Respiratory Innovation Summit
Dallas, May 17th-22nd

How Artificial Intelligence May Impact Respiratory Diagnosis and Treatment

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Application of Artificial Intelligence
to Imaging Research in Lung Fibrosis

NIHR | National Institute for Health Research

Fibrotic lung disease is a seriously under recognised problem for public health

MORE THAN 40,000

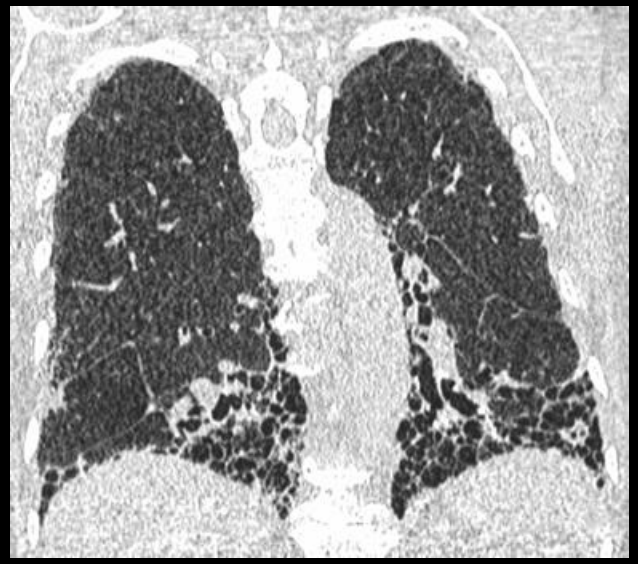
Deaths from idiopathic pulmonary fibrosis in the US since **RIS** in May last year

BREAST CANCER ≈ 41,760

LEUKEMIA ≈ 24,370

Fibrotic lung disease is a collective term for a group of disorders which cause scarring of the lungs

High Resolution Computed Tomography is central to diagnosis and management of fibrotic lung disease



Diagnosis

What type of fibrotic lung disease is this?

Monitoring

Can detect progression or improvement

Useful clinical information in the pixel data, undetectable to the human eye

“Frontiers” in lung fibrosis imaging research

- Early detection/screening
- Disease behaviour prediction
- Monitoring response to therapy
- Patient stratification in drug trials
- Diagnostics

All, in principle, amenable to AI-ML solutions

Early detection

Problem 1: Symptom-based diagnosis

- Symptoms alert clinician
- Established fibrosis on HRCT
- Early intervention “opportunity” missed
- Irrevocable lung function loss…

“Diagnosing coronary artery disease after myocardial infarction has occurred...”

David Lederer, AJRCCM, 2012;185:697-9

Research

Original Investigation

Association Between Interstitial Lung Abnormalities and All-Cause Mortality

Rachel K. Putman, MD; Hiroto Hatabu, MD, PhD; Tetsuro Araki, MD, PhD; Gunnar Gudmundsson, MD, PhD; Wei Gao, MS; Mizuki Nishino, MD; Yuka Okajima, MD; Josée Dupuis, PhD; Jeanne C. Latourelle, DSc; Michael H. Cho, MD, MPH; Souheil El-Chemaly, MD, MPH; Harvey O. Coxson, PhD; Bartolome R. Celli, MD; Isis E. Fernandez, MD; Oscar E. Zazueta, MD; James C. Ross, PhD; Rola Harmouche, PhD; Raúl San José Estépar, PhD; Alejandro A. Diaz, MD; Sigurdur Sigurdsson, BSc, MSc; Elías F. Gudmundsson, MSc; Gudny Eiríksdottír, MSc; Thor Aspelund, MSc, PhD; Matthew J. Budoff, MD; Gregory L. Kinney, PhD; John E. Hokanson, MPH, PhD; Michelle C. Williams, MD; John T. Murchison, MD; William MacNee, MD; Udo Hoffmann, MD, MPH; Christopher J. O'Donnell, MD, MPH; Lenore J. Launer, PhD; Tamara B. Harrris, MD, MS; Vilmundur Gudnason, MD, PhD; Edwin K. Silverman, MD, PhD; George T. O'Connor, MD; George R. Washko, MD; Ivan O. Rosas, MD; Gary M. Hunninghake, MD, MPH; for the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) and COPDGene Investigators

