

Fully Automated Volumetric Tumour Segmentation using Deep Learning AI

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PREDICT-Meso Aim and Key Questions



Aim

To build a large cohort of **Benign-MPM tissue pairs**, plus the technologies and infrastructure needed to

- Design effective MPM therapies
- Deliver future human trials, particularly in early stage disease or chemoprophylaxis

Key Questions

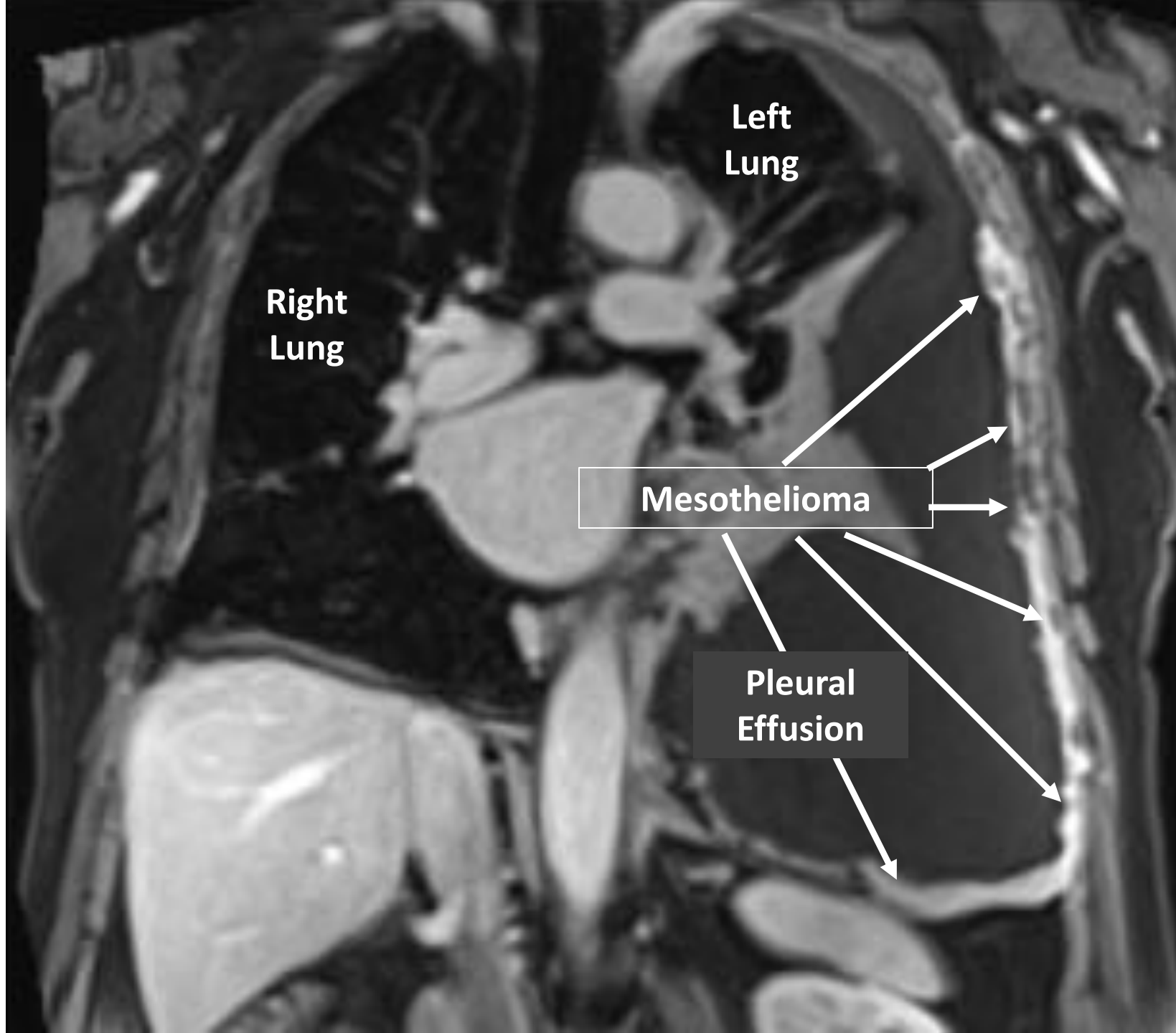
- How does asbestos-driven chronic inflammation evolve into MPM? What are the **key molecular events** and **vulnerabilities**?
- Can individuals destined to develop MPM be identified at a pre-malignant stage?
- **Can suitable treatment response tools be validated?**

Plan



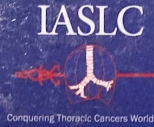
- Background: Why are new response tools needed?
- From modified RECIST to Volumetric Tumour Quantification
- Deployment of Volumetry on CT
- Development of Automated Volumetric Segmentation using the PRISM study cohort
- Next steps in Work Package 5

**Rind-like
morphology
makes response
assessment
difficult**



Tumour Size is not currently accounted for in Staging

8th Edition of the TNM Classification for Malignant Pleural Mesothelioma Proposed by the IASLC



T – Primary Tumour

T1	Tumour involving the ipsilateral parietal or visceral pleura only
T2	Tumour involving ipsilateral pleura (parietal or visceral pleura) with invasion involving at least one of the following: <ul style="list-style-type: none"> • diaphragmatic muscle • pulmonary parenchyma
T3 ¹	Tumour involving ipsilateral pleura (parietal or visceral pleura) with invasion involving at least one of the following: <ul style="list-style-type: none"> • endothoracic fascia • mediastinal fat • chest wall, with or without associated rib destruction (solitary, resectable) • pericardium (non-transmural invasion)
T4 ²	Tumour involving ipsilateral pleura (parietal or visceral pleura) with invasion involving at least one of the following: <ul style="list-style-type: none"> • chest wall, with or without associated rib destruction (diffuse or multifocal, unresectable) • peritoneum (via direct transdiaphragmatic extension) • contralateral pleura • mediastinal organs (oesophagus, trachea, heart, great vessels) • vertebra, neuroforamen, spinal cord or brachial plexus • pericardium (transmural invasion with or without a pericardial effusion)

N – Regional Lymph Nodes

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	Metastases to ipsilateral intrathoracic lymph nodes (includes ipsilateral bronchopulmonary, hilar, subcarinal, paratracheal, aortopulmonary, paraoesophageal, peridiaphragmatic, pericardial, intercostal and internal mammary nodes)
N2	Metastases to contralateral intrathoracic lymph nodes. Metastases to ipsilateral or contralateral supraclavicular lymph nodes

