X Rays in Medicine

For almost a century, x rays have been used for medical imaging and for radiation therapy. Now these two clinical regimes are converging in the latest technology.

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One hundred years ago this month Wilhelm Röntgen, a professor of physics at the Julius Maximilian University of Würzburg, discovered x rays while experimenting with cathode rays in a Crookes tube. Word of the discovery spread quickly, and by early 1896 the properties of x rays were under investigation in numerous physics laboratories in Europe and North America. By the turn of the century, physicians and physicists were exploiting the penetrating character of x rays to look inside the human body without cutting it open. They were also beginning to explore the therapeutic properties of x radiation.

The applications of x rays to medical diagnosis and therapy have expanded enormously since those early years. Today, in the US alone, 300 million clinical x-ray examinations are performed annually for purposes ranging from static imaging of fractures and cancers to the real-time guidance of tissue biopsies and cardiovascular angioplasties.[1] In addition, half a million cancer patients each year receive x-ray treatments, about half of them for curative purposes and the rest for pain relief.[2]

Until recently the diagnostic and therapeutic applications were relatively distinct, although images might be obtained periodically during extended x-ray treatments to verify alignment of the treatment beams and assess the response of the patient. Today, however, the boundary between the diagnostic and therapeutic applications of x rays in medicine is far less distinct. X-ray images are incorporated directly into treatment plans for cancer patients, and they may soon provide real-time tissue imaging during treatment.

A major contributor to the enormous progress of medicine in this century has been the development of noninvasive imaging techniques of various kinds. It all started in Röntgen's physics laboratory a hundred years ago. Half a century later, ultrasound imaging was developed with surplus sonar equipment. Imaging with radioisotopes at first exploited nuclear reactors constructed immediately after World War II. Magnetic resonance imaging had its origin in nuclear magnetic resonance spectroscopy. Other imaging methods, based on magnetic field measurements, infrared transmission or electrical impedance may one day achieve clinical acceptance.

Physicists have been instrumental in all of these diagnostic and therapeutic contributions. The American Association of Physicists in Medicine (one of the ten member societies of the American Institute of Physics) has almost 4000 members.[3] Graduate and postdoctoral training programs in medical physics increasingly attract bright young physicists.

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Planar imaging with x rays

Ordinary planar x-ray images are formed by placing a patient between an x-ray tube and an image receptor, usually a cassette containing an intensifying screen and a photographic film. The film is exposed by light emitted when transmitted x rays interact in the screen. The resulting "radiograph" is simply a static shadow image. Fluoroscopy is a variant of this procedure in which a fluorescent screen and an electronic image intensifier are used to form a continuous "moving picture."

As the x rays traverse the patient, they can be absorbed, scattered or transmitted undisturbed to the receptor. The scattered x rays merely interfere with the information conveyed by the shadow pattern of transmitted rays. So a mechanical grid is inserted behind the patient to prevent most of the scattered x rays from reaching the cassette.

For a parallel, monoenergetic x-ray beam incident along the z axis, the distribution $N(x, y)$ of transmitted x-ray photons at the image plane is given, in the absence of scattering, by

