CHAPTER 1

INTRODUCTION

The last two decades have witnessed significant advances in medical imaging and computerized medical image processing. These advances have led to new two-, three-, and multidimensional imaging modalities that have become important clinical tools in diagnostic radiology. The clinical significance of radiological imaging modalities in diagnosis and treatment of diseases is overwhelming. While planar X-ray imaging was the only radiological imaging method in the early part of the last century, several modern imaging modalities are in practice today to acquire anatomical, physiological, metabolic, and functional information from the human body. Commonly used medical imaging modalities capable of producing multidimensional images for radiological applications are X-ray computed tomography (X-ray CT), magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT), positron emission tomography (PET), and ultrasound. It should be noted that these modern imaging methods involve sophisticated instrumentation and equipment using high-speed electronics and computers for data collection and image reconstruction and display. Simple planar radiographic imaging methods such as chest X rays and mammograms usually provide images on a film that is exposed during imaging through an external radiation source (X ray) and then developed to show images of body organs. These planar radiographic imaging methods provide high-quality analog images that are shadows or two-dimensional (2-D) projected images of three-dimensional (3-D) organs. Recent complex medical imaging modalities such as X-ray CT, MRI, SPECT, PET, and ultrasound heavily utilize computer technology for creation and display of digital images. Using the computer, multidimensional digital images of physiological structures can be processed and manipulated to visualize hidden characteristic diagnostic features that are difficult or impossible to see with planar imaging methods. Further, these features of interest can be quantified and analyzed using sophisticated computer programs and models to understand their behavior to help with a diagnosis or to evaluate treatment protocols. Nevertheless, the clinical significance of simple planar imaging methods such as X-ray radiographs (e.g., chest X ray and mammograms) must not be underestimated as they offer cost-effective and reliable screening tools that often provide important diagnostic information sufficient to make correct diagnosis and judgment about the treatment.

However, in many critical radiological applications, the multidimensional visualization and quantitative analysis of physiological structures provide unprecedented clinical information extremely valuable for diagnosis and treatment.

Medical Image Analysis, *Second Edition*, by Atam P. Dhawan

Computerized processing and analysis of medical imaging modalities provides a powerful tool to help physicians. Thus, computer programs and methods to process and manipulate the raw data from medical imaging scanners must be carefully developed to preserve and enhance the real clinical information of interest rather than introducing additional artifacts. The ability to improve diagnostic information from medical images can be further enhanced by designing computer processing algorithms intelligently. Often, incorporating relevant knowledge about the physics of imaging, instrumentation, and human physiology in computer programs provides outstanding improvement in image quality as well as analysis to help interpretation. For example, incorporating knowledge about the geometrical location of the source, detector, and patient can reduce the geometric artifacts in the reconstructed images. Further, the use of geometrical locations and characteristic signatures in computer-aided enhancement, identification, segmentation, and analysis of physiological structures of interest often improves the clinical interpretation of medical images.

1.1. MEDICAL IMAGING: A COLLABORATIVE PARADIGM

As discussed above, with the advent and enhancement of modern medical imaging modalities, intelligent processing of multidimensional images has become crucial in conventional or computer-aided interpretation for radiological and diagnostic applications. Medical imaging and processing in diagnostic radiology has evolved with significant contributions from a number of disciplines including mathematics, physics, chemistry, engineering, and medicine. This is evident when one sees a medical imaging scanner such as an MRI or PET scanner. The complexity of instrumentation and computer-aided data collection and image reconstruction methods clearly indicates the importance of system integration as well as a critical understanding of the physics of imaging and image formation. Intelligent interpretation of medical images requires understanding the interaction of the basic unit of imaging (such as protons in MRI, or X-ray photons in X-ray CT) in a biological environment, formation of a quantifiable signal representing the biological information, detection and acquisition of the signal of interest, and appropriate image reconstruction. In brief, intelligent interpretation and analysis of biomedical images require an understanding of the acquisition of images.

A number of computer vision methods have been developed for a variety of applications in image processing, segmentation, analysis, and recognition. However, medical image reconstruction and processing requires specialized knowledge of the specific medical imaging modality that is used to acquire images. The character of the collected data in the application environment (such as imaging the heart through MRI) should be properly understood for selecting or developing useful methods for intelligent image processing, analysis, and interpretation. The use of application domain knowledge can be useful in selecting or developing the most appropriate image reconstruction and processing methods for accurate analysis and interpretation.

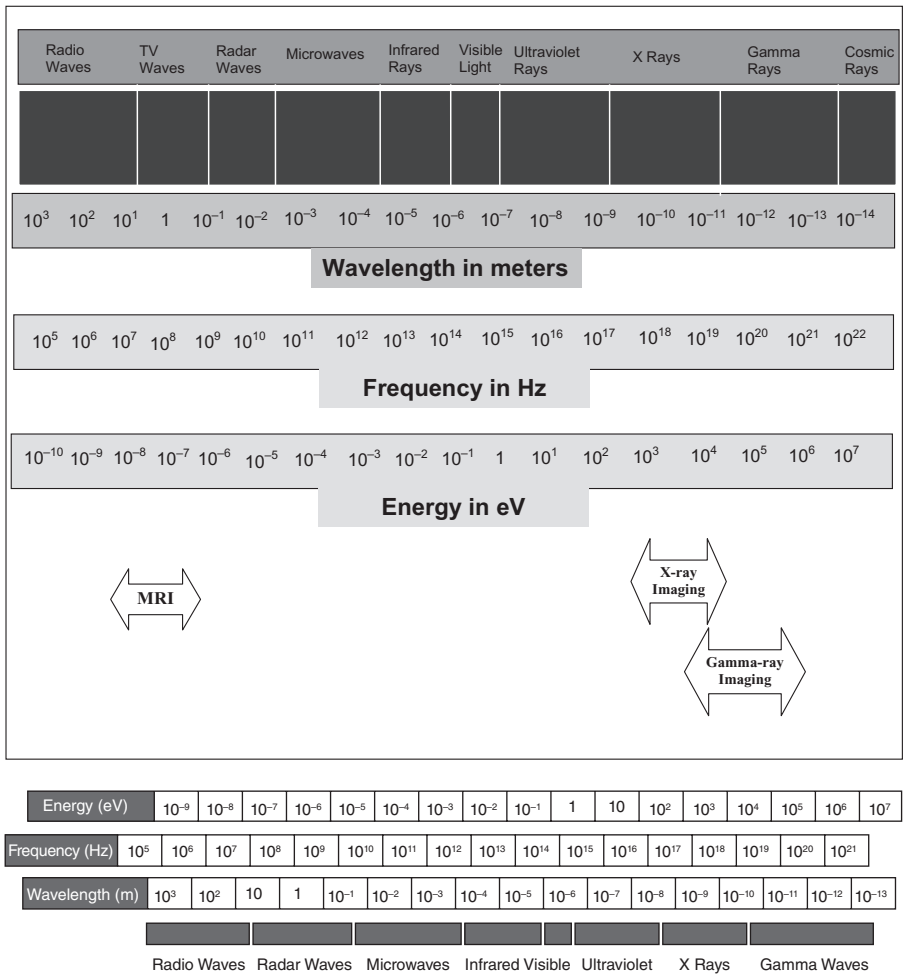


Figure 1.1 Energy sources for different medical imaging modalities.