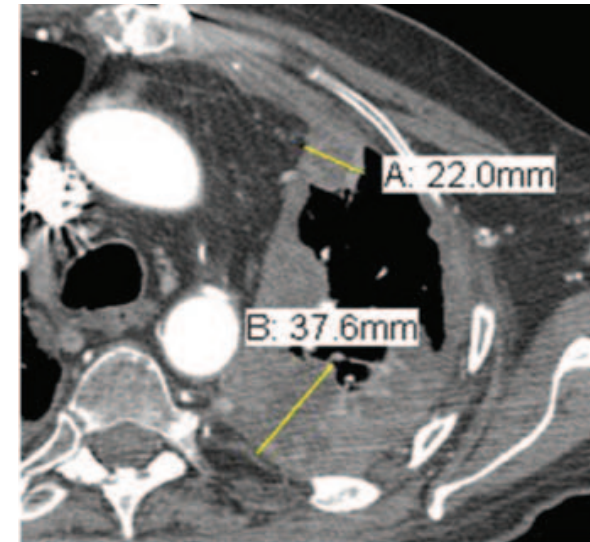
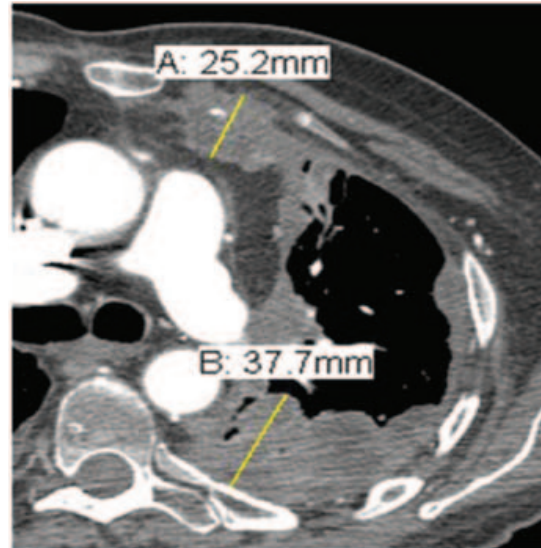
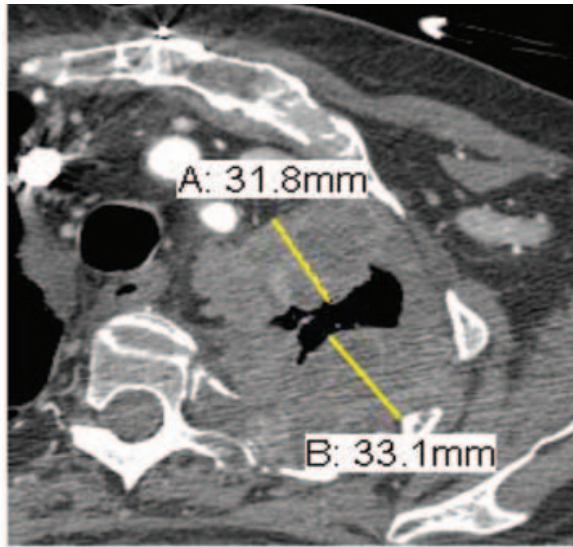
M – Distant Metastasis

M0	No distant metastasis
M1	Distant metastasis present

¹T3 describes locally advanced, but potentially resectable tumour.

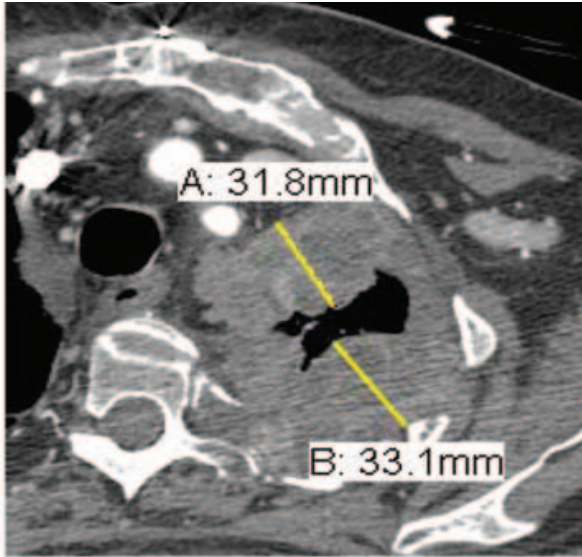
²T4 describes locally advanced, technically unresectable tumour.

How can we possibly assess response to therapy?

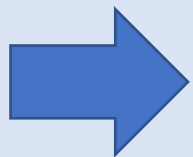


- Thickness associated with decreased OS and increased stage ¹
- **Modified RECIST:** Sum of 2 unidimensional measurements on 3 axial CT slices
- Compare summed values after treatment with baseline measures
- Partial Response (PR) and Progressive Disease (PD): -30% and +20% changes

Limitations of Modified RECIST



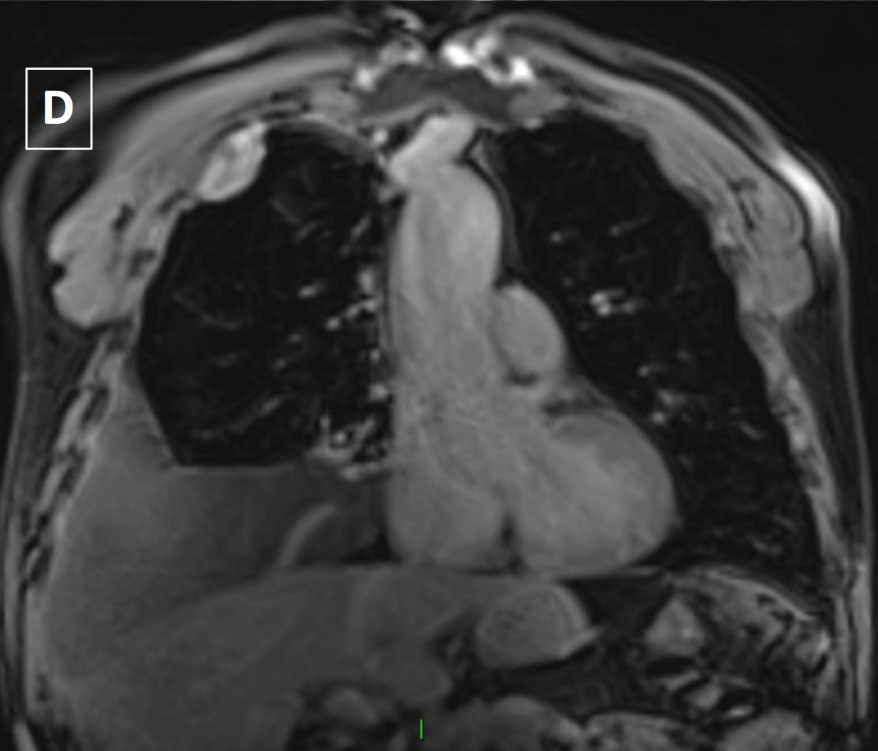
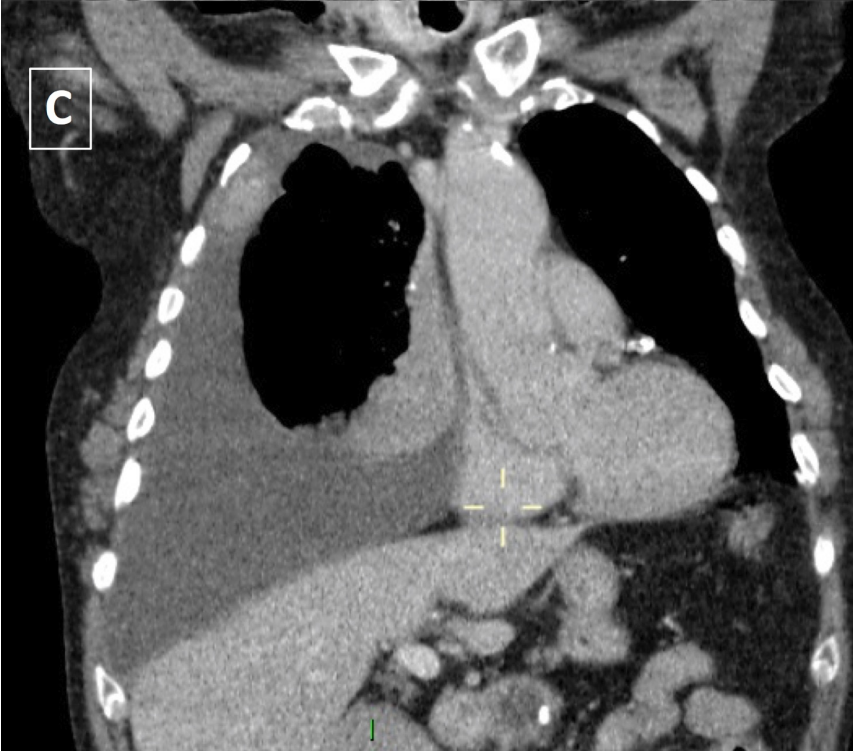
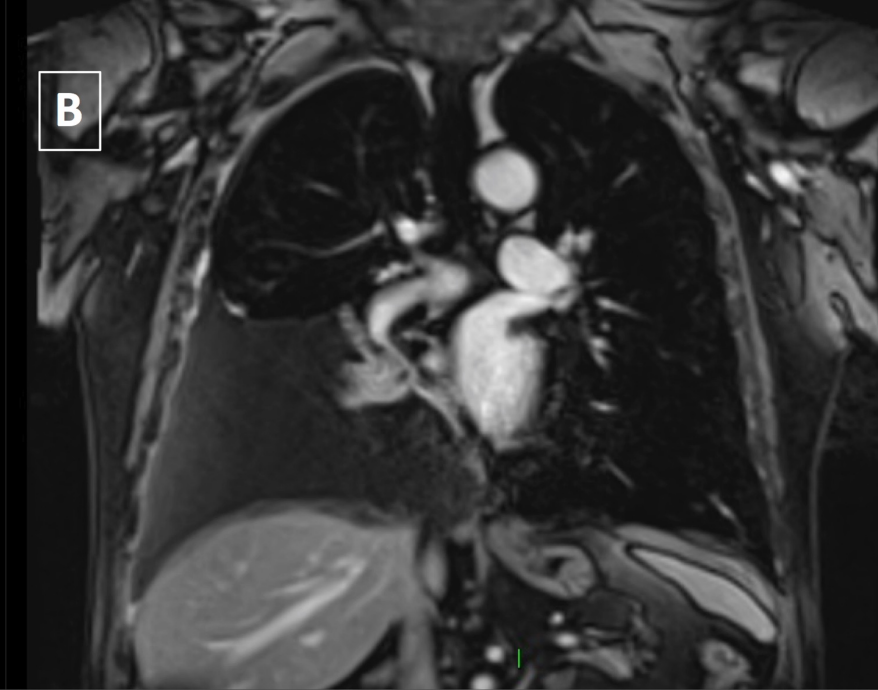
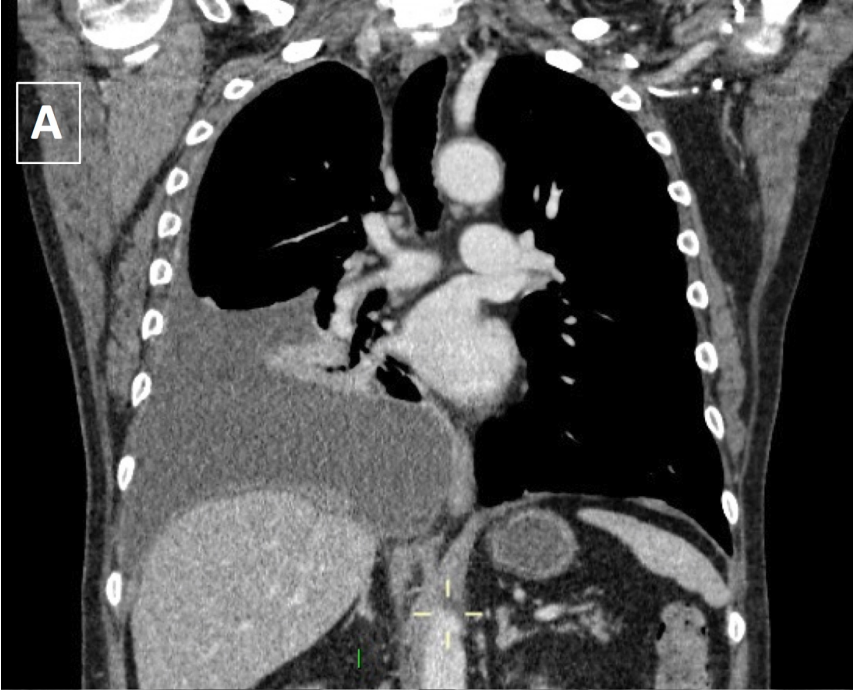
- Gross over-simplification of disease and response
- Radiologist required to replicate measurement sites
- Unsurprisingly, up to 30% variation between reporters ¹
- PFS correlates poorly with OS in Mesothelioma ²
- ‘Minimally measurable disease’ ³



