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Thorac Surg Clin 14 (2004) 125–133

THORACIC
SURGERY
CLINICS

Computer-aided diagnostics

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In this paper the authors provide an overview of recent work in using computer analysis of CT images of the lungs to aid the physician in diagnosing diseases of the lung and planning treatments, with particular attention to lung cancer. Computers can provide such aid in several domains:

1. Image visualization: by providing different viewing options, the computer can present image data to the radiologist in a more convenient form for diagnosis or to a surgeon in such a way that anatomic relationships can be recognized more easily
2. Detection: the computer can be used to detect lung abnormalities automatically, especially in typical situations in which whole-lung scans consist of hundreds of images and the abnormality is small and might only be visible on one image
3. Characterization: the computer can make measurements on a pulmonary nodule to determine its malignancy status; currently, the most accurate measurement for predicting malignancy is growth rate, which is determined from the change in nodule size in two time-separated scans
4. Abnormality documentation and treatment evaluation: if many nodules are present, the computer is ideal for the tedious cataloging and documenting task. Furthermore, for treatment evaluation the computer can be used to quantitatively measure the difference through the whole-lung region before and after surgical or nonsurgical treatments

Each of these domains is considered in turn. The lung is a particularly convenient organ for CT image analysis because many abnormalities show up as brighter image regions on the dark lung parenchyma background, which is in contrast to other organs, in which the contrast is much less and the delineation of abnormal tissue is typically more difficult. The lung also presents a unique challenge to accurate measurement because of its compressible nature. Image analysis is complicated, for example, by change in patient position, degree of inspiration, heart motion image artifacts, and body movement image artifacts.

CT technology has made considerable advances over the past decade, providing better information and greater challenges for the radiologist. Newer multislice scanners can capture many more images in a single breath-hold. Consequently, the radiologist is confronted with the task of examining several hundred images for a single whole-lung scan rather than the tens of images characteristic of older scanners. Furthermore, these images are now often recorded using a low-dose protocol, which means that there is much more image noise, making the reading more difficult. However, for computer analysis the thinner slices provide a tremendous opportunity for considering the CT scan as single three-dimensional (3D) image rather than the traditional viewpoint of a set of individual two-dimensional images. Computer methods can use true 3D geometric analysis, which is much simpler and more direct than the two-dimensional counterpart.

For 3D geometric techniques to be used, the 3D image must have a close to isotropic voxel size. The resolution in the axial direction (slice thickness) must be similar to the in-plane resolution (pixel size). For example, a typical whole-lung image has a pixel size of about 0.6×0.6 mm. If the slice thickness is

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1547-4127/04/$ – see front matter
doi:10.1016/S1547-4127(04)00030-1

10 mm, there is an anisotropic mismatch of 10 to 0.6 or about 18 to 1. For a 1 mm slice thickness the ratio is 1:0.6 or about 1.8:1. The most recent multislice scanners offer 0.5 mm slice thickness, in which the ideal 1:1 ratio is achievable.

The main benefits of computer-aided image analysis are realized when quantitative methods are used for measuring and classifying image characteristics. Image visualization, in which the computer provides a more human-convenient presentation of image data, has been the more traditional use of computer assistance; however, such a qualitative approach leaves the image analysis and decision making entirely up to the radiologist. In contrast, quantitative data analysis can provide three major benefits to the radiologist:

1. More accurate and repeatable measurements. The computer does not suffer from fatigue and will consistently use the same measurement algorithm with the same parameters every time it is applied. In contrast, humans use a number of subjective judgments in making measurements and there are many sources of measurement variation. However, the computer sometimes makes mistakes in locating the correct boundary for a region of interest. Therefore, a good strategy is to have the human observe the decisions made by computer and to manually override the measurement process when any incorrect computer decisions are observed.
2. Large database for diagnosis. Diagnosis by computer involves comparing the quantitative information from an image with knowledge of all previous examples that the computer has in its database. This knowledge can be recorded in the computer in many ways, from a set of actual images to a set of derived measurement parameters. However the data are organized, the general result is that the larger the knowledge database (number of cases), the better the quality of the computer diagnosis. Given that memory to store the cases is no longer a major consideration for modern computer technology, clinicians can anticipate that performance of computer diagnosis methods will continue to improve with time. Compare this scenario to the physician, who must typically make a judgment based on a lifetime personal experience of only a few hundred cases.
3. Management of large data sets. The computer is an excellent data manager ideally suited to the tedious task of documenting all abnormalities that might be present in a single whole-lung scan. Furthermore, it is equally well suited to matching two time-separated whole-lung scans and documenting the changes that have occurred in the period between them. For radiologists this is an arduous, time-consuming task that is difficult to perform consistently for long periods of time.