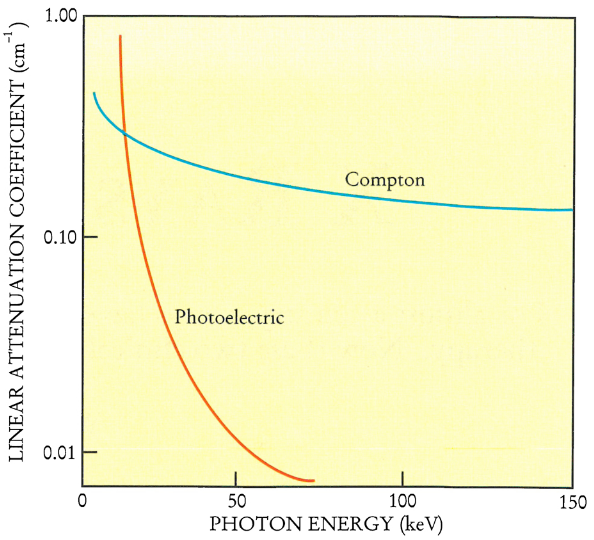
$$N_0 A \int e^{-\mu(z)}\, dz$$

where the line integral is taken over all tissues along the unscattered photon trajectory to the point (x, y) on the image plane, μ is the linear attenuation coefficient for x rays of the tissue encountered at (x, y, z) and A is the x-ray energy absorption coefficient of the intensifying screen. The distribution of x rays absorbed in the screen thus forms a two-dimensional projection image of the transmission of x rays through the three-dimensional volume of tissue exposed to the x-ray beam.

The linear attenuation coefficient μ is in fact the sum of the coefficients for various types of x-ray interactions. For the range of x-ray energies employed in medical imaging, two kinds of interactions predominate: the photoelectric effect, described by the linear attenuation coefficient τ, and Compton scattering, described by the linear attenuation coefficient σ. Thus $\mu = \tau + \sigma$. Figure 1 shows the x-ray energy dependence of these coefficients in human soft tissue.

The photoelectric coefficient increases with atomic number Z like Z^3, principally because x rays interact photoelectrically with the inner, tightly bound electrons of

LINEAR ATTENUATION COEFFICIENT for x rays traversing human soft tissue is the sum of two dominating contributions. Attenuation coefficients for these two contributors, Compton scattering and photelectric absorption, are plotted here as functions of the x-ray photon energy. FIGURE 1



an atom. The Compton coefficient, by contrast, is relatively independent of the atomic number of the tissue atoms, because x rays Compton scatter almost exclusively off the outer, loosely bound atomic electrons. Both coefficients increase linearly with the tissue density. To achieve contrast between soft tissues that differ only slightly in Z, one must use low-energy x rays, because they interact predominantly by the photoelectric effect. An example is mammography, whuch employs x rays in the range of 15–30 keV. For chest x rays, which involve tissues of greater intrinsic contrast, clinicians use x rays with energies ranging from 50 to 150 keV.

X-ray images represent a compromise among four kinds of resolution: spatial, contrast, temporal and statistical. Spatial resolution is related to the geometry of the image-forming process and the resolving capacity of the intensifying screen. Contrast resolution is affected by the attenuation characteristics of the various tissues, the x-ray energy and the glare from scattered x rays that cannot be kept from the screen. Temporal resolution refers to the blurring caused by the patient's movement during exposure. Statistical resolution is related to the number of x ray photons absorbed in the screen to produce the image; the more photons, the less statistical noise.

Unfortunately, improving any one of these resolution factors generally degrades one or more of the others.[4] The compromise among them represents a balance such that no single factor dominates the degradation of the image.

Sectional imaging

A fundamental limitation in conventional planar x-ray imaging is the projection of the three-dimensional distribution of attenuation coefficients as a shadow onto a two-dimensional detector. This projection obviously discards much information about tissue variation along the beam direction. For many years techniques of analog tomography were used in attempts to overcome this limitation. But they were restricted to certain specific applications, and the images were difficult to interpret.

A major breakthrough was achieved in 1972 with the introduction of x-ray transmission computed tomography (often abbreviated as CT or CAT). This technique was brought to clinical medicine through the efforts of Godfrey Hounsfield and Allan Cormack,[5] who shared the 1979 Nobel Prize in medicine. (See PHYSICS TODAY, December 1979, page 19.) Several other investigators contributed significantly to the foundations of this important x-ray imaging technique.[6]

To understand the principles of CT scanning, consider a highly collimated x-ray pencil beam in the plane of a slice of the body only a few millimeters thick. X rays transmitted all the way through the slice are measured with a collimated detector on the opposite side of the patient. The signal from the x-ray detector (an ionization chamber or a scintillation detector) is converted to digital output. The tight collimation of source and detector prevents scattered radiation from degrading image contrast. The number of x-ray photons recorded by the detector at one position constitutes a single pencil-beam projection of x-ray transmission data at a specific angle through the tissue slice. This process is repeated many times at slightly different angles to create a set of multiple projections of the entire tissue slice. (See figure 2a.)

