DIAGNOSTIC RADIOLOGY
A REVIEW OF COMPUTERS IN

Authors: **E. J. Hall**
S. J. Dwyer, III
C. A. Harlow
Department of Electrical Engineering
G. S. Lodwick
Department of Radiology
University of Missouri-Columbia
Columbia, Missouri

Referee: Arch. W. Templeton
Professor and Chairman
Department of Radiology
University of Kansas Medical Center
Kansas City, Kansas

I. INTRODUCTION

The use of computers in radiology has steadily increased over the last ten years, motivated by the desire to increase radiologists' efficiency and improve patient care. The computer has been shown to be an effective means of speeding health care by transmitting and storing radiologists' reports. For example, the MARS System (Missouri Automated Radiology System) has been developed and is currently used for over 95% of the radiology reports at the University of Missouri.[1] The use of MARS as a reporting system has greatly reduced the time elapsing between a patient's examination and the transmittance of the report to the referring physician. Furthermore, MARS also automatically stores the report for immediate recall for teaching or research use. Other types of reporting systems have been developed at Nebraska University,[2] Massachusetts General Hospital,[3] and in Sweden.[4]

Computer simulation of radiology departments is another area of computer applications in radiology. For example, a computer radiology department simulator[5] has been developed to study patient flow patterns, equipment requirements, and personnel requirements within a radiology department. This type of simulator may also be used to study several possible system designs in order to determine an optimum design prior to the construction of a new department. These uses of the computer can improve patient care by increasing the efficiency of both radiological personnel and equipment.

Computers are used routinely for clinical radiation dosimetry and the area of nuclear medicine is seeing increased usage of small computer systems for on-line applications, such as isotope bookkeeping functions, dosage and decay computation, and image manipulation. One of the most recent uses is direct computer interpretation of brain scans.[6]

In addition, several applications have been made of what we shall call computer-aided diagnosis. In this method the radiologist extracts the information from the film and the computer is used to aid in the decision-making regarding disease patterns based on the features extracted from the film by the physician. This work draws heavily upon the results derived in mathematical decision theory.

Finally, a new tool which we call automatic computer analysis is beginning to show promise of clinical applicability. In this method, the radiologist does not directly read the film. Rather, the computer reads the film and directly makes a diagnosis about abnormalities that might occur in the film. Automatic computer analysis draws upon the disciplines of what is often called image analysis and also results from mathematical decision theory. It also requires hardware capability in the implementation of scanning and display equipment.

In the remainder of this paper, we will review recent papers on computers in radiology and provide a state-of-the-art view of the field. To provide sufficient depth of coverage, the review will concentrate on current developments in automatic computer diagnosis and computer-aided diagnosis. Although these developments are now in the research stage, ultimate clinical use appears imminent.

First, several important papers dealing with computer-aided diagnosis will be reviewed. Computer-aided diagnosis implies the use of a computer to analyze information that has been extracted from the film by radiologists. The application of computer-aided diagnosis of lung cancer, gastric ulcers, bone tumors, congenital heart disease, and thyroid disease will be discussed as examples of the benefits of the human-computer interactive systems. The success of these efforts has motivated the development of automatic feature extraction techniques as a step toward automatic diagnosis. Therefore, several recent developments on automatic feature extraction from radiographs will be reviewed.

Next, we will give a detailed discussion of automatic computer analysis. This discussion will be divided into a discussion of image analysis techniques which will be followed with a discussion of some applications in radiology.

II. COMPARISON OF COMPUTER AIDED AND AUTOMATIC COMPUTER DIAGNOSIS

The science of radiological computer diagnosis has evolved over the last ten years in two directions. The first method involves computer-aided diagnosis in which the radiologists extract the information from a radiograph and use a computer for statistical calculations. The second, more recent, method consists of automatic computer diagnosis.

An interesting comparison of the similarities and differences between radiologists' diagnoses, computer-aided diagnosis, and automatic computer diagnosis has been given by Hall et al.[7] For example, consider the classic example of mitral stenosis shown in Figure 1.

A radiologist, upon viewing this case, notes and mentally describes the individual features which are abnormal; that is, the left atrial appendage, left atrial enlargement, and pulmonary vascular changes. This mental procedure is the feature extraction phase of the radiologist's diagnosis. Next, the radiologist compares and correlates the normal and abnormal features of this particular case with his past knowledge and experience in the diagnosis of rheumatic heart disease. This process may be compared to the computation of the prior probability matrix in a computer-aided diagnostic method or to a computation of training sample statistics in an automatic computer diagnosis. Next, the radiologist applies his decision scheme, which consists of "physiologic thinking" in which he notes that mitral stenosis causes obstruction of the blood flow at the left atrial level producing the enlarged left atrium, enlarged atrial appendage, and also explains the normal left ventricular size and normal aorta. These findings are explained by a stenotic mitral valve producing the radiographic changes. Radiologists' training stresses the "physiologic thinking" approach to diagnosis.

FIGURE 1. Example of mitral stenosis.

In computer-aided diagnosis, the radiologists again act as the feature extractors; however, they may be aided by computer questions concerning the possible features. In Templeton's system of computer-aided diagnosis of heart disease,[8] the radiologist answers 25 specific questions concerning the unknown case. Each of the radiologist's responses to the series of questions is related back to past experience stored in the computer memory in the form of a probability matrix. Based upon the radiologist's responses, a decision rule based on Bayes' theorem produces a distinct probability value for each of a set of possible diagnoses.

In automatic computer diagnosis, the radiologist is removed entirely from the feature extraction step. In the University of Missouri system, the chest radiograph is scanned with an image dissector camera system which converts the radiant image into a matrix of numbers stored on magnetic tape. The computer then performs the feature extraction function by a method which will be described later. Once the measurements have been obtained, the computer compares these values to past experience of normal and abnormal hearts. The comparison is made and a decision reached by use of a discriminant function.

Several differences between the three methods of diagnosis may be noted. The most striking difference is the automatic feature extraction phase of the automatic computer diagnosis method. Also, note that the trend is to increase radiologists' efficiency by automating more and more of the steps involved in a diagnosis. Finally, as will be clearly illustrated later, the computer may arrive at a correct diagnosis without having to make many of the smaller steps, such as quantifying specific heart chamber enlargements, which utilize the "physiologic thinking" approach.

This brief introduction will now be followed with a detailed review of several papers on computer-aided diagnosis and automatic computer diagnosis, illustrated by a recent example of automatic computer diagnosis of rheumatic heart disease.

III. COMPUTER-AIDED DIAGNOSIS

Computer-aided diagnosis implies the use of a computer to analyze information that has been extracted from the film by the physician. That is, the feature extraction step is performed interactively by the physician. Several important applications of computer-aided diagnosis of lung cancer, gastric ulcers, bone tumors, congenital heart disease, and thyroid disease have been reported.

The long-range goal of direct scanning of radiographic images requires the careful analysis of disease systems in order to determine which findings are most important for the recognition of disease. Radiologists are highly successful in their more intuitive approach to the recognition of disease, and thus computer-aided diagnosis was a natural starting point for the use of computers in radiologic diagnosis.

As early as 1963, a method for converting roentgenographic data into numerical sequences for subsequent computer analysis as an aid in the radiologic diagnosis in predicting biological behavior and operability in lung cancer, was performed by Lodwick et al.[9] Roentgenograms of 541 cases of primary lung cancer were studied to determine the individual characteristics which reflected the pathological process. These characteristics were enumerated: size and shape of tumor, contour of margin of tumor, calcification in lung tumors, attenuation of tumor edge, degree of contact between tumor and pleura, cavity formation in lung cancer, pleural effusion, pulmonary spread of neoplasm, and bone involvement. These characteristics were given numerical values and entered on punched cards for computer processing. One year survival statistics were computed on the 541 cases and were found to meet acceptable standards in predicting biological behavior and operability in lung cancer.

Differential diagnosis of benign and malignant gastric ulcers was made by computer analysis of significant predictor variables by Wilson et al.[10] Ninety-three histologically proven gastric ulcers were analyzed by clinical, laboratory, roentgenographic, and statistical methods and the *a priori* probability matrix was developed by use of frequency distributions and Chi-square testing. Of 70 radiographic signs and clinical findings related to ulcer incidence, 17 variables that met the minimum 0.05 significance level included physical characteristics of the ulcer crater, condition of the gastric wall, patient's age and previous history, and evidence of gastric acid, epigastric tenderness, and peristalsis through the lesion. The most useful roentgenographic data for differential diagnosis of benign and malignant gastric ulcers center about the crater. The computer program based on Bayesian theory provided correct diagnosis in a test series of 14 consecutive unselected histologically proven cases.

Computer-aided diagnosis of primary bone tumors was reported by Lodwick et al.[11] According to the authors, the accuracy of diagnosis is related to the consideration of all possible diagnoses. There are five essentials in the development of a program of instructions for use by a computer as an aid to diagnosis:

1. Assume that the proper diagnosis can actually be made in a large percentage of cases.
2. Develop a method of converting or coding data from roentgenograms into numerical sequences which may be manipulated by the computer.
3. Having developed a system for communication with the computer, devise a method of relating the digitized findings to the diagnostic possibilities. Bayes' formula of inverse probability has been used for this research. The use of this formula assumes all of the clinical and roentgenographic findings to be independent variables.
4. If the probability matrix is inaccurate, then the possibility of a proper diagnosis is slight. The accuracy is dependent on
   a. the skill of the radiologist in coding the roentgenograms,
   b. the ability of the pathologist to classify the tumor, and
   c. the number and character of the cases in each classification which influence the statistical validity.
5. Test the diagnostic system's ability to predict the histologic type of bone tumor from the roentgenogram.

A summary of the initial series of 77 cases (using 8 possible histologic diagnoses) is included. Further studies were also reported.

Templeton et al.[12] performed a computer diagnosis and evaluation of congenital heart disease using coded roentgenographic findings. A computer using Bayes' theorem and a frequency distribution matrix correctly diagnosed 78% of 231 cases (proved by autopsy, surgery, or angiography) of 9 common congenital heart defects. Radiologists using the work sheets prepared for programming the computer diagnosed 79% correctly. Different defects were reviewed randomly and without prior knowledge of the proven diagnosis. The close correspondence between the two percentages is partially due to the consistent method imposed by the work sheet. Eighty-four percent of the defects were correctly diagnosed by the two methods together. Twenty roentgenographic signs were used, but the computer was also able to correctly diagnose 71% of the cases when only five signs were tested: heart size, left ventricular size, main pulmonary artery size, peripheral vessel size, and peripheral vessel disparity.

Further evaluation of a computer program for diagnosis of congenital heart disease was reported by Toronto et al.[13] The physician fills out a list, noting with a check mark those symptoms present in the patient. The code numbers corresponding to these symptoms are punched on an IBM card and fed to the computer along with the cards containing the symptom-disease matrix and the computer program. The computer prints out a list of diseases with corresponding probabilities listing only those whose probability exceeds 0.01.

A computer program for diagnosis of thyroid disease based on signs, symptoms, and laboratory findings was developed by Fitzgerald et al.[14] A program for the diagnosis of thyroid disease based on experience gained with 1379 cases of suspected thyroid disease, was developed. The program makes use of a conditional probability model of medical diagnosis and is believed to imitate the thought processes of a physician experienced in thyroid disease. First, it evaluates the probability of a functional thyroid abnormality based on the signs and symptoms alone; it then evaluates the probability of a functional abnormality based on the laboratory data; finally, it considers all data together. Laboratory values and the probability values are routinely searched for some 10 to 15 specific combinations (such as those produced by acute thyroiditis, congenital deficiency of thyroid-binding globulin, masked hyperthyroidism, etc.) If a particular test may give a conclusive diagnosis, it is requested and, if present, a specific diagnosis is printed out. After the diagnosis has been made, all values are entered back into the basic data matrix so that the subroutine changes the basic data matrix after each diagnosis. In this way, the program may be said to "accumulate experience". In 500 cases of suspected thyroid disease examined by the program at the University of Florida College of Medicine, 14 mistakes in the diagnosis of the thyrometabolic status were made (2.8%) of which 7 could be easily corrected. Further work led to a fast computer program and increased diagnostic accuracy.[15]

Two methods of computer diagnosis of solitary pulmonary lesions were compared by Templeton et al.[16] Two methods of computer diagnosis, one assuming independence of variables and one assuming linear dependence, were tested on 242 histologically proved cases of solitary lung lesions covering 9 disease entities. The small number of patients made it necessary to group the diseases into four categories and to reduce the number of variables from 16 to 9. These last are smoker, zone of lesion, size of lesion, shape of lesion, character of border, calcification, cavitation, pleural fluid, and hilar adenopathy. Under these conditions, the method assuming linear dependence was most accurate. Difficulties such as those met in this study may be remedied by collecting more proved cases and by applying medical judgment in the selection of symptoms and diagnostic categories.

