Medical Imaging Strategies

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Computed tomography (CT), intravenous digital subtraction angiography (IV-DSA), digital radiographic image processing and dual energy subtraction are four examples of medical imaging strategies that have met with various degrees of success as *judged by diagnostic performance.* The success of CT has been spectacular; IV-DSA has provided modest benefits; digital image processing of chest radiographs has been singularly disappointing; and the verdict on dual energy subtraction is undecided. The degree of success of each of these techniques can be understood by considering the degree to which each simplifies image interpretation or isolates a fingerprint of disease.

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IF ONE BELIEVES that the purpose of medical imaging is to detect and delineate disease, then imaging strategies should be predicated upon the nature of disease and how it is likely to "appear" in an image. Effective imaging strategies produce images in which disease states are either transparently obvious or can be isolated unambiguously using some sort of image processing strategy. In the former case, resultant images must be simpler to interpret than images produced using competing approaches; in the latter case, the image appearance of disease must have a unique "fingerprint," by which it can be isolated from other image features. The degree of success of an imaging strategy is related to the degree to which it accomplishes one or the other of these tasks. Four specific diagnostic imaging approaches will be discussed to illustrate these points: computed tomography (CT), intravenous digital subtraction angiography (IV-DSA), image processing of digitized film based chest radiographs, and dual energy imaging.

COMPUTED TOMOGRAPHY

There is no question that computed tomography (CT) has revolutionized the practice of radiology.[1] By isolating radiographic information from a single slice, the radiographic image analysis task is simplified since only a small section of anatomy is examined at a time. Structures are laid out next to each other, not superimposed upon each other. Consequently, CT images are relatively simple to interpret when compared to the complicated image appearance of a chest radiograph.

While CT images derive benefits from efficient detectors and imaging geometry which rejects most scattered radiation and makes low contrast sensitivity possible, CT owes its great success to the simplification of the disease detection task. Most anyone can "see" a 1-cm tumor in a chest CT image, while the same tumor may go undetected by even the most experienced radiologist when recorded on a chest radiograph. Such a tumor may lie well above the threshold for detectability on the chest image, but go undetected because of confusing superimposed normal anatomy. Because CT produces images that are simpler to interpret, diagnostic benefits result.

INTRAVENOUS DIGITAL SUBTRACTION ANGIOGRAPHY (IV-DSA)

Following closely on the heels of the spectacular success of CT, digital subtraction angiography (DSA) systems were developed in the late 1970s and introduced commercially in 1980.[2] The principle upon which DSA was founded—image subtraction—is half a century old. Arterial image information is isolated from competing image contrast by subtracting unopacified from opacified anatomy. A pair of images, one obtained before and one after injection of iodinated contrast material, is used to perform the subtraction. The strategy is similar to that which made CT successful, but image subtraction rather than slice isolation, would produce an image simple enough to interpret that even low

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levels of vascular image contrast could be distinguished from the competing image contrast of the surrounding image anatomy.

From initial indications, intravenous DSA appeared to offer the potential to reduce the complexity and morbidity associated with selective angiography by substituting a peripheral intravenous (IV) route of contrast administration for arterial puncture and catheter guidance. Since less skill was required for the IV procedure and fewer complications were expected to be encountered than with selective angiography, IV-DSA was greeted with enthusiasm by many clinicians.

While initial image quality was judged to be inferior to that produced with film and selective arterial injections, the IV-DSA images were judged to be adequate for a number of diagnostic tasks, most notably evaluation of the extracranial carotid arteries. Since the technology was still new in 1980, many anticipated it would be just a matter of time before IV-DSA image quality approached that obtained with film and selective arterial injections.

Prior to the advent of DSA, images were recorded and subtraction was performed using film and film processing techniques. Such techniques required high levels of arterial contrast, which required injection of contrast material just upstream of the artery being studied. Since DSA was sensitive to lower concentrations of iodine in the bloodstream, injections could be made further upstream from the target artery than with film techniques. For some exams, intravenous injection of contrast material appeared to be adequate.

Experience with DSA revealed limitations in the technique, only some of which would be overcome via technological innovation. One limitation that was overcome was the reduction of excessive levels of image noise present in early DSA images. Another was the modest spatial resolution of which the technique was capable.

The first DSA systems offered 256 × 256 image matrices and slow framing rates (two to four per second). These matrices were rapidly increased to 512 × 512 and framing rates of 30 per second became available. Today, 1,000-line systems are available and spatial resolution approaching that of film, is possible. The spatial resolution capabilities of DSA are not at issue today.

