A century ago the ghostly shadow of X-ray pictures, laboriously made with temperamental and often home-made equipment, promised to revolutionize medicine. How will our insight into the body human change in the next one hundred years? (Courtesy of the Center for the American History of Radiology, Reston, Va.)
Epilogue: The Future of Imaging

James H. Thrall, M.D.

Progress and innovation are not regular and predictable but come in compelling bursts, followed by periods of assimilation and refinement even as the pathways beckon toward new breakthroughs. Taken in the broadest context, medical imaging has followed this pattern, but at a greatly accelerated pace in the past quarter-century. Technology transfer from core knowledge in electronics, computers, materials science, chemistry, physics, and mathematics has led to stunning developments of new imaging technology and to new applications of established imaging methods. As we approach the second century of medical imaging, this pattern will accelerate. It is daunting to attempt to forecast the future of medical imaging and impossible to predict specific inventions and breakthroughs, but important and overarching trends shaping overall directions for the future of medical imaging are clearly recognizable.

This chapter first addresses the importance of energy as the basis and unifying theme of all imaging methods, followed by a discussion of five overarching trends shaping medical imaging across the different imaging modalities. The chapter continues with a discussion of research directions and opportunities and concludes with selected observations about the implications of scientific and social changes on radiology education and clinical practice. The predictions in this chapter are firmly grounded in what is known today. From the perspective of twenty-five or fifty years in the future these predictions will be viewed by people holding the actual knowledge gained in the interim.

Energy: The Unifying Theme of All Imaging Methods

The details of medical imaging are so complex and absorbing, and the advances so stunning, that it is easy to lose track of integrative concepts that tie the field together. All medical imaging involves the detection of some form of energy emanating from biologic tissues and in most cases the exposure of the patient to a source of energy (Table 28.1). This basic medical imaging paradigm will not change in the future.

The kind of diagnostic information available from each modality is based on the nature of the interactions of the energy form employed with biological tissues. In conventional X-ray imaging, the differential absorption of X rays in air, water, fat, and bone allows their dis-
tinction in the image. The attenuation is determined by average electron density and effective atomic number. In medical sonography, the differing acoustic impedance of tissues is the basis of creating images. In contemporary clinical applications of magnetic resonance (MR) imaging, differences in hydrogen content and differences in the chemical and physical environments of hydrogen nuclei provide the basis for distinguishing tissues. In nuclear medicine, the body is imaged from “the inside out.” The internal distribution of radiopharmaceuticals is recorded externally in time and space. Radiotracer pharmacokinetics and selective tissue uptake form the basis of diagnostic utility.

The kind of information available from medical images is also determined by how the energy is applied and recorded. Taken alone, static, planar imaging with X rays is the single most frequently used medical imaging technique. However, much of the excitement and progress in the use of X rays in the first century after their discovery has come from the development of novel ways of applying and recording the X-ray beam. The development of fluoroscopy permitted continuous real-time imaging and the ability to combine physiologic observations with anatomic observations. Angiography requires rapid sequential recording of images. Computed tomography (CT) is simply a different way of applying and recording X rays. The resulting increase in image contrast and ability to view organs discretely without superimposition is a breakthrough of such magnitude that CT is often thought of as a distinct modality. Similar observations on methods of applying and recording energy can be made about sonography, MR imaging, and radionuclide scintigraphy.

A point of speculation as we enter the second century of medical imaging is whether there are as yet unknown kinds or sources of energy that will become important (Table 28.1). The electromagnetic spectrum has been explored in great detail but may still yield new opportunities. Early methods for breast transillumination light scanning were not effective, but applications of visible light, ultraviolet light, or infrared could become important with better understanding of the ways to apply these energy sources and the significance of their interaction with biologic tissues. Optical time-resolved and multifrequency approaches to imaging with light are both under vigorous investigation. In selected applications, optical imaging has the potential to become a powerful tool for characterizing tissues and their chemical composition. To the extent that pathological processes, including tumors, have characteristic biophysical “signatures,” spectral analysis with light could provide rapid automated diagnosis without the need for classic histopathologic examination. Optical imaging and spectroscopy also have the potential for endovascular application.

Electrical signals in the body have been used to record the activity of the heart, skeletal muscles, and brain. Low spatial resolution images are routinely created in electrical field mapping studies of the heart and brain. Improving the methods of recording these signals and even enhancing them will improve images made from them. Electrical field imaging has the potential advantage of following physiologic changes at millisecond time intervals—far faster than current methods based on recording changes in organ perfusion or biochemistry.

**TRENDS IN MEDICAL IMAGING**

In addition to the possibility that new energy sources will be found, at
least five overarching trends across all modalities are shaping the future of medical imaging (Table 28.II). These trends are closely linked and in many cases are synergistic.

The importance of these trends for the field of medical imaging is perhaps best illustrated by the observation that none of them was clinically important twenty-five years ago, and all of them are central to the practice of radiology at the celebration of its first century. All of these overarching trends will become more important in the future, primarily because the results of these trends collectively allow earlier diagnosis of disease and offer a greater role for the radiologist in treatment and management of patients. Quite simply, the advances embodied in these trends provide more information from medical images and, therefore, more value is derived from imaging in the care of patients.

Although much of the excitement in the future of medical imaging will revolve around the trends identified in Table 28.II, conventional procedures and methods will be enduring. Conventional radiography is still a mainstay of medical imaging practice in terms of the number of patients examined, and it will continue to be so for many years into the future, especially in emerging health care systems in developing countries around the world.

