New Instrumentation in Radiation Oncology

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Radiation oncology's contribution to cancer therapy is the local and regional control of malignant neoplasms, with complete regression as the usual result of definitive radiation therapy. Despite an overall local response rate of approximately 95 percent, permanent control in the treated regions does not always result. Of 12 sites of disease in which radiation therapy plays an important or adjuvant role, failure of local control resulted in an estimated 65,000 deaths in the United States in 1975.1 Failures occur when:

1. a tumor is so large that tolerable doses of radiation are insufficient to sterilize all the cells;
2. the volume encompassed by the high dose of radiation is inadequate to include the entire tumor, either because of its size or an inaccurate estimation of its actual extent;
3. a tumor contains a cell population that is resistant to conventional radiation;
4. a uniform dose distribution within the tumor volume is unachievable;
5. normal tissues of limited tolerance are situated in the irradiated volume.

Local control will become crucial as more successful chemotherapy is developed to provide more patients with longer survival and, thus, a longer period for local tumor regrowth.5 It will become necessary to improve the radiation therapy of primary and regional disease to provide local control during increasingly long remissions of metastatic disease. In addition, more effective radiation therapy will be required for patients with tumors in sequestered sites in which disseminated disease is effectively managed by chemotherapy or im-
munotherapy, e.g., brain irradiation of children with acute lymphocytic leukemia.

The development of new instrumentation in radiation oncology attempts to overcome current limitations. To improve results, a tumor must be identified earlier when it has fewer cells. Its total extent must be correctly delineated. It should then be encompassed with a sufficiently high dose of biologically effective radiation for sterilization, while minimizing the damage to normal structures. The advances in instrumentation that are of the greatest interest are those that improve tumor delineation, increase dose localization, and provide new sources of ionizing radiation with advantageous radiobiological properties.

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**TUMOR LOCALIZATION**

Computed Tomography

The computerized axial tomographic (CAT) scanner is an encouraging new instrument, which should greatly assist in early tumor detection and localization. Now in fairly common use for the head, CAT scanning is becoming more available for the whole body. (Fig. 1.) This device can locate very small lesions in sites such as the brain and pancreas which are now detected only at advanced stages.

CAT scanning measures the transmission of a narrow X-ray beam through a section of the body at numerous orientations. With the aid of a digital computer, the transmitted intensity at each orientation is mathematically reconstructed into an image that depicts tissue density variations in the anatomical cross-section. Commercially available head and whole-body CAT scanners are capable of detecting density variations of one percent or less, and are able to resolve three mm. structures. The dose is acceptable for individual exposures, but would be significant in a mass screening program. The data reduction process is
relatively slow and subject to possible error. At the University of Arizona, axial tomograms using a simpler and less expensive optical reconstruction technique are being investigated and show promise for the near future.

Axial tomography, computed or optically reconstructed, will have a major impact on radiation oncology, since it can delineate a tumor accurately in three dimensions in relation to the surrounding normal structures and provide highly detailed information on the radiation absorption characteristics of the tumor and the normal tissues through which the beam passes. The latter information is critically important in definitive treatment planning. Absorption coefficients derived from CAT scans can correct the treatment plan for differences in tissue density thus providing more accurate dose administration in each patient. This will represent a considerable improvement over the assumption of uniform density that forms the basis of most treatment today.

Heavy Ion Radiography
Accelerated charged particle beams, such as protons or carbon ions (heavy ions), are being investigated as a possibly superior method of delineating tumors and surrounding structures. The properties of charged particle beams are such that small density differences within an absorbing medium dramatically affect the depth of penetration. The range of these particles is very well defined and small differences in path length due to slight variations in density are readily detectable. With an appropriate detector, density differences of 0.1 percent are measurable within the volume of interest. This is an impressive improvement over present imaging systems and could provide a superior tool for low-dose, high-density discrimination radiography, capable of defining the extent of a neoplasm surrounded by soft tissues. In addition, density distribution plots in three dimensions can be reconstructed from particle radiographs. For example, it might be possible to precisely define the position of a gastric carcinoma and map its density as well as that of adjacent structures, in three dimensions from two views separated by 90° (a right angle pair of radiographs). This type of study would be of significant value in defining tumor volumes and providing information on tissue densities, thereby greatly facilitating accurate treatment.

