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CHEST

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Automatic detection of pulmonary nodules at spiral CT: clinical application of a computer-aided diagnosis system

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Abstract The aim of this study was to evaluate a computer-aided diagnosis (CAD) workstation with automatic detection of pulmonary nodules at low-dose spiral CT in a clinical setting for early detection of lung cancer. Eighty-eight consecutive spiral-CT examinations were reported by two radiologists in consensus. All examinations were reviewed using a CAD workstation with a self-developed algorithm for automatic detection of pulmonary nodules. The algorithm is designed to detect nodules with diameters of at least 5 mm. A total of 153 nodules were detected with at least one modality (radiologists in consensus, CAD, 85 nodules with diameter < 5 mm, 68 with diameter ≥5 mm). The results of automatic nodule detection were compared to nodules detected with any modality as gold standard. Computer-aided diagnosis correctly identified 26 of 59 (38 %) nodules with diameters ≥5 mm detected by visual assessment by the radiologists; of these, CAD detected 44 % (24 of 54) nodules without pleural contact. In addition, 12 nodules ≥5 mm were detected which were not mentioned in the radiologist's report but represented real nodules. Sensitivity for detection of nodules ≥5 mm was 85 % (58 of 68) for radiologists and 38 % (26 of 68) for CAD. There were 5.8 ± 3.6 false-positive results of CAD per CT study. Computer-aided diagnosis improves detection of pulmonary nodules at spiral CT and is a valuable second opinion in a clinical setting for lung cancer screening despite of its still limited sensitivity.

Keywords Lung · Nodule · CT · Computer programs · Computers · Diagnostic aid

Introduction

Spiral CT of the chest has the highest sensitivity for detection of pulmonary nodules compared to all other imaging techniques. It can demonstrate lesions with diameter as small as 2 mm. Low-dose spiral CT (LDCT) has the potential to demonstrate small, clinically unapparent bronchogenic carcinoma which can be treated with curative intention [1, 2, 3]. The reliable detection of even small pulmonary nodules is a crucial task for early detection of lung cancer with LDCT because close follow-up examinations may demonstrate growth as a sign of a potentially malignant lesion [4].

However, the radiologist's sensitivity for detection of small pulmonary lesions is unsatisfactory [5, 6, 7]. Especially in the central lung regions nodules can be missed because they are confused with blood vessels imaged in cross section. For differentiation between spherical (nodule) and tubular (vessel) structures contiguous slices have to be evaluated. This is a time-consuming task which is susceptible to errors; therefore, several approaches have been used to improve lung nodule detection:

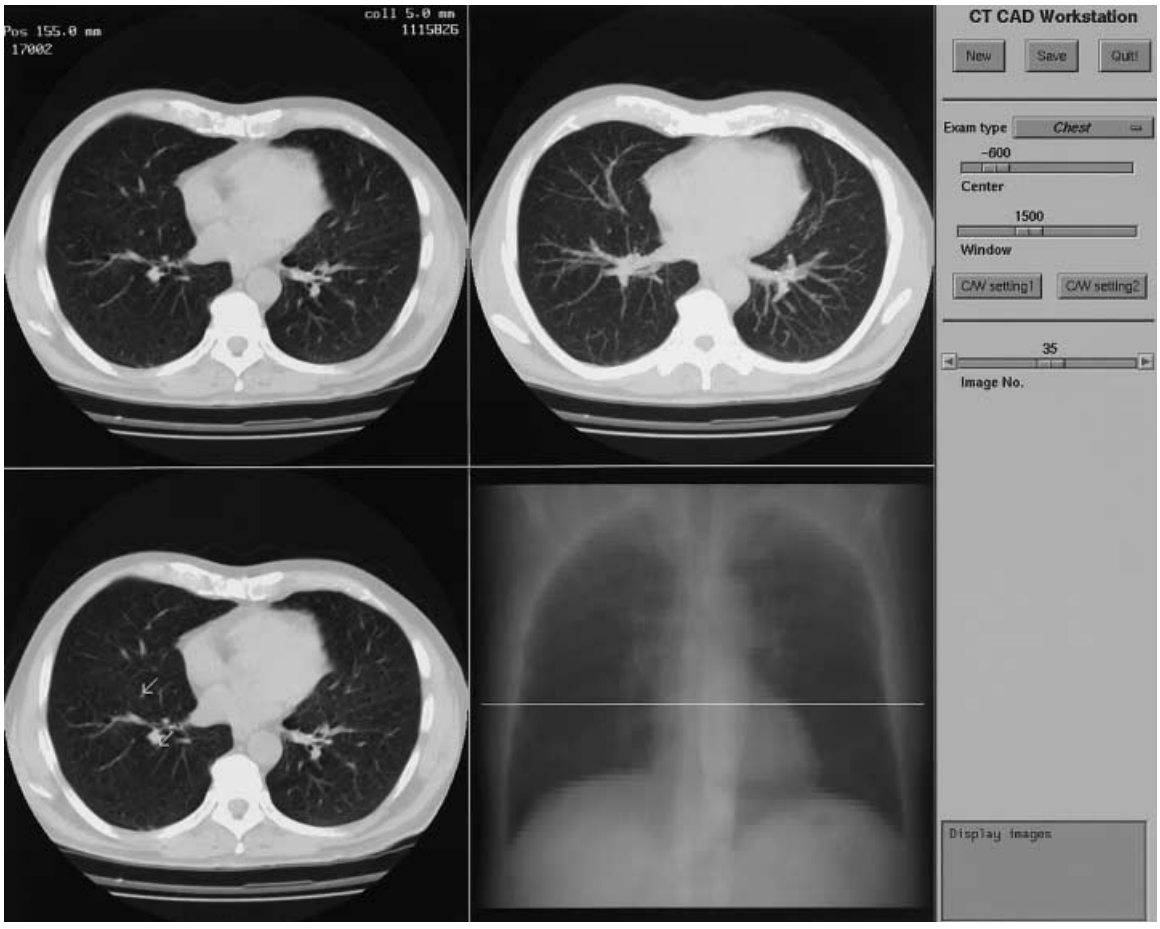

Fig. 1 Screenshot of the computer-aided diagnosis (CAD) system's user interface. Note the 5-mm pulmonary nodule (bottom left: *arrow* generated by the CAD system) in the right middle lobe, and a false-positive finding in the right lower lobe. *Top left:* axial image; *top right:* maximum intensity projection; *bottom left:* axial image with marked nodules; *bottom right:* reconstructed frontal view

1. Monitor viewing using cine mode allows for an easier distinction between tubular and nodular structures, compared with hardcopy viewing [6].
2. Axial thin-slab maximum intensity projection (MIP) delineates vessels as longitudinal structures and allows for easier detection of nodular structures [8].
3. Computerized analysis of CT scans has the potential for discrimination between tubular and nodular structures. Several algorithms have been described [9, 10, 11, 12, 13, 14].

It can be expected that a sufficient automatic nodule detection can guide the radiologist to questionable structures.

There are several ways to integrate these features into the radiologist's reporting work flow; a very convenient one is the integration into a softcopy viewing workstation. Utilization of automatic nodule detection in clinical routine has become possible due to dramatically increased computer performance over the past years which keeps calculation time within acceptable limits.

We developed a computer-aided diagnosis (CAD) workstation which includes automatic nodule detection and a conventional viewing workstation with cine mode and MIP as needed for reporting thoracic CT examinations. It is used for routine reporting for early detection of lung cancer with low-dose CT [3].

The purpose of our study was to evaluate the usefulness of this CAD workstation in clinical routine.

Materials and methods

CAD workstation

The hardware of the CAD system consists of a Silicon Graphics 02 workstation and a 21-in. cathode-ray tube (CRT) monitor. 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 [12, 13]. Firstly, soft tissue objects within the segmented lung borders are detected using a fixed density threshold value (approximately –600 HU). Evaluation is done after using a 3D region-growing algorithm. Objects with a detected volume of less than 10 voxels are ignored. For a spherical soft tissue density nodule this size corresponds to a diameter of approximately 5 mm due to partial-volume effect and the density threshold value. For the remaining objects the distinction between probable nodules and other structures (especially vessels and scars or subsegmental atelectasis) is 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.

The user interface provides four viewing modalities (Fig. 1):

1. The original axial CT image with cine mode capabilities
2. A thin-slab MIP in axial direction
3. The axial CT image with detected structures suspicious of nodules marked with arrows
4. A "projection radiograph" reconstructed from the CT data providing a frontal view of the chest with marked level of the axial image displayed.

Image segmentation takes approximately 2 min for a CT study with approximately 60 images and can be done before viewing. Segmentation results are stored together with the original images and are loaded whenever the corresponding CT study is opened. Region analysis is less time-consuming (approximately 20 s) and is done every time when loading a CT study.