1.2. MEDICAL IMAGING MODALITIES

The field of medical imaging and image analysis has evolved due to the collective contributions from many areas of medicine, engineering, and basic sciences. The overall objective of medical imaging is to acquire useful information about the physiological processes or organs of the body by using external or internal sources of energy (1–3). Figure 1.1 classifies energy sources for different medical imaging modalities. Imaging methods available today for radiological applications may use external, internal or a combination of energy sources (Fig. 1.2). In most commonly used imaging methods, ionized radiation such as X rays is used as an external energy source primarily for anatomical imaging. Such anatomical imaging modalities are based on the attenuation coefficient of radiation passing through the body. For

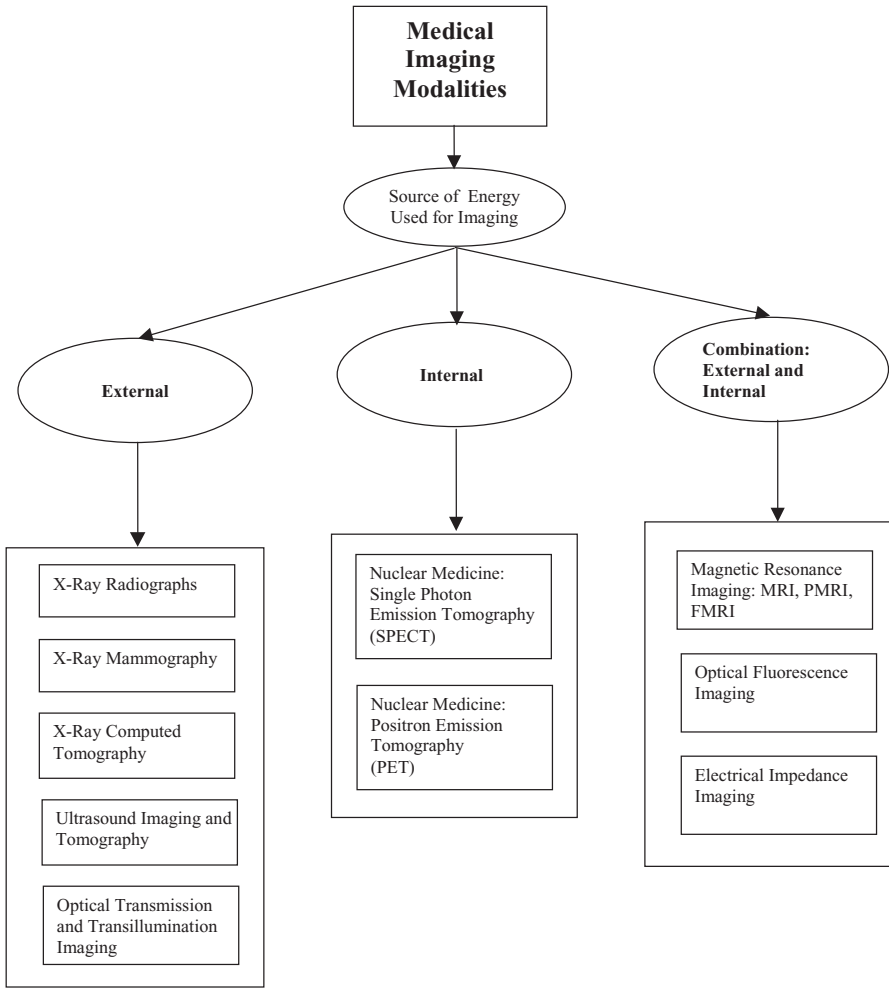


Figure 1.2 A classification of different medical imaging modalities with respect to the type of energy source used for imaging.

example, X-ray radiographs and X-ray CT imaging modalities measure attenuation coefficients of X ray that are based on the density of the tissue or part of the body being imaged. The images of chest radiographs show a spatial distribution of X-ray attenuation coefficients reflecting the overall density variations of the anatomical parts in the chest. Another example of external energy source-based imaging is ultrasound or acoustic imaging. Nuclear medicine imaging modalities use an internal energy source through an emission process to image the human body. For emission imaging, radioactive pharmaceuticals are injected into the body to interact with selected body matter or tissue to form an internal source of radioactive energy that is used for imaging. The emission imaging principle is applied in SPECT and PET. Such types of nuclear medicine imaging modalities provide useful metabolic

information about the physiological functions of the organs. Further, a clever combination of external stimulation on internal energy sources can be used in medical imaging to acquire more accurate information about the tissue material and physiological responses and functions. MRI uses external magnetic energy to stimulate selected atomic nuclei such as hydrogen protons. The excited nuclei become the internal source of energy to provide electromagnetic signals for imaging through the process of relaxation. MRI of the human body provides high-resolution images of the human body with excellent soft-tissue characterization capabilities. Recent advances in MRI have led to perfusion and functional imaging aspects of human tissue and organs (3–6). Another emerging biophysiological imaging modality is fluorescence imaging, which uses an external ultraviolet energy source to stimulate the internal biological molecules of interest, which absorb the ultraviolet energy, become internal sources of energy, and then emit the energy at visible electromagnetic radiation wavelengths (7).

Before a type of energy source or imaging modality is selected, it is important to understand the nature of physiological information needed for image formation. In other words, some basic questions about the information of interest should be answered. What information about the human body is needed? Is it anatomical, physiological, or functional? What range of spatial resolution is acceptable? The selection of a specific medical imaging modality often depends on the type of suspected disease or localization needed for proper radiological diagnosis. For example, some neurological disorders and diseases demand very high resolution brain images for accurate diagnosis and treatment. On the other hand, full-body SPECT imaging to study metastasizing cancer does not require submillimeter imaging resolution. The information of interest here is cancer metastasis in the tissue, which can be best obtained from the blood flow in the tissue or its metabolism. Breast imaging can be performed using X rays, magnetic resonance, nuclear medicine, or ultrasound. But the most effective and economical breast imaging modality so far has been X-ray mammography because of its simplicity, portability, and low cost. One important source of radiological information for breast imaging is the presence and distribution of microcalcifications in the breast. This anatomical information can be obtained with high resolution using X rays.

