PET Imaging in Interstitial Lung Disease (ILD)

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Tainan 2019

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University College London

University College London

- Research University (Biomedical Sciences)
- Based in Central North London
- Oldest College of University London (1826)
- 1st Non Sectarian University in UK
- 1st UK University to admit Women/Ethnic Minorities

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UCH Founded in 1834
Criciform Building 1906

INM/UCL

Opened 2005

Institute of Nuclear Medicine

Founded in 1961

22,000 clinical examinations a year

All Specialties – Oncology & Cardiology.

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Interstitial Lung Diseases

- Diffuse Parenchyma Lung diseases

- Known Causes
  - Rheumatological
  - Drugs
  - Chemicals (asbestos)

- No Known Causes
  - **Idiopathic Pulmonary Fibrosis**

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PET in ILD and IPF
OVERVIEW

FDG PET in ILD and IPF

-Initial Observations

- Predicting Mortality- Prognostic Biomarker

-Reproducibility of PET Signal

- Measuring Treatment Response Response Biomarker

Other PET Techniques in IPF

Applications of FDG PET in IPF in Clinical Practice

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Idiopathic Pulmonary Fibrosis

- Poor prognosis -median survival 3 years
- Lack of proven effective treatments
- Incidence is rising
- IPF more common than previously thought,
  estimated US prevalence 14- 43 per 100,000

IPF as prevalent as many common cancers that attract much more resources.

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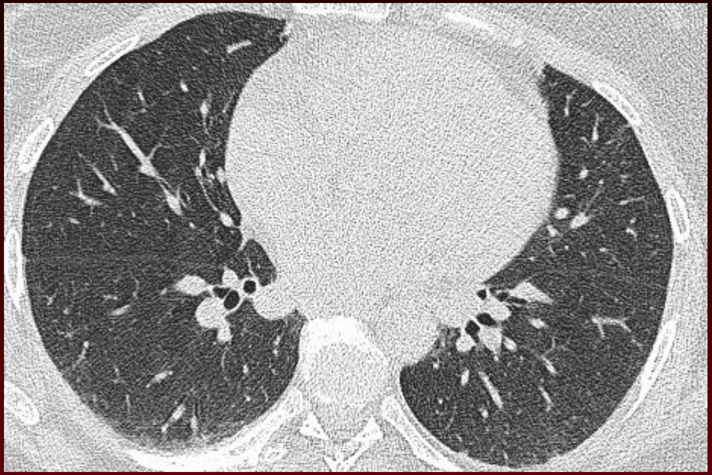
HRCT



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HRCT

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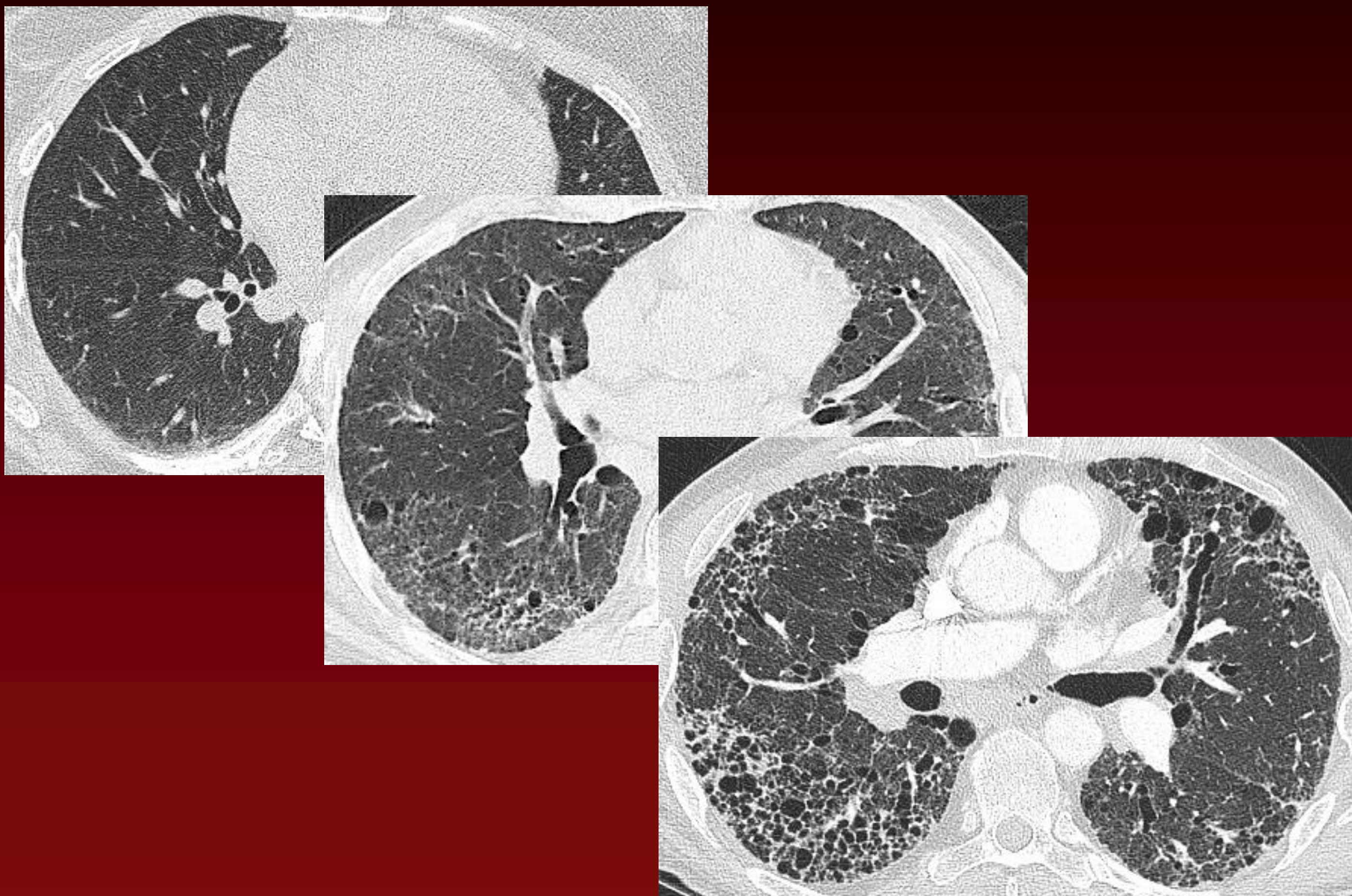
HRCT



Why use PET in IPF

- The disease mechanism is poorly understood
- Poor prognosis –lack of biomarkers
- Lack of effective treatments- lack of end points

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64 year male with IPF. CT images show classic honeycombing. A sign of established fibrosis

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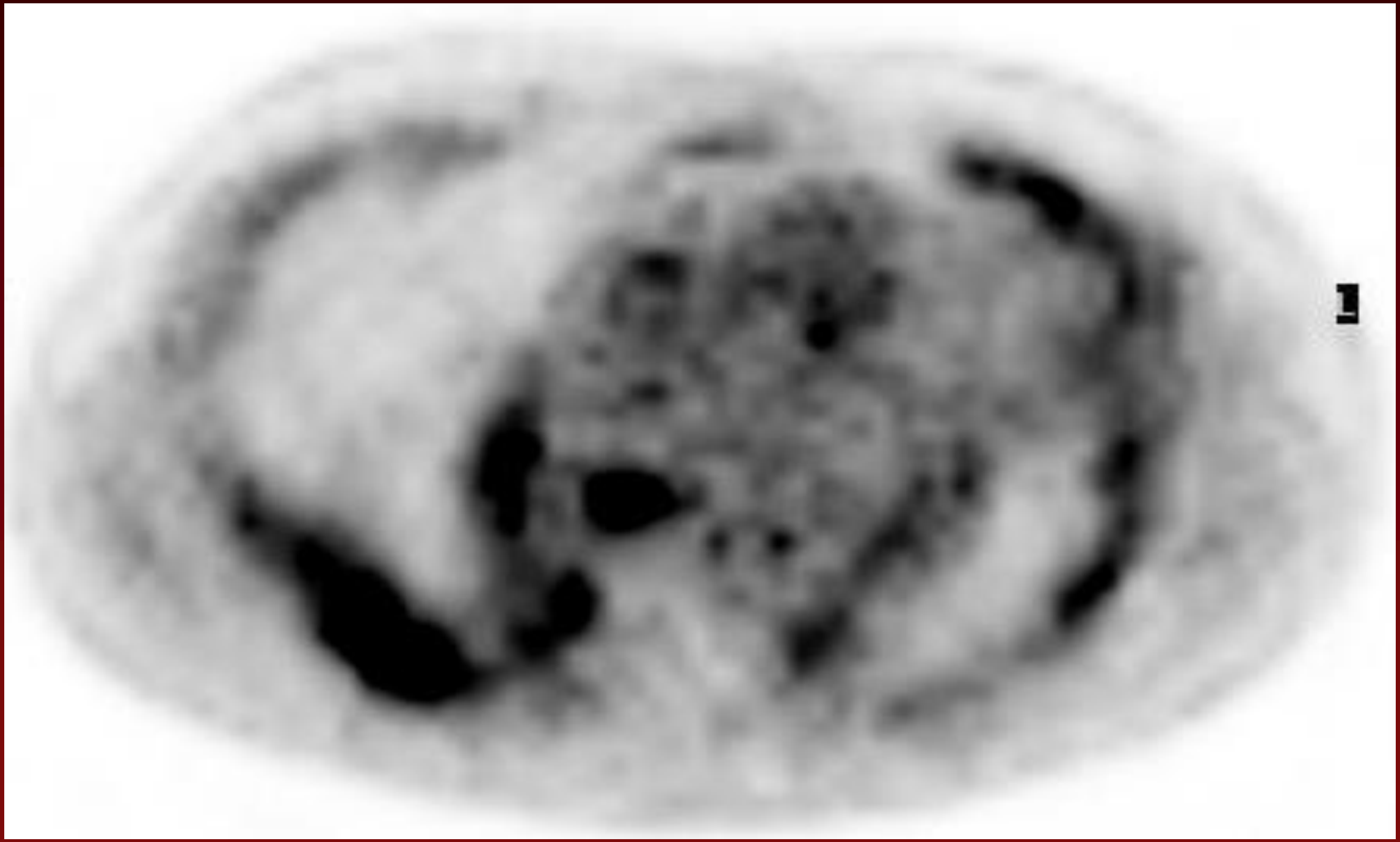
PET images from patient above showing highly metabolically active disease at the sites of the honeycombing on HRCT.



