Review Article

Computer Vision and Artificial Intelligence in Mammography

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The revolution in digital computer technology that has made possible new and sophisticated imaging techniques may next influence the interpretation of radiologic images. In mammography, computer vision and artificial intelligence techniques have been used successfully to detect or to characterize abnormalities on digital images. Radiologists supplied with this information often perform better at mammographic detection or characterization tasks in observer studies than do unaided radiologists. This technology therefore could decrease errors in mammographic interpretation that continue to plague human observers.

Remarkable advances in digital computer technology have allowed the practical development of sophisticated techniques such as CT and MR imaging. These advances have had virtually no effect on the manner in which radiologists interpret examinations in day-to-day practice, however. Images are presented to the radiologist without comment or assistance, but the variety and complexity of these images now challenge the ability of even the most diligent to remain current and expert in all the areas encompassed by diagnostic radiology. In response, an ever-increasing number of investigators have undertaken study of the application of computer vision and artificial intelligence to the analysis of radiologic images. The area of greatest interest has been the development of computer-aided diagnostic techniques for mammography. Investigators have thus confronted one of the most difficult diagnostic tasks faced by radiologists today. Their success portends changes in the way radiologists will practice in the future.

Computer-based diagnostic schemes presently center on the radiologist and the radiologist's basic approach to image interpretation. The radiologist must detect potential abnormalities on mammograms, and to the extent possible, characterize or classify them. Conceptually, it is simplest to consider these as sequential processes, although characterization of the features of mammographic findings plays a large role in determining whether they are, in fact, "detected." Most present computer schemes are devoted to one or the other aspects of this process, namely, detection or characterization. Most also have been designed to complement or to supplement the human observer, allowing him or her to come to a correct diagnosis more consistently—hence the often used term computer-aided diagnosis. The well-trained radiologist brings far too much insight and versatility to the diagnostic process in mammography to be casually relegated to a secondary role.

Limitations of Human Observers

When simple objects are detected on uniform backgrounds, the human observer is limited only by the noise in the image [1–3] and, in very low contrast situations, the (low) "internal noise" inherent in the eye-brain system [4]. Even though lack of information regarding the size or location of the target may decrease performance [5], the eye-brain system performs at a high level that can be further improved if viewing distance and/or magnification is varied [6, 7]. The possibility of improving detection by the use of computer techniques in such situations is only theoretical and has not been evaluated experimentally.

Very few, if any, radiographic diagnoses are made under image conditions that even approximate the simple situation

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just described, however. Rather, important disease is represented on the complex background of normal anatomy. The long-known fallibility of human observers in the early detection of masses on chest radiographs [8, 9] is related, in part, to "structured noise" arising from the superimposition of normal structures [10]. Such superimposition can be equally confusing to computer algorithms and, for example, is the cause of many of the false-positive detections in computer analysis of chest radiographs [11, 12]. Given the large variability in normal breast anatomy, an effectively converse situation also exists in mammography, with radiologists incorrectly interpreting localized lesions as normal anatomic structures.

Other deficiencies in human performance are more obvious targets for improvement through the introduction of computer-aided diagnostic techniques. Simple oversight of abnormalities contributes significantly to false-negative mammographic interpretations, even in high-quality practices [13, 14]. Further, once a basic level of training has been reached, additional improvements in detection may not be strongly dependent on experience [15, 16]. It has been suggested that mammographic interpretation by two radiologists would improve the detection of subtle abnormalities [17–19]. A natural alternative to this approach is the review of images by both human and computer observers with the results merged to form an improved diagnostic output. This output would then reflect the significant strengths of both forms of observer.

Computer Vision and Artificial Intelligence

Computer analysis of images can begin only after they are represented in suitable digital format. In virtually all investigations to date, this has involved digitization of existing film or xeroradiographic images. Requirements for digital representation of a mammogram include high spatial resolution and high contrast sensitivity. Researchers in the field believe that pixels on the order of 50 μm in size with 12-bit quantization may be required for adequate depiction of mammographic detail [20, 21].

Direct digital acquisition of images, now possible in certain clinical situations, will most likely form the eventual input for future practical computer-aided diagnostic systems. Whole breast direct digital acquisition systems under development include storage phosphor and phosphor/charge-coupled device area detectors as well as scanned beam detectors that can virtually eliminate scattered radiation from the image [21, 22].

Image processing is the first step in most detection algorithms based on computer vision [23, 24]. Such processing allows the signal-to-noise characteristics of certain findings in the image (such as microcalcifications in a particular size range) to be enhanced, while unwanted detail is suppressed. The processed images are then tested to identify potential targets of interest, with local or global thresholding of pixel values being the simplest examples. Features of potentially interesting areas of the image can then be extracted and serve as the basis for further detection or characterization decisions. In computer schemes devoted only to characterization of abnormalities located by other means, feature extraction is the principal role of computer vision.

