Pulmonary Vascular Properties in a Human Model of Acute Lung Injury Measured using DCE-MRI

Dr Tanuj Puri

Newcastle Magnetic Resonance Centre

Newcastle University

NHS National Institute for Health Research

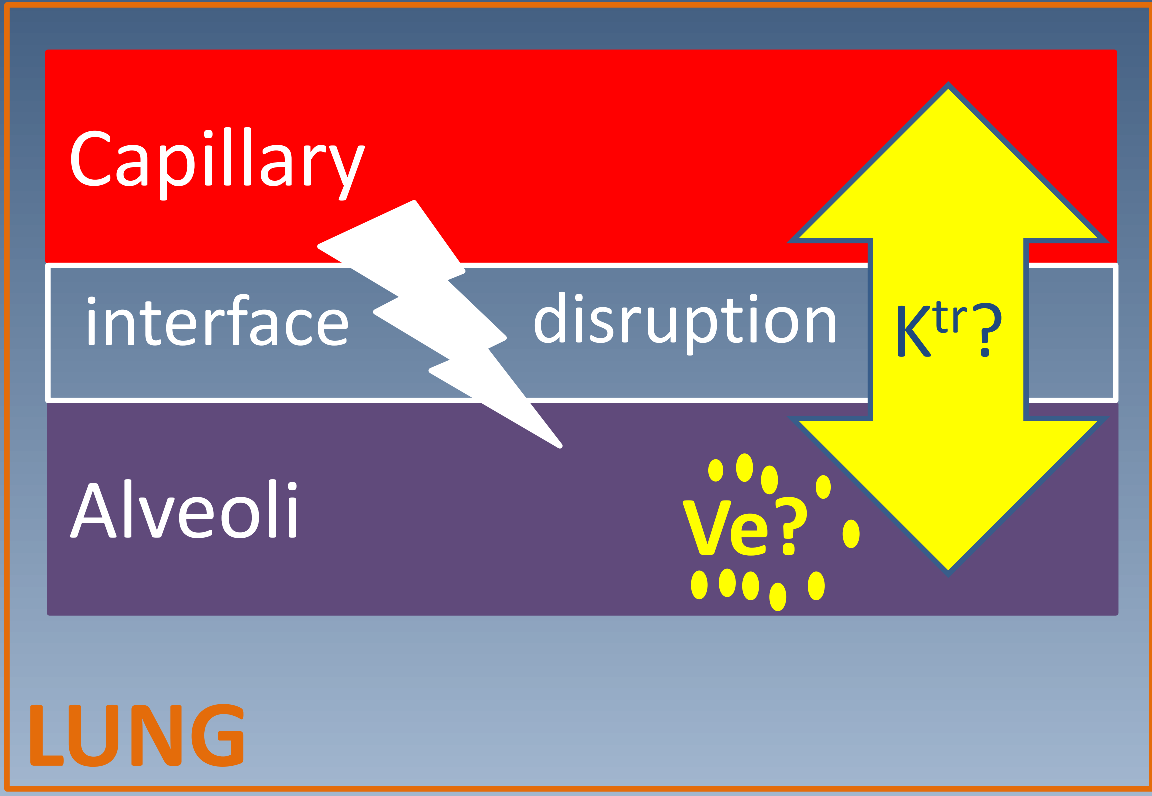
Introduction

ICU → 10% → ALI , ARDS → 43% Mortality

[1] Rubenfed et al. N Engl J, 2005
[2] Brun-Buisson et al. Intensive Care Med, 2004
[3] Zambon & Vincent. Chest, 2008

Introduction

Acute Lung Injury (ALI)



[1] Rubenfed et al. N Engl J, 2005
[2] Brun-Buisson et al. Intensive Care Med, 2004
[3] Zambon & Vincent. Chest, 2008

Introduction

- **Lipopolysaccharide (LPS)**
  - human model of ALI
  - induces pulmonary immune response (increased K^{tr}/Ve?)
  - to investigate processes underlying ALI
  - to develop treatment strategies

- **Invasive techniques**
  - Bronchoscopy, FDG-PET

- **Need for non-invasive imaging biomarkers**
  - DCE-MRI: K^{tr} ? , Ve ?

- **AIM:** to measure changes in lung vascular properties (K^{tr}, Ve) due to LPS-inhalation using DCE-MRI

Study design

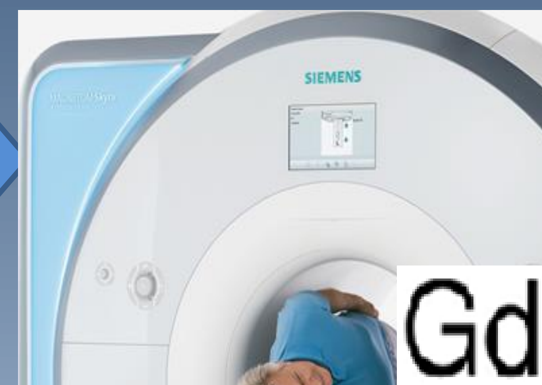
- Ethics: **16** subjects (**8** control, **8** LPS)
- Ongoing recruitment: healthy, non-smokers, no respiratory disease

Study design

SCAN-1

SCAN-2

6-hr

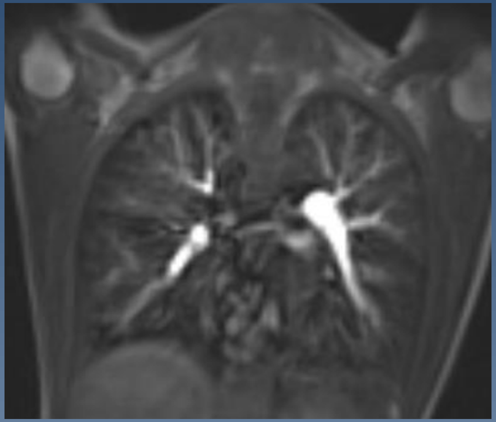


(No LPS)	LPS	N=2/8 (Changes)
N=5/16	or	
(No Saline)	Saline	N=3/8 (Precision)

