From the Watching of Shadows

“Our science is from the watching of shadows.”
Ezra Pound, Canto 85

One hundred years ago, the German physicist Wilhelm Conrad Roentgen (figure 1) happened upon X rays. Although no one realized it at the time, this most extraordinary and mysterious discovery foreshadowed the quantum upheavals that would turn the physical sciences upside down in the early decades of the twentieth century. More immediately and spectacularly, though, it flung open a door that led into a new and completely unanticipated dimension in the practice of medicine—the ability to look within a patient’s body without having to slice it open.

“A NEW KIND OF RAY”

It is difficult, from today’s vantage point, to imagine just how primitive medicine actually was a century or so ago. The idea of surgery can still make anyone a little nervous, but in earlier days, it elicited feelings of sheer horror. Many are the stories of the wounded or seriously ill who begged for a hard blow to the head, or even death itself, rather than the ordeal of the knife. Alcohol and opium could induce some degree of numbness, but anesthetics—the kind that really knock you out, like ether and chloroform—were not in wide use before the American Civil War. The painkilling properties of nitrous oxide gas and ether had been known since around 1860, but deep anesthesia was not used in surgery until midcentury.

In those days, moreover, something like half of all patients who did en-
Figure 1. An engraving of Wilhelm Conrad Roentgen, published in 1896, less than a year after his discovery.


dure the amputation of an arm or leg died of infection anyway. It wasn’t until the 1860s that Louis Pasteur, Joseph Lister, Florence Nightingale, and others recognized and began preaching the importance of cleanliness, disinfectants, and sterilized surgical instruments. But even with these improvements in the operating room (which, like anesthesia, took decades to gain general acceptance), death from infection was commonplace until penicillin and other antibiotics became readily available after World War II.

Medical diagnosis, too, was almost entirely art, and little science. The physician could measure body temperature, blood pressure, pulse rate, and a few simple chemical attributes of blood and urine, but not much else. Odors and subtle aspects of a patient’s appearance commonly provided equally important clues. But a doctor often had no way to know what was going on within the body other than to cut it open.

All of that changed overnight in 1895. Roentgen, a respectable but rather obscure professor at the University of Würzburg, had been experimenting with an apparatus of widespread scientific interest at the time, a vacuum tube through which electric charges were flowing. Late in the evening of November 8, working in a darkened room, something unusual caught his eye: when an electric discharge occurred in his tube, a nearby piece of paper coated with a chemical compound of barium, platinum, and cyanide produced a glow. With his glass tube completely enveloped in black cardboard, no light from it could be reaching the coated paper. So something invisible had to be passing through the cardboard and reaching the barium platinum cyanide, inducing it to give off light. Roentgen had, in fact, discovered X-ray radiation by observing X-ray fluorescence.
Figure 2. The earliest extant X-ray record, taken by Roentgen on December 22, 1895, of his wife’s hand and signet ring. Courtesy of the Deutsches Roentgen-Museum, Remscheid-Lennep, Germany.

(the emission of light caused by an X-ray stimulus) in a nearby fluorescent material.

By placing various objects between the tube and his fluorescent screen, Roentgen learned that they affected the brightness of the emitted light by different amounts. Paper and cardboard had little effect, but a thick sheet of metal quenched the light completely. And when he held his hand in the path of the X-ray beam, he could make out the bones of his fingers projected in silhouette upon the screen. A short while later, Roentgen produced the first X-ray record, capturing for all time his wife’s hand and signet ring on a glass photographic plate (figure 2).

Word of this wonder spread like wildfire, and the experiment was easy to reproduce. Within months, physicians throughout the world were using X-ray images to extract shrapnel and set broken bones. Roentgen had discovered “a new kind of ray,” as he described them, and in so doing he had created a splendid window for looking within the living body.

For the better part of a century thereafter, innovations in the field of medical imaging came slowly but steadily, and a few were quite remarkable. But the advances in recent years have been as revolutionary as the computers that have made them possible. If the people who developed the automobile, the airplane, the telephone, or the television were to run across modern versions of their inventions, they would probably understand a great deal of what they found. But if Roentgen were to wander through a medical imaging center today, with its computed tomography (CT) scans, magnetic resonance imaging (MRI), and positron emission tomography (PET), much of what he saw would mystify him.