Computer vision techniques have the distinct advantage of being as reproducible as the underlying computer code on which they are based. The computer will therefore always evaluate the corner of the film and will not be distracted by everyday clinical interruptions. Such consistency in performance can be of great value to the radiologist, who operates in a very different environment.

At some level in the execution of many computer diagnostic schemes, decisions related to characterization, or even to detection, have less and less directly to do with what the radiologist would consider the physical appearance of the image. Rather, the details of the mathematical pattern of individual physical features extracted by computer vision or by the radiologist become the most important factor in determining the final output or recommendation. This pattern can be analyzed in a straightforward manner by simple algorithms as was done by the earliest investigators in the field. However, complex patterns have more and more been analyzed by artificial intelligence techniques developed by mathematicians and physical scientists during the past decades [25, 26]. These include discriminant analysis methods, expert rule-based systems, and artificial neural networks. Such techniques can merge complex and varied features in reproducible ways, often more accurately than can human decision makers who are given the same tasks.

Historical Perspective

The earliest investigators in the field outlined many of the basic rationales, approaches, and limitations of computer-aided diagnosis in mammography. Winsberg and coworkers, the first published investigators in this field [27], were motivated by the problems inherent in the routine viewing of large volumes of screening mammograms performed on asymptomatic women, even before the validity of such screening had become well established [28]. They used the expected symmetry of right- and left-breast architecture as the basis for identifying areas in which local image attributes varied appreciably from one side to the other (Fig. 1). Greater variations corresponded to greater likelihood of disease.

Kimme et al. [29] expanded on this basic approach, introducing computer tracking of the skin line and improved registration of right and left images. They also used the concept of "feature" to define calculable attributes of a portion of an image that can be used in subsequent decision making, a usage that persists to this day. As appropriate for xeroradiographic images, many of these features were textural.

In 1972, Ackerman and Gose used a computer to extract and to subsequently merge four properties of mammographic lesions—calcification, spiculation, roughness, and shape—in order to classify them as benign or malignant [30] (Fig. 2). The computer performed as well as two expert radiologists in this classification task. Ackerman et al. [31] also merged by computer 30 imaging features extracted by human observers to differentiate benign from malignant lesions. Studies at the same institution later combined detection and classification algorithms in an attempt to form a fully automated system for screening xeromammograms [32, 33].

During the late 1970s, Wee et al. [34] and Fox et al. [35] developed methods to characterize clusters of microcalcifica-

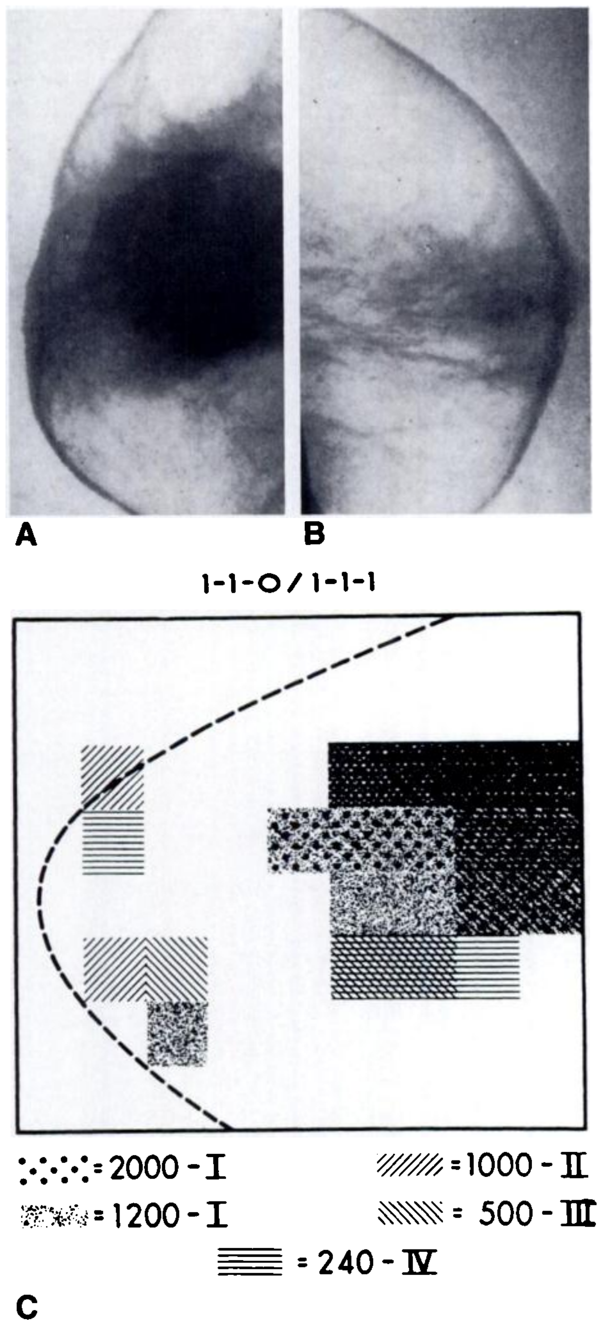


Fig. 1.—*A–C*, Computer detection of a large mass in breast by Winsberg et al. in 1967. Mass produces prominent asymmetry in characteristics of right (*A*) and left (*B*) craniocaudal mammograms. Calculable aspects of this asymmetry are portrayed in computer output (*C*) used to localize mass. (Reprinted with permission from Winsberg et al. [27].)

tions by computer as benign or malignant. Various aspects of the size, density, and morphology of individual microcalcifications as well as the pattern of clustering were analyzed by computer algorithms in this process. Spiesberger [36] first specifically studied the detection of microcalcifications, not only concentrating on the identification of individual calcifications but also evaluating strategies for the detection of clusters.