Image acquisition

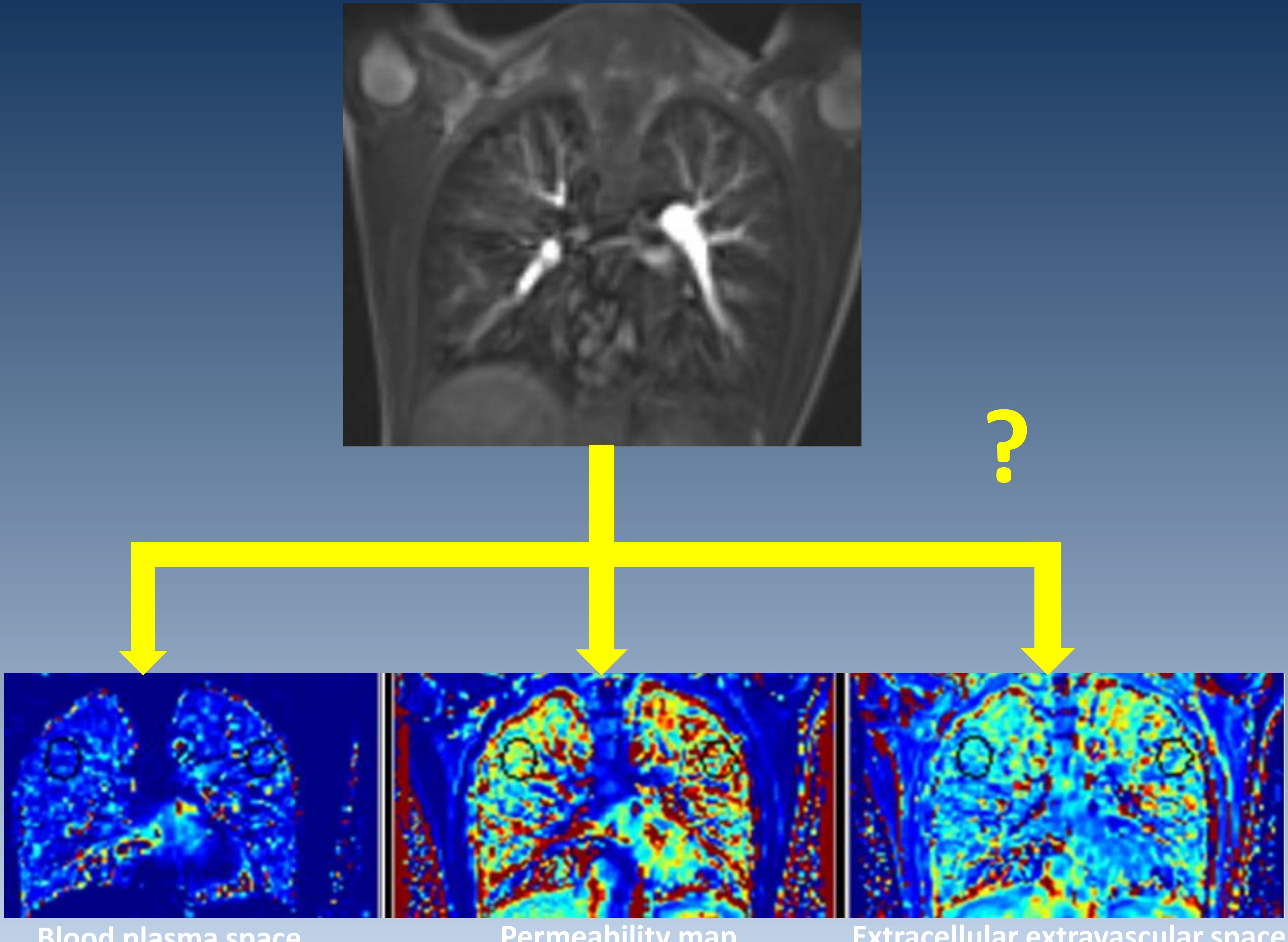
Baseline T1		DCE			
Scout	VFA	5 frames	Gd	Saline	135 frames

TIME

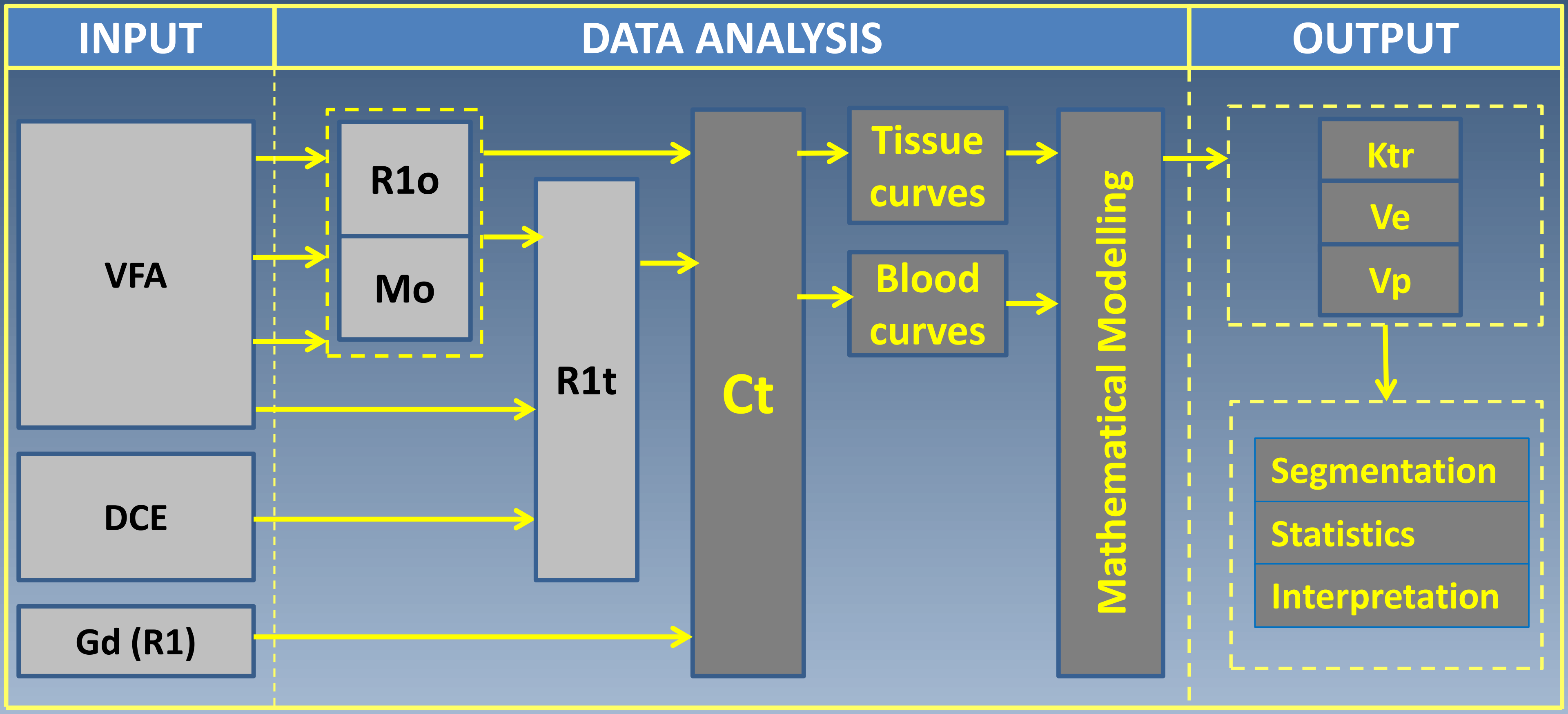


- Scanner: 1.5 Tesla SIEMENS
- Sequence: Spoiled Gradient echo (free breathing)
- Transmit, receive: body, 4-surface coil
- Baseline T1: 2^{o}, 5^{o}, 10^{o}, 19^{o}
- DCE scan
  - Gd, saline, injection: 0.2 mMol/kg, 20 ml, 4 ml/sec
  - FA, TR, TE, Frames: 19^{o}, 3.14, 0.91 ms, 140 frames
  - Spatial, temporal resolution: 2.74 x 2.74 x 5mm, 3.9 sec