From Analog to Digital Imaging

It is almost incredible in retrospect to realize that when astronauts landed on the moon in 1969, there was not a single clinically important or routine application of digital imaging in radiology. The tremendous new developments in computers during the space race of the 1950s initially bypassed medicine. However, in the decade of the 1970s the seeds were planted for one of the most notable trends in medical imaging, the shift from analog to digital imaging.

The pervasive trend toward digital imaging has developed in two ways. The availability of increasingly powerful digital computers was an enabling technology for the practical implementation of X-ray CT. The ability to operate in a digital environment created the capacity for a new modality or submodality. The same is true for MR imaging and spectroscopy, where no practical means are available to perform the techniques outside of a digital, computer-controlled environment. We have come to think of these techniques as inherently digital.

In parallel with the development of these new digital modalities there has been a broad trend toward converting conventional analog imaging techniques into digital techniques. In many institutions, nuclear medicine is now practiced almost entirely as a digital modality. Computer processing of digital data is an absolute requirement for single photon emission computed tomography (SPECT) and positron emission tomography (PET). Contemporary ultrasound devices are designed to facilitate digital image recording, and increasing use is being made of data capture in digital format for sonographic studies.

Similarly, digital techniques have now been developed for every conventional application of X-ray imaging and have been adopted to various degrees in clinical practice. Digital fluoroscopy and angiography are now widely accepted.

<table>
<thead>
<tr>
<th>CURRENT</th>
<th>EMERGING AND FUTURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Analog imaging</td>
<td>1. Digital imaging and image processing</td>
</tr>
<tr>
<td>2. Emphasis on gross anatomy and gross pathology</td>
<td>2. Physiology, biochemistry, and molecular processes</td>
</tr>
<tr>
<td>3. Qualitative analysis</td>
<td>3. Quantitative analysis</td>
</tr>
<tr>
<td>5. Emphasis on diagnosis</td>
<td>5. Image-guided interventional therapy</td>
</tr>
</tbody>
</table>
although the techniques do not yet provide the absolute spatial resolution of analog imaging. For example, conventional angiography still yields small-vessel detail superior to that yielded by digital angiography. However, the advantages of operating in a digital environment are enormous; these include the ability to immediately review acquired images to guide decision making during procedures and the ability to electronically generate essentially instantaneous subtraction images. Digital imaging also eliminates the time delay for mechanical transport of film, which is important in many fluoroscopic applications. Procedure times are generally shorter for digital angiography to the benefit of patient safety and efficient use of equipment. On balance, these factors in favor of digital angiography and fluoroscopy are compelling. The clear trend for the future is a further adoption of these digital techniques and further improvement in spatial resolution.

The final bastion of analog imaging will be conventional radiography. The sheer magnitude of studies performed, the flexibility of the conventional techniques, and the cost of acquiring new digital radiography systems inhibit conversion from analog to digital methods. Again, the currently available digital radiography systems do not provide the absolute spatial resolution of analog systems but have other features so advantageous that digital technology will increasingly be adopted in the future in practice environments where procedure volume justifies the initial expense of the equipment. For example, the exposure latitude, or range, offered by digital radiography is on the order of one thousand times greater than conventional film-based analog imaging. Wide exposure latitude and the ability to optimize the image parameters electronically "after the fact" result in consistently higher quality radiographs, especially in suboptimal imaging situations such as portable examinations, where both equipment and patient factors are frequently problematic.

Another factor that will drive radiology toward digital imaging is the increasing importance of quick access to information by health care providers. At least in the United States, the medical establishment is under tremendous pressure to become more efficient and cost effective. Any delay in diagnosis or in the availability of diagnostic information, including medical images, to clinicians creates unacceptable inefficiency and increases costs. Coupled with the trend toward consolidation of hospitals into health care systems or geographically distributed provider units, the use of hard copy to share image data is increasingly unacceptable and will be recognized as obsolete in major centers before the end of the twentieth century.

The development and increasing importance of "front end" digital imaging methods is now converging with parallel developments in electronic image management systems, often referred to as picture archiving and communications systems (PACS). The development of PACS has been a vision in the medical imaging world for well over a decade. Early attempts were undermined by inadequate componentry. Until recently, the large size of image data sets has been out of scale for even very powerful computing systems. Order-of-magnitude improvements in computing power, network speed, and archive size are creating a realistic expectation that PACS will soon exist to handle even the largest hospitals and health care systems.

A factor that has slowed the adoption of PACS in many institutions has been the widely held view that these systems represent another kind of radiology equipment or modality. Capital and operating funds for PACS have had to compete with funds for imaging equipment. Increasingly, PACS are now being viewed as the imaging component of health care and hospital information systems. In light of the extraordinary sums being devoted to information management in health care organizations, the capital and operating costs of PACS seem much more reasonable.

The term teleradiology has been coined to describe the transmission and sharing of image data over long dis-
tances. The equipment and technology are essentially identical to those used in PACS, and teleradiology may be thought of as "long distance" PACS. Tele-radiology is an important component of a larger trend toward telemedicine. Techniques are being developed in virtually every medical specialty to provide medical services through specialized telecommunications systems. Developments in the global telecommunications infrastructure will soon make it feasible for radiologists and other medical specialists to offer services to patients anywhere in the world.

