Anniversary Paper: A sampling of novel technologies and the role of medical physicists in radiation oncology

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Physicists have and continue to play a major role in the creation and introduction of novel technology into medical care. This review covers some of the highlights of contributions of medical physicists to the field of radiation oncology during the history of the AAPM. While not comprehensive, the broad scope of developments and their impact hints at the importance of the medical physicist in advancing the field in the past, present, and future. © *2008 American Association of Physicists in Medicine*. [DOI: 10.1118/1.3021006]

Key words: innovation, medical physics, history, radiation oncology

I. INTRODUCTION

One of the most important roles that medical physicists have played is the development and introduction of new and useful technologies into clinical medicine. Some of these technologies were invented and implemented within the medical physics community (e.g., linear accelerators, digital subtraction angiography, radiation therapy treatment planning). Others were outside technologies that were put to work in the clinical environment (e.g., radionuclides). Still others were developed for medical use outside the hospital and applied clinically with medical physics help (e.g., image intensifiers, gamma cameras). These devices unquestionably improved the diagnosis and treatment of patients during the 50 year AAPM era.

This article reviews a very limited selection of such technologies, with a specific focus on the field of radiation oncology. Reviews are never complete. The random walk presented below is largely colored by the experiences of the authors. Indulgence is requested from the multitude of medical physicists whose contributions equaled or exceeded the few discussed here.

Three benchmark years are 1958, the founding of AAPM, 1983, the 25th anniversary, and 2008, the 50th anniversary. To provide some focus, a hypothetical patient with pancreatic cancer and/or possible multiorgan metastasis is pictured at each benchmark.

II. 1958: AAPM FOUNDED

In 1958, the pancreas was essentially invisible to all of the available imaging modes. These were radiography using film or film-screen systems, GI fluoroscopy using direct fluorescent screens and barium, and nuclear detectors observing inorganic radionuclide compounds. Brain and liver metastasis were almost invisible. Lung metastases could be seen once they grew to a size of several centimeters. Definitive diagnoses were made using exploratory surgery. Treatment options for the pancreas were usually a choice of radon seeds or 250 kVp external beam therapy. A few centers offered megavoltage beams. External beam treatment planning was done by hand using water isodose curves and educated guesses regarding the locations of the tumor and nearby critical organs. Brachytherapy for a pancreatic cancer could not be planned. Post-implant radiographs were used to estimate the implanted dose. These calculations were generally based on the major diameters of the implant, the implanted activity, and an estimate of the homogeneity of the implant.

II.A. Treatment delivery

In 1958, there were few early cancers that could be identified using available imaging technologies. Exploratory surgery was the available alternative for the diagnosis and staging of disease. Radiation therapy was typically used to treat the inoperable cancers found by this process. Most "deep" external beam therapy was delivered using 250 kVp beams (Fig. 1) because there were only a few megavoltage machines available in the USA. Most of these were 1–2 MV x-ray sources. A few betatrons were available, producing both photons and electrons. Radon seed permanent implants were placed in deep seated lesions at the time of surgery. Removable implants using radium needles and capsules were applied in accessible locations (Fig. 2).

The first medical linear accelerator in the United States was put into use at Stanford University about the same time as the AAPM was founded. This system, a 6 MV accelerator, was developed by the physics group under the vision of Henry Kaplan, M.D. in Collaboration with EL Ginzton, and began treatments in 1956 (Fig. 3). Dr. Ginzton was a pioneer in the design of linear accelerators for national laboratories, as well as medical purposes, and was a cofounder of Varian Associates. The first clinical physicist working with the Stanford Medical Accelerator, Mitchell Weissbluth, described the characteristics of the system in one[1] of a series of reports on

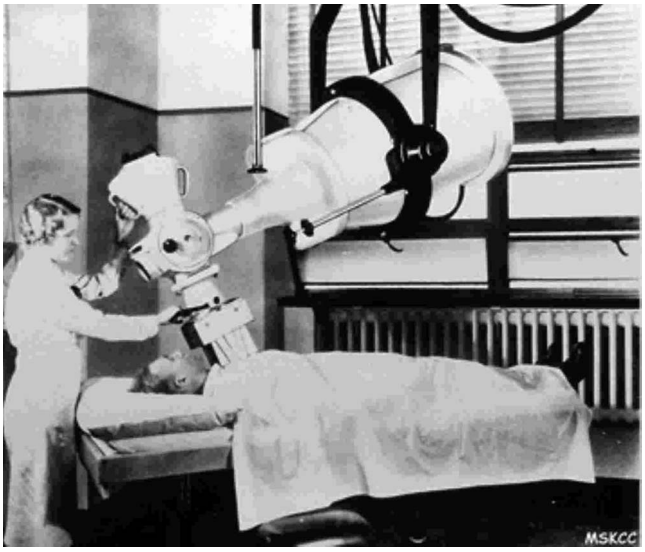


FIG. 1. 250 kVp at MSKCC. This photo was taken in the late 1930s. The machines in service in the late 1950s were quite similar in appearance.

the device,[2–4] and further studied biological properties of higher energy photons available on the Stanford Linear Accelerator.[5]

Particle therapy was initially proposed in 1946.[6] The first treatments at various high energy particle physics accelerators in the 1950s were followed by more dedicated treatments at the Harvard Cyclotron Laboratory. In this early period of particle therapy, various more exotic heavy and subatomic particles, such as neutrons,[7,8] pi mesons,[9] and heavier ions[10–12] were discussed and experimented with. The period from 1958–83 was a very active era in particle therapy research, with a wide variety of experiments report-

