Novel Machine Learning Algorithm Predicts All-cause Mortality in the National Lung Screening Trial

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Rationale

- There has been widespread interest in applying machine learning algorithms to chest computed tomography (CT) to improve early detection of interstitial lung disease (ILD) in at-risk populations.
- Computer-Aided Lung Informatics for Pathology Evaluation and Ratings (CALIPER) quantifies key features of fibrotic lung disease using traditional machine learning techniques (i.e. nearest neighbor).
- We compared the ability of **CALIPER** and a novel deep-learning based software, **DeepLTA** (Imbio Inc) to assess risk of mortality in current and former smokers in the National Lung Screening Trial (NLST).

Study Population and Methods

- NLST enrolled 12,247 current and former smokers 55-74 years old with a minimum 30-pack-year smoking history at 33 US sites and available data for multivariable modeling over 6 years of follow-up
- Combined fibrosis score: reticular opacity and honeycombing
- Total % ground glass and reticular opacity, honeycombing and combined fibrosis score were generated using CALIPER and DeepLTA
- The outcomes studied included incident lung cancer, lung cancer mortality, and all-cause mortality

Results

Table 1: Subject Demographics

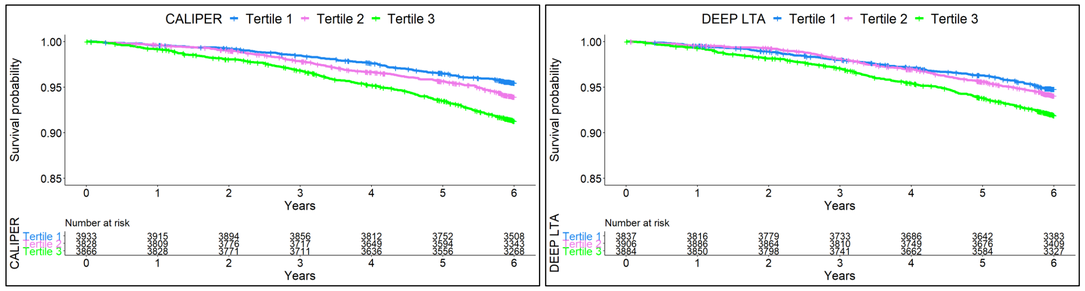
	Overall (N=11627)
Age	61.4 (5.0)
Race	
Hispanic or other	408 (3.5%)
Non-Hispanic Black	631 (5.4%)
Non-Hispanic White	10588 (91.1%)
Male	6861 (59.0%)
BMI, kg/m2	28.0 (5.0)
Smoking pack years	56.4 (23.9)
Quit years	3.8 (5.0)
Personal history of cancer	476 (4.1%)
Family history of lung cancer	2591 (22.3%)

Data are presented as means (standard deviation) for continuous variables and counts (percentages) for categorical variables.

Results

Figure 1: Kaplan Meier Curves of All-cause Mortality by Tertiles of Combined Fibrosis Score

CALIPER **DeepLTA**



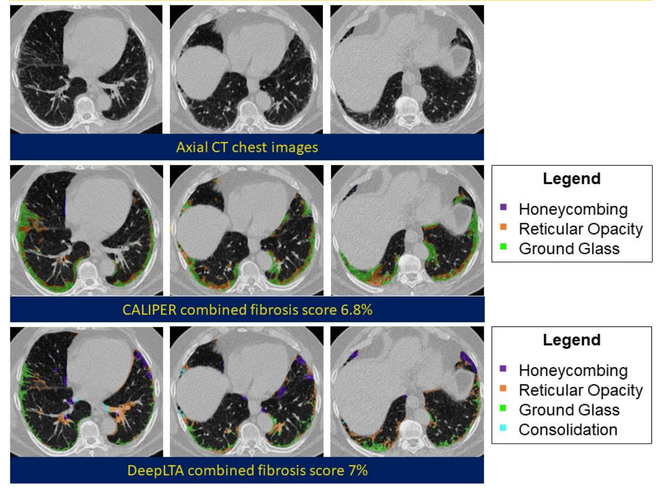
Multivariable Cox Regression Models of All-cause Mortality

- Model was adjusted for: age, race, highest education attained, gender, BMI, tobacco use (intensity and duration), time since smoking cessation, percent low attenuation area, and personal history of cancer and family history of lung cancer.

All-Cause Mortality								
	DeepLTA				CALIPER			
	Hazard Ratio, HR	95% Confidence Interval, CI	p value	C statistic	Hazard Ratio, HR	95% Confidence Interval, CI	p value	C statistic
Ground Glass Opacity	1.03	1.01 – 1.06	< 0.01	0.68	1.02	1.01 - 1.03	< 0.01	0.68
Reticular Opacity	1.17	1.10 – 1.25	< 0.01	0.68	1.05	1.03 - 1.08	< 0.01	0.68
Honeycombing	1.08	1.01 – 1.15	0.02	0.68	2.93	1.86 - 4.62	< 0.01	0.68
Combined Fibrosis Score	1.10	1.06 – 1.15	< 0.01	0.68	1.05	1.03 – 1.07	< 0.01	0.68

Results

Figure 2: CALIPER vs DeepLTA Images



Discussion

- For both DeepLTA and CALIPER an increased risk of death was observed for each percent increase in ground glass opacity, reticular opacity, honeycombing and the combined fibrosis score.
- Associations with lung cancer mortality did not reach statistical significance. Quantitative measures of fibrosis were not associated with incident lung cancer.
- Early, automated detection of ILD in a large at-risk screening population allows for timely follow-up and consideration of anti-fibrotic treatment

Conclusions

Both CALIPER and the novel deep-learning algorithm DeepLTA identified features of ILD on LDCT that were associated with risk of all-cause mortality in an at-risk screening population of current and former smokers.

Acknowledgements

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