Similar clinical associations to IPF

Putman et al. JAMA, 2016;315:672

ILA's: 7-9 per 100
IPF: 1-63 per 100,000

Searching for patterns which predict progressive fibrosis based on *subclinical* CT abnormalities

Disease behaviour prediction

Problem 2:The progressive fibrotic phenotype

Stable disease with or without treatment

Relentlessly progressive disease: “progressive fibrotic phenotype”

Once disease is established

It is currently not possible to reliably predict which patients will develop progressive fibrosis or remain stable using **BASELINE** information.

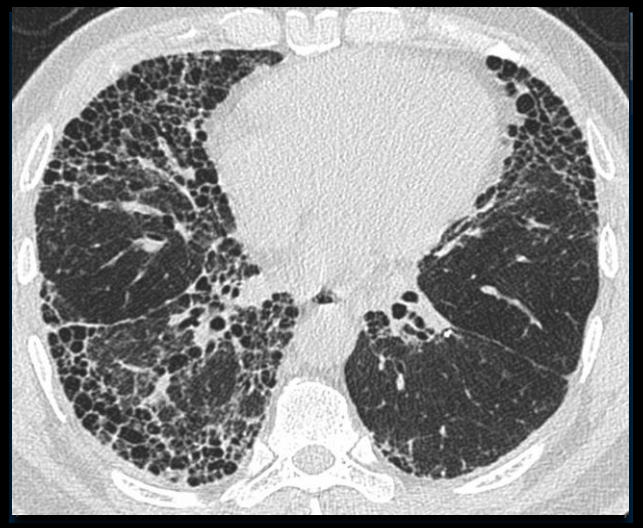
Precious time wasted (more than 1 year)

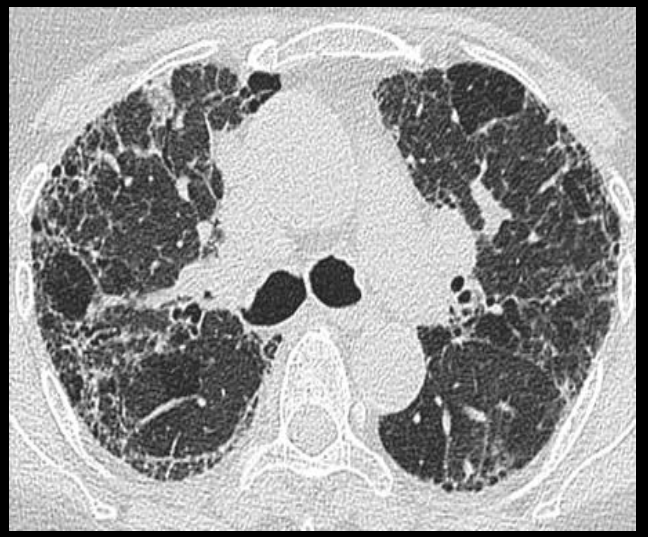
More lung biopsies (2%, 30 day mortality)

Patient exposure to harmful medications

Increased healthcare costs

"PROGRESSIVE"