There is no perfect imaging modality for all radiological applications and needs. In addition, each medical imaging modality is limited by the corresponding physics of energy interactions with human body (or cells), instrumentation, and often physiological constraints. These factors severely affect the quality and resolution of images, sometimes making the interpretation and diagnosis difficult. The performance of an imaging modality for a specific test or application is characterized by sensitivity and specificity factors. Sensitivity of a medical imaging test is defined primarily by its ability to detect true information. Let us suppose we have an X-ray imaging scanner for mammography. The sensitivity for imaging microcalcifications for a mammography scanner depends on many factors including the X-ray wavelength used in the beam, intensity, and polychromatic distribution of the input radiation beam, behavior of X rays in breast tissue such as absorption and scattering coefficients, and film/detector efficiency to collect the output radiation. These factors eventually affect the overall signal-to-noise ratio leading to the loss of sensitivity of

detecting microcalcifications. The specificity for a test depends on its ability to not detect information when it is truly not there.

1.3. MEDICAL IMAGING: FROM PHYSIOLOGY TO INFORMATION PROCESSING

From physiology to image interpretation and information retrieval, medical imaging may be defined as a five-step paradigm (see Fig. 1.3). The five-step paradigm allows acquisition and analysis of useful information to understand the behavior of an organ or a physiological process.

1.3.1 Understanding Physiology and Imaging Medium

The imaged objects (organs, tissues, and specific pathologies) and associated physiological properties that could be used for obtaining signals suitable for the formation of an image must be studied for the selection of imaging instrumentation. This information is useful in designing image processing and analysis techniques for correct interpretation. Information about the imaging medium may involve static or dynamic properties of the biological tissue. For example, tissue density is a static property that causes attenuation of an external radiation beam in X-ray imaging modality. Blood flow, perfusion, and cardiac motion are examples of dynamic physiological properties that may alter the image of a biological entity. Consideration of the dynamic behavior of the imaging medium is essential in designing compensation methods needed for correct image reconstruction and analysis. Motion artifacts pose serious limitations on data collection time and resolution in medical imaging instrumentation and therefore have a direct effect on the development of image processing methods.

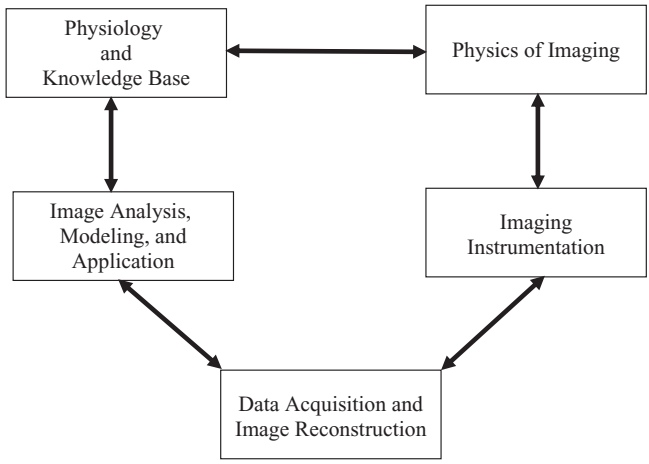


Figure 1.3 A collaborative multidisciplinary paradigm of medical imaging research and applications.

1.3.2 Physics of Imaging

The next important consideration is the principle of imaging to be used for obtaining the data. For example, X-ray imaging modality uses transmission of X rays through the body as the basis of imaging. On the other hand, in the nuclear medicine modality, SPECT uses the emission of gamma rays resulting from the interaction of a radiopharmaceutical substance with the target tissue. The emission process and the energy range of gamma rays cause limitations on the resolution and data acquisition time for imaging. The associated methods for image formation in transmission and emission imaging modalities are so different that it is difficult to see the same level of anatomical information from both modalities. SPECT and PET provide images that are poor in contrast and anatomical details, while X-ray CT provides sharper images with high-resolution anatomical details. MRI provides high-resolution anatomical details with excellent soft-tissue contrast (6, 7).

1.3.3 Imaging Instrumentation

The instrumentation used in collecting the data is one of the most important factors defining the image quality in terms of signal-to-noise ratio, resolution, and ability to show diagnostic information. Source specifications of the instrumentation directly affect imaging capabilities. In addition, detector responses such as nonlinearity, low efficiency, long decay time, and poor scatter rejection may cause artifacts in the image. An intelligent image formation and processing technique should be the one that provides accurate and robust detection of features of interest without any artifacts to help diagnostic interpretation.

1.3.4 Data Acquisition and Image Reconstruction

The data acquisition methods used in imaging play an important role in image formation. Optimized with the imaging instrumentation, the data collection methods become a decisive factor in determining the best temporal and spatial resolution. It is also crucial in developing strategies to reduce image artifacts through active filtering or postprocessing methods. For example, in X-ray CT, the spatially distributed signal is based on the number of X-ray photons reaching the detector within a time interval. The data for 3-D imaging may be obtained using a parallel-, cone-, or spiral-beam scanning method. Each of these scanning methods causes certain constraints on the geometrical reconstruction of the object under imaging. Since the scanning time in each method may be different, spatial resolution has to be balanced by temporal resolution. This means that a faster scan would result in an image with a lower spatial resolution. On the other hand, a higher spatial resolution method would normally require longer imaging time. In dynamic studies where information about blood flow or a specific functional activity needs to be acquired, the higher resolution requirement is usually compromised. Image reconstruction algorithms such as backprojection, iterative, and Fourier transform methods are tailored to incorporate specific information about the data collection methods and scanning geometry. Since the image quality may be affected by the data collection methods,

the image reconstruction and processing methods should be designed to optimize the representation of diagnostic information in the image.

1.3.5 Image Analysis and Applications

Image processing and analysis methods are aimed at the enhancement of diagnostic information to improve manual or computer-assisted interpretation of medical images. Often, certain transformation methods improve the visibility and quantification of features of interest. Interactive and computer-assisted intelligent medical image analysis methods can provide effective tools to help the quantitative and qualitative interpretation of medical images for differential diagnosis, intervention, and treatment monitoring. Intelligent image processing and analysis tools can also help in understanding physiological processes associated with the disease and its response to a treatment.

