

Alex M. Aisen, MD
Lynn S. Broderick, MD
Helen Winer-Muram, MD
Carla E. Brodley, PhD
Avinash C. Kak, PhD
Christina Pavlopoulou, MS
Jennifer Dy, PhD
Chi-Ren Shyu, PhD
Alan Marchiori, BS

Index terms:

Computed tomography (CT), thin-section, 60.12115
Computers, diagnostic aid, 60.12115, 60.12118
Computers, educational aid, 60.12115
Lung, CT, 60.12115, 60.12118
Lung, diseases, 60.12115

Published online

10.1148/radiol.2281020126
Radiology 2003; 228:265–270

Abbreviations:

ASSERT = automated search and selection engine with retrieval tools
PBR = pathology-bearing region

¹ From the Department of Radiology, Indiana University School of Medicine, UH 0279, 550 N University Blvd, Indianapolis, Indiana 46202 (A.M.A., H.W.M.); Department of Radiology, University of Wisconsin, Madison (L.S.B.); and Department of Electrical and Computer Engineering, Purdue University, West Lafayette, Ind (C.E.B., A.C.K., C.P., J.D., C.R.S., A.M.). Supported by National Science Foundation grant IRI9711535 and National Institutes of Health grant 1 RO1 LM06543-01A1. From the 2001 RSNA scientific assembly. Received February 28, 2002; revision requested April 30; final revision received September 20; accepted October 24. Address correspondence to A.M.A. (e-mail: aaisen@iupui.edu).

Author contributions:

Guarantors of integrity of entire study, A.M.A., C.R.S.; study concepts, A.M.A., L.S.B., C.E.B., A.C.K., H.W.M.; study design, A.M.A., L.S.B., H.W.M., C.E.B., A.C.K.; literature research, A.M.A.; experimental studies, A.M.A., C.E.B., C.P.; data acquisition, A.M.A., L.S.B., H.W.M.; data analysis/interpretation, all authors; statistical analysis, C.E.B.; manuscript preparation, A.M.A.; manuscript definition of intellectual content, A.M.A., L.S.B., H.W.M., C.E.B., A.C.K.; manuscript editing, A.M.A., L.S.B., H.W.M., C.E.B.; manuscript revision/review, A.M.A., L.S.B., H.W.M., C.E.B.; manuscript final version approval, A.M.A., L.S.B., H.W.M., C.E.B., A.C.K.

© RSNA, 2003

Automated Storage and Retrieval of Thin-Section CT Images to Assist Diagnosis: System Description and Preliminary Assessment¹

A software system and database for computer-aided diagnosis with thin-section computed tomographic (CT) images of the chest was designed and implemented. When presented with an unknown query image, the system uses pattern recognition to retrieve visually similar images with known diagnoses from the database. A preliminary validation trial was conducted with 11 volunteers who were asked to select the best diagnosis for a series of test images, with and without software assistance. The percentage of correct answers increased from 29% to 62% with computer assistance. This finding suggests that this system may be useful for computer-assisted diagnosis.

© RSNA, 2003

In this article, we describe the development, implementation, and preliminary evaluation of a computer-based system designed to aid image interpretation of thin-section computed tomographic (CT) images of the chest by means of pattern recognition coupled with a database of scans with known diagnoses.

Thin-section CT of the chest has been developed over the past several decades and has proven to be a valuable diagnostic tool to assist in the diagnosis of usually diffuse parenchymal disease of the lung. Diagnosis is based on understanding, identification, and analysis of a normal or abnormal appearance of the lung parenchyma. Important features include (i) linear and reticular opacities, (ii) nodules and nodular opacities, (iii) increased lung opacity, and (iv) abnormalities asso-

ciated with decreased lung opacity, including cystic lesions, emphysema, and airway abnormalities" (1). Correct recognition of the patterns of pulmonary architecture allows the formation of an intelligent differential diagnosis.

When a radiologist, perhaps an individual without specialized expertise in thin-section CT of the chest, encounters a challenging case, he or she may recognize that there is pathologic lung parenchyma but may wish to use computer-based assistance to determine a likely specific diagnosis. This interactive "physician-in-the-loop" approach, in which the physician identifies the abnormal region of interest before computer evaluation, is simpler than the use of a computer to interpret an entire image without user interaction (2). The purpose of our study was to design, implement, and validate a computerized database of thin-section CT images of the chest and demonstrate the use of a Web-based tool with this database to assist the radiologist.