- Misclassification risk mandates multiple reporters in trials, increasing costs and barriers to site delivery. Low volume excluded
- Strong case for improved response assessment, e.g. Volumetry

CT

- Widely Available
- Cheaper
- Familiar to Radiologists
- Embedded in Clinical Care and Trials



MRI

- Limited Availability
- More expensive
- Unfamiliar to some

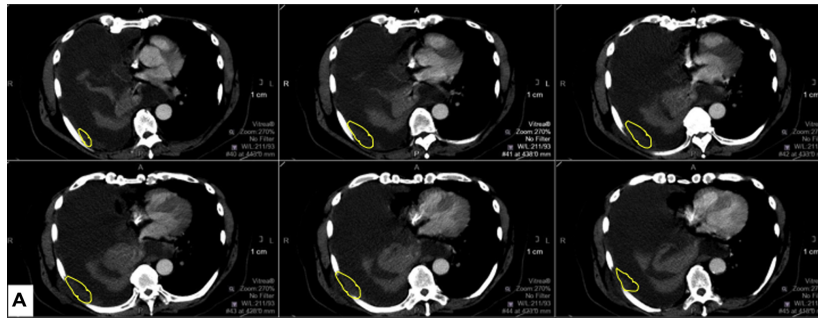
BUT

- ✓ Superior soft tissue contrast
- ✓ More sensitive to T3 and T4
- ✓ Established adjunctive staging tool