The implications of working in a digital environment are enormous. Image data can be postprocessed to bring out important features. Postprocessing can be as simple as windowing and centering, as is done routinely in CT and MR imaging, or it can involve sophisticated techniques like histogram equalization and edge enhancement. Analysis and display of tomographic data can be done in three dimensions. Three-dimensional reconstructions of CT and MR imaging volume data sets have already become standard for many applications. Figure 28.1 illustrates standard transaxial and three-dimensional renderings of a facial fracture. The three-dimensional CT image portrays the extent of the injury and the relationship of the displaced bone to surrounding structures, including the orbit. Other projections of data using special systems are being explored to aid planning for surgery and other therapies. The term virtual reality has been applied to projections of image data in space.

The work paradigm for radiologists in the first century of medical imaging has been to view an analog, hard-copy film on a light box. The paradigm for the second century will be to view a soft-copy computer-generated display of a digital image.

From Anatomy and Gross Pathology to Physiology, Biochemistry, and Metabolism

In its first century, clinical research in radiology has been heavily directed at describing and understanding the anatomic and pathologic significance of image patterns. Understanding the "roentgen signs" historically has been based on radiologic-pathologic correla-
tion. The traditional level of focus has been gross anatomy and gross pathology.

Imaging in the twenty-first century promises to be increasingly oriented to measurements of physiology, biochemistry, and metabolism. The development of ever more versatile and powerful digital imaging methods, coupled with the development of the ability to extract quantitative parameters from image data, is enabling this paradigm shift.

The trend toward an increasing focus on physiology, biochemistry, and metabolism is perhaps best illustrated by recent experience with functional neurological imaging. It has been known for years that brain function is closely coupled to brain metabolism and blood flow. Areas of the cerebral cortex activated by physical or cognitive stimuli demonstrate increased glucose and oxygen metabolism and blood flow. These parameters and many others can be measured by PET imaging, and there is a rich literature describing the mapping of brain metabolism in response to a wide variety of cortical task activation paradigms (Fig. 28.2). Recent advances in MR have permitted similar functional neuroimaging of blood volume and flow. The MR approach has the advantage of being repeatable for serial studies without exposure of the patient to ionizing radiation. Fast MR imaging can capture subsecond changes. Combinations of PET and MR studies now provide a wide choice of functional and metabolic parameters.

In the early demonstrations of functional neuroimaging, this powerful capability was in some ways no more than an interesting technical tour de force of little practical clinical value. More recently, brain mapping through functional neuroimaging has been increasingly used to study patients with neurologic and psychiatric disorders to gain a better understanding of what parts of the brain are actually affected. For example, in patients with obsessive compulsive disorders who are studied under baseline conditions and then again after obsessive behavior is triggered, portions of the brain can now be shown to clearly and reproducibly demonstrate increased metabolism and blood flow. The potential importance of this is enormous, because it means there are now objective physiologic and biochemical markers to study psychiatric disorders. As new therapies become available, these objective, image-derived parameters have a potentially important role in assessing therapeutic effect.

Functional neuroimaging serves as only one example from a growing list of image-based measurements of function and biochemistry. Through these methods radiology and medical imaging will participate in the era of molecular medicine. In many disease processes, function becomes abnormal long before gross anatomic changes are apparent. For example, patients with adrenal medullary hyperplasia may have life-threatening and even fatal episodes of catecholamine release before adrenal enlargement is detected by anatomic imaging. Adrenal medullary hyperplasia is readily detected by metabolic radionuclide imaging with radioiodine-labeled metaiodobenzylguanidine (MIBG).

---

Fig. 28.2 Three transverse sections at the level of the centrum semiovale from a PET cortical activation study. From left to right the images represent control, side-to-side tongue movement, and the subtraction image which clearly exhibits bilateral areas of sensory-motor activation. The study was obtained to localize sensory-motor function as an aid in surgical planning. The images were obtained with O-15-CO2 to measure blood flow. (Courtesy of Nathaniel M. Alpert, Ph.D.; Bradley R. Buchbinder, M.D.; and Alan J. Fishman, Ph.D., M.D.; Department of Radiology, Massachusetts General Hospital, Boston)
The thresholds and horizons for functional imaging are far from being defined. For example, it has been known for some time that patients with Alzheimer's disease demonstrate altered glucose metabolism in areas of involvement. A high degree of correlation exists between the decreased use of glucose demonstrated by PET scanning and functional MR brain maps of cerebral blood volume (Fig. 28.3). However, loss of memory is the earliest cognitive deficit that occurs in Alzheimer's disease. Fig. 28.4 illustrates the results of a visual memory task performed within an MR system. Changes in focal brain oxygenation occur during brain activation and are measured during the memory task using fast MR imaging. The utility of this kind of testing in suspected Alzheimer's disease is being explored. Multiparametric studies have the potential for earlier and more specific diagnoses in Alzheimer's disease, which serves as an example for directions in functional imaging research.

Physiologic and biochemical or molecular measurements will lead to a far greater role for medical imaging in the understanding of disease mechanisms and natural history. Indeed, for psychiatric disease there are no animal models, and functional imaging techniques now represent a unique opportunity for research progress. Physicians can now literally watch the brain think at a physiologic and molecular level!!