Fig. 2.—Digital printout of a mass lesion with defining circle in 1972 work of Ackerman and Gose. Circled lesion was subsequently characterized on the basis of features extracted by computer. (Reprinted with permission from Ackerman and Gose [30].)

Early researchers in the field realized that the extremely large memory and computational requirements of digital mammography and computer analysis of mammographic images limited the practical application of their techniques. Digital computers continued to evolve rapidly, however, and more sustained interest in computer-based approaches developed within a decade.

Virtually no articles on the topic of computer-aided diagnosis in mammography appeared in medical publications between 1981 and 1987. Since that time, a virtual explosion in interest in the field has occurred, with between 50 and 100 centers now actively pursuing such work (Doi K, personal communication). This greatly renewed interest has been driven by the ever-increasing use of mammography as a screening tool, as well as by rapid advancements in digital computer technology.

Most recent work in the field has focused on the detection of particular targets or on approaches to the characterization of detected abnormalities. Recent research is also distinguished from that of the early investigators by greater use of image processing, more sophisticated feature analysis, and use of artificial intelligence methods. Refinement of promising techniques, important in achieving performance levels that would be acceptable in actual clinical practice, also represents a significant fraction of current investigative efforts.

Detection of Microcalcifications

Microcalcifications are ideal targets for computer detection algorithms because of their clinical relevance, their potential subtlety, and the lack of coexisting normal structures that have the same appearance. Of recent investigations, the most influential work in computer-aided detection has been by Chan, Doi, and coworkers who studied microcalcifications. Their approach illustrates many of the basic aspects of computer detection schemes and so will be discussed briefly next.

Chan et al. [37, 38] used a subtraction-image approach at the image-processing stage of their detection algorithm. The original digital mammogram is spatially filtered twice, once to enhance microcalcifications and once to suppress them. A subsequent subtraction of these images not only improves the signal-to-noise ratio of most microcalcifications but also largely suppresses the underlying soft-tissue anatomy of the breast (Fig. 3). The subtracted image is then subjected to thresholding with all signals above a certain pixel value retained. The threshold value is routinely chosen to subsequently yield a high sensitivity for detection of true abnormalities at a reasonable false-positive detection rate. The remaining features in the thresholded image are, in turn, analyzed to decrease false-positive detections of microcalcifications, with one potential approach shown in Figure 4. Various criteria

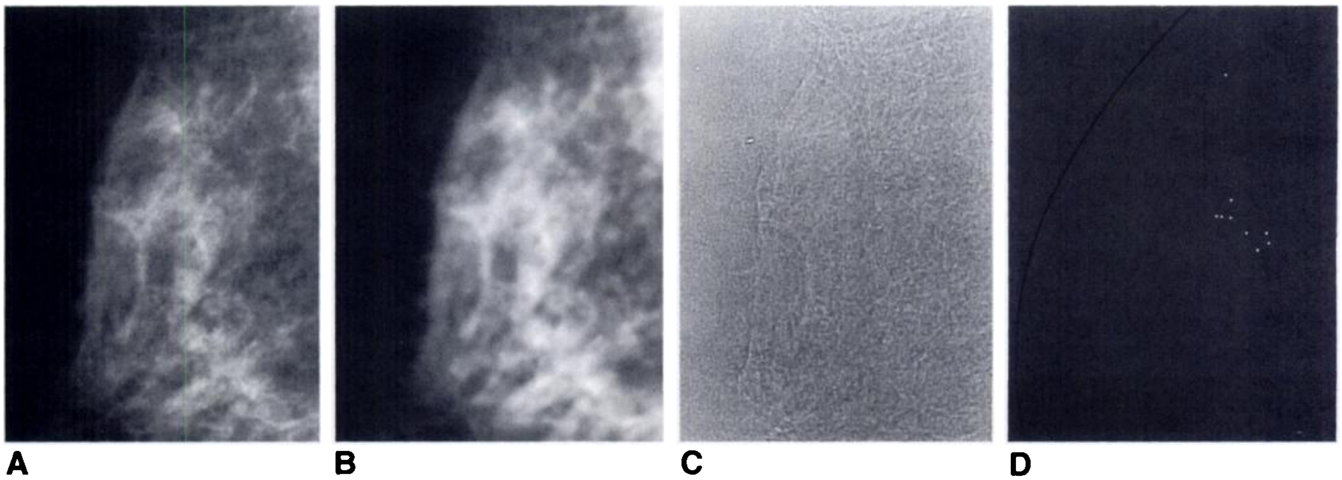


Fig. 3.—Subtraction form of image processing for detection of clustered microcalcifications.
***A,* Digital mammogram filtered to enhance small signals, including subtle microcalcifications.**
***B,* Digital mammogram filtered to suppress small signals.**
***C,* Subtraction mammogram in which background parenchymal densities are strongly suppressed but microcalcifications remain readily visible.**
***D,* Computer detection of cluster of microcalcifications after feature analysis.**
(Courtesy of Robert Nishikawa, Chicago.)

