The Perception of Medical Images 1941-2001

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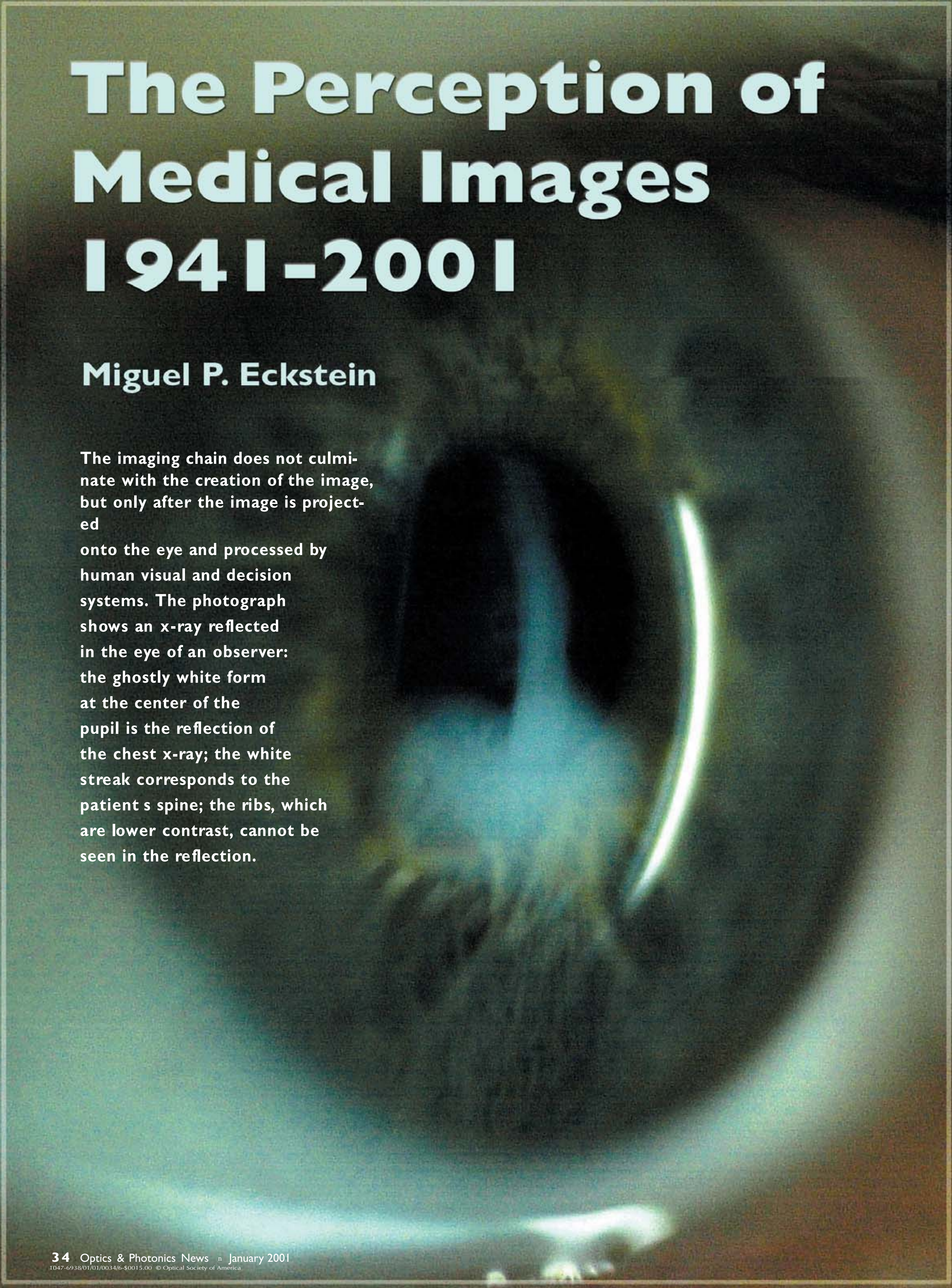

The imaging chain does not culminate with the creation of the image, but only after the image is projected onto the eye and processed by human visual and decision systems. The photograph shows an x-ray reflected in the eye of an observer: the ghostly white form at the center of the pupil is the reflection of the chest x-ray; the white streak corresponds to the patient s spine; the ribs, which are lower contrast, cannot be seen in the reflection.