From Qualitative to Quantitative Analysis

A strong correlative trend to the growing importance of functional and biochemical assessments is a shift from qualitative analysis of images to higher levels of quantitative analysis. In the first century of medical imaging, the overwhelmingly dominant interpretive approach has been to draw inference through a qualitative analysis of image findings. Although the qualitative will continue to remain dominant into the foreseeable future, there is a clear trend toward the extraction of more and more quantitative information from medical images. This trend may be obvious for many of the newer studies obtained with one of the digital modalities, but it is also true for conventional procedures where quantitative analysis improves accuracy and reproducibility and allows more information to be extracted from the images.

Analysis of cardiac images is an example that spans a broad range of measurements. Ventricular volumes and ejection fractions have been calcu-
lated from contrast ventriculograms for
some time. By adding temporal and
physiologic information, numerous
other functional parameters can also be
derived from these studies, including
rates of ventricular filling and empty-
ing, rates of myocardial wall thickening,
and pressure-flow relationships.

The assessment of coronary artery
stenosis is increasingly done quantita-
tively. Visual estimates of vascular
stenosis are notoriously variable
between observers and from one time
to another by the same observer.
Reproducible, semiautomated analysis
programs are now available. It is highly
likely in the near future that the
absolute standard for analysis of car-
diac images will require quantitative
measurements; patients and third-party
payers at some point will no longer
accept a purely qualitative analysis of
coronary angiograms. These quantita-
tive measurements of coronary artery
stenosis are much easier to make in a
digital environment than by hand-trac-
ing structural outlines on projected
analog images.

In conventional practice, tumors are
often described qualitatively as being
small, moderate, or large in size. After a
course of oncoytic therapy, the follow-
up qualitative assessment describes the
tumor as larger, unchanged, or smaller
than previously seen. In the future these
assessments will be made quantitatively
using a combination of three-dimension-
al volume imaging and tissue segmenta-
tion algorithms. The oncologist will be
able to follow response to therapy quan-
titatively. For example, the aggregate
tumor burden in the liver before and
after a course of chemotherapy will be
the future quantitative standard of prac-
tice, as opposed to the measurement of a
few selected tumor diameters.

Quantitative techniques have also
created the opportunity to make meas-
urements that are simply not possible or
relevant qualitatively. An excellent ex-
ample is the measurement of bone mineral
content using a variety of single- and
dual-energy techniques employing
radionuclides, X rays, and CT. By com-
bining transmission data calibrated to
reference standards of calcium, it is pos-
sible with CT to quantitatively deter-
mine the mineral content of both
cortical and cancellous bone. These
quantitative measurements are suffi-
ciently accurate and reproducible to
permit serial assessment of bone loss
and the response of bone mineral con-
tent to therapy. Qualitative assessment
of bone mineral content is not in any
way suitable for either purpose.

PET and MR imaging and spec-
troscopy offer opportunities for quanti-
tative analysis at a functional and even
molecular level as noted above. Absolu-
te quantitation of radiopharmaceutical localization is possible in PET
imaging with the use of transmission
scanning to correct for attenuation.
Sequential imaging, combined with
blood sampling and the use of sophisti-
cated analytic models, then allows the
quantitative assessment of numerous
metabolic and biochemical parame-
ters, including regional rates of glucose
and oxygen metabolism, blood flow,
blood volume, and pH. Important mea-
surements can also be made of recep-
tor binding and saturation in studies of
the brain. Thus the threads of digital
imaging, quantitative analysis, and
functional measurements are woven
closely together. This convergence of
developmental trends will become
even stronger in the future.

Quantitative methods clearly are
adding new capabilities and new
avenues for diagnosis and patient man-
agement through medical imaging.
The paradigm shift from qualitative to
quantitative analysis parallels the same
trend in other medical disciplines.
Whenever reasonable quantitative
methods become available in medical
practice they have tended to replace
qualitative methods. Yet the best and
most astute physicians are still those
who are able to assimilate both their
qualitative impressions and available
quantitative data to draw diagnostic
inference. In many settings, the same
will hold true for medical imaging. It
will be the creative application of quan-
titative methods when they are appro-
priate and not a slavish devotion to
them that will underwrite progress in the future.

From Nonspecific to Tissue- and Disease-Specific Contrast Enhancement

The clinical utility of nuclear scintigraphy is based largely on the diversity of available radiopharmaceuticals. Most radiopharmaceuticals are a combination of a radioactive moiety that permits external detection and a chemical or biologically active moiety that is responsible for biodistribution (Fig. 28.5). Each radiopharmaceutical has a different mechanism of localization that is critical to its clinical application and to the range of its diagnostic utility. The “best” radiopharmaceuticals are those that provide a high degree of specificity in portraying a physiologic system or pathologic process. Radiopharmaceuticals have the additional highly desirable property that they do not perturb function; the historic term tracer is actually a rather good one because it implies the ability to study or follow a process without disturbing the process. The paradigm of tissue and physiologic process specific radiopharmaceuticals is now being replicated as a major trend in the development of enhancement media for all other imaging modalities.

Current intravascular agents for contrast radiographic enhancement are iodinated derivatives of benzoic acid. These agents have been incredibly useful in the history of radiology and will continue to enjoy broad clinical application into the future, but their drawbacks include rapid clearance from the vascular space, nonspecificity of their localization in normal and pathologic tissues, and the need for multiple dosage administrations during the course of many procedures. Moreover, because these agents cannot distinguish between many structures of interest or provide reliable diagnostic specificity in diseased tissues, new classes of contrast media offer potential benefit and value.