DOSE LOCALIZATION

The radiosensitivity of malignant cells often approximates that of normal cells in the tissues surrounding and intermixed with a tumor. Consequently, the most important factor in determining whether a tumor can be destroyed, without severely damaging normal tissues, is the ability to restrict the high-dose zone of irradiation to the tumor. The smaller the volume of tissue irradiated to high dose, the greater the tolerance of intermixed and adjacent normal tissues. Some of the instrumentation developed to assist the radiation oncologist in achieving this goal is described below.

Computerized Treatment Planning
Dose localization has been improved by the use of computers that have been developed for calculating the radiation dose distribution within a patient for a given treatment set-up. With computerized treatment planning, it is possible to optimize dose distributions resulting from sophisticated treatment techniques, an exceedingly difficult and time-consuming task to compute by hand. Computerized treatment planning assists in optimizing the use of special radiation techniques, which include:

- Multiple angle beam entry to shape a high-dose radiation volume within the
patient while sparing tumor-free tissue in the path of radiation.

- Arc-therapy techniques, in which the radiation source circumscribes the tumor volume during treatment. This procedure also has the goal of sparing normal tissue. Rotational therapy uses a full 360° arc, analogous to employing an infinite number of stationary multiple beam entry points.

- Wedge-shaped radiation absorbers in the beam paths to modify the beam penetration characteristics to tailor high-dose zone to treatment volume.

The quantitative tissue density information available from CAT scanning or heavy ion radiography can be applied directly to improve the accuracy of planning calculations. Computer planning systems are relatively fast and display the results electronically, enabling the physician to examine a number of treatment plans in rapid succession and to select the optimal plan.

Simulators

Dose localization is further improved with the radiation therapy simulator. Simulators (Fig. 2.) are radiographic units that reproduce the physical configuration of a treatment machine. In combination with a patient couch, which duplicates the motions of the treatment couch, the simulator can perform either fluoroscopy or diagnostic radiography under conditions identical to that used during therapy, thereby enabling the radiation oncologist to observe the exact region in a patient’s body that will be traversed by the therapy beam. Treatment fields can be more precisely shaped to selectively irradiate a tumor. In addition, simulators are valuable as teaching devices.

Reproducibility of Treatment

Having determined the desired treatment plan, reproducibility of treatment set-ups on a day-to-day basis is critical,
whether a few or many treatment sessions are used to deliver the therapeutic dose.  

Modern therapy equipment is capable of various beam angulations and couch orientations. The radiation source can rotate 360° to direct the beam at any angle through the center of rotation. In addition, the treatment couch can translate the patient in any direction and rotate in the horizontal plane, providing a wide variety of beam orientations. To fully utilize this versatility, new instrumentation is continuously being developed to aid in accurate repositioning of the patient and the machine.

Patient Repositioning
Patient repositioning and immobilization are most often accomplished by restraining devices, which include plaster casts and, more recently, plastic molds. Head and neck repositioning is achieved with bite-blocks, which are individual dental impressions rigidly fixed in relation to the beam.

The beams of lasers mounted on the treatment room walls and accurately aimed to converge at the center of machine rotation are also useful as repositioning devices. The position of each laser beam on the patient’s skin is marked at the initial set-up and used for subsequent repositioning.

Machine Repositioning
Modern therapy equipment provides indicators to aid in repositioning. Physical scales with pointers are most common. In some equipment, positioning is monitored electronically to provide digital readouts of the machine parameters, such as field size, beam angle and couch position. Lasers may also be mounted on the accelerators to help reposition the beam angle. A laser mounted perpendicular to the central axis of the radiation beam and directed toward the treatment room wall acts as a long lever arm to provide a very sensitive indication of beam angle. In this manner, the machine angle can be reproduced to within 0.1 degree.

