Innervision
Volume 25 Number 6 (Issue 291)
Outtake from the June 2010 Issue

Special Report

Joint Industrial-Academic Seminar JRC2010

The Possibilities Tomosynthesis Brings to Lung Cancer Screening

Low-dose Tomosynthesis is a Useful Tool in Lung Cancer Screening

Noriyuki Moriyama
Director of Research Center for Cancer Prevention and Screening, National Cancer Center

A Technical Evaluation of Low-dose Tomosynthesis with the SONIALVISION safire

Kaoru Shimizu
Department of Radiology, Hospital East, National Cancer Center

Shimadzu Corporation

Joint Industrial-Academic Seminar JRC2010

The Possibilities Tomosynthesis Brings to Lung Cancer Screening

Japan Radiology Congress 2010 (JRC 2010) was held over the four-day period from Thursday, April 8 to Sunday, April 11, 2010. On April 9, the Japan Radiological Society (JRS), the Japanese Society of Radiological Technology (JSRT), and the Japan Society of Medical Physics (JSMP) partnered with Shimadzu Corporation to hold the Joint Industrial-Academic Seminar under the title of "The Possibilities Tomosynthesis Brings to Lung Cancer Screening." Keigo Endo, M.D., Ph.D, Professor of Diagnostic Radiology and Nuclear Medicine of Subdivision of Oncology, Division of Biosystem Medicine, Gunma University Graduate School of Medicine presided as Chairperson. The Seminar featured two presentations: "A Technical Evaluation of Low-dose Tomosynthesis with the SONIALVISION safire" by Kaoru Shimizu, Department of Radiology, Hospital East, National Cancer Center, and "Low-dose Tomosynthesis is a Useful Tool in Lung Cancer Screening" by Noriyuki Moriyama, M.D., Director of Research Center for Cancer Prevention and Screening of the National Cancer Center.

Chairperson
Keigo Endo, M.D., Ph.D.
Professor, Diagnostic Radiology and Nuclear Medicine, Subdivision of Oncology, Division of Biosystem Medicine, Gunma University Graduate School of Medicine

A Technical Evaluation of Low-dose Tomosynthesis with the SONIALVISION safire

Kaoru Shimizu
Department of Radiology, Hospital East, National Cancer Center

The SONIALVISION safire, which features 17-inch by 17-inch direct-conversion flat-panel detector (FPD) was introduced at Hospital East of the National Cancer Center in April 2006. The SONIALVISION safire produces very high-definition images, and its Tomosynthesis imaging capabilities are the device's greatest asset. In 2008, Hospital East started associated research with Shimadzu Corporation and the Research Center of the National Cancer Center for Cancer Prevention and Screening to apply Tomosynthesis to chest imaging. The research has already shown Tomosynthesis to perform satisfactorily in lung cancer screening and detection of the presence of nodules. In this presentation, I will report the findings of our investigation of lower dose Tomosynthesis for lung cancer screening.

Evaluating the Ability of Tomosynthesis to Detect Tumors

Phase 1 : The Usefulness of Tomosynthesis in Chest Imaging

Lung cancer screening is performed on the people in normal health and therefore must identify early-stage cancer that is still curable while minimizing the dose. Solid nodules measuring at least 5mm and pure ground glass opacity (GGO) measuring at least 15mm are subject to treatment. A report by the "Anti-Lung Cancer Association" calls for imaging under screening CT conditions of LSCT phantom (LSCT-001 chest phantom by Kyoto Kagaku) should be able to detect a 6mm diameter simulating GGO.

I will next report the findings of an investigation by Hospital East on the imaging of simulated tumors with Tomosynthesis. The investigation began in 2008. We used general chest radiography, computed tomography (CT, under screening conditions), and Tomosynthesis to image LSCT phantom implanted with simulated tumors in the apex and basal of the lung and bifurcation of the trachea. The simulated tumors in the left lung measured 2, 4, 6, 8, and 10mm