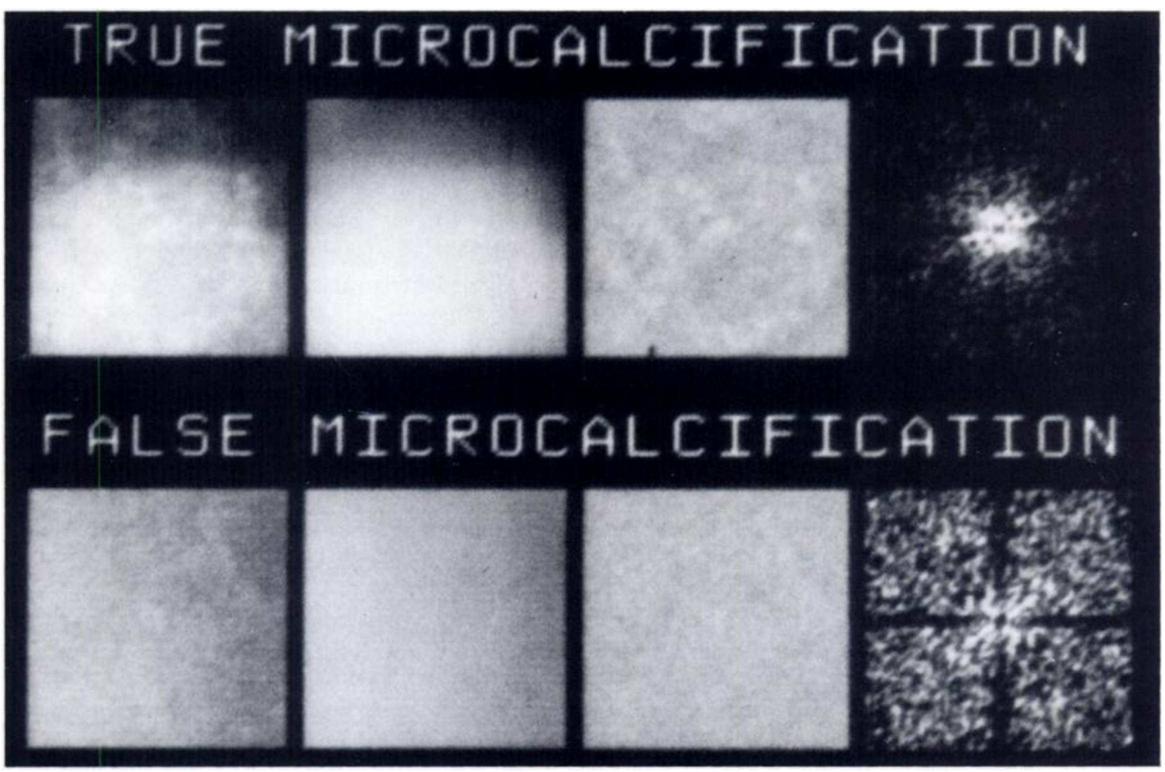


Fig. 4.—One approach to feature analysis for microcalcifications. Small signals at center of either box at far left are detected by thresholding and are further analyzed. Smoothed background trends are determined and subtracted from original images (second and third boxes). Power spectra for true-positive microcalcifications contain more low-frequency information because they represent actual structures and not a fortuitous appearance of noise. (Reprinted with permission from Chan et al. [39].)

are then used to determine which of the remaining detections are most likely the result of true clusters of microcalcifications. Mathematical morphology [40], new clustering filters [41], and artificial neural networks [42] have been used to improve the overall performance of this basic scheme, most notably by Nishikawa and coworkers [41, 42].

Many other approaches to microcalcification detection have been reported in the past 5 years, including work by Fam et al. [43], Davies and Dance [44, 45], Astley et al. [46], and Karssemeijer [47]. Each uses novel methods for image processing, feature analysis, or decision making that the interested reader can find in their publications. Microcalcification detection has also recently attracted a large number of new investigators to the field who have developed innovative image processing (Fig. 5) or classification techniques [48–55].

