ILD highlights from the ERS 2023 Congress

(Tiêu điểm về bệnh phổi mô kẽ tại Hội nghị Hô hấp Châu Âu 2023)

Milan, 09 – 13 tháng 09, 2023

Boehringer Ingelheim

External report, SC-CRP-14278, NP-VN-100019

Contents

Jump to section

Abbreviations are defined in the slide notes

AI-derived imaging biomarkers

(Biomarkers hình ảnh học có nguồn gốc trí tuệ nhân tạo)

Boehringer Ingelheim

A deep learning algorithm for predicting disease progression in IPF[1] (Walsh S *et al.*)

(Nghiên cứu sâu về thuật toán giúp dự đoán bệnh tiến triển trong xơ phổi vô căn – IPF)

- This **retrospective study** aimed to investigate the use of a deep learning algorithm for predicting the risk of progression in patients with IPF based on baseline HRCT data
  - Progression was defined as a 10% decline in FVC % predicted at 12 months, death or transplantation
- The algorithm was trained using HRCTs from the OSIC database (**N=731**) and tested using data from the AIPFR (**N=501** patients with suspected IPF)
  - The prognostic utility of the algorithm was evaluated against conventional measures of disease severity (eg visual-based total fibrosis extent) and SOFIA-based UIP probability scores[2]
- Using the full AIPFR test data set, the algorithm independently predicted progression (HR: 1.02; *P*<0.0001), even when controlling for total fibrosis extent (HR: 1.03; *P*<0.0001)
  - A 1% increase in the probability of PPF was associated with a 2% increase in the risk of mortality
- Progression probability scores generated by the algorithm were then converted to PPF_PIOPED scores using the PIOPED diagnostic probability thresholds*[3]
- Multivariable analysis revealed that PPF_PIOPED scores, SOFIA UIP PIOPED scores and total fibrosis extent independently predicted progression, and hence mortality (**Table**); therefore, PPF_PIOPED scores were able to predict the risk of mortality, even when controlling for CT phenotype or disease severity
  - In a sub-analysis, PPF_PIOPED scores predicted mortality in patients with an 'indeterminate for UIP' HRCT pattern (n=82; HR 8.06, *P*<0.0001) and patients who underwent lung biopsy (n=86; HR 2.27; *P*<0.0001)
- When using the AIPFR criteria to define progression,† an increase in PPF_PIOPED score by one category was associated with a three-fold increased likelihood of disease progression (OR: 3.21; *P*<0.0001), even when controlling for total fibrosis extent (OR: 1.04; *P*<0.0001)

Table. Multivariable analysis of PPF_PIOPED scores, SOFIA-based UIP PIOPED scores and total fibrosis extent in predicting the risk of mortality in patients with IPF from the AIPFR

Disease severity

CT phenotype

PPF probability and…

Variable (n=497)	HR	*P* value	95% CI
PPF_PIOPED scores	2.35	<0.0001	1.88–2.93
SOFIA UIP PIOPED scores	1.22	<0.0001	1.01–1.03
Total fibrosis extent	1.02	<0.0001	1.11–1.34

Author conclusion: Deep learning may be used to identify patients with suspected IPF at risk of progression at 12 months.

*Absent (0–4% [score 1]); low probability (5–29 % [score 2]); intermediate probability (30–69% [score 3]); high probability (70–99% [score 4]); pathognomonic (100% [score 5]); †10% decline in FVC % predicted at 12 months, a 15% decline in DL_{CO} % predicted (sustained at 18 months), transplantation or death

1. Walsh S *et al.* Oral presentation at ERS International Congress 2023:OA4852; 2. Walsh S *et al. Lancet Respir Med* 2018;6:837–45; 3. PIOPED investigators. *JAMA* 1990;263:2753–9

e-Lung biomarkers as predictors of clinical outcome in patients with non-IPF ILDs

(E-lung biomarkers được dùng như những dự đoán về kết cục lâm sàng trên bệnh nhân bệnh phổi mô kẽ không phải IPF)