A general purpose computer program for roentgen diagnosis was developed by Tsien et al.[17] Instead of a system for use in making differential diagnosis of a specific disease group, their present general purpose computer program is designed for assisting the roentgen diagnosis from reading films of a specific anatomical region. Following the natural stages of recognition of roentgen signs by the radiologist to the final report of possible conclusions, at each stage the program enables the radiologist to obtain information prestored in the computer to supplement his own knowledge, to help him minimize errors, or to analyze the statistical data when such data are available. The input data are the roentgen signs observed by the radiologist. The program contains two main sections with the possibility of using all or part of the program, as may be desired by the radiologist.

IV. AUTOMATIC COMPUTER DIAGNOSIS

An automatic computer diagnosis requires an image-scanning system and automatic feature extraction methods followed by computer decision analysis. Several important advances in both image scanning and computer equipment and feature extraction techniques from images have been made in the past five years.

Automatic computer diagnosis devices have long been anticipated. For example, Lee B. Lusted[18] in 1960 described "...an electronic scanner-computer to look at chest photofluorograms and to separate the clearly normal chest films from the abnormal films. The abnormal chest films would be marked for later study by the radiologists." Perhaps one reason that such techniques are not completely established is that, as stated by Gwilym S. Lodwick,[19] "the computer is not sufficiently accessible to medical users."

In the following section we will discuss some general image analysis techniques and some applications of automatic computer diagnosis in radiology. First, a tutorial review of image analysis as applied to diagnostic radiology will be given. The general image analysis system can usually be divided into three steps: preprocessing, feature extraction, and classification. For automatic computer analysis, these steps are preceded by image scanning and may be followed by image display. The preprocessing techniques are designed to enhance selected features and remove irrelevant detail. Feature extraction techniques, designed to extract significant information from images, may be accomplished interactively by humans or automatically by computer. Several automatic feature extraction methods will be described. Diagnosis or pattern classification using the extracted information is usually the final step and provides a means of evaluating the overall image analysis system.

A. An Overview of Image Analysis Techniques

The design of a computer-aided diagnostic system may be divided into three phases: image pattern recognition, evaluation, and implementation. The image pattern recognition problem is usually considered to consist of three major steps: (1) preprocessing, (2) feature extraction, and (3) classification.

The most difficult step in image pattern recognition is still, as it was stated some 15 years ago by Selfridge,[20] "The extraction of significant features from a background of irrelevant detail." This fact is particularly relevant with respect to radiographic image analysis. Several authors, such as Uhr,[21] have even cautioned against assuming the existence of significantly distinguishable features. An obvious example is that quite different three-dimensional objects can yield identical two-dimensional projections. The question about features has not raised serious doubts in biomedical image processing, mainly because feature extraction and pattern classification can be accomplished with reasonable success by radiologists. Thus, a more pertinent question might be whether or not a computer can successfully duplicate or compete with the procedures employed by a trained radiologist.

Practical models for the pattern recognition of images have been discussed by Levine,[22] Tretiak,[23] and others. The block diagram of a realistic pattern recognition system for image analysis is shown in Figure 2. Image preprocessing usually consists of an application dependent technique for enhancing pre-selected features or for removing irrelevant detail. The feature extractor will thus have an image function for its input. The purpose of this step is to extract features from the image. The features may contain coordinates, areas, average values, topological functions, etc., but must consist of a real-valued vector function of a set of images. The outputs of the feature extractor are then used by a pattern classifier. The following theoretical difficulty has been pointed out by Nagy.[24] The features must be evaluated in terms of the classification stage rather than during the feature extraction process. This results in the need for an adaptive supervisor. At the present time, this adaptive supervisor, in most applications, is represented by a radiologist or a programmer.

Most image processing techniques which have been applied to biomedical situations have been found to be very application dependent. Thus, starting with a large repertoire of techniques, one can converge toward the best technique for a particular application.

Preprocessing Techniques

The diagnostic information content in a radiograph is more semantic than statistical in nature. That is, the features necessary for diagnosing a particular disease are determined both by the disease and the class of images. For example, heart size is relevant in the diagnosis of rheumatic heart disease, but is probably irrelevant in the diagnosis of lung cancer. Also, the resolution required in a particular disease application, for example, may be an order of magnitude lower than that necessary for all general diseases using the same class of images.

In this section, several useful preprocessing techniques will be described. The techniques are designed to enhance the extraction of selected features and to eliminate irrelevant information in an image. First, a distribution linearization technique will be described. Second, spatial digital filtering methods will be described. Third, a contrast enhancement technique is illustrated. Finally, image subtraction, a simple technique for removing irrelevant information, is considered.

Distribution Linearization

Because image digitization requires that each gray level value be quantized over a finite range (e.g., six bits/picture element), a histogram of the gray level distribution values may be computed.

The gray level histogram (first order probability density function) of most images exhibits a brightness peak which is heavily biased to the dark side of the histogram.[25,26] Figure 4, a 64 level histogram of the chest radiograph pictured in Figure 3, is an example of this. The digital representation of the radiograph has 256 X 256 brightness values over a 33 X 33 cm face, with a

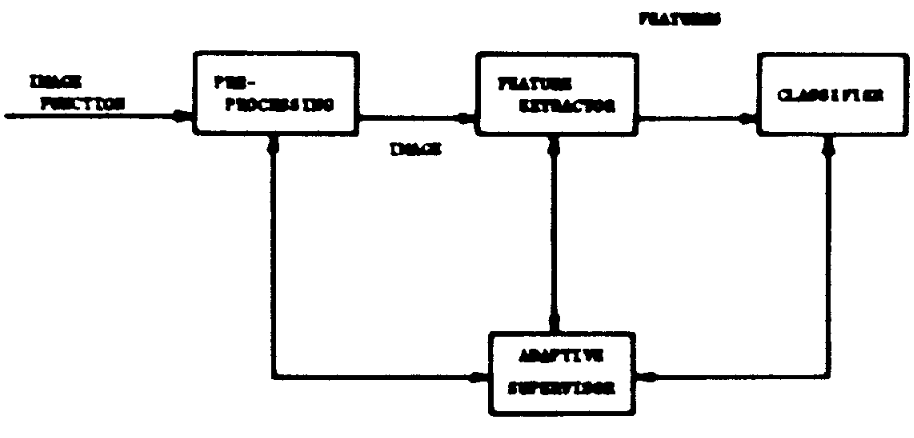


FIGURE 2. Pattern recognition system block diagram.

FIGURE 3. Chest radiograph.

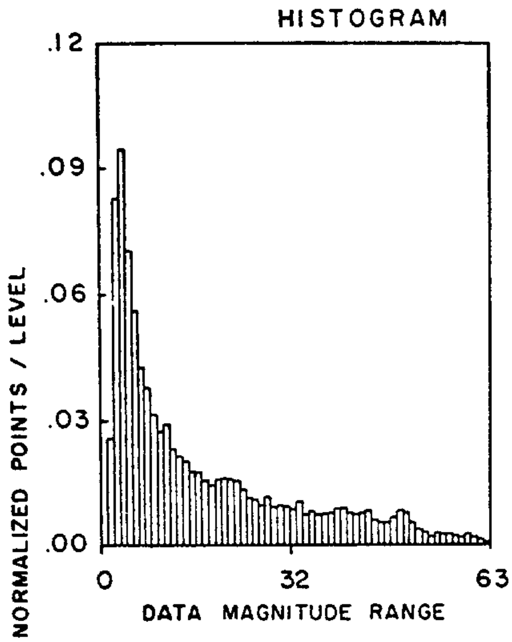


FIGURE 4. Gray level histogram of chest radiograph.

sampling frequency in either dimension of .78 lines/mm. The effect of having a large percentage of the 65536 picture elements (pixels) concentrated into such a narrow portion of the histogram is an image with little visible detail. Many contrast ratios that define edges are simply not displayable. One technique frequently used to correct this is the application of logarithmic conversion of the brightness pixels. This yields pixels which are proportional to image film density rather than brightness[27]. The log operation has the effect of

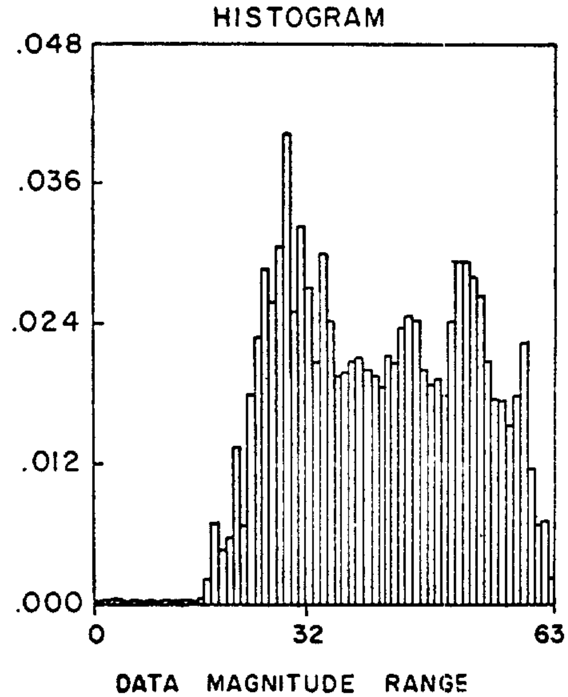


FIGURE 5. Gray level histogram after logarithmic conversion.

expanding the gray range of the lower brightness pixels while compressing that of the higher brightness pixels. However, because of the shape of the brightness histogram, there is much more contrast expansion than compression. Figure 5 is a gray level histogram of the original chest radiograph after logarithmic conversion.

Because a more rectangular histogram is advantageous, a position invariant, nonlinear histogram equalization technique, similar to the distribution transform in statistics,[28] is useful. Since the distribution transformation is only true for continuous variables, some care must be taken to obtain the desired result for the discrete approximation. The resulting histogram, Figure 6, is the best discrete approximation to a rectangular histogram.

Linear Filtering

Several techniques for spatial and frequency domain design of spatial digital filters will now be considered.

Digital smoothing is designed to remove noise from images so that later processing will be made easier. Smoothing, or preprocessing digitally within a computer, is usually done by either spatial or frequency domain operations.

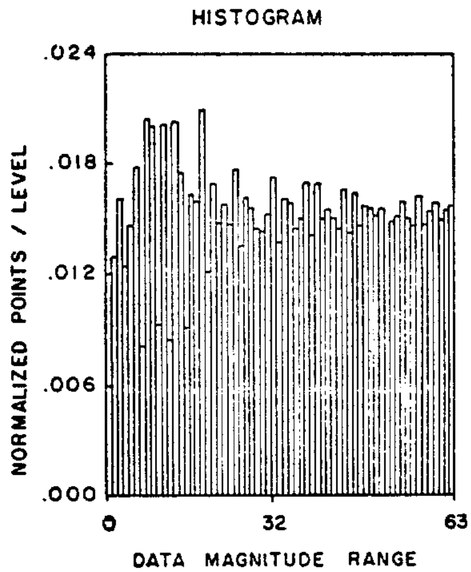


FIGURE 6. Gray level histogram after distribution linearization.

One method is to average over a neighborhood in the spatial domain. The basic idea is simply to assign a neighborhood to a point and then change the intensity value of the point by performing an average of all its neighbors.[29] In addition, gradient functions may be set up in various directions in order to test whether or not the averaging process should be performed. An attempt is made to prevent blurring edges or points where significant pictorial information occurs. Noise removal depends chiefly upon the nature of the pictures which are being processed. For example, what appears to be noise may be a significant feature of a human face.