One new class of radiographic contrast agents proving to be quite versatile is based on nanometer-size particles. Depending on their exact size and the method of formulating them, these iodinated nanoparticles demonstrate prolonged half-time in the circulation (thirty minutes or more) providing a “blood pool” agent (Fig. 28.6). With a different formulation, clearance into the reticuloendothelial cells of the liver and spleen is quite rapid, and the contrast between normal parenchyma and disease processes is excellent (Fig. 28.7). In yet another formulation they are rapidly taken up in lymphatics following subcutaneous administration (Fig. 28.8). This approach to indirect lymphography may be used in many sites, including the upper and lower extremities and internal mammary chain. All of these applications...

![Image of scintigraphy](image-url)
have analogies among radiopharmaceuticals. The common goal is to confer greater target organ specificity and achieve a better diagnostic yield. Full clinical exploration for these new radiographic media awaits, but the future direction is clear.

The potential for new MR imaging enhancement agents is, if anything, even greater than for radiographic media, because any one of a number of magnetopharmaceutical “labels” can be used. The diversity of chemical moieties that can be used to confer biologic localization is also far greater than that for radiographic media although it does not yet approach the diversity among radiopharmaceuticals.

Small superparamagnetic iron oxide particles are a versatile magnetopharmaceutical label for a wide variety of conjugate materials. Various ligands, including antibodies and receptor binding agents, can be conjugated into tissue- and dis-

Figs. 28.7a and b CT images of a rabbit liver with experimental tumors implanted (arrows). Contrast enhancement in (a) is with a new nanoparticulate reticuloendothelial system agent and in (b) with a conventional non-ionic agent. Note the far superior enhancement with the experimental agent. (The sections are slightly different angles through the liver)

Figs. 28.7c and d Paired images with conventional nonionic contrast medium (c) and experimental reticuloendothelial system nanoparticulate agent (d) in a rabbit with an experimentally induced liver abscess (arrows). Again the contrast is far greater with the nanoparticulate agent that is fixed in the reticuloendothelial cells of the liver and is cleared from the blood background. (Courtesy of G. Scott Gazelle, M.D., Department of Radiology, Massachusetts General Hospital, Boston)
Fig. 28.8a CT section through the popliteal nodes in a rabbit with a VX2 carcinoma in the right popliteal node.

Fig. 28.8b Following subcutaneous administration of the nanoparticulate agent on the dorsum of the feet, the normal left popliteal lymph node is well visualized with incomplete opacification of the cancerous node on the right. The contrast seen on the right is in residual normal tissue. (Courtesy of Gerald L. Wolf, Ph.D., M.D., Department of Radiology, Massachusetts General Hospital, Boston)

Fig. 28.9 This figure illustrates lesion specific uptake of iron oxide antibody in an experimental infant in the rat heart (left hand image). Control images with free iron oxide nanoparticles (middle image) and saline (right) fail to demonstrate any signal loss on these MR microscopic T2-weighted images. (Courtesy of Ralph Weissleder, M.D., Ph.D., Department of Radiology, Massachusetts General Hospital, Boston. From Weissleder, R.; Lee, A.S.; Khaw, B.A.; Shen, T.; and Brady, T.J., “Antimyosin-labeled Monocrystalline Iron Oxide Allows Detection of Myocardial Infarct: MR Antibody Imaging,” Radiology 182 (1992):381–385. Reprinted with permission)

ease-specific magnetopharmaceuticals (Fig. 28.9). The particles themselves can also be sized and formulated in a manner similar to that for the nanoparticulate radiographic contrast media. Localization in the reticuloendothelial system, blood pool, and lymph nodes can be achieved. The lymph node application has the additional advantage of allowing visualization of all nodal structures following intravenous rather than subcutaneous injection. Other magnetolabels, including dysprosium, manganese, and gadolinium, are being synthesized with chelating agents and macromolecules to confer desired enhancement and biologic distribution properties (Fig. 28.10).

Again, these examples are offered only as indicators of future directions. After decades of no really new agents or mechanisms of localization for radiographic contrast media, the dam has been broken, and it is highly likely that agents for indirect lymphography, blood pool, and reticuloendothelial system imaging will be available for clinical use in the future. For MR the ability to bring together moieties conferring magnetic susceptibility and biological localization provides enormous opportunities, and the challenge will be to select the most clinically useful agents to take through the expensive development and approval process.

Diagnostic pharmaceuticals in some respects have been stepchildren in the pharmaceutical world. The term pharmacokinetics is used to describe the time course of biodistribution of drugs. The term pharmacodynamics is used to indicate both therapeutic and side effects of a drug on organ function. But there is no term that describes what physical effect a drug has on a medical image directly or indirectly. Because physical effects on the recorded image are in fact central and critical to the understand-
emerges: Diagnosis is based on quantitative analysis of metabolic or physiologic parameters from digital image data obtained using pharmaceutical image enhancement media. An increasing number of medical imaging procedures will contain one or more of these elements in the future.

From Emphasis on Diagnosis to Image-Guided Therapy

Image-guided therapy is one of the fastest-growing areas of radiology practice. There has been a convergence of developmental activities from medical disciplines, surgical disciplines, and radiology toward less-invasive therapies using conventional operative procedures as the reference standard. This trend is likely to become even more important in the future.