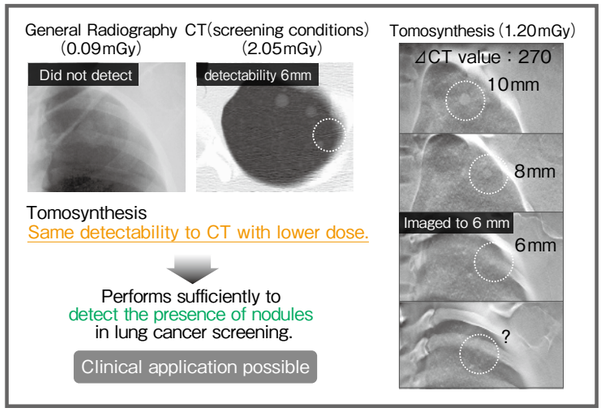


Fig.1 Comparison of detectability of simulated tumors (The amount of doses indicates absorbed dose at center of the phantom)

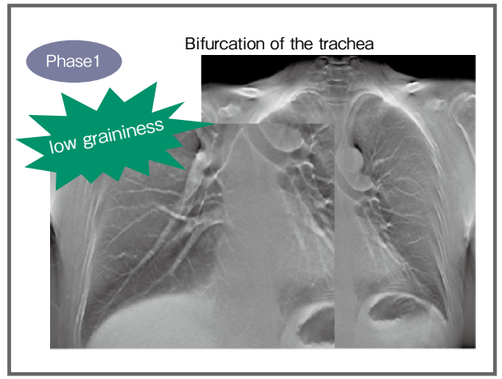


Fig.2 Images generated with conventional (phase 1) Tomosynthesis

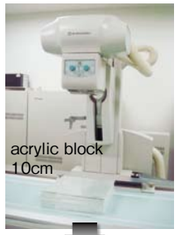
(⊿CT value : 270), and those in the right measured 4, 6, 8, 10, and 12mm (⊿CT value : 100). Focusing on the apex of the left lung, you can see that general chest radiography was unable to detect simulated tumors covered by the ribs, while CT and Tomosynthesis described simulated tumors down to 6mm (**Fig.1**). The absorbed dose at the center of the phantom was 0.09mGy, 2.05mGy, and 1.20mGy, respectively. **Fig. 1** shows that Tomosynthesis has almost the same detectability as CT screening using less X-ray dose. Tomosynthesis performs sufficiently for detecting the presence of nodules.

Working on Low-dose Tomosynthesis

Phase 2 : The Efficacy of Low-dose Tomosynthesis in Lung Cancer Screening

Fig.2 shows the sample image of Tomosynthesis obtained under X-ray conditions in phase 1. It seems possible to reduce X-ray dose with respect to image quality because it keeps a high S/N ratio not only in the lung region but also in high-absorption areas such as the heart and liver. By increasing analog gain (AG) of the FPD, tumors are detectable in lower dose conditions. As lung cancer screening requires the reduction of X-ray dose as much as possible. We investigated the way to reduce the dose through increasing FPD gain. In fact, our goal was to lower the dose with keeping the detectability of tumors achieved previously.

1) 10cm thick acrylic block was used.
2) With the acrylic block imaged at different FPD gains, the equivalent digital levels on the FPD output were determined.



Exposure, acquisition, and reconstruction conditions (fixed)

Tube voltage	120kV
Matrix size	1440×1440 (17inches)
Acquisition time	Slow mode 5.0 seconds
Acquired number of frames	High-resolution mode 74 frames
Exposure angle	40°
SID	110cm
Reconstruction method	FBP Reconstruction kernel:Thickness++

Fig.3 Optimal X-ray conditions at increased FPD gain

	Analogue gain (AG)	Tube voltage (kV)	X-ray conditions per frame (fixed) mA	msec	mAs
Phase1	×3 (former value)	120	160	3.2	0.51
	×10		80	1.6	0.13
	×20		25	1.6	0.04
	×30		10	1.4	0.014

Fig.4 Optimal X-ray conditions at different FPD gains

Investigation 1: Optimal Doses with increased FPD Gain

We tried to get lower X-ray conditions by changing FPD AG (**Fig.3**). We set X-ray conditions in order to get the same digit output from the FPD with the AG increased by a factor of 3 (as in phase 1) as well as factors of 10, 20, and 30, using a 10cm thick acrylic block. The 10cm thick acrylic block has the same X-ray penetration than that of chest

