Abstract. We evaluated a computer-aided diagnosis (CAD) system with automatic detection of pulmonary nodules for lung cancer screening with computed tomography (CT). Five hundred and eighteen participants were examined with low-dose helical CT during a lung cancer screening by three respiratory physicians according to the General Rule edited by the Japan Lung Cancer Society. Four cases were detected by CAD and pathologically diagnosed as lung cancer. We compared the detection capability of the physician and CAD in 301 participants. Three physicians determined 75/301 (24.9%) participants as "e" (suspicious of lung cancer) in consensus without CAD, while 3 participants were added to "e" with CAD. Three physicians did not independently judge as "e" in 14 (18.7%), 16 (21.3%) and 16 (21.3%) out of 75 participants. CAD could not identify 17 (22.7%) nodules of 75 participants, and all 17 were less than 6 mm in diameter. The CAD system offers a useful second opinion when physicians examine patients at lung cancer CT screenings.

Few studies on lung cancer screening have been reported using low-dose helical computed tomography (CT) scanning (1-6). Helical CT scanning has the highest sensitivity for detection of pulmonary nodules compared to other examinations and has the potential to demonstrate small, clinically unapparent, curable lung cancer (2, 3). The reliable detection of small pulmonary nodules is an important task for early detection of lung cancer with low-dose helical CT because a follow-up examination can demonstrate growth as a sign of a potential malignancy (7). The sensitivity of small pulmonary nodules detected by physicians is not satisfactory (8, 9), especially at a mass screening for lung cancer.

Sufficient automatic nodule detection may be useful to guide physicians to questionable structures. There are some ways to integrate these features into the physician's work. A very convenient one is the integration of a softcopy viewing workstation. Utilization of automatic nodule detection in the clinical routine has become possible due to the dramatic increase in computer performance within acceptable limits (10-12). The Moriyama research group in Japan has developed a computer-aided diagnosis (CAD) system, which includes automatic nodule detection and a conventional viewing workstation needed to report thoracic CT examinations (10, 13, 14). In this study, we used this CAD system to detect pulmonary nodules on CT scans performed for a lung cancer screening with helical CT scan. In this report, we present the usefulness of the CAD system at a mass screening for lung cancer.

Materials and Methods

Subjects. All participants gave informed consent for CT screening of lung cancer and filled out questionnaires about respiratory symptoms, smoking and past histories. All participants were living in the surrounding areas of the National Kanagawa Hospital, Japan. From October 2001 to January 2003, a total of 518 CT screening procedures were performed. All 518 procedures were baseline screenings and there were no repeat screenings. This included 301 without CAD system assistance in the first half of the period and 217 which utilized the CAD in the second half. The
Table I. Characteristics of participants.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>without CAD</th>
<th>with CAD</th>
</tr>
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<tbody>
<tr>
<td>Participant number</td>
<td>301</td>
<td>217</td>
</tr>
<tr>
<td>Age median (range)</td>
<td>60 (26-91)</td>
<td>54 (21-84)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>220/81</td>
<td>156/61</td>
</tr>
<tr>
<td>Smoking index*</td>
<td>785.7</td>
<td>766.1</td>
</tr>
</tbody>
</table>

CAD: computer-aided diagnosis, * cigarette counts x smoking year

characteristics of the participants are summarized in Table I. The majority of participants (72.6%) were men between 20 and 85 years old. The frequency of current or former smokers was 174 (33.6%) and 66 (12.8%), respectively.

CT scanning. A helical CT scanner [Xvision/SR (TSX-002A), Toshiba, Japan] was used for this study. The scanning parameters were 120 kilovolt peaks, 50 mA, 10-mm collimation and 2.0 pitches. The whole lung field was scanned and completed at deep inspiration during a single breath-hold of about 15 sec. The total time between entering and leaving the room was only about 10 min. Ten-millimeter reconstructed images were stored on optical disks (650 megabytes of volume per disk). After scanning, high resolution CT (HRCT) scanning was added on the same day, when the lesion was strongly suspected of being lung cancer. The scanning parameters of HRCT were 120 kilovolt peak, 150 mA 2-mm collimation and 1.0 pitch reconstructed images at the HRCT scanning.