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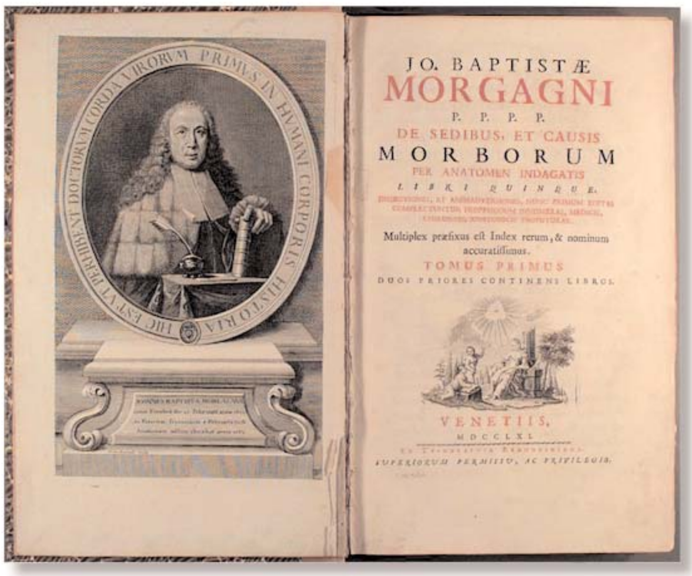

Figure 1. In his book *De sedibus et causis morborum* (The seat and causes of disease, 1761) Giovanni Battista Morgagni documented his use of a microscope to observe dissected corpses, and the relation of his observations to the course of disease.

The purpose of medical images is to visualize aspects of human anatomical structure and function that are not apparent to the naked eye. We can trace the origins of visualization of human anatomy as a tool to study disease to the work of Giovanni Battista Morgagni, an Italian professor of medicine and anatomy at the University of Padua.[1] Using the microscope (which had arrived in Venice around 1623), Morgagni related meticulous observations on dissected corpses to clinical histories and the course of disease. In 1761, at age 79, he documented his findings in the book *De sedibus et causis morborum* (The seat and causes of disease); see Fig. 1. By the 1850s, the magnifying power of microscopes had improved dramatically, a factor which moved pathology from inspection with the naked eye to a microscopic dimension, making possible the first descriptions of leukemia, thrombosis, and embolism, among others.[1]

Modern medical imaging was born on November 8, 1895, when Wilhelm Conrad Roentgen was studying cathode rays arising from a tube and observed a dim light reflected on a bench in the laboratory. The light was coming from a small screen of barium platinum cyanide. He also observed that when holding "the hand between the discharge apparatus and the screen, one sees the darker shadows of the bones within a much fainter shadow of the picture itself." He named these new rays with the symbol for an unknown, X, and published his findings in a manuscript entitled: "A New Kind of Rays: A Preliminary Communication." Soon after January 1896, newspapers and journal articles reported the new x-rays would allow for the diagnosis of diseases as well as for photographing injuries of bones.[1]

Since then, medical imaging has expanded into many new types of modalities with different underlying physical processes and distinct abilities to visualize different anatomical structures and/or functions: These include gamma-ray imaging, ultrasound, computer tomography, positron emission tomography (PET), magnetic resonance (MR), and single photon emission tomography (SPECT).

The value and potential of imaging the inside of the living body was quickly embraced by the world. What was not immediately appreciated was that the creation of an image was not the final step in the imaging chain. The final decision about the presence or absence of disease occurs only after the image is projected onto the physician's retina, stimulating the retinal receptors, and the subsequent transduction of the image through the bipolar, amacrine and ganglion cells, the lateral geniculate, and on to the primary visual cortex and other areas and finally reaching a decision system in the brain where the physician makes the judgment.

The importance of the viewer in diagnostic decisions

The key role of the viewer of the image in medical diagnostic errors and the value of understanding the process by which viewers detect and classify aspects of the image were not given great importance until the 1940s. A crucial turning point was a lecture by W. Edward Chamberlain at the 27th annual meeting of the Radiological Society of North America in 1941.[2] In this lecture, Chamberlain related the inherent limitations of fluoroscopy to the dim light levels of the fluoroscopes and the properties of the human visual system. A fluoroscopic imaging chain entails use of a specialized x-ray tube and a fluoroscopic screen as the image receptor for real-time viewing of the anatomy during an x-ray exposure. Early fluoroscopic screens, introduced by Edison,[1] were very dim. Radiologists were required to spend 20-30 minutes in darkness to adapt their visual systems to the low light levels of the fluoroscopes. Chamberlain argued that a significant drawback of the fluoroscopes was the fact that the human ability to detect changes in intensity and notice details (visual acuity) was highly degraded at such low levels of luminance. He related this degradation to human visual physiology: the existence of the two distinct types of retinal receptors, cones operating at high luminance levels and rods at low, basing his arguments on classic work by Helmholtz.[3] Soon after, image intensifiers capable of amplifying the image to higher luminance levels were introduced by Westinghouse, and the earlier dim fluoroscopes were banned.