Detection of Masses

In many ways, breast masses are more difficult to detect than microcalcifications because masses can be simulated or obscured by normal breast parenchyma [56–58]. Giger and colleagues have expanded on the basic approach of using left-to-right breast asymmetries for the detection of subtle masses [59–61]. At the image-processing stage, multiple subtraction images are formed to enhance asymmetries (Fig. 6). Feature extraction that uses morphologic filtering, or that determines the size and shape of lesions or their distance from the breast border, is used to decrease the number of false-positive detections. Other investigators have used template matching and multiresolution image processing for the initial identification of possible masses [62].

Kegelmeyer has focused on the detection of stellate abnormalities in the breast for the identification of early spiculated masses [63]. The orientation of edges throughout the image is analyzed to identify areas in which locally radiating structures exist (Fig. 7). False-positive detections can be decreased by texture analysis. Astley et al. [46] and Ng and Bischof [64] have proposed different approaches to image processing and feature analysis for the detection of radiating patterns of spiculation.

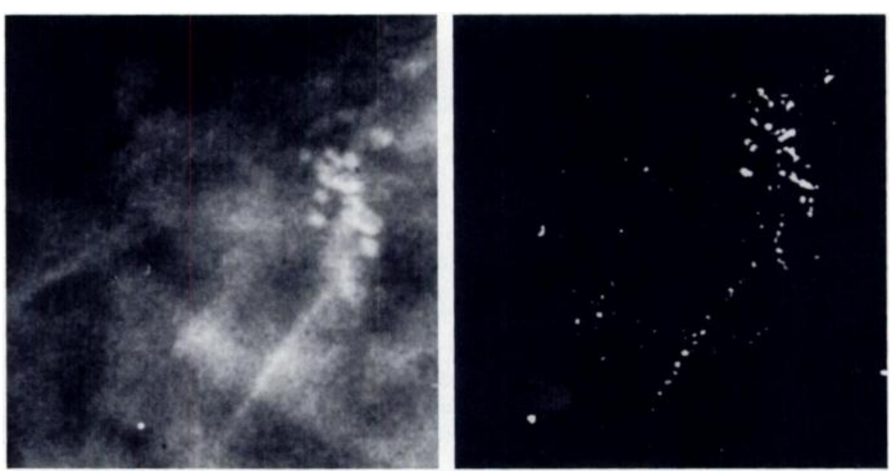
Computer Classification of Abnormalities

Despite improved criteria for differentiating benign from malignant lesions of the breast [65–68], considerable misclassification of lesions persists. This results in low or variable positive predictive values of recommendations for biopsy of indeterminate lesions [69]. Computer analysis of abnormalities can play a useful role in this classification process and thus in important decisions related to patients' management. Algorithms of this sort use a wide variety of approaches; in many of these, human observers play a significant role in the process. For example, the image features on which computer classifications are based can be extracted by the computer or by the radiologist. In other schemes, computers provide considerable support to what remains an essentially human classification decision.

As discussed earlier, Ackerman, Wee, and Fox with their coworkers used features extracted by computers to classify masses or clusters of microcalcifications as benign or malignant [30, 34, 35]. More recently, Magnin et al. [70] automatically extracted the characteristics of individual microcalcifications in order to distinguish phosphate and oxalate forms. Patrick et al. [71] used features of individual microcalcifications and individual clusters to differentiate benign from malignant groupings with the aid of an expert learning system.

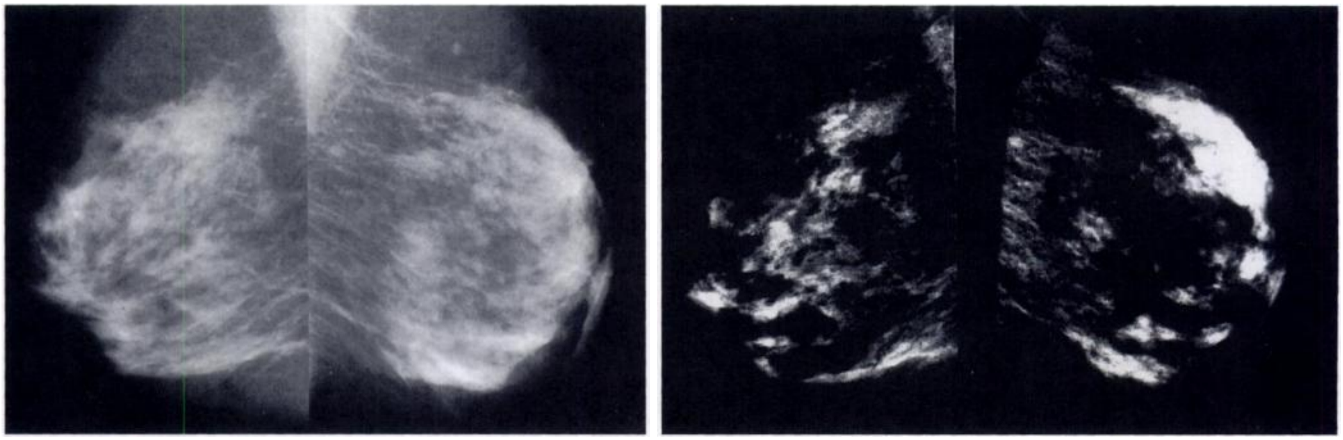
Giger et al. [59] have developed a classification approach based on measures of spiculation extracted by computer. This approach compares the closely tracked and smoothed margins of mass lesions to assess spiculation as shown in Figure 8. Brzakovic et al. [72] use area, shape, edge distance variation, and edge intensity variation determined by computer to differentiate benign from malignant lesions.