Materials and Methods

Our project was approved by the institutional review boards. Because the use of image data from patient scans was retrospective, the requirement for informed consent was waived. The volunteer physicians in the preliminary trial freely gave verbal approval to participate.

System Description

We named our system "automated search and selection engine with retrieval tools" (ASSERT). The software is written in the C++ computer language and is used with a server (Sun Microsystems, Sunnyvale, Calif). The user-interface software for the preliminary evaluation is

written in Java and can be accessed over the Web by using a standard browser.

The software is designed to store and index medical images. The system is used interactively: The physician-user identifies abnormal pulmonary parenchyma and marks it by using an electronic cursor. The major objective is to permit "unknown" or "query" images to be matched reliably against images that are already in the database so that scans with similar patterns of disease can be retrieved. By retrieving and displaying known cases that are similar in appearance to the query image, information regarding the diagnosis can aid in the interpretation of the query image. Currently, we match and retrieve on the basis of a "pathology-bearing region" (PBR) present in a single section of the query thin-section CT scan; demographic and other textual information is not used in the matching and retrieval process.

There are two types of procedures for managing the database of the PBR: (a) procedures for storing the PBR with known diagnoses into the database and (b) procedures for matching an unknown image with a PBR by querying the PBR in the database, so that similar images can be retrieved. Many of the processing steps for these two functions are similar. The steps are shown schematically in Figure 1; a technical description appears elsewhere (3).

As images from patients with known diagnoses were added to the database, a trained specialist or subspecialist radiologist (L.S.B., H.W.M.) examined each image and marked the regions of interest that depicted the pathologic condition or the PBR. Major anatomic landmarks, such as the pleural fissures, were also marked. The time required for this physician interaction was short, typically less than 1 minute per image. On the basis of information from the medical record or the appearance of the image, the expert recorded the appropriate diagnosis. Once the process was complete, the remainder of the image storage process was automated.

The software then applied a region-extraction algorithm that segmented out the tissue type of interest in this case, the pulmonary parenchyma. This segmentation allowed the system to work with any PBR that was marked imprecisely, since soft tissues other than the pulmonary parenchyma will be ignored by the software.

