Growth patterns of screen-detected malignant pulmonary nodules: Accuracy of doubling-time models

A. Creamer[1], C. Horst[1], J. Dickson[1], S. Tisi[1], H. Hall[1], P. Verghese[1], R. Prendecki[1], A. Bhamani[1], J. Mccabe[1], J. Teague[2], A. M. Hacker[2], L. Farrelly[2], K. Gyertson[3], A. Devaraj[4], A. Nair[5], A. Hackshaw[2], S. Janes[1]

[1]Lungs for Living, University College London; [2]Cancer Trials Center, University College London; [3]Cancer Clinical Trials Unit, University College London Hospital; [4]National Heart and Lung Institute, Imperial College; [5]University College London Hospitals NHS Foundation Trust

Background

- The use of volume-doubling time (VDT) to guide management decisions in indeterminate pulmonary nodules implies early-stage lung cancers follow a consistent exponential pattern of growth
- However, there is limited *in vivo* evidence for this
- Previous research in early lung cancer presenting as solid lung nodules has suggested shown exponential growth models closely fit observed growth[1]
- The aim of this analysis was to determine the accuracy of exponential functions in modelling observed growth of early-stage lung cancer presenting as solid (volume) and subsolid (mass) nodules in the SUMMIT study

Methods: The SUMMIT Study

- The SUMMIT study is a prospective observational cohort study to examine the performance of delivering a LDCT screening service to a high-risk population in London and to validate a multi-cancer early detection blood test (NCT03934866)
- Eligible participants were 55–77 years old, met the US Preventive Services Task Force 2013 screening criteria or had a $PLCO_{m2012}$ risk of ≥1.3%
- Participants attended three annual lung health checks (baseline (Y0), year 1 (Y1) and year 2 (Y2)) with LDCT at Y0 and Y2 and randomization at Y1.
- Nodule management was based on British Thoracic Society guidelines[2]

Methods: Nodule Analysis

- Images were read by thoracic radiologists using computer aided detection (CADe) software (Veolity V.1.4, MeVIS Medical Solutions, Germany)
- Individual nodules were tracked across serial study scans
- Nodule volume analysis was semi-automated with CADe
- Mass was calculated by transforming CT attenuation into physical density (mg/ml) and multiplying nodule volume by mean nodule density and was provided by CADe
- Accuracy of exponential growth functions to observed growth was assessed with the coefficient of determination (R^2)
- Statistical analysis and graph production was performed with R (V4)

References:

1. Heuvelmans, M. A. et al. Quantification of growth patterns of screen-detected lung cancers: The NELSON study. Lung Cancer 108, 48–54 (2017).
2. Callister, M. E. J. et al. British thoracic society guidelines for the investigation and management of pulmonary nodules. Thorax (2015)
3. Mackintosh, J. A., Marshall, H. M., Yang, I. A., Bowman, R. V & Fong, K. M. A retrospective study of volume doubling time in surgically resected non-small cell lung cancer. Respirology 19, 755–762 (2014).
4. de Margerie-Mellon, C. et al. The Growth Rate of Subsolid Lung Adenocarcinoma Nodules at Chest CT. Radiology 297, 189–198 (2020)

Results

Volume growth of solid nodules

- 21 histologically confirmed lung cancers diagnosed in solid nodules seen on 3 or more CTs were identified
- The measured growth fit an exponential growth model in the majority of cases with R^2 >0.90 in 14/21 cancers
- Median R^2 0.9740, IQR 0.849-0.9985, range 0.6507 – 1.0

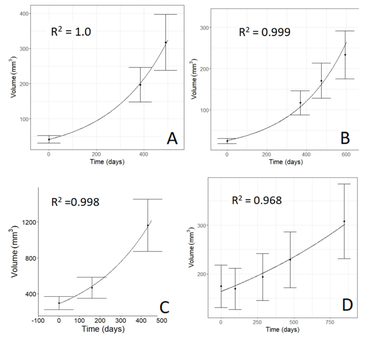

Figure 1: Example growth-patterns of screen-detected lung cancers derived from solid nodules
Points are measured volume and trend lines are modelled growth curves using an exponential growth function. Error margins are +/- 25% volume error. R^2 values are given for each nodule.

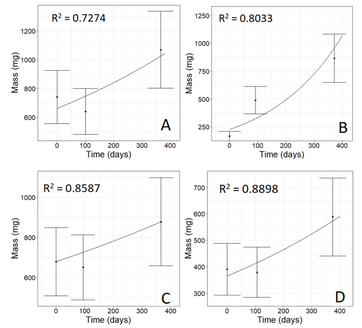

Figure 2: Example growth-patterns of screen-detected lung cancers derived from subsolid nodules
Points are measured mass and trend lines are modelled growth curves using an exponential growth function. Error margins are +/- 25% volume error. R^2 values are given for each nodule.

Mass growth of subsolid nodules

- 21 histologically confirmed lung cancers derived from subsolid nodules seen on 3 or more SUMMIT scans were identified.
- Compared to volume growth curves in solid malignant nodules, the mass growth of subsolid nodules was significantly less well described by an exponential model. 7/21 nodules had R^2 ≥0.9.
- Mean R^2 0.687, median 0.8033, IQR 0.4456-0.9080, p= 0.0054).

Conclusions

1. Volume growth of early-stage lung cancer presenting as solid nodules is well described by an exponential growth function
2. Mass growth of early-stage lung cancer presenting as subsolid nodules is less accurately modelled by an exponential growth function
3. These results support current guidelines that subsolid nodules require longer-term surveillance due to less predictable future growth

Cancer Research UK and UCL Cancer Trials Centre
90 Tottenham Court Road, London, W1T 4TJ
Enquiries: +44 (0)20 7679 9858, F: +44 (0)20 7679 9899

lungsforliving
Leading Lung Cancer Research