Video Repositioning
A video system has been developed to reposition both the patient and the machine. A video disc stores the closed
Fig. 4. Electrons. From this versatile and more sophisticated accelerator, a higher energy X-ray beam is produced (10-MV). In addition, the target can be retracted to allow extracted electrons to be used as a therapy modality. This accelerator can produce five discrete electron energies of 6, 9, 12, 15 and 18 MeV, thus enabling a variable depth of penetration for treatment. The electron collimator, which extends to within two cm. of the skin surface, is shown connected to the X-ray collimator assembly.

Modern Radiation Sources

Very high energy X-rays from betatrons or linear accelerators deliver relatively little dose to the skin and subcutaneous tissues (skin sparing), a characteristic that significantly reduces the morbidity of radiotherapy. Linear accelerators (Fig. 3.) are tending to replace the versatile and highly successful Co-60 therapy units. Advantages being sought in this transition to newer equipment are:

- more sharply defined radiation beam;
- improved sparing of superficial tissues and better dose at target depth;
- higher dose rates and shorter treatment times, which reduce errors in position due to patient motion.

The X-rays from a 4 MeV accelerator are significantly better focused and slightly more penetrating than the gamma-rays of Co-60. X-rays of 10-45 MV are much more penetrating than Co-60 gamma-rays, and deliver a much lower dose to normal tissues when treating deep-seated tumors.
Electron beams (Fig. 4.) are produced by commercially available high-energy linear accelerators or betatrons. The physical characteristics of electrons provide an advantage over X-rays, resulting from their finite mass and limited range in tissue as compared with X-rays which are attenuated exponentially in tissue. Electrons are useful when the tumor volume is situated directly over a critical organ or tissue. By varying the energy of the beam, penetration can be adjusted to treat the tumor while sparing the deeper tissue.

Protons also provide an opportunity for improved dose localization. Due to their larger mass, protons scatter less than electrons and their range in tissue is sharply defined. Protons exhibit a characteristic referred to as the Bragg peak phenomenon, in which the dose at the end of the range is greatly enhanced, and the protons deposit a significant amount of energy at the very end of their path. Proton beams can be localized with a precision measured in terms of millimeters. In most clinical situations, definition of the exact volume at risk is far less precise than the ability to localize a proton beam. Consequently, utilization of the extreme precision of this interesting form of irradiation rests on the development of our abilities to more precisely localize tumor volumes and to handle the problems of density variation in normal tissues (bone or lung versus muscle tissue). Unless corrections are made for variations in tissue density, the precise stopping region of protons can result in the dose being localized in precisely the wrong place. This is a general problem in charged particle therapy.

NEW TYPES OF RADIATION

The major thrust in the development of new therapy machines is derived from studies indicating that densely ionizing radiations have certain radiobiological properties that might be advantageous in treating cancer. Conventional modes of irradiation, such as X-rays, gammarays and electrons, are all forms of low LET radiation (linear energy transfer). LET refers to the average loss of energy of a radiation particle per unit length of the path in an absorbing medium. Densely ionizing radiations have a relatively high LET. Examples of high LET radiation include neutrons, negative π mesons and heavy ions (nuclei of carbon or nitrogen). High LET radiations have a greater effect on anoxic tumor cells for a given degree of damage to normal, well-oxygenated cells.

Neutrons

Neutron accelerators are now commercially available (Fig. 5.) and imaginative new models are being planned, such as the proton linear accelerator with beryllium target, studied at Los Alamos. (Fig. 6.) Neutron beams are the most readily produced form of high LET radiation and are currently being used in clinical trials. They have been compared with megavoltage X-rays in the control of advanced head and neck cancers at Hammersmith Hospital in London, and appear to be more than twice as effective in producing complete tumor regression for a given degree of normal tissue damage. With the current availability of commercial neutron sources, these encouraging results should stimulate much more intensive clinical trials.

