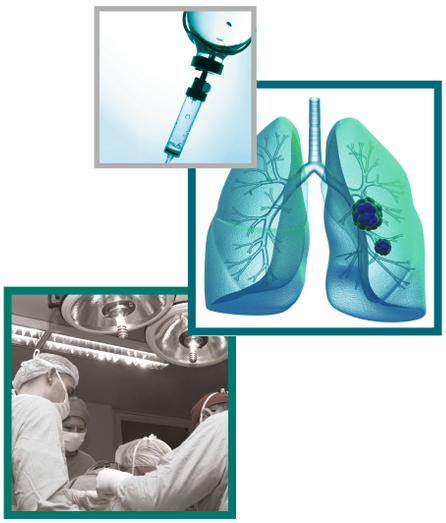
EDITORIAL



Is lung cancer screening possible with digital chest tomosynthesis?

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"...chest digital tomosynthesis could become the first-line lung cancer screening tool..."

Tomography & tomosynthesis

Tomography, also known as stratigraphy, was developed in the 1930s by the Italian radiologist Alessandro Vallebona [1] and proved to be useful in reducing the problem of superimposition of structures in projectional radiography. A chest tomogram is a picture of the chest area created by moving the x-ray machine in one direction, while moving the recording film the other way. Consequently, structures in the focal plane appear sharper, while structures in other planes appear blurred. Different focal planes that contain the structures of interest can be selected by modifying the direction and extent of the movement. Until the 1980s, before the advent of more modern computer-assisted techniques, chest stratigraphy was a pillar of the diagnosis and preoperative evaluation of patients who had to undergo lung surgery. The ideas used in the first stratigraphy techniques led to the development of computed axial tomography. Computerized techniques allowed conventional tomography to evolve and solve many of the problems associated with tomography, such as radiation dose given to the patient and long positioning time when multiple sections were required. In tomosynthesis, by collecting a number of projection images at different angles with a digital detector, an unlimited number of section images at arbitrary depths can be produced by using a suitable reconstruction algorithm [2].

In 2008, Vikgren *et al.*, using a multidetector computed tomography (CT) scan as reference, demonstrated that chest digital tomosynthesis can detect 100% of lung nodules with a diameter between 6 and 8 mm, and 91% of those from 4 to 6 mm [3].

More recently in a phantom study, Gomi *et al.* demonstrated that chest digital tomosyntesis was also able to detect artificial pulmonary nodules 5–8 mm in diameter, with ground glass opacity, and concluded that digital tomosynthesis may be a valid alternative to CT scans for the detection of artificial pulmonary nodules [4]. However, according to Zhao *et al.*, the detection sensitivity of chest digital tomosynthesis appeared to be lower than that of CT for ground glass opacity 5–8 mm in diameter with a density of -800 HU [5].

"The cost of tomosynthesis is one-fifth of that of low-dose computed tomography."

The lung cancer 'epidemic'

A century ago, lung cancer was considered to be a rare disease. Now, lung cancer is the

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leading cause of death from cancer in developed countries and its incidence in developing countries is rising to an epidemic level. In China, 67% of the male population are smokers; the prevision of deaths for lung cancer by the middle of the 21st century is very high. The principles of treatment have changed little in the last few years: surgery, chemotherapy and radiotherapy alone or in combination. Improvement in staging led to the avoidance of futile thoracotomies in approximately 20% of patients previously believed to be operable. Chemotherapy has improved and personalized medicine for lung cancer is focusing on targeted agents and radiation therapy has improved. Nevertheless, in spite of all the improvements, in the last 20 years, the 1- and 5-year survival rates have only slightly changed.

> "...the percentage of ... lung cancer detected with chest digital tomosynthesis was comparable with that reported for low-dose computed tomography."

Lung cancer is the most preventable respiratory disease worldwide and educational efforts have succeeded in reducing lung cancer incidence to some extent in developed countries. However, for smokers, the only chance of being cured of lung cancer is for it to be detected at a very early stage.

