of RILD

N=33 CT scans pre-RT and 12-months post-RT reviewed by a multidisciplinary team

- ❑ Categorised findings into 3 main categories.
- ❑ Radiological change was present in all subjects (at least 2 out of 3 categories)



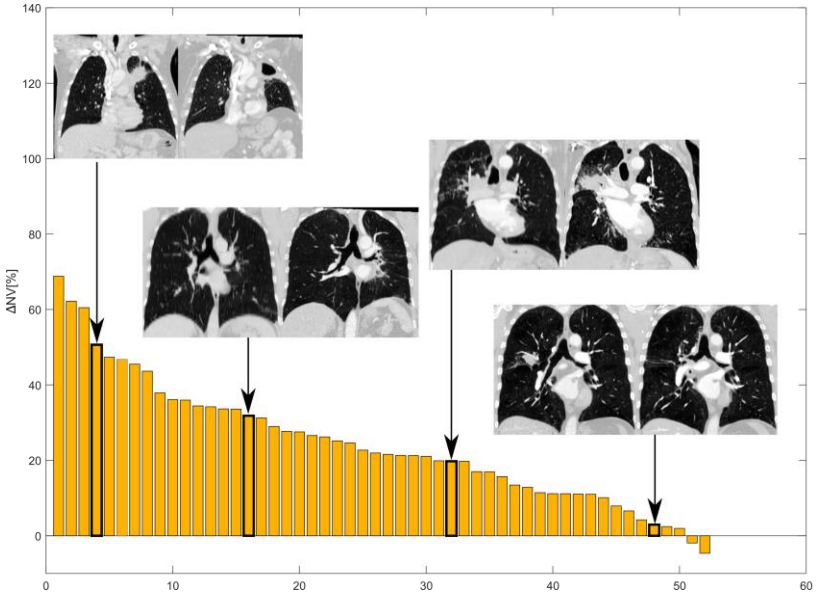


[2] Veiga et al, Radiother Oncol 2018 126(2):300-306

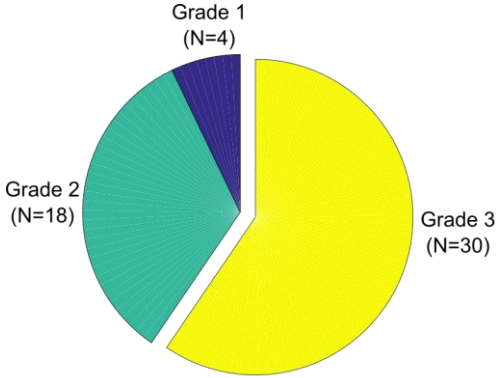
CT-based biomarkers of RILD

Developed a set of objective CT-based biomarkers to quantify RILD [5]

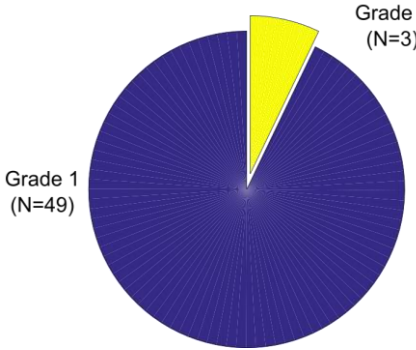
- Measures of parenchymal, volume reduction and pleural change
- Objective and continuous measures
- Interpretable (not abstract)
- But not easily quantifiable by human observers



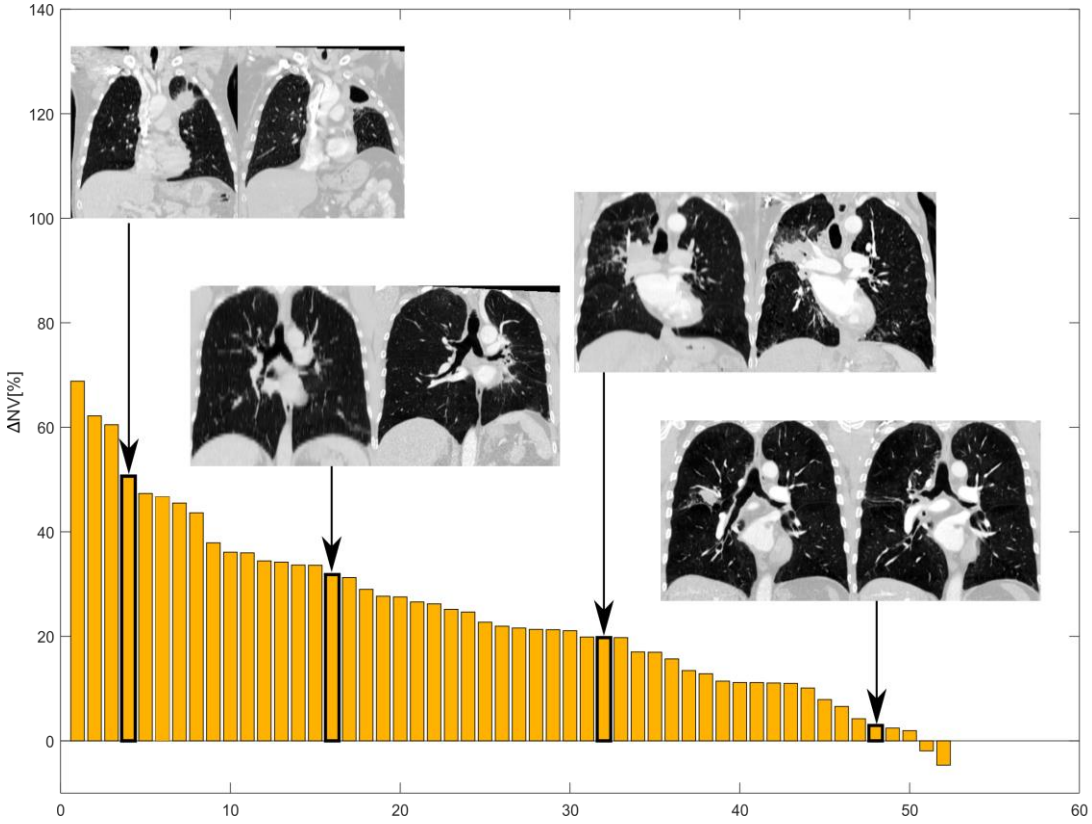
[4] Veiga et al, ASTRO 2018 Annual Meeting
[5] Veiga et al, Int J Radiat Oncol Biol Phys 2018 102(4):1287-1298