If x-ray projection data are collected at a sufficient number of angles, a matrix of values of the attenuation coefficient μ for different $\delta x\,\delta y$ cells can be calculated by a simple back-projection technique, thus yielding the two-dimensional distribution $\mu(x, y)$ over the whole tissue slice. By displaying the variation of the attenuation coefficient pictorially in shades of gray, one creates an image that shows the various anatomical features of the tissue slice.

In practice the back projection is calculated by Fourier transforming the projection data into (spatial) frequency space. In that way the back-projection computations can easily be combined with ramp and cutoff-frequency filters to improve image quality and enhance subtle features.

The first CT scanners employed a single collimated x-ray source and two detectors, so that data could be collected from two contiguous tissue slices. The source and each detector mapped out projection data in a translate–rotate geometry, one x-ray path at a time. That scheme required several minutes to acquire enough data to reconstruct a single image.

Efforts to collect data faster soon led to the successive generations of fan-beam scanners shown in figures 2b, 2c and 2d. Figure 2b shows an array of detectors that move in a translate–rotate configuration; 2c shows a bank of detectors that move in a purely rotational geometry; finally, 2d shows a ring array of stationary detectors. With these fan-beam geometries, a whole tissue slice can be imaged in a few seconds. By combining these geometries with the patient gantry moving continuously along its long axis, one can get cross-sectional images of many slices of the patient in minimum time. This procedure is called spiral scanning. Finally, images of vertical (sagittal or coronal) slices through the body can be constructed by compiling arrays of attenuation coefficients along axes parallel to the patient's long axis.

Although the evolution of x-ray scanning geometries greatly shortened the time required to acquire images, none of the three fan-beam generations permitted data acquisition in a time (less than 0.1 seconds) short enough to capture images of the heart and other blood-perfused organs without significant degradation caused by motion. For that one needed to find a way of producing x-ray projection data without mechanical moving parts. To that end the so-called 5th generation of scanners employs an electron-beam gun that generates x-ray beams in different directions by scanning over a stationary concave metal target. The resulting scan times are only a few milliseconds.[7]

Digital imaging

The combination of intensifying screen and photographic film has many advantages for capturing and recording x-ray images. It is simple, portable and inexpensive, and it yields excellent spatial resolution. But it is limited to a narrow range of acceptable exposures and offers little flexibility for image processing or data compression. Film images are bulky to store, and they must be transported physically from one location to another.

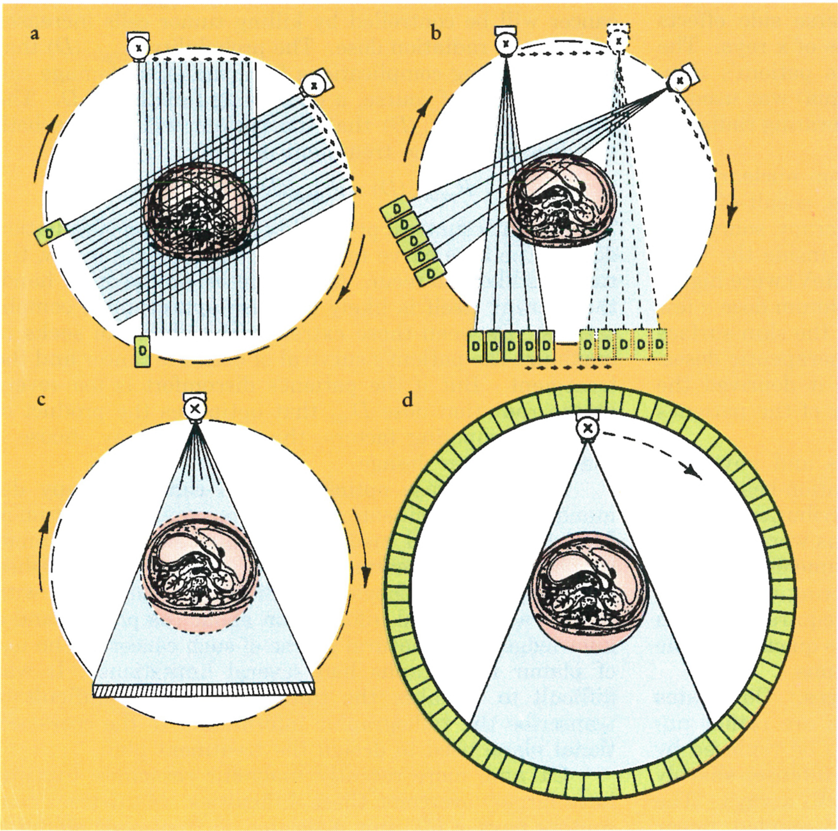
Digital imaging methods overcome these limitations, but currently they are more expensive and more complex. Digital methods employ a variety of approaches for x-ray detection and measurement: fluorescent crystals with photomultipliers, semiconductor detectors, channel electron multipliers and photostimulatable phosphors with laser-scanning readout. As these techniques evolve, medical imaging is becoming increasingly reliant on digital technologies. It is likely that clinical imaging will be entirely digital in the not-too-distant future.[8]