Many investigators have taken advantage of the ability of radiologists to extract image features such as smoothness or spiculation in an efficient and reproducible manner when developing their computer-based diagnostic systems. They have used discriminant analysis [73–75], rule-based expert systems [76], and artificial neural networks [77] to merge the ratings of the features provided by human observers into final determinations of the likelihood of malignancy. Many have found that their computer systems merge these fea-



A B

Fig. 5.—Enhancement of microcalcifications by high-frequency analysis.
A, **Portion of a digitized mammogram containing microcalcifications.**
B, **Mammogram after processing and thresholding to emphasize high frequencies. Microcalcifications, many of which are very subtle, are apparent, as are scattered false-positive detections. (Courtesy of Laura Mascio, Livermore, CA.)**



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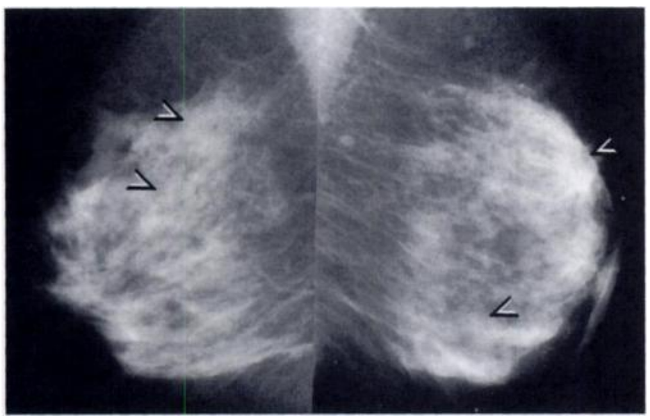


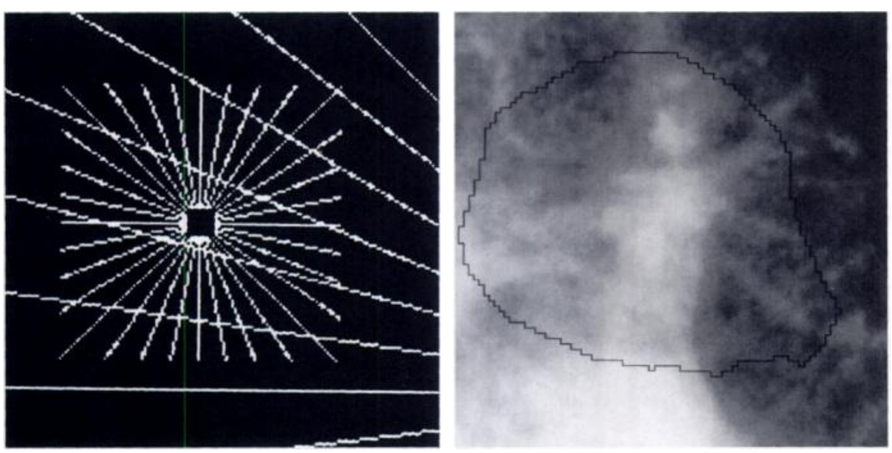
C

Fig. 6.—Detection of a mass lesion by analysis of optical density asymmetries.

A, **Original paired mediolateral oblique mammograms show a mass in upper portion of left breast.**

B, **Images obtained after multiple subtractions enhance density asymmetries.**

C, **Mammograms after feature analysis show correct identification of mass by computer along with three false-positive detections (*arrows*).**



A B

Fig. 7.—Detection of a breast mass by analysis of local orientation of edge structures.

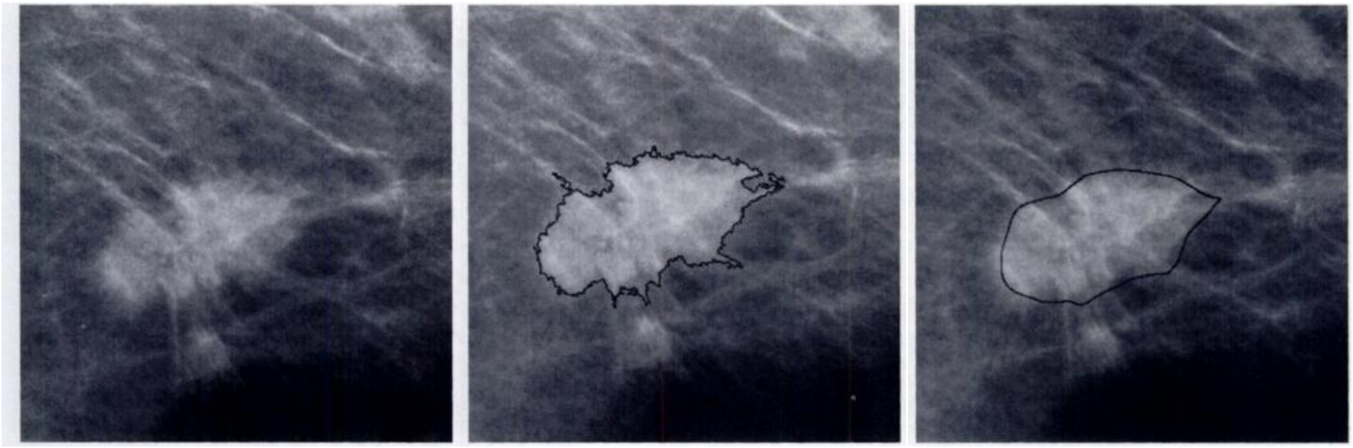
A, **Schematic illustration of differences in edge orientations of a spiculated lesion and adjacent normal parenchyma.**