Image material

The evaluation of the CAD workstation was embedded in a project for early detection of lung cancer using low-dose spiral CT of the chest. Informed consent of all patients was obtained for participation in the study and for scientific work-up of their data. The CT studies were obtained with 50-mAs tube current, 120-kVp tube voltage, 5-mm collimation, 10-mm table feed per rotation and 5-mm reconstruction interval at a Philips AVE scanner (Philips, Eindhoven, The Netherlands) in one breath-hold of less than 30 s. Images were displayed on hardcopies and on the CAD monitor using a lung window with 1500-HU window width and –600-HU window level on both modalities.

All CT studies are routinely reported using hardcopy and softcopy viewing including cine mode. Axial softcopy images were viewed stepwise and in cine mode on a conventional Windows-based workstation (Pentium MMX 200, 21-in. Monitor with Windows NT 4.0) with commercially available viewing software RadWorks 2.0 (Applicare Medical Imaging). A written report was based on consensus decision of two experienced radiologists. After the routine reporting procedure, CT studies were viewed by one experienced radiologist (D. W.) using the CAD workstation described above which additionally provides the results of automatic nodule detection and axial thin-slab MIP. At that time the reader had knowledge about the location of the nodules mentioned in the written report.

Time for viewing a CT study on hardcopy and for CAD monitor viewing was recorded. For both modalities, the overall time for making the decision as to whether the CT study contained nodules, and for recording the location of detected nodules on a reporting form, was measured using a stopwatch. Wilcoxon rank-sum test was used to test for differences between both methods, and $p < 0.05$ was regarded as significant.

The results of the automatic nodule detection were recorded and compared with the written report. The structures detected by the CAD system were divided into three groups:

1. Nodules found by the CAD system. A structure was considered a nodule if it was also described in the written report. A degree of certainty was recorded. If the written report mentioned uncertainty about the nodule, it was considered questionable; otherwise, it was recorded as definite. These nodules were regarded as true-positive results of the CAD system
2. Structures which were marked by the CAD system and were not mentioned in the written report. If this structure could not be considered a nodule in retrospect, it was counted as a false-positive result of the CAD system.
3. Structures which were not mentioned in the written report but were confirmed at repeat analysis of the images. A degree of certainty was recorded ("definite" or "questionable" nodule). These structures were also regarded as true-positive results of the CAD system and therefore as false-negative results of the routine reporting procedure without using the CAD system.

The decision whether a structure marked by the CAD system belonged to group 2 or 3 was made by both radiologists in consensus at repeat analysis of the CT study.

Nodules mentioned in the written report and not found by the CAD system were recorded as false-negative results of the CAD system.

To evaluate the diagnostic performance of radiologists with and without the CAD system sensitivity for nodule detection was calculated. All nodules found with any method (hardcopy or softcopy viewing, CAD system) and considered definite or questionable by two radiologists in consensus were used as gold standard. The analysis compared all nodules described in the written report to all nodules detected by the CAD system and recorded as true-positive findings (groups 1 and 3).

Nodule location was recorded as peripheral if the distance to the nearest pleural surface was less than 2 cm; otherwise, it was recorded as central location. The nodule was considered to have pleural contact if there was no lung density tissue visible between the nodule and the pleural surface.

Results

Between November 1999 and March 2000, 88 CT examinations of 85 subjects (56 men, 29 women; age range 41–76 years, mean age 58.3 ± 8.9 years) were enrolled in the study. On average, a CT study contained 61.8 (± 8.2) slices. In all cases at least one previous CT examination was available at time of consensus reporting since all studies were follow-up examinations.

Radiologists mentioned 138 pulmonary nodules in their written report, detected with hardcopy and softcopy viewing; of these, 132 nodules were reported as definite findings. Six nodules were reported to be questionable on the initial scan but were constantly seen on subsequent CT examinations. Mean nodule diameter was 4.6 ± 2.2 mm, ranging from 2 to 16 mm. Size distribution of the nodules is given in Table 1.