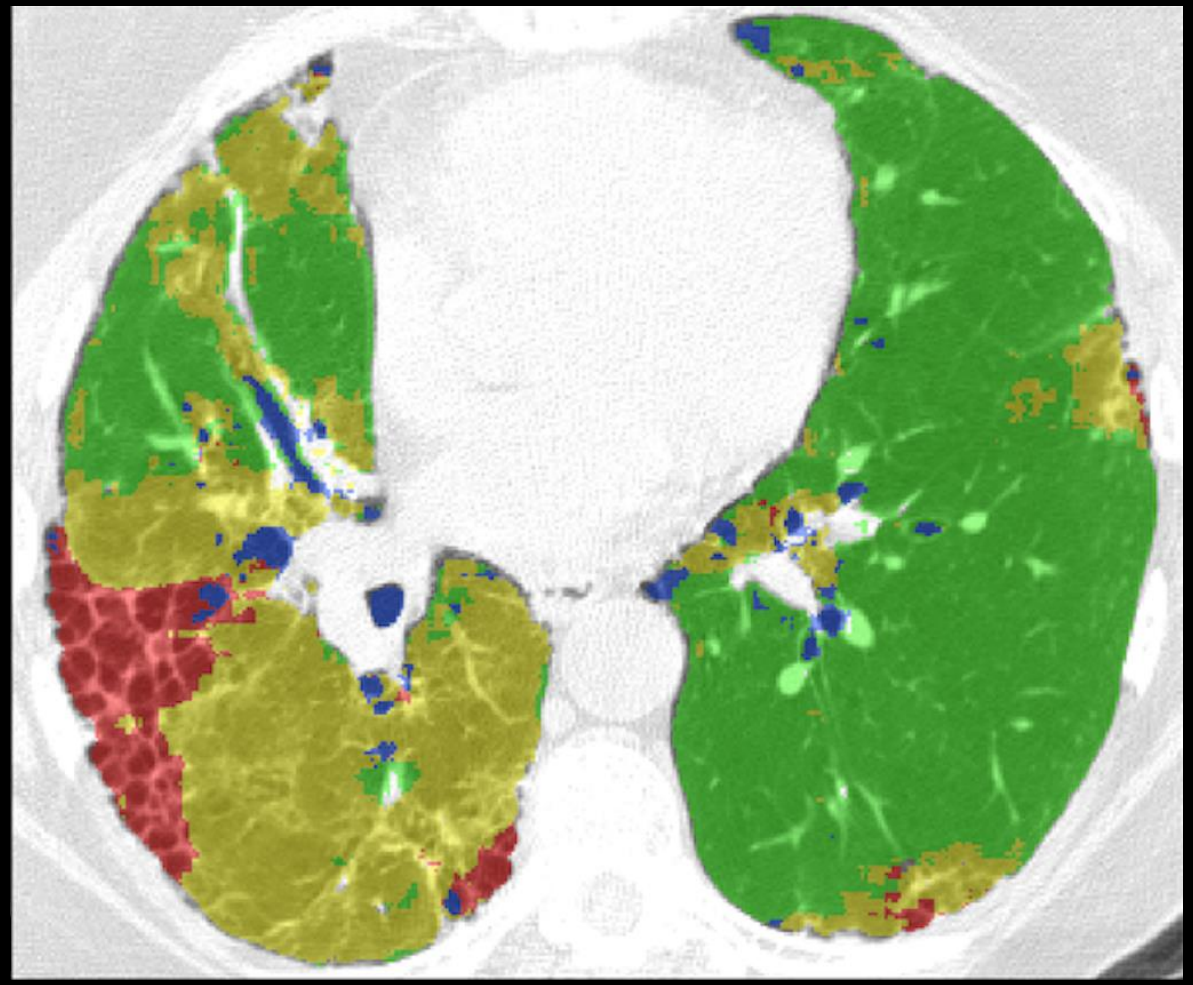
"STABLE"

Both are disease phenotyping problems amenable to **DEEP LEARNING**

Training label
ILA progression?
FLD progression?

FIND PATTERNS

PREDICTIVE ALGORITHM



Disease quantification using deep learning

Monitoring subtle disease progression or response to therapy

Humphries SM, et al Radiology. 2017 May 10;285:270-8
Humphries SM, et al Eur Respir J 2018; 52:1801384

Diagnostics

Problem 3: Experts often cannot agree

ORIGINAL ARTICLE

Interobserver agreement for the ATS/ERS/JRS/ALAT criteria for a UIP pattern on CT

Simon L F Walsh,[1] Lucio Calandriello,[2] Nicola Sverzellati,[3] Athol U Wells,[4] David M Hansell,[5] on behalf of The UIP Observer Consort

Walsh et al, Thorax 2016;71:45-51

IMPACT:

Imaging plays a major role in assessing drug trial eligibility

ELIGIBLE → ✗ IMAGING MISREAD

ELIGIBLE → ✓ ELIGIBLE

INELIGIBLE → ✓ IMAGING MISREAD

INCREASED SCREEN FAILURES

Longer and more expensive drug trials

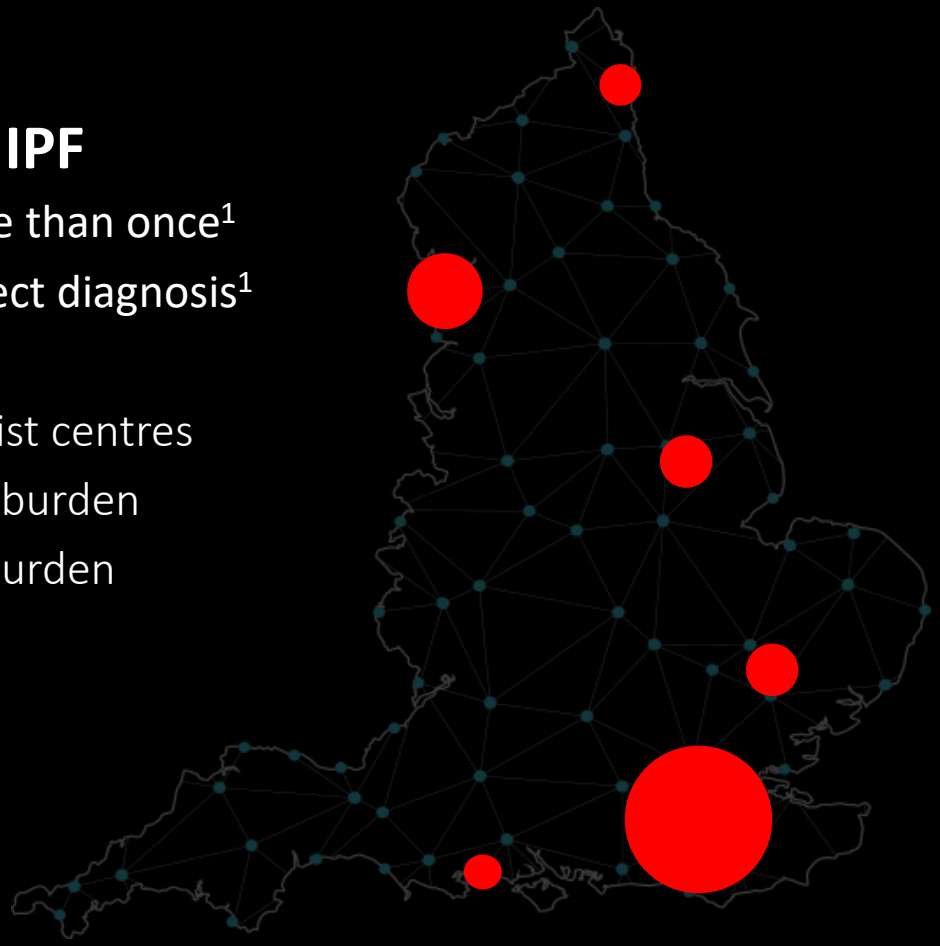
IMPACT:

Misdiagnosis in IPF

>50% once, 33% more than once[1]

>1 year to reach correct diagnosis[1]

- Reliance on specialist centres
- Increased financial burden
- Increased patient burden



Presents an opportunity for automated diagnostic support in IPF

[1]*Cosgrove et al. BMC Pulmonary Medicine 2018;18:9*

Our early work

THE LANCET
Respiratory Medicine

Deep learning for classifying fibrotic lung disease on high-resolution computed tomography: a case-cohort study

Simon LF Walsh, Lucio Calandriello, Mario Silva, Nicola Sverzellati

Summary

Background Based on international diagnostic guidelines, high-resolution CT plays a central part in the diagnosis of fibrotic lung disease. In the correct clinical context, when high-resolution CT appearances are those of usual interstitial pneumonia, a diagnosis of idiopathic pulmonary fibrosis can be made without surgical lung biopsy. We investigated the use of a deep learning algorithm for provision of automated classification of fibrotic lung disease on high-resolution CT according to criteria specified in two international diagnostic guideline statements: the 2011 American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society (JRS)/Latin American Thoracic Association (ALAT) guidelines for diagnosis and management of idiopathic pulmonary fibrosis and the Fleischner Society diagnostic criteria for idiopathic pulmonary fibrosis.