RTOG/EORTC



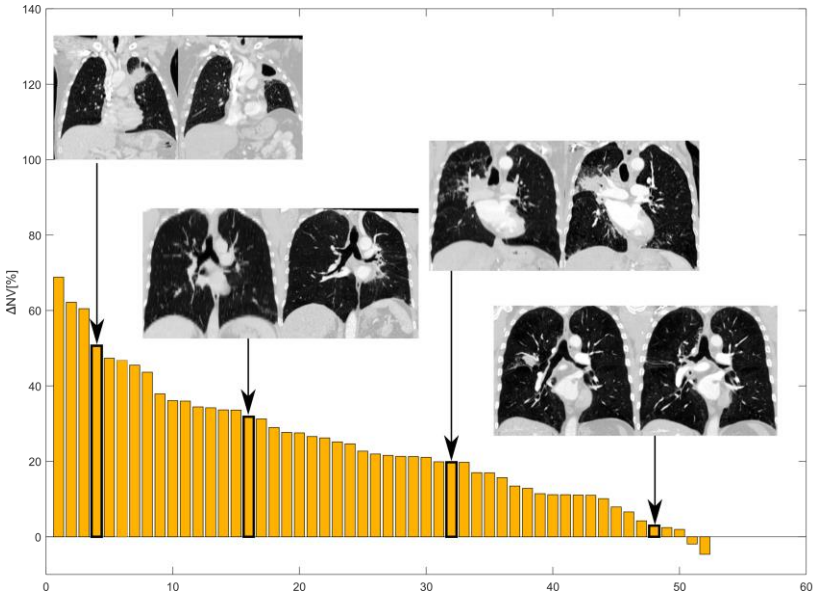
CTCAE



[4] Veiga et al, ASTRO 2018 Annual Meeting

Applications:

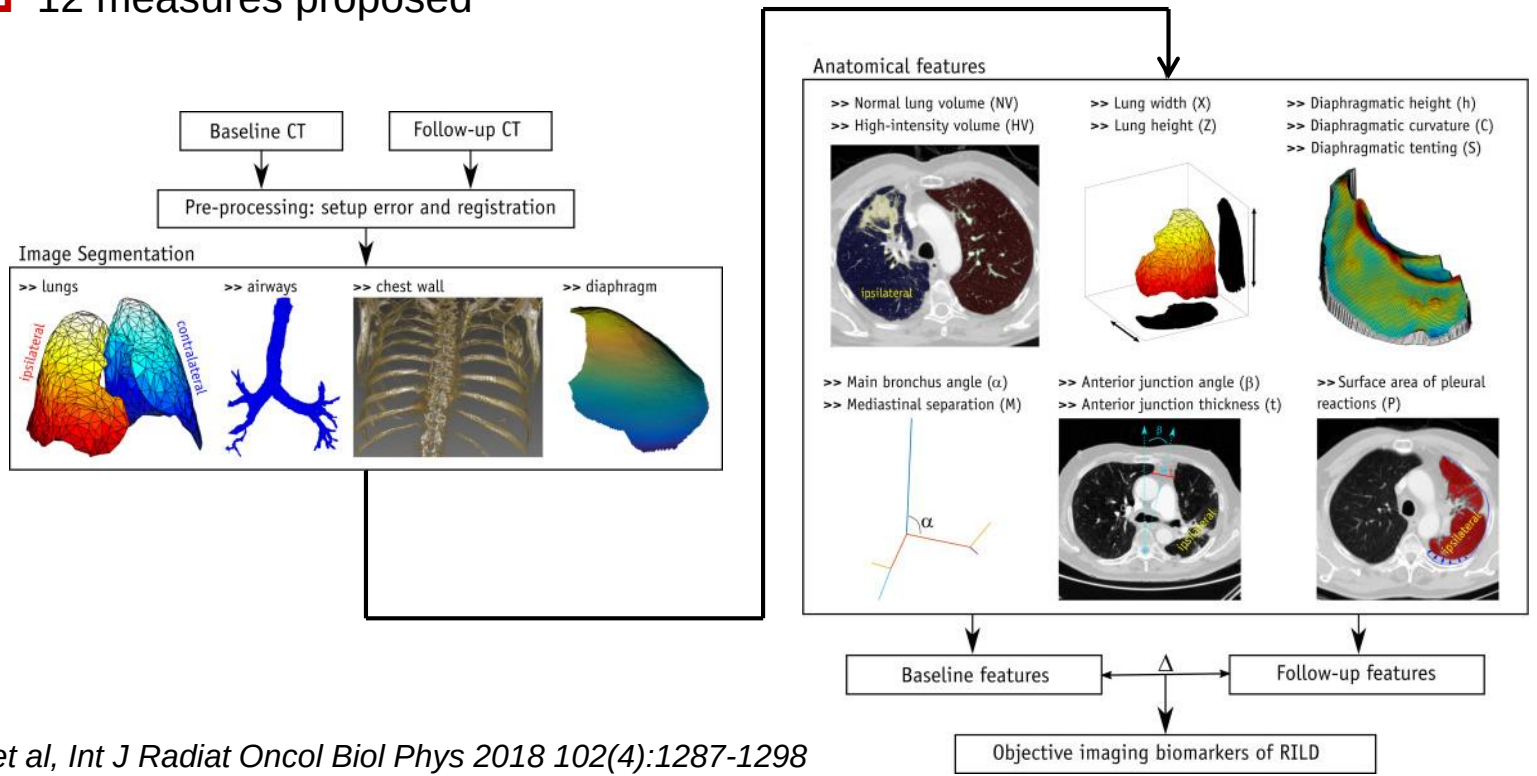
- Facilitate correlation with clinical end-points
- Development of objective scoring system of RILD
- Understanding how RILD appears and evolves following RT