Looking Within will walk Herr Professor Roentgen, and anyone else who
would like to come along, through a modern imaging department, explaining the medical marvels that would so amaze him. But let’s start with a technology Roentgen should feel quite comfortable with, and show how an ordinary X-ray film study of a hand is produced and used today.

**CASE STUDY**

**X-RAY FILM OF A CRACKED BONE**

When a patient shows up at her door, a physician will listen to the symptoms, do a physical examination, and perhaps take some blood or urine specimens (which today can provide highly specific and valuable information). From her interpretation of the results, she can probably limit the diagnosis to one or a few possibilities. Medical imaging may now step in to play a decisive role in confirming, refining, modifying, or refuting the initial diagnosis. Imaging may also be invaluable in planning the treatment and in following the patient’s progress over time.

It may not be readily apparent to the patient, but this general process of gathering relevant information on the malady, considering the possible explanations, and focusing first on the most likely ones goes on quietly even with as simple a problem as a broken bone.

Kathleen Nealon, the sixteen-year-old star pitcher for her high school softball team, took a hard blow to the left hand from a batted ball, causing a great deal of pain and rapid swelling. Her older sister, Kelly, who had dropped by to watch part of the game, drove her to the emergency room of the local hospital.

After carefully inspecting the hand, the emergency room physician sent Kathleen to the radiology department for an X-ray film. An imaging study was needed for a correct diagnosis that would, in turn, guide Kathleen’s treatment. If no bones were damaged, Kathleen could get by with elevation of her hand, intermittent application of a cold pack, and medication to reduce swelling and discomfort. If the radiologist found a hairline crack, the hand might need a cast to counteract any stresses on the injury during healing. If a bone had been broken into separate pieces, it might even be necessary to wire them together surgically for proper setting. Before there were X-ray films, a physician would have had to stabilize a bone without being able to see clearly how to position the pieces, and that could result in weakness and deformity after mending.

Kathleen’s X-ray took less than five minutes. The radiographer (also known as a radiologic technologist) positioned her swollen hand on a cassette, which contained a sheet of radiographic film, adjusted the height of the X-ray tube above it, and reduced the dimensions of the rectangular X-ray beam until it barely covered the hand (figure 3a). Then he protected
Kathleen’s body and neck with a lead-lined apron, which strongly absorbs any stray X rays. He stepped behind a shielding wall, set the controls of the X-ray machine, and kept watch on his patient through a lead-glass window as he shot the film. He then replaced the exposed film in the cassette with a fresh one, repositioned the hand, and took a second film.

In a few minutes, the films were developed and ready for inspection (figure 3b). Both were of high enough quality for the radiologist to identify the problem and guide Kathleen’s treatment. As with most radiographic studies, the contrast between bone and soft tissue was high. There was almost no visual noise interfering with what had to be seen. And the films had sufficient sharpness and resolution of detail to reveal a clean, simple break in one of the bones into two separate pieces. These had not been displaced relative to one another, but the radiologist recommended a cast anyway, to ensure that the bone would be rigidly immobilized.

A month later, when the bone was nearly healed, the cast came off. A few weeks after that, Kathleen was back in there pitching.

Figure 3. X-ray study of a hand. (a) A modern X-ray unit, with the X-ray tube (within the horizontal, white cylindrical housing) pointing its beam downward at the hand, which is resting on a film cassette. The corrugated hose carries the high voltage cables from the generator, which is outside the room, and tubes for circulating the coolant oil. The two knobs on the collimator assembly allow adjustment of the beam size, to minimize the amount of tissue irradiated. (b) In this film of the left hand, the arrow points to a clean break in the fifth metacarpal bone. Compare it with the normal fourth metacarpal, below.
WHAT A PHYSICIAN NEEDS FROM A MEDICAL IMAGE

My wife and I live in Washington, and even though we visit the Lincoln Memorial with out-of-town friends two or three times a year, we never tire of it. We love it for the strength and integrity carved into the wonderfully lifelike face of the man, along with his gentle understanding and acceptance of human frailties (figure 4a). It’s all right there, in the stone.

