The Possibilities Tomosynthesis Brings to Lung Cancer Screening

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

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

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Shimadzu Corporation
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.

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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
Tomosynthesis 

Same detectability to CT with lower dose. 

Performs sufficiently to detect the presence of nodules in lung cancer screening. 

Clinical application possible 

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

1) 10mm 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. 

Watching on the apex of the left lung, you can see that general chest radiography was unable to detect simultaneously both 6mm and 8mm simulated tumors due to low contrast. However, Tomosynthesis obtained under lower dose conditions was able to detect the tumors simultaneously. 

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

Investigation 1: Optimal X-ray conditions at increased FPD gain 

**Analogue gain (AG) Tube voltage (kV) X-ray conditions per frame (fixed) 

<table>
<thead>
<tr>
<th>AG</th>
<th>Tube voltage (kV)</th>
<th>X-ray conditions per frame</th>
<th>Dose absorbed (over 74 frames)</th>
<th>Skin Dose (mGy)</th>
<th>Skin Dose (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>× 3</td>
<td>120</td>
<td>160 3.2 0.51</td>
<td>× 10 80 1.6 0.13</td>
<td>0.04</td>
<td>0.09</td>
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<td></td>
<td></td>
<td></td>
<td>× 20 25 1.6 0.04</td>
<td>0.04</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>× 30 10 1.4 0.014</td>
<td>0.04</td>
<td>0.09</td>
</tr>
</tbody>
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**Fig.4** Optimal X-ray conditions at different FPD gains 

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

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**Fig.6** Absorbed Dose of LST phantom at different FPD gains 

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**Fig.7a** and **Fig.7b** show Tomosynthesis images of the lung apex. The 6, 8, and 10mm simulated tumors were visible at the AG x20 as well as in AG x3 images. But at AG x30, the 6mm simulated tumor was not visible, only slightly visible. Both images show the diaphragm. As in the agaric tumors, the simulated tumors of all sizes appear similarly at AG x20 as they do in AG x3 image, but the effects of noise in adjacent high-absorptive regions reduce the visibility of the 6 and 8mm simulated tumors.

Investigation 4: Evaluating Visibility of Images in Volunteers 

We concluded from the results of investigations 1 to 3 that Tomosynthesis reduces radiation exposure when AG results in low X-ray dose, but simultaneously, the graininess and CNR values become worse. 

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

Noting that graininess increased as AG was increased in AG x20, we wondered if a similar marked difference would appear when we used an LST phantom with similar to the human body. We decided to determine an allowable range of dose reduction that would keep simulated tumors visible in conventional imaging. We used the LST phantom used in phase 1. 

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 visible at AG x20 as well as in AG x3 image. But at AG x30, the graininess increased, although it was not as clear as AG x20. In the AG x3 image, the effects of noise in adjacent high-absorptive regions reduced the visibility of the 6 and 8mm simulated tumors.

Investigation 4: Evaluating Visibility of Images in Volunteers 

We concluded from the results of investigations 1 to 3 that Tomosynthesis reduces radiation exposure when AG results in low X-ray dose, but simultaneously, the graininess and CNR values become worse.
This team found that although the AG x 20 images had slight-ly higher graininess in regions of high absorbance than the AG x 3 images, graininess remained low in the lungs and nod-ule visibility was almost identical. It was concluded that even AG x 20 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 espe-cially in the high absorption ranges, resulting in higher grain-iness. However, nodule imaging, comparable to that at the conventional AG x 3, was possible at up to AG x 20 with lower doses of radiation and the image quality was ade-quate for detecting the presence of nodules in lung cancer screening. Low-dose Tomosynthesis at 0.21 mGy (the dose absorbed at the center) — which is one-sixth of the exposure of 1.2 mGy in conventional Tomosynthesis (again the dose absorbed at the center) — resolved lesions comparably to those obtained by computed tomography (CT) imaging 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 presenta-tion.

We at the Research Center for Cancer Prevention and Screening have partnered with Hospital East of the National Cancer Center and Shimadzu Corpora-tion 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 Cen-ter. The device, equipped with Tomosynthesis func-tionalities, produced high-definition images compara-ble to those obtained by computed tomography (CT) imaging 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 presenta-tion.

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 observa-tion of a whole intestinal area. Tomosynthesis, by which an ar-bitrary plane and continuous tomo-graphic 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.

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

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tion 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) imaging 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.

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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 1.2mGy for Tomosynthesis, 0.09mGy for chest X-ray radiography, and 2.05mGy 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 3mm by 3mm. 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.

  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 3mm.
  
  (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 of 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.

**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 0.21mGy, 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 detect (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 were 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.
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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.

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