Screening

Most lung cancer is detected at an advanced stage and the prognosis is dismal. In an attempt to detect lung cancer at an early asymptomatic stage, attempts to screen at-risk populations by chest x-ray were made in the 1970s and 1980s. The results of these trials using chest roentgenograms were completely unsatisfactory and failed to show a reduction in lung cancer mortality. Until recently, the use of low-dose CT (LDCT) scans for screening also failed to demonstrate a reduction in lung cancer mortality in the screened population. Many uncontrolled trials using spiral CT showed that CT was able to detect much more lung cancer at an early stage than chest x-ray, but they failed to demonstrate a reduction in lung cancer mortality until the results of the NLST, a trial that involved more than 50,000 subjects [6]. A 20% reduction in lung cancer-specific deaths was demonstrated in subjects who had screening performed with LDCT. The question of the optimal time, horizon and screening interval remains, to date, unanswered; moreover, the costs of the screening and radiation dosage must be taken into consideration. As a matter of fact, NLST was the most expensive (US$200 million) randomized trial of a single cancer screening test ever undertaken in the USA. Because the optimal screening interval remains unanswered, the cumulative radiation dosage of multiple LDCT scans, radiation from natural sources and possible radionuclide investigations can rise to levels that pose individuals at risk of developing a new cancer.

Lung cancer screening with chest digital tomosynthesis

With digital chest tomosynthesis, the effective radiation dosage is approximately 0.13 mSv compared with an average effective dosage of 2 mSv of a LDCT scan. The estimated radiation dose that each NLST participant received was approximately 8 mSv. The cost of tomosynthesis is one-fifth of that of LDCT. Lung cancer detection rates in the first published observational study on approximately 2000 subjects compare with those of most LDCT lung cancer screening [7].

Recently, a study for computerized detection of lung nodules in digital chest tomosynthesis has been published [8]. The baseline results on the use of digital chest tomosynthesis in the early detection of lung cancer are encouraging; the detection rate is comparable with the rates reported for LDCT and is attained at a far lower cost and radiation dosage. In this study involving nearly 2000 subjects, the percentage of lung nodules and lung cancer detected with chest digital tomosynthesis was comparable with that reported for LDCT. The lung cancer detection rate was 0.9%.

It can be easily understood that, if present data on the ability of chest digital tomosynthesis to detect lung nodules and lung cancer in the same percentage of LDCT [3–5,7,8] can be confirmed by other studies and clinical trials, chest digital tomosynthesis could become the first-line lung cancer screening tool among patients at high-risk of lung cancer (who should undergo a CT scan).

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References

1 Vallebona A. Axial transverse laminagraphy. *Radiology* 55(2), 271–273 (1950).

2 Dobbins JT III, Godfrey DJ. Digital x-ray tomosynthesis: current state of the art and clinical potentials. *Phys. Med. Biol.* 48(19), R65–R106 (2003).

3 Vikgren J, Zachrisson S, Svalkvist A *et al.* Comparison of chest tomosynthesis and chest radiography for detection of pulmonary nodules: human observer study of clinical cases. *Radiology* 249(1), 1034–1041 (2008).

4 Gomi T, Nakajima M, Fujiwara H *et al.* Comparison between chest digital tomosynthesis and CT as a screening method to detect artificial pulmonary nodules: a phantom study. *Br. J. Radiol.* 85(1017), e622–e629 (2012).

5 Zhao F, Zeng Y, Peng G *et al.* Experimental study of detection of nodules showing ground-glass opacity and radiation dose by using anthropomorphic chest phantom: digital tomosynthesis and multi detector CT. *J. Comput. Assist. Tomogr.* 36(5), 523–527 (2012).

6 The National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N. Engl. J. Med.* 365(5), 395–409 (2011).

7 Terzi A, Bertolaccini L, Viti A *et al.* Lung cancer detection with digital chest tomosynthesis: baseline results from the observational study SOS. *J. Thorac. Oncol.* 8(6), 685–692 (2013).

8 Wang J, Dobbin JT III, Li Q. Automated lung segmentation in digital chest tomosynthesis. *Med. Phys.* 39(2), 732–740 (2012).