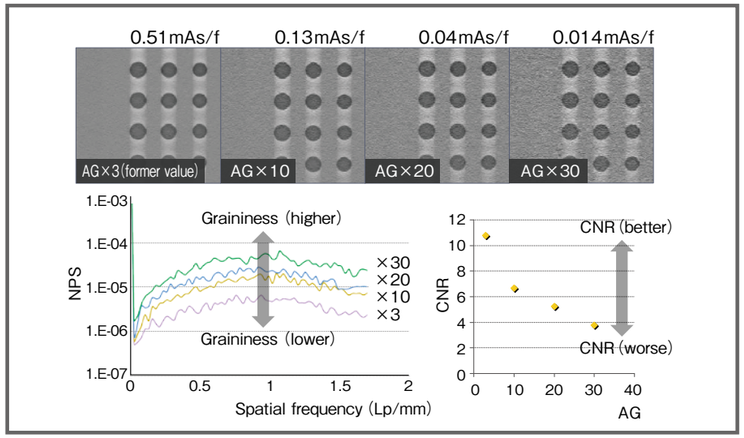


Fig.5 The effects of changing FPD gain on graininess and CNR

Analogue gain (AG)	Tube voltage (kV)	X-ray conditions per frame (fixed) mA	msec	mAs	Dose absorbed (over 74 frames) Skin Dose (mGy)	Dose absorbed in center (mGy)
×3 (former value)	120	160	3.2	0.51	4.2	1.2
×10		80	1.6	0.13	1.5	0.42
×20		25	1.6	0.04	0.71	0.21
×30		10	1.4	0.014	0.55	0.14
Reference : General Radiography (CR) : 140kV 5mAs					0.22	0.09
CT (screening) : 120kV 30mA 0.5s/rot (Aquilion64)					—	2.05

Medical institution mean : 0.28mGy
From the "The Grasp of Patient Exposure in CR"
Japanese Journal of Radiological Technology. 2005 ; 61 (11) : 1510-1520

Fig.6 Absorbed Dose of LSCT phantom at different FPD gains

region.

The results are shown in **Fig.4**. X-ray conditions per-frame were 0.51mAs at an AG of x3, 0.13mAs at an AG of x10, 0.04mAs at an AG of x20, and 0.014mAs at an AG of x30. The dose required for imaging can thus be lowered as AG increases.

Investigation 2: Assessing Graininess and Measuring Contrast-to-Noise Ratio

Secondly, using an acrylic block and a Burger phantom, we assessed graininess with noise power spectra (NPS) and measured the contrast-to-noise ratio (CNR) (**Fig.5**).

We set a Burger phantom in a 9cm acrylic block and acquired the image for it with the changing AG value by factors of 3, 10, 20, and 30, and X-ray conditions obtained in Investigation 1. We set Regions of interest on the object and background of the obtained images, and measured CNR. NPS was measured at 5 points: in the center of the acrylic block and at the 4 corners. Consequently, higher AG results in low X-ray dose, but simultaneously, the graininess and CNR values become worse.

Investigation 3: Measuring Absorbed dose and Evaluating Visibility on Simulated Tumors

Noting that graininess increased as we increased AG when imaging the uniform acrylic block, we wondered if a similar marked difference would appear when we used an LSCT phantom which is similar to the human body. We decided to determine an allowable range of dose reduction that would keep simulated tumors visible as in conventional imaging. We used the LSCT phantom used in phase 1.

The LSCT phantom was imaged with AG increased by factors of 3, 10, 20, and 30 at the respective optimal doses. Absorption was measured with dosimeters placed in the center and surface of the LSCT phantom, and the visibility of the simulated tumors in the LSCT phantom was assessed.

The absorbed doses are shown in **Fig.6**. As in investigations 1 and 2, the per-frame dose from imaging decreased as AG increased. The absorbed dose at the center and skin of the phantom likewise decreased as AG increased.

The images observed in the visual assessment are shown in **Fig.7a** and **7b**. **Fig.7a** shows Tomosynthesis images of the lung apex. The 6, 8, and 10mm simulated tumors were as visible at up to AG x20 as they were in the AG x3 image. But at AG x30, graininess increased, albeit only slightly. **Fig.7b** shows images of the diaphragm. As in the apical images, the simulated tumors of all sizes appear similarly at up to AG x20 as they do in the AG x3 image, but the effects of noise in adjacent high-absorbance regions reduce the visibility of the 6 and 8mm simulated tumors.

Investigation 4 : Evaluating Visibility in Images of Volunteers

We concluded from the results of investigations 1 to 3 that AG to x20 has a lesion detection capability equivalent to that of conventional AG x3. We imaged about 20 volunteers at AG x3 and x20, using the optimal doses. We then asked 3 pulmonologists and 5 radiologic technologists to assess the visibility of the images.