The automated e-Lung CT algorithm is more prognostic than lung function in patients with non-IPF fibrotic ILD; a validation study[1] (George P *et al.*; Sponsor: Brainomix)

- e-Lung produces automated outputs reflecting ILD extent on CT, including WRVS and GGO score[2]
- The aim of this **retrospective study** was to validate baseline WRVS as a predictor of TFS and FVC decline over 12 months in two independent cohorts of patients with non-IPF fibrotic ILDs (test cohort: **n=180**; validation cohort: **n=172**)
  - Using data from the OSIC database,[3] CT scans and contemporaneous FVC data were analyzed using e-Lung
- After adjusting for age and lung function, baseline WRVS was more strongly associated with TFS than FVC, both in the individual cohorts and when pooled (pooled C-indices: 0.72 [WRVS] and 0.65 [FVC])
  - When dichotomized at the medians, patients with a WRVS score ≥7.3 had a significantly greater risk of mortality than patients with a WRVS score <7.3 (HR [CI]: 3.6 [2.4–5.3]; *P*<0.001; **Figure 1**)
- Baseline WRVS was shown to be more than twice as predictive of a ≥10% future decline in FVC over 12 months (OR [CI]: 5.3 [2.6–11.8]; *P*<0.001) than baseline FVC (OR [CI]: 2.2 [1.2–4.4]; *P*=0.019)

Novel e-Lung CT biomarkers combine to provide higher prognostic discrimination than FVC in patients with non-IPF fibrotic ILD[2] (George P *et al.*; Sponsor: Brainomix)

- Similarly, this **retrospective study** using OSIC data explored the relationship between e-Lung GGO score, at baseline and over time, with survival in patients with non-IPF fibrotic ILDs (**N=109**)
- Patients with a low baseline GGO score in addition to a high baseline WRVS had a significantly higher risk of mortality compared to patients with 'normal' scores (HR [CI]: 4.0 [1.77–9.04]; *P*=0.00032)
- In contrast, patients with an increase in both GGO and WRVS on serial CT scans had a significantly greater risk of mortality vs patients with 'normal' scores (HR [CI]: 2.96 [1.24–7.06]; *P*=0.01; **Figure 2**)

Figure 1. Kaplan–Meier curve of survival probability in patients with non-IPF fibrotic ILD with a baseline WRVS ≥ or <7.3 for the pooled dataset

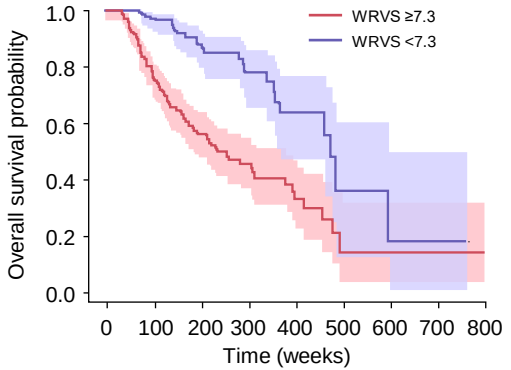
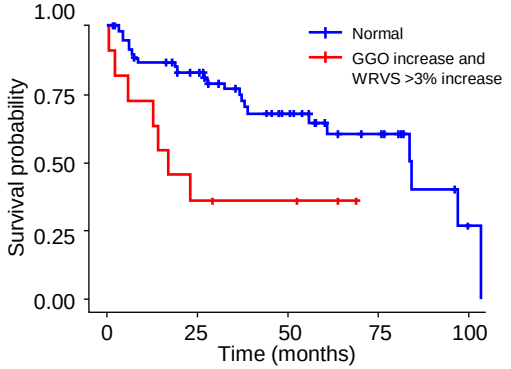


Figure 2. Kaplan–Meier curve of survival probability in patients with non-IPF ILD with normal vs increased GGO and WRVS on serial CT scans