In early IV-DSA systems, image noise was dominated by sources other than x-ray quantum statistics. Much early work centered on improving the signal-to-noise ratio (SNR) in DSA images by removing this noise. In this effort, video camera dynamic range performance was improved and digitizers capable of faithfully recording this dynamic range were introduced. Eventually, the extraneous sources of noise were largely eliminated, leaving mostly the unavoidable mottle associated with quantum statistics. Today, cameras with >1,000:1 dynamic range and 10-bit digitizers are standard.

In spite of these efforts, many IV exams were still compromised by inadequate SNR. Improvements in image intensifier construction somewhat raised the quantum detection efficiency of IV-DSA systems. Image averaging, temporal filtering, and other forms of image processing were pursued in a further effort to take fuller advantage of the available x-ray statistics. Injection techniques were optimized and gradually, more central injections were used to deliver adequate concentrations of iodine to the arteries of interest. Still, the prevalence of inferior IV exams persisted. The problem was not the technology.

As it turned out the severest limitation to IV-DSA image quality was the patient being examined. The culprits were low cardiac output and involuntary (and sometimes voluntary) patient motion. Low cardiac output resulted in images in which vessel opacification was inadequate to overcome the quantum noise. Patient motion produced severe misregistration artifacts, whose presence too often masked arterial anatomy. This latter consequence was the most severe.

To make matters worse, these factors reduced image quality greatest in those patients in whom the diagnostic outcome of the exam was most crucial—the sick. Patients suffering from atherosclerotic disease were more likely to have low cardiac outputs than healthy patients, and ill patients found it more difficult to remain motionless for the 20 or so seconds required for a successful exam.

Temporal image subtraction techniques did not overcome the intrinsic problems associated with the nature of the IV-DSA exam, atherosclerotic disease and human physiology. The persistence of patient motion and low levels of image contrast produced IV-DSA images that were not simple to interpret. Today, while DSA systems are used routinely, selective arterial injections are used in the vast majority of exams; occasionally, injections are made into the aortic arch; rarely are IV injections used. It is safe to say that while the use of DSA systems may have facilitated selective arteriographic procedures (in terms of reduced procedure time and decreased radiation), the anticipated diagnostic benefits of IV-DSA did not materialize because images that were simple to interpret did not result.

RADIOGRAPHIC IMAGE PROCESSING OF CHEST RADIOGRAPHS

Researchers have been digitizing and processing film radiographs for years. In answer to the question: Why digitize a piece of film?, researchers often refrained, "to improve diagnostic performance by highlighting heretofore 'invisible' image features through established methods of digital signal processing." For example, structures in a radiograph are generally easier to appreciate if they possess sharp edges. By artificially accentuating the edges of all structures in a radiograph, using standard spatial filtering techniques, these structures should be easier to see.

Since projection radiographs are intrinsically complicated, it was hoped that disease (ie, lung nodules) would contain some identifying image characteristic or "fingerprint" that could be isolated with image processing. If this characteristic differed enough from those that characterized normal tissues, the appearance of disease could be enhanced. This logic has motivated many years of research effort, with little reward.

The simplest image processing technique that can be applied to a digitized film radiograph is grey scale manipulation through interactive control of "window level" and "window width." Since the film exposure may cover a 1.5 to 2.0 optical-density-unit range, better display is achieved by isolating a reduced range of densities while simultaneously expanding this reduced range to fill the full display range available on the display device as is done in CT. Unfortunately, this approach does not work well for chest radiography. For example, while an uncalcified lung nodule may usually lie between -50 and $+150$ Houndsfield units on a CT image, there is no way to know a priori within which range of optical density the same nodule will appear on a radiograph. The range will vary depending on whether the nodule is superimposed over lung or the mediastinum.

While anecdotal examples of improved disease detection using digitized chest radiographs and interactive grey scale manipulation have been reported, such processing has several drawbacks. Apart from the time required to interact with the display, only a subset of the information recorded on the radiograph is displayed at a time. Viewing multiple parts of a radiograph can adversely affect diagnostic performance, even when the sum of those parts equals the whole. Viewing the entire image in one piece is preferred. Also, there is no a priori way to choose the "right" window settings for any class of disease. Improper window settings are as likely to obscure a structure as to make it more visible.

More sophisticated grey scale manipulation techniques allow the entire radiograph to be viewed simultaneously. Histogram equalization is one such technique. By computing the frequency distribution of grey scale values in a digitized image, a one-to-one grey scale transformation can be used to equally populate all the possible grey levels. Such processing produces regional contrast stretching that accentuates low contrast structure, including noise. Some strange processing artifacts also are produced. The overall effect is often displeasing to a radiologist's eye.