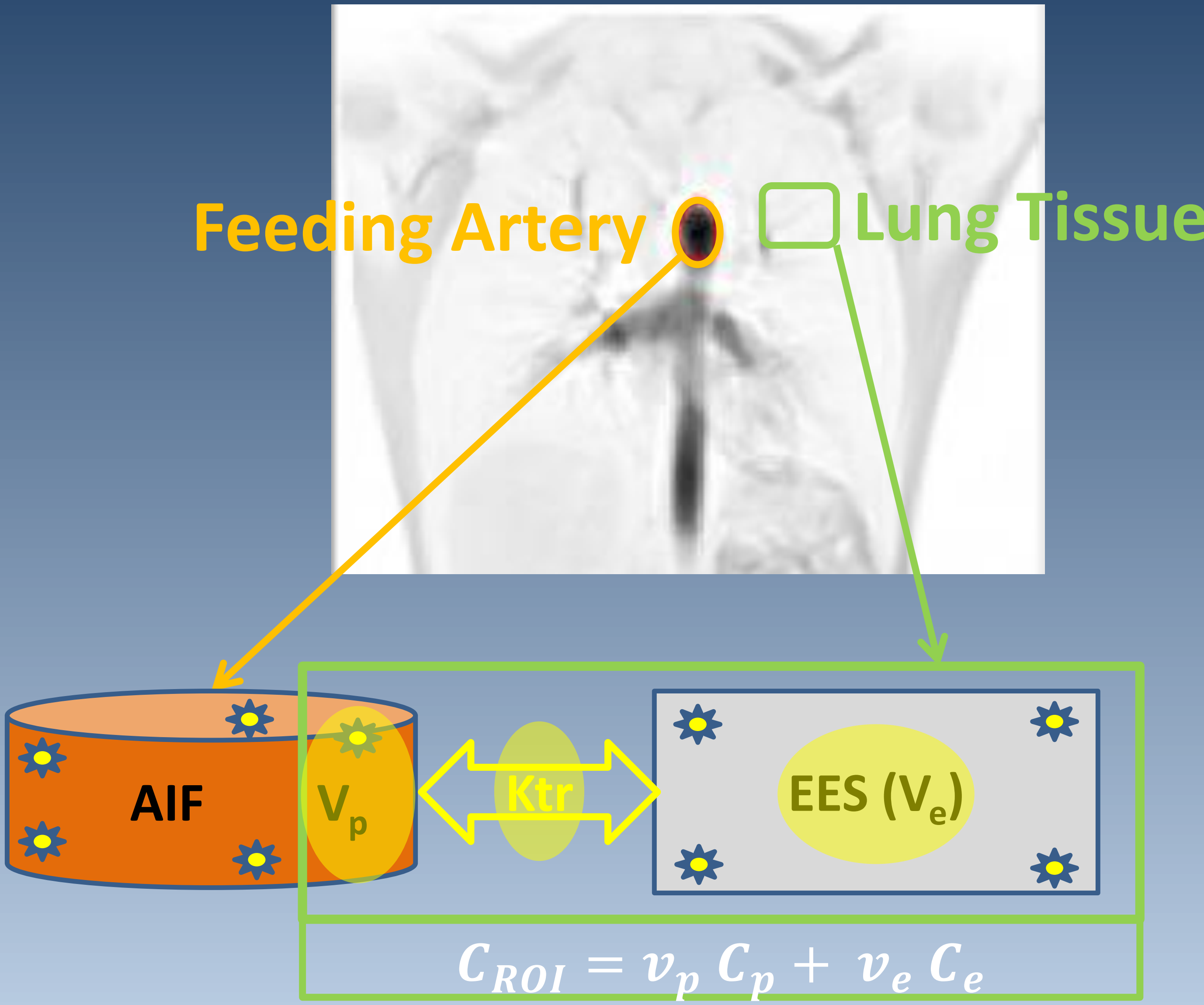
Naish et al. Magnetic Resonance in Medicine 61:1507–1514 (2009)