In 1949, Burger stressed the importance of determining the perceptibility associated with different roentgen (x-ray) methods. Drawing an analogy with the microscope, he suggested that investigators should be familiar with the "resolving power" (i.e., the smallest object that can be distinguished) of every roentgen method under the conditions in which it was used.[9] Until that time the quality of specific x-ray images had been evaluated only in a subjective way. Burger proposed replacing the subjective method with an objective one based on measuring the perceptibility of a synthetic "phantom" that would closely match the x-ray absorbing properties of a real lung.[4]

In the late 1940s and early 1950s, a number of radiologists brought to the attention of the medical profession the concept that many diagnostic errors had to do with human error in viewing images. L. Henry Garland was probably the first radiologist to pursue the idea that physicians make diagnostic errors and that many of the errors can be attributed either to higher level perception or to decision making.[9] Garland also argued that there were both "objective" and "subjective" reasons for a failure on the part of the physician to detect a lesion. The objective reasons included inadequacy of roentgenographic exposure and processing, inadequacy of viewing arrangements, inexperience or fatigue of the person interpreting the image, and lack of interest. Garland argued that the subjective reasons were of unknown nature, saying: "There are times when an experienced physician sees a visible lesion clearly and times when he does not. This is the baffling problem, apparently partly visual and partly psychologic. They constitute the still unexplained human equation in diagnostic procedures."[5]

William Tuddenham pointed out the limited efficacy of concentrating on increasing radiographic definition and contrast, given the fact that diagnostic errors derive most often from higher level perceptual effects such as failure to "organize" the visual field effectively.[6] He viewed the challenge of finding a lesion among the clutter in a medical image as a problem of organizing the visual scene and separating the "figure" from the "ground," much in the same way Gestalt psychologists conceived perception. Tuddenham believed that efforts should be directed to developing new teaching materials to attack the problem of "reader error."[7]

Harold Kundel and colleagues, then at Temple University, also emphasized the observer's importance in diagnostic decisions and suggested the possibility of improving performance through image-processing technique.[8]

The rise of signal detection theory

The fact that the physician's decision contained a component of randomness—what Garland referred to as the "human equation"—was a fundamental observation that would play a significant role in the development of the field. Randomness in the human decisions related to detection of a faint visual or auditory signal was studied in the 1940s by psychophysicist H. Richard Blackwell. Blackwell attributed it to variability (later referred to as noise) in the environment and in the observer, variability capable of producing sensory-neural activity that could be confused with the sensory activity produced by the stimulus itself.[10,11] The variability inherent in human perceptual decisions would make statistical decision theory, an area of statistics that dealt with hypothesis testing in the presence of uncertainty, the skeleton of much of medical image perception as well as the field of visual/auditory perceptual judgements.

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In the early 1950s, Wesley W. Peterson and Theodore G. Birdsall, engineering graduate students at the University of Michigan, applied statistical decision theory to the problem of radar detection, giving rise to the theory of signal detectability (also known as signal detection theory).[12,13] Then John Swets and Wilson Tanner, two graduate students in psychology studying under Blackwell at the University of Michigan, applied the theory of signal detectability to observers' perceptual judgments in the area of simple tasks in which the signal could appear with a certain probability and the observers had to decide on the presence or absence of the signal (i.e., a yes/no task).[13,14]