Recent advances in qualitative image visualization are considered in the next section, followed by the advantages of using quantitative methods for detection, characterization, and general documentation.

Visualization

Unlike chest radiographs (the original standard for chest radiography), the visualization of CT images has always required computer assistance in the form of digital reconstruction algorithms, even when the images are presented to the radiologist on a film base. To acquire CT image data, several parameters, including the dose and slice thickness, need to be preestablished; however, to view a CT image a radiologist must specify a number of post hoc parameters when the raw CT image data has been acquired. These parameters include brightness and contrast (level and widow), spatial enhancement, and the field of view (magnification). The use of film fixes these parameters while the use of a soft-copy computer display device permits the radiologist to modify these parameters in real time while viewing the image data.

The standard radiology soft-copy viewing station is designed to accommodate a range of imaging modalities. Constraints on projective images such as chest radiographs and mammograms require high resolution and a well-controlled viewing environment; hence, most such soft-copy systems are costly and involve a special high-resolution grayscale monitor.

The viewing requirements for high-contrast lung CT scans are, in general, less stringent than for projective images. Many standard PCs offer adequate quality viewing characteristics for viewing CT image data, especially for the characterization of previously identified nodules. Furthermore, they offer color as one means of drawing attention to regions of interest such as lung abnormalities. Standard computer graphics methods coupled with simple computer analysis offer alternative modes for viewing CT image data, and vendors are introducing such methods. Acceptance of these methods by radiologists has been rather slow; possibly one factor is the difficulty in

Fig. 1. Axial CT image with a small pulmonary nodule outlined.

incorporating such techniques on the traditional high-resolution, grayscale, soft-copy workstations.

To illustrate some of the visualization options, the visualization of a single lung nodule is presented. In Fig. 1, a conventional axial CT image of the lung is shown with a 10 mm nodule outlined in the left lung. All scanners and soft-copy workstations support this conventional visualization. Fig. 2 shows the image slices through that nodule at the same time in a montage display. Fig. 3 shows an alternative method of viewing these data using standard computer graphics techniques. A visualization is generated to resemble how the nodule might look if it were perfectly extracted from the lung, if it had a perfectly reflecting matt surface, and if it was illuminated by a single, simple light source with some uniform background illumination. Because this method involves creating a 3D model of the nodule (which is made possible by the isotropic property of the thin slice scan), the nodule can be viewed from different viewpoints than just the conventional axial direction. On a viewing workstation the nodule can be rotated and viewed from any arbitrary direction. In Fig. 3, visualizations from the three canonical viewpoints, axial, sagittal, and coronal, are provided.

A second conventional nodule image is shown in Fig. 4. The visualization of that nodule using standard ray tracing techniques is shown in Fig. 5. In this case the body tissue is given an opacity related to its radiograph density, then computer algorithms identify the nodule region and colorize the other dense image objects in the lung according to their geometric form, hence using color to highlight the region of prime interest to the radiologist (Fig. 6). A magnified image of the nodule is shown in Fig. 7.

In Fig. 8A a CT image of a nonsolid nodule or ground-glass opacity (GGO) is shown. For this important nodule type there is a distinctive difference in density between the nonsolid material and other solid tissue (eg, vessels and chest wall). To visualize the nonsolid tissue the authors use a translucent rendering method as shown in Fig. 8B. The interaction between the vessels and the nodule can now be