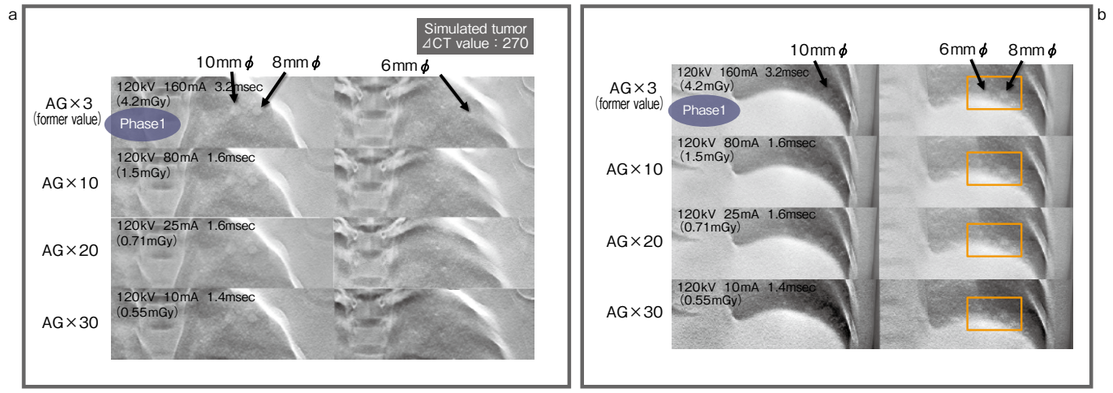


Fig.7 Evaluation of visibility on simulated tumors at the apex of lung (a) and diaphragm (b) (Doses indicate skin dose)

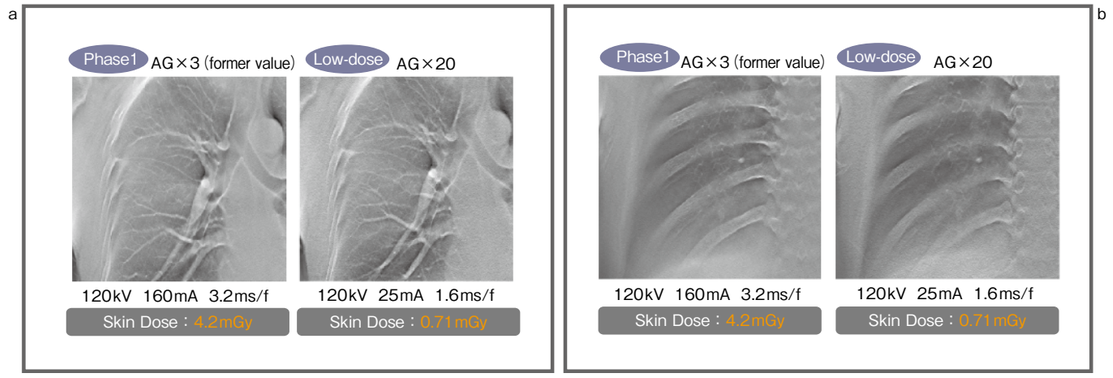


Fig.8 Evaluation of mage quality (Volunteers without lesion)

This team found that although the AG x20 images had slightly higher graininess in regions of high absorbance than the AG x3 images, graininess remained low in the lungs and nodule visibility was almost identical. It was concluded that even AG x20 images are of a level acceptable for detection of the presence of nodules (**Fig. 8a, 8b**).

Conclusions

Although imaging was possible at lower doses of radiation when the FPD gain was increased, noise increased especially in the high absorption ranges, resulting in higher graininess. However, nodule imaging, comparable to that at the conventional AG x3, was possible at up to AG x20 with lower doses of radiation and the image quality was adequate for detecting the presence of nodules in lung cancer screening. Low-dose Tomosynthesis at 0.21mGy (the dose absorbed at the center) — which is one-sixth the exposure of 1.2mGy in conventional Tomosynthesis (again the dose absorbed at the center) — resolved lesions comparably to conventional Tomosynthesis. Here at Hospital East, we raised our AG setting from x3 to x20 to image at 120kV, 25mA, and 1.6 ms/f, taking into account the thickness of the body.