The PBRs were stored and indexed in the database based on software image

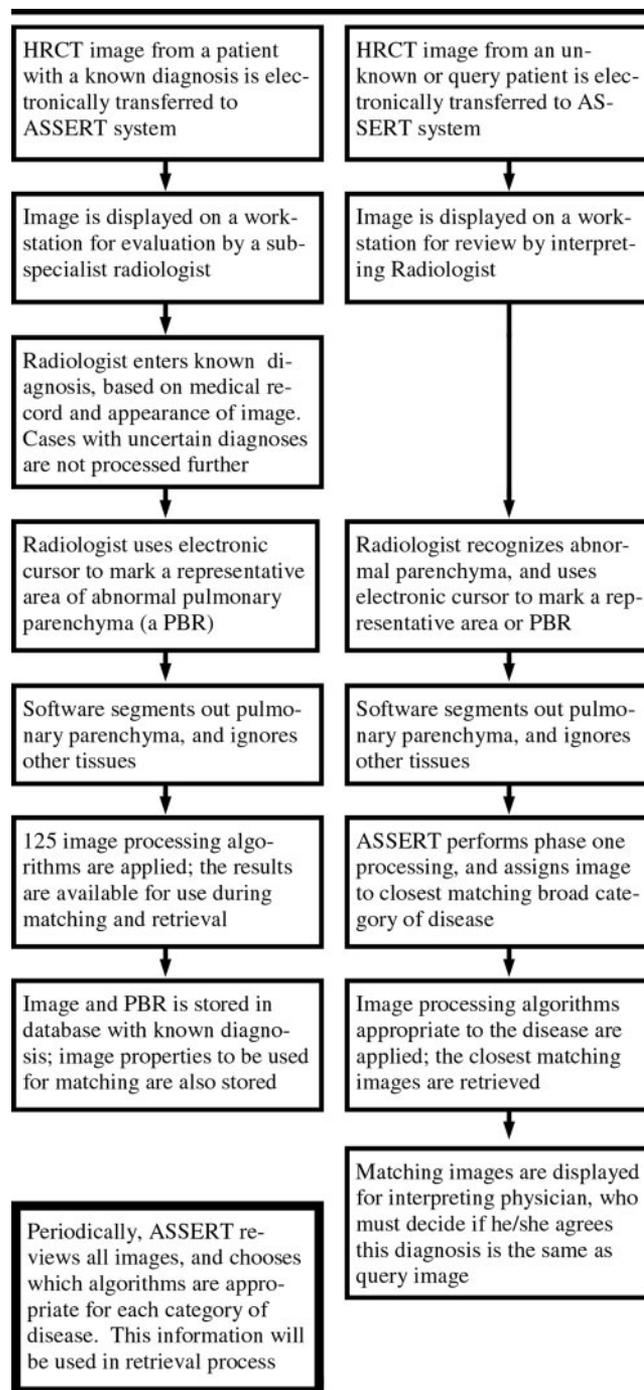


Figure 1. Schematic shows the software steps and user interactions necessary to store an image in the database. Left: Procedures in a patient with a known diagnosis. Right: Procedures to retrieve images from the database that are similar to query images with unknown diagnoses. Periodically, the software determines which image properties to use for matching and retrieving images for each type of disease, as shown in the box at the bottom left. *HRCT* = high-resolution (thin-section) CT.

processing. In the current study, 125 image-processing algorithms were applied to the PBRs. We have found that there is no single set of image properties that best characterizes all disease types. That is,

properties that might be useful in discriminating among subtypes of one disease (eg, emphysema) might not be well suited to separating varieties of nodular lung disease. For this reason, we imple-