?
Blood plasma space
Permeability map
Extracellular extravascular space

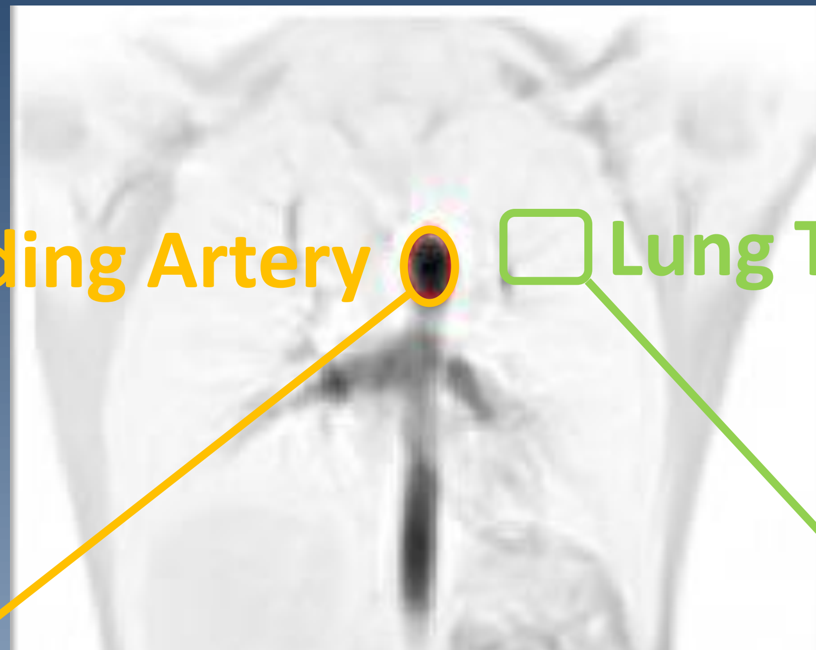
Data analysis pipeline



Mathematical modelling



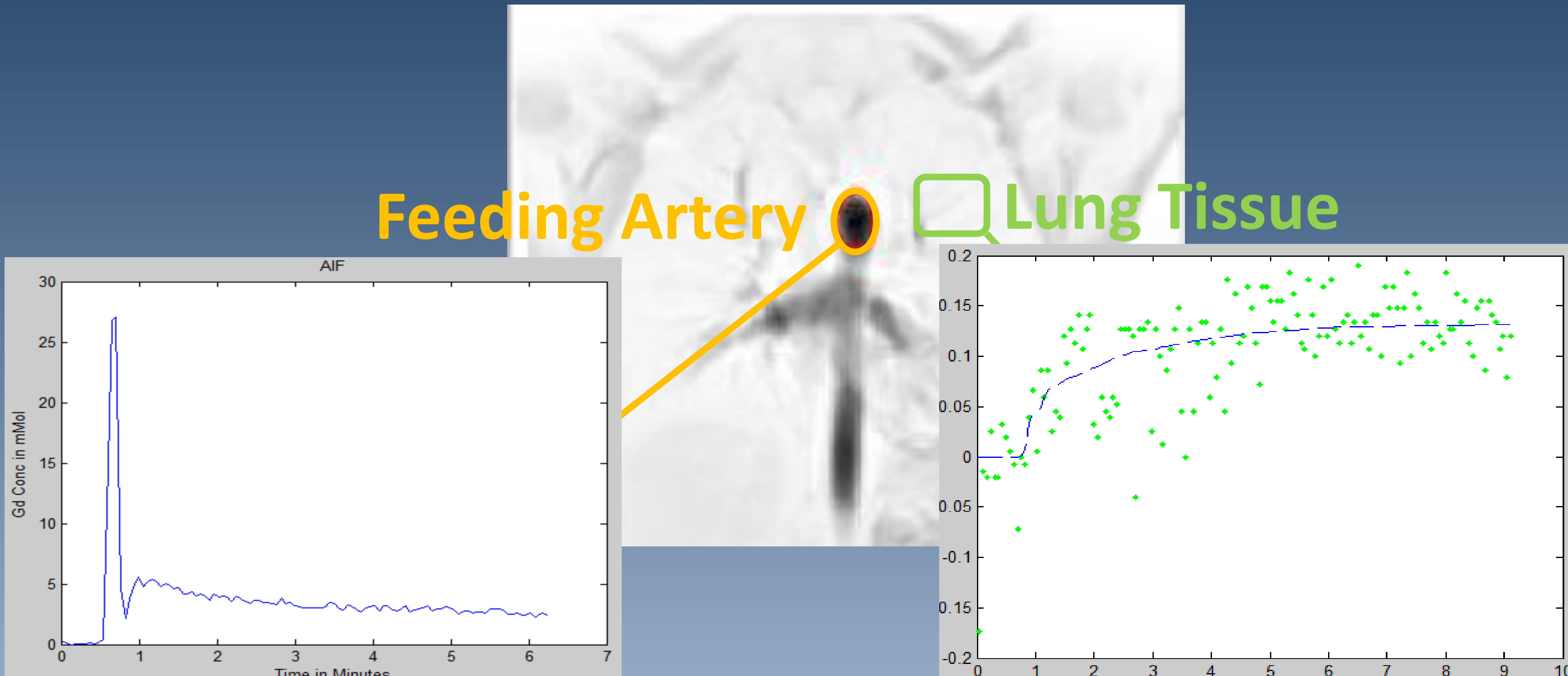
Extended Kety model



$$v_p C_p(t-\omega) + K^{tr}\int_0^{t-\omega} \exp\left(-\frac{K^{tr}}{v_e}\tau\right) C_p(t-\omega-\tau)\,d\tau = C_{ROI}(t)$$

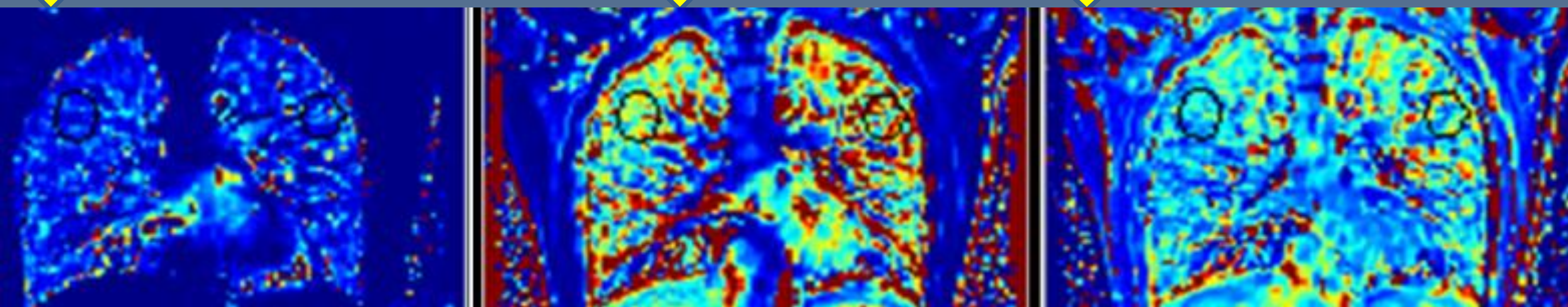
Naish et al. Magnetic Resonance in Medicine 61:1507–1514 (2009)

Extended Kety model



$$v_p C_p(t-\omega) + K^{tr}\int_0^{t-\omega} \exp\left(-\frac{K^{tr}}{v_e}\tau\right) C_p(t-\omega-\tau)\,d\tau = C_{ROI}(t)$$