[4] Veiga et al, ASTRO 2018 Annual Meeting

Implementation details

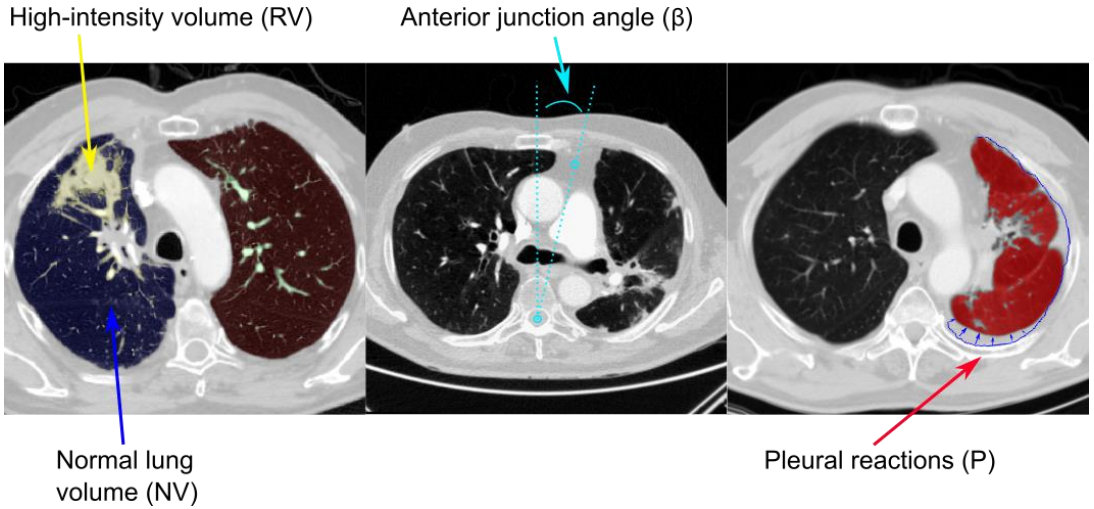
- Semi-automated pipelines implemented in MATLAB
- Segmentations visually assessed and edited if needed.
- 12 measures proposed



[5] Veiga et al, Int J Radiat Oncol Biol Phys 2018 102(4):1287-1298

Selected imaging biomarkers provide complementary information:

- Volume of consolidation (RV) → parenchymal change
- Pleural change (ΔP) → pleural effusion/thickening
- Normal lung volume shrinkage (ΔNV) → lung volume loss
- Anterior junction line rotation (Δβ) → anatomical distortions



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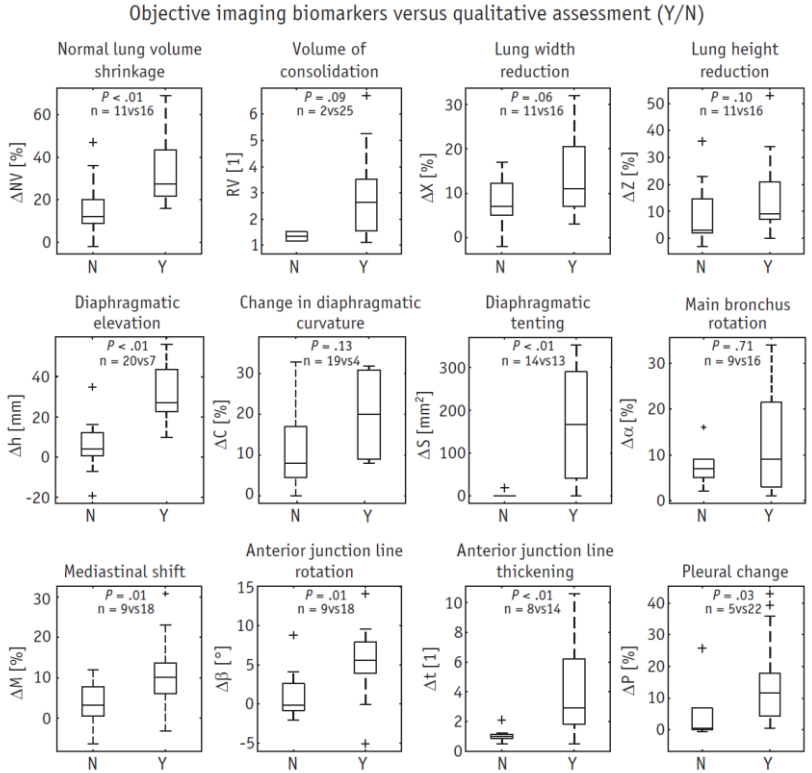
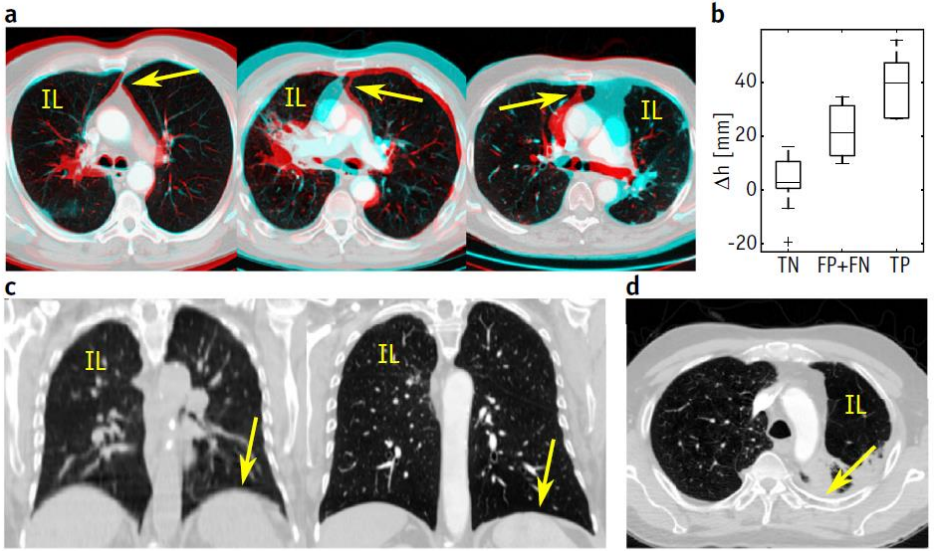
Evaluation