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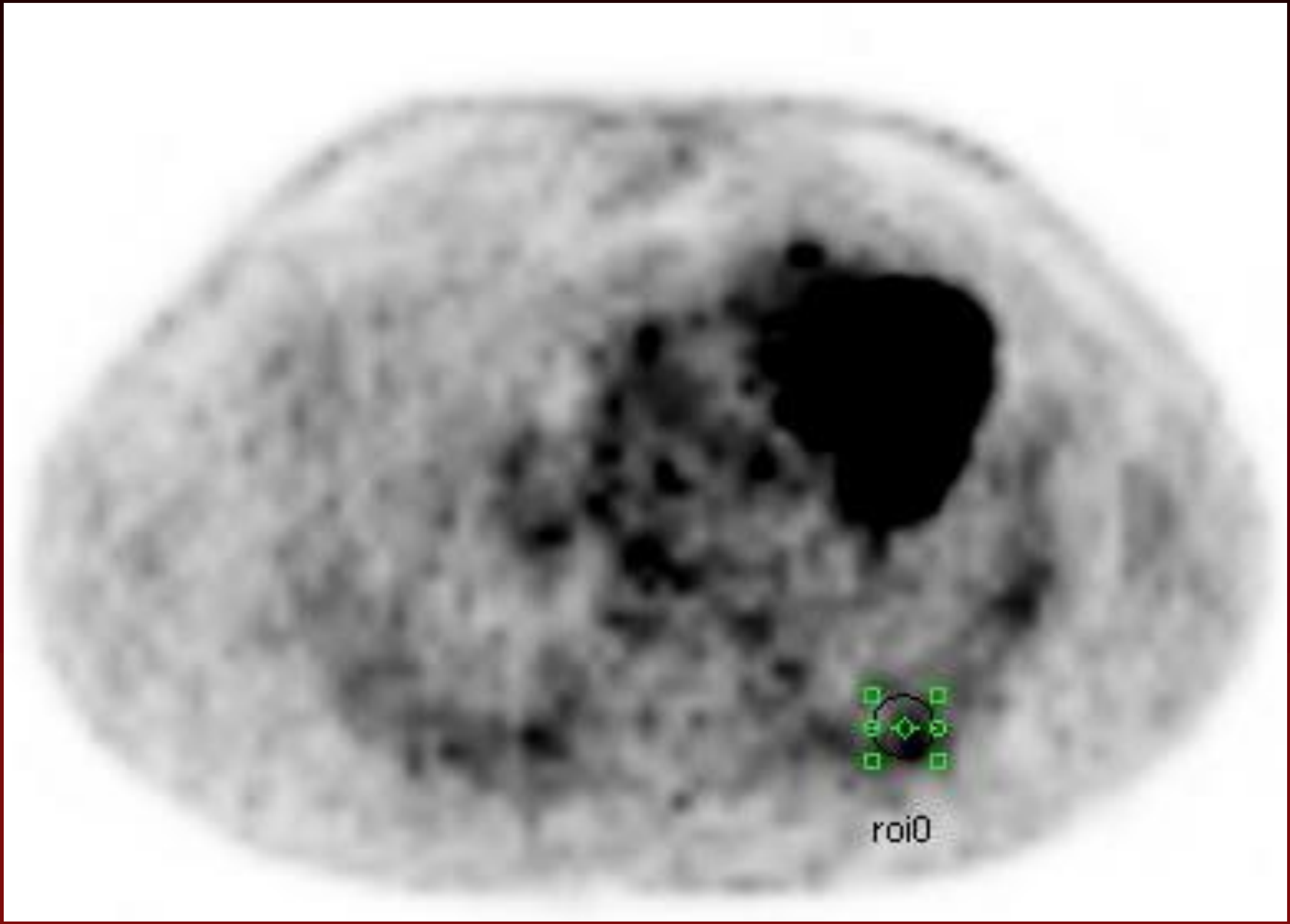
Region of Interest analysis to derive Maximal FDG uptake on PET; SUV (max/mean)



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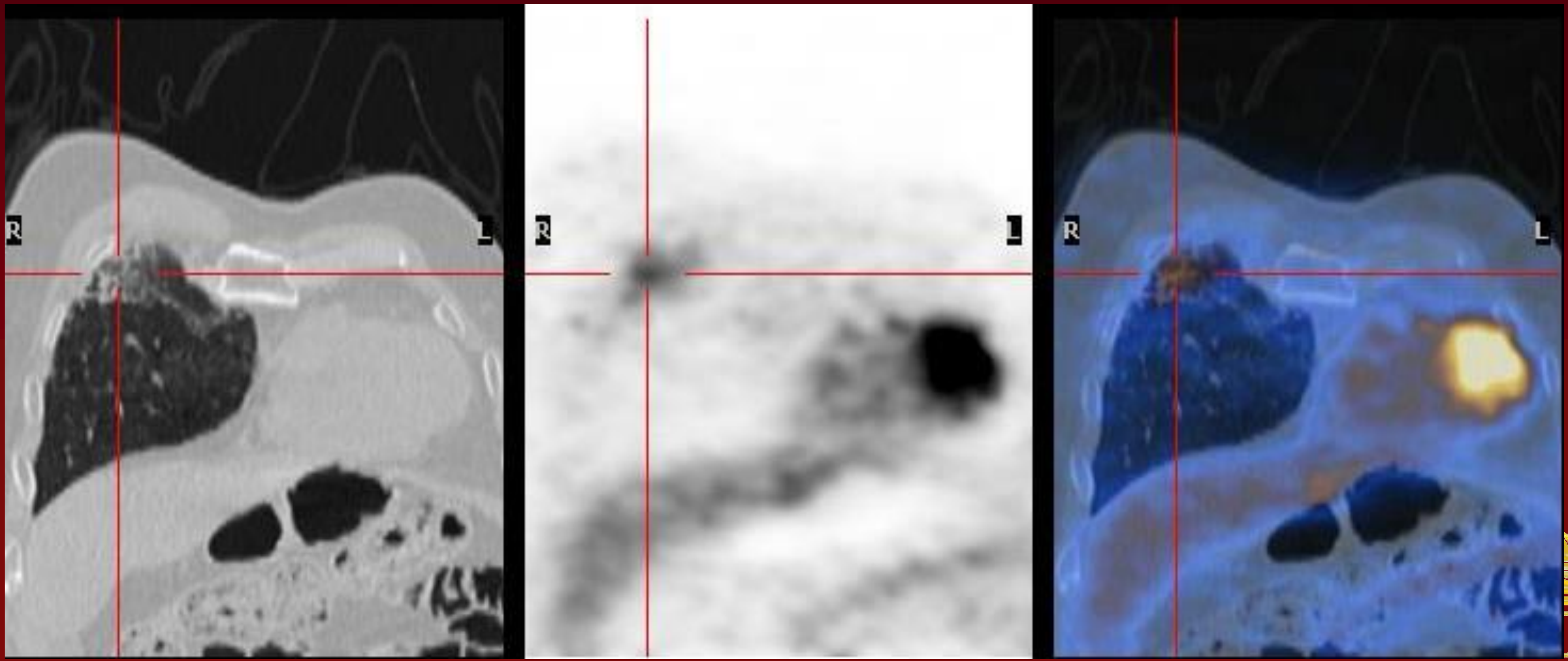
Where ever there was CT parenchymal changes of ILD a FDG PET signal was obtained.

N=36



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Pulmonary ^{18}F-FDG Uptake & PFTS

Significant correlation between Pulmonary FDG uptake (SUV) and % predicted

- FVC $r=0.41$, $p=0.014$
- KCO $r=0.37$, $p=0.042$

$N=36$

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Pulmonary ^{18}F-FDG Uptake and Quality of Life

Significant correlation between Pulmonary FDG uptake and general activity Score

r=0.50, *p*=0.004

N=36

Implications

- Honeycomb lung is highly metabolically active
- Honeycombing could be susceptible to metabolic manipulation
- ?Role of PET CT in Prognosis and Treatment monitoring

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PET as a PROGNOSTIC Biomarker in ILD

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IPF Survival and PET

- 113 IPF patients
- PET >10 years of data
- Lung FDG Uptake (TBR)
- Survival analysis via KM
- Comparison with GAP Analysis
  - Gender
  - Age
  - Physiology

EJNMMI 2018 45 806-15

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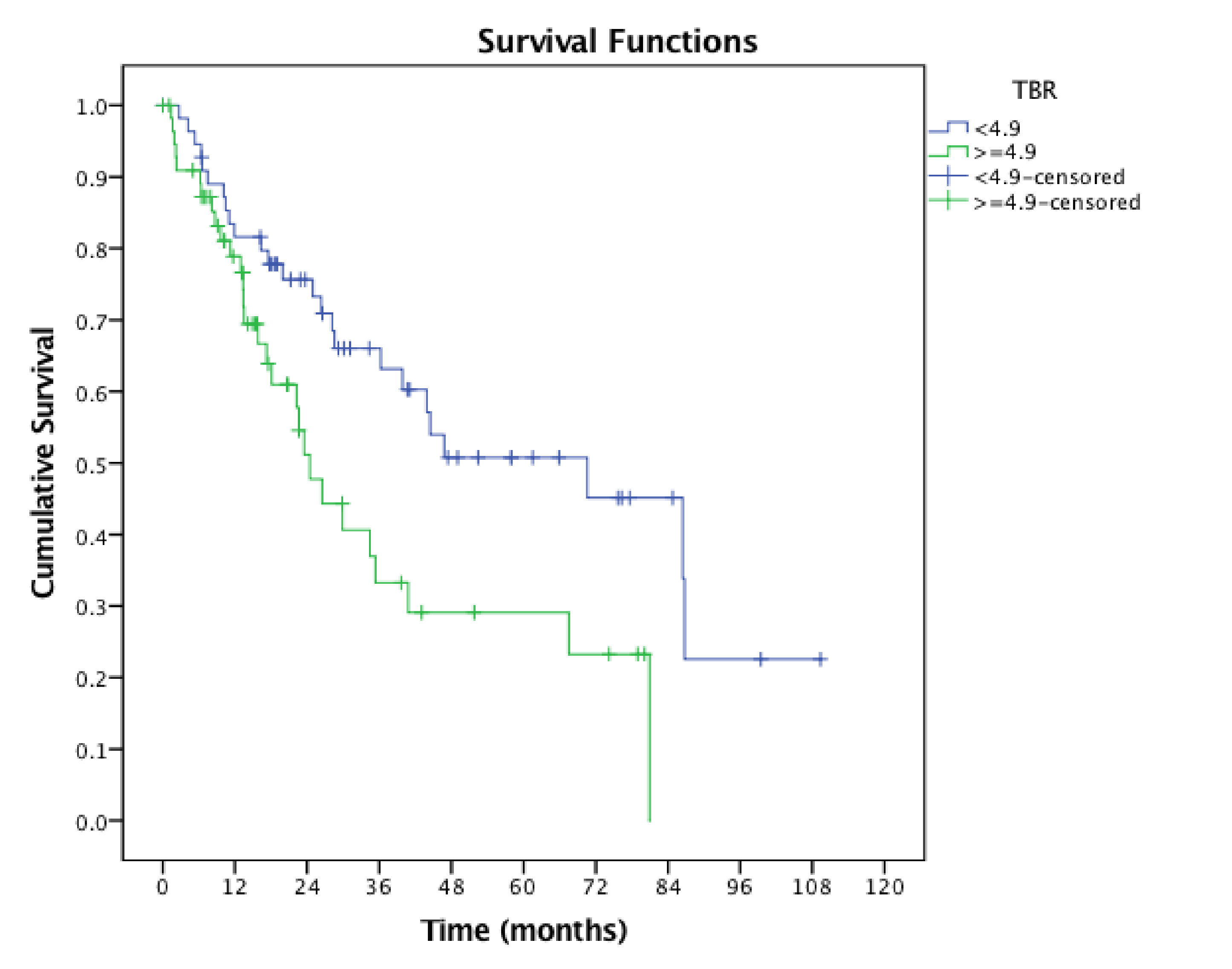
High TBR = Poor Survival

p = 0.009 (4 fold cross validation)