Tomosynthesis is easy to perform, and low-dose Tomosynthesis can improve lesion imaging from a general chest radiography at about 2.4times the exposure. Moreover, Tomosynthesis has the same level detectability comparable to low-dose CT at approximately one-tenth the exposure. These points make it an effective new option in lung cancer screening. We will continue investigating image processing to accelerate lower exposures while increasing image quality and keep working to expand the possibilities that Tomosynthesis offers.

(Excerpted from the JRC2010 JRS/JSRT/JSMP Shimadzu Joint Industrial-Academic Seminar : The Possibilities Tomosynthesis Brings to Lung Cancer Screening, corresponding author: Editing Department)

Biography

Kaoru Shimizu graduated from the Department of Radiological Sciences of the School of Health Sciences, International University of Health and Welfare in March 2002 and began working in the Department of Radiology of the National Tochigi Hospital in April 2002. She began working in the Department of Radiology of Hospital East, National Cancer Center in April 2005.

Low-dose Tomosynthesis is a Useful Tool in Lung Cancer Screening

Noriyuki Moriyama, M.D.
Director of Research Center for Cancer Prevention and Screening, National Cancer Center

We at the Research Center for Cancer Prevention and Screening have partnered with Hospital East of the National Cancer Center and Shimadzu Corporation to bring Tomosynthesis to lung cancer screening. Lung cancer screening must identify early-stage lesions that are still curable at as low dose as possible. We carried out an experiment with the SONIALVISION safire with a direct-conversion flat-panel detector (FPD) by using a chest phantom located at Hospital East of the National Cancer Center. The device, equipped with Tomosynthesis functionalities, produced high-definition images comparable to those obtained by computed tomography (CT) screening with lower dose exposure.
We then compared the detectability of lung nodules of general radiography, which is usually used in lung cancer screening, with that of Tomosynthesis to validate the usefulness of Tomosynthesis for lung cancer screening. We conducted the same trial with low-dose Tomosynthesis, which needs only one-sixth of the dose of conventional Tomosynthesis. I am pleased to report the results in this presentation.

The Benefits of SONIALVISION safire with Tomosynthesis

SONIALVISION safire, with its large 17-inch by 17-inch FPD, produces excellent general radiographic images and is also useful for G.I.exams, for example, double contrast gastrography and observation of a whole intestinal area. Tomosynthesis, by which an arbitrary plane and continuous tomographic images can be obtained in a single acquisition, is not only able to observe lesions three dimensionally but also has very few metal artifacts compared to CT, making it more advantageous for orthopedic purposes (**Fig.1**). The SONIALVISION safire, a multi-purpose device, can be used for lung cancer screenings, not just for for routine examinations. We hope to eventually apply the SONIALVISION safire to the field of mammography.

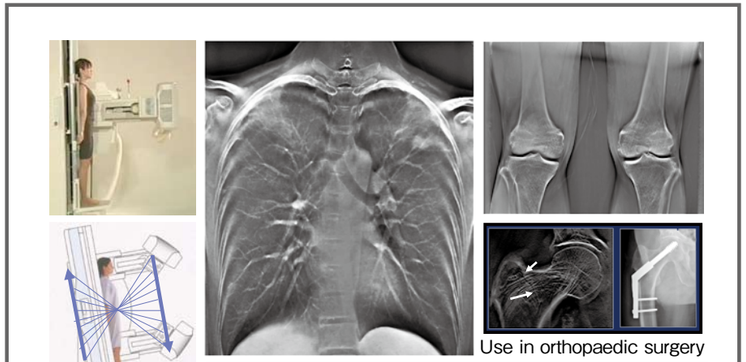


Fig.1 The potential of Tomosynthesis

Lung Cancer Screening with General Radiography and CT

Deaths by cancers in Japan are on an incessant uptrend and have reached 340,000 annually. Lung cancer is the biggest killer of men. Chest X-ray is normally used to screen lung cancer and is capable of detecting small nodules provided the lesions are solid. While CT detects the ground-glass opacity (GGO) found in alveolar cell cancer at the stage when the lesions contain a large amount of air which is difficult in general radiography. A solid lesion and GGO carry very different prognoses even when the masses are of the same size. GGO has a much better prognosis.
Anti-Lung Cancer Association based in Tokyo, which has used helical CT to screen lung cancer since 1993, released the data comparing the stages of lung cancer detected by chest X-ray and CT. Slightly more than 40% of all lung cancer was in stage IA when detected in screenings by general radiography prior to the introduction of CT. The percentage of IA stage increased significantly to almost 80% after CT use commenced. This indicates that lesions including GGO