In a digital planar radiographic unit, as shown in figure 3, the x-ray source and receptor are computer-controlled to provide digital images that can be displayed in real time on video screens. Digital images can be stored on magnetic media or optical disk, and a film-writing device may be used to produce permanent analog copies of the images, if they are wanted. Digital image storage and display are used routinely in x-ray CT and magnetic resonance imaging. The convenience and utility of digital technology is encouraging its adoption for other imaging modalities.

Two types of image receptors are used in digital radiography. One type records the entire image simultaneously; the other acquires a complete image by scanning the x-ray beam and receptor in synchrony across the patient, a technique known as scanned-projection radiography. Various data acquisition methods are available, including the use of image intensifiers, ionographic chambers, solid-state detector arrays and stimulated-luminescence plates. Commercially available stimulated-luminescence plates employ a phosphor that absorbs x-ray photons and reradiates their energy in the visible when scanned with a laser beam.[9] The emitted light is detected by a photomultiplier tube and digitized with an 8- or 16-bit analog-to-digital converter. The digitized image is displayed on a video monitor and stored.

Conventional film images also can be digitized with a scanning microdensitometer. Although that approach is inefficient, it is used to convert selected film images into digital data for transmission to distant sites for interpretation and consultation. It can also be used to integrate analog images into an electronic image network.

Scanning systems for digital radiography have the advantage of excellent rejection of scattered radiation by means of tight collimation of the x-ray beam near the source and the detector. The beam may be scanned as a point or line across the patient. Line scanning requires several seconds to compile data for a single image. But the exposure of any particular region of tissue is so brief



EVOLUTION OF GEOMETRIES of x-ray CT scanners. **a:** First-generation scanner, in which the pencil x-ray beam is both translated and rotated to cover the body being imaged; the moveable detector is shown in green. **b:** Second-generation scanner, with a diverging fan beam and detector array that are translated and rotated. **c:** Third-generation scanner, with a fan-beam source that rotates around the body together with its detector bank. **d:** Fourth-generation detector, with a rotating fan-beam source and a stationary ring of detectors.
FIGURE 2

that the image suffers little motion blurring.[10] With point scanning, one can vary the dwell time for different tissue locations so that the detector sees a constant photon flux, more or less. This technique, called scan-equalization radiography, is designed to control statistical unsharpness.[11]

Digital images offer numerous advantages over screen and film radiography. They can be processed to highlight selected features (edge sharpening, contrast enhancement, noise smoothing), and the data can be compressed for rapid electronic transmission. They require less storage space, and copies can be presented for viewing without risk of misplacing the original. The acquisition of digital x-ray images sometimes requires less radiation exposure than does conventional analog imaging. Also, computer subtraction of images taken at different times can quickly reveal changes in a patient's state.