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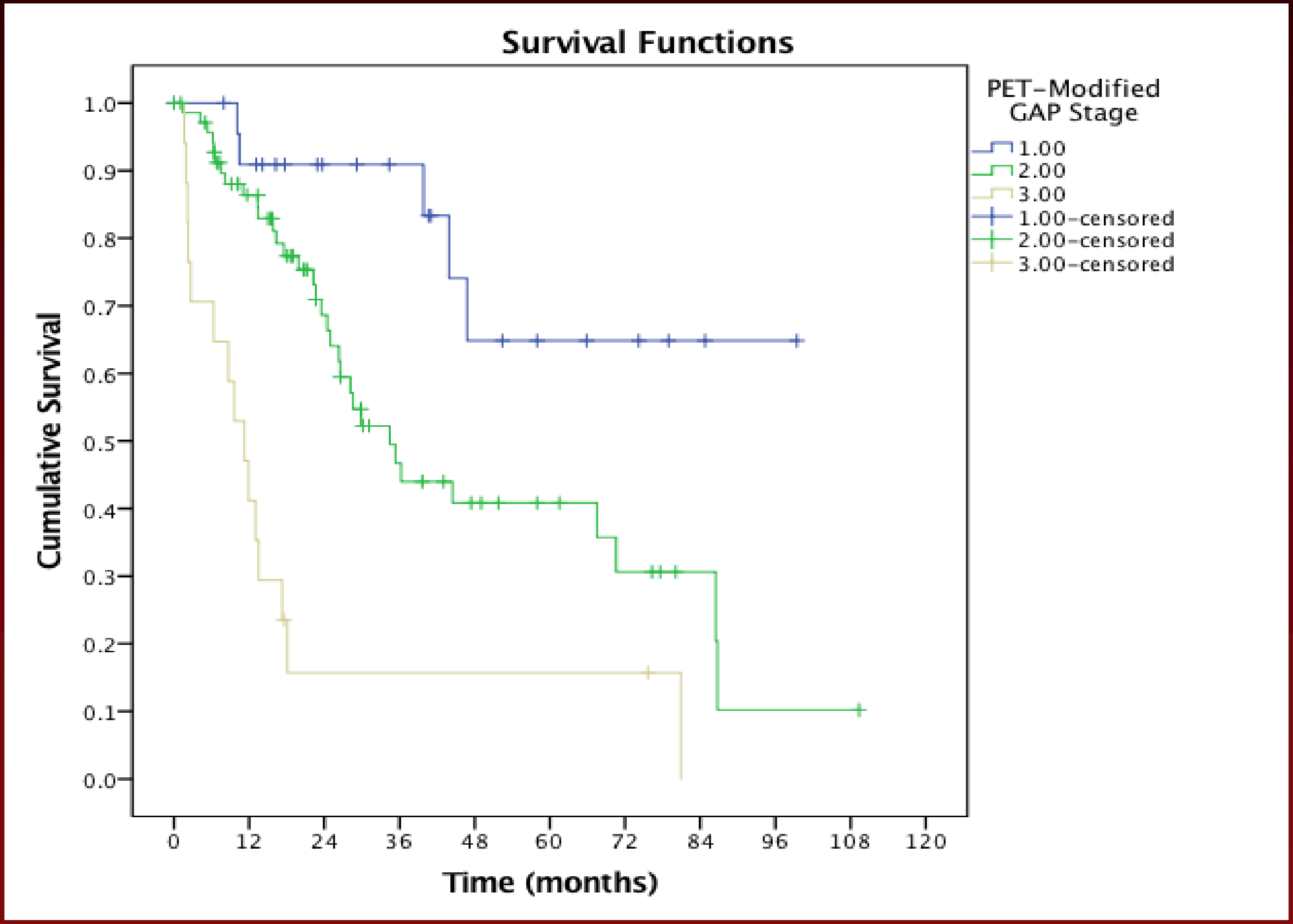
Modified (using TBR) GAP = Poor Survival

p = 0.001 (4 fold cross validation)



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IPF Survival with PET and QCT

- 91 IPF patients
- PET and quantitative CT (e.g vessels)
- 10 years of data
- Survival analysis via KM
- Comparison with GAP analysis

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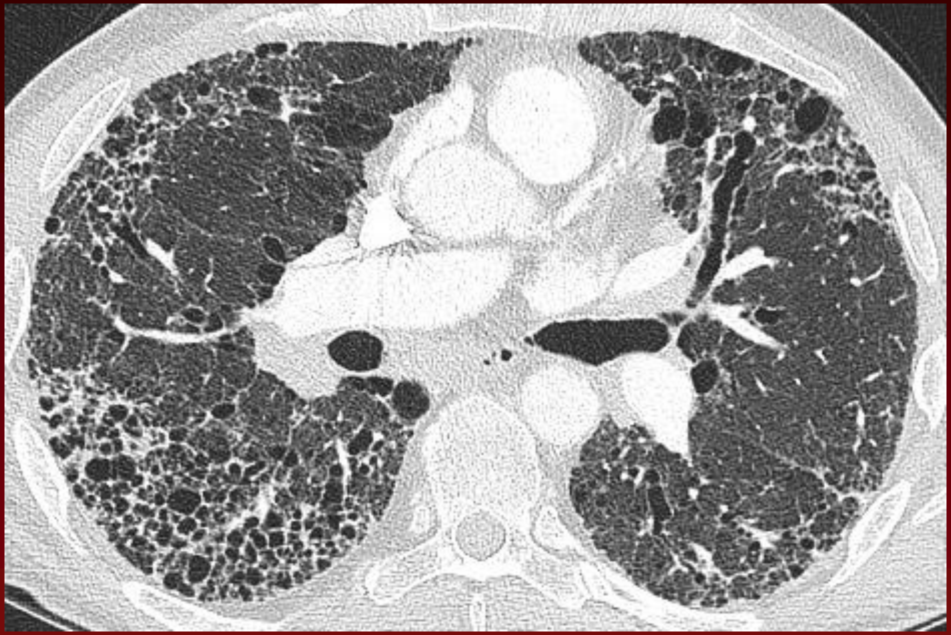
QCT



Software (IMBIO) analyses the images e.g. textural analysis to quantify characteristics e.g.
Reticulation
Vessels
Emphysema

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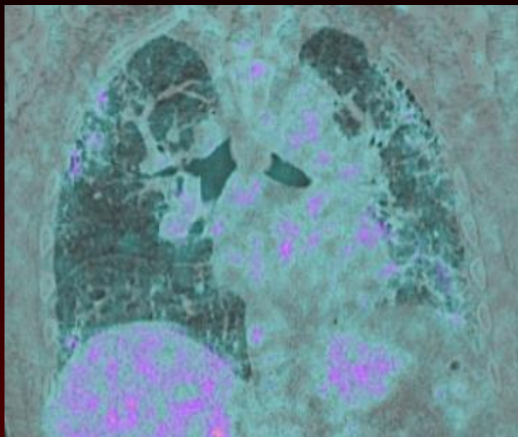
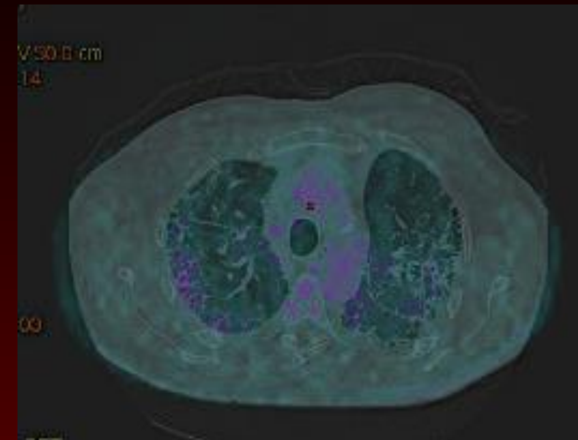




PET-derived parameters
SUV Max
SUV Min
TBR

TEXTUR

NORMAL

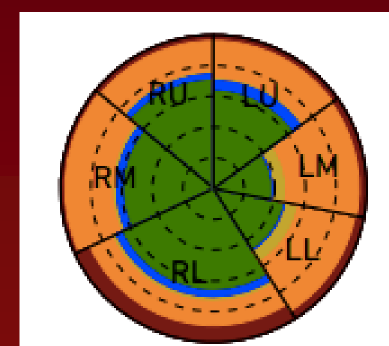
EMPHYSEMA

GROUND GLASS

RETICULAR

HONEYCOMBING

VESSELS



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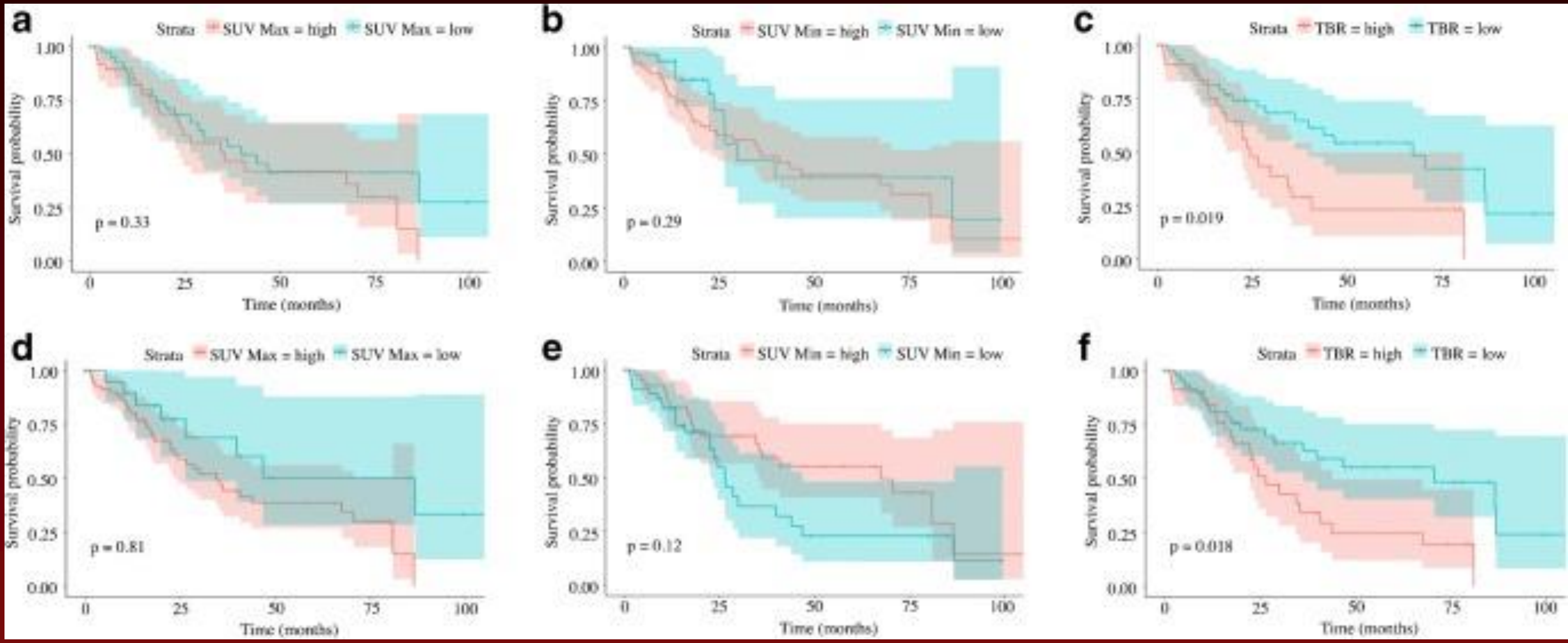
KM analysis FDG Uptake v Survival *p*=0.0180