While the radiobiological qualities of neutron beams partially exhibit the favorable characteristics of high LET irradiation, the physical properties of the neutrons make them less than ideal for clinical therapy. Neutrons scatter widely and are absorbed exponentially like X-rays. Many of the available neutron sources for clinical work generate beams of insufficient energy for good tissue penetration. For these reasons, it is relatively difficult to selectively irradiate the tumor bearing volume of tissue without...
Fig. 5. Neutrons. In this commercially available neutron generator, deuterons are accelerated to 15-MeV in a cyclotron (A.) and then magnetically transported and focused on a beryllium target. The target is isocentrically mounted and capable of rotation through a 240° arc. The penetration of this neutron beam is less than that for a Co-60 beam. The Cyclotron Corporation is currently building a neutron generator that will utilize the fusion of deuterium with tritium to produce 14-MeV monoenergetic neutrons to overcome the penetration difficulties of this machine. Field definition is provided by a set of collimator inserts. A dose monitoring system, field definition light and range projector for clinical applications are provided. (B.) Isocentric neutron therapy system with head in vertical position, with shroud.
also delivering large quantities of irradiation to intervening and surrounding normal tissues.

Negative \( \pi \) Mesons

Negative \( \pi \) mesons are even more densely ionizing than neutrons near the end of their range. They interact with tissue atoms producing an explosion of densely ionizing particles termed “nuclear stars,” which deposit biologically effective energy in the target tissue. Unfortunately, the equipment necessary to produce a \( \pi \) meson beam is expensive and complex, presently limiting their availability to a few large physics accelerators (Los Alamos, New Mexico, Vancouver, British Columbia and Zurich, Switzerland). A design for a hospital based \( \pi \) meson facility, exclusively for medical use, has been developed at Stanford University, California.

Heavy Ions

Heavy ions, such as the nuclei of carbon and nitrogen, can be accelerated to energies sufficient to provide a beam with excellent tissue penetration. These particles exhibit a very high LET and a pronounced Bragg peak, which permits them to be localized with extreme precision. Heavy ions provide both desirable radiobiological characteristics and precise beam localization. At the present time, there are few heavy ion facilities
Fig. 7. Heavy Particles. This figure illustrates a possible configuration for a hospital-based medical heavy ion accelerator with four treatment rooms (with co-functions for particle radiography). This preliminary conceptual drawing is derived from a joint feasibility study between the Accelerator Division of the Lawrence Berkeley Laboratory and the Division of Radiation Oncology and the Physics Department at the University of Arizona. Shown in the extreme left-hand position of the figure is the accelerator room housing a synchrotron, utilizing a cyclotron for particle injection into the main accelerator. Since the injector requirements are not stringent, the cyclotron can be used to operate an in-house isotope production facility. After extraction, the beam transport systems will switch the therapy beams between the four treatment rooms as indicated. The design criteria in the feasibility study are to accelerate ions up to carbon or neon nuclei at intensities of approximately 10^7 particles per second. The goal will be to treat the tumor volume at about 200 rads/min., thus providing for short treatment times.

in the world, and the equipment currently used for their production is expensive. However, the few heavy ion beams available for clinical use are derived from accelerators designed for research in basic nuclear physics. Clinically dedicated heavy ion accelerators are being developed (Fig. 7.) and may be available for clinical trials within the next five years.

SUMMARY

Technological advances of the past decade have resulted in the current commercial availability of linear accelerators capable of producing high-energy X-rays and electron beams of great advantage in the treatment of human cancer. The use of low LET irradiation has been optimized to provide improved local tumor control with less normal tissue damage, for example, a better therapeutic ratio. X-ray and electron beams of higher energy would have no additional clinical advantage. Consequently, future development of new medical radiation sources will concentrate on the investigation of charged particle beams and neutrons.

It seems probable that the use of densely ionizing radiation could double the rate of local control of many cancers,
an improvement which would save countless lives and prevent an enormous amount of suffering. However, many patients will continue to succumb to metastatic disease even if the primary tumor is eliminated. The use of adjuvant chemotherapy and possibly immunotherapy to destroy microscopic metastases before they become clinically apparent, may greatly increase the cure rate of patients with primary tumors eradicated by combinations of surgery and irradiation. If adjuvant chemotherapy and/or immunotherapy are found to be even moderately successful, improved local and regional tumor control by irradiation will, to a great extent, be translated into cures.

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