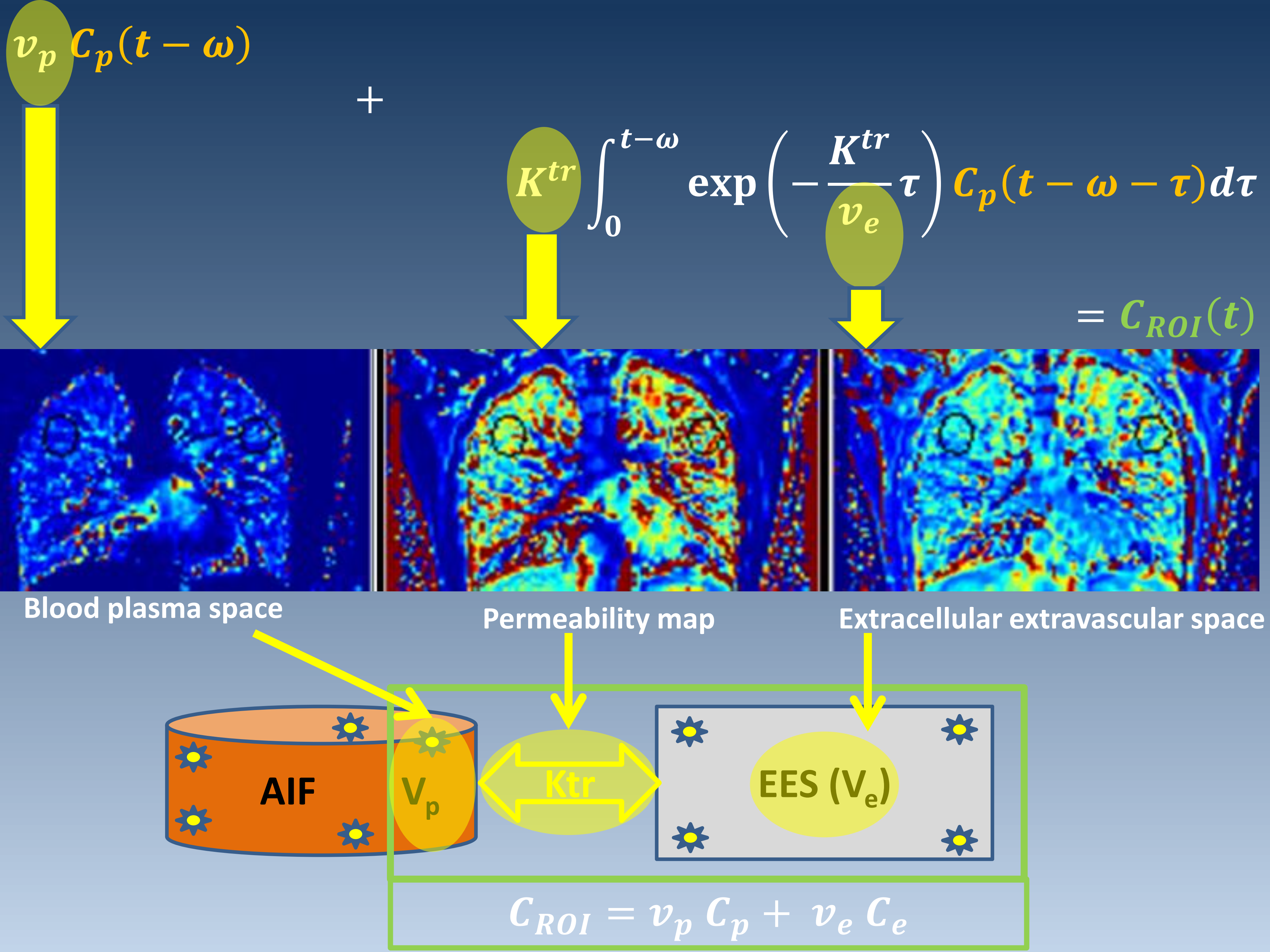
$$v_p\, C_p(t-\omega) + K^{tr}\int_0^{t-\omega} \exp\left(-\frac{K^{tr}}{v_e}\tau\right) C_p(t-\omega-\tau)\,d\tau = C_{ROI}(t)$$