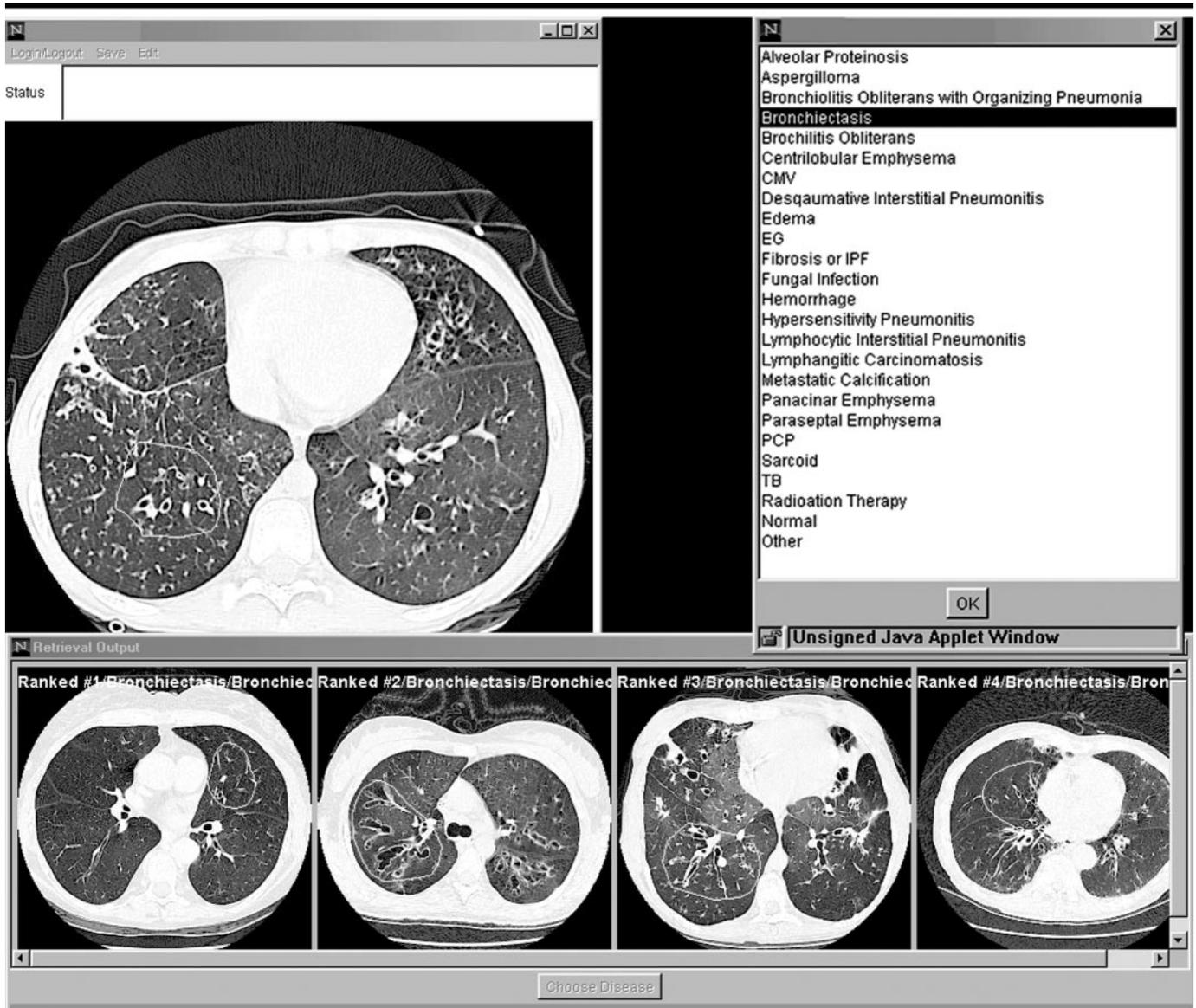


Figure 2. Screen capture of user interface for phase 2 of the trial. User has identified and outlined a PBR. ASSERT software chose four images that contain similar-appearing abnormalities and displayed them, as well as the known diagnosis for these images (bronchiectasis). In the list of diagnostic possibilities, the user has made a selection.

mented a two-stage process, which we call “customized queries,” in which the set of image parameters to be used (a subset of the 125 properties) was determined automatically for each broad category of disease (4–7). In the first of the two steps, an initial analysis was performed to categorize a query image into a broad disease category. Once this was done, the software determined which select subset of image processing algorithms was appropriate to the specific disease entity. The basic idea was to choose those image parameters that best discriminated among disease entities for the first stage and that best characterized each specific disease for the second stage.

The matching or retrieval process occurred when an unknown image was presented to the system; this process was somewhat similar to the storage process. First, a PBR was marked on an unknown query image by the physician user, after which the computer identified lung parenchyma in the PBR. First-stage matching, in which the system decided the broad category of disease, was then performed. Next, the second phase of image retrieval was performed by measuring and then matching those image attributes that were determined previously to be appropriate for the specific disease (2). The resulting closest matching images with the predicted disease are then

displayed with their known diagnosis for the physician user.

In this initial phase of the project, 1,888 PBRs in 1,069 images from 173 patients were entered into the database. Images were selected retrospectively from routine clinical examinations performed at our institutions during the previous 3 years. The cases were identified by means of systematic review of the scanner logs for thin-section CT cases. There were no specific selection criteria for the patients. We attempted to include as many patients with as broad a range of diagnoses as was feasible. Toward the end of the process, we stopped adding cases with diagnoses already well represented nu-

merically in the database (eg, emphysema). Diagnoses were confirmed with pathologic or clinical data. The diagnoses of centrilobular emphysema and paraseptal emphysema were made on the basis of their characteristic thin-section CT appearance. Cases for which the diagnosis was known with reasonable reliability in the judgment of an experienced chest radiologist (L.S.B. or H.W.M.), on the basis of available information in the medical record and the appearance of the images, were entered. Patients who had more than one diagnosis (possibly resulting from overlap of abnormalities on thin-section CT images) were not included. The most common disease entities were centrilobular emphysema, paraseptal emphysema, sarcoidosis, invasive aspergillosis, bronchiectasis, *Mycobacterium avium-intracellulare* infection, panacinar emphysema, and idiopathic pulmonary fibrosis.

Preliminary Evaluation of System

To conduct a preliminary evaluation of the utility of ASSERT, special evaluation software was designed, implemented, and then executed by 11 volunteers who were not otherwise participants in this project: two chest radiologists, each with 5 or more years of experience in thin-section CT; five general radiologists, each with more than 10 years of experience; and four residents or fellows (two residents, one in the 2nd year and one in the 3rd year, and two non-chest radiology fellows). The evaluation was performed in two phases. In both phases, the same set of 29 test images, which were selected randomly from the database to provide a disease distribution similar to that of the overall database, were used. The most common disease entity was centrilobular emphysema. The 29 images were obtained in 23 patients; images from these patients were removed from the database before the system was trained, as well as from the set of images available for retrieval.