Another, and altogether different, visual treat is Marcel Duchamp’s Nude Descending a Staircase (figure 4b). Duchamp interprets the human form by portraying its flow, and his painting is as abstract and impersonal a representation as Lincoln is solid and familiar.

Some would argue that Lincoln is a more important work, of greater inherent value because of its directness and traditional authenticity. No one ever has to ask what it means. Such a perspective would miss a crucial point: the two representations are intended to do very dissimilar things, and both succeed splendidly in their individual ways of depicting reality—but an informed interpretation is essential for a true appreciation of either.

The situation is much the same for a medical image. You might suppose that the value of a picture increases with its visual similarity to the part of the body that it examines. But much of that information content will invariably be medically irrelevant at best, or detract from or even hide the diagnostically critical features. Take a look at the studies by X ray, nuclear medicine, and magnetic resonance angiography (all of which we shall discuss later) in figure 5, and you’ll see that what a physician has to work with can be quite distinct from photographic reality. What is important is
what he can “read” in the image. His job is to detect any significant anomaly in it, and identify a corresponding irregularity in the patient’s body. He must then interpret this in terms of a deviation from normal anatomy or physiology—the what, how, and why of what has actually gone wrong with the cells, tissues, and organs. Only then, after settling on at least a tentative diagnosis, is it possible to choose the best treatment. A medical image will be considered good if it helps make any or all of this happen reliably and easily. A diagnostic imaging system must therefore be able to display the specific, distinctive aspects of a patient’s anatomy or physiology that are causing a problem, and be sensitive enough to pick up even very faint signs of it.

The specificity, sensitivity, and other characteristics of the various imaging tools, in turn, are determined by how they work—and they work in remarkably disparate ways. But although the several imaging tech-
The gamma-ray probes used in nuclear medicine originate within the body, and are detected after they leave it, but the basic idea is much the same.

A test that is not specific, or selective, enough may light up and suggest a medical problem when, in fact, none exists; such a false positive result can cause the patient needless anxiety and lead to unnecessary further tests, treatments, and costs. A false negative from an insufficiently sensitive measurement, on the other hand, may preclude the treatment of a condition that is actually serious. Unfortunately, no test can be perfectly specific and sensitive, so there always will be some incorrect readings.

tologies use quite different physical processes in carrying out their appointed tasks, as we shall see, they do share a fundamental commonality of approach: they create medical images by following and recording, by some means, the progress of suitable probes that are attempting to pass through a patient’s body. The body must be partially, but only partially, transparent to the probes. If the probes all slip right through bones and organs without interacting with them, like light through a pane of clear glass, no differences among the tissues can be visualized. Similarly, if their passage is completely blocked, nothing much shows up. But if we choose probes that are only somewhat absorbed, scattered, reflected, delayed, or otherwise affected, we may be able to detect small differences in how they interact with different biological materials. And these differences can then serve as the raw material for the creation of diagnostically useful pictures.

When a uniform beam of X rays entered Frau Roentgen’s or Kathleen Nealon’s hand, for example, the bones and muscles attenuated it (i.e., removed energy from it, reducing its intensity) by different amounts, thereby casting a distinctive pattern of X-ray shadows in it. The no-longer-uniform beam that emerged from the hand then fell upon and exposed a photographic plate or film cassette. Finally, the X-ray shadow pattern was distilled into a permanent visual record when the photographic plate or film was developed.