Lancet Respir Med 2018

Department of Radiology, King's College Hospital Foundation Trust, London, UK (S L F Walsh MD); Department of Radiology, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy (L Calandriello MD); and Department of Medicine and

Our early work

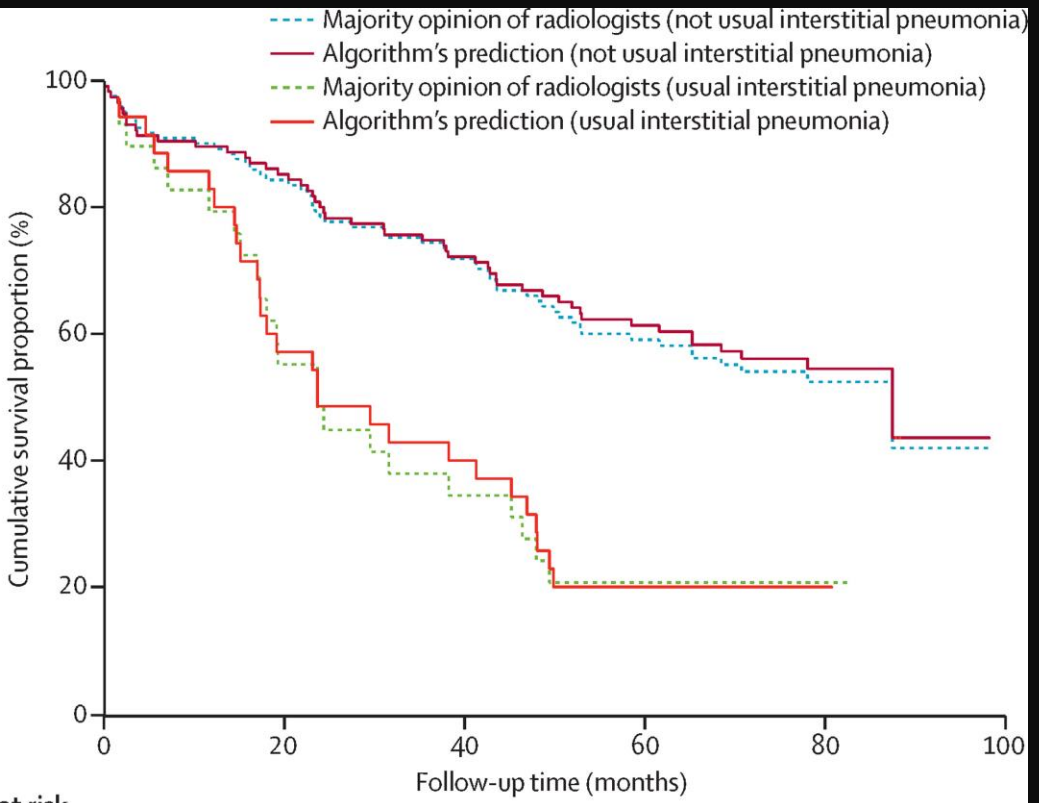
Performance classifying HRCTs based on ATS/ERS/JRS/ALAT IPF guideline criteria

92

Thoracic radiologists

Out performed on
diagnosis and outcome

Can be deployed anywhere easily for reproducible, expert-level diagnosis support



Number at risk						
Majority opinion of radiologists (not usual interstitial pneumonia)	121	102	87	64	30	0
Algorithm's prediction (not usual interstitial pneumonia)	115	98	83	63	31	0
Majority opinion of radiologists (usual interstitial pneumonia)	29	16	10	5	2	0
Algorithm's prediction (usual interstitial pneumonia)	35	20	14	6	1	0

← Not UIP

← UIP

Algorithm provided equivalent prognostic discrimination between "UIP vs not UIP" than majority opinion of **92 thoracic radiologists**

THE TIMES

Algorithm rivals doctors in lung disease diagnosis

Meeting Coverage > ERS

Machine Tops Humans in Fibrotic Lung Disease Classification

— Nearly instantaneous results also matched prognostic abilities

PARIS -- Robots scored another win against humans,

Podcast: Deep learning and fibrotic lung disease

"This is human plus machine performance.....we are not trying to replace radiologists."