These averaging methods can also be performed in the frequency domain. One takes the input picture in digitized form and performs the discrete Fourier transform or equivalent methods. The smoothing operations that have been discussed can be performed by removing the high frequencies in the frequency domain. This operation is called low pass filtering. Instead of merely deleting the high frequencies of a picture in order to remove noise, often a selected band of frequencies will be deleted while enough of the high frequencies are left to keep the edges clear.

When an image is low pass filtered, the image contrast is generally unaffected. However, edge detail is effectively removed.[30] This effect is seen in the image displayed in Figure 7. The most common application of low pass filtering of images

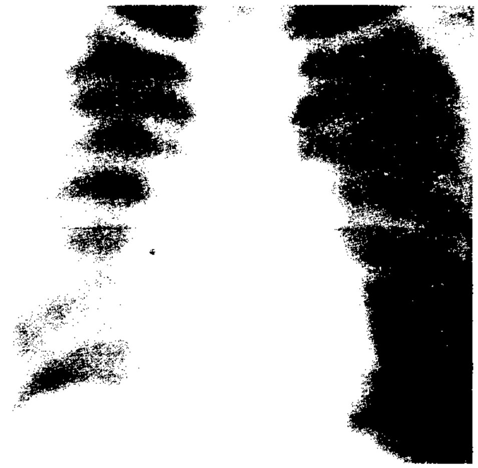


FIGURE 7. Low pass filtered image.

is to reduce the effect of random picture noise when the image is used for measurement selection and pattern recognition purposes. Other types of filters can be developed based on a low pass prototype.

Enhancement techniques have an obvious potential for assisting roentgenographic diagnosis. The ability to sharpen detail, for example, and to employ non-isotropic filters to make a hairline fracture more evident, could result in more correct diagnoses, especially when combined with high resolution display equipment for human viewing.

The effect of high pass filtering an image as seen in Figure 8 is to remove the contrast information of the image while outlining edges. The edge outlining effect can be seen most obviously at sharp, high contrast ratio edges, such as along the patient's diaphragm. A major application of high pass filters is in the visuali-

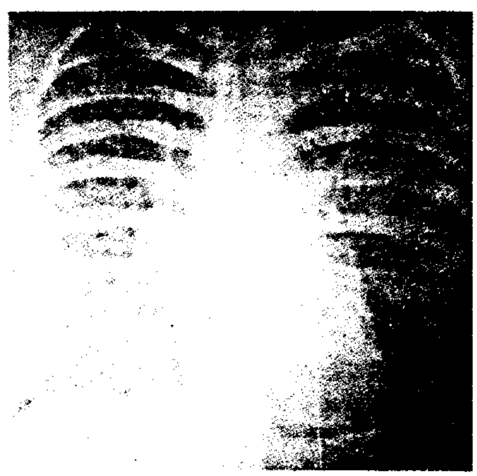


FIGURE 8. High pass filtered image.

zation of small, low contrast features superimposed onto uniform backgrounds.[31,32]

A filter which partially suppresses the lower frequency components while enhancing those higher is the high emphasis filter. It should be noted that both the high emphasis and high pass filters create negative brightness pixels. These usually appear as dark bands surrounding the sharper, high contrast ratio edges in an image. The application of a high emphasis filter to an image has an effect on image edges quite similar to the photographic technique of unmasked sharpening.[33] This technique overemphasizes edges, reinforcing the Mach phenomenon. The filtering result is shown in Figure 9.

Post-Filtering Contrast Enhancement

While high emphasis filtering is useful as an edge sharpening procedure, it has the somewhat undesirable effect of reducing image contrast. A useful gray level transformation may be developed with the distribution linearization technique, which has the added advantage of being adaptive. Figure 10 is an example of contrast enhancement by distribution linearization of the high emphasis filtered image shown in Figure 6. This technique visually enhances the image because the edge sharpness is retained while contrast ratios that define small edges are expanded.

Image Subtraction

When two radiographs differ only in certain details, a subtraction of the two images can be performed to accentuate the differences in the two films. Image subtraction is a commonly used

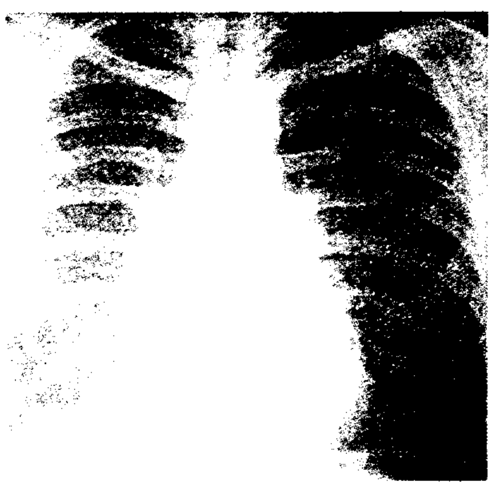


FIGURE 9. High emphasis filtered image.

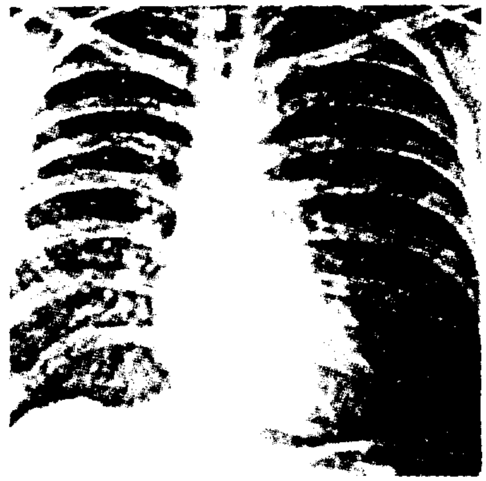


FIGURE 10. Contrast enhanced image.

technique in serial angiography. The photographic subtraction method requires precise registration of the films, a precise inverse relation between the copy print negative and the original, correct exposure, and controlled development of gamma 1.0.

The subtraction may also be performed digitally. Although prevention of motion, correct exposure, and precise registration are still important, a contact print is not necessary. Also, the effects of motion, exposure, and registration can be compensated for on the computer. Registration must be carefully accomplished during scanning and small adjustments may be made by correlation or matched filtering.

Feature Extraction

As previously defined, feature extraction consists of the extraction of significant features from a background of irrelevant detail. Methods for the enhancement of selected features and elimination of irrelevant detail were described in Section A. Several techniques for the extraction of significant features from an image function will be described in this section.

The selection of an image feature set is a significant problem in itself, and no general theoretical solution exists. One reason for this difficulty is that the set of features required for classification of normal or abnormal samples for a particular disease is relative not only to the class of images but also to the diagnostic problem under consideration. Also, information which is pertinent to one diagnostic problem may be irrelevant to the solution of another problem.

Fourier Transform Frequency Signatures

The utility of spatial frequency power-spectrum sampling for automatically classifying patterns in images was demonstrated by Lendaris and Stanley,[34] particularly in detecting targets in aerial photographs. The purpose of this section is to consider the applications to biomedical images.

The usefulness of frequency sampling is based on the fact that certain features of an image function may be more distinguishable in the frequency domain than in the spatial domain. Also, a large data reduction may be effected and the features still distinguished.

The frequency signature consists of a set of n samples, where n is the number of sampling areas for a given sampling geometry. Several sampling geometries may be used. An annular ring sampling geometry is suited to the detection of circular objects, whereas a wedge shaped geometry can be used to detect periodic line structures in an image. A horizontal or vertical slit may be used to detect on axis features. An example of this technique will now be presented. A well-known property of the two-dimensional Fourier transform is that the transform of a circularly symmetric object is also circularly symmetric. Thus, if one is trying to detect circular objects, an annular ring sampling geometry is appropriate. Peaks in this circular sampled signature would correspond to energy at a given radial distance in the transform space.

Template Matching

Suppose that an image function of known form which is nonzero only over a finite rectangular region is perturbed by additive noise. The filter which maximizes the ratio of signal power to average noise power at the filter output at some spatial position is called a matched filter.[35] A detection decision may be made by sampling the matched filter output at the position and comparing this value to a threshold.

A matched filter detection is not affected by a translation of the signal; however, it is sensitive to rotation. The matched filter is also sensitive to magnification changes. If only a small size variation in the desired signal is expected, then a search through several sizes may be reasonable.

One of the first methods applied to automated analysis was template matching. Filtering techniques, primarily using the fast Fourier transform, have been widely applied to scene analysis. Template matching is a special case of filtering where one uses a matched filter. Some success has been achieved in character recognition using template matching but it has not been used successfully on other scene classes. If one considers the characters to be separated, then character recognition is not a difficult image analysis problem, compared to some others. Template matching has several problems. One such problem is that the process is not size invariant and that different templates for different size objects must be utilized. Also, it appears to be more appropriate for one bit pictures; that is, pictures with only two shades of gray such as a picture of a character. One can define template for pictures that are not one bit, but it is not clear that the recognition is sharp in this case. Template matching is a global technique, which is in its favor.

Directional Signatures

A simple but powerful technique for locating objects in fixed frame images consists of gray level directional signatures, e.g., Meyers, et al.[36] A fixed frame image set consists of images of similar objects; for example, chest, head, or leg x-rays. Normalization is a significant but solvable problem. The directional signature consists of a function which is the sum of the gray level pixel values along a line normal to a reference line. The x and y direction signatures for a chest x-ray are shown in Figure 11. Note that major objects such as the clavicle, the lungs, the heart, and the diaphragm may be located from the signatures. The signature information allows one to "zoom" in on a particular object. After an object has been located, measurements such as size or texture may be made.

Contour Tracing

A study of the human visual system (HVS) gives important insights into the feature extraction problem. It is known that the HVS responds linearly to the logarithm of the observed image brightness. It is also known that the subjective effect of image acuity or sharpness is more closely related to the rendition of objects much larger than those barely visible.[37] The Mach phenomenon relates to the physiological fact that the eye creates dark and light bands near contours of abrupt changes in image brightness and that this phenomenon results in the subjective enhancement of a sharp brightness change. In summary, the

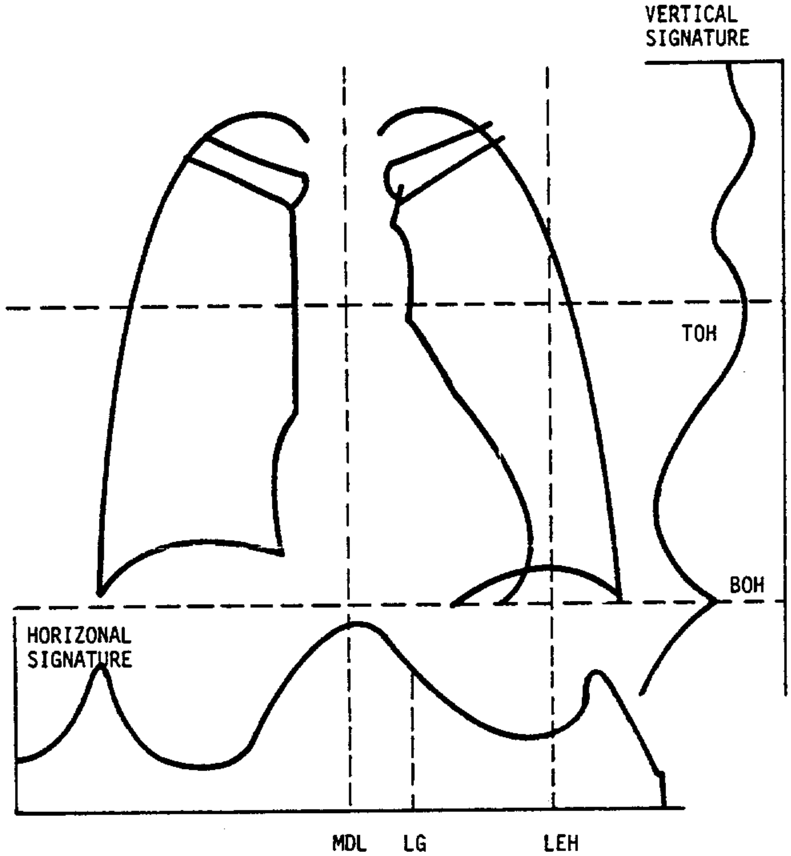


FIGURE 11. Directional signatures for chest radiograph.