A fundamental aspect of signal detection theory is awareness of the fact that an observer's propensity to report detection of a signal may change on the basis of factors including the likelihood—as perceived by the observer—that the signal will or will not be present and the relative cost of each of the decisions. A consequence is that in the context of a simple yes/no task, human performance cannot be assessed simply by analyzing the proportion of trials or images in which the observer correctly calls "signal-present" (hit rate). For example, an observer might close his/her eyes, report seeing the signal in every image, and then score a hit rate of 1.0; on the other hand, if one analyzed the proportion of trials in which the observer reported a signal although the image contained none (false alarm rate), one would also obtain a false alarm rate of 1.0 in this case. Analysis of the hit rate and the false alarm rate together would demonstrate that the observer was responding "signal present" regardless of whether the image contained a signal or not. In this context, an observer's ability to determine whether a signal is present or absent is not determined by the hit rate or the false alarm rate alone but by the relative amounts of both. The receiver operating characteristic (ROC) plots the hit rate as a function of the false alarm rate.[12] In practice, the ROC curve is typically derived from observers' ratings of their confidence about presence of the signal. From the ROC curve one can infer a bias-free measure of performance known as the area under the curve (AUC).[12]

Lusted,[15] who reanalyzed some older data originally presented by Garland, pointed out the need for a bias-free measure of accuracy in medical diagnosis. Since then, ROC analysis of physician's confidence ratings about lesion presence has established itself as the primary method to evaluate medical image quality. More recent efforts in this arena have concentrated on how best to combine the responses of the observers to optimally estimate the area under the curve,[16,17] combining responses across many observers, along with other modified ROC techniques.[12,18]

Toward image-based objective metrics of quality

ROC analysis allows investigators to evaluate physicians' performance in detecting or classifying a signal in medical images; however, it does not allow investigators to predict human performance directly from imaging system parameters and/or from image properties such as noise magnitude, signal contrast, or resolution.

Among the first of the fundamental image properties to be investigated were the random luminance variations thought to contribute to the variability in observers' ability to detect a signal. Albert Rose at RCA, who had been involved in the development of electronic television camera tubes, was interested in the evaluation of camera sensitivity. He investigated human performance in detecting disks of different sizes on a TV screen limited by the fluctuation in the number of photons (quantum noise). He related the level of quantum noise to the contrast necessary for the disk to be detected.[19,20]

In the 1960s, Russell H. Morgan was the first person to apply Rose's ideas to medical imaging.[21] He also introduced the idea of analyzing what he referred to as the frequency-response function, the imaging system's response to sine waves of different spatial frequencies, now known as the modulation transfer function, or MTF.[22] The idea was to represent the signal, the imaging system's response and the eye's response in terms of their individual spatial and temporal frequency content. The human visual system is characterized by a drop-off in sensitivity to low and high spatial frequencies (slow and rapid spatial sinusoidal luminance changes). Morgan used the relative overlap of the combination of the frequency response of the imaging system and of the eye with respect to the frequency content of the signal and related it to the visibility of the signal to a human observer. In essence, Morgan assumed observers combined information across all spatial frequencies in the image to reach a decision and could only control the relative weighting of the different spatial frequencies by adjusting their viewing distance to the image.

Noting that there was no single physical measure of image quality, Kurt Rossmann, first of Kodak and then of the University of Chicago, recognized the importance of the observer's role in defining image quality.[23] Like Morgan, Rossmann attempted to relate human performance to the imaging system MTF and to the frequency content of the signal and noise. In 1974, Rossmann stated: "In the last ten years, our basic knowledge of physics of radiological images has increased to such an extent that it cries out to be linked with observer performance studies."[24,25] This statement foreshadowed some of the formal modeling that would later be carried out in this field.