Users accessed the evaluation software by using standard personal computers with standard Java-enabled Web browsers. Figure 2 shows a screen capture of the user interface. In the first phase, each volunteer was presented with the test images one at a time and was asked to choose one best diagnosis from a pull-down list. The order of the images was random and was varied from volunteer to volunteer. The pull-down list contained all diagnoses present in the database, many of which were not represented in the small

set of 29 test images. The volunteers' answers were scored on the basis of the number of correct choices for each. In the second phase, which was conducted after a minimum 1-week delay, each user was presented with the same images, in a different randomly selected order. This time, they were asked to mark a pathologic region on the query image, after which a set of four "matching" images was presented by the system. The four matching images were labeled with their known diagnoses. In the implementation of our software used in the current study, the diagnosis for all four retrieved images was the same. This is because of the two-stage matching process used in the current design of our retrieval method.

The volunteers were informed in advance that the matches might or might not be correct. After the matching images were examined, the volunteers were asked to select the appropriate diagnosis from the pull-down menu of diseases; again, they were free to select or not to select the same disease as was indicated for the matching images. The number of correct answers was again tallied and compared with the results of the first phase. Logistic regression by means of the Wald test (8) was used to compare the performance of the 11 volunteers in the two phases of the trial.

Results

The distribution of diagnoses for the 29 images in the trial is given in Table 1. The results of the trial are given in Tables 2 and 3. Overall, the percentage of correct answers increased from 29% (94 of 319) without computer assistance to 62% (198 of 319) with computer assistance ($P < .001$); the improvement was greater for the general radiologists than that for the specialized chest radiologists.

For each of the 29 test images, a specific disease was predicted by the ASSERT software; this disease was represented in the four matching images retrieved and displayed by the system. The diagnosis that was chosen depended on the PBR marked by each of the volunteers and was not necessarily the same for all 11 users. In this trial, the diseases chosen by the ASSERT software were correct in approximately 70% of cases.

Discussion

Computer-aided image interpretation is an area of rapid technologic growth that is likely to play a growing role in the

TABLE 1
Diagnoses in 29 Cases Chosen Randomly from the Database for the Preliminary Trial

Diagnosis	No. of Cases
Centrilobular emphysema	12
Paraseptal emphysema	1
Aspergillus	2
Panacinar emphysema	2
Sarcoidosis	2
Idiopathic pulmonary fibrosis	5
<i>Mycobacterium avium-intracellulare</i> infection	1
Bronchiectasis	4

clinical practice of radiology. This technology has been used to assist with both lesion detection and diagnosis. There are several systems approved by the U.S. Food and Drug Administration that perform computer-aided detection for mammography, and the U.S. Congress has approved increased reimbursement for mammography when interpretation is supplemented with computer-aided detection techniques. Findings in other trials suggest that computer-based tools can substantially enhance diagnostic sensitivity (9,10).

There are many approaches to computer-assisted image interpretation. In one approach, rule-based, or what may be termed "artificial intelligence," methods are used. In the field of mammography, for example, computers are used to characterize breast masses as likely malignant or likely benign on the basis of properties such as lesion density, character of the margin, and the presence of microcalcifications. Shape, margin spiculation, and some types of microcalcifications indicate malignancy; computer-based tools have been developed to assist with both the identification and classification of such findings (11–20). These methods are applied with varying degrees of user interaction by the interpreting physician. In one of these studies, the performance of a fully automated method for identifying (segmenting) and classifying breast masses exceeded that of nonspecialist radiologists and approached that of experts (11).

Another area of radiologic diagnosis to which computer-aided interpretation has been applied is screen-film or digital radiography of the chest (21,22,23) for the detection (21,23) and characterization (22) of radiographic abnormalities. In chest CT, software has been developed for nodule detection (24,25) and for such

TABLE 2
Number and Percentage of Correct Answers for Volunteers in the Two Phases of the Trial

Volunteers	Without Computer Assistance	With Computer Assistance
Chest radiologists (<i>n</i> = 2)	23 of 58 (40)	38 of 58 (66)
General radiologists (<i>n</i> = 5)	36 of 145 (25)	98 of 145 (68)
Radiologists in training (<i>n</i> = 4)	35 of 116 (30)	62 of 116 (53)
Overall (<i>n</i> = 11)	94 of 319 (29)	198 of 319 (62)*

Note.—Data are the number of images. Numbers in parentheses are percentages.