1. George P *et al.* Oral presentation at ERS International Congress 2023: OA850; 2. George P *et al.* (presented by Devaraj A) Oral presentation at ERS International Congress 2023: OA855;
3. Open Source Imaging Consortium. Available at: https://www.osicild.org/ (accessed September 2023)

A novel diagnostic tool for ILD
(Công cụ chẩn đoán ILD mới)

Boehringer Ingelheim

The use of electronic nose (eNose) technology in the detection and differential diagnosis of ILD *(Sử dụng công nghệ "mũi điện tử" phát hiện và chẩn đoán phân biệt bệnh phổi kẽ)*

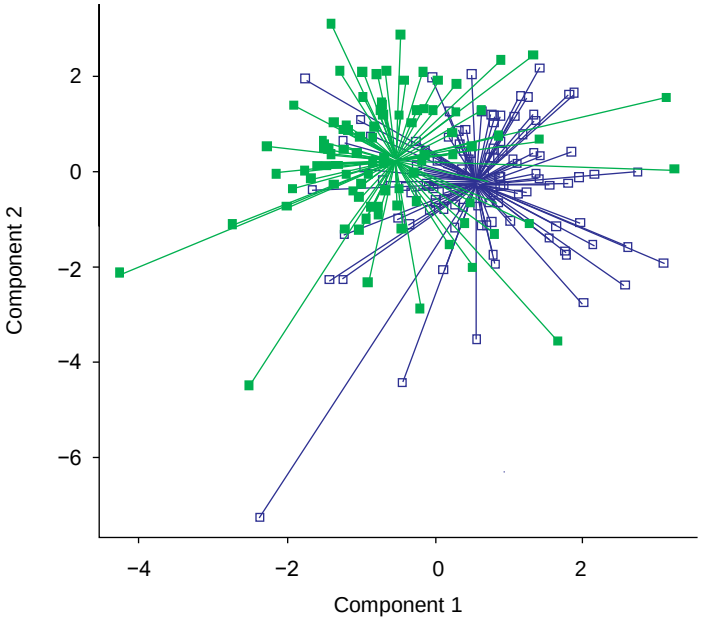
Electronic nose technology detects CTD-ILD[1] (Moor K *et al.*)

- This **cross-sectional, single-center study** performed exhaled breath analysis using eNose technology and assessed its ability to differentiate patients with CTD-ILD (**n=123**) from patients with IPAF (**n=25**) and other forms of ILD (**n=122**)
  - eNose sensors analyzed the 3000 types of VOCs found in exhaled breath and produced a breath profile
- The eNose successfully discriminated between patients with CTD-ILD and patients with other ILDs, with an AUC of 0.92 for the test set, and between patients with CTD-ILD and IPAF, with an AUC of 0.99 for the test set
- Similar discriminative ability was seen in a follow-up study in patients with SSc (**N=223**), where the eNose was able to differentiate between patients with SSc-ILD and SSc without ILD with an AUC of 0.84 for the test set (**Figure**)
  - These results were not influenced by the type of SSc, antibodies, gender, smoking status or the use of immunosuppressive drugs

Electronic nose technology differentiates ILDs from other chronic respiratory diseases[2] (Van der Sar IG *et al.*)

- This **cross-sectional, multicenter study** evaluated whether eNose technology accurately distinguishes patients with ILD (**n=161**) from patients with asthma (**n=65**), COPD (**n=50**) and lung cancer (**n=46**)
- The eNose distinguished patients with ILD from the full cohort of patients with asthma, COPD and lung cancer, with an AUC of 0.99 for the test set
  - Additionally, the eNose showed high accuracy in differentiating ILD from each individual respiratory disease, with AUCs of 1.00, 0.96 and 0.98 (for the test set) for asthma, COPD and lung cancer, respectively

Figure. Breath profiles of patients with SSc-ILD vs SSc without ILD



1. Moor K *et al.* Oral presentation at ERS International Congress 2023: OA852; 2. Van der Sar IG *et al.* Oral presentation at ERS International Congress 2023: OA1427