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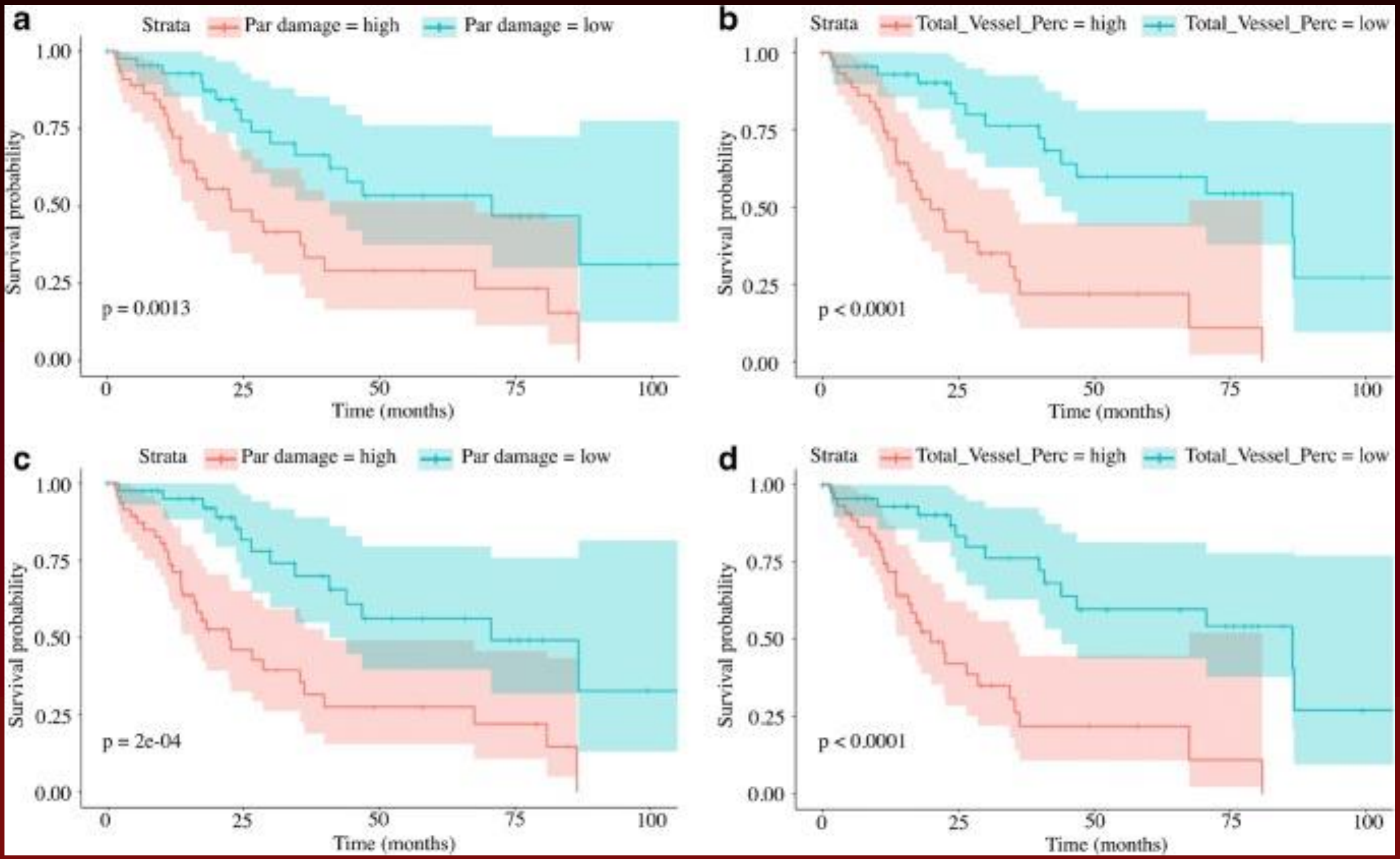
KM analysis QCT v Survival *p*=0.0002



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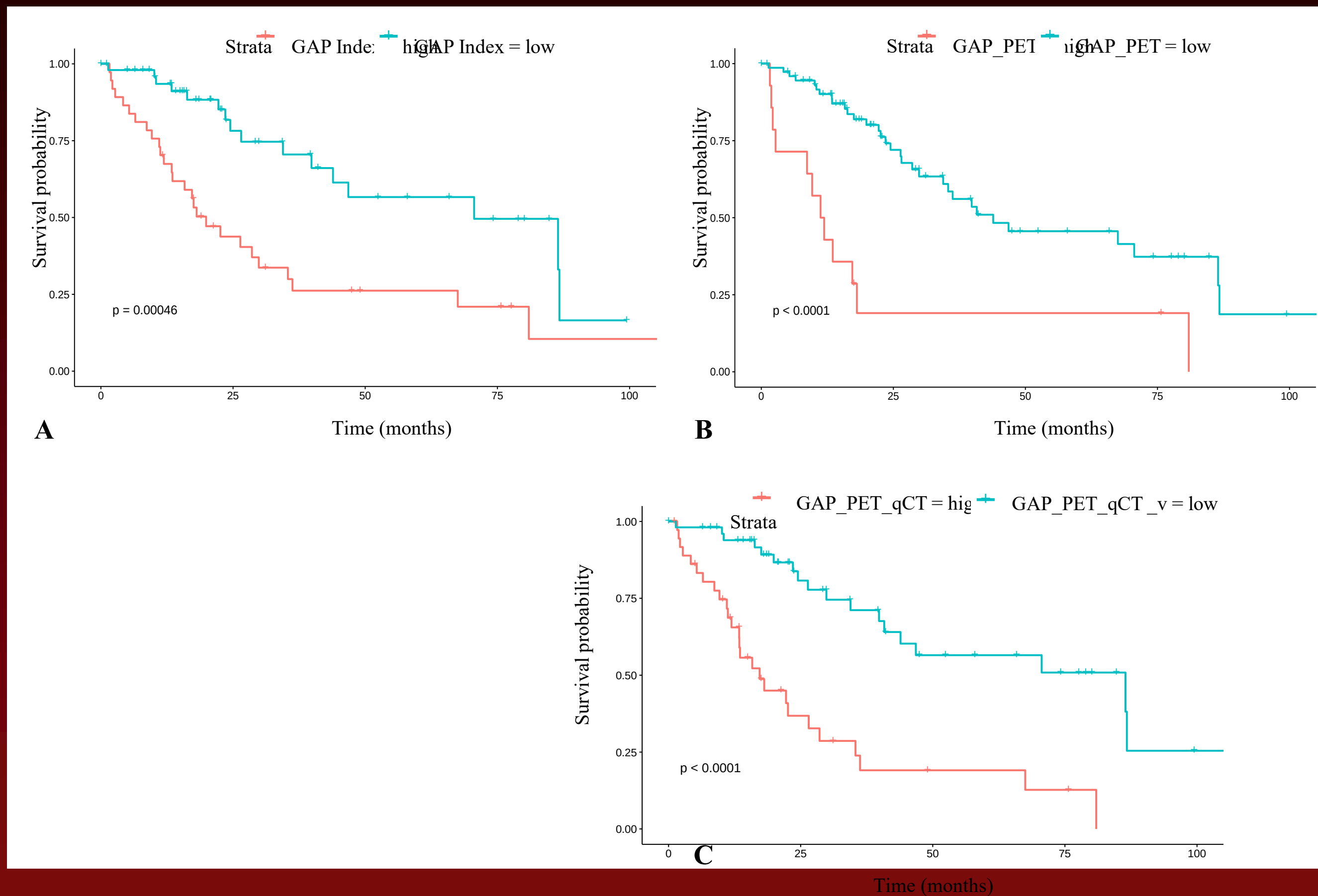
KM analysis FDG, QCT and GAP v Survival *p*<0.0001



GAP score statistically significant predictors of survival
Adding PET and qCT improved the differentiation between better and worse prognoses

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PET as a Response Biomarker in ILD

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PET Signal Reproducibility and Measurements in IPF

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	Correlation Between SUV values from different scan dates	Correlation Between Corrected SUV values from different scan dates
FDG S1	0.981	0.985
FDG S2	0.966	0.976
FDG S3	0.910	0.956
FDG S4	0.908	0.837
FDG S5	0.968	0.985
Ga S1	0.784	0.948
Ga S2	0.991	0.994
Ga S3	0.989	0.977
Ga S4	0.917	0.942
Ga S5	0.884	0.782

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Conclusion

There is excellent short term FDG PET/CT reproducibility in IPF

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Measuring treatment response in patients with NSIP using ^{18}F-FDG-PET/CT Imaging;

A proof of concept study

12-patients (4-male, 5-female mean age 67.2±9.0). ILD with NSIP on HRCT. 1 Bx NSIP

Pre and Post Treatment ^{18}F-FDG-PET, HRCT, PFTs

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Axial HRCT. Female amiodarone lung. Parenchymal pattern of mixed ground glass & reticular opacity

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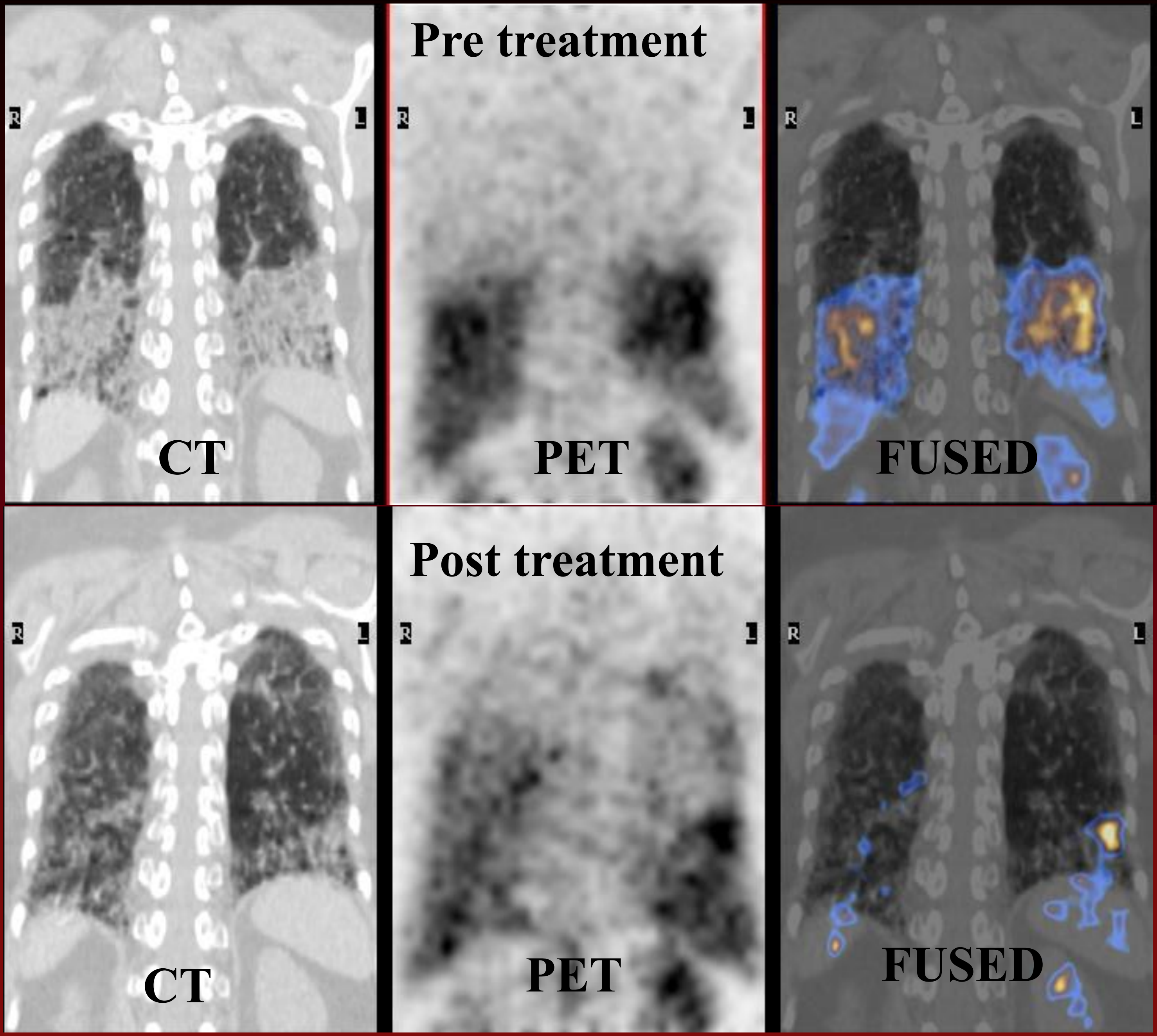