HVS is most sensitive to contrast ratios and acuity properties of image edges, and least sensitive to the absolute brightness levels.

This knowledge of the importance of edge structure to the HVS has been used to advantage by Graham[38] and others to develop data compression techniques. Also, in diagnosing a patient's condition from a radiograph, a radiologist obtains a large amount of information from visible line or boundary structure.

These facts clearly indicate the importance of edge structure as significant features in many radiographic images, and motivate the development of computer algorithms for extracting edge information.

Therefore, many early attempts were made to identify the lines in a picture. These programs are often called contour trace programs. A position in a picture where two objects meet will be characterized by a change in the gray shades in a picture array, Figure 12b. This has suggested a search for points where the rates of change (deviations) of the picture array PIC(I,J) are large. Once these points are found, some form of logic is then used to connect these points together to form (see Figure 12a) the boundary of the object. There are variations in these techniques including level slicing and contour tracing, but the results tend to remain much the same. This method has several problems. First, due to the noise that will invariably be present in the picture array, contour trace algorithms will tend to give false edges. If there are touching and overlapping objects, a contour trace program will tend to switch from one object to another before a boundary of an object is completely traced. Contour trace programs are local algorithms and as such have the following problems. If mistakes are made, such as gaps, they must be corrected later. If there are several objects in the scene, a contour trace algorithm has no way of knowing that it is following a particular object and must be careful not to stray from it. Therefore this technique suffers from the problem of making mistakes which are passed on to the later stages for corrections, namely the pattern recognition stage.

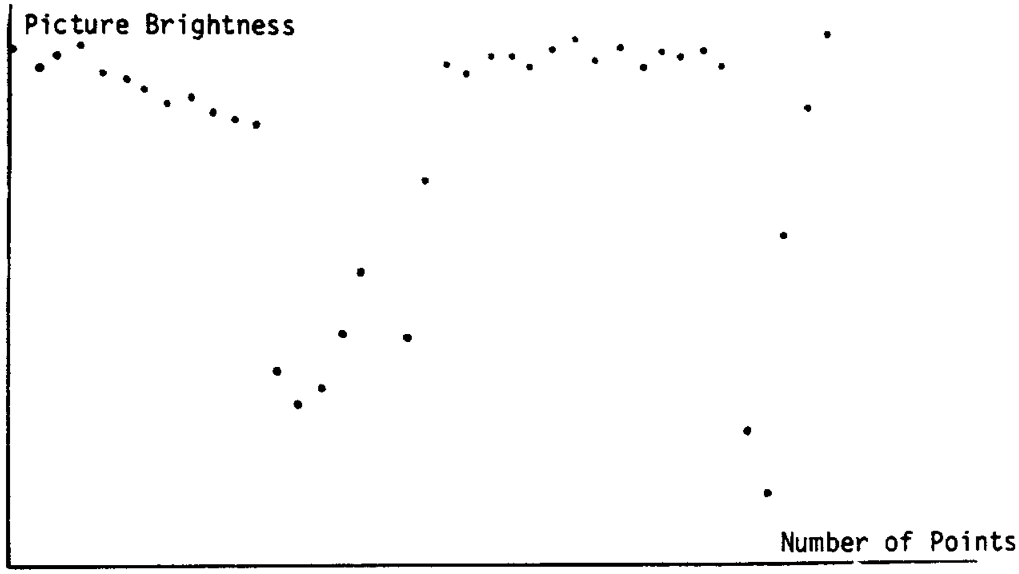


FIGURE 12b. One line plot of picture data from AP x-ray of the knee.

Thus, there is the very real problem of errors accumulating through the various processing stages. Also, it is bound to fail in complex images because it has no mechanisms to sort out the objects. Contour trace programs of this type must be limited to picture classes that are simple.

Another method that has shown some utility is often called region enumeration. This method tends to be the inverse of contour tracing. In this method a point x = (i,j) in the picture array is located, perhaps by a raster scan, and one desires to identify the points that lie in the same region with x. There will be a property P(y) that one uses to determine if a point y is in the region. First, one finds x; then one examines the eight neighbors of x. Let y be one of these points. If y has the property P, then y is placed in the region with x, otherwise it is not placed in the region. The process is repeated spreading out from x until all the contiguous points with the property P are placed in the same region. Often the property P will relate to the gray level of the point. For example, does point y have the same picture value as x? Or an average gray value of the region may be kept and y is tested to see if its picture value PIC(y) is close to the average value. Other P's can also be used. There are variations of these techniques in which one uses thresholding with region enumeration. Thus we see that region enumeration seeks to identify all the points in a

FIGURE 12a. X-ray of the lower leg, tibia and fibula, antero-posterior view.

region, not the boundary points. To do this, it places points in the region if it is not on the edge of the object, while contour tracing looks for edge points. Region enumeration has an advantage in that it is an integration type process where one builds up the points in the regions which should tend to approximate the region properties as the number of points is increased. In contour tracing it is hard to imagine an average gradient around an object, in other than simple pictures. Thus region enumeration tends to be somewhat more reliable than contour tracing but it is still a local process and shares the same problems that are inherent in local algorithms.

The Descriptive Approach to Image Analysis

Another approach that has been suggested in recent years is the linguistic approach. This approach was formulated as an alternative to the categorizor model. In the categorizor model, one has a transducer that extracts from the input picture a list of values for a set of features. Therefore, the pattern reorganizer must decide to which class a given vector in R^n belongs. An entire discipline called mathematical decision theory has been developed to study the problem of the optimal manner to partition R^n into disjoint subsets, each associated with a particular pattern class. Many different schemes have been devised including metric methods where one tries to choose the features so that vectors in the same class are close together according to some metric. Partitioning the space R^n with linear functions, polynomials, and potential functions has been extensively studied. Also, statistical methods have been used when one can reasonably estimate conditional probabilities.

The categorizor model was originally used in image analysis because the first problem attempted was the character recognition problem. This problem was so simple that the method worked well enough for commercial models to be constructed for multifont and hand printed characters.

This approach breaks down on complex pictures such as x-rays or landscapes. One can analyze such pictures only if he can decompose the picture into its various subparts and interpret the complex way the subparts interrelate to constitute the entire picture.

Many authors including Narasimham[39] and Shaw[40] recognized the inadequacies of the categorizor approach and developed the linguistic approach as an alternative. Since then, many others have examined the linguistic approach and it is used in the analysis of chromosomes and bubble chamber pictures. In the linguistic methods, one usually has some type of a generative grammar that gives the coded strings which represent the scenes. There will necessarily be some extra symbols, such as +, *,[40] or tie points,[41] etc., which reflect the manner in which the objects form their two-dimensional connections. The scenes are often considered to consist of line-like scenes. The primitive objects then are simple line strokes. One is then faced with the problem of finding these primitive lines in the scene. It is interesting to note that many of the papers on the subject assume that the primitive lines are somehow available with some type of offhand comment that there exist methods for finding them. This is a gross assumption to say the least. One of the main sources of interest in the linguistic approach derives from the fact that it may offer the means for finding the primitive lines in the picture. The information about the scene class is available; one has to devise a means for using the description to guide the feature extraction phase of the processing.

To summarize: the linguistic approach is of interest because it does contain a description of the scene class which is used to recognize the objects. It is not clear to the authors that it has been used to solve the feature extraction problem. It certainly could be used for scene generation in graphics applications. It appears to have the disadvantage that, as the theory is now formulated, it is more appropriate for line-like scenes.

Discussion of another approach that is being advocated follows. We usually refer to it as the descriptive approach. It is a method that is linguistic in nature; however, it tends to be much more of a semantic rather than syntactic approach. Since semantics is not a defined concept, we are subject to criticism here, but it is certain that it is a descriptive approach. The interpretation of the picture that arises from the processing which is guided by the description of the picture constitutes the meaning of the picture, since it represents what one wants to know about the scene. Before we begin a description of some applications in radiology, we will describe some of the literature on the descriptive method.

In reference 42 the authors advocate an approach to scene analysis based upon the concepts that:

a. regions will be the primitive objects – not lines;

b. the identification of objects should be done in a vertical search, i.e., from large objects to their details;

c. a graph contains the information describing the scene class. The graph gives information about the vertical ordering and geometrical arrangements of the object-such as object A is to the right of object B.

The authors apply the method to the analysis of landscapes. The model is used for the recognition stage, not feature extraction.

In reference 43 a structural approach is advocated. A structural description is a description which encodes an object organization in terms of its parts and the relationship between them. The important point is made that the structural description depends upon the articulation of the input into regions where the points in the region have some properties in common. Two important types of properties are mentioned, internal properties and boundaries. Global processing is advocated; the author appears to share our aversion to strictly local techniques. That is, he prefers to proceed from large objects in their entirety to their details, rather than vice versa. Also, an important idea is mentioned in this paper: "In a picture processor descoped in fairly general input material we should not be concerned if regions are not bounded initially by distinct edges, for some more complex property or relationship is no doubt involved and may enable us to perceive boundaries which are not present as sudden changes in the density." Some boundaries may be "invisible" when the load density values are examined.

In reference 44 a descriptive approach is also chosen. The authors use regions of uniform brightness and merge them to produce sufficient regions. The regions are then described in terms of properties such as average, brightness, and centroid. They then merge regions if the boundary between them is weak. After this is done, the picture is divided into regions that represent objects in the picture. Various relations are computed between these regions, such as adjacent beside convex and others. The picture description is in the form of a graph. The picture description model has relations between the objects. These relations are compared with those actually found to exist between the regions and the picture is interpreted according to these matches.

In reference 45, Bruce and Fennemer describe a method for identifying objects using regions. They first consider the atomic regions which are those whose points have identical gray shades. (This is an extremely restricted definition of an atomic region since most regions have significant variations.) These atomic regions are then joined together to form the regions used in object identification. They use a clever way of representing a region based on boundary points that are superimposed in the original grid of picture points. Regions are joined according to two heuristics, the first merging if two regions have a weak boundary (small difference in gray shades) that is a significant part of the total boundary intersection between the two objects. After the regions are merged, a line fitting method is employed which represents the line with straight line segments. The goal of the scene analysis is to give an interpretation of the picture data. The analysis extracts easily recognized regions first. In their case, the authors first look for floor and walls using the expected locations and attributes of the object. The remaining regions are then grouped by comparing vertices. The objects are then recognized based on the decomposition of each into quadrilaterals and triangles. The scenes are, of course, scenes of the inside of buildings.

In reference 46, Duda and Hart describe a scene analyzer. Their system consists of two components. One is a baseboard tracking program that locates a baseboard in the room. It finds the baseboard by knowing its gray shade and the width of the object. Then it scans the picture column by column looking for dark sections of a known width. This output is a two bit picture with all the problems of contour trace picture output. Next a straight line fitting program is applied to the data. Utilizing the fact that the scenes are of rooms, the program recognizes that there may be two walls in the scene. After one straight line is found, it searches for a baseboard of a second wall using concepts from projective geometry. Next, it recognizes objects. It operates on two levels. At the first level, the tests are made on the gradient picture; an edge detector is used. Straight line fitting is done. Measurements are made of the positions of the line from the baseboard – distance between a point and the edge of the scene. Also the absolute (relative to the camera) location of objects is found. The supervisor is in the form of a decision tree. Each node is a hypothesis about the scene. Each following node is a fixed text that is used to sharpen the hypothesis about the scene. Backtracking in the tree search is implemented. When a path of a tree terminates and an object is recognized, the object is removed from the scene and analysis proceeds in the remainder. The executive makes its decisions about objects by calling the low level tests and using its knowledge of the scene class.

In reference 47 an approach, which has some similarities to those just described, has been implemented and applied to x-rays. This method will be discussed further in the next section on radiographic applications.