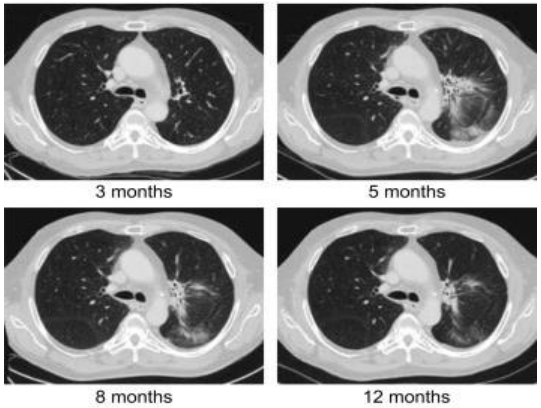
- Comparison with expert assessment
- Critical assessment: variability in scans acquisition and segmentations

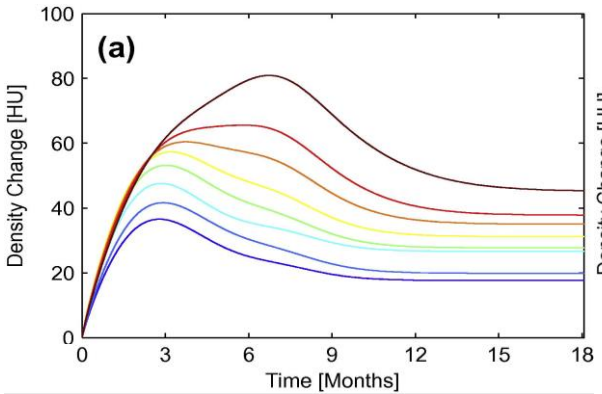


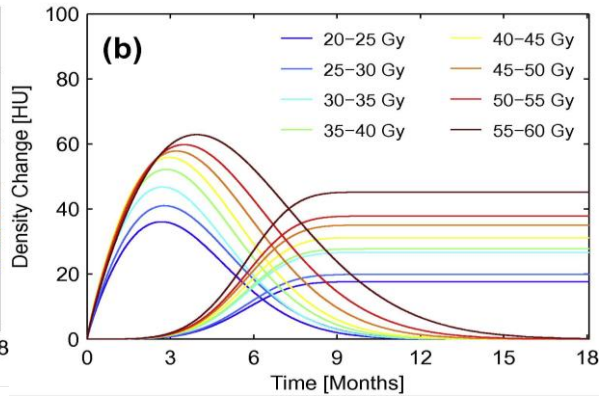


[5] Veiga et al, Int J Radiat Oncol Biol Phys 2018 102(4):1287-1298

Evolution of RILD on CT imaging and PFTs







RILD has a time/dose evolution [6, 7]

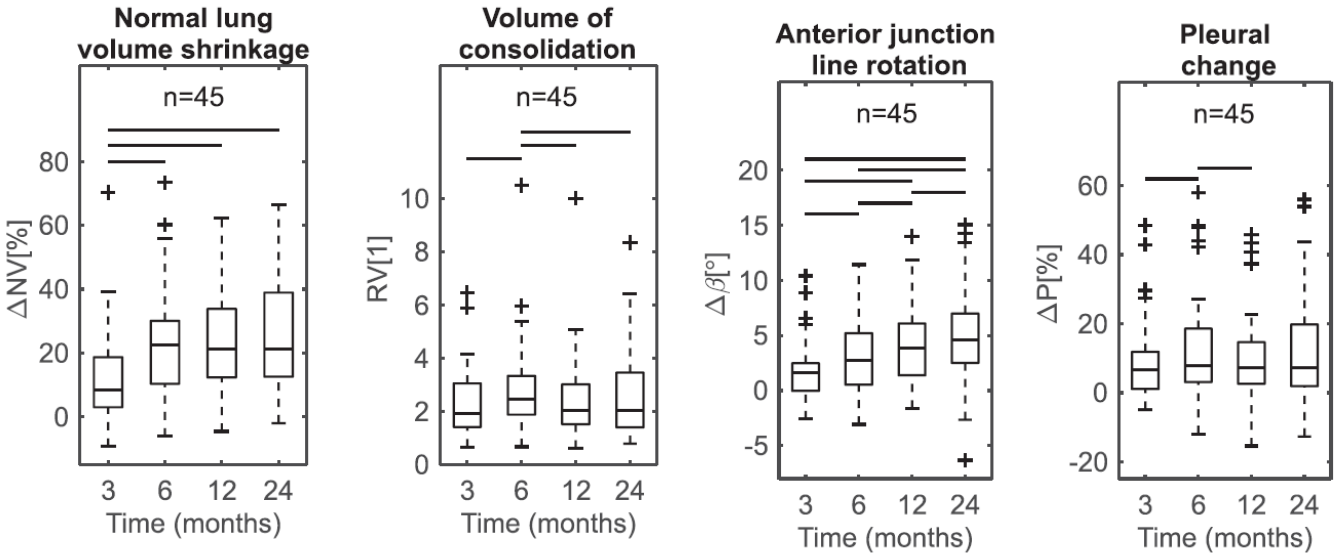
- Evolution of local CT density over time (parenchymal change)
- Fitted curves of the two-component model:
  - early transient component (skewed bell shape) – peaks 3-4months
  - late persistent component (sigmoid shape) – stabilize >12months

[6] Bernchou et al, Radiother Oncol 2013 109(1):89-94
[7] Veiga et al, Radiother Oncol 2020 148:89-96

N=45 subjects for which biomarkers were calculated at 3, 6, 12, and 24-months

Overall population findings:

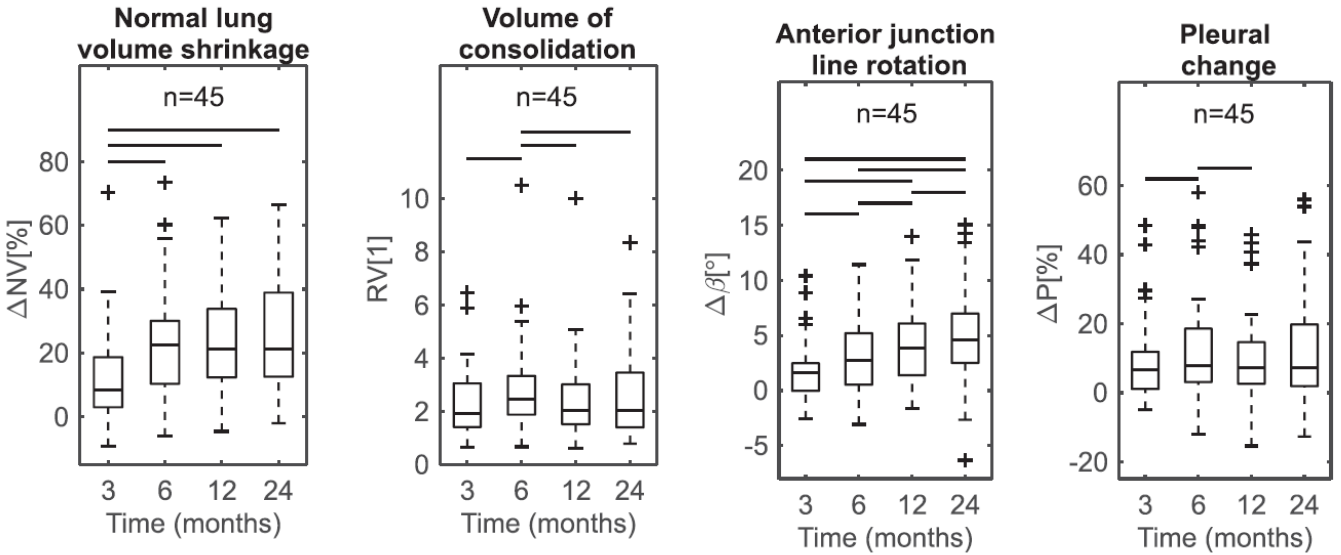
- Radiological findings have a temporal dependency
- Findings present from 3-months
- Largest variation occurring from 3 to 6-months



[7] Veiga et al, Radiother Oncol 2020 148:89-96

Overall population findings:

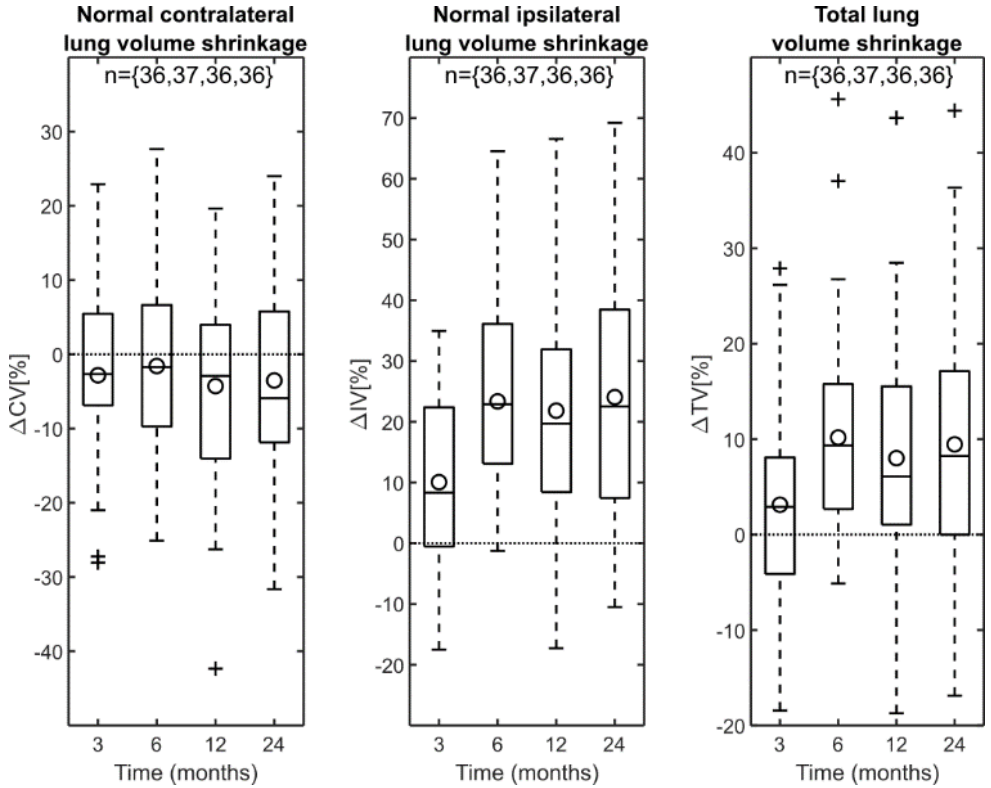
- ❑ Parenchymal change peaks at 6-months
- ❑ Lung volume and anatomical distortions progressively worsen up to 24-months
- ❑ Pleural change variable across the patient group



[7] Veiga et al, Radiother Oncol 2020 148:89-96

Overall population findings:

