

Helical computed tomography for lung cancer screening

Given the controversy over this strategy, Australia should be involved in its evaluation

LUNG CANCER IS the leading cause of cancer death in Australia and has a dismal prognosis, with 7800 new cases and 6800 deaths each year, and a 5-year post-diagnosis survival of only 12%. New cases increasingly occur in ex-smokers.¹ Helical computed tomography (CT) is a fast and sensitive screening technique that can detect early-stage lung tumours, potentially increasing the proportion of patients who can be offered curative treatment. Newer scanners can perform studies with lower radiation exposure. However, use of this technique is controversial; the studies suggest that it has benefits that are uncontrolled, with no concurrent or randomised comparison group.

Proponents of helical CT screening argue that its high sensitivity and the early results of studies showing that it detects small, early stage and operable cancers demonstrate its clear benefits.^{2,3} In the Early Lung Cancer Action Project in the United States, 1000 asymptomatic smokers or former smokers aged over 60 were screened with low-dose helical CT and conventional chest x-rays; 23% had non-calcified pulmonary nodules detected by CT, while only 7% had abnormalities detected by chest x-ray. Of those with nodules on CT, 12% were eventually diagnosed with malignancy, of which 85% were stage I tumours.^{4,5} In contrast, only 20% of lung cancers in patients presenting in Victoria in 1995 were localised.⁶ Other similar uncontrolled studies in the United States, Japan, Germany and Finland showed that from 5%⁷ to over 50%⁸ of people screened have an abnormality detected. While many can be investigated with non-invasive

tests and reassessment, the substantial rate of false-positive scans requiring potentially hazardous interventions is a real concern.

Others argue that studies with no control group are open to severe biases and give misleading results.^{9,10} Non-randomised comparisons between screen-detected and conventionally diagnosed patients that assess outcomes such as tumour size and survival are open to selection, lead time, prevalence-duration and overdiagnosis bias, all of which tend to make the outcomes in the screened group appear more favourable.¹¹ The experience with previous trials of screening for lung cancer, using chest x-ray and sputum cytology, shows these problems. A randomised trial in Czechoslovakia demonstrated that, in the screening group, 53% of tumours were at an early stage, 25% were operable, and 5-year survival was 23%, compared with figures of 21%, 16% and zero 5-year survival in the unscreened group.¹² However, the death rate from lung cancer over the subsequent 15 years was actually higher in the screened group; this discrepancy arises from the biases noted above. A trial at the Mayo clinic in the United States showed similar results.¹³ A Cochrane meta-analysis of trials of lung cancer screening shows no difference in all-cause mortality (relative risk, 1.01; 95% CI, 0.94–1.08), and a higher mortality from lung cancer in the screened groups (relative risk, 1.11; 95% CI, 1.00–1.23).¹⁴

Randomised trials of helical CT screening have begun. The US National Lung Screening Trial started in 2002 and

plans to recruit 50 000 high-risk subjects aged 55–74 over 2 years; in the first 6 months, 16 000 subjects have been recruited. The intervention group will be offered helical CT, and the comparison group will be offered conventional chest x-ray, each at baseline and annually for 2 years. Follow-up will continue to 2009.^{15,16} The trial will have power to detect a 20% reduction in mortality, and costs are estimated at US\$200 million. Other smaller randomised trials are in progress. A trial with 40 000 participants has been planned in the United Kingdom, but funding has not been approved. Many non-randomised trials, most linked to the Early Lung Cancer Action Project, are in progress.

In 2002, the National Cancer Control Initiative in Australia set up a working group and a wider advisory group to review the state of knowledge of helical CT screening and make recommendations about its future in Australia. Their report recommends that a coordinated analysis of Australian clinical experience with helical CT screening be undertaken, along with a study to determine the prevalence of benign nodules in Australia, which may differ from that in other countries.¹⁷ Cost-benefit studies are recommended, largely to assess what degree of mortality benefit would have to be shown by the randomised controlled trials to fulfil acceptable economic criteria for screening. The report concludes that an Australian-based randomised trial would be impractical and too expensive, but recommends that one or more Australian centres should be involved in the international randomised trials. Such involvement would need funding of around \$1 million for 3–5 years; but would let us fully contribute to the essential evaluation of a challenging new approach to our leading cause of cancer deaths.

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