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Correlations between **Initial** SUV and Change in PFT

Lung Volumes

FVC	*r* = -0.76, *p*= 0.005
FEV1	*r* = -0.69, *p*= 0.015
TLC	*r* = -0.68, *p*= 0.017

Gas Transfer

TLCO	*r* = -0.73, *p*= 0.014
KCO	*r* = -0.56, *p*= 0.076

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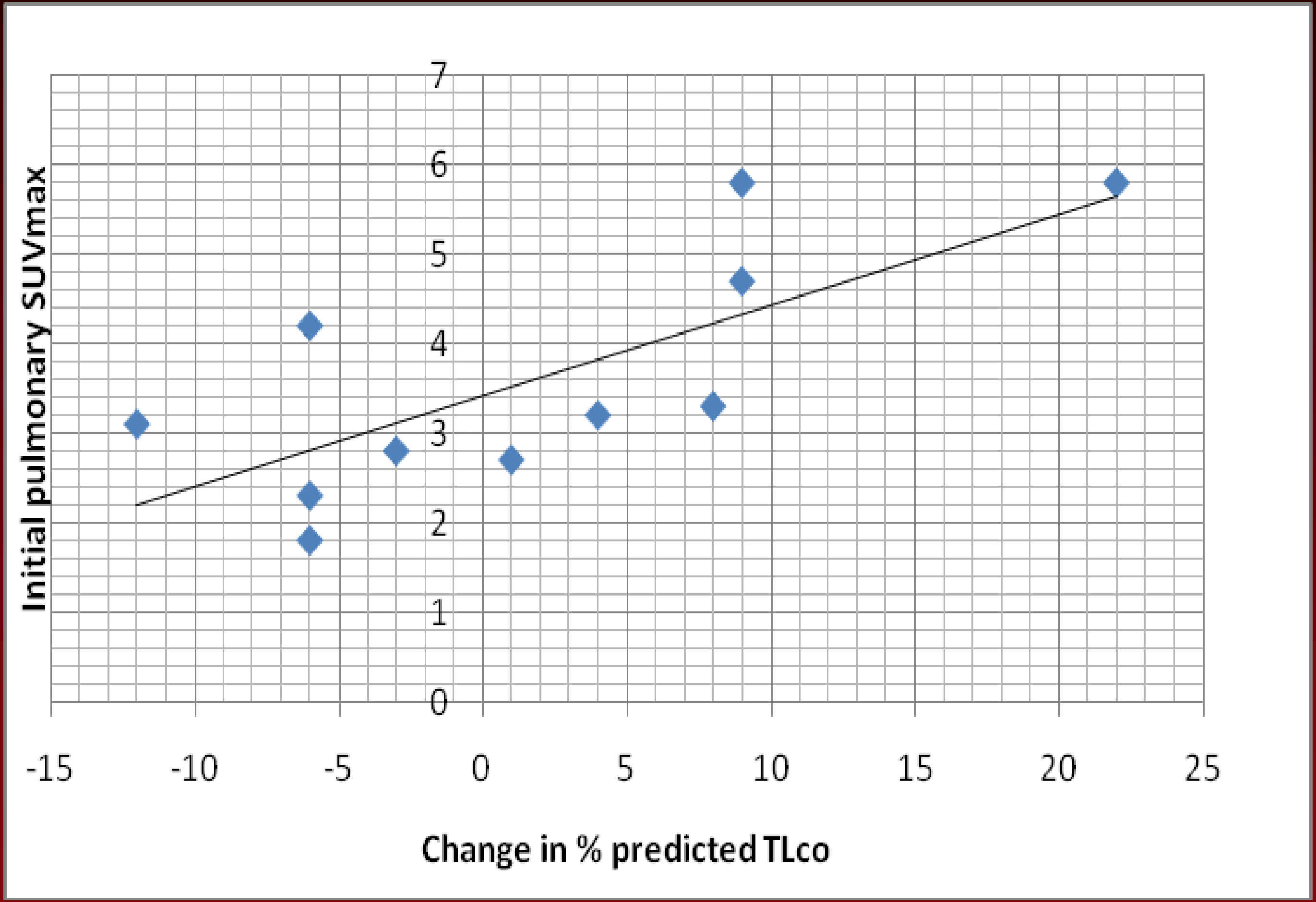
Correlations between Initial SUV and Change in Tlco (p=0.014)



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Correlations between change in SUV and change in PFTS

Lung Volumes

FVC	*r* = -0.75, *p*= 0.006
FEV1	*r* = -0.77, *p*= 0.005
TLC	*r* = -0.68, *p*= 0.017

Gas Transfer

TLCO	*r* = -0.71, *p*= 0.016
KCO	*r* = -0.76, *p*= 0.009

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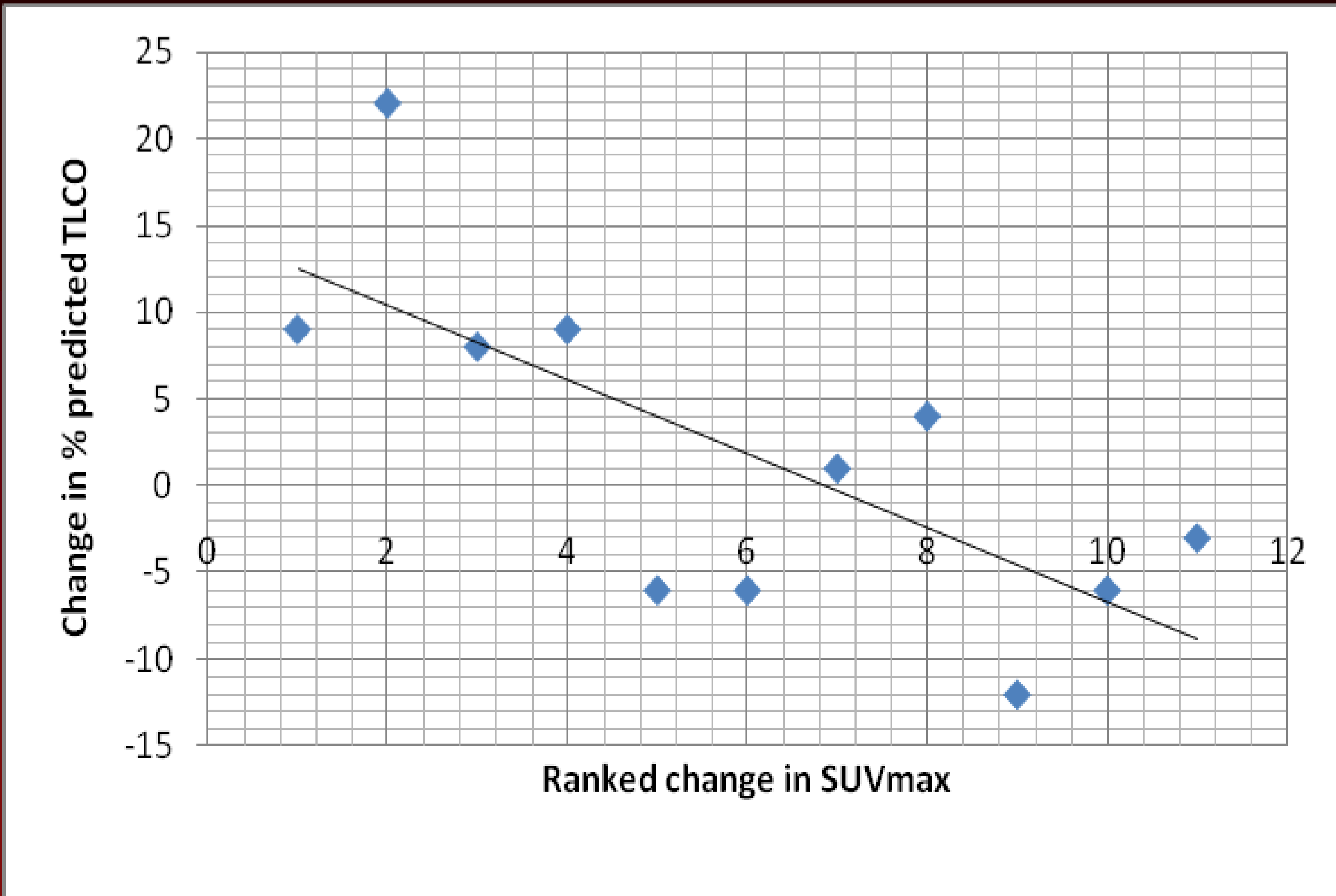
Correlations between Change in SUV and Change in TLco $p=0.016$PFT



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Conclusions

Potential for ^{18}F-FDG PET/CT as a

Predictive and Responsive Biomarker for

Therapeutic planning and monitoring in NSIP patients.

A randomised, placebo-controlled study of omipalisib (PI3K/mTOR) in IPF

- 17 IPF patients (3:1) randomized for PI3K/MTOR inhibitor
- 3 different dose schedules
- FDG PET/CT pre and mid cycle treatment (TBR)
- Dose dependent TBR changes

Eur Respir J 2019; 53: 1801992

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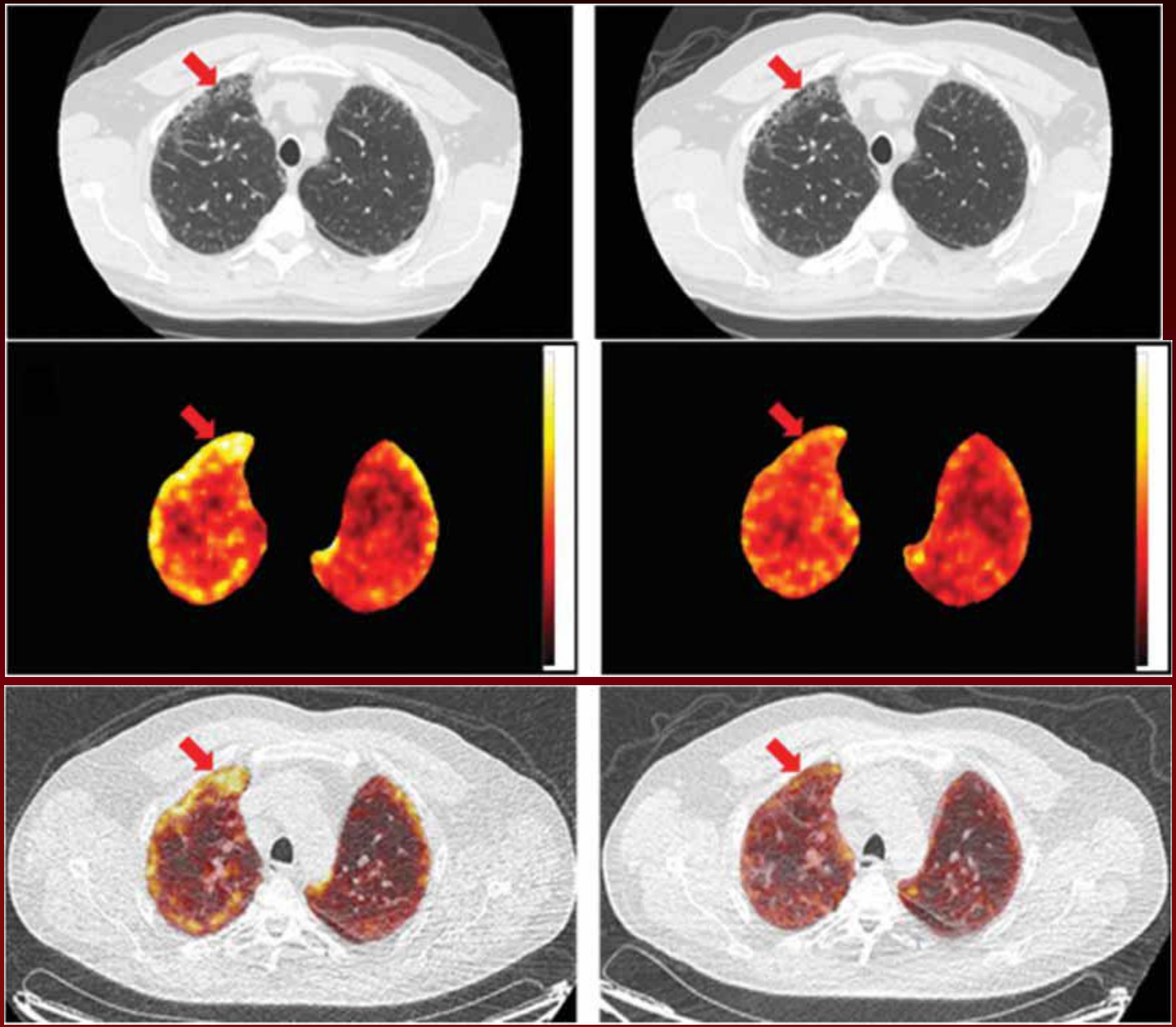
Baseline | Mid Cycle