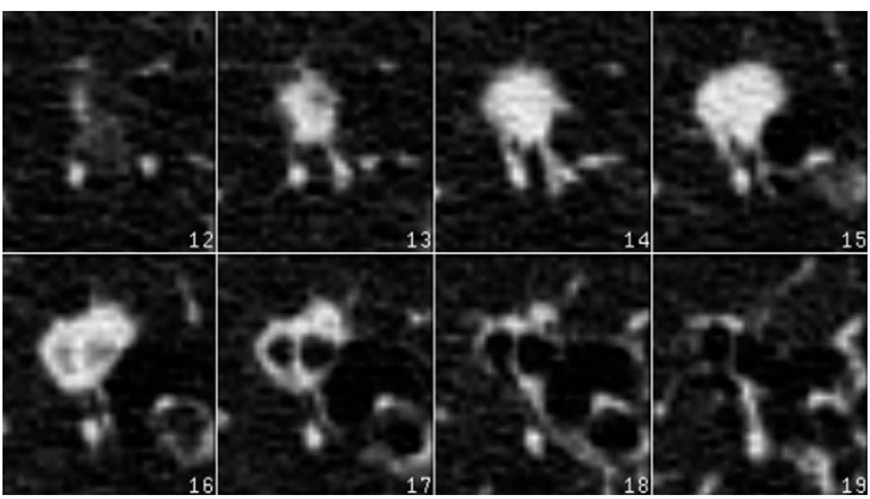

Fig. 2. Consecutive 1 mm image slices through the nodule shown in Fig. 1.

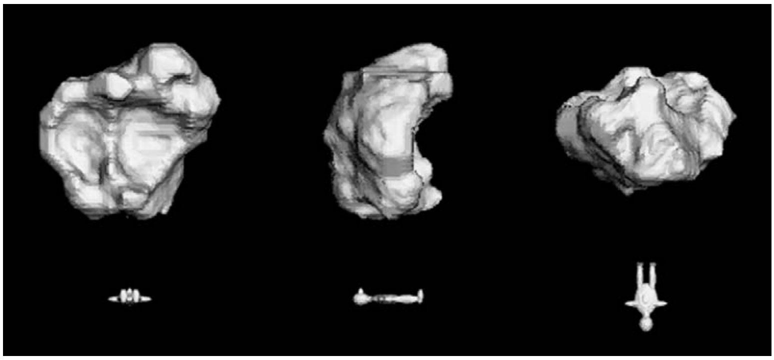

Fig. 3. 3D reconstructions of the nodule shown in Fig. 2 rendered from three orthogonal viewing directions: axial, sagittal, and coronal.

seen. Further, the authors can remove the vessels from consideration as shown in Fig. 8C to have an unobstructed view of the whole nodule's shape.

While visualization is important, especially for the correct interpretation of image data by radiologists, the real power of the computer is in the *quantitative* analysis of the data to directly determine clinically relevant information. The visualizations shown in Fig. 9 show a rendering of a geometrical model of a nodule derived from the nodule size measurements extracted from the computer segmentation process. This reference (see Fig. 3) is derived from the quantitative analysis, whereas other renderings are computed without explicit segmentation, and measurements cannot be made from them.

Detection

A computer assistant for detection examines a whole-lung CT scan for any evidence of pulmonary nodules and reports the locations of suspected nodule to the radiologist. The most common scenario (one that is currently the most likely to be approved by the U.S. Food and Drug Administration) is to use computer-detected results as a second read. When the

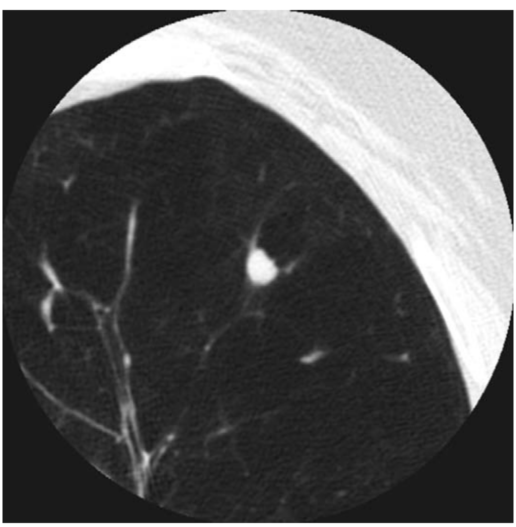

Fig. 4. Conventional focused study image of a small, solid pulmonary nodule.

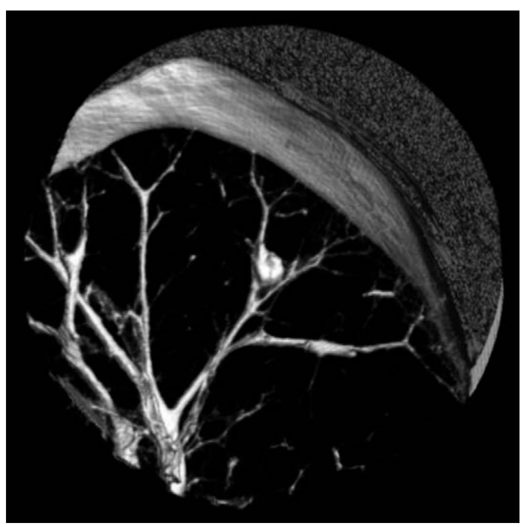

Fig. 5. Ray-traced rendering of the nodule shown in Fig. 4.