Mammographic radiography, nuclear medicine, magnetic resonance imaging, and ultrasound use different physical probes in examining the body. These probes interact with the tissue immediately around them, and the nature of that interaction can be highly sensitive not only to the specific physical characteristics of the tissue, but also to the nature of the probe. It should be no surprise, then, that each imaging technology, with its own particular kind of probe, is suitable for the study of only certain kinds of medical problems. A fine crack in a small bone that would not show up at all with ultrasound imaging (which uses high-frequency sound waves) or with magnetic resonance imaging (magnetic fields and radio waves) may be fully visible in an ordinary X-ray film and perhaps in some kinds of nuclear medicine studies as well (gamma rays). Conversely, subtle differences among the various soft tissues of the abdomen that cannot be seen with the X rays of radiography or even CT may be easy to spot with ultrasound or MRI. Different probes, different interactions with the tissues, and different means of detecting the probes give rise to different images conveying different types of clinical information.
THROUGH A GLASS, BUT NOT TOO DARKLY

Selecting the technology that employs the most appropriate probe is only the first step. Given that the physician chooses a suitable diagnostic test, the resulting pictures will be of little clinical use unless they are of good enough image quality. Although there are other critical factors as well, the three gold standards by which images (and the imaging systems that produce them) are most commonly judged are contrast, resolution, and visual noise.

When contrast is good, significant physical differences among the tissues show up as substantial differences in shades of gray (or color) in the image. The contrast between bone and the soft tissues of muscle or the internal organs, for example, is almost always strong in a radiograph, even in Roentgen’s first plate—but there is little inherent radiographic contrast among the organs themselves, so it is sometimes difficult to see them at all. The same organs might show up with dazzling contrast, however, with an MRI or a nuclear medicine scan.

Some kinds of investigations, such as the search for calcifications in the breast (tiny flecks of bonelike material that may sometimes be suggestive of cancer), require high resolution (also called sharpness), the ability to display fine detail. X-ray films tend to provide extremely good resolution, and tiny objects and linelike features of interest within the body (such as the crack in Kathleen’s finger, figure 3b) may show up well in a radiograph or mammogram. One important source of unsharpness is the blur introduced by patient movement—which is the reason for the inevitable “Take a deep breath and hold it!” that accompanies chest films. With some kinds of imaging, such as ultrasound and nuclear medicine, the power of resolution is inherently not great; but although those technologies may get low marks in visualizing anatomic detail, they do display the contrast needed to provide other (sometimes much more important) sorts of information on the patient’s medical condition—such as how healthy the tissues of a particular organ are.

Visual noise refers to anything that interferes, a little or a lot, with an image, just as static noise from lightening in a storm will degrade a radio broadcast. An all-too-familiar example of visual noise (before the advent of cable) was the irritating snow that blew across your TV screen whenever the signal was too weak. But noise may assume more subtle forms, as anyone who has enjoyed an afternoon in the park with Georges Seurat well knows. His Sunday on La Grande Jatte is composed of countless little dabs of paint of various colors. From a distance, the image seems quite smooth and realistic (figure 6a), but the finer features are indistinguishable. At close range, the size of the individual dabs causes the picture to take on
a speckled texture (figure 6b), and that, too, limits the amount of sharpness possible. Fine detail is not what Seurat had in mind, but the objectives of medical imaging are different. A digital image, for example, is composed of a hundred thousand or more tiny dots of different shades of gray or color, and the imaging system must be designed to ensure that they are small and numerous enough for a picture to be clinically useful—otherwise, it may appear blotchy, too noisy to be of value.

We have been discussing the factors that underlie the selection of a technology with sufficient specificity and sensitivity for a given job, and the need for its images to be of adequate quality. Figure 7a, a candid portrait of young Nadine Wolbarst, nicely illustrates these ideas. So as not to produce just one more cute-kitten photo, I worked diligently to reveal the essence of her character by capturing, specifically, her glazed-over, catnip-deranged stare. The imaging equipment had to be sensitive enough, moreover, to perform in the challenging environment of a dimly lit suburban Washington den. Fortunately, disposable-camera film technology (with flash) was up to the demands, and the results exceeded my wildest artistic aspirations.