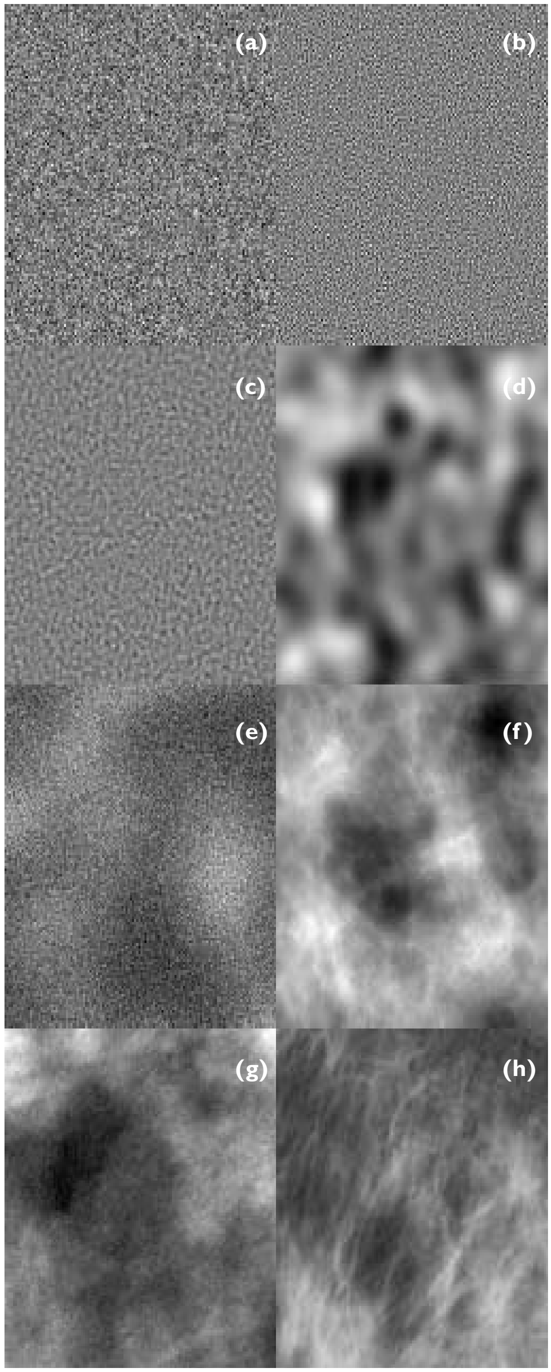

Figure 2. Researchers have studied visual detection of simulated signals (lesions) in a variety of noisy backgrounds. Studies have progressed from simpler backgrounds to more complex simulated backgrounds and to real medical image backgrounds.

From left to right, top to bottom: **a)** white noise,[32-34] **b)** high-pass, ramp noise,[35] **c)** low pass Gaussian noise,[42] **d)** mid/high frequency pass noise,[40] **e)** clustered lumpy background,[60] **f)** lumpy background,[42] **g)** real mammographic background,[46] **h)** real coronary angiographic background.[46]

Otto Schade[26] and Dwight North[27] at RCA Laboratories assessed the performance of electronic devices such as television receptors. Robert Wagner, a physicist at the Food and Drug Administration (FDA), formalized the relation between the signal, the modulation transfer function of the imaging system, the noise—on the one hand—and human performance based on different hypothetical strategies that might be adopted by the observer to integrate information across spatial frequencies on the other.[28,29] In particular, he considered a detector model in which the image data were weighted by the spatial frequency content of the signal (matched filter model) and related it to the optimum detector (the ideal Bayesian observer). This type of detector would make predictions different from those made by Morgan's model. Some of the models brought into medical imaging by Wagner led the way for experimental work comparing model vs. human performance in simple tasks in noise.

At the same time Arthur Burgess, a physicist at the University of British Columbia who was doing work on optimization of magnification angiography, realized that optimization of the imaging chain required understanding of how the eye-brain processed the information in the image. In 1979, Burgess spent half of his sabbatical year at Cambridge collaborating with Horace Barlow, who had also been studying how the human visual system dealt with noise—in this case not noise in images but quantum noise in the light reaching the retina and the noise intrinsic to the visual system, what he referred to as "dark current."[30] Barlow had also become interested in comparing human performance to the performance of the optimum detector (the ideal Bayesian observer) through a measure known as the absolute efficiency.[31] Later, Burgess went to the FDA to work with Wagner on experiments comparing the optimal detector and a suboptimal matched filter model to human detection or discrimination performance in Gaussian distributed spatially uncorrelated noise, or white noise, an approximation to quantum noise in medical images; see Fig. 2, top left.[32] In the 1980s, Burgess used a suboptimal Bayesian observer model based on matched filtering to predict human performance in white noise as a function of a variety of conditions including number of possible signal locations, noise magnitude, signal contrast, and observers' prior information.[32,33]

At the same time, psychologist Richard Swensson and physicist Phil Judy at Harvard Medical School were also investigating the validity of the matched filter model in white noise,[34] using the model to study human performance of simulated signals in computed tomographic images of the liver.[35] Researchers at the University of Chicago combined the matched filter approach with a contrast sensitivity (or MTF) of the eye[36] and used the model to study more applied issues such as the number of gray levels, display window width, and x-ray exposure.[37] This and other work by investigators in the field of basic human vision[38] contributed to increased understanding of visual performance in the presence of white noise. Yet by the mid-1980s there was also awareness of the fact that white noise was only one of the many sources of variability in real images, such as anatomy and correlations in the noise arising from image receptor blur or reconstruction algorithms (in computed tomography, for example). In fact, Kundel and his colleagues had for many years emphasized the influence of what they called "structured noise," anatomical structures in the image not relevant to the diagnostic task at hand.[39]