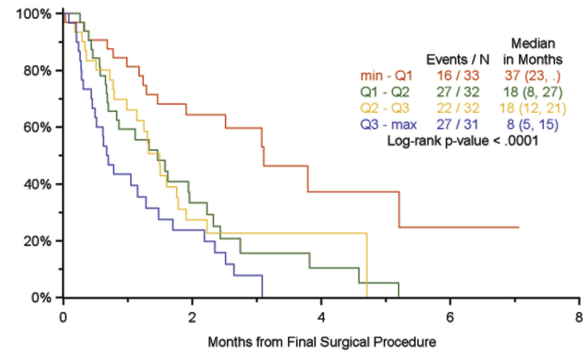
Volumetric Tumour Quantification



CT Volumetry *Gill et al, Ann Thor Surg 2016*

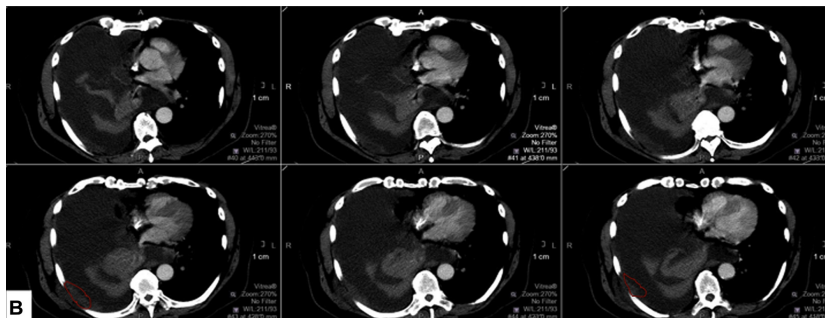


583
cm³



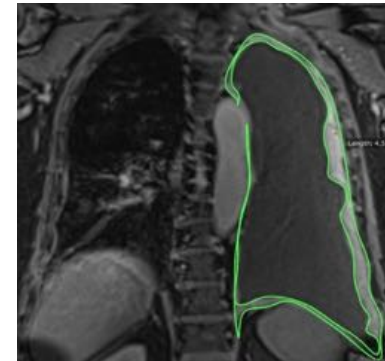
Volume Tertiles ⁴

- 91 cm³
- 245 cm³
- 513 cm³

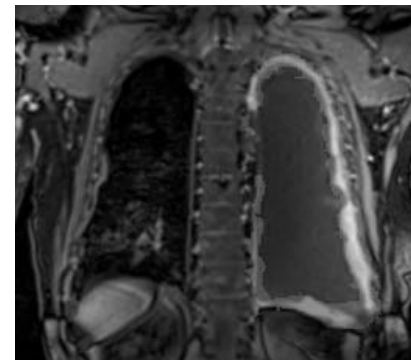


267
cm³

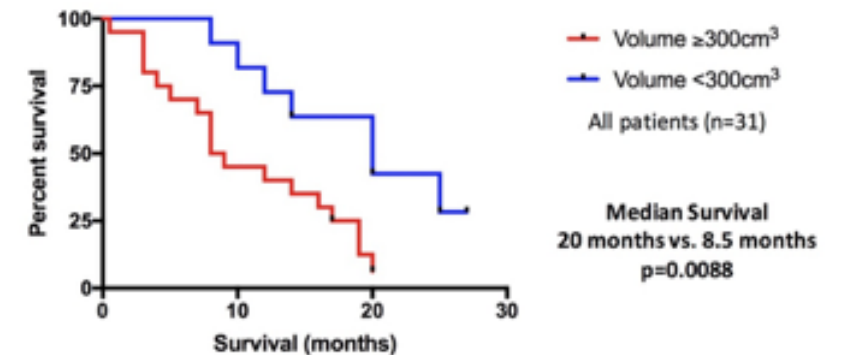
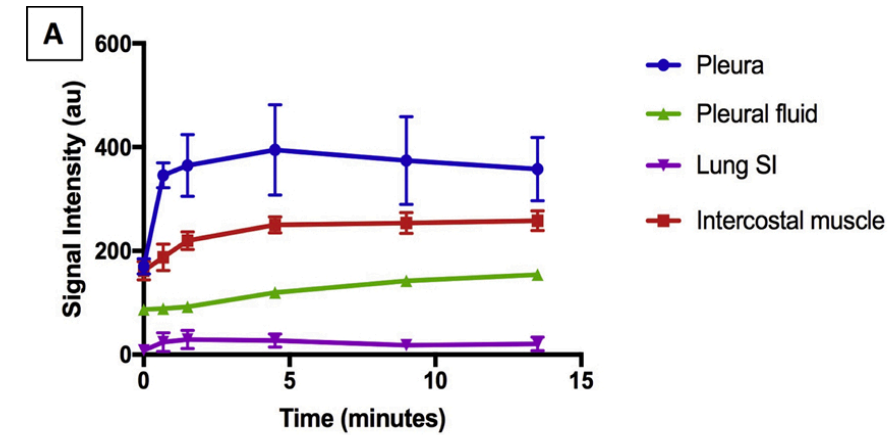
MRI Volumetry *Tsim et al, Lung Cancer 2020*



Manual tumour contouring
(one every 8-10 slices)



Perfusion Tuned Tumour
Segmentation



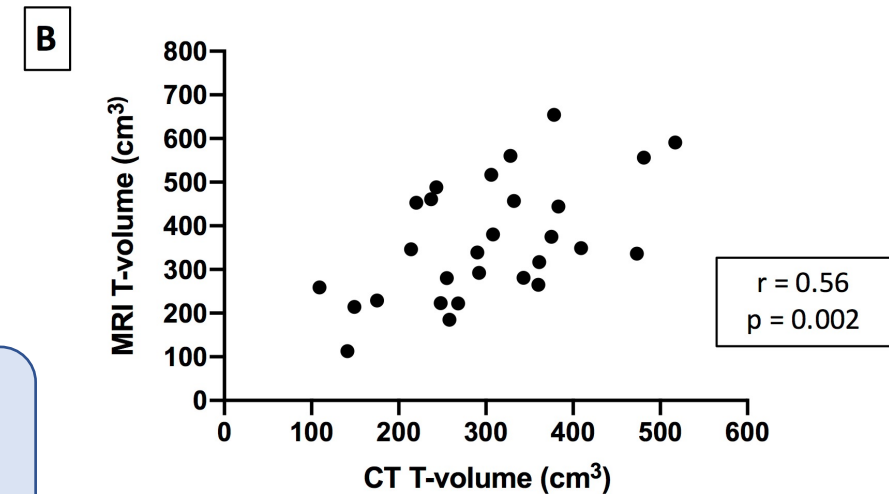
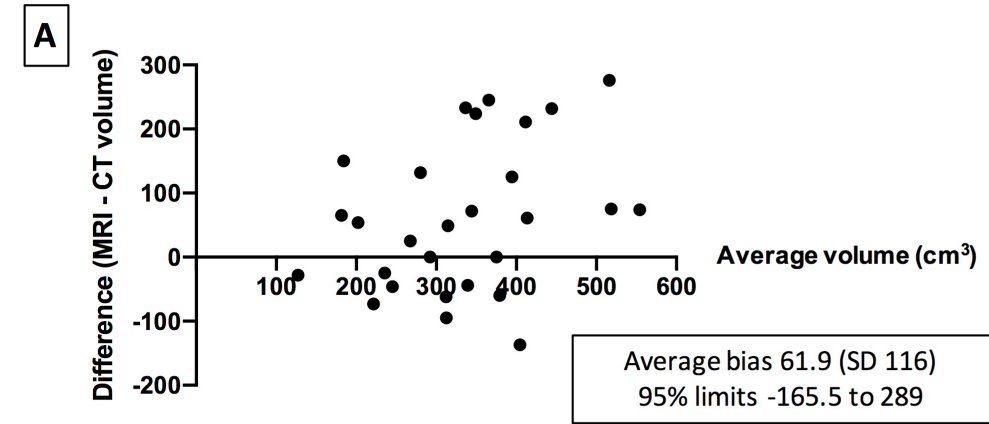
Comparison between CT and MRI Volumetry



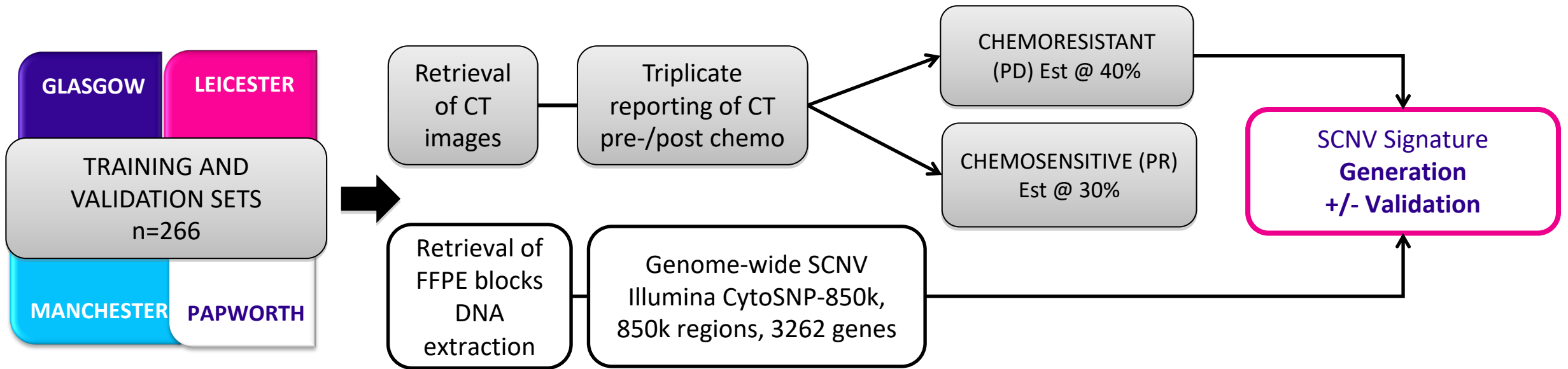
- 31 patients with Mesothelioma
- CT and MRI at first presentation
- Median interval: 19 days

- MRI and CT volumes correlate but do not agree
- MRI more strongly associated with survival
- MRI could be semi-automated (14 mins)
- CT had to be fully manual (2.5h, 225 slices/case)

- ➔ MRI probably better volumetric tool in longer term
- Enhanced post-processing for CT in the short term ?