The most promising techniques have been those associated with "unsharp masking" and variations on this theme.[3-5] The rationale for this type of image processing is that the variations in density within a radiograph that occur over large distances are unimportant to the diagnostic task. In its simplest implementation, a deliberately blurred replica of an original image is created and subtracted from the original. The remaining image contrast is windowed for display. When applied to an image, unsharp masking suppresses the low spatial frequencies in a radiograph and allows the higher spatial frequencies to be contrast enhanced without saturating the image display. Generically, unsharp masking is a form of spatial filtering in which the higher spatial frequencies are accentuated. Carried to an extreme, edge enhancement results.

Modest (unsharp masking) to aggressive (edge enhancement) spatial filtering has been applied to radiographs. Again, anecdotal incidences of diagnostic improvement have been observed.[6] Disturbingly, many incidences in which important diagnostic information is suppressed have also been reported. The net result has been that such processing produces little diagnostic benefit, relative to the original film, in only a few limited detection task, such as the detection of lung nodules, wires, and tubes in the retrocardiac and subdiaphragmatic spaces. For other detection tasks, performance has suffered from such processing.

As the technology has progressed, making faster, low cost image processing workstations available to researchers, more sophisticated approaches to spatial filtering have evolved and been applied to radiographs. One such technique is called adaptive histogram equalization.[7] Adaptive histogram equalization can be thought of as a hybrid processing technique that combines aspects of spatial filtering with histogram equalization. This technique attempts to take best advantage of each in hopes of optimizing both. But again, a significant improvement in disease detection has yet to be demonstrated.

Image processing of digitized, film-based chest radiographs has failed to increase diagnostic accuracy for a number of reasons. Of course, it can be argued that the film recording process corrupts the radiographic information to such an extent that no image processing algorithm can recover the "lost" information because of the inadequacies of film. In the over- and underexposed regions of a radiograph, image contrast can be washed out completely. While this is undoubtedly true, it is not the key issue.

The failure of digital image processing techniques to produce significant improvements in diagnostic accuracy when applied to such radiographs is likely to persist. Even if film is replaced by an electronic detector with infinite dynamic range and perfect linearity and powerful image processing computers are given away free at grocery stores with each purchase, without the introduction of a new imaging strategy that better isolates the appearance of diseases of the chest, no image processing methodology is likely to alter the present situation. The issue goes beyond the properties of film to the nature of an x-ray projection image and the nature of disease. Simply put, there exists no unique fingerprint for disease, such as a lung nodule, that appears on a conventional projection radiograph that is not shared by many normal tissues.

ENERGY SUBTRACTION

X-ray energy subtraction, as applied to chest radiography, presents an imaging strategy that attempts to produce a simplified image in which the soft tissue or calcium fingerprint of cancer can be isolated.

Two interactions—Compton scattering and the photoelectric effect—dominate the attenuation of x-rays in the diagnostic energy range, 20 to 150 keV. The effects each produces on radiographic image contrast are energy dependent and can be separated using a pair of radiographs, each acquired at a different effective energy. Analogously, low atomic number tissues (soft tissue) can be separated from higher atomic number tissues (bone) using a dual energy pair of radiographs.

Two possible diagnostic tasks have been suggested as candidates for dual energy subtraction in chest radiography—nodule detection and calcification determination.[8-10] By eliminating bone shadows in the lungs (bone subtraction), it is hoped that potential underlying soft tissue nodules will be more clearly visualized. For lung nodules previously identified on a standard chest radiograph, potential nodule calcification can be determined by eliminating soft tissue image contrast (soft tissue subtraction). Each of these applications has undergone preliminary study and some promising results have been demonstrated in well-defined imaging tasks.

In order for dual energy subtraction to show improvements in diagnostic accuracy for lung nodule detection, two things must be demonstrated. Since the energy subtraction process results in a significant loss of residual tissue contrast, image noise must be appropriately reduced to preserve adequate SNR for either nodule detection or calcification determination. What level of noise can be tolerated is not known. It must also be demonstrated that removal of rib shadows produces image simplification adequate to increase diagnostic accuracy. Only if these two things can be demonstrated clinically can an increase in diagnostic accuracy be anticipated.

CONCLUSION

The degree of success of a medical imaging strategy has depended on the degree to which image interpretation has been simplified or the degree to which a fingerprint of a particular disease has been isolated from image features that characterize normal tissues. Spectacular improvements have followed if one of these criteria has been met to a sufficient degree, as in CT. Modest improvement has resulted if one of these criteria has been met only marginally, as in IV-DSA. Little benefit has resulted if neither of these criteria has been met, as with the digital processing of projection chest radiographs. Other medical imaging strategies for the future, such as dual energy chest radiography, will only offer improvements in diagnostic accuracy if one or both of these criteria is met to a sufficient degree.

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