Figure 7b shows how the photo was made: Nadine was bathed in light, some of which was reflected toward the camera. The lens projected the pattern of light coming from her onto the film. The more light that struck a tiny area of film, the darker it would become when it was chemically de-
Figure 7. Contrast, resolution, and noise level are three important qualities that affect the ability of any image to convey information. (a) Nadine Wolbarst appears with high contrast, sharp resolution, and little visual noise. (b) The making of a photograph: light reflecting from a spot on Nadine’s coat is focused onto a corresponding point on the film within the camera.

veloped later; thus, the camera produced a “negative.” The process was then repeated, in effect, but this time with the negative (rather than Nadine herself) serving as the source of the incoming pattern of light; the negative from this negative was the “positive” shown in figure 7a.

Technically speaking, figure 7a is not a bad picture. There is good contrast, easily picking up the shades of gray in Nadine’s coat. The resolution is fine enough for us to make out her whiskers, and there is virtually no visual noise. Most important, at least with respect to the storage and transfer of information, the specificity, sensitivity, and overall visual quality are sufficient for you or me, the final link in the imaging chain, to determine that this is indeed a cat. And I, with access to certain additional data, can even assert with a fair degree of assurance which cat she usually is. If the film were underexposed or blurry, or in some other sense carried less information or more noise, then that would not necessarily be true.

Turning these thoughts back to medicine: no single technology can perform all imaging tasks well, so a physician must understand what the different types of medical images can reveal about a patient’s condition.
Only then can he or she choose the technology most likely to provide the essential, specific piece of information needed to address a given medical problem. Then it’s up to the medical imaging staff to produce pictures of high enough quality to allow a reliable interpretation and diagnosis. And all of this has to be done with minimal risk to the patient and staff, and at an acceptable cost.

**WHAT IMAGING STUDIES REVEAL**

Six general kinds of imaging are used routinely in modern diagnostic clinics: radiography, fluoroscopy (including studies that involve the computer), computed tomography, nuclear medicine, magnetic resonance imaging, and ultrasonography. The most familiar of these, of course, is radiography, the taking of X-ray films.

*Radiography*

As indicated above, medical images are generally produced by tracking the progress of suitable probes as they pass through the body. A beam of X rays consists of such probes (figure 8a). Think of an X-ray beam as a stream made up of vast numbers of small, discrete, particlelike bundles of energy, called photons. (Appendix A provides an elementary review of atoms and radiation.) X-ray photons propagate through space in straight lines and at the speed of light. Most important, they can collide with atoms and in this way be removed from the beam. In conventional radiography, a uniform, penetrating beam produced by an X-ray tube exposes a part of the body for a fraction of a second (figure 8b). Since the various tissues reduce the intensity of different areas of the beam by different amounts, an X-ray shadow is imprinted in the beam before it exits the patient. The shadow pattern that emerges is then captured on special photographic film. The more a bone or other tissue in the beam path absorbs or scatters X rays, the smaller the number of them that make it completely through to expose the film—and the clearer (less dark the corresponding region of film will appear after it is developed.

X-ray films are most useful in locating and examining objects that have densities significantly greater or less than the surrounding soft tissues—as with bullets, bones, or lungs. X rays are also excellent for examining veins and arteries or parts of the gut if these areas can be filled with “contrast agent,” such as certain compounds of iodine or barium, which soak up X rays particularly well. A tumor, unfortunately, presents more of a challenge. Because its density may be close to that of the surrounding healthy organ and muscle tissues, a cancer growth may give rise to little radiographic contrast, and so may be difficult (or impossible) to see di-
Figure 8. Standard X-ray filming, or radiography. (a) An X-ray image of a part of the body can be produced by keeping track of the fate of "probes" that enter it and do, or do not, interact with it. (b) Overview of the radiographic process. During the fraction of a second that the exposure switch is closed, so that high voltage from the generator is briefly being applied to the X-ray tube, the tube creates a nearly uniform X-ray beam, which enters a part of the body. Only some X-ray photons pass through; the rest are scattered or absorbed, predominantly in the denser tissues, especially the bones. The patterns imprinted in the (no longer uniform) residual X-ray beam emerging from the far side of the patient are captured on specialized photographic film in a cassette. Where more radiation passes through the patient and reaches the cassette, the developed film will be darker.

directly on an X-ray film. Yet a tumor may reveal its presence by altering the appearance of an adjacent body (such as the wall of bowel that contains contrast agent) that can be visualized.