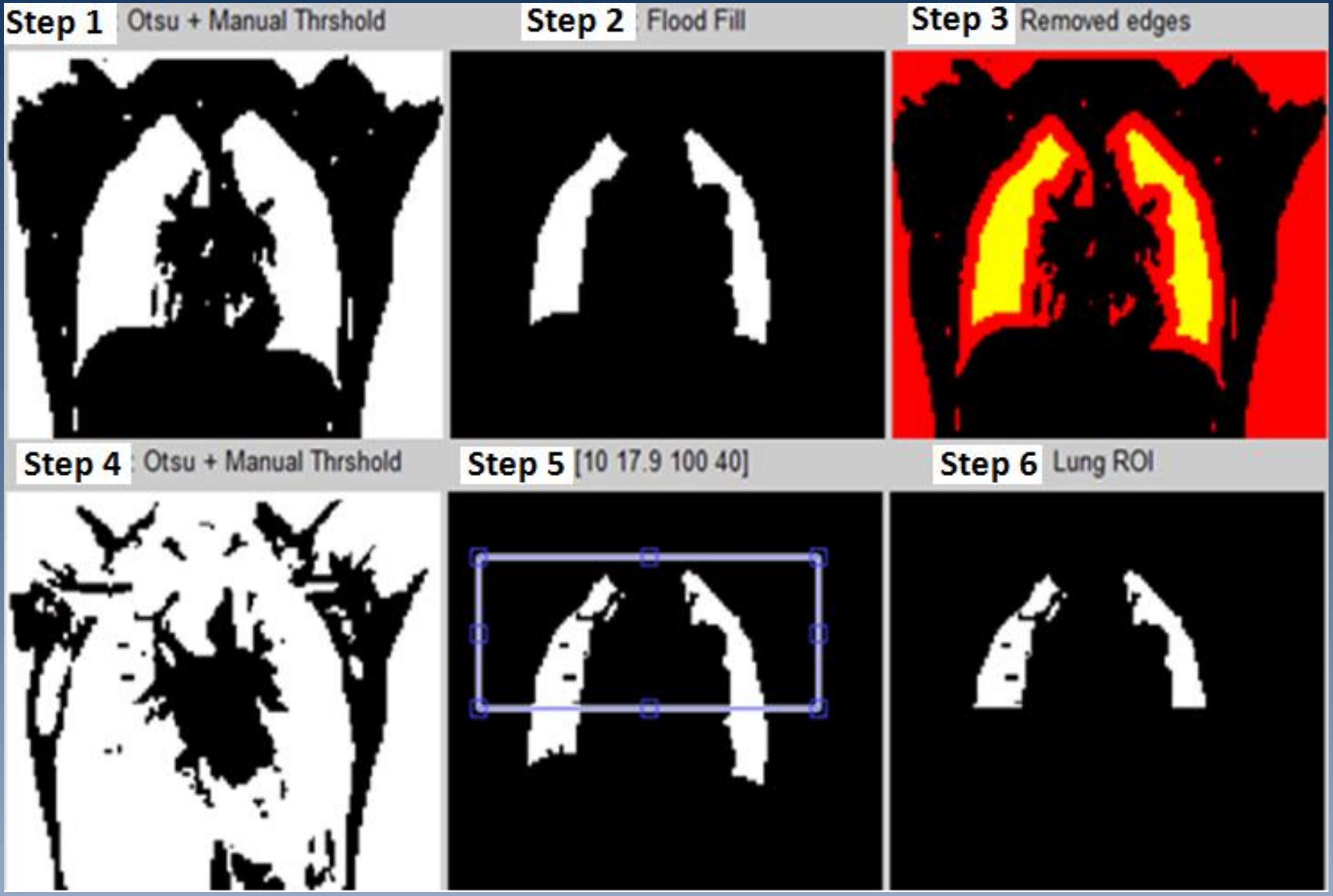
Blood plasma space

Permeability map

Extracellular extravascular space

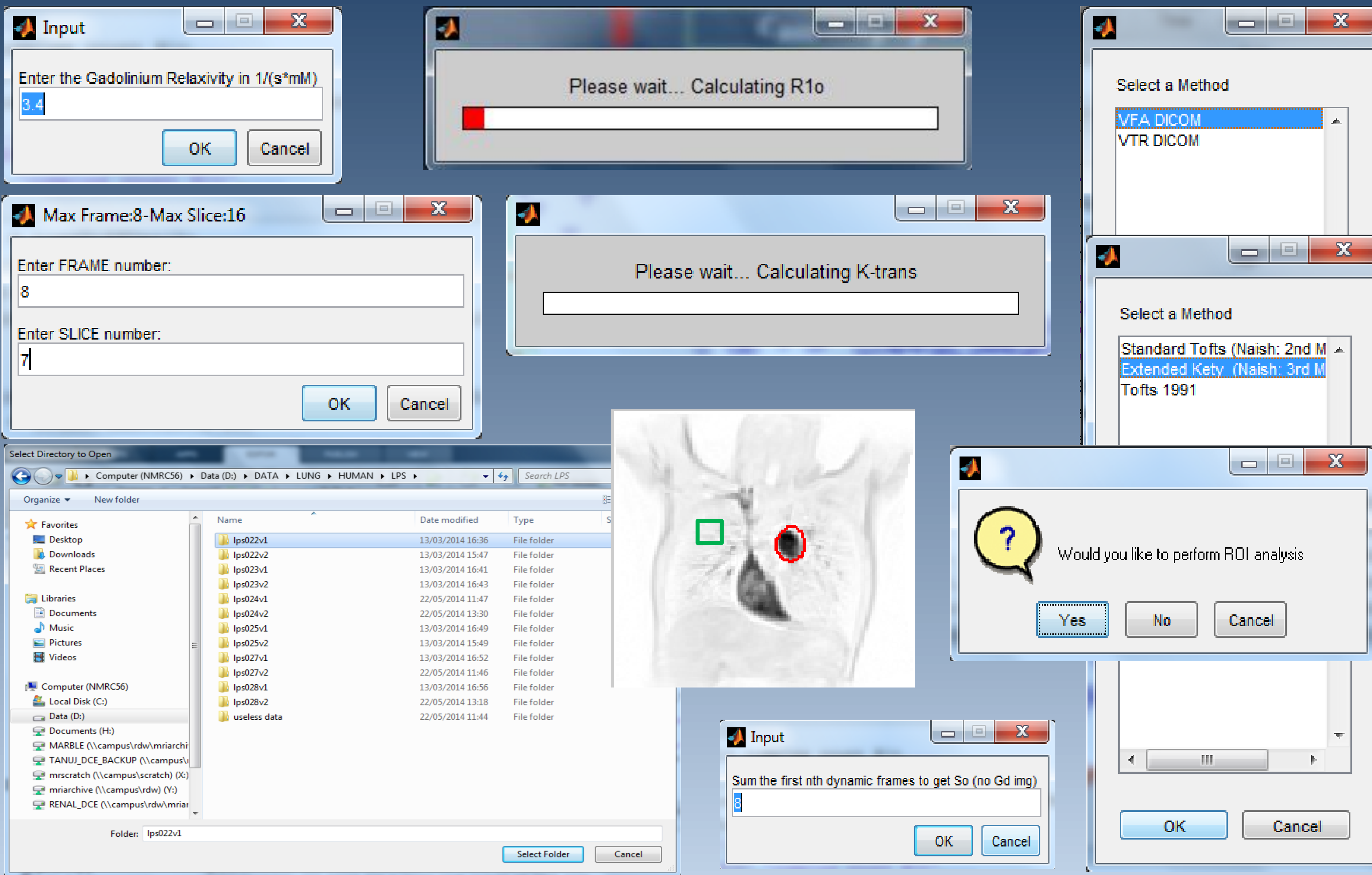


$v_p \, C_p(t-\omega)$
$+$
$K^{tr} \int_0^{t-\omega} \exp\left(-\frac{K^{tr}}{v_e}\tau\right) C_p(t-\omega-\tau) d\tau$
$= C_{ROI}(t)$
Blood plasma space
Permeability map
Extracellular extravascular space
AIF
V_p
Ktr
EES (V_e)
$C_{ROI} = v_p \, C_p + \, v_e \, C_e$