Digital techniques have the potential of moving medical imaging toward an on-line, real-time diagnostic regime that promises more efficient and responsive medical care. In addition to permitting the almost instantaneous transmission of images to distant locations, digital imaging facilitates the retrieval and intramural movement of images within a medical institution. Remote transmission, called teleradiology, is already important in military medicine as a means of providing expert consultation on battlefield injuries.[12]

X-ray therapy

Very soon after Röntgen's discovery, x rays began to be used to treat cancer and a variety of other illnesses. For several decades these treatments were undertaken with x rays produced at tube potentials of a few hundred volts. Although such treatments helped many thousands of patients, some indiviuals experienced adverse side effects caused by the tissue-destroying properties of x rays. The x rays delivered the highest dose to the patient's skin, and the degree of skin reddening (erythema) was used as a measure of how well the patient was tolerating radiation treatment.

After World War II, radioisotopes from nuclear reactors became available. One such isotope, cobalt-60, had excellent attributes as a so-called teletherapy source for external-beam treatment of tumors deep inside the body. Its energetic gamma rays (1.17 and 1.33 MeV) were highly penetrating *and* they delivered their maximum dose a few millimeters below the skin surface. With the skin surface spared, patients could tolerate greater therapeutic doses. This was a major clinical advance, but it deprived the clinician of skin response as an indicator of the patient's dose tolerance.

In place of skin response, clinicians and physicists combined detailed measurements of radiation-beam characteristics with calculations of dose distributions to develop treatment plans. At first these plans were compiled manually. Soon, however, computers became essential for handling the large data volume and meeting the need to generate individualized plans. All this requires as much physics as medicine. So medical physicists quickly became pivotal members of radiation therapy teams.

Cobalt-60 does have its disadvantages. Dose rates are quite limited and the beam margins are rather unsharp. In the 1960s ^{60}Co units began to be replaced by linear accelerators designed to produce intense, sharply defined beams of high-energy (a few MeV) x rays. The development of the standing-wave, side-coupled linear accelerator was a major design breakthrough. It gave clinicians a compact high-energy accelerator ideal for use in radiation therapy where space is limited and positional flexibility is desirable.[13] Linear accelerators have now replaced ^{60}Co units for almost all external-beam radiation treatment. In addition to x rays, these units provide electron beams for treating relatively superficial tumors. Linear accelerators require extensive dosimetry and quality management, further enhancing the need for oversight by medical physicists.

For treatment of cancers in accessible organs and body cavities, implanted radioactive sources have competed over the years with external radiation sources. Implanted sources are the preferred treatment for cancers in specific organs, including the prostate, bladder, cervix and uterus. Generally they emit gamma rays, but one popular source (iodine-125) also emits characteristic x rays. The use of implanted radioactive sources is an elaborate process requiring care to protect the patient and attending personnel from excessive exposure. Detailed procedures and computations are used to ensure proper source placement and adequate radiation-dose delivery. This requires the involvement of medical physicists, working collaboratively with clinicians to meet the exacting demands of optimal patient care.