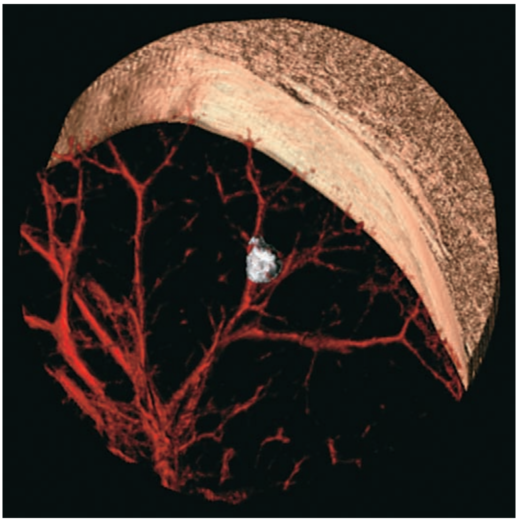

Fig. 6. Color-coded rendering of the nodule shown in Fig. 4.

radiologist has performed a conventional reading of the scan, the computer highlights possible nodule locations that have not been documented by the radiologist. The radiologist then examines these locations with a view to modifying the report.

The critical issue is that the detection system must be sensitive enough to detect essentially all nodules without indicating too many false alarms (false-positives). To achieve this performance, the detection algorithm must have a high sensitivity and specificity. Furthermore, a sensitivity parameter needs to be set to fix the sensitivity/specificity tradeoff to the optimal value for a given clinical reading task.

Of importance to a detection system is the definition of a nodule or a reportable event. In general, large nodules are easier to identify for the radiologist and the machine. The task of nodule identification becomes increasingly more difficult as the nodule size approaches the voxel size of the scanner. Furthermore, as nodules of a smaller size are detected and characterized, there is a higher probability that smaller, benign nodules will be detected. Clinically relevant nodules are currently considered to be in the 3 mm to 3 cm size range. In addition, other lung abnormalities might be of interest to the radiologist, and the issue of reporting these abnormalities should be addressed.

Experimental computer-aided systems for lung nodule detection are currently being developed and evaluated. Basic algorithms now exist for nodule detection [1–3]; however, more work is needed to optimize these methods and to establish appropriate parameters for general clinical use. For example, the specification of exactly what abnormalities are to be reported and the appropriate size and sensitivity settings commiserate with an acceptable rate of false-positives for clinical use must be determined. Furthermore, as technology improves and more experience is gained, it is anticipated that future methods will achieve a significant improvement with respect to sensitivity and specificity.

Characterization

The computer can aid the physician in a number of ways by characterizing the detected nodule. Beyond a variety of special visualizations, the computer can provide quantitative measurements on that nodule for the physician to interpret or it can perform a classification on these measurements (based on a large number of previously diagnosed nodules) to directly determine the probability of malignancy.

The basic procedure for nodule characterization is

1. Segmentation, determining which voxels belong to the nodule and which do not
2. Feature extraction, making quantitative measurements on the nodule voxels
3. Diagnosis/classification, determining the probability of malignancy from a statistical analysis of the extracted features

Two basic methods have been explored to determine the malignancy status of a nodule by computer evaluation: shape features and size change. In the

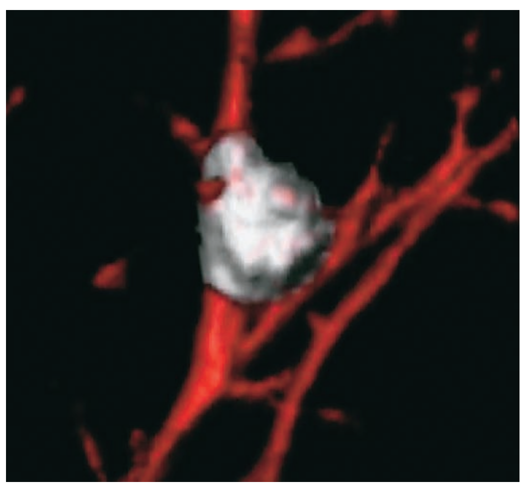

Fig. 7. Magnified view of the nodule shown in Fig. 6.