Harrison Barrett and his graduate students at the University of Arizona, influenced by the work of another University of Arizona professor, George Seeley, began investigating human performance in a variety of more complex scenarios including object variability and correlated noise (see Fig. 2).[40,41,42] A property of correlated noise (also known as colored noise) is that its spectrum energy is not uniform across frequencies. High-pass noise has more energy in the high frequencies and low-pass noise has more energy in the low frequencies (see Fig. 2). When the noise is not uniform in the frequency domain, the optimum detector departs from the matched to signal filter by adjusting its strategy to emphasize spatial frequencies with less noise. A focus of much of the research carried out in the late 1980s and the 1990s has been whether observers can use knowledge about noise statistics to adjust their visual strategy to improve their performance. There is evidence that for detection tasks, humans have the ability to adjust their strategies for dealing with low-pass noise[42,43] but not high-pass noise.[40] Myers added to the model a set of channels, or sensors, tuned to a fixed number of spatial frequencies determined on the basis of previous research in the area of human visual psychophysics. The channels effectively constrained the model in the amount of information it could extract from the images.[44] Most human detection performance has been accounted for by the channelized Hotelling model, which can adjust its strategy linearly to the frequency content in the noise but is constrained by the spatial frequency channels.[41,43]

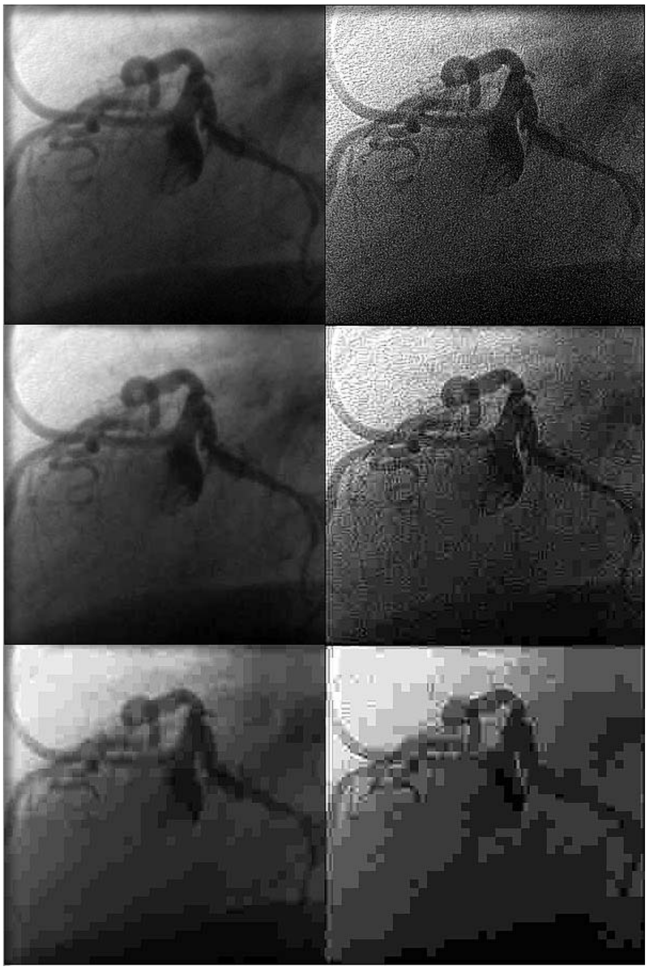

Figure 3. A frame from a digital x-ray cine coronary angiogram that has undergone different degrees of lossy image compression.

Left column: From top to bottom, increasing degrees of image compression.

Right column: From top to bottom, edge-enhanced images with different degrees of image compression. Lossy image compression alters the images irreversibly and introduces image artifacts. Model observers have been used to evaluate the effect of different image compression algorithms on human visual detection performance.

Since the mid 1990s, advances in computer technology have allowed for the digitization of large amounts of real medical images recorded on film. Modeling human performance in tasks that combine computer-simulated lesions with real medical backgrounds, rather than simulated backgrounds, has increased the applicability to the clinical setting of the quantitative models developed. Many of the models have been extended to include a set of channels with responses to spatial frequency[43,45,46,47] and/or orientation[45,46] more consistent with physiological measurements of the responses of cells in the cat visual cortex.