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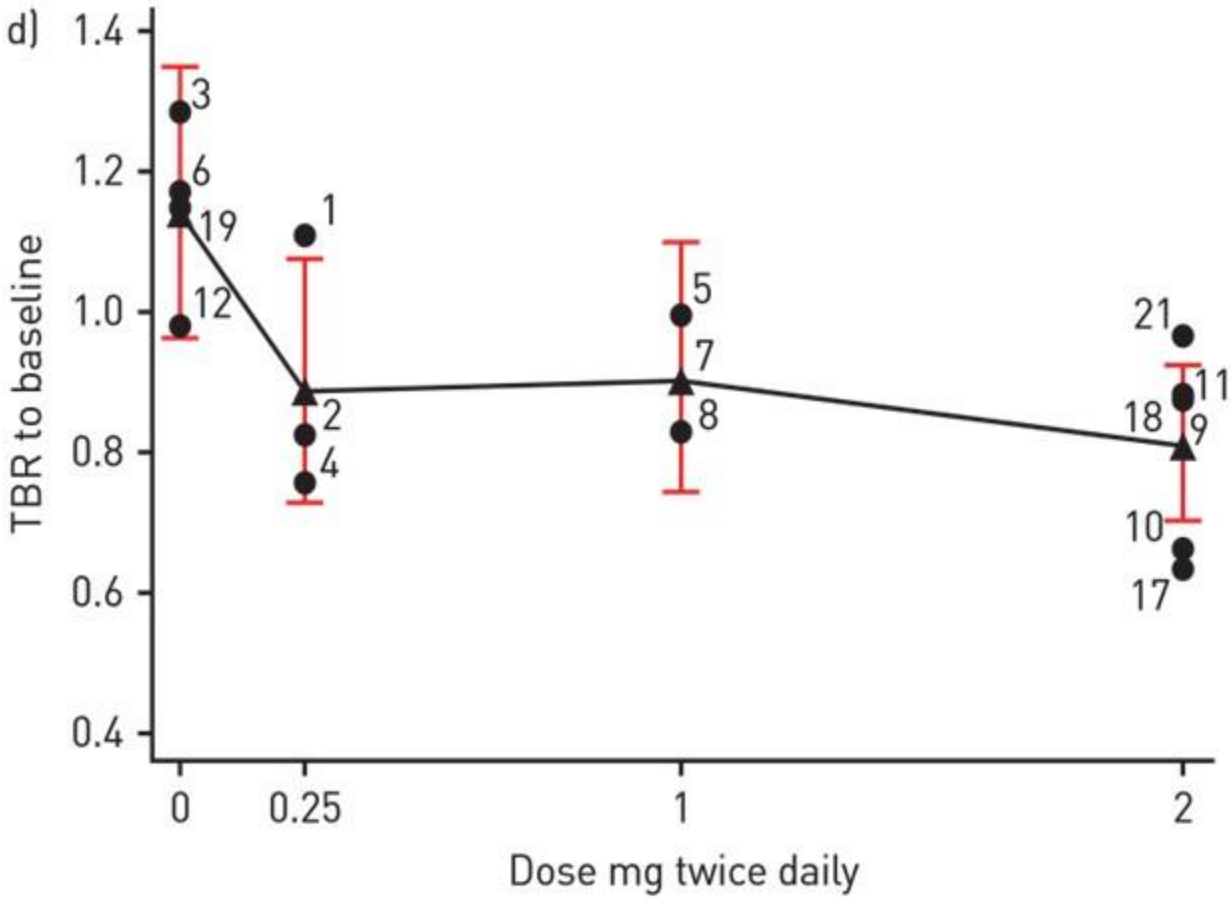
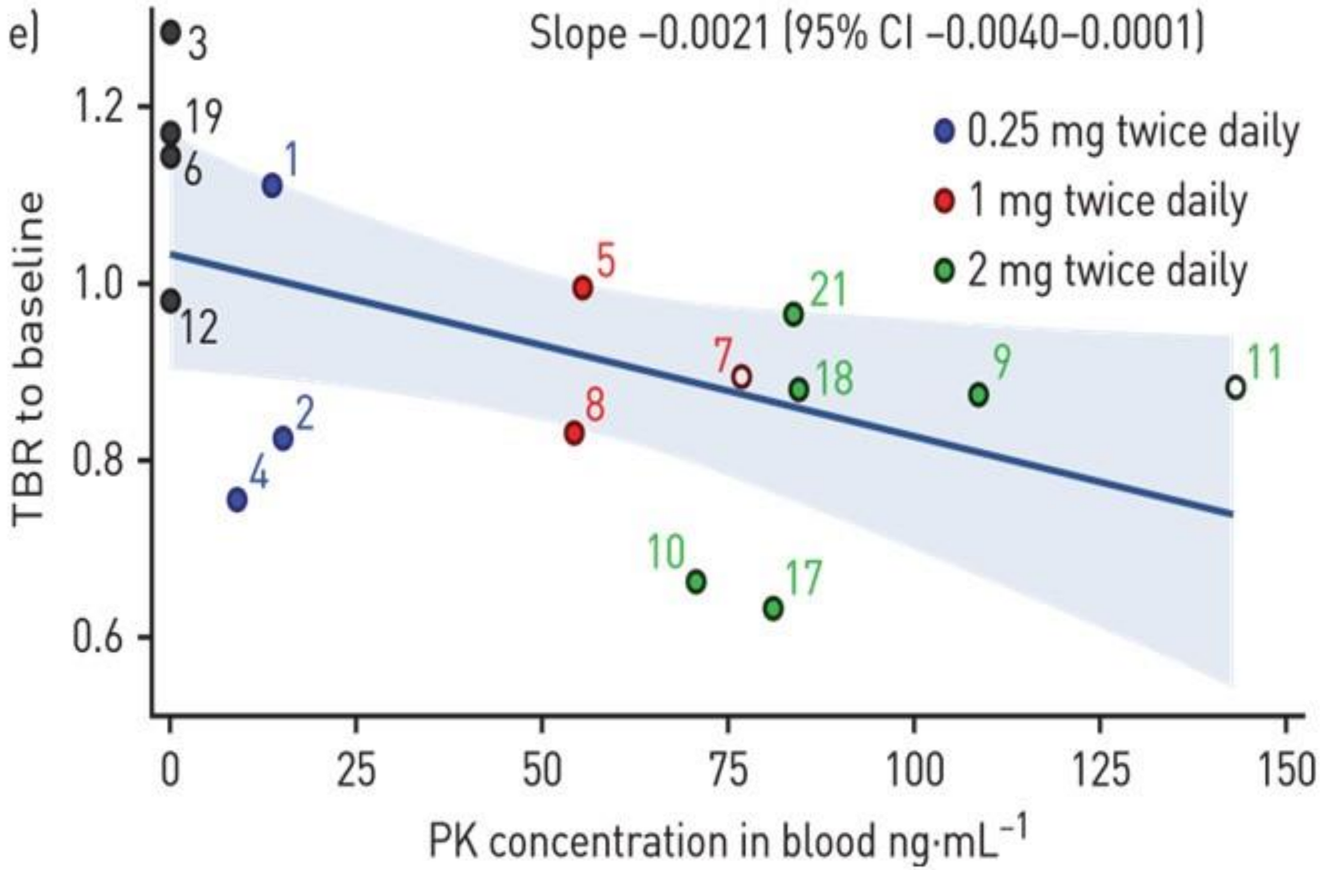

d)
TBR to baseline
1.4
1.2
1.0
0.8
0.6
0.4
0
0.25
1
2
Dose mg twice daily
3
6
19
12
1
2
4
5
7
8
21
11
18
9
10
17


e)
Slope –0.0021 (95% CI –0.0040–0.0001)
0.25 mg twice daily
1 mg twice daily
2 mg twice daily
TBR to baseline
PK concentration in blood ng·mL⁻¹
0.6
0.8
1.0
1.2
0
25
50
75
100
125
150
3
19
6
1
12
5
21
7
18
9
11
2
8
4
10
17

Other PET Techniques in IPF

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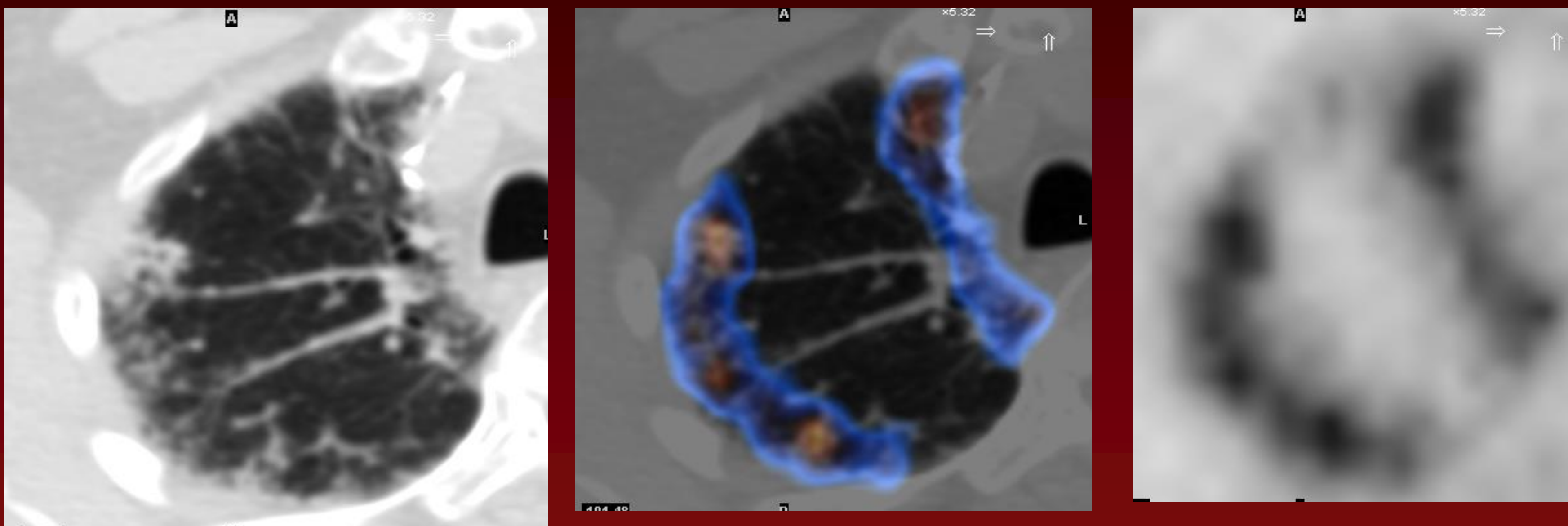
82 yo Female with IPF
^{68}GA DOTATATE
Somatostatin Analogue