The inherently very high resolution of X-ray films enables them to
provide critical details of fine structure, revealing hairline cracks in bone, for instance, and irregularities in narrow blood vessels enhanced with contrast agent.

Finally, it’s easy to control most visual noise in film radiography, and it rarely causes difficulties, unless the film is under- or overexposed.

Conventional X-ray radiography is still the most common and least expensive way of obtaining diagnostic medical and dental images, and for many tasks it is perfectly adequate. But imaging departments have other options to choose from, as well, and in many situations one or more of them may offer a far better approach to a clinical problem.

Fluoroscopy

Fluoroscopy is radiography’s first cousin. Here, the X rays that pass through and emerge from the patient do not immediately expose a film. Instead, they are projected onto the front face of an image intensifier (figure 9), an electronic vacuum-tube device that transforms a life-size pattern of X-ray shadows into a small, bright optical image. This visible image can be fed into a film camera; more commonly, it goes to a television (video) camera, where it is converted into an electrical signal and sent to a video camera.

Figure 9. Fluoroscopy. The radiant energy from an X-ray tube passes through the patient, and the resulting X-ray shadows are transformed by the image intensifier into a bright image of visible light three centimeters or so in dimensions. This optical image, in turn, is captured by a 100 mm camera, a movie camera, or a video camera.
Figure 10. Digital subtraction angiography. For this DSA image of a carotid artery of the neck, a narrow catheter is threaded into a leg artery, up the aorta, and into the carotid. Images are obtained both (a) before, and (b) after a bolus of iodine-based contrast agent is injected through the tip of the catheter. (c) Aligning the two pictures and subtracting the “before” image from the “after,” point by point, yields a “difference” image that shows only the vessels just filled with the iodine. (d) It may help with interpretation to reintroduce some faint background landmarking.

monitor for live display. The image can be recorded on videotape for subsequent playback and further processing.

As with X-ray filming, fluoroscopy is most adept at distinguishing objects that differ significantly from soft tissue in density. Its major advantage is that it lets a physician watch bodily processes in “real time,” as they happen—for example, the movement of barium contrast agent (given orally or by enema) past partial obstructions in the gut, or the passage of injected iodine-based compounds through constrictions in blood vessels.

By itself, fluoroscopy finds many routine applications in the clinic, but its considerable powers are extended even further when it is coupled to a computer. Digital subtraction angiography (DSA), in particular, is splendid for imaging arteries and veins—nothing else shows up on the screen but the arteries and veins (figure 10). The computer stores separate fluoroscopic images before and after contrast agent is injected into the patient’s bloodstream. It then subtracts the first image from the second, point by point, and displays the difference between the two as a new image. This third, “difference” image highlights those (and only those) places where the first and second images differ, that is, where blood vessels hold contrast agent; all the uninteresting, and easily confusing, background patterns are eliminated.
Computed Tomography (CT)

Conventional radiographic and fluoroscopic images are relatively straightforward and inexpensive to produce—even the smallest X-ray clinics have the equipment—and the trained eye can often derive more than enough from them for an accurate diagnosis. But the superimposed shadows from overlapping tissues sometimes obscure the critical details that a physician needs to see.

What is captured by film or fluoroscopy, and is thereby available for diagnosis, is the pattern of X rays transmitted through the body. The radiographic process is thus a kind of condensation, or deflation, of patient anatomy from the real world of three dimensions into a visual image in two. In the process, the shadows from an intricate three-dimensional structure, like a head, can be flattened into hopeless chaos on film, as in figure 5a. Although a radiologist may be able to perform near magic in detecting and interpreting slight irregularities amidst all the junk, in many cases there is simply too much visual confusion.

Digital subtraction angiography provides one path around that problem, but it works only for blood vessels. Computed tomography achieves the same end for a wide variety of organs, but it produces images quite differently. CT (called “see-tee” or “cat scanning”) uses X rays, an elaborate radiation detection system, and a computer that carries out millions of calculations to construct the image of a thin, breadlike (transverse) slice