* $P < .001$.

TABLE 3
Number of Answers Changed from First Phase of Study (without computer assistance) to Second Phase (with computer assistance)

Volunteers	Wrong to Right	Right to Wrong	Wrong to Wrong
Chest radiologists (<i>n</i> = 2)	15 of 58 (26)	0 of 58 (0)	11 of 58 (19)
General radiologists (<i>n</i> = 5)	67 of 145 (46)	5 of 145 (3)	28 of 145 (19)
Radiologists in training (<i>n</i> = 4)	33 of 116 (28)	6 of 116 (5)	31 of 116 (27)
Total (<i>n</i> = 11)	115 of 319 (36)	11 of 319 (3)	70 of 319 (22)

Note.—Data are the number of images. Numbers in parentheses are percentages.

quantitative analysis as quantification of emphysematous change by means of measurement of pulmonary parenchymal density (26). In one study, chest radiograph interpretation was assisted with a computer to analyze lung texture and flag areas of potential interstitial abnormality (21). For thin-section CT, computer analysis is being applied to automatic detection of abnormal pulmonary lung parenchyma (27). Other domains for which computer tools have been described include quantification of stenoses on angiograms (28,29), detection and identification of liver lesions (30), detection of colonic polyps (31), and evaluation of the trabecular pattern of bone (32). In addition to rule-based systems, neural-network techniques have been applied to image interpretation (27,33).

Most previous work has been concerned with the selection and development of algorithms for feature detection and image analysis. Our current study dealt with a different, though related, aspect of computer-aided image interpretation: the development of database methods and tools for classifying, indexing, and retrieving images that depict similar radiographic appearances. Such a search engine is called a content-based image retrieval system. From the perspective of computer science, this problem of automated classification, indexing, storage, and retrieval of images or image regions represents an important and complex problem and one that, to our knowledge,

has received only limited attention in the medical arena.

In our "physician-in-the-loop" approach, the problem of computer-assisted diagnosis and not detection is dealt with, because the physician is required to identify the abnormal pulmonary parenchyma. Computer analysis is performed with respect to this region, with use of both regional and global algorithms. Thus, the ASSERT software is designed to work with local regions of abnormal pulmonary parenchyma or PBRs and not with entire tomographic images.

In practical terms, it is unlikely that the computer could outperform an experienced specialist radiologist in selecting similar images among a limited data set. As the database grows, however, the computer will be able to search through a set larger than would be feasible for a human to examine. With our software, the user is presented with similar images with known diagnoses. This can help a non-subspecialist radiologist by suggesting potential diagnoses. For example, the thin-section CT pattern of lymphangitic spread of malignancy is well known to radiologists experienced in the reading of thin-section CT images but may be less familiar to other radiologists. Thus, if our system is presented with an unknown image, and the appearance of the pathologic parenchyma is that of lymphangitic spread, the system is expected to retrieve other images from patients with this diagnosis. The physician posing the query

would then have the opportunity to examine the retrieved images and reach a conclusion about whether the unknown case was similar. It is our hope that results with our software will duplicate the success of others in related domains (10,21) and enhance diagnostic efficacy.

Our current implementation has limitations. At present, we are limited to working in one narrow domain, thin-section CT of the lung. We are expanding into several additional areas. At present, the software can not evaluate clinical information or context other than the images themselves. In future enhancements, we hope to include contextual information, including sex, age, and perhaps other clinical or laboratory information in both the database and perhaps the retrieval process itself. For example, the retrieval software could be modified to give preference to patients with the same sex or age as the patient with the query image.

Our present implementation will fail to find any appropriate matching images if, in the first step of software processing, the wrong major diagnostic category is chosen. This appears to occur in approximately 10%–30% of cases. It is noteworthy that the failure rate in this trial was more than 30%, which is greater than that for preliminary tests conducted by some of the investigators. This may have contributed to the failure rate for the second part of the trial because, in practice, the users did not include the same area of lung in the PBR as was included by the investigators who helped create the database. Fortunately, relatively simple modifications to the software can be made that will improve the functionality; such modifications are being implemented. A major design change will be to allow the several retrieved matching images to represent more than one disease.

It should be noted that normal regions of lung were not included in the database because our system is designed to assist with the diagnosis of areas of pulmonary parenchyma that a physician believes are abnormal. In our approach, we assume that the physician is able to recognize pathologic parenchyma.