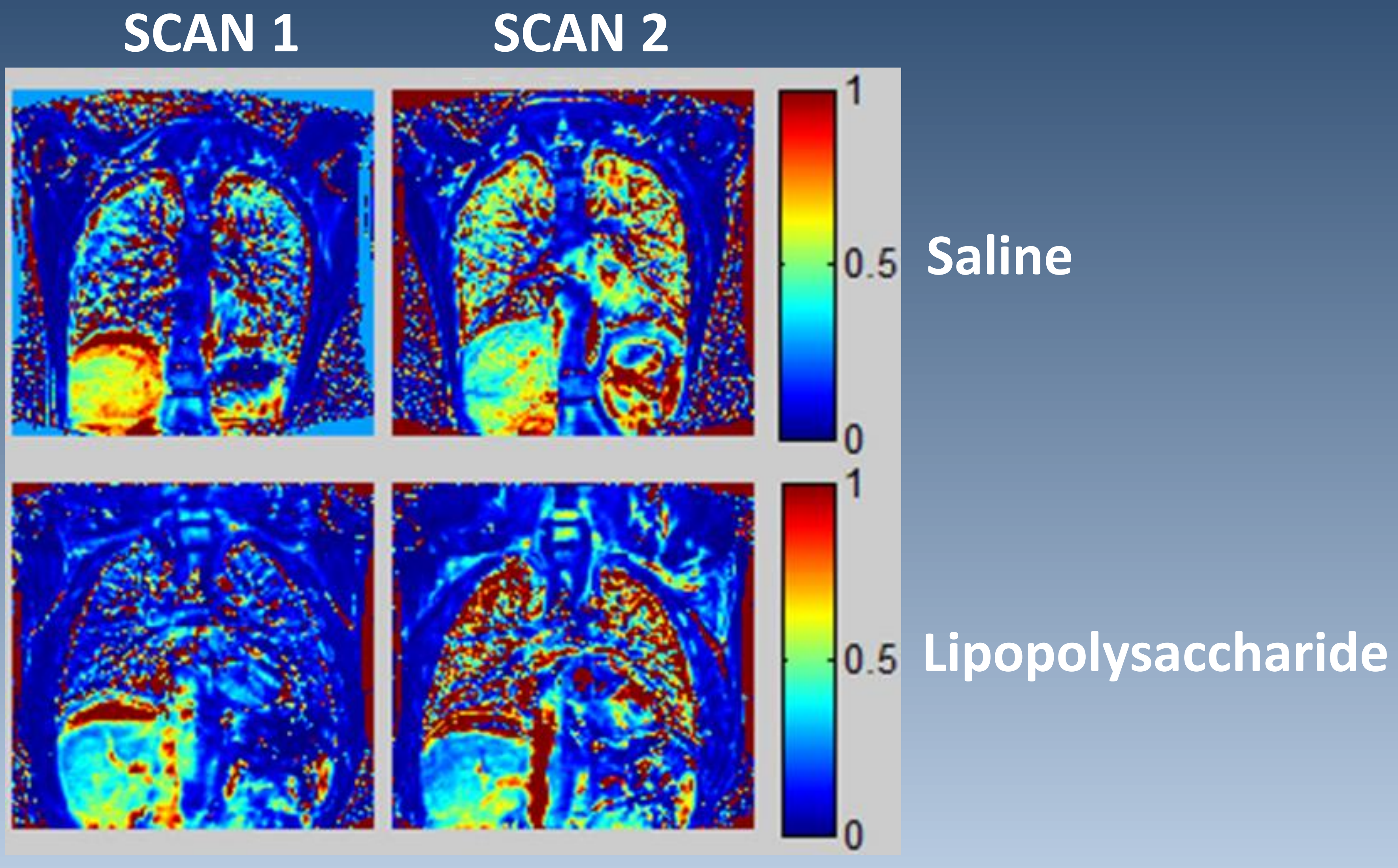


T1o	Semi-automated	Circular ROI
SNR	4-8	2-4
COV	3.7 %	6.8 %

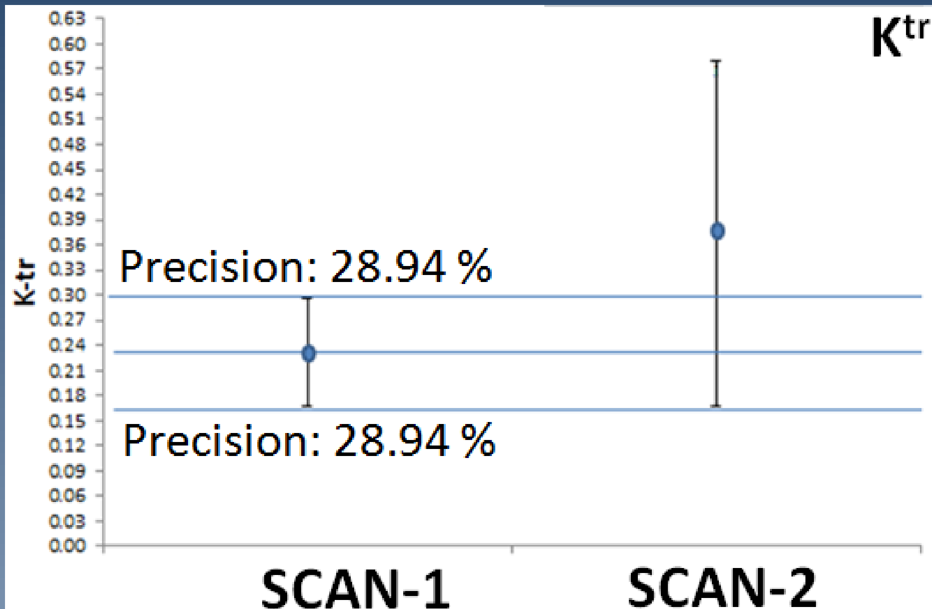
Data analysis tool (MATLAB)