B. Application in Radiology

One of the first relatively successful attempts at computer-directed feature extraction and classification of biomedical images was accomplished by Ledley[48] concerning automatic chromosome analysis and karyotyping. The analysis was carried out by an on-line, real time, high speed and resolution FIDAC system utilizing a flying spot scanner. Automatic chromosome karyotyping was performed by means of syntax-directed contour-analysis to identify the arm ends and centromeres of chromosomes from which measurements were made for typing and normality determination. The FIDAC system also has been used to extract and measure certain white blood cells called monocytes by means of characterization in terms of significant boundary concavities and convexities.

This research has led to a general effort to automate the analysis of this type of biomedical image. Mendelsohn and Prewitt[49] have delineated a set of descriptors to classify leucocytes using a nonstandard staining process. Young[50] concerned himself with simulation of a system to perform a six-class automated leucocyte classification by extraction and measurement of certain features of cell images using photomicrographs of Wright's stained leucocytes. Green[51] also used Wright's stained photomicrographs to develop a method for extraction and measurement of erythrocytes. The cells are separated from the background by thresholding a global gray level histogram of the entire image field. Once the background and cell field areas have been separated, the contours of a suspected cell are traced, as well as a local gray level histogram of the suspected cell area. The measurements extracted from these features are used to determine authenticity of the suspected cell. The features that were measured included cell area, perimeter, first and second moments, average optical density, and several other measurements that were combinations of the previously stated ones. The feature extraction and measurement strategy used in this case was to make quantitative measurements similar in conception to the qualitative measurements usually obtained manually.

One of the first applications of the digital computer to the analysis and display of radioisotope scans was described by Brown.[52] The processing included a statistical correction in which each point in the scan was compared to its eight neighboring points. If it deviated by more than one standard deviation from the mean, it was replaced by the mean. Resulting images were printed out using characters of different density on an on-line printer. Several lesions were clearly demonstrated by this technique which were only suspected on conventional photoscans. Brown[53] later reported a comparison between computed and conventional scans. He found that the photoscans contained more diagnostic information in two cases and that the photoscan was technically superior in five cases. In these five cases processing errors were found to be the cause of decreased quality. Thirteen computed scans were judged superior in diagnostic information and six computed scans were technically superior.

Tauxe[54] used an IBM 7090 to produce digital quantitative scans with 20 levels of gradation which perform background corrections corrections for radioactive decay, statistical analysis, and corrections for movement of the scanning radiation detector. Tauxe[55] also extended his method to produce displays with 100 levels of activity.

Levi[56] has used a small 8K work PDP-116 computer to store and process scans. An iterative smoothing process is used to decrease irregularities caused by statistical fluctuations in count rate. MacIntyre[57] developed a smoothing and Cal-Comp display program for scan data which was useful in showing nonhomogeneous blood flow to various organs.

Sprawls[58] has developed an automated procedure for normal-abnormal classification of scintigram images of the thyroid gland. For this study, 60 radioisotope scans were selected and hand-digitized. Twenty-one of the scans were normal. For the patterns of the human thyroid gland, a 24 x 24 array was used with each element representing a body surface area of $1/4 \text{ cm}^2$. An 18-dimensional feature vector was taken whose values were derived from three measurements (dispersion, skewness, and kurtosis), taken relative to two perpendicular axes in each of three specified areas (total gland, right lobe, and left lobe). The describing characteristics could also be defined in terms of the moments about the mean of the image in the specified area. The extracted features were used for classification and computer interpretation. The computer classification results were compared to physician interpretation with agreement in 57 of the 60 cases.

A more recent development was reported by Lehr et al.[59] It consisted of automatic tumor detection and classification in digitized brain scintigrams. The techniques of variable gray level thresholding, region enumeration, and the Freeman chain code were used to detect both those abnormalities which project clear of the calvarium and those which merge with it. The classification results were based on 16 films and were competitive with manual interpretation. The authors also point out the potential advantage of quantitative computer diagnosis to reduce the inconsistencies in medical diagnosis discussed by Garland.[60]

Meyers et al.[61] were among the first to apply automatic computer analysis to medical radiographs. Using an IBM 1401 in conjunction with a flying spot scanner system, they digitized 70mm chest photofluorograms. Then they computed a spatial signature and used it to measure cardiothoracic ratios. The computer-determined measurement was compared to values measured by 4 investigators for 36 cases. The computer value was within 15% of the average value determined by the investigators in 35 of the cases. This study clearly demonstrated that an automatic computer system could extract useful diagnostic information from a medical radiograph.

An application of a computer in the detection of radiographic abnormalities in mammograms was reported by Winsbert et al.[62] A facsimile scanner was used to convert the film information to an analog signal which was then analog-to-digital converted using a CDC 160A computer. The digitized image was stored in an 8 x 8 array with 16 gray levels. The system was designed to indicate the presence of breast cancer which is indicated by an area of increased density on the radiograph. The digitized information in each of the 64 areas was characterized by four vectors representing the distribution of density values, the number of subareas containing a given density level, the uniformity of density levels, and the continuity of a particular density. The vector set for each breast is compared to the vector set for the corresponding film of the contralateral breast, resulting in the detection of the presence and location of roentgen abnormalities.

Rockoff[63] has extracted trabecular bone measurements to locate and measure the width and orientation of their shadows but did not attempt classification.

In reference 64, an approach with some similarities to those just described has been applied to the analysis of AP chest x-ray with the goal of diagnosing abnormality in the heart and lungs. Since that time, the same program has been applied to AP x-ray of the knee. There are several basic assumptions behind this method which we will now discuss because we believe this method can be fruitfully applied to a variety of biomedical pictures.

1. The analysis of a scene should be top down. That is, one should first analyze the large objects in the scene at the lowest possible resolution and later analyze the finer objects in the scene as details of the large objects.

We believe that this assumption is justified for the following reasons:

a. It is easier to find large objects than small ones.

b. Restricting the search for small objects to a region within a previously analyzed larger object should make it much easier to locate the object.

c. Searching for large objects at a course resolution and then for their details at, perhaps, a different resolution should make for a more efficient utilization of both the computer's time and memory.

2. Feature extraction and pattern

recognition must be combined into a reinforcing system, i. e., a system with feedback. That is, feature extraction is not a separate process from pattern recognition. Pattern recognition is an integral part of feature extraction and must be included from the beginning.

We believe that this assumption is justified from an experience and the following intuitive argument. In a complicated scene, if one desires to recognize the objects in the scene, then one must find the relevant features in the image. Suppose the contours are sufficient. Then one must extract the contours of all the objects in the scenes. In a complex scene, one must have a knowledge of object A before one can extract the contour, otherwise one will, in some situations, deviate from A's contour into another object in the scene. But, one must know that he is in fact on object A, which means he has in fact found the object. Thus, one cannot extract the features of A until he has recognized A and one cannot recognize A until he has extracted the features of A. This seeming paradox of course implies an approach combining feature extraction and recognition.

3. One must have within the program a comprehensive description of the class of scenes to be analyzed. This description must guide the scene analysis system from beginning to end. The description should be in the form of data to scene analysis supervisor so that one can readily analyze different scene classes without extensive reprogramming.

4. Regions enumeration rather than some form of contour trace program should be used in primitive object identification. As previously discussed, due to the integrating effort of regions enumeration, we believe the process is inherently more stable than some form of contour tracing which is very sensitive to perturbations. Also, we believe it is easier to implement assumption 3 using regions enumeration for primitive object identification.

5. All parameters in the program must be selfadjusting. There will necessarily be parameters to some of the programs. The program that enumerates the regions will certainly have some parameters, which indicates when a region terminates. For a scene class that is large, one cannot expect one setting of the parameters to suffice. Thus all parameters must be adjusted internally in the program.

6. The concept of field of vision is important in locating the true boundaries of objects. In many applications one must not only recognize the objects, but must also determine the exact boundary of the object. An example is chest x-rays where one needs an accurate contour of the heart in order to diagnose heart disease. We believe that there are advantages in recognizing the fact that a scene is composed of objects that completely fill its area, i.e., every point in the picture is in some region and one always sees something even though it may be lumped into a catch-all category of background. These objects all fit together in jigsaw fashion to completely fill the space of the scene. Therefore, one may say that one object begins where another one terminates. Thus, rather than locating boundary points where there is great activity, one should first locate the regions, areas of constant gray shade, and then let those regions spread into the questionable areas of the scene, i.e., the boundaries between objects, so that the decisions about the boundary points are made last, not first, when one has some information about the scene available.

A graphical description seems natural in implementing assumptions one and three. In particular a tree structure very naturally gives a top down (vertical) description of the scene class. See Figures 13, 14, and 15 for some examples. In the program described,[47] each node of the tree represents an object in the picture. The graph is data to the program. Thus when one changes picture classes, one changes the data which describe the scene class. Attached to each node is a list of attributes for that object and a predicate that describes the object's relation to the other objects in the picture. The attributes might include such facts as:

a. average gray level
b. average number of points
c. shape description such as higher order moments.

An important point to note is that by using a top-down search, the objects can be located with widely different resolutions. For example, our current version for the chest searches for the level one objects (diaphragm, mediastinum, right lung region, and left lung region) at a 16 x 16 resolution.

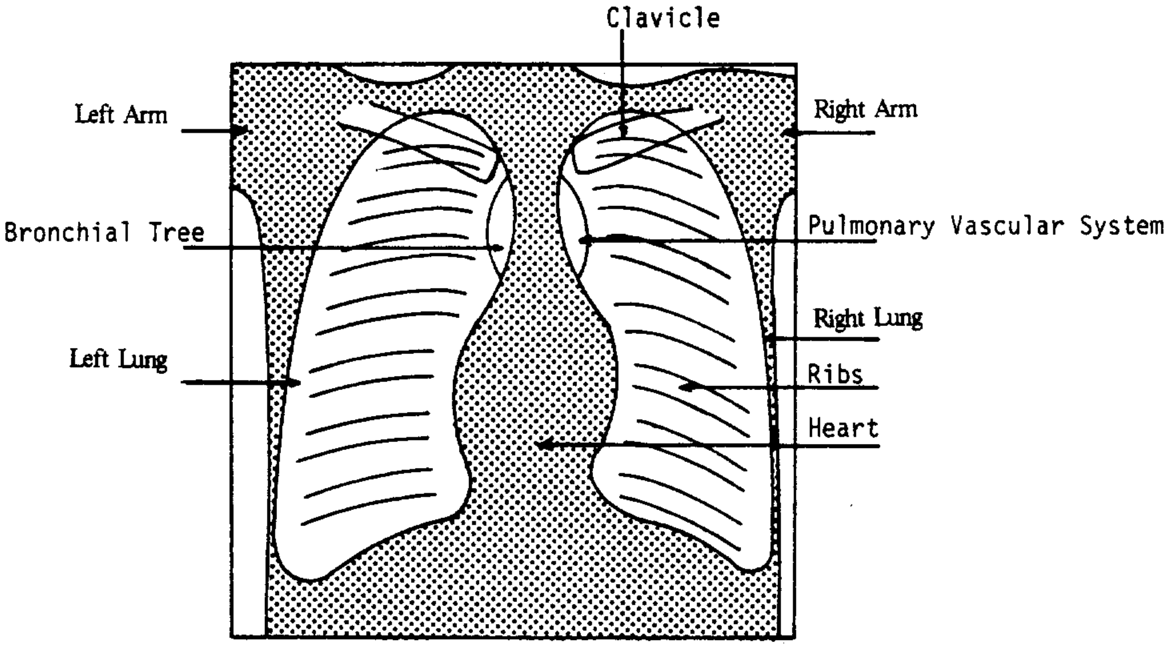


FIGURE 13. Anteroposterior view of chest.