The current study is preliminary, with a relatively small number of test images and a limited distribution of diagnoses. Overall accuracy of the volunteers in identifying the images increased from 29% without computer assistance to 62% with assistance. The benefit for the two chest radiologists was less than that for the general radiologists. The fact that the accuracy is not higher is an artifact of the

experimental design and not of the skills of the volunteers. Several factors contributed to this low accuracy. First, for scoring purposes, we allowed the choice of only one diagnosis, when, in fact, the images might have been reasonably ascribed to any of several diseases (eg, interstitial lung disease secondary to connective tissue disease and usual interstitial pneumonitis). This may have contributed to the improvement in the scores of the expert chest radiologists. Second, only single images were presented, without the ability to adjust the window and level settings. Clinical interpretation of thin-section CT scans requires examination of images of the entire lung, which was not done in this preliminary trial. Third, no context, such as patient age, sex, or medical history, was provided. Fourth, if the region of interest was not placed on the appropriate area of disease by the user, the retrieved images may not represent the correct principal diagnosis.

In summary, we developed and tested a computerized database for the intelligent storage and retrieval of medical images. We believe our system will be useful both as an aid in image interpretation and as an educational tool, since the user will be able to view similar images with their respective diagnoses. We are continuing to develop our system and are in the process of both expanding the database of thin-section CT images and extending the system to other organ systems and imaging methods. The results of our preliminary trial suggest that a tool such as ours can substantially improve diagnosis, particularly for nonspecialist radiologists.

Acknowledgements: The authors thank the volunteers for participating.