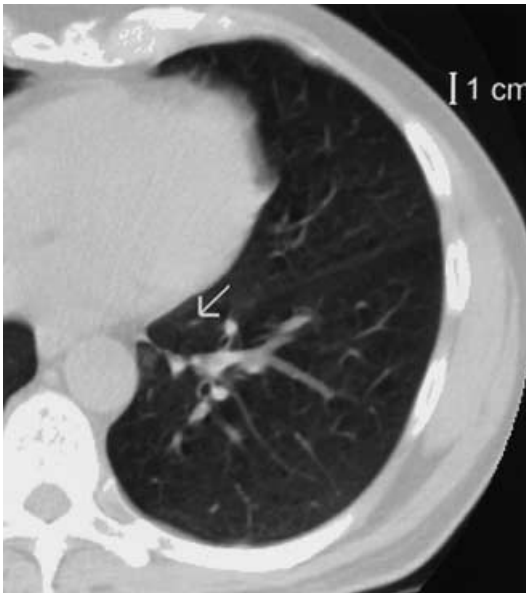

Fig. 2 A 5-mm nodule in the left lower lobe *(arrow)* adjacent to the interlobar fissure only detected by the CAD system and missed by the reporting radiologists on previous examinations, although it was visible in retrospect

Table 1 Size distribution, diagnostic confidence and location of nodules detected by both modalities

	< 5 mm	5–9 mm	≥10 mm	Total
All nodules	85	63	5	153
Definite nodules	80	60	5	145
Questionable nodules	5[a]	3	0	8[a]
Pleural contact	16	4	1	21
Central location	2	15	1	18

[a]Two questionable nodules were not mentioned in the radiologist's report but were detected by the CAD system and were considered a questionable nodule in retrospect

The CAD system was not designed to detect nodules < 5 mm in diameter to keep the amount of false-positive findings within acceptable limits. Taking into account only lesions with a diameter of at least 5 mm, 58 pulmonary nodules were described by the radiologists in their consensus report; 3 of them were initially reported as questionable finding. Sixteen of these lesions were detected by the CAD system. In addition, CAD found 10 nodules which were not mentioned in the written report but did represent true nodules in retrospect (Fig. 2), all of which were considered definite findings. Using all modalities (hardcopy and softcopy reading, CAD) a total of 68 nodules ≥5 mm were detected; of these, 85 % (58 of 68) were described by the radiologists in their consensus report, and 38 % (26 of 68) were detected by the CAD system. Ten nodules (15 %) would have been missed without use of the CAD system (Table 2).

Table 2 Influence of size and location of nodules on detection by visual assessment of radiologists and computer-aided diagnosis (CAD)

	N	Nodules found by:		
		Radiologists only	Radiologists and CAD	CAD only
All nodules	153	116 (76)	22 (14)	15 (10)
Nodules ≥5 mm	68	42 (62)	16 (24)	10 (15)
No pleural contact	108	74 (69)	21 (19)	13 (12)
No pleural contact ≥5 mm	54	30 (56)	15 (28)	9 (17)
Peripheral location	135	106 (79)	17 (13)	12 (9)
Central location	18	10 (56)	5 (28)	3 (17)

Numbers in parentheses are percentages

Taking into account all nodules regardless of their size, 153 lesions were detected by at least one modality (hardcopy and softcopy viewing, CAD); of these, 138 (90 %) were reported by the radiologists in consensus without using CAD, and 37 (24 %) were demonstrated by the CAD system. Fifteen nodules (10 %) would have been missed by the radiologists.

Location adjacent to the pleural surface was noticed in 21 (14 %) nodules; none of them were detected by the CAD system because the segmentation routine regarded the nodules as a part of the chest wall (Fig. 3). Of the remaining nodules without pleural contact, 31 % of all nodules and 44 % of nodules ≥5 mm were detected by CAD.

On the basis of all nodules demonstrated by at least one modality, sensitivity of radiologists was 90 % (138 of 153) for all nodules and 85 % (58 of 68) for nodules ≥5 mm. This difference is due to the fact that CAD found more additional nodules ≥5 mm than smaller ones. Sensitivity of CAD was 24 % (37 of 153) and 38 % (26 of 68), respectively. The CAD system was designed to detect nodules ≥5 mm without pleural contact. Sensitivity for these nodules was 83 % (45 of 54) for radiologists and 44 % (24 of 54) for CAD.

Nodule location was peripheral in 135 cases and central in 18 cases. The CAD detected 21 % (29 of 135) of the peripheral and 44 % (8 of 18) of the central nodules. Twelve (9 %) peripheral and three (17 %) central nodules would have been missed without the CAD system (Table 2).

On average, the CAD system marked 5.8 ± 3.6 false-positive results per CT study (1–18 structures, median 6 structures). This corresponds to one false-positive finding on every tenth CT image. All these structures proved to be blood vessels imaged in cross section.