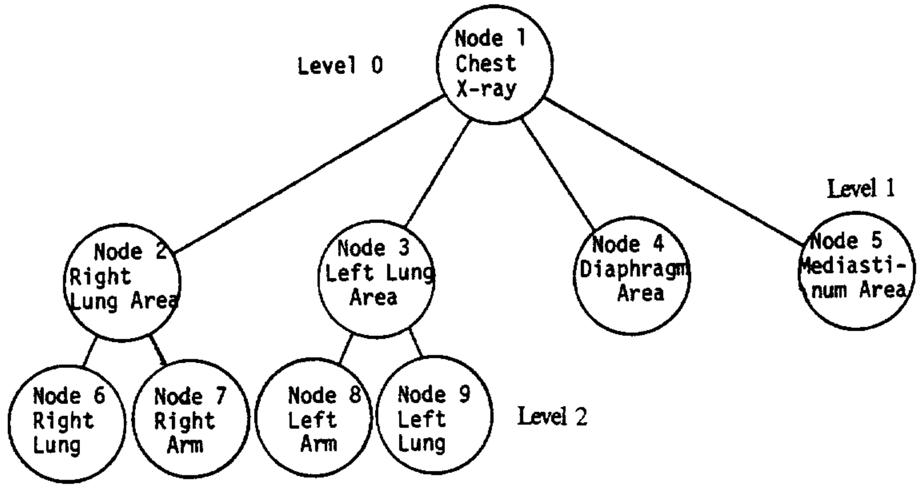


FIGURE 14. Partial vertical ordering of AP chest x-ray picture.

One does not have to analyze the entire x-ray at once. First, just distinguish these objects from each other. If one desires very accurate descriptions of the borders, one can easily switch resolutions, retaining the information found at the lowest level. When our present program switches resolutions, it merely declassifies the boundary points between objects, then switches resolution and reenters the point classification program which decides to which object the point belongs. Thus, in moving to higher resolutions one merely reshapes the boundary to get an accurate description of the object.

The predicates attached to each node can be very valuable in identifying the objects. Many times an object in a picture has a border that has wide variations in the intensity of the picture function at the border. In places the border may not be visible at all. The predicates are a way to define the boundary of an object when the boundary may not be visible. For example, in Figure 14 consider Node 7 and the predicate

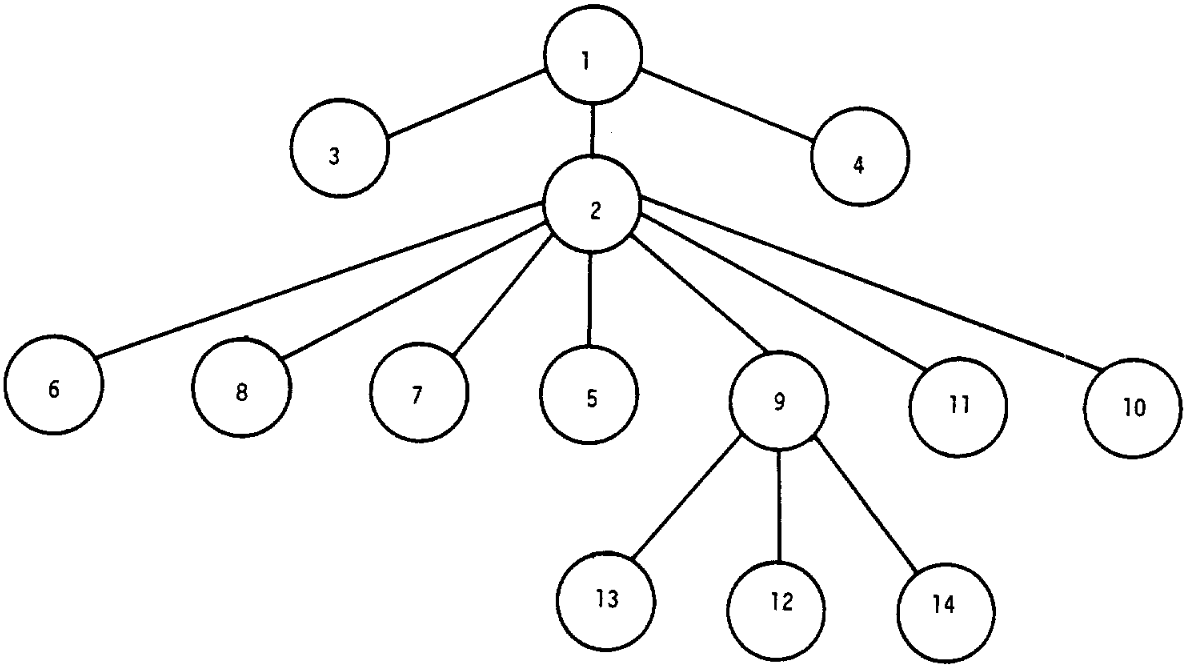


FIGURE 15. Partial vertical ordering of AP x-ray of the knee.

expressed in PL/1 notation when 1 is the or and & is the and symbol.

(L(7)|B(7)|(R(7)& (B(6)L(6))))
(U(7)&(B(4)|B(6)| L(6))))|
(L(7)&R(7)))|(U(7)&B(7))

This says that a point x can be put in a region associated with the left arm region only if one of the following conditions holds for the initial regions linked to the node which represents the left arm, Node 7.

a. Region 7 is to the left of the point. This lets the region 7 grow without hindrance to the edge of the picture.

b. Region 7 is below the point. Hence, the arm region can move toward the top of the picture without hindrance.

c. Region 7 is to the right of the point and region 6 is either below or to the left of the point.

The other parts of the predicate are interpreted similarly.

Observe that the left arm region is thus controlled by the left lung region and points cannot be added to the region unless the left lung region lies to its left. Hence, the border is controlled by the predicate which reflects what the picture represents as well as its gray level characteristics.

A program for the automatic computer diagnosis of rheumatic heart disease has been developed recently at the University of Missouri.[65] The goal for this study was classification of the heart size from the standard PA chest radiograph into a normal or abnormal category. If the cardiac size was judged abnormal, a further sub-classification was accomplished into four separate categories of rheumatic valvular involvement. To test the basic normal-abnormal classification further, some non-rheumatic cardiac abnormalities in adults were also used as test cases. A test set of 320 cases was used. This set included 194 cases of rheumatic heart disease representing all combinations of rheumatic valvular involvement.

All patients in the abnormal group have had right and left heart catheterization and appropriate cineangiography to establish the correct diagnosis. Eighty-eight normal chest examinations were also selected from patients with no history of cardiac disease, no murmurs, and no cardiac symptoms. These were obtained from routine psychiatric admission chests, preoperative chest exams, and employee chests. The normals were selected generally from the age group of 20 to 45 in an attempt to match the age group range of the rheumatic heart disease patients included in the set of abnormals. To further test the normal-abnormal classification, 38 adult patients with other types of cardiac disease were included. These were proven examples of coarctation, ventricular septal defect, atrial septal defect, and pericardial effusions. The total test set included 320 cases.

The first 135 cases selected as the computer testing and training set were put aside as the radiologist test set library. This separate library, which includes both normals and all categories of rheumatic heart disease, forms the basis for comparing the diagnostic accuracy of the computer and the radiologist.

The 14" x 17" PA chest radiographs were scanned with an image dissector camera under the control of an SEL 840A computer into a 256 by 256 point array in which each element represents the image density at a discrete point on the film.

The first step in the feature extraction process was to extract size, contour, and shape of the heart from the standard PA film. This was accomplished by an algorithm that constructs a cardiac rectangle around the heart. The cardiac rectangle is variable in size, depending upon the heart size. This cardiac rectangle is obtained by spatial signature analyses similar to those developed by Sprawls[75] and Becker.[76] The initial horizontal and vertical signatures are computed by summing the pixels (numerical picture elements) in the columns and rows of the image array, respectively. The horizontal and vertical signatures are characteristic in their shape. A typical horizontal and vertical signature can be seen in Figure 13.

Once the cardiac rectangle was located, a technique for obtaining the closed cardiac surface was developed. The technique involved thresholding a gray level histogram to produce a one-bit (two level) representation of the chest image within the cardiac rectangle (Figure 16). The algorithm, using a gray level histogram, determines the threshold for converting the extracted cardiac rectangle into a two-bit representation (black and white) image of the heart.

The next step was to outline the cardiac contour from this black and white representation. With the left and right outlines determined, the intersection of the right cardiac edge and the diaphragm was determined, and a line was drawn from this point across to the intersection of the left cardiac edge with the diaphragm. A line was also drawn to connect the right and left top of heart (TOH) outlines so that the entire heart and portions of the pulmonary arteries are enclosed. A typical example is shown in Figure 16.

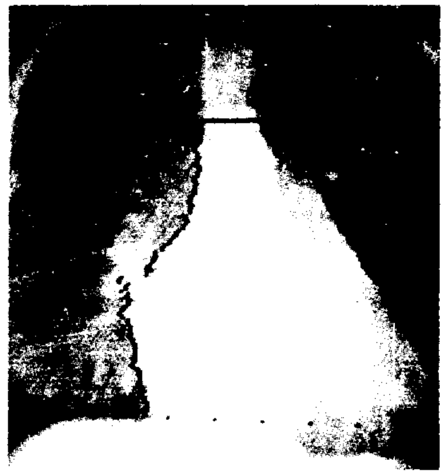


FIGURE 16. Cardiac contour outlined by computer.

Area and extent measurements are now easily made from this closed contour. At this point, nearly all information from the standard PA chest radiograph needed for the diagnosis and classification of heart disease had been extracted, and the next step was measurement of the heart.

The following are definitions of the extracted heart measurements.

1. THr–The thoracic distance is the lateral width of the thoracic cavity at the level of the intersection of the right diaphragm and right pleura. This measurement is used to normalize all the extent measurements which follow.
2. MDL–The chest midline is a vertical line which divides the thoracic cavity into two more or less equal parts.
3. MLE–The normalized maximum left extent is the distance from MDL to the left cardiac boundary.
4. CTR–The cardiothoracic ratio is the one measurement commonly used clinically to detect cardiac enlargement. It is the sum of MLE and MRE divided by THr.
5. DIAG–The diagonal thoracic ratio normalized by division by THr.
6. TA–The estimated thoracic area is a rectangular approximation of the thoracic cavity which is used to normalize all cardiac projection area measurements. It consists of a rectangle with a horizontal dimension equal to THr and vertical

dimension equal to the vertical distance between the pleural apex and the right cardiac-diaphragm intercept (RCDI).

7. LA–The left cardiac area is the normalized area of the heart between the chest midline (MDL) and the left cardiac border.

8. RA–This is the corresponding normalized right heart area, similarly defined.

9. TCA–The total normalized cardiac area is defined as the sum of LA and RA.

10. ALPHA–This is an angular measurement which measures the angle of the line extending from the left cardiac-diaphragm intercept (LCDI) to the right cardiac apex and is designed as an indicator of cardiac inclination within the thoracic cavity.

11. DIAGI–This is an extent measurement from the left cardiac diaphragm intercept to the right cardiac apex. It is designed as a cardiac height measurement.

12. RP–This right polynomial is a mathematical expression of the contour of right mediastinal boundary.

13. LP–This is a mathematical expression of the contour from below the aortic arch to just below the left atrial appendage. It is likewise approximated by a fourth order polynomial and is designed to detect the presence of an enlarged left atrial appendage, as caused by mitral stenosis.

All cardiac measurements were normalized so that a ratio figure was obtained. The linear measurements were divided by Thr, the thoracic width, and the area measurements were divided by TA, the thoracic area. This allows correction for variation in heart sizes related to the patient's overall size. This same algorithm can also be used for different film input sizes, i.e., standard 14 x 17 inch, 35 mm reduction, or chest photofluorograms.

Once these series of heart measurements had been extracted from the cardiac rectangle, this information was used as the basis for first classifying the case as normal or abnormal. If a particular case was abnormal, the classification went further by placing the case into the correct group of rheumatic heart disease.

The diagnoses were divided into 5 classes and the 16 possible combinations of aortic and mitral valve disease were divided into 4 separate groups. The classes considered by the classification scheme were:

Class 1. Normal

Class 2. Mitral stenosis only

Class 3. Other mitral valve lesions - MSMI; MI only

Class 4. Aortic and mitral involvement

Class 5. Aortic involvement - ASAI, AS only, AI only

Computer classification was accomplished through the use of linear and quadratic discriminant function.[68] This classification method was selected because of its relative simplicity and speed. Initially each part of the classification was processed using both the linear and quadratic discriminant functions. The selection for using a quadratic or linear discriminant function for each group in the final classification scheme was determined by the results: that discriminant function was chosen which gave the best results. If the accuracy was equal for both discriminant functions, the linear discriminant function was selected for the final classification scheme because it required less computer processing time.