1.4. GENERAL PERFORMANCE MEASURES

Let us define some measures often used in the evaluation of a medical imaging or diagnostic test for detecting an object such as microcalcifications or a physiological condition such as cancer. A "positive" observation in an image means that the object was observed in the test. A "negative" observation means that the object was not observed in the test. A "true condition" is the actual truth, while an observation is the outcome of the test. Four basic measures are defined from the set of true conditions and observed information as shown in Figure 1.4. These basic measures are true positive, false positive, false negative, and true negative rates or fractions. For example, an X-ray mammographic image should show only the regions of pixels with bright intensity (observed information) corresponding to the microcalcification areas (true condition when the object is present). Also, the mammographic image should not show similar regions of pixels with bright intensity corresponding to the

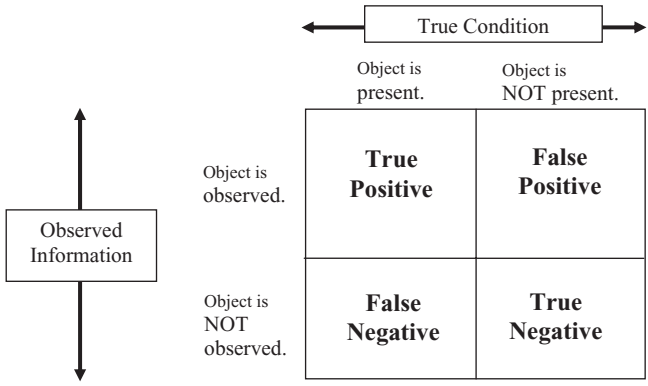


Figure 1.4 A conditional matrix for defining four basic performance measures of receiver operating characteristic curve (ROC) analysis.

areas where there is actually no microcalcification (true condition when the object is not present).

Let us assume the total number of examination cases to be N_{tot}, out of which N_{tp} cases have positive true condition with the actual presence of the object and the remaining cases, N_{tn}, have negative true condition with no object present. Let us suppose these cases are examined via the test for which we need to evaluate accuracy, sensitivity, and specificity factors. Considering the observer does not cause any loss of information or misinterpretation, let N_{otp} (true positive) be the number of positive observations from N_{tp} positive true condition cases and N_{ofn} (false negative) be the number of negative observations from N_{tp} positive true condition cases. Also, let N_{otn} (true negative) be the number of negative observations from N_{tn} negative true condition cases and N_{ofp} (false positive) be the number of positive observations from N_{tn} negative true condition cases.

Thus,

$$N_{tp} = N_{otp} + N_{ofn} \quad \text{and} \quad N_{tn} = N_{ofp} + N_{otn}.$$

1. True positive fraction (TPF) is the ratio of the number of positive observations to the number of positive true condition cases.

$$\text{TPF} = N_{otp}/N_{tp}. \tag{1.1}$$

2. False negative fraction (FNF) is the ratio of the number of negative observations to the number of positive true condition cases.

$$\text{FNF} = N_{ofn}/N_{tp} \tag{1.2}$$

3. False positive fraction (FPF) is the ratio of the number of positive observations to the number of negative true condition cases.

$$\text{FPF} = N_{ofp}/N_{tn} \tag{1.3}$$

4. True negative fraction (TNF) is the ratio of the number of negative observations to the number of negative true condition cases.

$$\text{TNF} = N_{otn}/N_{tn} \tag{1.4}$$

It should be noted that

$$\begin{aligned} &\text{TPF} + \text{FNF} = 1 \\ &\text{TNF} + \text{FPF} = 1. \end{aligned} \tag{1.5}$$

A graph between TPF and FPF is called a receiver operating characteristic (ROC) curve for a specific medical imaging or diagnostic test for detection of an object. Various points on the ROC curves shown in Figure 1.5 indicate different decision thresholds used for classification of the examination cases into positive and negative observations, and therefore defining specific sets of paired values of TPF and FPF. It should also be noted that statistical random trials with equal probability of positive and negative observations would lead to the diagonally placed straight line as the ROC curve. Different tests and different observers may lead to different ROC curves for the same object detection.

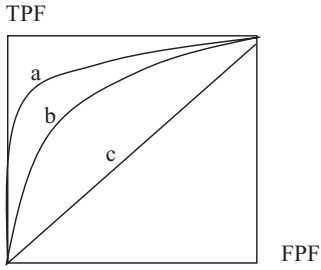


Figure 1.5 ROC curves, with "a" indicating better classification ability than "b," and "c" showing the random probability.

True positive fraction is also called the sensitivity while the true negative fraction is known as specificity of the test for detection of an object. Accuracy of the test is given by a ratio of correct observation to the total number of examination cases. Thus,

$$\text{Accuracy} = (N_{otp} + N_{otn})//N_{tot}. \tag{1.6}$$

The positive predictive value (PPV) considered to be the same as precision of a diagnostic test is measured as

$$\text{PPV} = N_{otp}/(N_{otp} + N_{ofp}). \tag{1.7}$$

In other words, different imaging modalities and observers may lead to different accuracy, PPV, sensitivity, and specificity levels.

The accuracy, sensitivity, and specificity factors are given serious consideration when selecting a modality for radiological applications. For example, X-ray mammography is so successful in breast imaging because it provides excellent sensitivity and specificity for imaging breast calcifications. In neurological applications requiring a demanding soft-tissue contrast, however, MRI provides better sensitivity and specificity factors than X-ray imaging.

1.4.1 An Example of Performance Measure

Let us assume that 100 female patients were examined with X-ray mammography. The images were observed by a physician to classify into one of the two classes: normal and cancer. The objective here is to determine the basic performance measures of X-ray mammography for detection of breast cancer. Let us assume that all patients were also tested through tissue-biopsy examination to determine the true condition. If the result of the biopsy examination is positive, the cancer (object) is present as the true condition. If the biopsy examination is negative, the cancer (object) is not present as the true condition. If the physician diagnoses the cancer from X-ray mammography, the object (cancer) is observed. Let us assume the following distribution of patients with respect to the true conditions and observed information:

1. Total number of patients = $N_{tot} = 100$
2. Total number of patients with biopsy-proven cancer (true condition of object present) = $N_{tp} = 10$
3. Total number of patients with biopsy-proven normal tissue (true condition of object NOT present) = $N_{tn} = 90$
4. Of the patients with cancer N_{tp}, the number of patients diagnosed by the physician as having cancer = number of true positive cases = $N_{otp} = 8$
5. Of the patients with cancer N_{tp}, the number of patients diagnosed by the physician as normal = number of false negative cases = $N_{ofn} = 2$
6. Of the normal patients N_{tn}, the number of patients rated by the physician as normal = number of true negative cases = $N_{otn} = 85$
7. Of the normal patients N_{tn}, the number of patients rated by the physician as having cancer = number of false positive cases = $N_{ofp} = 5$

Now the TPF, FNF, FPF, and TNF can be computed as

$$\text{TPF} = 8/10 = 0.8$$
$$\text{FNF} = 2/10 = 0.2$$
$$\text{FPF} = 5/90 = 0.0556$$
$$\text{TNF} = 85/90 = 0.9444$$

This should be noted that the above values satisfy Equation 1.5 as

$$\text{TPF} + \text{FNF} = 1.0 \quad \text{and} \quad \text{FPF} + \text{TNF} = 1.0$$

1.5. BIOMEDICAL IMAGE PROCESSING AND ANALYSIS

A general-purpose biomedical image processing and image analysis system must have three basic components: an image acquisition system, a digital computer, and an image display environment. Figure 1.6 shows a schematic block diagram of a biomedical image processing and analysis system.