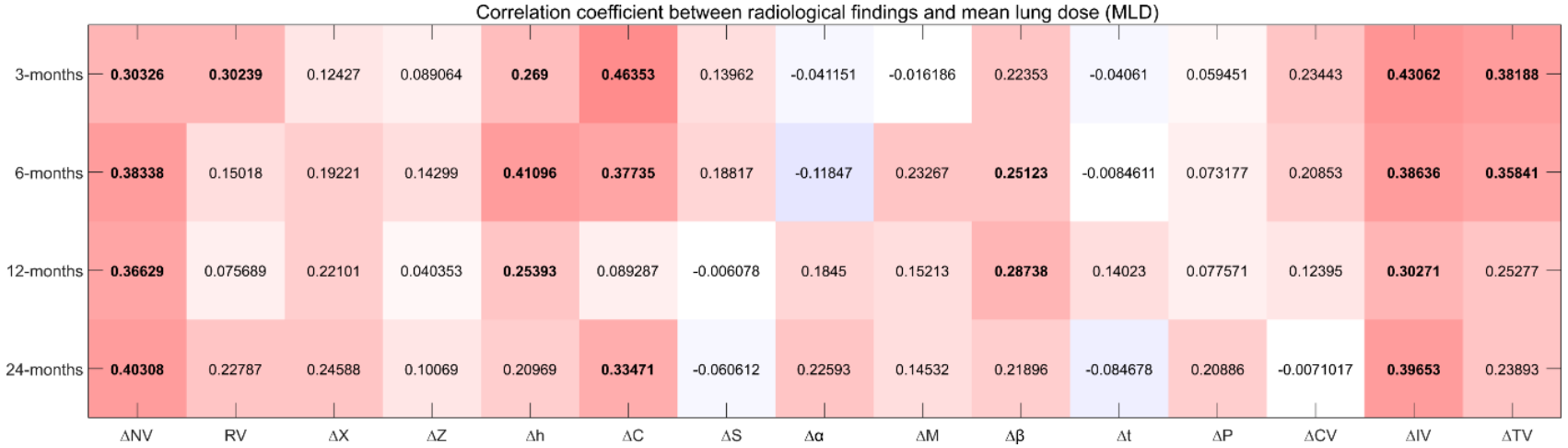
- Total lung volume loss with inflation of the contralateral lung

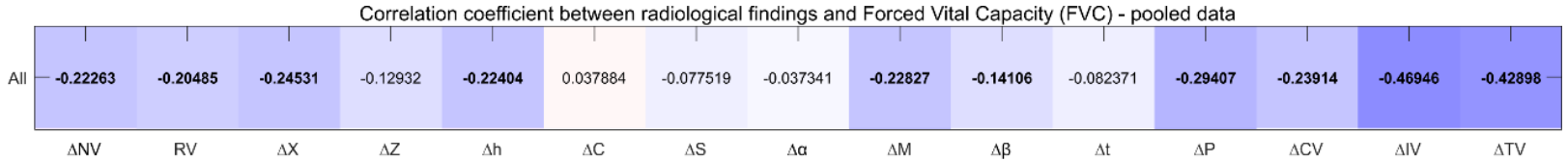


[7] Veiga et al, Radiother Oncol 2020 148:89-96

Overall findings:

- Correlation between radiological findings and dosimetry/pulmonary function tests
- Modest but significant correlations with lung volume loss



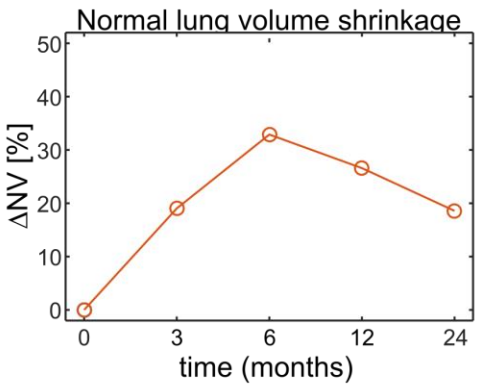


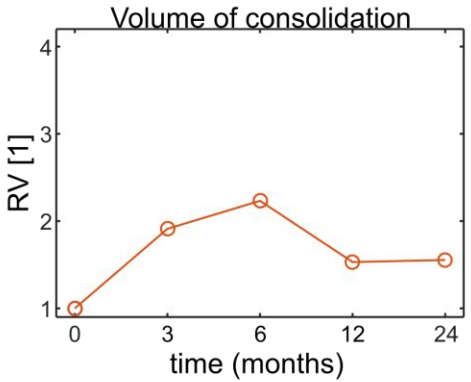
[7] Veiga et al, Radiother Oncol 2020 148:89-96

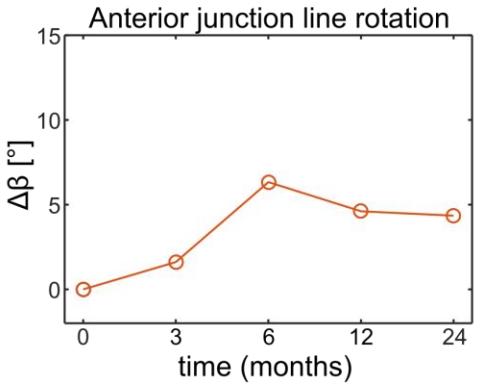
Considerable variation between patients: severity and temporal patterns