In order to estimate the unbiased capabilities of the computer diagnostic classification scheme for the evaluation of new samples, the "jackknifing" test procedure was instituted. This procedure consists of first withdrawing 10% of the cases from each of the five classes. The remaining 90% of the cases in each class with their measurement parameters and polynomials are then used to train the classification scheme. Each case in the withdrawn group is subsequently tested and classified into one of the five diagnostic classes. This withdrawn 10% of the cases are then replaced into their respective classes, whereupon a different 10 % is withdrawn, tested, and replaced in an identical manner until all the cases have been tested. No case was tested more than once. This is a fair test, since in each case the algorithm had not "seen" the withdrawn test set until asked to make a diagnostic classification. A better test would probably have been to remove one case at a time and test each using the "jackknifing" procedure until all of the cases had been classified. However, this was not practical because of the large amount of computer time involved.

One further test was performed. The hypothesis was proposed that a normal-abnormal diagnosis for rheumatic heart disease would also make possible a reliable normal-general abnormal class diagnosis. This hypothesis was tested on the mixed group of

39 abnormal cases that included adults with ASD, VSD, coarctation, or pericardial effusion. A simple normal-abnormal diagnosis was instituted by submitting the mixed group abnormals to the classification algorithm derived for the diagnosis of rheumatic heart disease. Of the 38 cases submitted, 75% were correctly diagnosed as abnormal. The test missed four patients with coarctation. However, on review of the films, the heart proved to be of normal size; the diagnosis could have been made only from the presence of rib notching. This parameter is not now included in this cardiac algorithm.

It would be difficult to judge the value of this automated feature extraction and classification algorithm unless its accuracy could be compared to the diagnostic accuracy of radiologists. For this reason, the following study was instituted.

Ten radiologists were asked to individually diagnose 135 representative cases of the 282 rheumatic and normal cases evaluated by the computer. This group of radiologists consisted of seven board certified academic radiologists and three third-year residents whose training was nearly completed. Each radiologist was given the PA and lateral views and told that each case was either normal or rheumatic heart disease. He was asked to make a complete radiological diagnosis and record his answers on a form designed for the study. Each case diagnosed was counted as one physician observation. Information on the forms was then transferred to punched cards and computer programs were written to separate the 639 physician observations collected. Not all of the physicians completed the task of reading all 135 films. A comparison of the physicians' results with the computer results is shown in Figure 17. It is not an entirely valid comparison since the computer used only the PA chest film and the radiologists used the PA and lateral for their diagnoses.

The table in Figure 17 shows the correct classification rate, false positives, and false negatives for both the radiologists and computer. The correct classification rate for each disease category is found along the diagonal of the table. Reading each group along the horizontal reveals into what group the incorrect diagnoses were placed. For example, the third line (MI; MSMI) shows that the computer interpreted 3% of the patients who actually had MSMI or MI as normal (underdiagnosis). Continuation of the same line shows that the computer correctly classified 23.8% as having a mitral valve lesion (MSMI or MI), then overdiagnosed 66% of the group as having bivalvular involvement, and 9% as aortic valvular disease. In the combined aortic and mitral row, radiologists incorrectly classified 42% of the true bivalvular disease patients as having mitral disease only. The last column shows the total number of cases or observations viewed for each group.

Comparing the relative accuracy figures shows that the computer incorrectly classified too many cases as combined aortic and mitral valvular disease while the radiologists incorrectly classified too many into group three (MSMI, MI only). Figures also show that the radiologists as a group overdiagnosed the normals (diagnosed normals as abnormal) more frequently than the computer.

Overall accuracy was 73.3% for the computer and 61.8% for the group of radiologists. The 73% computer accuracy was also higher than that attained by any single radiologist. The overall accuracy was computed from the following equation:

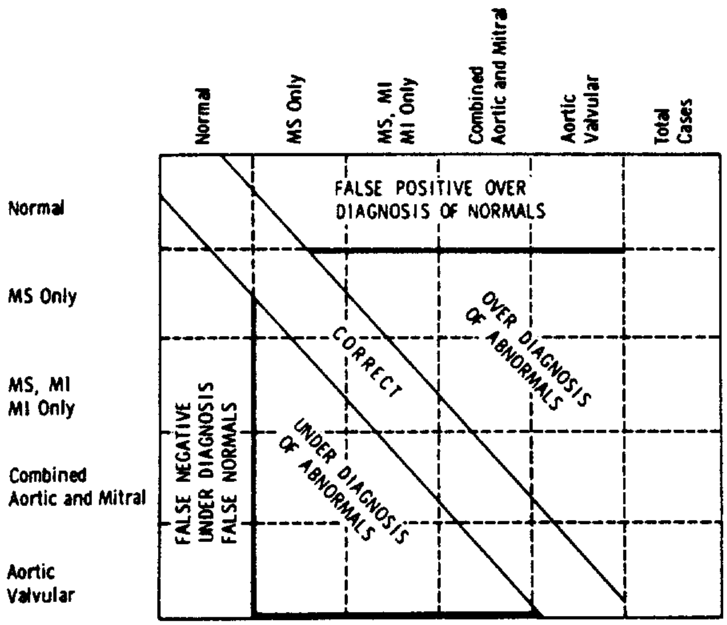
$$\textit{Overall accuracy} = \frac{\textit{Total number correct diagnoses}}{\textit{Total number of cases in test group}}$$

The abnormal classification rate was 93.6% for radiologists and 93.8% for the computer. These figures indicate that the computer and the radiologists have equal accuracy in determining a particular heart as abnormal, but that the computer is more accurate in placing abnormal cases into the correct class of rheumatic heart disease.

This example illustrates that although automatic computer diagnosis is quite different from the other methods, it is competitive and may outperform them.

V. Conclusion

The historical developments described in this paper show that in many particular situations, the use of computers in radiology can increase radiologists' efficiency and improve patient care. The examples of automatic computer diagnosis, the most recent application area, show the definite potential of computer diagnosis with an accuracy comparable to that of a radiologist. However, further applications need to be developed before this method is ready for clinical use. A pertinent question is: What are the possibilities in this area



	Normal	MS Only	MS, MI, MI Only	Combined Aortic and Mitral	Aortic Valvular	Total Cases	
Normal	88.6%	1%	0	6%	4.5%	88	Computer Accuracy
	83 %	1 %	1 %	3 %	12 %	221	Radiologist Accuracy
MS Only	9%	56%	3%	28%	3%	32	
	4.5 %	50 %	26 %	13.5 %	5.8 %	155	
MS, MI, MI Only	3%	0	23.8%	66%	9%	21	
	4.2 %	21 %	54 %	13%	7%	95	
Combined Aortic and Mitral	3.3%	6.6%	2.2%	82%	4.5%	90	
	4.2 %	21 %	42 %	29 %	6.3 %	95	
Aortic Valvular	20.6%	0	2%	26.5%	59%	50	
	20 %	0	0	2.7 %	76 %	73	

PHYSICIAN ACCURACY RATE

Total radiologist observations from films 639
Normal Classification Rate 83 %
Abnormal Classification Rate 93.6 %
Overall Classification Accuracy 61.8 %

COMPUTER ACCURACY RATE

Total computer test set 281
Normal Classification rate 89%
Abnormal Classification rate 93.8%
Overall Classification Accuracy 73.3%

FIGURE 17. Comparison of the computer's and radiologist's results. The top line horizontally in each class represents the computer results and the second line in each class represents the radiologists' results. The correct classifications in each class can be found along the diagonal of the table. All the other figures represent percentages of incorrect diagnosis.

and what approaches are valid? Several observations are clear. First, it is important to note that because a picture has some details that require a high resolution, one is not prohibited from analyzing the picture. Just because a chest may have some details that require a resolution of 1024 x 1024 does not mean that the entire million data points must be considered in the initial analysis. Rather, we believe that as little information as possible must be brought in. Then analyze these data and make deductions according to the computer's knowledge about its picture environment. When these deductions are verified, proceed to look at more of the picture data until all the information desired is obtained.

We might point out that in the area of scene analysis one can correctly assess a method only if he has in fact used the method himself. Since we have not tried everything, we will invariably make some incorrect assessments. We hope other investigators can contribute to this assessment of other techniques. The reason it is so difficult to judge methods from the published reports is the ease with which the data can be masked. Typical published results show a few examples of the results of a program. It is difficult to determine if these are typical results or if the investigator has fine-tuned his program on one picture, and if this is the only one, it works on without numerous adjustments by the investigator. Even when testing is reported there is still a possibility that the camera input and a lot of knob twisting and template arranging has put the data into just the right form. So, unless one has actually tested a method, one should be skeptical of it.

The principal question in scene analysis is: Given a class of pictures for investigation, how does one proceed to build an automated system to recognize the objects in the scene? First, we might mention some characteristics of a picture class that are important in the implementation of a scene analysis system.

1. Scene complexity - A scene is complex if there is a large variety of overlapping objects in the scene.
2. The number of pictures to be interpreted.
3. Quantified information should be important. There should be some characteristics of the objects whose numerial measurement is valuable.
4. The pictures should contain important information.
5. The pictures should be standardized. There should be a fixed frame of reference from which the pictures are taken, rather than a wide variety of oblique views.

Because these concepts are necessarily vague, we shall elaborate on each of them.

1. Examples of simple scenes are pictures of isolated blocks. The object is isolated and the implemenation of a system for analyzing such a class of scenes would be straightforward. A complex scene might be one of a landscape, the inside of a building, or a chest x-ray. There is a wide variety of objects in these scenes that touch and overlap. Analysis is difficult.

2. The number of pictures in the picture class to be analyzed is important due to the present state of the art. The cost of implementing an automated system is high. Only if there are a large number of pictures to be interpreted can one hope to have a reasonable cost effectness. Also, one should remember that humans interpret images fairly well. They are particularly good at interpreting a few pictures with great perception. However, for a large number of pictures, boredom becomes a factor and humans will tend to perform poorly. Needless to say, machines now do only a crude form of scene analysis, but they will not "fatigue."

3. It is obvious that an automated system could provide a lot of quantified information that is not readily available to human observers. For example, in chest x-rays one could measure the size of the heart. In bubble chamber pictures one can compute conjectories.

4. The pictures must be important; else, why analyze them in the first place. There are many classes of biomedical pictures that are important because they contain disease diagnostic information. Since it does not appear that a completely general scene analysis program is on the horizon, one should develop these programs on important picture classes so that the cost of the programs can be justified. Most biomedical images are important, but this is not always true in other studies.

5. It is a great help in the analysis of scenes if the pictures have a standard frame of reference. Lateral and AP chest x-rays and any of

the nuclear medicine pictures are standarized, but pathology slides and reconnaissance pictures are not because the objects in the scene can appear in all sizes and orientations, or not at all. In pathology slides a cell may be there in any size or part of it may be there. In photo reconnaissance pictures, an airport may or may not be in the picture, or half of it may appear.

We believe that the more of these characteristics a scene class possesses, the easier it is to implement an automated system. The fewer it has the less feasible it is to implement a system. For example, a scene class with the properties that

1. The scenes are simple
2. The class contains a vast number of pictures
3. Useful measurements can be made on the pictures
4. The pictures contain important information
5. The pictures have a standard view

would be most appropriate for an automated system.

Chest x-rays have properties number two through five. Nuclear medicine images have all the properties if one uses a lower interpretation of "vast" in number two. Photo-reconnaissance pictures have the properties two and four, but not one and five which makes the problem difficult, if not impossible, to solve at present.

We believe that picture classes with a fixed frame of reference will be amenable to automatic computer diagnosis. Some examples are:

1. AP chest x-rays
2. Lateral chest x-rays
3. Thyroid scans images
4. Brain scan images
5. AP x-rays of the knee
6. Lateral x-rays of the knee
7. Liver scans
8. Lung scans

If this criterion is not met, and unless some other simplifying assumptions are present, one is apt to have much difficulty implementing a system.