In multiple disciplines researchers are seeking creative new ways for visualizing the operative or therapeutic field. Surgeons have classically achieved visualization by cutting through normal tissues. The use of endoscopes greatly reduces damage to normal tissues while preserving optical visualization of anatomic structures. In the context of image-guided therapy, medical images, instead of direct line of sight, are used to view the therapeutic field of interest.

Simple image-guided interventions were begun decades ago. For example, patients with tuberculosis were frequently treated with pneumothorax introduced under fluoroscopic control. The introduction of transmural angioplasty a decade and a half ago accelerated interest and creative thinking about less-invasive approaches to major therapeutic problems. Although endoscopic surgery has been practiced for many years, the recent introduction of laparoscopic cholecystectomy and nephrectomy has now stimulated great interest among contemporary surgeons in minimally invasive procedures. Coupled with parallel developments in other specialties, including urology and gastroenterology, the concept of minimally invasive therapy has come to center stage.

In a real sense there has been a blurring of specialty borders as physicians from multiple disciplines work together in treatment teams to the benefit of their patients. In some cases the new procedures are definitive; in other situations they precede or follow a surgical operation. For example,

---

**Table 28.III**

<table>
<thead>
<tr>
<th>MODALITY</th>
<th>EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>X ray</td>
<td>Attenuation of portions of X-ray beam by contrast media.</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>Increased acoustic impedance mismatch and reflectivity at “contrast media” surface.</td>
</tr>
<tr>
<td>MR imaging</td>
<td>Proton relaxation rate (T1, T2) enhancement in tissues near enhancement media.</td>
</tr>
<tr>
<td>Nuclear medicine</td>
<td>Radioactive emission from radionuclide.</td>
</tr>
</tbody>
</table>
many patients with previously untreatable cerebral aneurysms and arteriovenous malformations are being treated by endovascular techniques alone or in combination with surgery (Figs. 28.11 and 28.12).

Imaging techniques are frequently well suited for following therapeutic outcomes. Figure 28.13 illustrates percutaneous treatment of a solitary liver tumor with image-guided injection of alcohol. Marked tumor regression between the initial and follow-up images is clearly demonstrated. Early response to chemotherapy and radiotherapy is being studied with metabolic PET imaging; PET imaging is also being used with receptor binding agents to assess therapeutic effects of central nervous system drugs. In these latter applications, “image guidance” is used after an initial therapy is administered in order to manage subsequent therapeutic decisions.

One of the important implications for the future is the need to redesign treatment and procedure rooms. In most institutions around the world the operating room provides excellent patient support and monitoring in a controlled, clean environment with limited imaging and image display capability. At the same time treatment and procedure rooms in departments of radiology and cardiology have excellent imaging capabilities but historically have not been designed for administration of anesthetics and for the most sophisticated patient monitoring and support. The procedure and treatment rooms of the future will meld the best features of operating rooms and radiology special procedure rooms.

The next generation of image-guided therapies will take advantage of major developments in computer processing and graphics. For example, data obtained from patients will be used in virtual-reality simulations so that physicians can plan and even practice image-guided therapeutic procedures before approaching the patient. These virtual-reality systems will also become a tool for training physicians in performing both the newer minimally invasive procedures and standard surgical procedures.

Additional image processing and image fusion will be accomplished during procedures. Video images of the operative or treatment field can be superimposed on medical image three-dimensional data sets so that the therapist (whether surgeon or radiologist) performing a procedure can visualize both the direct field of view and deep anatomic and functional structures as a scalpel, needle, catheter, or laser penetrates the tissue. These fused images will be presented by both conventional monitors and novel, head-up displays that allow the physician performing the procedure to “look through” image data while maintaining direct line of sight visualization of the surface of the treatment field.

The successful registration of video and medical image data will permit “frameless” stereotaxy. This in turn will lessen the invasiveness and morbidity of stereotactic surgery while increasing the flexibility of patient positioning, especially with respect to intraprocedure imaging. Eventually, frameless stereotaxy will allow real-time feedback and positioning of robotically controlled devices that can be positioned with greater efficacy than currently possible. The efficacy will come from more precise anatomic localization as well as incorporation of functional information.

Computer systems are already being used to bring anatomic and functional information together. The fusion of images from PET and MR imaging or CT allows both kinds of information to be visualized in the same image scene. For example, PET activation paradigms can exactly localize the areas of the cerebral cortex involved in critical motor functions (as seen in Fig. 28.2). The superimposition of the PET image data with three-dimensional registration onto CT or MR scans provides a combined functional and anatomic map for planning therapy to avoid damaging the motor cortex in dealing with lesions adjacent to it. Likewise, in patients with partial epilepsy, functional images pinpointing the focus of abnormal brain metab-
olism can be fused with anatomic MR and CT images. In the future this level of image guidance will become the standard of practice for many applications. The technology will move out of academic research centers to become broadly available.

These examples again illustrate the synergy between the overarching trends shaping the future of radiology. That is, the image data are in digital rather than analog form; the critical assessments are functional as well as anatomic, and they are generated by quantitative analysis of contrast-enhanced studies. All of the image handling and analysis will be performed in open-architecture PACS environments. PACS will provide the basic networking to send image data sets to specially designed workstations customized for end user applications. PACS networks will further support transmission of image data to display and workstations in the specialized treatment rooms of the future.