- Reversible parenchymal change without progressive anatomical distortions

BIOMARKERS

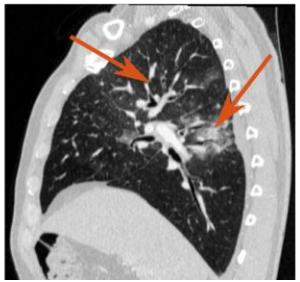




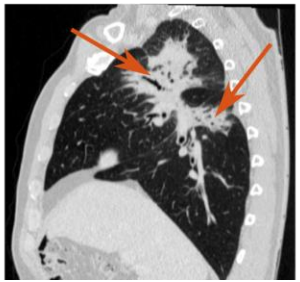


PRE-RT

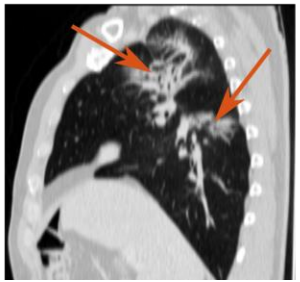
3-MONTHS



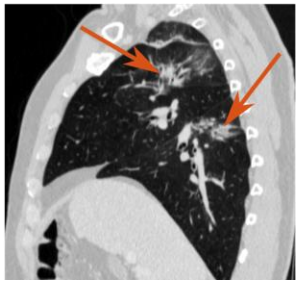
6-MONTHS



12-MONTHS



24-MONTHS



[7] Veiga et al, Radiother Oncol 2020 148:89-96

Considerable variation between patients: severity and temporal patterns

- Reversible parenchymal change with progressive anatomical distortions

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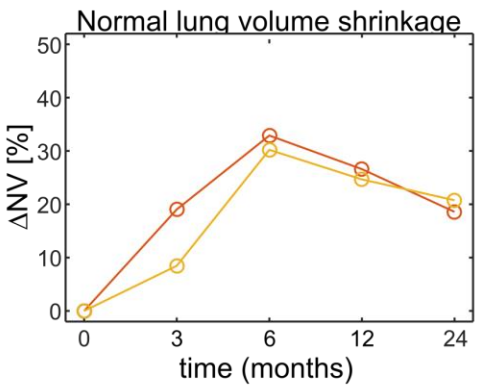

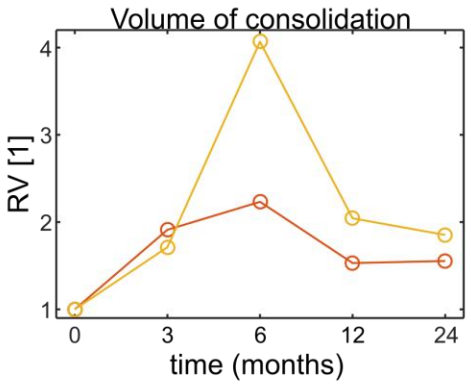

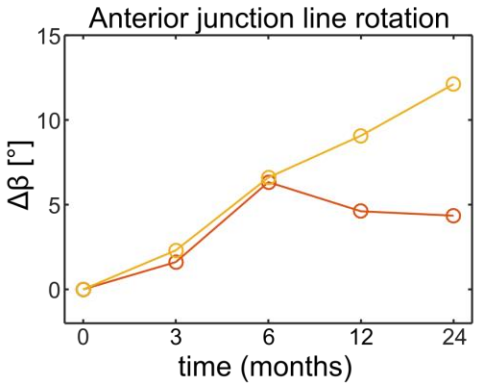

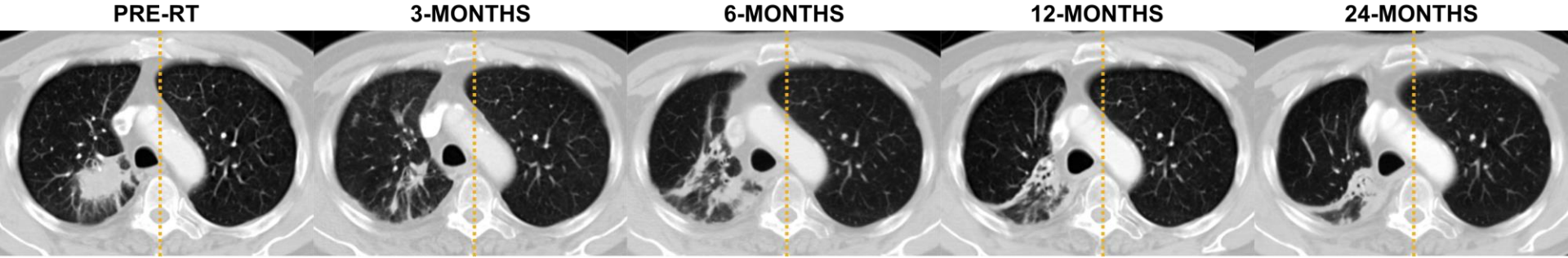

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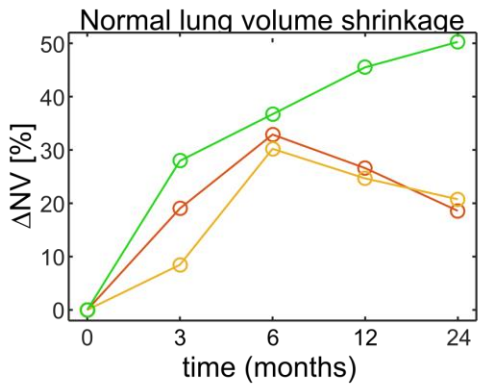
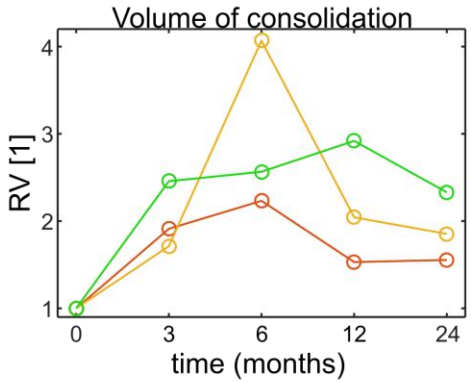
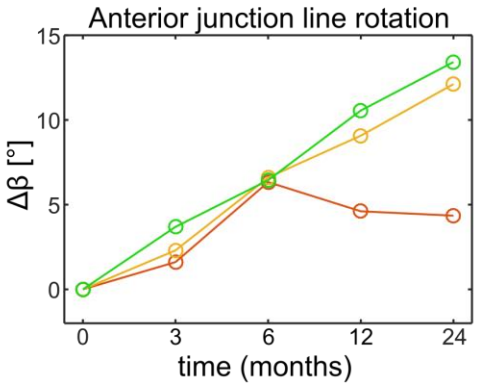