Treatment planning

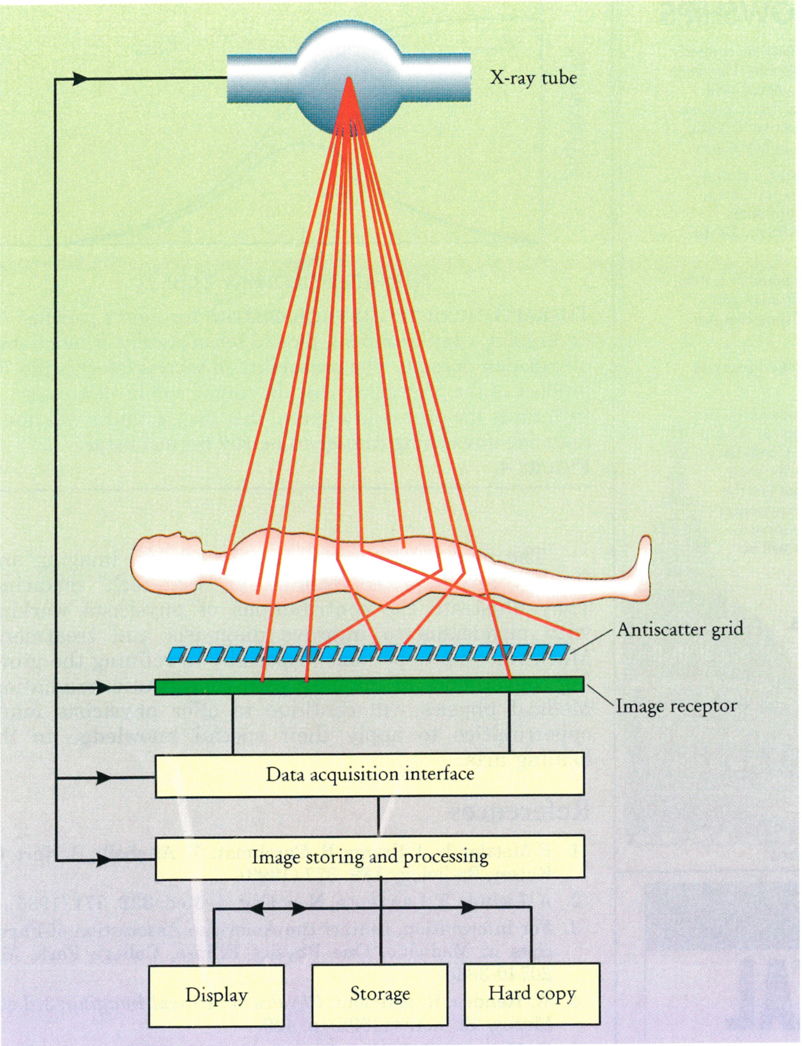
The successful treatment of cancer with x rays requires that the tumor and all of its microscopic extensions into normal tissue receive a radiation dose sufficient to kill the cancer cells. At the same time one must avoid the serious complications that result from overexposing nearby normal tissue. Figure 4 depicts the balance between these doses.[14] The probability $P_{\text{tumor}}(D)$ that the cancer will be controlled by killing tumor cells increases with D, the radiation dose. The probability $P_{\text{organ}}(D)$ that life-threatening complications from radiation damage can be avoided is, of course, a decreasing function of D. The probability $P_{\text{patient}}(D)$ that the patient will survive both the disease and the treatment is

$$P_{\text{patient}}(D) = P_{\text{tumor}}(D) \times P_{\text{organ}}(D)$$

The patient's survival probability as a function of radiation dose is the blue curve in figure 4. If the dose is low, the tumor is likely to recur. At high doses, on the other hand, the therapy itself is likely to cause unacceptable complications. Between these extremes the physician seeks to maximize the patient's survival of both the cancer and the treatment. But if the patient's discomfort is too severe at the radiation dose D_{opt} that optimizes the product of the two competing factors, the physician may choose a somewhat lower dosage.

Radiation dose optimization in cancer therapy demands careful delineation of the margins of the tumor. That requires good medical imaging. Before CT, tumor localization and treatment planning were accomplished primarily with orthogonal radiographs combined with clinical and surgical information about the patient and a knowledge of the natural course of such cancers. The use of planar radiographs had several limitations. It was difficult to visualize the tumor clearly, and difficult to transcribe the radiographic information to the cross-sectional plane used to design the treatment plan.

CT and, more recently, magnetic resonance imaging have largely overcome these difficulties. Many treatment centers have a CT unit dedicated to treatment planning



DIGITAL RADIOGRAPHIC SYSTEM creates digital x-ray images that can be displayed in real time or stored. X rays that traverse the patient unscattered are recorded at the digital receptor screen and the data are passed on for processing and display. Scattered x-ray photons are kept from the receptor screen by an antiscatter grid. FIGURE 3

and monitoring. The images not only provide a cross-sectional representation of the patient's internal anatomy, but also yield an accurate representation of the body contour and, often, excellent visibility of the tumor and surrounding normal tissues. Because the data are digital, they can be entered directly into the treatment-planning computer so that proposed treatment plans can be superimposed directly onto the CT images. Then the plan can be implemented on the treatment machine.