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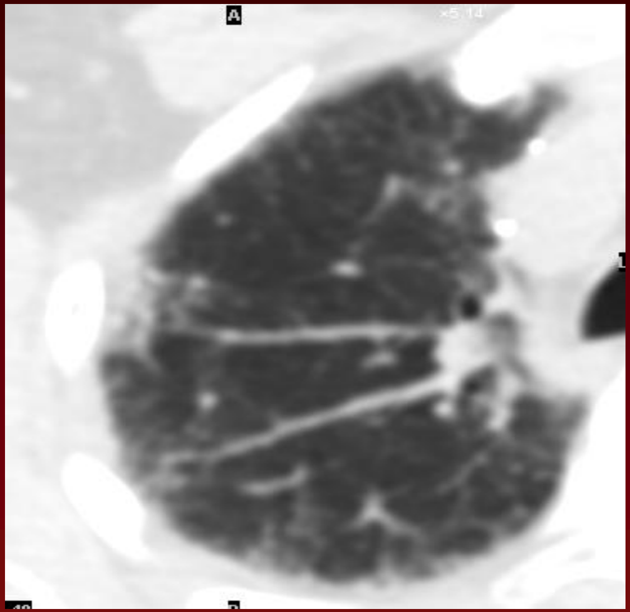
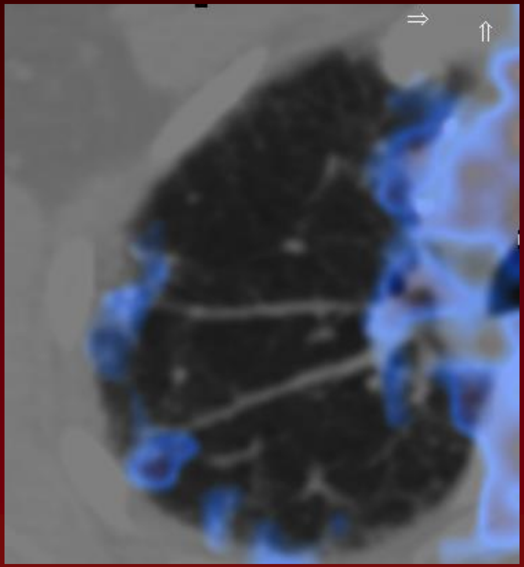
82 yo Female with IPF
FDG





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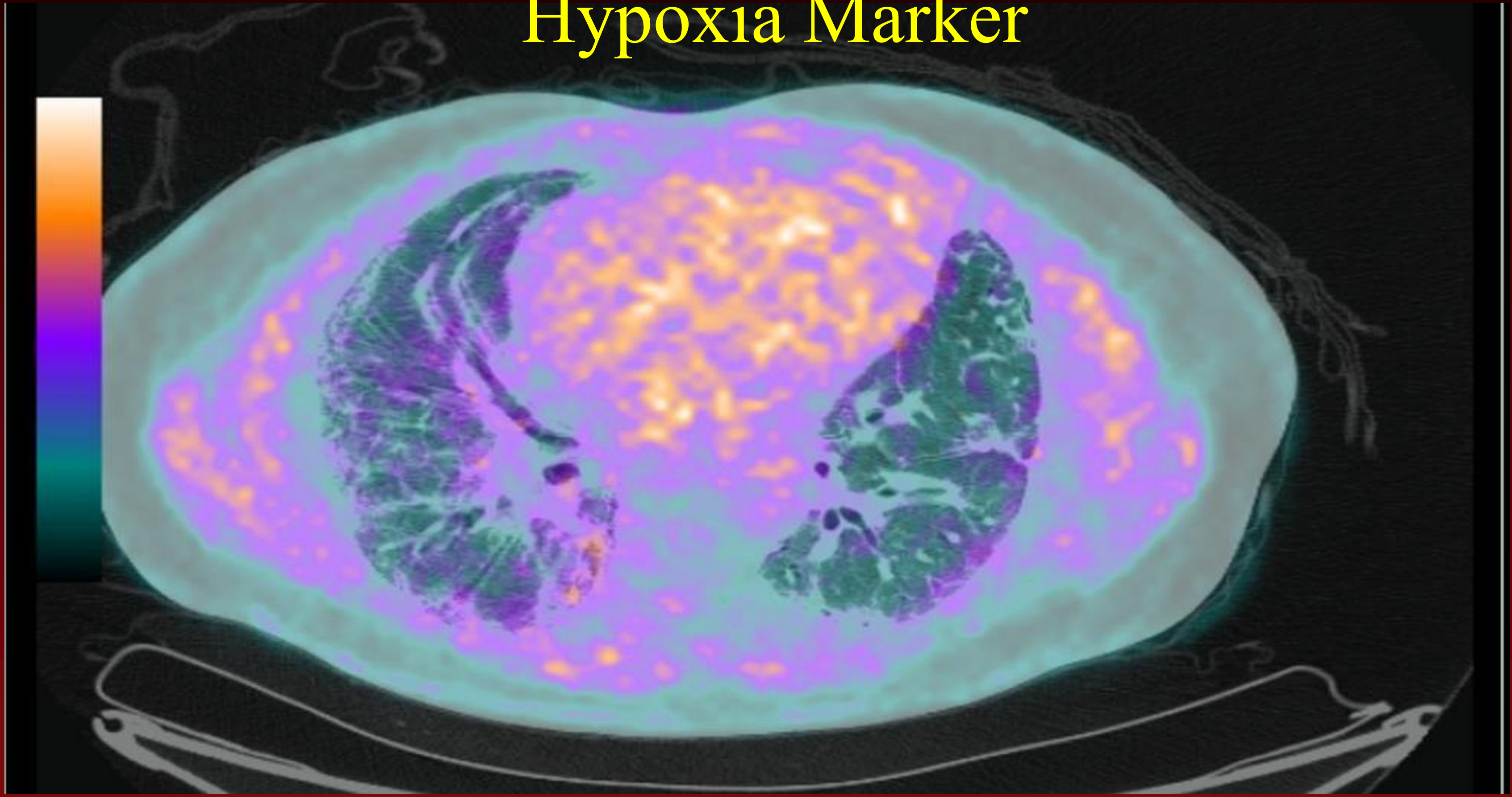
Hypoxia imaging in IPF Using FMISO PET Hypoxia Marker



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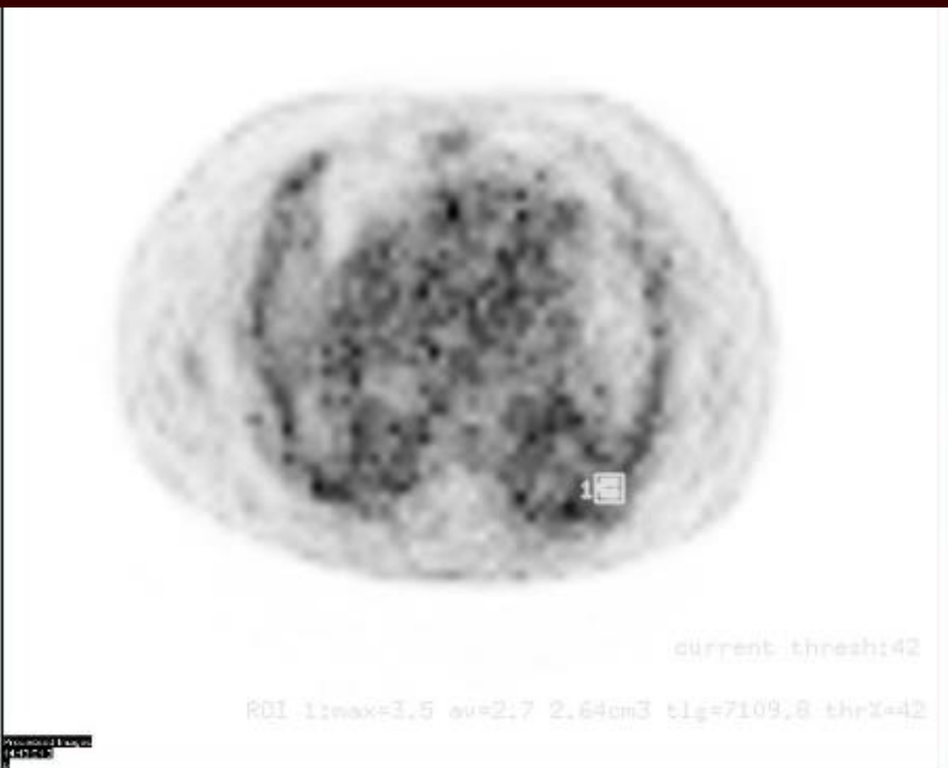
Integrin PET Tracer
Measuring possible fibroblast metabolism



UCL
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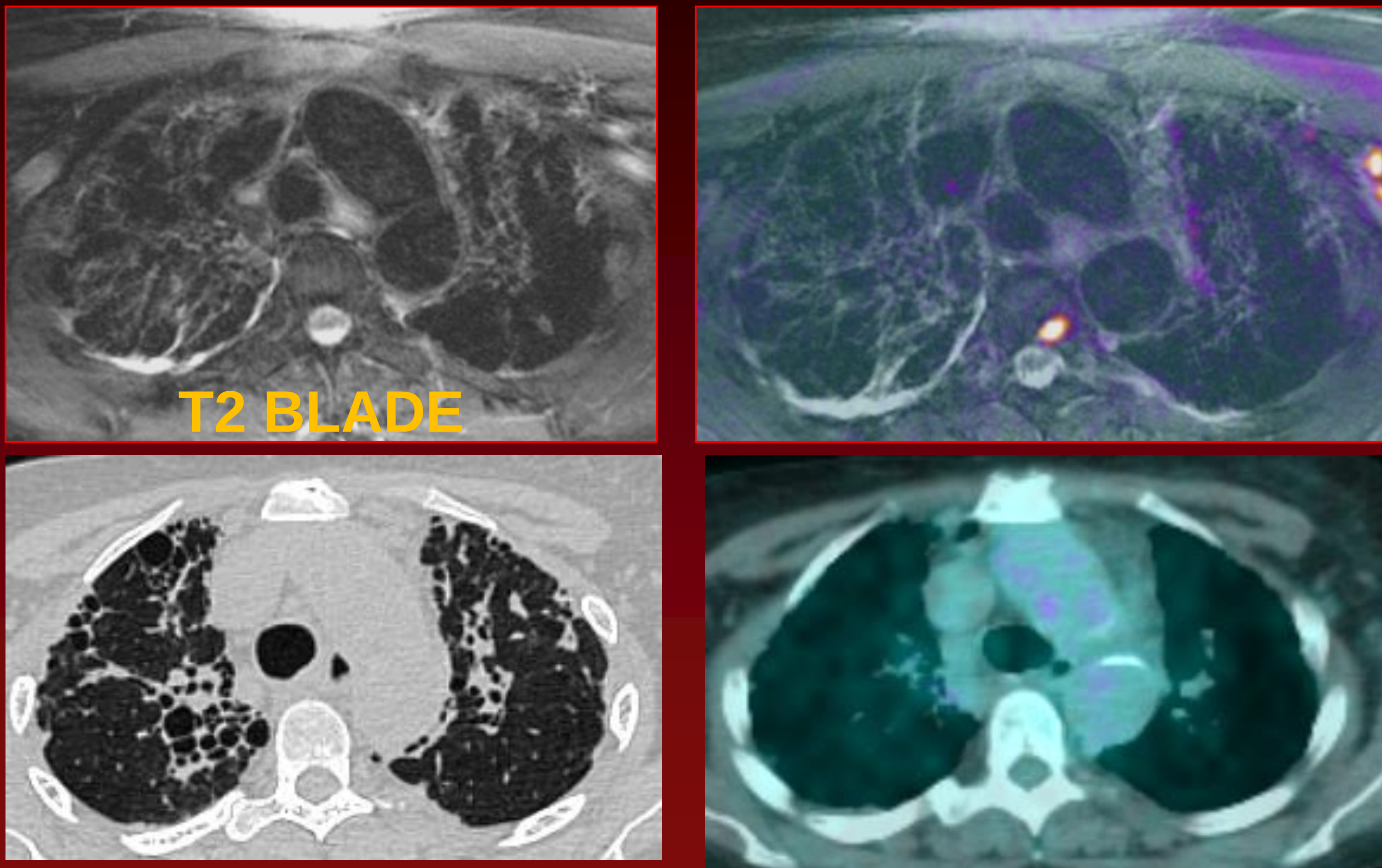
PET/MRI in IPF