CAD workstation. The Moriyama research group kindly provided us with the CAD system they had developed. The hardware of the CAD system consists of a Toshiba AS 7000 U5 workstation (10, 14). A screenshot of the CAD system’s user interface is shown in Figure 1. This CAD system is equipped with automatic image diagnosis and an image screening function. When the automatic image diagnosis process is started in advance, the physician can begin lung cancer diagnosis at any time. Four centimetre slice CT images are always displayed and the physician can easily search the chosen image. When the physician clicks the mouse button on the image, the marker displays at the position of the cursor. The diagnostic results from all subjects are recorded on the hard disk drive. Network transfer of CT data from the CT scanner to the CAD workstation is realized with DICOM protocol. The CAD software includes a detection algorithm for pulmonary nodules and a user interface. The detection algorithm includes a complex segmentation of lung parenchyma (deletion of the CT table and soft tissue of the chest wall), followed by detection of structures with soft tissue density within the lung parenchyma and a region analysis to evaluate detected structures in the 3D data set (15). First, soft tissue objects within the segmented lung borders are detected using a fixed density threshold value (approximately 600 Housefield Units [HU]). Evaluation is done after using a 3D region-growing algorithm. Objects with a detected volume of less than 10 voxels are ignored. A spherical soft tissue density nodule this size corresponds to a diameter of approximately 5 mm due to the partial-volume effect and density threshold value. For the remaining objects, the distinction between probable nodules and other structures (especially vessels and scars or subsegmental atelectasis) are based on object geometry, especially on the length/width/height ratio, because it can be assumed that vessels and scars have a non-spherical shape.

Interpretation. All images were obtained at window settings appropriate for lung parenchyma (level, -600 HU; width, 1800 to 1600 HU). As for the CAD’s performance, the time required to obtain images and diagnose them was about 7 min, but the CAD cannot simultaneously obtain images from a CT scan when a CT scan is running another thoracic examination. Three respiratory physicians separately interpreted all cases according to the General Rule for the Clinical and Pathological Record of Lung Cancer edited by the Japan Lung Cancer Society (16). We made a judgement without CAD system assistance in the first half. In the second half, we used the CAD system and three physicians separately interpreted initially and then made a final judgement with CAD assistance (Figure 2). When they could not reach a consensus, a final conclusion on the findings was reached by consensus at the conference.

Results

Between October 2001 and January 2003, lung cancer screening with helical CT scan was performed on 518 participants (376 men, 142 women; age range 20-85 years, mean age 57.9 years). The three respiratory physicians made judgements in consensus according to the General Rule for the Clinical and Pathological Record of Lung Cancer (the Japan Lung Cancer Society) ("a", undetermined; "b", within normal limit; "c", old inflammatory lesion; "d", suspicion of disease other than lung cancer; "e", suspicion of lung cancer). We made judgement for 301 participants without the CAD system in the first half and for 217 participants with the CAD system in the second half.

In the first half, 75/301 (24.9%) participants were determined as "e" without CAD, while 55/217 (25.3%) participants were "e" with the CAD system in the second half (Table II). Four participants were histopathologically diagnosed with lung cancer in all periods. The sizes of four lung cancer cases were 9 x 9 mm, 18 x 15 mm, 32 x 20 mm and 50 x 45 mm in diameter. One case with a lesion 9 x 9 mm in diameter was diagnosed with pathologically bronchioloalveolar carcinoma. Besides lung cancer, other pulmonary diseases were diagnosed such as active pneumonia, non-tuberculous mycobacterium infection, bullae and chronic obstructive pulmonary disease.

The diagnosis by each physician of 301 cases in the first half is shown in Table III. The judgements of "e" by three physicians (Dr. A, Dr. B and Dr. C) were 62 (20.6%), 54 (17.9%) and 61 (20.3%), respectively. Three physicians determined 75/301 (24.9%) participants as "e" in consensus.
without CAD. All three physicians independently judged as "e" 46/75 (61.3%) participants, while one or two physicians judged 29 other participants as "e". We re-evaluated 301 participants and judged them with CAD. With CAD, three participants were added to "e" from other judgements in the first half without CAD. These three nodules were 8 mm, 5 mm and 5 mm in diameter. CAD picked up three cases overlooked by all three physicians, one nodule being 8 mm in diameter and highly suspicious of early lung cancer (Figure 3A). All 4 participants, who were histopathologically diagnosed as lung cancer, were detected by CAD.

Three physicians determined 75/301 (24.9%) participants as "e" in consensus without CAD, while 3 participants were added to "e" with CAD. Three physicians did not independently judge as "e" 18.7%, 21.3% and 21.3% of the 75 participants, while CAD could not identify 22.7% of the nodules of the 75 participants. The CAD system may provide a useful second opinion at lung cancer CT screenings, despite its limited sensitivity.

The CAD system is able to demonstrate some nodules overlooked by the physicians because they were located in more central areas of the lung. In this study, 3 cases were overlooked by all three physicians and reassessed to an "e" judgement with CAD assistance. One of these three was 8 mm in diameter and highly suspicious of early lung cancer. All three physicians might have overlooked this case because of a faint shadow located in the subpleural lesion. Midthun et al. reported that 21% of nodules 8-20 mm in size were malignant and that lesions 8-20 mm in size require further evaluation (17). We must make further examinations in this case.