For such a process to succeed, however, the geometry used to acquire the CT data must correspond precisely to the patient's setup for each of the subsequent treatments. That is accomplished by laser alignment employing reference marks on the patient, and then periodic verification with a treatment simulator constructed to reproduce the proper geometry. The medical physicist must closely monitor the alignment of radiation-dose delivery with the tomographic input data and the computed treatment plan.[15]

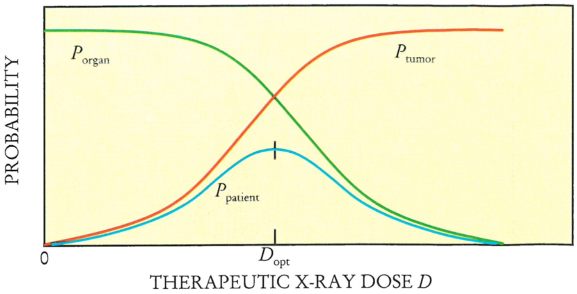
Tomographic therapy

Most applications of x-ray CT information to radiation treatment planning rely on a commercial CT scanner and various external techniques to maintain the alignment of the scanner and the accelerator with the treatment plan. But a number of medical physicists have built CT scanners on treatment-simulator gantries.[16] Usually such units compile image projections by digitizing the output from a television camera that monitors the transmitted x-ray intensity imaged on an image-intensifier screen. Although these units do not provide resolution comparable to that from a diagnostic CT scanner, they duplicate the treatment geometry and yield images good enough for treatment planning.

The images from a CT unit are gray-scale representations of the matrix of attenuation-coefficient values across a planar section through the tumor. If the matrix could be measured at the x-ray energies used in treatment, then the dose distribution could be corrected for the presence of nonhomogeneous structures in the irradiated tissue, and patient alignment could be monitored during the treatment. Several groups have successfully developed detectors and computer algorithms to accomplish these objectives with megavolt treatment machines.[17]

Most radiation treatments nowadays involve the use of multiple fixed radiation fields converging on the tumor from different angles. Thus the dose can be concentrated in the tumor while much lower doses are delivered to surrounding normal tissues. In many cases one can get an even better dose distribution by continually rotating the gantry of the x-ray accelerator around the patient during treatment so that only the tumor is constantly in the path of the beam. But this rotating-beam therapy is complicated by the fact that malignant tumors are notoriously asymmetrical. Therefore the size of the radiation field has to be varied continuously as the beam direction through the tumor changes. The dose distributions could be improved even further by also varying the beam intensity during the rotation. This approach, called conformal therapy, is being pursued in several centers in the US and overseas.[18] It requires detailed three-dimensional knowledge of the anatomy of the irradiated tissue. It also requires exquisite computerized positioning control of the accelerator, the gantry and the patient's couch.

A significant advance in conformal therapy would be the convergence of CT and megavoltage therapy in a single gantry, so that tomographic images could monitor alignment and dose distribution continually during treatment. This hybrid approach remains to be developed in full.[19] It presents a number of challenges, but the potential benefit is considerable.



THERAPEUTIC OUTCOME PROBABILITIES for cancer patients undergoing x-ray treatment, plotted schematically as functions of radiation dose D. The probability of success (blue) is the product of the probability that the tumor will be destroyed (red) times the probability (green) that the treatment will not cause life-threatening damage to nearby normal tissue. FIGURE 4

The modern uses of x rays for clinical imaging and therapy are a prime example of "high-tech" medicine. They illustrate the contributions of physicists working with physicians to improve diagnosis and treatment. Much remains to be done, especially in refining the growing convergence of imaging with therapeutic irradiation. Medical physics will continue to offer physicists many opportunities to apply their special knowledge to the healing arts.

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