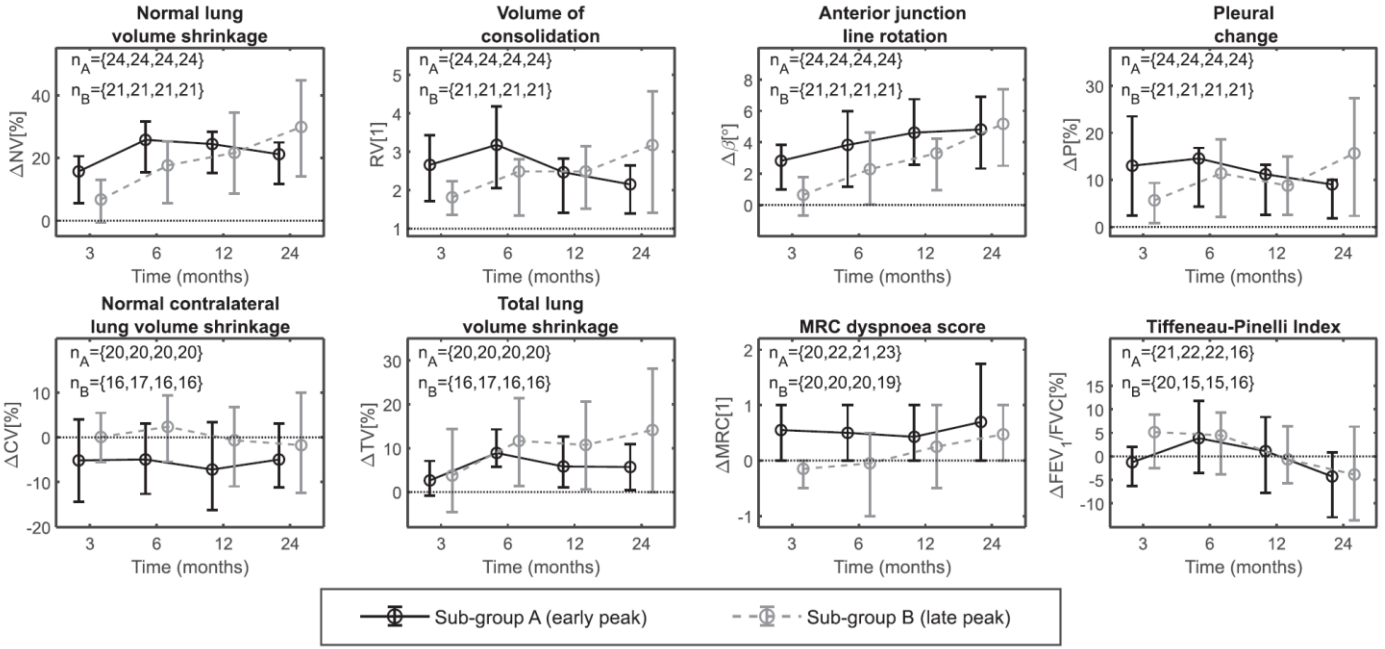




[7] Veiga et al, Radiother Oncol 2020 148:89-96

Identify two sub-groups based purely on radiological findings

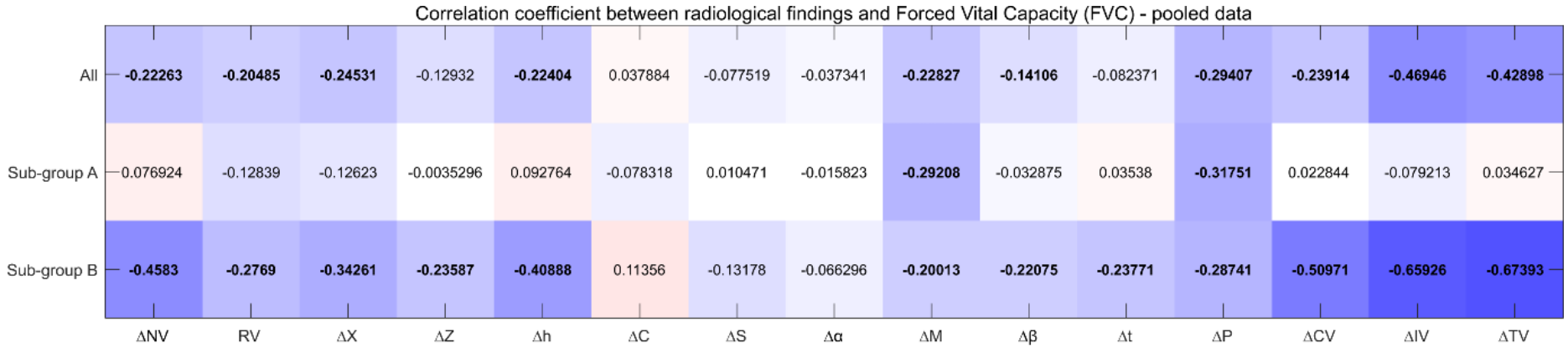
- The sub-grouping differentiated subjects with predominantly acute inflammatory reactions versus patients with mostly persistent fibrotic RILD
- Majority of subjects progressed to develop late RILD when imaging findings were absent or mild in the early phase



[7] Veiga et al, Radiother Oncol 2020 148:89-96

Identify two sub-groups based purely on radiological findings

- Differing functional patterns (PFTs) in the radiologically-stratified sub-groups
- Patients in the early change group had better pulmonary function pre-RT.



[7] Veiga et al, Radiother Oncol 2020 148:89-96

Discussion

Image-based biomarkers provide quantitative information on the evolution of RILD

- The evolution of RILD is not easily quantifiable by human observers
- Findings with high level of detail but interpretable

We can identify patterns of radiological evolution of RILD

- early acute inflammation phase (3-6 months), characterised by reversible parenchymal change
- chronic inflammation (6-24 months), characterised by irreversible scarring, progressive lung volume loss and anatomical distortions

Interpatient variability seems to indicate sub-groups for the evolution of RILD

- Subjects with better pre-RT PFTs had a more severe early phase

Limitations

Small number of subjects included

- Findings are exploratory and have to be validated in larger cohorts

Uncertainties in the biomarkers

- Caused by variation in inhalation level, segmentation, scanner acquisition parameters, resolution, patient positioning …

Confounding factors

- Patient-specific factors (e.g.: age, baseline pulmonary function, smoking history, …)
- Treatment-specific factors (e.g: RT modality, concurrent chemotherapy, …)
- Other pathologies with similar radiological patterns

Acknowledgments

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Natalie Yip
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Royal Academy of Engineering

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