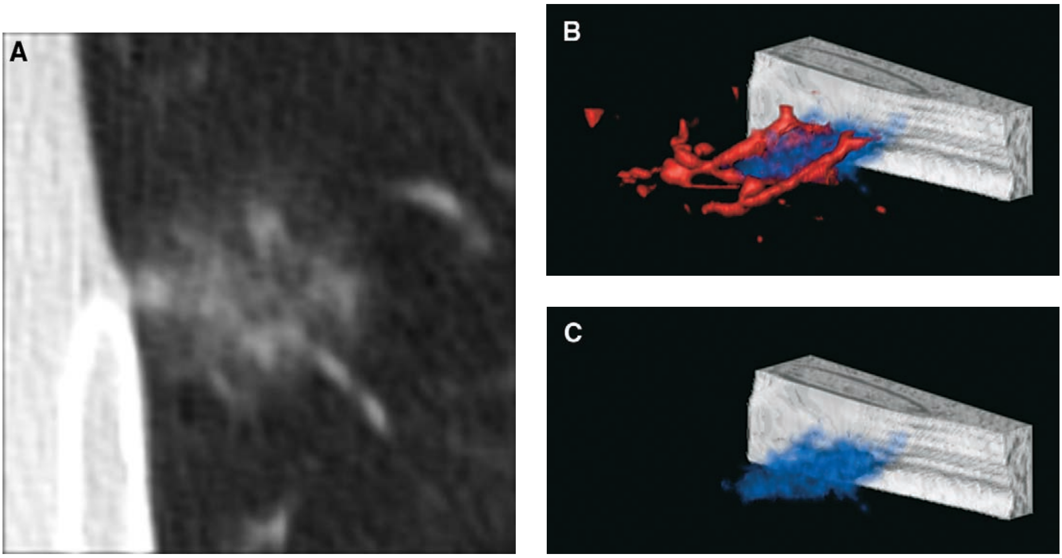

Fig. 8. Visualization of a nonsolid nodule. (*A*) CT image. (*B*) Rendered as a translucent blue region with vessels marked in red. (*C*) With vessels removed.

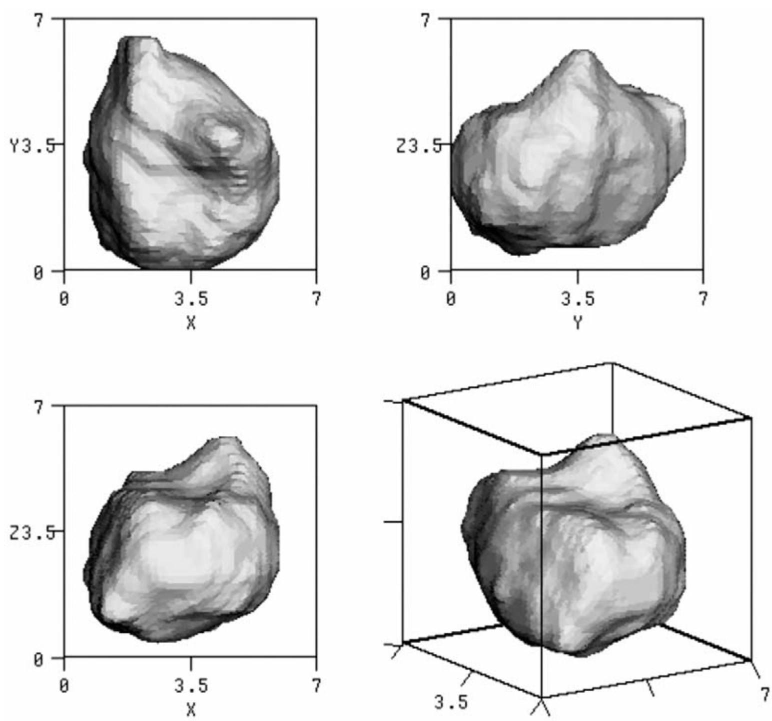

Fig. 9. Light-shaded views of the segmented nodule in Fig. 4.

shape feature method a number of measurements are made on the nodule voxels from a CT scan and these features are used to predict malignancy by way of a classifier that has been trained on a database consisting of documented malignant and benign nodules. This method has been explored in research settings, and while the initial results are quite promising [4], more research is needed. The second method is to measure growth rate from the nodule size change in two time-separated CT scans. In preliminary studies [5] a high growth rate has been found to be an excellent predictor of malignancy; however, this approach has the drawbacks of requiring a second CT scan and the delay in diagnosis caused by the required time period between scans

CT manufacturers and other vendors are now providing 3D nodule growth estimation tools. Issues with this approach are that the two scans must be of a high quality and recorded with the same CT scan parameters, and the time delay between scans must be long enough to obtain a sufficiently accurate measurement to predict malignancy, but this delay needs to be minimized to reduce patient anxiety. For current CT scanner technology, this optimal time period might be several months for small nodules, reducing to perhaps less than 1 month for larger (1 cm) nodules.