REFERENCES

1. Lehr, J. L., Lodwick, G. S., Reichertz, P., and Nicholson, B., Experience with an on-line system, presented at Computer Application in Radiology, University of Missouri, Columbia, September 1970.

2. Wilson, W. J., An automated system for coding radiology reports, presented at Computer Application in Radiology Conference, University of Missouri, Columbia, September 1970.

3. Bauman, R. A., Pendergrass, H. P., Greenes, R. A., and Kayolan, R. J., Further development and initial use of an on-line computer system of radiology reporting, presented at Computer Applications in Radiology, University of Missouri, Columbia, September 1970.

4. Brolin, I., Experience with an automated reporting system, presented at Computer Application in Radiology, University of Missouri, Columbia, September 1970.

5. Lodwick, G. S., Braaten, M. O., Williams, D., and Meyer, P., Use of a simulator in development of an automated scheduling system, presented at Computer Application in Radiology Conference, University of Missouri, Columbia, September 1970.

6. Lehr, J. L., Parkey, R. W., Harlow, C. A., Garrotto, L. J., and Lodwick, G. S., Computer algorithms for the detection of brain scintigram abnormalities, *Radiology*, 97, 269, November 1970.

7. Hall, D. L., Lodwick, G. S., Kruger, R. P., and Dwyer, S. J., Computer diagnosis of heart disease, Department of Radiology and Electrical Engineering, University of Missouri, Columbia, June 1971.

8. Templeton, A., Bryan, K., Waid, R., Townes, J., Huque, M., and Dwyer, S. J., Computer diagnosis and discriminant analysis schemes, *Radiology*, 95, April 1970.

9. Lodwick, G. S., Keats, T. E., and Dorst, J. J., The coding of roentgen images for computer analysis as applied to lung cancer, *Radiology*, 81, 185, 1963.

10. Wilson, W. J., Templeton, A. W., Turner, A. H., Jr., and Lodwick, G. S., The computer evaluation of roentgenographic signs in benign and malignant gastric ulcers, presented at the 1965 meeting of Association of University Radiologists.

11. Lodwick, G. S., Haun, C. L., Smith, W. E., Keller, R. F., and Robertson, E., Computer diagnosis of primary bone tumors, *Radiology*, 80, 273, 1963.

12. Lodwick, G. S., A systematic approach to the roentgen diagnosis of bone tumors in *Tumors of Bone and Soft Tissue*, 49, Year Book Publishers, Chicago, 1965.

13. Templeton, A. W., Lehr, J. L., and Simmons, G., The computer evaluation and diagnosis of congenital heart disease using roentgenographic findings, *Radiology*, 87, 658, October 1966.

14. Toronto, A. F., Veasy, L. G., and Warner, H. R., Evaluation of a computer program for diagnosis of congenital heart disease, *Prog. Cardiovasc. Dis.*, 5 (4), January 1963.

15. Fitzgerald, L. T., Overall, J. E., and Williams, C. M., A computer program for diagnosis of thyroid disease, *Amer. J. Roentgen.*, 97, 4, 901, 1966.

16. Fitzgerald, L. T. and Williams, C. M., Modified program for computer diagnosis of thyroid disease, *Radiology*, 82, 334, February 1964.

17. Templeton, A. W., Jansen, C., Lehr, J. L., and Hufft, R., Solitary pulmonary lesions, *Radiology*, 89, 4, 605, October 1967.

18. Tsien, K. C. and Peterson, M. D., Development of a general purpose computer program for roentgen diagnosis consultation, *AAPM Quarterly Bulletin*, (2), June 1968.

19. Lusted, L. B., Logical analysis of roentgen diagnosis, *Radiology*, 74, 1960.

20. Lodwick, G. S., Computer diagnosis in radiology, *J. Mich. State Med. Soc.*, 61, 1239, October 1962.

21. Selfridge, O. G., Pattern recognition and modern computers, Proceedings Western Joint Computer Conference, March 1955, 91.

22. Uhr, L., Feature discovery and pattern recognition, *Pattern Recognition*, Kanal, L. N., Ed., Thompson, Washington, D.C., 159, 1969.

23. Levine, M. D., Feature extraction: A survey, *IEEE*, 57, 1391, August 1969.

24. Tretiak, O. J., Pattern recognition, Notes of Image Proceedings Workshop, Massachusetts Institute of Technology, June 1970.

25. Nagy, G., State of the art in pattern recognition, *Proc. IEEE*, 56, 836, May 1968.

26. Kunio, D., Optical transfer function of the focal spot of x-ray tubes, *Amer. J. Radiat. Ther. Nuc. Med.*, October 1965.

27. Morgan, R. H., An analysis of the physical factors controlling the diagnostic quality of roentgen images, *Amer. J. Radiat. Ther. Nucl. Med.*, December 1965.

28. Kruger, R. P. and Dwyer, S. J., Image analysis of radiographs, *SWIEEECO Record of Technical Papers*, Dallas, Texas, 147, April 1970.

29. Selzer, R., Improving biomedical image quality with computers, JPL Technical Report, 32, 1336, October 1968.

30. Rosenfeld, A., *Picture Processing by Computer*, Academic Press, New York, 1969.

31. Hall, E. L. and Dwyer, S. J., Frequency domain design of spatial digital filters, *IEEE Information Theory Conference*, June 1970. Also, University of Missouri, Columbia, Image Analysis Laboratory, Technical Report 101, June 1970.

32. Stockham, T. G., et al., Nonlinear filtering of multiplied and convolved signals, *Proc. IEEE*, 1264, August 1968.

33. Neblette, C. R., *Photography, Its Materials and Processes*, Van Nostrand Company, New York, 1951.

34. Lendaris, G. G. and Stanley, G. L., Diffraction-pattern sampling for automatic pattern recognition, *Proc. IEEE*, 58, 198, February 1970.

35. Andrews, H. C., Automated interpretation and classification of images by use of the Fourier Domain, in *Automatic Interpretation and Classification of Images*, Academic Press, New York, 1969, 187.

36. Meyers, P. H., Nice, C. M., Becker, H. C., Nettleton, N. J., Sweeney, J. W., and Meckstroth, G. R., Automated computer analysis of radiographic images, *Radiology*, 83, 1029, December 1964.

37. Morgan, R. H., Visual perception in fluoroscopy and radiography, Fifty-First Annual Meeting of the Radiological Society of North America, Chicago, Illinois, November 1965, 403.

38. Graham, D. N., Image transmission by two dimensional contour coding, *Proc. IEEE*, 55, 336, March 1967.

39. Narasimham, R., Labeling schemata and syntactic description of pictures, *Information and Control*, 7, 151, 1969.

40. Shaw, A. C., The formal description and parsing of pictures, Stanford Linear Accelerator Report 84, March 1968.

41. Feder, F., Linguistic specification and analysis of classes of line patterns, TR-403-2, April 1969, New York University School of Engineering and Science, Department of Electrical Engineering, Laboratory for Electroscience Research.

42. Preparata, F. and Ray, S., An approach to artificial non-symbolic cognition, UILC-ENG 70, 223, University of Illinois, Urbana, Illinois, July 1970.

43. Macleod, I., On finding structure in pictures, *Picture Language Machines*, Kaneff, S., Ed., Academic Press Inc. London-Ltd., 1970.

44. Barrow, H. G. and Popplestone, R. J., Relational descriptions in picture processing, *Machine Intelligence*, 6, American Elsevier Publishing Company, 1971.

45. Brice, C. R. and Fennema, C. L., Scene analysis using regions, Technical Note 17, Stanford Research Institute, April 1970.

46. Duda, R. O. and Hart, P. E., A generalized hough transformation for detecting lines in pictures, Technical Note 36, Artificial Intelligence 6, Stanford Research Institute, July 1970.

47. Harlow, C. A., Otto, J. L., Hall, D. L., Lodwick, G. S., Feature Extraction in Images, Technical Report, Image Analysis Laboratory, Electrical Engineering Department and Radiology Department, University of Missouri, Columbia, July 1971. Also appears in *Proceedings of Joint Conference on Major Systems*, Los Angeles, California, October 1971.

48. Ledley, R. S., Automatic pattern recognition for clinical medicine, *Proc. IEEE*, 57, 11, November 1969, 2017.

49. Mendelsohn, M. and Prewitt, J., Analysis of cell images, *Ann. N.Y. Acad. Sci.*, 128, Article 3, 1035, 1966.

50. Young, I. T., Automated leukocyte recognition, Ph.D. Dissertation, Department of Electrical Engineering, M.I.T., Cambridge, June 1969.

51. Green, J. E., Computer methods for erythrocyte analysis, *IEEE Conference Record of the Symposium on Feature Extraction and Selection in Pattern Recognition*, Argonne National Laboratory, October 5-7, 1970, 100.

52. Brown, D. W., Digital computer analysis and display of the radioisotope scan, *J. Nucl. Med.*, 5, 802, 1964.

53: Brown, D. W., Digital computer analysis and display of the radionuclide scan, *J. Nucl. Med.*, 7, 740, 1966.

54. Tauxe, W. N., Chaapel, D. W., and Sprau, A. C., Contrast enhancement of scanning procedures by high-speed digital computer, *J. Nucl. Med.*, 7, 647, 1966.

55. Tauxe, W. N., 100-level smoothed scintiscans processed and produced by a digital computer, *J. Nucl. Med.* 9, 2, 58, 1968.

56. Levy, L. M., Some clinical aspects of computer-processed scintiscans, (abst.) *J. Nucl. Med.*, 8, 388, 1967.

57. MacIntyre, W. J., Christie, J. H., and Curtis, G. S., Three dimensional computer read-out of radioisotope scan data, *Radiology*, 90, 22, January 1968.

58. Sprawls, P., The Development and Analysis of a Computer Method for Interpretation of Radioisotope Distribution Patterns, Ph.D. Dissertation, Bioengineering Department, Clemson University, Clemson, S. C.

59. Lehr, J. L., Parkey, R. W., Harlow, C. A., Garrotto, L. J., and Lodwick, G. S., Computer algorithms for the detection of brain scintigram abnormalities, *Radiology*, 97, 269, 1970.

60. Garland, L. H., Studies on the accuracy of diagnostic procedures, *Amer. J. Roentgen.*, 82, 25, 1959.

61. Meyers, P. H., Nice, C. M., and Becker, H. C., Automated computer analysis of radiographic images, *Radiology*, 93, 1029, 1964.

62. Wisberb, F., Elkin, M., and Macy, J., Detection of radiographic abnormalities in mammograms by means of optical scanning and computer analysis, *Radiology*, 89, 211, 1967.

63. Rockoff, S. D. and Selzer, R. H., Radiographic trabecular quantization of human lumbar vertebrae in situ, Proceedings of the Conference on Progress in Methods of Bone Mineral Measurement, Bethesda, Maryland, February 15-17, 1968.

64. Harlow, C. A., Otto, J. L., Hall, D. L., and Lodwick, G. S., Feature extraction in images, Technical report, Image Analysis Laboratory, Electrical Engineering Department and Radiology Department, University of Missouri, Columbia, Columbia, Missouri, July 1971. Also appears in Proceedings of Joint National Conference on Major Systems, Los Angeles, California, October 1971.

65. Kruger, R. P., Hall, D. L., Lodwick, G. S., and Dwyer, S. J., III, Computer-aided diagnosis of radiographic cardiac size and shape detectors, Technical Report, University of Missouri, June 1966.

66. Sprawls, P., The Development and Analysis of a Computer Method for Interpretation of Radioisotope Distribution Patterns, Ph.D., Dissertation, Bioengineering Department, Clemson University, Clemson, S.C.

67. Becker, H. C., Nettleton, W. J., and Meyers, P. H., Digital computer determination of a medical diagnostic index directly from a chest x-ray image, *IEEE Transactions on Biomedical Engineering*, 11, 67, July 1964.

68. Townes, J. R., The gaussian mixture decomposition of estimated probability density functions, Ph.D. Dissertation, University of Missouri, Columbia, August 1971.