On the other hand, the CAD system has an obvious weakness in the detection of nodules adjacent to the pleural lung surface because the image segmentation algorithm recognizes the nodule as a part of the chest wall and excludes it from further image processing. The algorithm is designed to detect nodules with diameters of at least 5 mm (10, 14). All 17 tiny nodules, detected by physicians and not identified by the CAD system, were less than 6 mm in diameter: ≤6 mm and >5 mm, 8 nodules; ≤5 mm and >4 mm, 4 nodules; ≤4 mm and >3 mm, 5 nodules (Figure 4). No apparent characteristics of CT number were noted in these 17 tiny nodules. Four nodules out of 17 were adjacent to the pleural lung surface and another four nodules were adjacent to the vessels.

Discussion

In this study, we evaluated a computer-aided diagnosis (CAD) system at a lung cancer CT screening. Three physicians determined 75/301 (24.9%) participants as "e" (suspicious of lung cancer) in consensus without CAD, while 3 participants were added to "e" with CAD. Three physicians did not independently judge as "e" 18.7%, 21.3% and 21.3% of the 75 participants, while CAD could not identify 22.7% of the nodules of the 75 participants. The CAD system may provide a useful second opinion at lung cancer CT screenings, despite its limited sensitivity.

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and the other four were adjacent to the vessels. Many pulmonary nodules including ground glass opacity (GGO) were picked-up by the helical CT scan (1), and a part of GGO is thought to be pulmonary adenocarcinoma at an extremely early stage (18). The General Rule for Clinical and Pathological Record of Lung Cancer edited by the Japan Lung Cancer Society notes that further examinations are necessary for cases with nodules more than 5 mm in diameter in helical CT screening for lung cancer (16). Further analysis will reveal the standard pick-up size of small nodules.

Table III. Judgements of 301 participants by each of the three physicians.

<table>
<thead>
<tr>
<th>Judgement*</th>
<th>Dr. A</th>
<th>Dr. B</th>
<th>Dr. C</th>
</tr>
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<tbody>
<tr>
<td>b/c/d/e</td>
<td>82/31/126/62</td>
<td>91/46/110/54</td>
<td>99/38/103/61</td>
</tr>
<tr>
<td>% e</td>
<td>20.6%</td>
<td>17.9%</td>
<td>20.3%</td>
</tr>
</tbody>
</table>

*We made judgements according to the General Rule for the Clinical and Pathological Record of Lung Cancer (the Japan Lung Cancer Society: "b", within normal limit; "c" old inflammatory lesion; "d", suspicion of diseases other than lung cancer; "e", suspicion of lung cancer). The three respiratory physicians (Dr. A, Dr. B and Dr. C) independently judged the 301 participants.

Figure 2. The detection of pulmonary nodules by CAD. (A) Original image of the location. (B) Detection result- a lesion was detected by the CAD system.

Figure 3. (A) Small pulmonary nodules detected by CAD without the physicians’ detection were 8 mm in diameter and -709 Hounsfield Units (HU) in CT number. (B) CT scan revealed a pulmonary nodule (5 mm, CT number -720 HU) detected by physicians but one that CAD could not identify.
The CAD system for the analysis of pulmonary nodules has the following advantages: (1) great speed of numerical calculation, allowing precise, quantitative and reproducible measurements, (2) an ever-increasing knowledge base to provide diagnostic information, and (3) non-susceptibility to fatigue (11). Armato et al. reported that 84% of missed cancers in a database of low-dose CT scans were detected correctly with the CAD system (19). Great benefits may well be seen in the quantitative results that can be derived from the analysis of a large number of subjects in a reproducible, efficient manner. These characteristics are very adequate for mass screenings for lung cancer. In this study, the "e" judgements determined by three physicians varied from 17.9% to 20.6% in the reevaluation of participants. The coincidence of all three physicians in "e" participants was not particularly high at 61.3%. The CAD system may provide physicians with tools to obtain more accurate diagnoses for lung cancer (20), especially in cases diagnosed by one physician.

Lung cancer screening using low-dose helical CT scanning is still a controversial issue (21, 22). The helical CT scan has the highest sensitivity for detection of pulmonary nodules compared to other examinations (2, 3). Nawa et al. reported that low-dose helical CT might be a promising method for screening early lung cancer at health examinations (23). There is currently insufficient evidence to support screening for lung cancer with any screening modality (20). Well-designed clinical trials are necessary to establish the guidelines for mass screening for lung cancer (24, 25).

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References


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