Documentation and health evaluation

Beyond detecting and measuring nodules, the computer system should also be capable of facilitating other operations such as whole-lung health monitoring and automated nodule cataloging. This is especially important for repeat scans in a screening or treatment scenario. This operation in itself does not require any new technological developments; rather, it requires the development of a patient management system that goes beyond conventional Radiological Information Systems (RIS). For example, the authors have built into their data management system a whole-lung volume and emphysema analysis capability. The computer automatically delineates the whole lung parenchyma region from the CT images and computes the lung volume. An analysis of the density distribution of the lung parenchyma is also computed to produce a visualization of the spatial distribution of emphysema. The outcome of this analysis presented

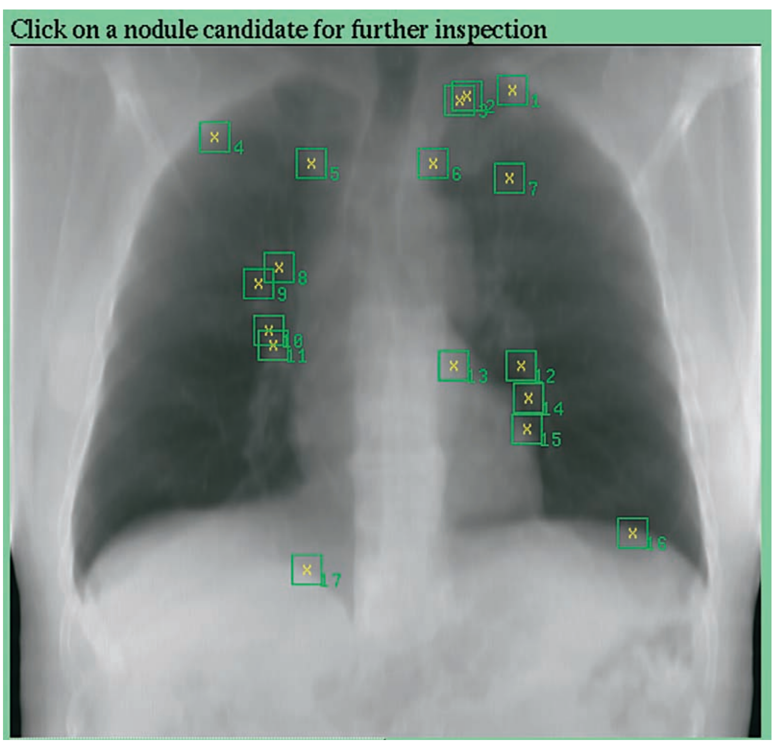

Fig. 10. Nodule candidate locations displayed on a coronal projection image of the lungs.

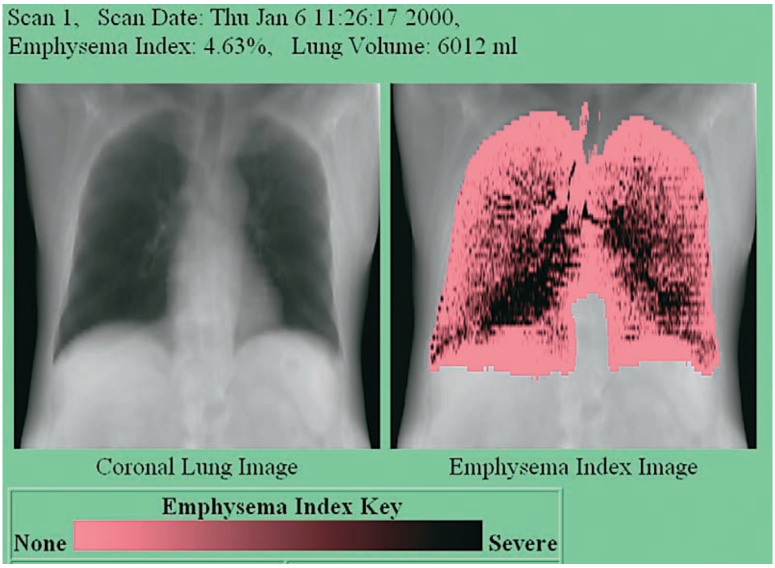

Fig. 11. Emphysema visualization on a coronal projection of the lungs.

from a coronal viewpoint is shown in Figs. 10,11. Whole-lung analysis of this type can be applied automatically to all CT scans before physician evaluation on a routine basis.