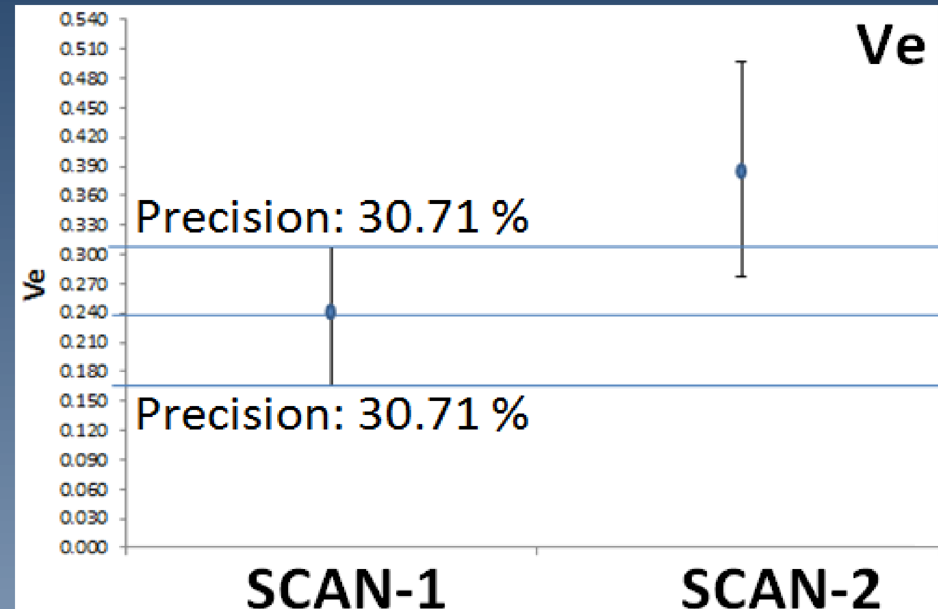


Lung permeability map



Results



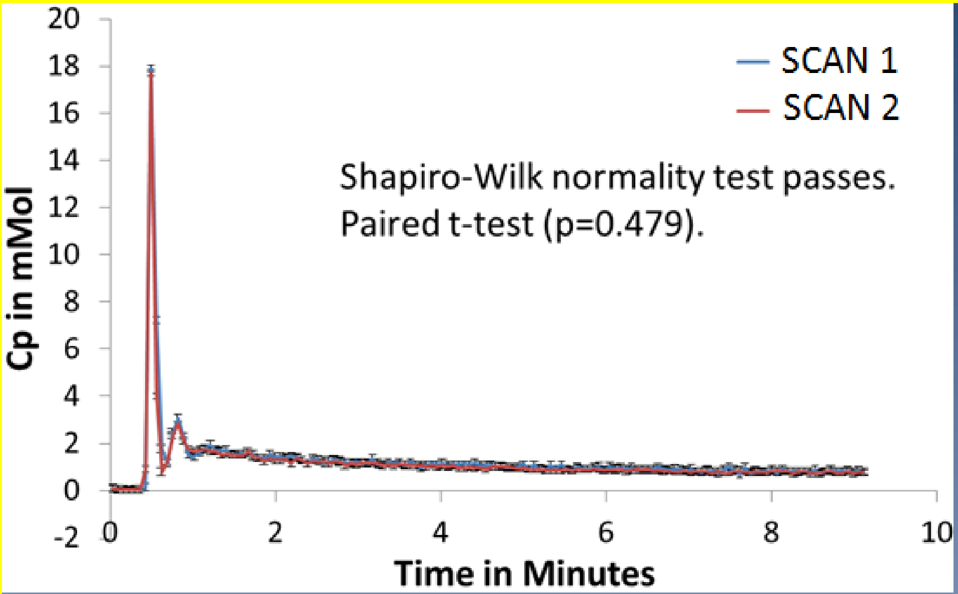


Hypothesis:

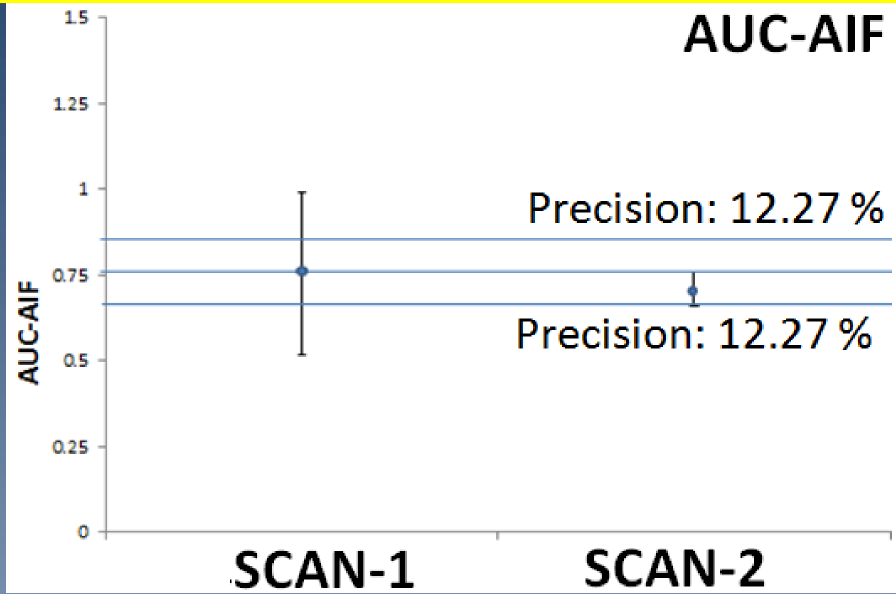
LPS induces changes in
K^{tr} (vascular permeability) & Ve (alveolar fluid content)
that can be detected with DCE-MRI

Ng et al 2010; Ashton et al 2010; Morgan et al 2006

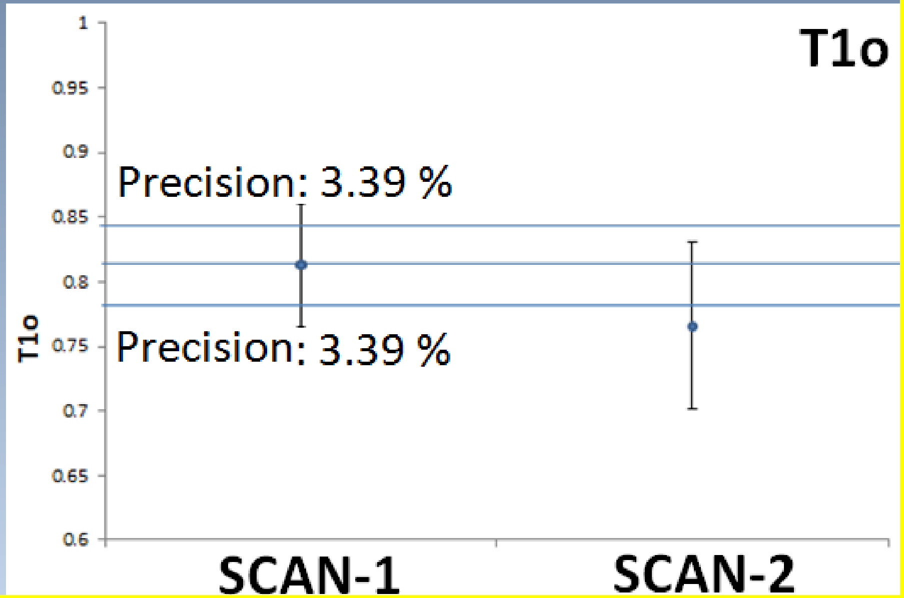
Results



SCAN 1
SCAN 2
Shapiro-Wilk normality test passes.
Paired t-test (p=0.479).
Cp in mMol
Time in Minutes



AUC-AIF
Precision: 12.27 %
Precision: 12.27 %
SCAN-1
SCAN-2



T1o
Precision: 3.39 %
Precision: 3.39 %
SCAN-1
SCAN-2

Summary

- Our hypothesis
  - LPS-induces changes in K^{tr} , Ve that can be detected with DCE-MRI
- Naish et al. 2008
  - Higher K^{tr} in smoker lungs than in non-smokers using DCE-MRI
- Used for clinical trials of novel drugs for ALI
- If no significant differences are observed then the precision errors of K^{tr} , Ve in the lung will be reported

Acknowledgements

- Co-authors
  - Sarah Wiscombe: Subject recruitment and ethics
  - Sally Marshall: Funding
  - John Simpson: Clinical oversight of the project
  - Josephine Naish: Advice on image acquisition and analysis
  - Pete Thelwall: Data acquisition and project coordination
- Staff
  - Freeman Hospital, Newcastle Magnetic Resonance Centre
  - Colleagues in Tyne room and Millennium room
- This work was funded by the NIHR Newcastle Biomedical Research Centre

Newcastle University

tanuj.puri@newcastle.ac.uk
tanujpuri82@gmail.com

NHS National Institute for Health Research

SCAN-1 SCAN-2

Saline

LPS