THE LANCET Respiratory Medicine

The best science for better lives

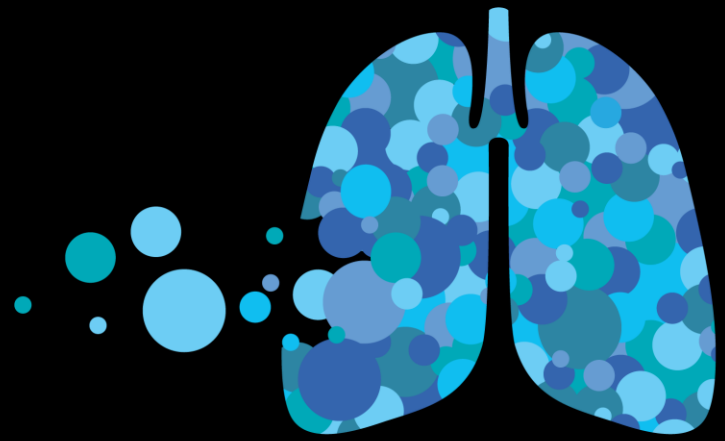
AUGMENTED INTELLIGENCE

"Automated decision support"

AI-based biomarker research in IPF

Issues – hype and real questions

- ***The "black box" issue***
  - Overstated or critically important?
  - Other black boxes in medicine
- ***The "buy-in" issue***
  - Data bias and algorithm generalizability
  - Accountability and governance
- ***The "data" issue***
  - How much is needed?
  - Common datasets for benchmarking
    - No comparative research in QCT
    - Human vs machine covered. What about machine vs machine?
    - The Cancer Imaging Archive



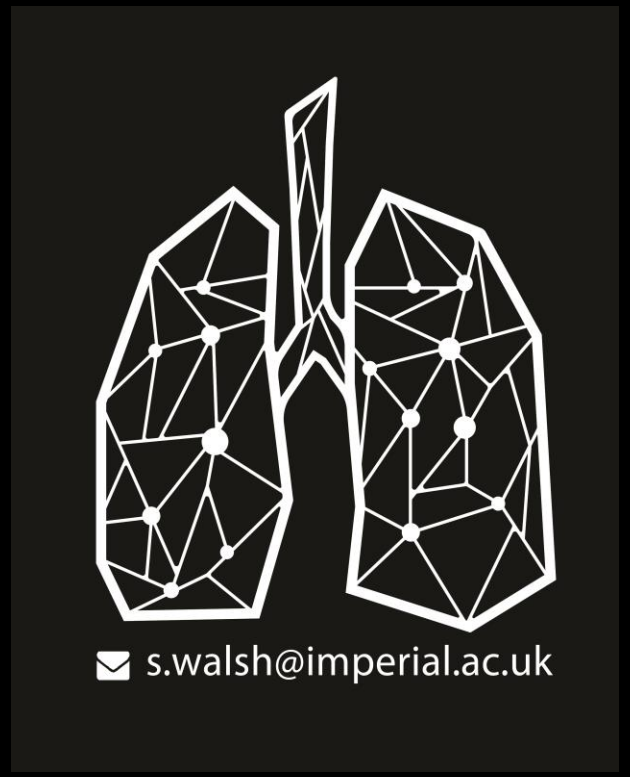
OPEN SOURCE IMAGING CONSORTIUM

against ***Interstitial Lung Disease***

DEVELOP A LARGE AND DIVERSE **IMAGING REPOSITORY**

ENGAGE WIDER MACHINE LEARNING COMMUNITY

INCREASE **COLLABORATION**



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