**RESEARCH**

Many current themes in clinical research in medical imaging will continue into the future. As new methods of applying and recording energy are developed to either modify existing modalities or create new ones, the significance of image patterns and findings associated with different diseases will continue to be explored. This exploration has been the heart and soul of clinical research in radiology and
medical imaging for decades. As the "roentgen signs" are understood, they become the basis of clinical image interpretation and clinical practice.

Largely because of economic pressures on health care in the United States, technology assessment is emerging as another extremely important area of clinical research in medical imaging. New medical imaging technologies are expensive, and the medical imaging community is being challenged to prove the value of both new and old procedures. Historically, the concept of technology assessment in medical imaging was to first demonstrate the safety of a new method and then to determine its diagnostic accuracy. While these basic concepts remain important, simply demonstrating the safety and accuracy of imaging technology is no longer sufficient. It is now also necessary to demonstrate a positive benefit in the outcome of individual patients, to populations of patients, and to society in general. This task is far more challenging and poses a
particular problem for diagnostic procedures that occur early in the management of a disease process. The ability to assess ultimate effect on outcome is often blunted by almost imponderable influences of later therapeutic decisions. A research challenge for the future is to develop better technology assessment methodologies that allow medical imagers and other health care researchers to rigorously answer both medical and social cost benefit questions.

It has been possible to critically study the cost and benefit of an imaging procedure on patient outcome in screening mammography. Specific guidelines continue to be debated, but the hypothesis is at least currently accepted that population screening of some kind is appropriate and beneficial. Better clinical epidemiology will be necessary to converge on the most cost effective screening strategy.

A counterexample is the use of ultrasound in uncomplicated pregnancies. Over two decades, certain patterns of application became almost unanimously accepted and employed without answering the basic question of outcome benefit. Routine application has now been challenged as not benefiting outcome and therefore not worth the cost. We must expect that more and more conventional wisdom and apparently "medically" obvious and intuitive conclusions will be challenged vigorously in the future. For economic, social, and political reasons, a significant portion of clinical research in medical imaging must be devoted to technology assessment in the next decade. Technology assessment data will be used to establish practice guidelines and standards of care.

Basic research in medical imaging will proceed along two fronts: (1) development of better imaging methods and (2) use of imaging methods to study problems of fundamental biomedical interest. Within this first avenue of basic research, academicians and industrial researchers will seek to find new energy sources that allow new and different kinds of imaging assessments and will continue to modify existing methods in order to produce studies that are safer, have higher information content from either an anatomical or functional standpoint, and facilitate better methods for handling, analyzing, and distributing image data.

Each existing modality will undergo continued development. Conventional radiography will become safer as better film screen systems and more sensitive digital detectors permit a reduction in radiation dose. Anatomic resolution and digital radiography applications will improve. Digital angiography systems will be developed with faster framing rates, better spatial resolution, and improved image contrast. Better spatial resolution and image contrast will improve conspicuity.

Development in CT reached a plateau briefly in the 1980s and has now resumed. This trend will continue in the future. Better componentry will permit ever faster imaging, which in turn will facilitate three-dimensional volume imaging and studies of organ function. The significance of faster imaging is illustrated in Figure 28.14. Dynamic events must be sampled at short enough time intervals to capture their details. For example, at normal heart rates a sampling interval of forty milliseconds or less is required to fully "capture" the peaks and valleys of ventricular volume through the cardiac cycle. CT with contemporary spiral scanning systems is fast enough to follow perfusion patterns through major organs such as the brain and the kidney (Fig. 28.15), but is not fast enough to study ventricular function. Ultrafast CT scanners capable of twenty images per second or more are required for this purpose. Continued improvement in price and performance may make such systems more widely available. Special CT scanners will be adapted for use in operating rooms and procedure rooms, and portable CT scanners that can be moved from one room to another will be developed to keep costs more reasonable.

Developments in MR imaging defy brief summary. The ability to use computers to control imaging sequences, coupled with creative developments in
magnets, gradient coils, and surface coils, provides almost unlimited opportunity. Faster imaging will continue to be an important developmental goal to support functional measurements (Fig. 28.15), to fully exploit new contrast enhancement media, and to bring procedure cost down. MR has the greatest potential of current imaging modalities for tissue characterization. Coils and imaging sequences will be developed to exploit this potential.

Modality developments in ultrasound will continue to be aimed at better spatial resolution, better penetration in tissues, and more integration of functional and anatomic information. The development of enhancement media for ultrasound has lagged developments in other modalities but has just as much potential to become important in the future. Obvious developmental candidates are blood pool agents and tissue-targeted agents. Rapid, real-time imaging is a strength of ultrasound of particular value for cardiac studies and for guidance of interventional procedures. The ability to miniaturize transducer systems also makes ultrasound an ideal candidate for endovascular, intracavitary, and intraorgan applications. Fiducial markers will be used to register objects in space, such as a surgeon's hand,
oped at an astonishing pace for both single-photon and PET applications. In some cases a class of tracer is explored through PET imaging and then a single photon analog is developed. New agents for brain imaging are examples of this synergistic developmental pattern. Because PET systems including radionuclide production facilities are extraordinarily expensive, this technology migration pathway is invaluable for achieving routine clinical applications.

SPECT and PET systems are close to their theoretical limits of spatial resolution with existing materials. However, spatial resolution and count rate response can be vastly improved if novel fiberoptic-based detector systems can be successfully developed.