PRiSM: Prediction of Resistance to chemotherapy using Somatic Copy Number Variation in Mesothelioma



STUDY OBJECTIVES

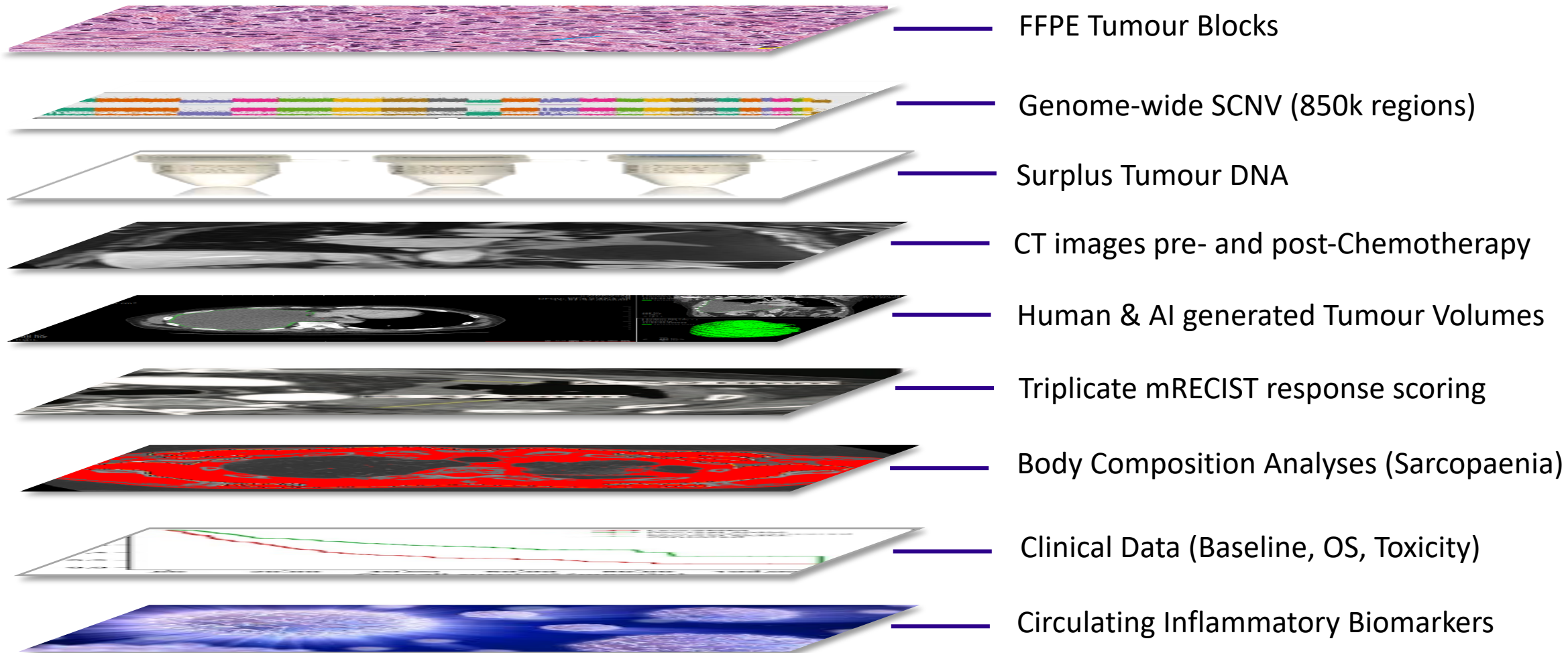
1. To define a predictor-classifier of chemoresistance (defined as Progressive Disease (PD) on triplicate assessment by mRECIST on CT) based on Somatic Copy Number Variation (SCNV)
2. To validate any SCNV predictor in an independent cohort