The image acquisition system usually converts a biomedical signal or radiation carrying the information of interest to a digital image. A digital image is

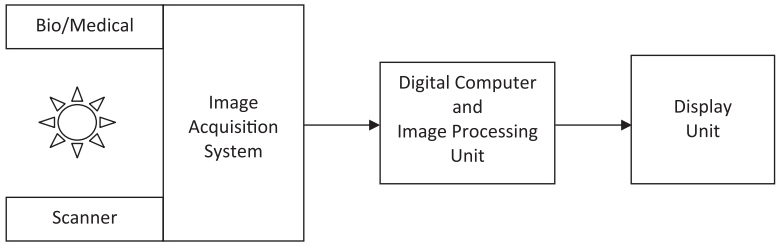


Figure 1.6 A general schematic diagram of biomedical image analysis system.

represented by an array of digital numbers that can be read by the processing computer and displayed as a two-, three, or multidimensional image. As introduced above, medical imaging modalities use different image acquisition systems as a part of the imaging instrumentation. The design of the image acquisition system depends on the type of modality and detector requirements. In some applications, the output of the scanner may be in analog form, such as a film-mammogram or a chest X-ray radiograph. In such applications, the image acquisition system may include a suitable light source to illuminate the radiograph (the film) and a digitizing camera to convert the analog image into a digital picture. Other means of digitizing an image include several types of microdensitometers and laser scanners. There is a variety of sources of biomedical imaging applications. The data acquisition system has to be modified accordingly. For example, a microscope can be directly hooked up with a digitizing camera for acquisition of images of a biopsy sample on a glass slide. But such a digitizing camera is not needed for obtaining images from an X-ray CT scanner. Thus, the image acquisition system differs across applications.

The second part of the biomedical image processing and analysis system is a computer used to store digital images for further processing. A general-purpose computer or a dedicated array processor can be used for image analysis. The dedicated hardwired image processors may be used for the real-time image processing operations such as image enhancement, pseudo-color enhancement, mapping, and histogram analysis.

A third essential part of the biomedical image processing and analysis system is the image display environment where the output image can be viewed after the required processing. Depending on the application, there may be a large variation in the requirements of image display environment in terms of resolution grid size, number of gray levels, number of colors, split-screen access, and so on. There might be other output devices such as a hard-copy output machine or printer that can also be used in conjunction with the regular output display monitor.

For an advanced biomedical image analysis system, the image display environment may also include a real-time image processing unit that may have some built-in processing functions for quick manipulation. The central image processing unit, in such systems, does the more complicated image processing and analysis only. For example, for radiological applications, the image display unit should have a fast and flexible environment to manipulate the area of interest in the image. This manipulation may include gray-level remapping, pseudo-color enhancement, zoom-in, or split-screen capabilities to aid the attending physician in seeing more diagnostic information right away. This type of real-time image processing may be part of the image-display environment in a modern sophisticated image analysis system that is designed for handling the image analysis and interpretation tasks for biomedical applications (and many others). The display environment in such systems includes one or more pixel processors or point processors (small processing units or single-board computers) along with a number of memory planes, which act as buffers. These buffers or memory planes provide an efficient means of implementing a number of look-up-tables (LUTs) without losing the original image data. The specialized hardwired processing units including dedicated processors are accessed and

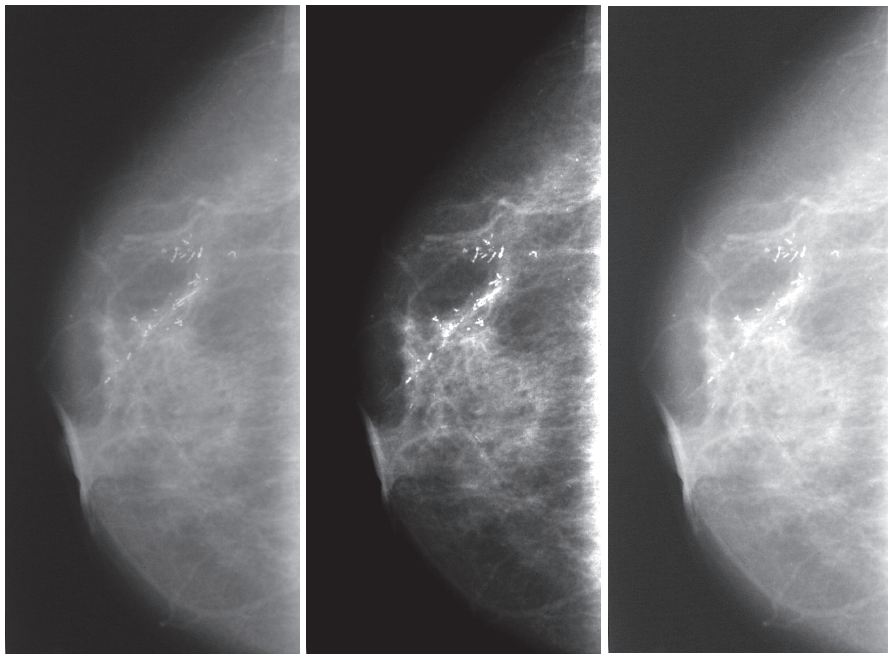
communicated with by using the peripheral devices such as keyboard, data tablet, mouse, printer, and high-resolution monitors.

There are several image processing systems available today that satisfy the usual requirements (as discussed above) of an efficient and useful biomedical image analysis system. All these systems are based on a special pipeline architecture with an external host computer and/or an array processor allowing parallel processing and efficient communication among various dedicated processors for real-time or near real-time split-screen image manipulation and processing performance. Special-purpose image processing architectures includes array processors, graphic accelerators, logic processors, and field programmable gate arrays (FPGA).