At least in some of the real backgrounds studied, a channelized Hotelling model and a simpler model with both a matched to signal filter and the frequency sensitivity of the human visual system seemed to predict human performance across levels of added white noise as well as a function of image processing techniques such as image compression.[46]

The past decade has also seen the extension of the perceptual models to the temporal domain with the inclusion of spatiotemporal noise applicable to imaging systems using x-ray fluoroscopy, cine coronary angiography, intravascular and transthoracic ultrasound.[48,49,50]

Finally, there has been an increasing use of models to answer practical questions regarding, for example, optimization of the aperture size[47] and exposure time in nuclear medicine,[42] stopping criteria for iterative reconstruction algorithms,[47] acquisition strategies in hepatic single photon emission computed tomographic (SPECT) imaging[51] and evaluation and optimization of image compression in x-ray coronary angiograms.[52]

Understanding the physician s search strategies and decisions

Although the development of quantitative models has been very useful in relating viewers' performance to the properties of images, a shortcoming is that these models are generally applied to simple tasks (detection of a simulated signal in one of a few specified locations) because they are computationally and theoretically easier to analyze. Such simple tasks are clearly far less complex than the work done by a typical physician in analyzing a real medical image: the process actually entails searching for one or more lesions varying in size and shape over the entire image, with thousands of possible locations. One limitation of the quantitative models is that they cannot now be used to study questions that more closely resemble such complex real-life tasks. Some investigators have sought to address this shortcoming by combining a more psychological approach to the problem of visual search in medical images with the quantitative tools developed to measure performance (ROC analysis). This re-search has often led to new insights and helped answer clinically relevant questions well before it was possible to model such problems.

One important question that has been thoroughly investigated is whether knowledge of a patient's clinical history aids the physician in visual detection and/or classification of lesions. Through an investigation of the effect of knowledge of clinical history on visual detection of a variety of lesions in chest and bone x-rays, Kevin Berbaum of the University of Iowa has shown that knowledge of a patient's history does indeed improve visual diagnostic performance.[53,54]

The search process involves directing the high-resolution foveal area of the eye to regions of interest. Recording eye position during visual search allows the investigator to determine where in the image the observer is directing his/her fovea (fixating). This technique has been instrumental in understanding how physicians search for lesions, the search patterns associated with diagnostic errors, and the effects of training.

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Figure 4. A typical scan pattern of a radiologist searching a bone x-ray image for a fracture (located in the large circle). Each small circle represents the image location where the radiologist has fixated (directed his/her high resolution fovea). The lines in between each circle represent the temporal order in which each fixation was generated. Courtesy of Elizabeth Krupinski, University of Arizona.

The first study monitoring eye position during visual search in medical images was carried out by Thomas and Lansdown.[55] They looked at the search scans of observers starting their medical training and found great variability in scanning strategies. Harold Kundel has monitored eye position to investigate the visual search strategies of physicians. In 1974, he showed that radiologists fixated areas in the images that they rated as having high information content.[56] In a later study, fixation position and fixation duration were used to classify diagnostic errors in three categories: scanning errors when radiologists did not fixate the lesion location, recognition errors when radiologists briefly fixated the lesion but still continued the search, and decision errors when the radiologists fixated the lesion for some time but ultimately decided not to "call it."[57]

Recent studies by Elizabeth Krupinski[58] and Nodine *et al.*[59] have looked at the effect of training on search patterns. Their finding is that experienced observers tend to find lesions earlier in the scanning process and also tend to spend less time searching in lesion-free areas.

Medical image perception: 1941-2001

In the past sixty years, researchers in the field of medical image perception have made substantial progress in applying quantitative methods to the assessment of visual diagnostic performance by physicians and to the evaluation of the quality of medical images in terms of task performance. Quantitative models developed on the basis of statistical decision theory have also allowed investigators to predict human performance as a function of basic image properties such as signal contrast and noise magnitude, as well as image-acquisition and processing parameters. In addition, studies in which eye position has been monitored have increased our understanding of the search strategies adopted by physicians as well as of the different types of diagnostic errors that may arise. Finally and most importantly, the field is now being recognized as a necessary complement to understanding the physics of medical imaging, with the goal of optimizing the quality of the medical images that physicians examine in the course of actual clinicial practice.

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