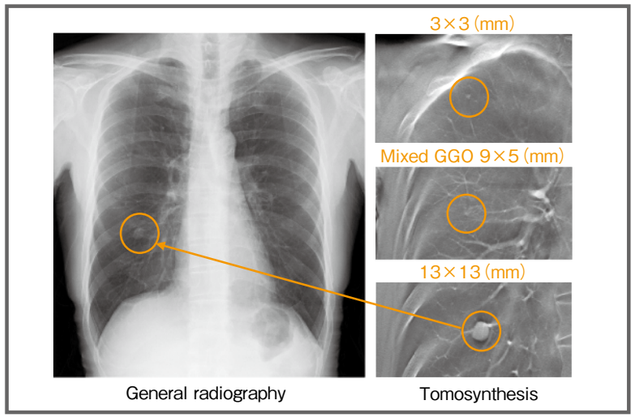


Fig. 2 Comparison of general radiography and Tomosynthesis images

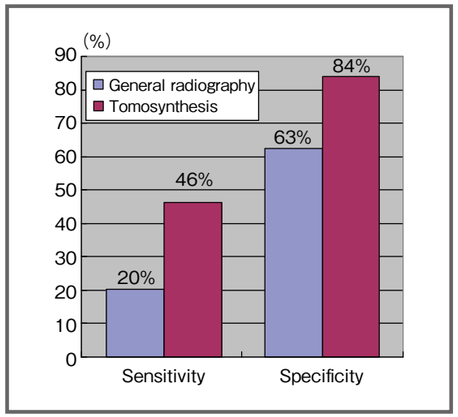


Fig. 3 Sensitivity and specificity achieved in detection of lung nodules in phase 1

are difficult to detect in general radiography. The 5-year survival rate among those with the cancer was 49% before the introduction of CT and increased to 75% after the introduction of CT. Given that the 5-year survival rate for lung cancer generally in Japan is about 20%, screening with chest X-ray could be useful, but CT performed better in identifying lesions.

Validation of Tomosynthesis in Detecting Lung Nodules

Lung cancer screening is satisfactory when it can detect masses measuring at least 5 mm and GGO measuring about 10 mm or larger. This makes Tomosynthesis — which requires less dose than CT and produces higher-definition images than general radiography — an ideal means to screen for lung cancer. We compared the nodule detectability of Tomosynthesis with that of general radiography to assess the usefulness of Tomosynthesis in lung cancer screening.

Phase 1 : Comparing Tomosynthesis Images to General Radiography Images

・Validation conditions

Two radiologists and two pulmonologists interpreted the images from chest X-ray and Tomosynthesis and checked whether any nodules could be found or not in 38 patients bodies. CT screening had revealed the nodules in 24 patients, while 14 people had nothing. The dose was 1.2 mGy for Tomosynthesis, 0.09 mGy for chest X-ray radiography, and 2.05 mGy for CT.

・Results

Fig. 2 compares general radiography images with Tomosynthesis images. The smallest tumors detected by chest X-ray were 13 mm by 13 mm, while Tomosynthesis easily revealed solidified nodules down to 3 mm by 3 mm. Although the minimum detectable GGO size is a little bit larger, we can point out where GGO was after the onset of lung cancer and will be very likely to be able to detect it with Tomosynthesis alone provided the interpreters are well trained.

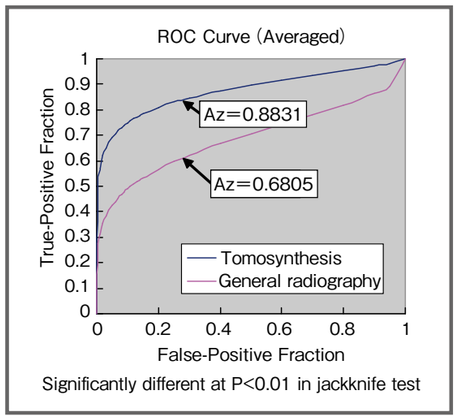


Fig. 4 ROC curve in phase 1 (mean Az values of 4 physicians)

The four image interpreters had the following comments about Tomosynthesis:

(1) Tomosynthesis makes cancer appear more cancer-like, robustly showing spiculations of semi-solidified cancers, for example.
(2) Tomosynthesis is able to detect even very small calcified lesions measuring about 3 mm.
(3) Although the images are far superior to chest x-ray, the area directly above the diaphragm has somewhat poorer contrast due to obstructive shadow.
(4) The contrast is lower behind the heart. But in the areas to the sides of the heart and elsewhere with no obstructive shadow show even small nodules well.
(5) The images radiographed by Tomosynthesis have a quality different from general radiography and therefore require some familiarization to interpret, but they are easy to be read once the reviewer has got used to them.
(6) Tomosynthesis images appear more like CT images than chest X-ray.
(7) Unlike general radiography, which produces only one image per exposure, Tomosynthesis shows nodules in multiple slices, adding credibility to diagnoses.