As discussed above, every imaging modality has limitations that affect the accuracy, sensitivity, and specificity factors, which are extremely important in diagnostic radiology. Scanners are usually equipped with instrumentation to provide external radiation or energy source (as needed) and measure an output signal from the body. The output signal may be attenuated radiation or another from of energy carrying information about the body. The output signal is eventually transformed into an image to represent the information about the body. For example, an X-ray mammography scanner uses an X-ray tube to generate a radiation beam that passes through the breast tissue. As a result of the interactions among X-ray photons and breast tissue, the X-ray beam is attenuated. The attenuated beam of X-ray radiation coming out of the breast is then collected on a radiographic film. The raw signals obtained from instrumentation of an imaging device or scanner are usually preprocessed for a suitable transformation to form an image that makes sense from the physiological point of view and is easy to interpret. Every imaging modality uses some kind of image reconstruction method to provide the first part of this transformation for conversions of raw signals into useful images. Even after a good reconstruction or initial transformation, images may not provide useful information with a required localization to help interpretation. This is particularly important when the information about suspect objects is occluded or overshadowed by other parts of the body. Often reconstructed images from scanners are degraded in a way that unless the contrast and brightness are adjusted, the objects of interest may not be easily visualized. Thus, an effective and efficient image processing environment is a vital part of the medical imaging system.

Since the information of interest about biological objects often is associated with characteristic features, it is crucial to use specially designed image processing methods for visualization and analysis of medical images. It is also important to know about the acquisition and transformation methods used for reconstruction of images before appropriate image processing and analysis algorithms are designed and applied. With the new advances in image processing, adaptive learning, and knowledge-based intelligent analysis, the specific needs of medical image analysis to improve diagnostic information for computer-aided diagnosis can be addressed.

Figure 1.7a,b shows an example of feature-adaptive contrast enhancement processing as applied to a part of the mammogram to enhance microcalcification areas. Figure 1.7c shows the result of a standard histogram equalization method commonly used for contrast enhancement in image processing. It is clear that standard image processing algorithms may not be helpful in medical image processing.



(a) (b) (c)

Figure 1.7 (a) a digital mammogram image; (b) microcalcification enhanced image through feature adaptive contrast enhancement algorithm; and (c) enhanced image through histogram equalization method (see Chapter 9 for details on image enhancement algorithms).

Specific image processing operations are needed to deal with the information of radiological interest. The following chapters will introduce fundamental principles of medical imaging systems and image processing tools. The latter part of the book is dedicated to the design and application of intelligent and customized image processing algorithms for radiological image analysis.

1.6. MATLAB IMAGE PROCESSING TOOLBOX

The MATLAB image processing toolbox is a compilation of a number of useful commands and subroutines for efficient image processing operations. The image processing toolbox provides extensive information with syntax and examples about each command. It is strongly recommended that readers go through the description of commands in the help menu and follow tutorials for various image processing tasks. Some of the introductory commands are described below.

1.6.1 Digital Image Representation

A 2-D digital image of spatial size $M \times N$ pixels (picture elements with M rows and N columns) may be represented by a function $f(x, y)$ where (x, y) is the location of

a pixel whose gray level value (or brightness) is given by the function $f(x, y)$ with $x = 1, 2, \ldots, M$; $y = 1, 2, \ldots, N$. The brightness values or gray levels of the function $f(x, y)$ are digitized in a specific resolution such as 8-bit (256 levels), 12-bit (4096 levels), or more. For computer processing, a digital image can be described by a 2-D matrix [F] of elements whose values and locations represents, respectively, the gray levels and location of pixels in the image as

$$\mathrm{F} = \begin{bmatrix} f(1,1) & f(1,2) & . & . & f(1,N) \\ f(2,1) & f(2,2) & & & f(2,N) \\ & & & & \\ & & & & \\ f(M,1) & f(M,2) & & & f(M,N) \end{bmatrix}. \tag{1.8}$$

For example, a synthetic image of size 5×5 pixels with "L" letter shape of gray level 255 over a background of gray level 20 may be represented as

$$\mathrm{F} = \begin{bmatrix} 20 & 20 & 255 & 20 & 20 \\ 20 & 20 & 255 & 20 & 20 \\ 20 & 20 & 255 & 20 & 20 \\ 20 & 20 & 255 & 20 & 20 \\ 20 & 20 & 255 & 255 & 255 \end{bmatrix}. \tag{1.9}$$

It is clear from the above that a digital image is discrete in both space and gray-level values as pixels are distributed over space locations. Thus, any static image is characterized by (1) spatial resolution (number of pixels in x- and y-directions such as 1024×1024 pixels for 1M pixel image), and (2) gray-level resolution (number of brightness levels such as 256 in 8-bit resolution image). In addition, images can also be characterized by number of dimensions (2-D, 3-D, etc.) and temporal resolution if images are taken as a sequence with regular time interval. A 4-D image data set may include, for example, 3-D images taken with a temporal resolution of 0.1 s.

Images that are underexposed (and look darker) may not utilize the entire gray-level range. For example, an underexposed image with 8-bit gray-level resolution (0–255 gray-level range) may have gray-level values from 0 to 126. Thus, the maximum brightness level in the image appears to be at about half the intensity it could have been if it was stretched to 255. One solution to this problem is to stretch the gray-level range from 0–126 to 0–255 linearly. Such a method is commonly known as gray-level scaling or stretching and can be shown as a linear mapping as

$$g(x, y) = \frac{(d-c)}{(b-a)}(f(x, y) - a) + c \tag{1.10}$$

where an original image $f(x, y)$ with gray-level range (a, b) is scaled linearly to an output image $g(x, y)$ with gray-level range (c, d).

Sometimes an image shows some pixels at the maximum brightness intensity level, yet the rest of the image appears to be quite dark. This may happen if there are some very high values in the image but most of other pixels have very low values. For example, a Fourier transform of an image may have a very high dc value

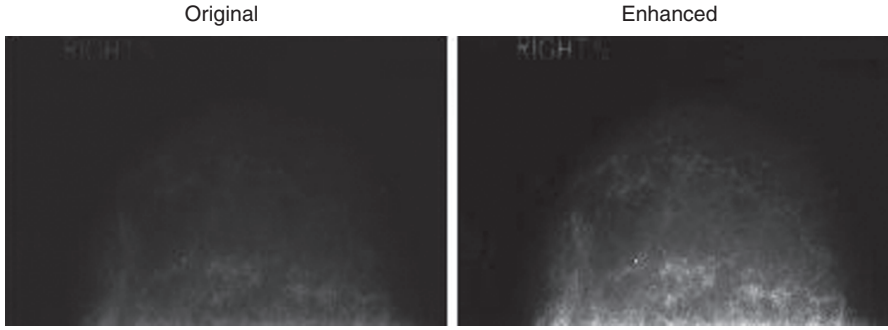


Figure 1.8 An original mammogram image (left) and the gray-level scaled image (right).

```
x = imread(f);
x = rgb2gray(x);
figure('Name', 'Contrast
Enhancement');
subplot(1,2,1)
imshow(x);
title('Original');
subplot(1,2,2)
imshow(x, []);
title('Enhanced');
```