Mean viewing time was 2:55 ± 0:48 min using hardcopies. Viewing using the CAD system was significantly

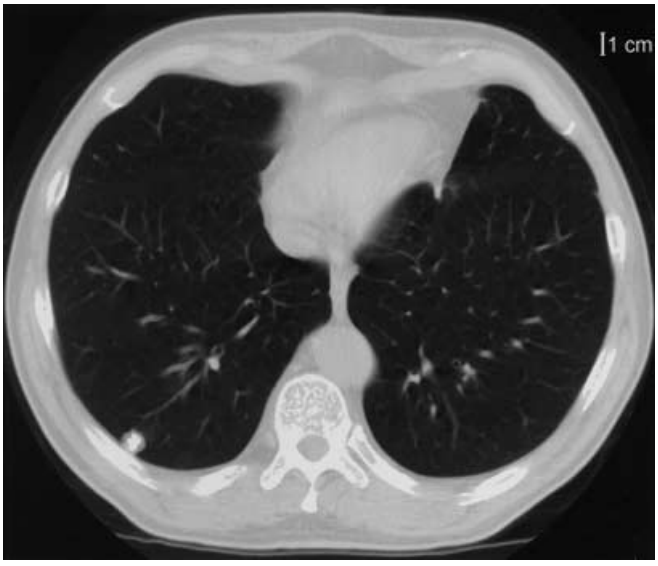

Fig. 3 A 16-mm partially calcified nodule in the right lower lobe not detected by the CAD system because of contact with the pleura which led to segmentation as a chest wall structure

($p < 0.05$) more time-consuming; mean time was 3:44 ± 0:47 min.

Discussion

The increasing discussion on lung cancer screening with low-dose CT [2, 3, 15] leads to the requirement of high sensitivity for pulmonary nodules at analysis of CT scans. Radiologists are far away from detecting every nodule which needs to receive attention in the context of a screening for bronchogenic carcinoma with low-dose spiral CT in order to ensure appropriate follow-up or further diagnostic work-up as required by the screening algorithms. Especially in that specific clinical setting the radiologist should use any available technical help to detect every pulmonary nodule.

At present, neither the radiologist using visual assessment nor the CAD system are able to find every pulmonary nodule; however, the results demonstrate that both detection methods can be used in a complementary fashion. The CAD system has obvious weaknesses in 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. Fortunately, there are no large blood vessels near the pleural surface; therefore, every soft tissue structure in the subpleural space is probably a nodule (or another lesion, e.g. a scar), and the radiologist has no difficulty to detect it. On the other hand, the CAD system was able to demonstrate some nodules overlooked by the radiologists mainly because they were located in more central areas of the lung and were probably mistaken by the radiologist as vessels.

A problem that remains to be solved are nodules adjacent to vascular structures which are difficult to detect for the radiologist and are likely to be taken as a part of the vessel by the CAD system. Further improvement of the region-analysis algorithm is necessary to detect these nodules which would be an effective help for the radiologist. Analysis of structure diameter, especially seeking for abrupt changes, might be a possible way to find nodules adjacent to blood vessels.

Sensitivity of nodule detection by CAD was lower (overall detection rate 37 of 153) compared with other published results [11, 14]. This is mainly due to different nodule size, as nodules in our healthy subjects were much smaller compared with other studies using CT scans from patients with metastatic lung disease to test detection algorithms [11]. Another study does not provide information about nodule size [14]; thus, our study is more likely to reflect the typical conditions in a screening setting.

Motion artefacts may result from patient movement (e.g. breathing) during the CT scan or from pulsation of heart and great vessels. Both may lead to failure of the region-growing algorithm because the continuity of tubular structures in z-direction is disrupted, resulting in a nodular appearance of the vessel "fragments"; therefore, numerous false-positive results are caused by these artefacts.

Compared with other known approaches [9], the detection algorithm is combined with a user interface which allows easy integration into the normal work flow. Furthermore, the additional information provided by the CAD system can assist the radiologist in nodule detection:

1. The cine mode allows better nodule detection due to the easier distinction between nodules and vessels [6].
2. The thin-slab MIP view is able to demonstrate nodules more clearly separated from vessels especially on CT studies with thin reconstruction intervals [8].
3. The possible nodules marked by the CAD system lead the radiologist to questionable structures.

The increased reporting time using the CAD system is due to the additional information available for every axial CT image.

Conclusion

The evaluated CAD system proved to be useful in routine reporting of low-dose screening CT examinations. It improves detection of pulmonary nodules particularly in the central lung areas and, therefore, is a valuable "second opinion". Furthermore, it can improve the radiologist's diagnostic confidence by providing additional information.

Although the current version already allows comfortable application, an improvement in sensitivity and a reduced amount of false-positive results can be expected with ongoing development of the detection algorithm.

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