AI Volumetry Development using multi-layered PRiSM Dataset



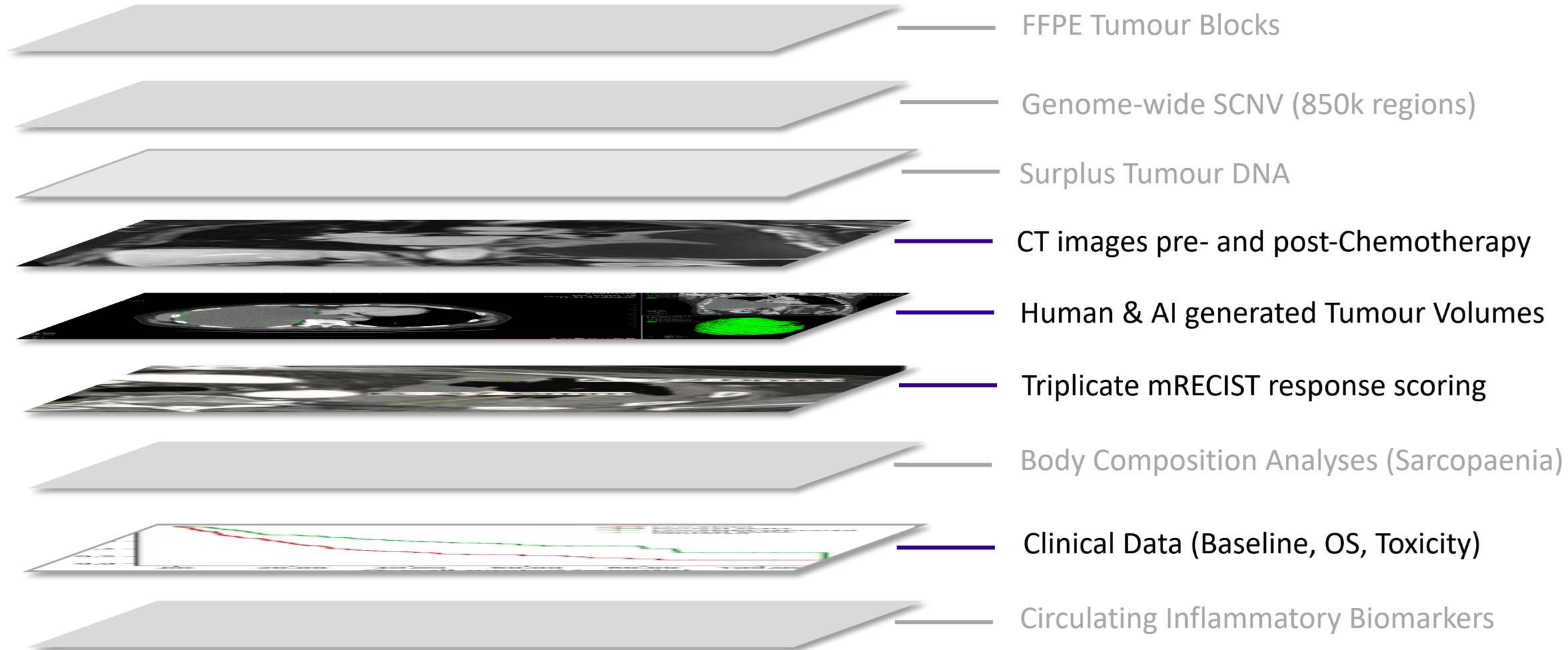
n=266



AI Volumetry Development using multi-layered PRiSM Dataset



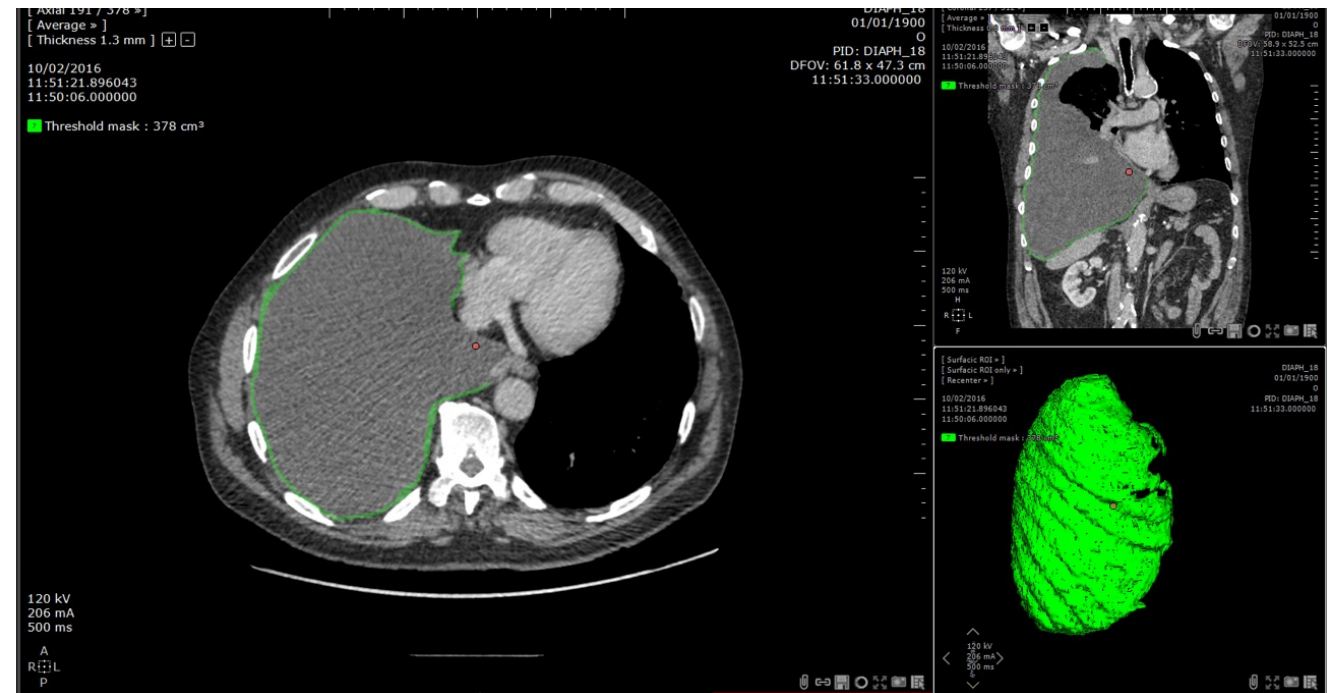
n=266



AI Volumetry: Design and Funding



- 183 CT datasets
- Training and Internal Validation (n=123)
- Blinded External Validation (n=60)
- High quality ground truth based on manual human tumour annotation
 - 2.5 hours/scan, 225 slices/scan
- Convolutional Neural Network with a two-dimensional U-Net architecture

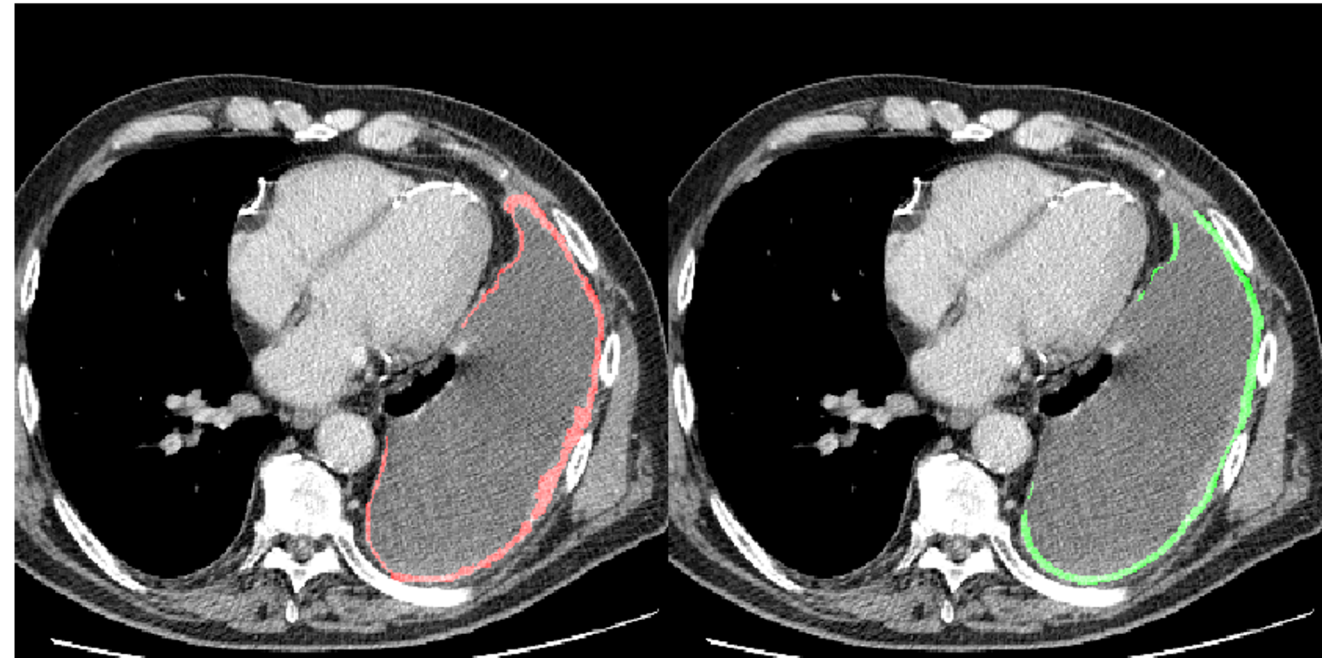
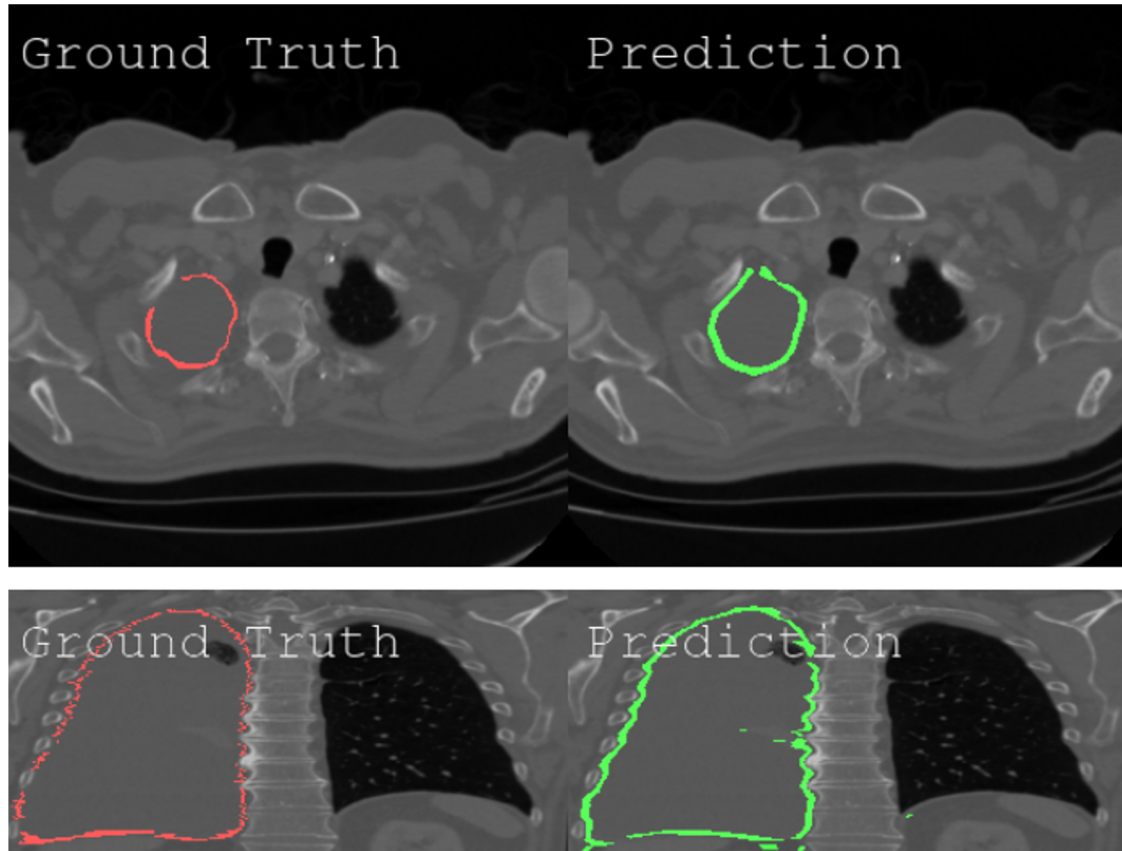