HRCT + FDG PET

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Physics Considerations

- Correction for Movement
- Correction for Density
- Correction for Blood Volume
- Correction for Blood Flow
- Correction for Positron Range

- *Eur J Nucl Med Mol Imaging. 2011;38(12)2238-46*
- *Phys Med Biol. 2015 Sep 21;60(18):7387-402*
- *Phys Med Biol. 2016 Apr 21;61(8):3148-63*
- *Phys Med Biol. 2019 Oct 16;64(20):205010.*

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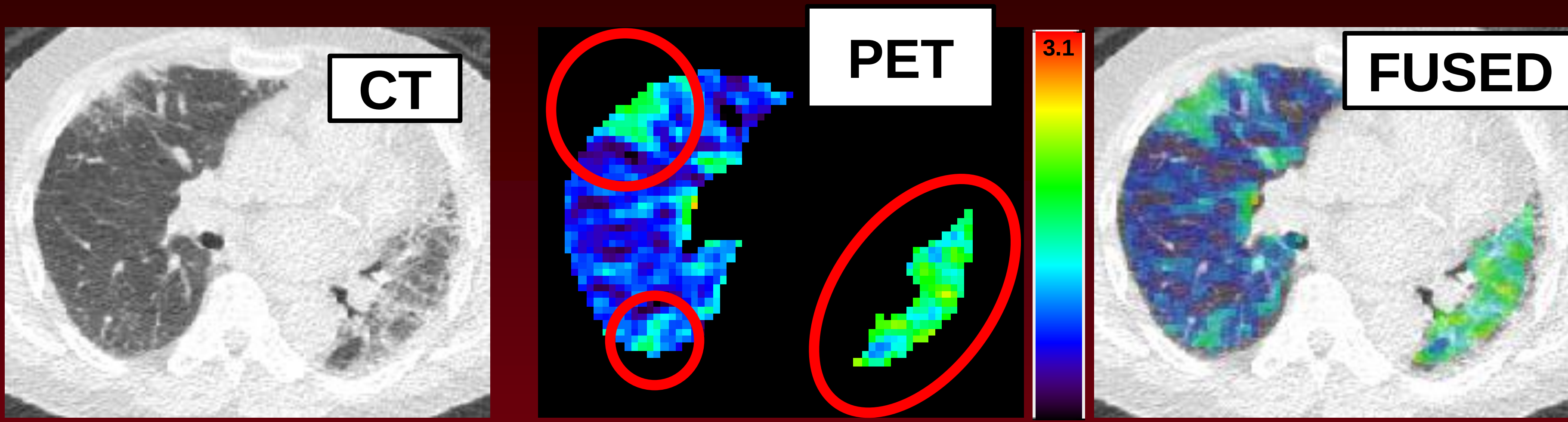
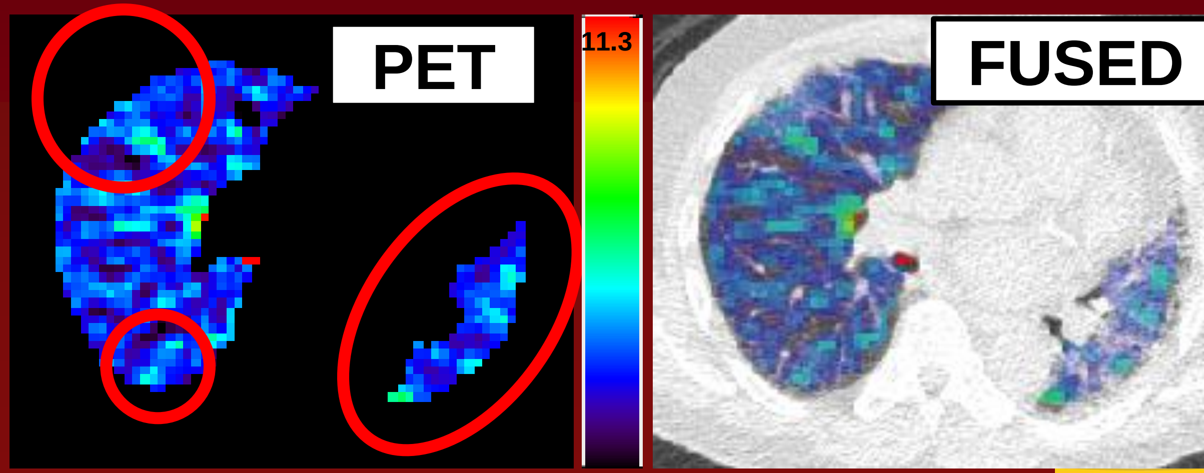
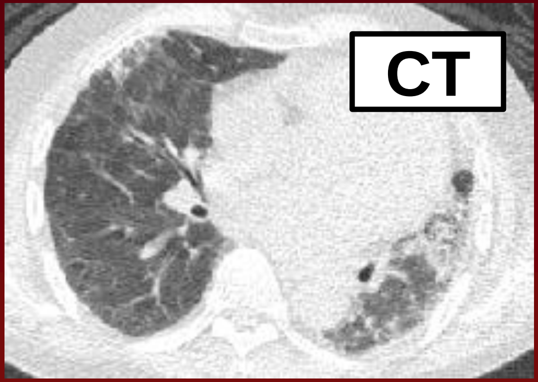
Introduction: Air Faction Correction



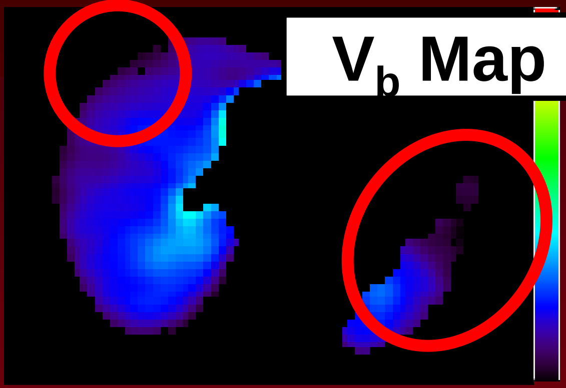
After Air Fraction Correction



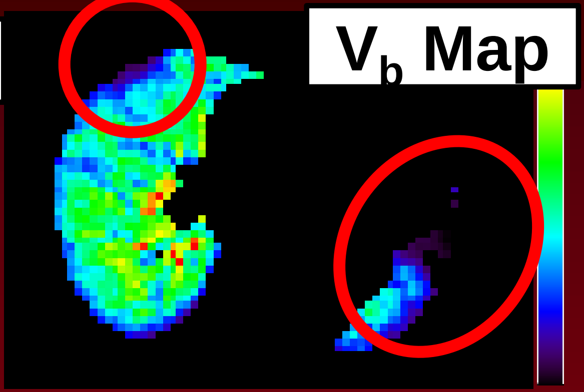
V_b Maps

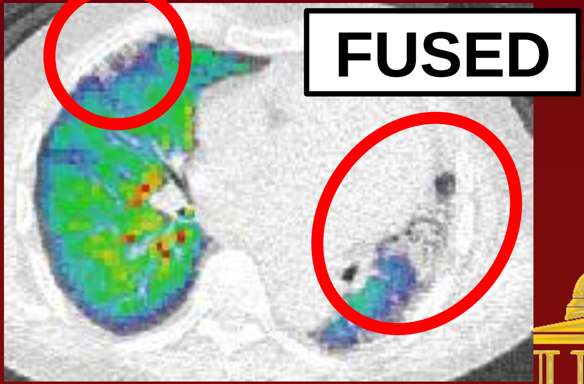


Blood Volume as a fraction of the voxel



Blood Volume as a fraction of the tissue





Areas in which nuclear PET scans may be helpful in clinical ILD

1. Refining mortality prediction
2. Assessing response to therapy
3. Targeting site of lung biopsy
4. Predicting patients at risk of interstitial lung disease

C/O Joanna Porter, Head of UCLH ILD Service

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1. Refining mortality prediction

- Prognostic value
- Timing of referral and listing for lung transplantation
- Stratification for clinical trials

2. Targeting site of lung biopsy

SH

- 52 yr old woman 2012 with shortness of breath.
- Normal CXR 2009
- Radiologically stable 2012-2013
- May 2012: V_A 96% FVC 99% and Dlco 79%
- April 2013: V_A 69% FVC 80% and Dlco 52%
- SUVmax rose from 2.85 to 5.35 over this time.
- Area of highest metabolic activity was targeted for biopsy together with adjacent area.

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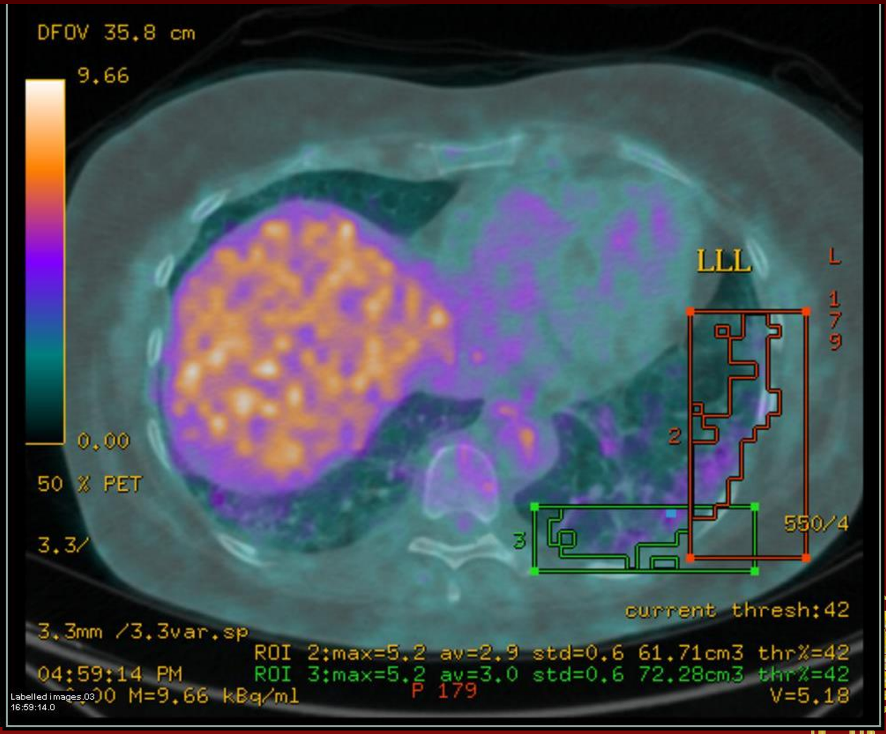
SUVmax right lower lobe 5.5/ left lower lobe 4.7



Summary

- FDG PET gives a signal in all IPF/ILD Patients

- FDG PET signal associated with Mortality

  Prognostic Biomarker

- Short term FDG PET signal is stable in IPF

- Measureable changes in PET signal with treatment in patients with ILD

  Response Biomarker

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Imperial

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Cambridge

Nick Screaton

GSK

Pauline Lukey, Fred Wilson

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