References

- Webb RW, Muller NL, Naidich DP. High resolution CT of the lung. 2nd ed. Philadelphia, Pa: Lippincott-Raven, 1996; 41.
- Shyu C, Brodley CE, Kak A, Kosaka A, Aisen A, Broderick L. ASSERT, a physician-in-the-loop content-based image retrieval system for HRCT image databases. *Computer Vision and Image Understanding* 1999; 74:111-132.
- Dy JG, Brodley CE, Kak AC, Aisen A, Broderick LS. The customized-queries approach to image retrieval. *IEEE Transactions on Pattern Recognition and Machine Intelligence* 2003; 25:373-378.
- Brodley CE, Kak AC, Dy JG, Shyu CR, Aisen A, Broderick L. Content-based retrieval from medical image databases: a synergy of human interaction, machine learning and computer vision. In: *Proceedings of the Sixteenth National Conference on Artificial Intelligence*. Los Alamitos, Calif: IEEE Computer Society, 1999; 760-767.
- Dy J, Brodley CE. Feature subset selection and order identification for unsupervised learning. In: *The Seventeenth International Conference on Machine Learning*. San Francisco, Calif: Morgan Kaufman, 2000; 247-254.
- Kohavi R, John GH. Wrappers for feature subset selection. In: *Artificial intelligence*. Amsterdam, the Netherlands: Elsevier, 1997; 273-324.
- Dy JG, Brodley CE, Kak A, Shyu C, Broderick LS. The customized-queries approach to CBIR using EM. In: *IEEE Conference on Computer Vision and Pattern Recognition*. Los Alamitos, Calif: IEEE Computer Society, 1999; 400-406.
- Hosmer DW, Lemeshow S. *Applied logistic regression*. New York, NY: Wiley, 1989; 33.
- Warren Burhenne LJ, Wood SA, D'Orsi CJ, et al. Potential contribution of computer-aided detection to the sensitivity of screening mammography. *Radiology* 2000; 215:554-562.
- Freer TW, Ulissey MJ. Screening mammography with computer-aided detection: prospective study of 12,860 patients in a community breast center. *Radiology* 2001; 220:781-786.
- Huo Z, Giger ML, Vyborny CJ, Wolverton DE, Schmidt RA, Doi K. Automated computerized classification of malignant and benign masses on digitized mammograms. *Acad Radiol* 1998; 5:155-168.
- Rymon R, Zheng B, Chang YH, Gur D. Incorporation of a set enumeration trees-based classifier into a hybrid computer-assisted diagnosis scheme for mass detection. *Acad Radiol* 1998; 5:181-187.
- Sahiner B, Chan HP, Petrick N, Helvie MA, Goodsitt MM. Computerized characterization of masses on mammograms: the rubber band straightening transform and texture analysis. *Med Phys* 1998; 25: 516-526.
- Buchbinder SS, Leichter IS, Bamberger PN, et al. Analysis of clustered microcalcifications by using a single numeric classifier extracted from mammographic digital images. *Acad Radiol* 1998; 5:779-784.
- Thurfjell E, Thurfjell MG, Egge E, Bjurstam N. Sensitivity and specificity of computer-assisted breast cancer detection in mammography screening. *Acta Radiol* 1998; 39:384-388.
- Mudigonda NR, Rangayyan RM, Desautels JE. Gradient and texture analysis for the classification of mammographic masses. *IEEE Trans Med Imaging* 2000; 19:1032-1043.
- Rangayyan RM, Mudigonda NR, Desautels JE. Boundary modelling and shape analysis methods for classification of mammographic masses. *Med Biol Eng Comput* 2000; 38:487-496.
- Nappi J, Dean PB. A multiscale algorithm for segmenting calcifications from high-resolution mammographic specimen radiographs. *J Digit Imaging* 2000; 13(2 suppl 1):130-132.
- Jiang Y, Nishikawa RM, Wolverton DE, et al. Malignant and benign clustered microcalcifications: automated feature analysis and classification. *Radiology* 1996; 198:671-678.
- Huo Z, Giger ML, Vyborny CJ, et al. Analysis of spiculation in the computerized classification of mammographic masses. *Med Phys* 1995; 22:1569-1579.
- Monnier-Cholley L, MacMahon H, Katsuragawa S, Morishita J, Ishida T, Doi K. Computer-aided diagnosis for detection of interstitial opacities on chest radiographs. *AJR Am J Roentgenol* 1998; 171: 1651-1656.
- Kido S, Ikezoe J, Tamura S, Nakamura H, Kuroda C. A computerized analysis system in chest radiography: evaluation of interstitial lung abnormalities. *J Digit Imaging* 1997; 10:57-64.
- Xu XW, Doi K, Kobayashi T, MacMahon H, Giger ML. Development of an improved CAD scheme for automated detection of lung nodules in digital chest images. *Med Phys* 1997; 24:1395-1403.
- Giger ML, Bae KT, MacMahon H. Computerized detection of pulmonary nodules in computed tomography images. *Invest Radiol* 1994; 29:459-465.
- Kanazawa K, Kawata Y, Niki N, et al. Computer-aided diagnosis for pulmonary nodules based on helical CT images. *Comput Med Imaging Graph* 1998; 22: 157-167.
- Archer DC, Coblenz CL, deKemp RA, Nahmias K, Norman G. Automated in vivo quantification of emphysema. *Radiology* 1993; 188:835-838.
- Kauczor HU, Heitmann K, Heussel CP, Marwedel D, Uthmann T, Thelen M. Automatic detection and quantification of ground-glass opacities on high-resolution CT using multiple neural networks: comparison with a density mask. *AJR Am J Roentgenol* 2000; 175:1329-1334.
- Cherrak I, Paul JF, Jaulent MC, et al. Automatic stenosis detection and quantification in renal arteriography. In: *Proceedings of the American Medical Informatics Association Fall Symposium* 1997. Bethesda, Md: American Medical Informatics Association, 1997; 66-70.
- Sarry L, Boire JY, Zanca M, Lusson JR, Cassagnes J. Assessment of stenosis severity using a novel method to estimate spatial and temporal variations of blood flow velocity in biplane coronary angiography. *Phys Med Biol* 1997; 42:1549-1564.
- Chen EL, Chung PC, Chen CL, Tsai HM, Chang CI. An automatic diagnostic system for CT liver image classification. *IEEE Trans Biomed Eng* 1998; 45:783-794.
- Summers RM, Beaulieu CF, Pusanik LM, Malley JD, Jeffrey RB Jr, Glazer DI, Napel S. Automated polyp detector for CT colonography: feasibility study. *Radiology* 2000; 216:284-290.
- Korstjens CM, Geraets WG, van Ginkel FC, Prahj-Andersen B, van der Stelt PF, Burger EH. Longitudinal analysis of radiographic trabecular pattern by image processing. *Bone* 1995; 17:527-532.
- Kalman BL, Reinus WR, Kwasny SC, Laine A, Kotner L. Prescreening entire mammograms for masses with artificial neural networks: preliminary results. *Acad Radiol* 1997; 4:405-414.