Phase 1: £35,000

Phase 2 : £140,000

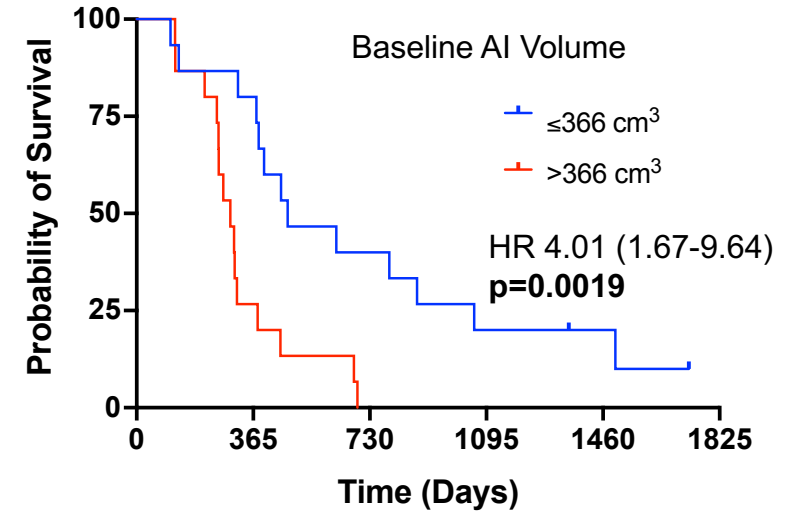
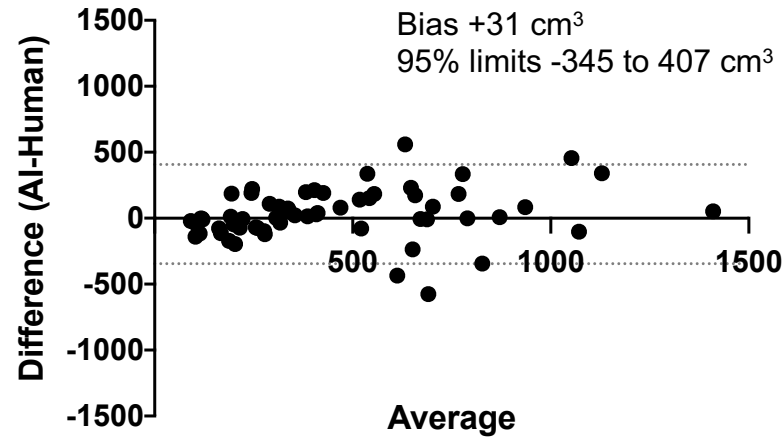
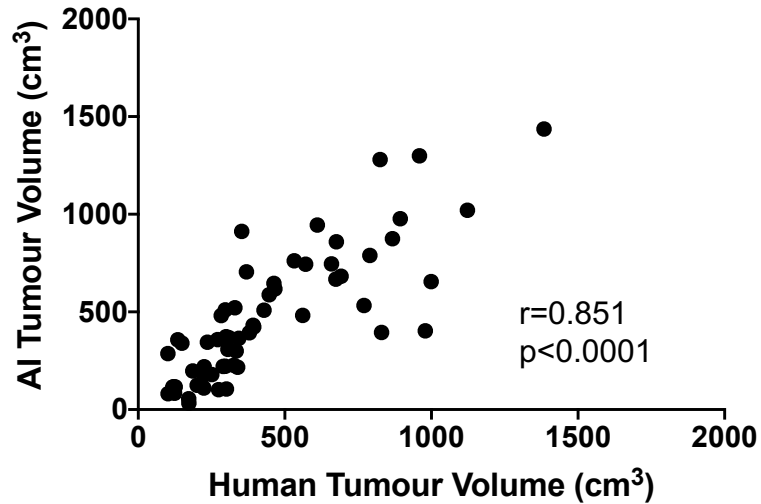


Human Ground Truth v AI Segmentation: Internal Validation Set (n=123)

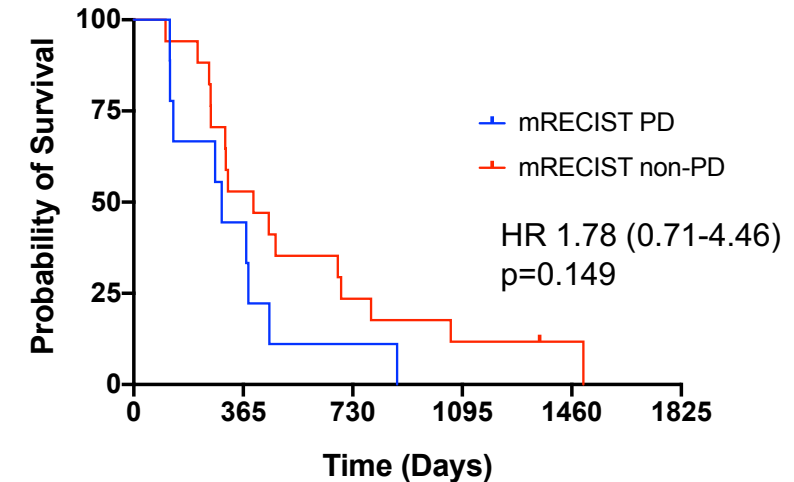


— Human
— AI

AI Performance in External Validation Set (n=60)