B, **Mammogram after computer analysis indicates location of a subtle spiculated mass based on its local edge characteristics.**

(Courtesy of W. Philip Kegelmeyer, Jr., Livermore, CA.)

tures into a correct diagnosis more often than do general radiologists, with the performance of the computers being similar to those of expert radiologists.

A computer can provide valuable assistance even if it does not recommend a final classification. Swett et al. [78–80] have described systems that provide visual and cognitive feedback to the radiologist so that he or she can perform at a higher level of expertise. The computer can assess a priori patient risk factors or determine whether the input data support the working diagnosis. The computer can also display images similar to the case at hand as an aid in the classification process.



A B C

Fig. 8.—Characterization of a mass by analysis of spiculation.
***A*, Original digital mammogram shows region containing a malignant mass.**
***B*, Digital mammogram showing computer-extracted tracked margin of mass illustrates roughness and spiculation of margin.**
***C*, Digital mammogram shows smoothed margin of mass in which spicules have been removed. Difference between the two computer traces yields an indicator of likelihood of malignancy.**

Present Status

Although they share many basic approaches, techniques for the computer detection of mammographic abnormalities vary markedly in their structure and execution. Most methods require that a number of empirical decisions be made regarding parameters that occur during the execution of the programs, such as filter characteristics or threshold levels. Therefore, no simple or complex theory can be used to predict from first principles which approach to computer detection will work best. Rather, this must be evaluated by testing the schemes on actual case material. Unfortunately, the results of such evaluations are very strongly influenced by the clinical cases examined, and for this reason, no reports of sensitivity, specificity, or other measures of computer performance are given here. It has been proposed that a standard set of images be developed as a common data base and made available to all investigators in the field so that their results can be compared in a meaningful way [81]. Until this occurs, the merits of individual schemes can be evaluated only by comparing their performance to that of radiologists or, more appropriately at the present stage of development, assessing their ability to improve the performance of radiologists under realistic conditions of image interpretation.

Such an experiment was first performed by Chan et al. and published in 1990 [39]. Their computer program analyzed a number of films containing subtle clusters of microcalcifications. The performance of radiologists interpreting these images under simulated screening conditions was shown to be significantly better when they were also given the detection information generated by the computer (Fig. 9). Their results also attest to the remarkable ability of human observers to use incomplete or imperfect information to improve their performance. The computer program yielding the computer-aided diagnostic information detected only 87% of the clusters in the case material and did so with an average of four false-positive findings per image. Nevertheless, this information was a definite aid to radiologists who were rapidly interpreting films, resulting in a statistically significant improvement in their detection performance. The radiologists performed at an even higher level when the false-positive rate was, in 1990, artificially reduced to one-

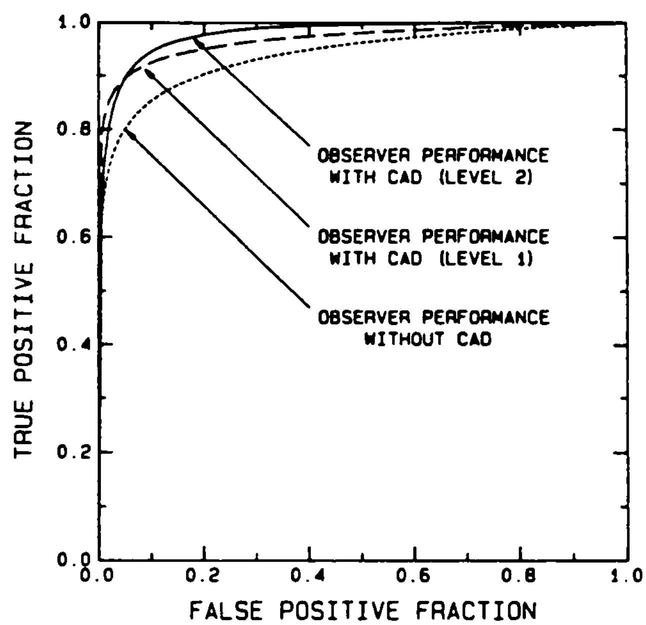


Fig. 9.—Receiver operating curves show statistically significant improvement in radiologists' performance in detecting clusters of microcalcifications when computer aid is used. Level 1 corresponds to radiologists' use of a computer aid that had an 87% true-positive detection rate with an average of four false-positive clusters per image. Level 2 corresponds to use of a simulated computer aid that had the same 87% true-positive detection rate but an average of only one half false-positive cluster per image. (Reprinted with permission from Chan et al. [39].)

half per image. This low level of false-positive detections has recently been obtained in actual practice on the same case material with the aid of improved feature analysis [41].