An analysis of the results showed that chest X-ray had a sensitivity of 20% and a specificity of 63%, while Tomosynthesis had a sensitivity of 46% and a specificity of 84%. Tomosynthesis had 2.3 times the sensitivity and 1.3 times the specificity (**Fig. 3**). A receiver operating characteristic (ROC) curve also showed Tomosynthesis to be significantly better (**Fig. 4**).

We concluded that Tomosynthesis, which features excellent detectability characteristics and low dose in lung cancer screening, is very clinically useful.

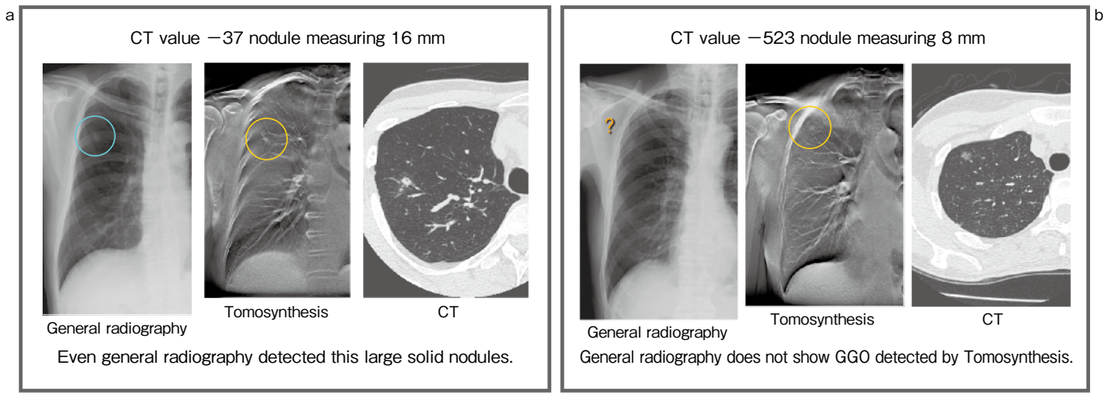


Fig. 5 Nodule diagnosis with general radiography and Tomosynthesis images

Phase 2: Comparing Low-dose Tomosynthesis Images to Chest X-ray Images

・Validation conditions

We next conducted a similar validation using low-dose Tomosynthesis, which has an exposure of 0.21 mGy, or about one-sixth the exposure of the Tomosynthesis in phase 1. Four pulmonologists interpreted general radiography images and low-dose Tomosynthesis images of 33 patients with nodules confirmed with thin-slice CT (49 nodules) and 22 healthy persons for a total of 55 persons. The results were analyzed. The dose condition of general radiography and CT were the same as in phase 1.

・Results

Fig. 5 shows the results of a comparison of nodule detection with low-dose Tomosynthesis and general radiography images. Both general radiography and Tomosynthesis detected a large size nodule (16 mm) with a low CT value of -37 (**Fig. 5a**). However, an 8 mm GGO with minus 500 CT value was hardly detected by general radiography but well detected by low-dose Tomosynthesis (**Fig. 5b**). Low-dose Tomosynthesis detected a 5 mm nodule that chest X-ray did not (**Fig. 5c**).

An analysis of the findings of image interpretation showed that chest X-ray had a sensitivity of 24% and a specificity of 45%, while Tomosynthesis had a sensitivity of 48% and a specificity of 76%. Tomosynthesis had twice the sensitivity and 1.7 times the specificity. As some large but low-density nodules were not detected, we also investigated the sizes and densities of nodules that chest X-ray and Tomosynthesis are capable of detecting. The results are shown in **Fig. 6**. Chest X-ray was able to recognize only large and dense nodules, while low-dose Tomosynthesis detected even small, low-density nodules. The image interpreters were also asked to record nodule locations and the diagnostic confidence. Free-response receiver operating characteristic (FROC) and ROC analysis showed that all 4 interpreters had a higher figure of merit (FOM) for low-dose Tomosynthesis.