Discussion

Recent computer methods have been used to enhance the visualization of CT images for diagnostic purposes and to provide quantitative measurements on these images. It is in the latter respect that computer methods are most powerful as a diagnostic tool. The advantages to diagnostic radiology are self-evident; however, these methods can also be applied to aid treatment and intervention.

Many quantitative and qualitative improvements can be anticipated in the anatomic analysis of the chest CT. Algorithms have been developed for the automatic segmentation of major anatomical regions from chest CT scans; however, the authors anticipate that future algorithm development will result in the automatic segmentation of all major bone and tissue regions in the thorax. The lung regions themselves are extracted easily, as are the trachea and major bronchi. Current efforts include the bone structures.

For the surgeon, these methods can be used for surgical planning in the preoperative phase. The boundaries of the lobes can be visualized and the abnormality can be viewed from different directions to present its spatial relationship to other structures within the lung. The health of other structures can be evaluated; the diameters of vessels, for example, can be measured. The amount of healthy lung that is being resected can be measured in emphysema patients so that the amount of tissue removed can be modified. Another area of development includes methods to model how the lobes and the remaining lung will remodel after surgery to anticipate any complications. In addition, better scanner sensitivity coupled with new algorithmic developments can achieve a more precise evaluation of invasion, especially in critical areas of the major vessels and the mediastinum.

This 3D visualization can be made available at the operating table on a flat-panel screen, where it can be referred to and manipulated in real time. Such facilities can also be integrated with video-assisted thoracic surgery (VATS) camera images. Additional integrated visualizations can be provided based on camera viewpoint, previous camera images, and available CT images.

In the postoperative domain, image analysis can also provide a number of benefits. The effects of medication can be measured accurately, and the volume capacity of the lungs can be compared before and after surgery and as healing progresses. Further, the healing process itself can be monitored carefully; the development of scar tissue and its growth pattern can be ascertained. The effects of medication can be evaluated and the optimal strategies for recovery can be determined for an individual patient and for refining the methods of standard practice.

Summary

The computer can be used in a number of ways to aid the physician to interpret CT lung images. Commercial tools are becoming available to assist the radiologist in growth rate determination, hence cancer diagnosis. Computer algorithms are in development that will permit lung health evaluation, including nodule detection. Finally, the results of such efforts will probably produce more detailed visualizations of the lung region, including depictions of the location and state of lung abnormalities. While computer methods have found a first application with the radiologist, these methods should also provide a valuable aid to surgery and pathology.

References

[1] Lee Y, Hara T, Fujita H, Itoh S, Ishigaki T. Automated detection of pulmonary nodules in helical CT images based on an improved template-matching technique. IEEE Trans Med Imaging 2001;20(7):595–604.

[2] Fan L, Qian J, Ordy B, Shen H, Naidich D, Kohl G, et al. Automatic segmentation of pulmonary nodules by using dynamic 3D cross-correlation for interactive CAD systems. In: Sonka M, Fitzpatrick JM, editors. Proceedings of the SPIE 2002;4648:1362–9.

[3] Taguchi H, Kawata Y, Niki N, Satoh H, Ohmatsu H, Kakinuma R, et al. Lung cancer detection based on helical CT images using curved surface morphology analysis. SPIE Conference on Image Processing 1999; 3661:1307–14.

[4] Reeves AP, Kostis WJ, Yankelevitz DF, Henschke CI. Three-dimensional shape characterization of solitary pulmonary nodules from helical CT scans. In: Lemke HU, Vannier MW, Inamura K, Farman AG, editors. Proceedings of Computer Assisted Radiology and Surgery (CARS '99). New York: Elsevier Science; 1999. p. 83–7.

[5] Yankelevitz DF, Reeves AP, Kostis WJ, Zhao B, Henschke CI. CT evaluation of small pulmonary nodules based on volumetrically determined growth rates. Radiology 2000;217:251–6.