Figure 1.9 M-Script code for the example shown in Figure 1.8.

but other parts of the frequency spectrum carry very low values. In such cases, a nonlinear transformation is used to reduce the wide gap between the low and high values. A commonly used logarithm transformation for displaying images with a wide range of values is expressed as $\log\{\text{abs}(f)\}$ or $\log\{1+\text{abs}(f)\}$ such that

$$g(x, y) = \log(|f(x, y)|)$$

or

$$g(x, y) = \log(1 + |f(x, y)|) \tag{1.11}$$

Examples of image scaling and log-transformation operations in the MATLAB image processing toolbox are shown in Figures 1.8 and 1.9. More image processing operations are described in Chapter 9.

1.6.2 Basic MATLAB Image Toolbox Commands

In the MATLAB environment, an image can be read and displayed using the image processing toolbox as

>> f = imread('filename.format');

There are several image storage and compression formats in which the image data is stored and managed. Some of the common formats are JPEG (created by Joint Photography Expert Group), graphical interchange format (GIF), tagged image file format (TIFF); and Windows Bitmap (BMP).

The format could be any of the above allowed formats. The semicolon (;) is added if the program is continued, otherwise the MATLAB displays the results of the operation(s) given in the preceding command. Directory information can be added in the command before the filename such as

≫ f = imread('C:\medimages\mribrain1.jpg');

The size information is automatically taken from the file header but it can be queried using the command *size(f)* that returns the size of the image in M × N format. In addition, *whos(f)* command can also be used to return the information about the image file:

≫ whos(f)

which may provide the following information

Name	Size	Bytes	Class
f	512 × 512	262,144	uint8 array

Grand total is 262,144 elements using 262,144 bytes

To display images, *imshow* command can be used:

≫ imshow(f)

To keep this image and display another image in a spate window, command *figure* can be used:

≫ imshow(f), figure, imshow(g)

Scaling the gray-level range of an image is sometimes quite useful in display. Images with low gray-level utilization (such as dark images) can be displayed with a scaling of the gray levels to full or stretched dynamic range using the *imshow* command:

≫ imshow(f, [ ]) or

≫ imshow(f, [low high])

The scaled images are brighter and show better contrast. An example of gray-level scaling of an X-ray mammographic image is shown in Figure 1.8. On the left, the original mammogram image is shown, which is quite dark, while the gray-level scaled image on the right demonstrates the enhanced contrast. M-script commands are shown in Figure 1.9.

To display a matrix [f] as an image, the "scale data and display image object" command can be used through *imagesc* function. This MATLAB function helps in creating a synthetic image from a 2-D matrix of mathematical, raw, or transformed data (such as transformation of red, green, and blue [RGB] to gray-level format can be done using the command *rgb2gray(f)*). The elements of the matrix can be scaled and displayed as an image using *colormap* function as

≫ imagesc(x, y, f)

or

≫ imagesc(f)

and

≫ colormap(code)

In the *imagesc* function format, *x* and *y* values specify the size of data in respective directions. The *imagesc* function creates an image with data set to scaled values with direct or indexed colors (see more details in the MATLAB manual or helpdesk Web site http://www.mathworks.com/access/helpdesk/help/techdoc/ref/imagesc.html). An easier way is follow-up *imagesc* function with a *colormap* function choosing one of the color code palettes built in MATLAB as gray, bone, copper, cool, spring, jet, and so on (more details can be found on the helpdesk Web site http://www.mathworks.com/access/helpdesk/help/techdoc/ref/colormap.html). An example of using *imagesc* and *colormap* functions can be seen in the M-script given in Figure 1.11.

Figure 1.10 (left) shows an image whose Fourier transform is shown in the middle. The Fourier transform image shows bright pixels in the middle representing very high dc value, but the rest of the image is quite dark. The Fourier transformed image after the logarithm transform as described above in Equation 1.11 is shown at the right. M-script is shown in Figure 1.11.

After image processing operation(s), the resultant image can be stored using the *imwrite* command:

≫ imwrite(f, 'filename', 'format')

More generalized *imwrite* syntax with different compression formats are available and can be found in the MATLAB HELP menu.

The MATLAB image processing toolbox supports several types of images including gray-level (intensity), binary, indexed, and RGB images. Care should be taken in identifying data classes and image types and then converting them appropriately as needed before any image processing operation is performed.

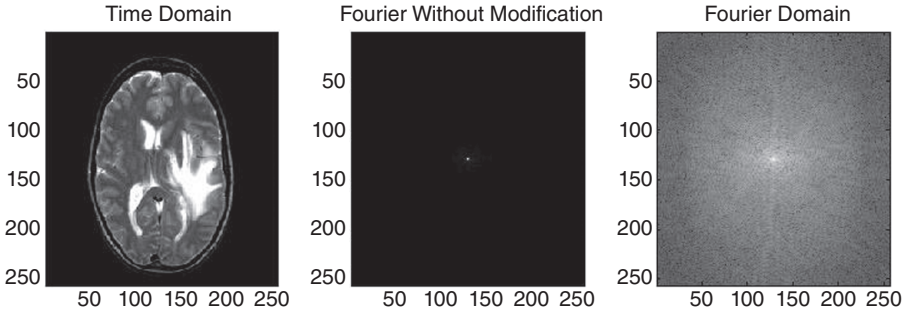


Figure 1.10 An original MR brain image (left), its Fourier transform (middle), and Fourier transformed image after logarithm transformation (right).

```
figure
subplot(1,3,1)
pic=imread(f);
pic=rgb2gray(pic);
imagesc(pic);
title('Time Domain')
colormap(gray)
subplot(1,3,2)
%To show importance of log in image display
imagesc(fftshift(abs(fft2(pic))));
title('Fourier Without Modification');
subplot(1,3,3);
%Now with log
qb=fftshift(log(abs(fft2(pic))));
imagesc(qb);
title('Fourier Domain')
colormap(gray)
```

Figure 1.11 M-script code for the example shown in Figure 1.10.