Recently, Astley et al. [46] have also reported an improvement in radiologists' performance when they were supplied with computer detection information for clustered microcalcifications. Kegelmeyer has shown that radiologists can detect subtle spiculated masses more sensitively when they are given information generated by his detection scheme [82].

At present, no classification method in which the computer extracts the image features has been shown to aid radiologists in making correct diagnoses. The eventual goal of these programs is to provide the basic input to other computer programs that merge image features to improve correct classification of abnormalities, however. Such programs, as discussed next, have already been shown to be of great value when used with human-extracted features.

The work of Getty et al. [74] and Swets et al. [75] shows that artificial intelligence can be used to merge individual image features into correct mammographic diagnoses more reliably than can general radiologists; other artificial intelligence methods perform rather at the level of expert radiologists. Recently, Wu et al. [77] have reported the ability of neural networks to correctly classify lesions as benign or malignant when using individual image features extracted by radiologists (Fig. 10). When adapted to patient management, the neural network output also proved superior to all radiologists in the study for determining whether biopsy was indicated.

As the field matures, it will become ever more important that promising techniques be evaluated in relation to the performance of radiologists. New, partially empirical, approaches will continue to emerge, but increasingly, the question of clinical efficacy will arise much as it does now when, for example, new chemotherapy protocols are introduced in medical oncology.

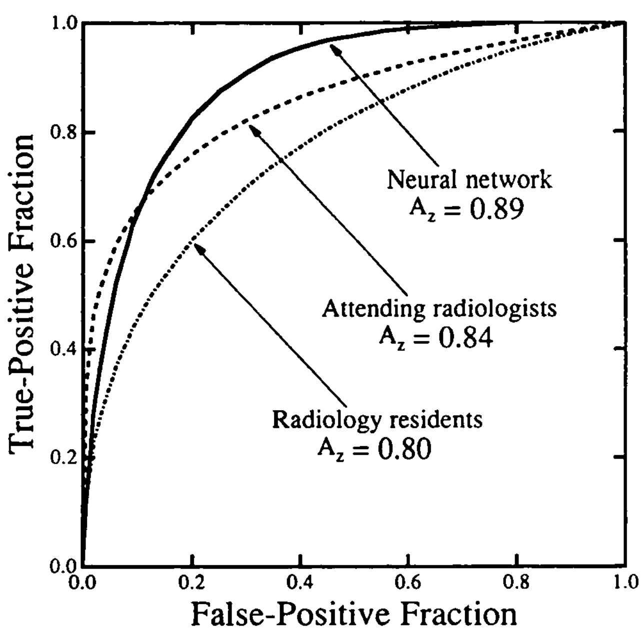


Fig. 10.—Receiver operating curves comparing performance of attending radiologists, radiology residents, and a neural network that used features extracted by an experienced radiologist in characterizing 60 mammographic lesions as benign or malignant. (Reprinted with permission from Wu et al. [77].)

Future Directions

The large-scale effort being invested in computer-aided diagnosis in mammography virtually assures that significant advances will be made in the future. These will likely be in the form of continued refinements of present methods and in the introduction of new and novel techniques or approaches.

The implementation of computer-based systems in everyday practice will be further advanced with the advent of primary digital mammograms. Although digitization of mammographic films allows similar information to be obtained, and is available today, digitization of film is not as efficient in terms of time and effort as are systems for direct acquisition of digital images. Given that digital mammographic systems are still several years from commercial reality, it is likely that such systems will contain some computer diagnostic capabilities at or shortly after their introduction. The superior latitude and noise characteristics of digital images [21] will, in turn, allow improved performance of available computer algorithms.

Even in the time frames described, the memory and data handling requirements of computer-aided diagnostic systems performing in near real time will be daunting. Considerable design will be needed to assure that the various algorithms run with high efficiency and that the different algorithms required for detection and classification purposes are combined as seamlessly as possible. The manner in which the computer information is displayed to radiologists will also require careful development. Such information, if appropriately presented, should not slow the radiologist or decrease his or her ability to do a day's work in a day.

These and other obstacles to the practical implementation of computer-aided diagnostic techniques in mammography will almost certainly be overcome in time, if not in the foreseeable future. As this occurs, radiologists and their patients will experience another benefit of the revolution created by the digital computer, and the practice of radiology will change yet again.

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