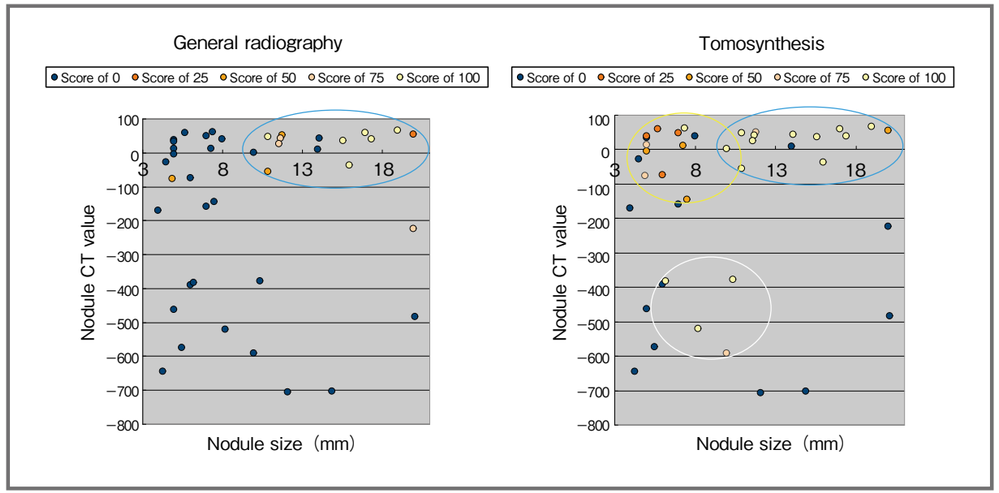


Fig.6 Nodule distribution and detection score comparison
(A score of 100 represents nodules identified by all 4 physicians)

The mean figure of merit (FOM) of the 4 physicians was 0.68 for Tomosynthesis and 0.44 for general radiography. Tomosynthesis detected nodules significantly better than general radiography (P<0.05).

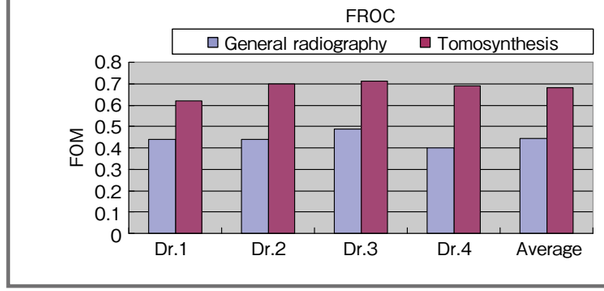


Fig.7 Phase 2 FROC results

In FROC analysis, the mean FOM was 0.68 for low-dose Tomosynthesis and 0.44 for chest X-ray (Fig.7). The ROC curve showed a significantly higher mean Az value for low-dose Tomosynthesis at 0.86 than for chest X-ray at 0.68.
In conclusion, low-dose Tomosynthesis, which has just one-sixth dose of conventional Tomosynthesis, detected nodules significantly better than general radiography.

Conclusions

The diversification and sophistication of imaging modalities are rapidly increasing the number of test data and images that we must interpret. Physicians will need to enlist the help of trained radiologic technologists and CAD-based techniques, which I suspect will first appear in lung cancer screening based on high-definition Tomosynthesis.
The age of lung cancer screening by general radiography is nearing an end. Let us hope that the new age of Tomosynthesis — with its low dose exposure and higher sensitivity and specificity when detecting lung nodules than general radiography — dawns in the near term.

[Acknowledgements]
The work was supported in part by the Health and Labour Sciences Research Grants for Third Term Comprehensive Control Research for Cancer.

(Extracted from the JRC2010 JRS/JSRT/JSMP Shimadzu Joint Industrial-Academic Seminar : The Possibilities Tomosynthesis Brings to Lung Cancer Screening, corresponding author : Editing Department)

Biography

Noriyuki Moriyama graduated from the School of Medicine of Chiba University in 1973 and was a visiting clinician at the Mayo Clinic in 1986. He was appointed Director of the Department of Radiology of Hospital East of the National Cancer Center in 1992 and Director of the Department of Radiology of the National Cancer Center Hospital in 1998 before assuming his current position in 2004.