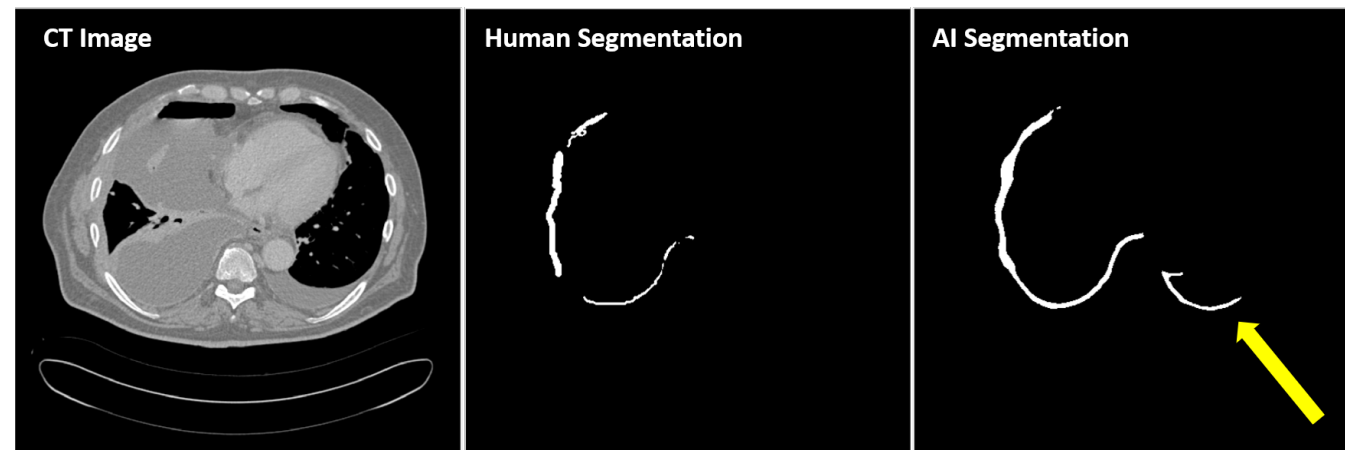
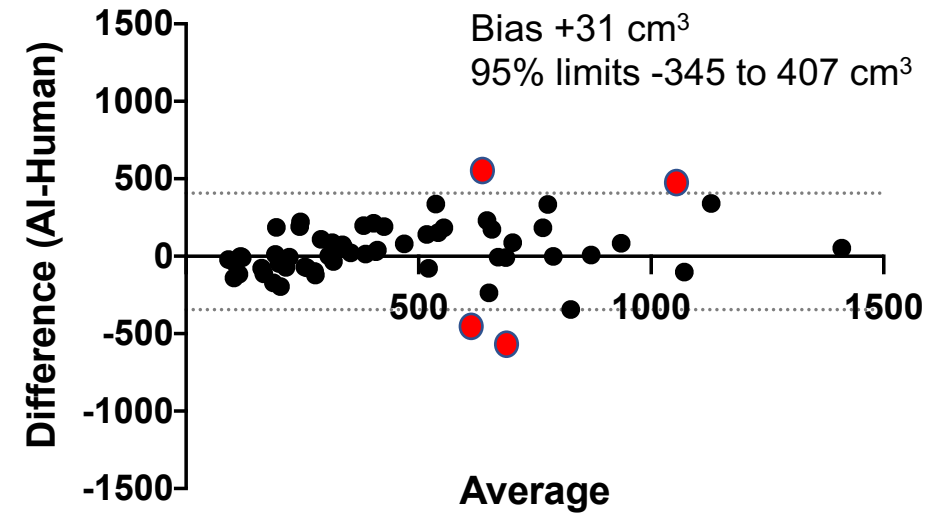
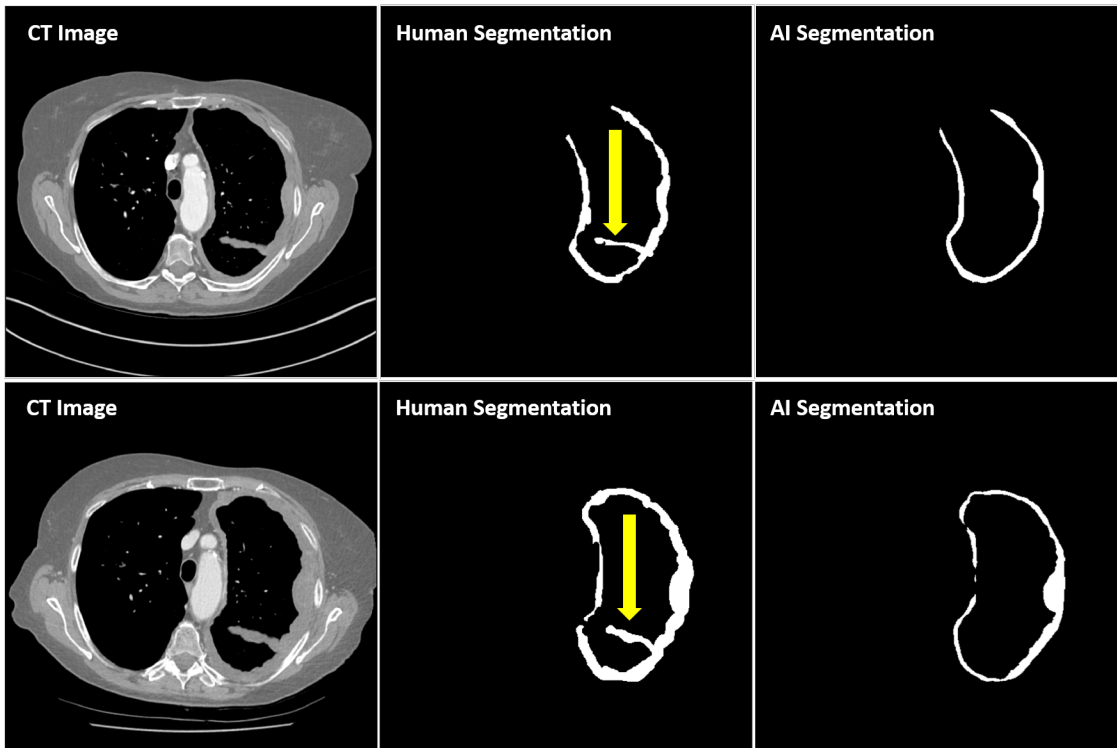


- Human inter-observer ICC 0.732 (Moderate)
- AI intra-observer ICC = 1.0 (Perfect)



Next Steps: Minimising AI Segmentation Errors

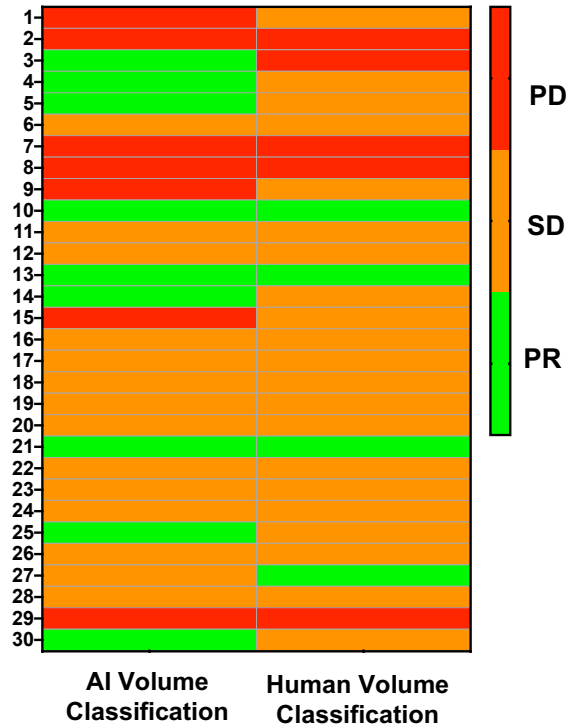
- AI significantly over- or under-segmented disease in 4/60 external validation cases (6.7%)
- Associated with infrequent anatomical features



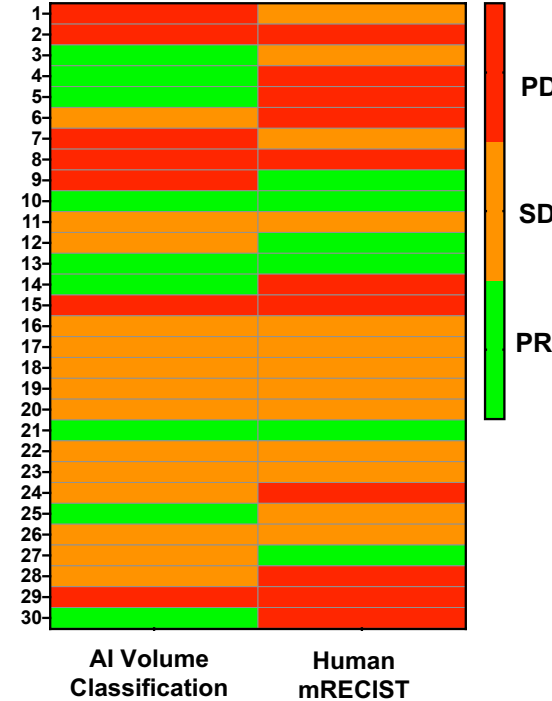
Next Steps: Calibration of Volumetric Response Thresholds also Essential



- AI v Human volumetric response
- Agreement in 20/30 (67%)
- kappa = 0.439 (0.178-0.700)



		AI Volume		
		PR	SD	PD
Human Volume	PR	3	5	1
	SD	1	13	0
	PD	0	3	4



		AI Volume		
		PR	SD	PD
Human mRECIST	PR	3	2	1
	SD	2	9	2
	PD	4	3	4

- AI volumetric v Human mRECIST response
- Agreement in 16/30 (55%)
- kappa = 0.284 (0.026-0.543)

mRECIST Thresholds:
 PR: -30% PD: +20% Uni-D
 AI Volume Thresholds:
 PR: -30% PD: +20% Volume

Conclusion



- First fully automated tool for volumetric segmentation of Mesothelioma
- First study to report an AI imaging output that predicts Survival
- Largest volumetry study in Meso, but small in context of Deep Learning AI
- Manuscript under review
- Further optimisation essential in a larger dataset
- CT scans from 1000 patients (at least 2000 scans) will be used in WP5.2, working with NCIMI and Canon
- AI PDRA post advertised. Clinical PhD involved in Ground Truth: Aug 2021

Partners



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