Hybrid imaging rooms will be developed to facilitate studies requiring more than one modality. For example, an angiographic or fluoroscopic device may be incorporated into a room to facilitate initial placement of vascular catheters; then CT or MR scanning can evaluate the distribution of an injected material.

As mentioned earlier, the second broad direction of imaging research that will become far more important in the future is the use of imaging methods to study problems of fundamental biomedical interest. In the “anatomic” era of medical imaging, imaging methods were not important for this kind of application. In the digital, quantitative, functional, and biochemical era of imaging, this situation has changed dramatically. Indeed, many important questions can only be feasibly studied by imaging. As previously discussed, the mapping of brain function and metabolism under basal conditions and following activation paradigms is uniquely performed through imaging studies.

Imaging methods are increasingly being used to study the pharmacology of therapeutic drugs. The term 21st-century pharmacology is suggested to describe the use of imaging to study pharmacokinetic and pharmacodynamic properties of new pharmaceuticals. Many therapeutic agents can be radio-labeled with positron-emitting radionuclides. This labeling permits absolute quantitation of pharmaceutical distribution in both time and space. Instead of having to sacrifice a series of animals at different points in time, researchers can use a single experiment to follow the pharmacokinetics of a drug. Likewise, organ function and response of lesions to therapy can be assessed through imaging.

By establishing imaging baselines, researchers can allow experimental subjects and patients to serve as their own controls, thereby reducing the number of measurements necessary to assess drug efficacy. Twenty-first century pharmacology has the potential to greatly reduce both the expense and time involved in drug development. The potential is underexploited by the pharmaceutical industry as we approach the beginning of the second century of medical imaging. The opportunity for this kind of research is therefore enormous.

The imaging community must determine its role in these new research directions. Scientists from outside the traditional imaging disciplines have been actively exploiting the new quantitative functional and biochemical capabilities, especially of PET and MR. We are at a watershed at the end of the first century of medical imaging, when we will see whether these new research capabilities strengthen radiological research activities or become fragmented. As knowledge from multiple disciplines is brought to bear on important research questions that require these new imaging capabilities, it seems likely that once again the borders between radiology and other medical specialties will be blurred.

**EDUCATION**

The future holds an interesting challenge for educational programs in medical imaging. Enormous amounts of new information must be added to the curriculum to reflect advances in all of the basic modalities as well as in computer science and functional imaging. Future radiologists who are not comfortable working in a digital, computer-oriented environ-
ment will be at a disadvantage. Similarly, radiologists who do not go beyond anatomic interpretations will fall behind the forefront of practice in many areas. Radiology training curricula in the future will need to add these components.

The educational process in radiology is likely to benefit from many of the advances in computer technology and image processing technology that are shaping clinical practice. PACS will be used to distribute more efficiently teaching files and reference images. Interactive teaching programs will be used to reinforce learning. Computer simulations will be used to teach both diagnostic and therapeutic procedures.

At the same time, the trend toward image-guided therapy suggests the need for an almost separate pathway for training. These procedures are becoming increasingly complex and require high levels of training in technique as well as traditional training in cognitive skills. As the borders between radiology, surgery, and medicine blur in the development and application of image-guided therapy, decisions will have to be made concerning the training time allocated in different components of medical imaging. Too little time devoted to technical performance aspects will relegate radiologists to observer status in image-guided therapy procedures. However, they must spend enough time in traditional core training to acquire the unique knowledge that distinguishes the specialty.

**Radiology Practice in the Future**

Social, economic, and even technical trends beyond the control of radiology or medicine will profoundly shape future practice. The wonderful developments benefiting the field and its patients that have been briefly discussed here will have to be adapted to rapidly changing health care systems and philosophies around the world. Many countries will need to set priorities and in some cases restrict the promulgation of new and established imaging methods. Practice standards will be increasingly imposed to guide clinical decision making. We hope that these standards will be based on valid research into assessment of the relevant technologies and not on economic factors alone. This process will be carried out differently in each country. While the developmental potential of medical imaging appears limitless, economic resources are not. A major challenge is to achieve a sustainable balance between cost and innovation.

Telecommunications and information management technologies will bring medical providers and patients together so that geography no longer limits the application of many services, including medical imaging services. Information superhighways are being developed for commercial and consumer purposes. These will be available for medical applications, including teleradiology. We envision a future practice of radiology and medicine in which key specialists can come together through teleconferencing as a "virtual group" to discuss or analyze particularly difficult cases, and where high-quality imaging services can be provided anywhere in the world through electronic linkage between remote areas and centers of specialty excellence.

The safest prediction for the future is that it will be different from anything we can now imagine. Who could have envisioned before Röntgen's discovery of the X ray in 1895 what a revolutionary turn the practice of medicine would take? And who, learning of the X ray, could have predicted all of the subsequent events in medical imaging of the last one hundred years? Scientific and medical knowledge are growing exponentially as we enter the second century of medical imaging. What we know today will soon be subsumed by enormous advances in new knowledge. This would be frightening if we were somehow faced with the prospect of suddenly being transported many years into the future. Just imagine traveling in a radiology time-capsule instantaneously from 1970 to 1995 and being confronted with ultrasound, CT, MR, and digital radiography! Rather, it is exciting to realize that we will continue to have the opportunity to participate day-by-day in the discovery and assimilation of new knowledge to create even more value for the care of patients through medical imaging in the future.