1.7. IMAGEPRO INTERFACE IN MATLAB ENVIRONMENT AND IMAGE DATABASES

The website for this book (ftp://ftp.wiley.com/public/sci_tech_med/medical_image/) provides access to all figures and images included. In addition, an Imagepro Image Processing Interface in the MATLAB environment and several medical image databases can be downloaded from the Web site to implement image processing tasks described in the book as part of MATLAB exercises.

The image databases include X-ray mammograms, multimodality magnetic resonance–computed tomography (MR–CT) brain images, multimodality positron emission tomography-computed tomography (PET–CT) full-body images, CT brain images of intracerebral brain hemorrhage, and multispectral optical transillumination images of skin lesions. "Readme" instructions are provided in each database folder with a brief description of the images and associated pathologies wherever available.

1.7.1 Imagepro Image Processing Interface

The Imagepro Image Processing Interface provides various image processing functions and tools with a user-friendly graphical user interface (GUI). On the GUI, six buttons corresponding to the six interfaces are provided to include

1. FIR filter interface
2. Morphological operation interface
3. Histogram interface
4. Edge detection interface
5. Noise reduction interface
6. Wavelet interface

An "Info" button is provided in each interface to obtain information about the different controls and abilities. Information about the image processing functions is also provided. Although the purpose of this interface is for demonstration, users can load the image of their choice and see the effects of the different image processing functions on the image.

1.7.2 Installation Instructions

Download all files for the Imagepro MATLAB interface from the Web site* ftp://ftp.wiley.com/publicisei_tech_med/medicalimage/ on your computer in the Impagepro folder in the MATLAB program directory. Open MATLAB and using the "set path" option under the File Menu select "add to path," or current directory selection to open the folder in which Imagepro files are copied.

Once the Imagepro folder is set up as the current directory, just type "imagepro" in the MATLAB command window to open the GUI. Help files are attached on each tool on the respective interface screens.

The software tools and images are intended to be used as an instructional aid for this book. The user needs to have a version of MATLAB to use the full software included in the image database files. Each folder included with the software has a separate "Readme" or Instructions file in text format. These files give information about the images or the interface installation instructions.

1.8. IMAGEJ AND OTHER IMAGE PROCESSING SOFTWARE PACKAGES

There are software packages other than MATLAB that readers can download and install on their personal computers for Windows, MAC, and other operating systems. One of the popular software packages, ImageJ, can be downloaded from the Web site http://rsbweb.nih.gov/ij/index.html. ImageJ software packages can be installed on personal computers with Windows, Mac OS, Mac OS X, and Linux operating systems.

ImageJ software provides a complete spectrum of image processing features with GUI-based functions to display, edit, analyze, process, save, and print 8-bit, 16-bit, and 32-bit images (8). The software reads multiple image formats including TIFF, GIF, JPEG, BMP, DICOM, FITS, and "raw," and supports series of images as "stacks" sharing a single window. It provides sophisticated 3-D image registration image analysis and visualization operations.

Another free open-source software package for image visualization and analysis is 3D Slicer, which can be downloaded from the Web site http://www.slicer.org/. 3D Slicer can be installed on personal computers with Windows, Linux, and Mac Os X operating systems (9). The user-friendly GUI-based 3D Slicer image analysis

software package provides a spectrum of image processing functions and features, including multiple image format and DICOM support, 3-D registration, analysis and visualization, fiducial tractography, and tracking analysis for image-guided surgery and therapy.

1.9. EXERCISES

1.1. Is it necessary to understand the physics and instrumentation of medical imaging modality before processing the data for image reconstruction, processing, and interpretation? Give reasons to support your answer.

1.2. What are the measures for evaluation of a medical imaging modality?

1.3. Explain the significance of the receiver operating characteristic (ROC) curve?

1.4. A chest phantom was implanted with different sizes and types of nodular lesions and was imaged with a new X-ray scanner. Let us assume that there are 156 radiographs of the chest phantom screened for detection of nodular lesions. The radiographs showed 44 lesions, out of which four lesions were verified to be false. The radiographs also missed three lesions that could not be seen by an observer. Compute accuracy, sensitivity, and specificity of the X-ray scanner in imaging nodular lesions in the chest.

1.5. A false positive fraction (FPF) or rate is defined and characterized by (choose the best answer)

a. Number of negative observations divided by number of positive observations.

b. Number of negative observations divided by number of true positive conditions.

c. Number of positive observations divided by number of negative observations.

d. Number of positive observations divided by number of true negative conditions.

1.6. In the evaluation of two imaging scanners, A and B, the following set of TPF and FPF are observed for detection of lung tumors:

A. TPF = 0.8; FPF = 0.5

B. TPF = 0.7; FPF = 0.1

Which of the above scanners would you recommend to use and why?

1.7. Compared with image processing methods used in computer vision, do you think medical image processing methods should be customized based on the physics of imaging and properties of the imaging medium? Explain your answer.

1.8. In the MATLAB environment, display an image of a breast mammogram from the MAMMO database. Apply gray-level scaling, histogram equalization, and an LOG enhancement mask for image enhancement as given below. Compare the enhanced images to original image qualitatively.

LOG enhancement mask to be convolved with the image:

$$\begin{matrix} -1 & -1 & -1 \\ -1 & 9 & -1 \\ -1 & -1 & -1 \end{matrix}$$

1.9. Repeat Exercise 6 for a magnetic resonance image of the brain from the MRI_BRAIN database. Do you see the same type of enhancement effect in each method for two images from different imaging modalities? Look for edge and object definitions in the original and enhanced images. Also, comment on the saturation and noise artifacts in the enhanced images.

1.10. In the MATLAB environment, display an X-ray CT image of the chest and compute its Fourier transform image as logarithmic magnitude folded to display dc value at the center of the image. Use *imagesc* and *colormap* functions to display the Fourier transformed image in gray, spring, and jet color maps built in MATLAB. Compare these displays and comment on the visualization of frequency components in the Fourier transform image.

1.10. REFERENCES

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1.11. DEFINITIONS

Accuracy: Accuracy is the ability to measure a quantity with respect to its true value. In normalized sense, this is the difference between measured value and true value divided by true value.

Precision: The precision of a measurement expresses the number of distinguishable values or alternatives from which a given result is selected. Precision makes no comparison with the true value. Therefore, high precision does not mean high accuracy.

Resolution: The smallest incremental quality that can be measured with certainty is the resolution.

Reproducibility: The ability to give the same output for equal inputs applied at different times is called reproducibility or repeatability. Reproducibility does not imply accuracy.

Sensitivity: The sensitivity of a test is the probability of yielding positive results when a given condition is true. This is also provided in terms of true positive fraction (TPF).

Specificity: The specificity of a test is the probability of yielding negative results in patients who do not havNe a disease. This is also provided in terms of true negative fraction (TNF).