Commentary

Optimizing the lung cancer screening interval: the world is waiting

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Although lung cancer is the leading cause of cancer death throughout the world, until recently, there has not been an accepted screening test for this deadly disease. Fortunately, the National Lung Screening Trial (NLST) has now shown that screening with low dose computed tomography (CT) can reduce lung cancer-specific mortality by 20% compared to chest radiography (1). This test thus has the potential to substantially reduce lung cancer deaths throughout the world.

To date, however, national implementation of CT lung cancer screening has only commenced in the United States (US). The international medical community is therefore poised to observe the clinical application of the US screening program and to await the results of ongoing international trials as both are likely to form the basis of an international approach to lowering lung cancer mortality. Optimizing the screening interval for CT screening has important implications for cost-effectiveness, with the potential to make screening more feasible within areas of limited health care resources. In the words of Drs. Field and Duffy from the United Kingdom, it is thus important that the international community "get this right" (2).

We therefore read with interest the findings of Dr. Patz and colleagues who published a retrospective cohort analysis of all NLST participants and performed a subgroup analysis of patients who had a negative prevalence (T0) low-dose screening CT study to determine whether subsequent CT at 1 (T1) and 2 (T2) years offered a lung cancer mortality benefit (3). A negative prevalence screening CT was defined as the absence of any non-calcified nodule 4 mm in longest diameter. The group also hypothesised the potential effect on mortality if a T1 screening CT had not been performed.

The group's analysis revealed that the yield of lung cancer at the T1 screen among participants with a negative T0 screen was 0.34% compared with a yield at the T0 screen among all T0-screened participants of 1%. The hypothetical effect of ceasing screening after a negative prevalence CT was an additional 28 deaths from lung cancer out of 19,066 patients with a negative T0 screening CT (0.001%). The lung cancer incidence in this group was 2% at last follow-up with a median follow-up time from T0 to diagnosis of 3.3 years compared to 4% of all patients with a median time from T0 screen to diagnosis of 2.2 years.

The mortality rate due to lung cancer during the trial was lower in participants with a negative T0 screen (185 per 1,000 person years) compared with that in all participants who had a T0 screen (277 per 1,000 person years) but any positive CT at T0, T1 or T2 had a substantial impact on lung cancer specific mortality rate, for example any patient with a negative and subsequent positive screening CT was shown to have a lung cancer specific mortality rate of 528 per 100 person years. Those patients with a negative T0 and positive T1 had a lung cancer mortality of 521 per 100 person years suggesting that the T1 scan adds little mortality benefit in those with a negative T0 screen.

In addition, emphysema on the T0 CT, or a patient reported history of chronic obstructive pulmonary disease (COPD) were found to be significant predictors of risk of lung cancer diagnosis in participants with a negative T0 screen (hazard ratio 1.9 for both parameters) as well as in all study participants.

It is important to note that patients with a negative T0 CT included both patients with no nodules and patients with micronodules <4 mm in longest diameter. Interestingly, it has been estimated that at least 1% of lung cancers detected in the CT arm of the NLST developed among such micronodules (RF Munden, personal communication,

12 August, 2016). Considering the small but significant malignant potential of micronodules in this population, a separate subanalysis of T0 screening participants with no nodules and those with micronodules should be considered for future research in this area. Moreover, in keeping with the rapidly changing landscape of lung cancer screening, the nodule size threshold for a positive screening CT has recently increased from 4 to 6 mm (4). Thus, it is unknown whether these results can be generalized to those patients with a "negative" CT screening exam under current guidelines who have nodules between 4–6 mm in diameter.

We emphasize that the findings of this study suggest that subsequent CT surveillance after a negative T0 screen is necessary to detect future lung cancers. It is important that this information be disseminated to referring clinicians and participants alike, to avoid loss to follow-up after the reassurance of a negative T0 screen.

As noted by the authors, evidence from pooled datasets of larger screened populations is necessary to develop a fully validated prediction model that is applicable globally. Pooling of the existing data of the European randomized lung cancer CT screening (EUCT) trials would create an additional lung cancer screening population of >37,000 patients, but long-term follow-up data is still awaited in this study (5). Moreover, because the NLST did not directly test the effectiveness of longer screening intervals, the optimal screening regimen for patients with negative T0 screens is still uncertain.

In summary, the value of CT screening for lung cancer is dependent on achieving a favourable balance between its potential benefits and risks. As the harms of cumulative radiation exposure, added costs and the potential for additional testing increase with overly frequent screening, lengthening the screening interval in participants with a negative low-dose CT prevalence screen may result in a more favourable risk-benefit ratio for selected participants with a negative T0 screen, particularly in the setting of limited healthcare resources. The world is thus waiting for a proven, efficient CT screening regimen for patients with negative baseline screening exams. The study by Patz *et al.* (3) is an important step forward in this process.

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Footnote

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References

1. Aberle DR, DeMello S, Berg CD, et al. Results of the two incidence screenings in the National Lung Screening Trial. N Engl J Med 2013;369:920-31.
2. Field JK, Duffy SW. Lung cancer CT screening: is annual screening necessary? Lancet Oncol 2016;17:543-4.
3. Patz EF Jr, Greco E, Gatsonis C, et al. Lung cancer incidence and mortality in National Lung Screening Trial participants who underwent low-dose CT prevalence screening: a retrospective cohort analysis of a randomised, multicentre, diagnostic screening trial. Lancet Oncol 2016;17:590-9.
4. Ruchalski KL, Brown K. Lung Cancer Screening Update. J Thorac Imaging 2016;31:190-200.
5. Heuvelmans MA, Vliegenthart R, Oudkerk M. Contributions of the European trials (European randomized screening group) in computed tomography lung cancer screening. J Thorac Imaging 2015;30:101-7.