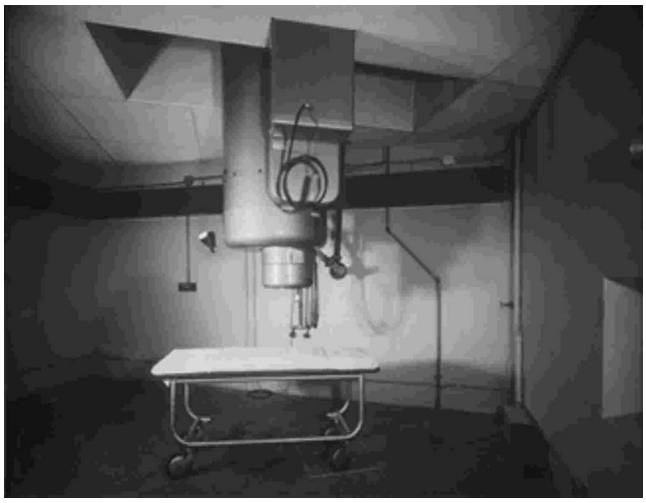


FIG. 3. The first medical linear accelerator at Stanford University (courtesy of R. Hoppe).

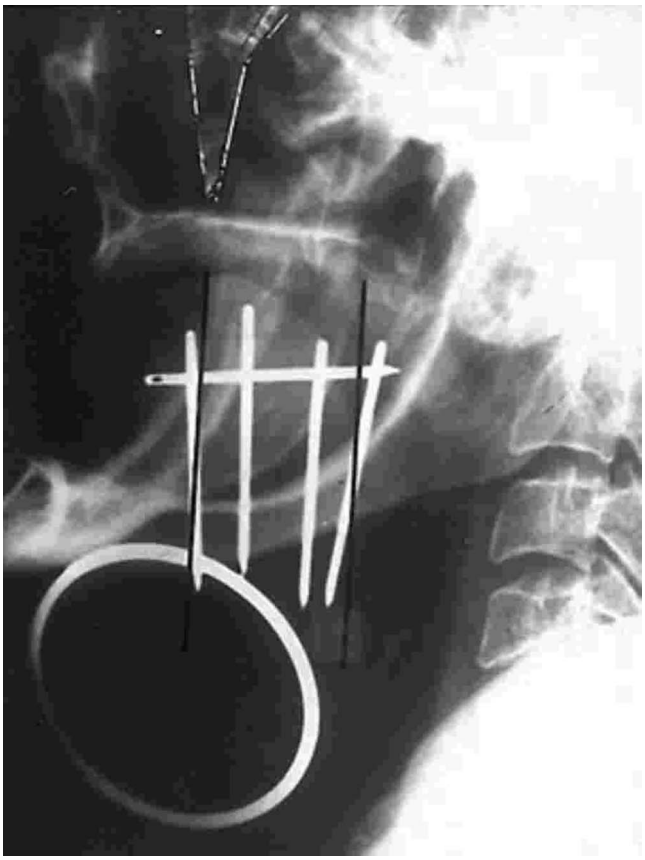


FIG. 2. Radium needle implant to the tongue. Patterson–Parker dose calculations accounted for only one end of the implant being crossed. Note the magnification ring.

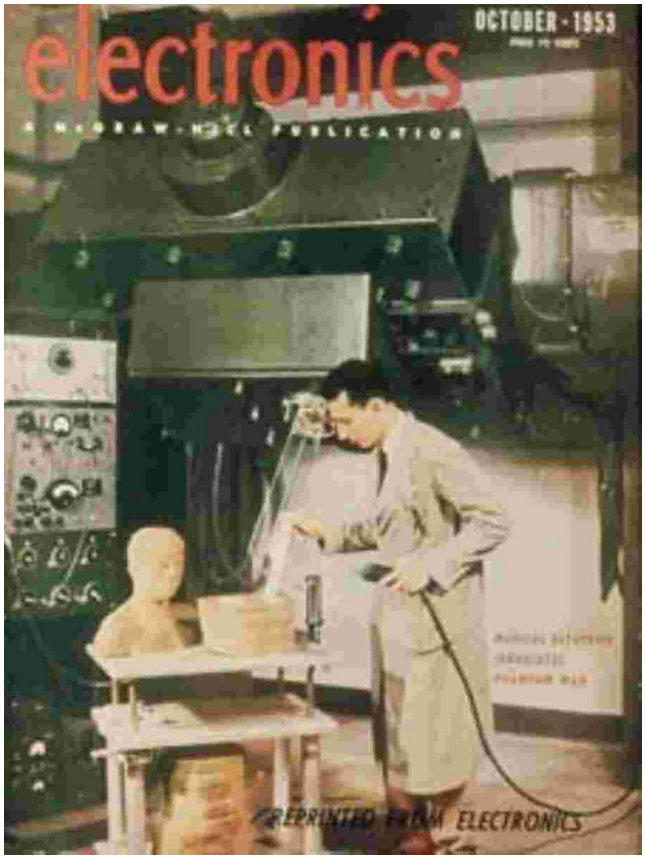


FIG. 4. MSKCC Betatron (electrons only) and phantom with inhomogenieties.

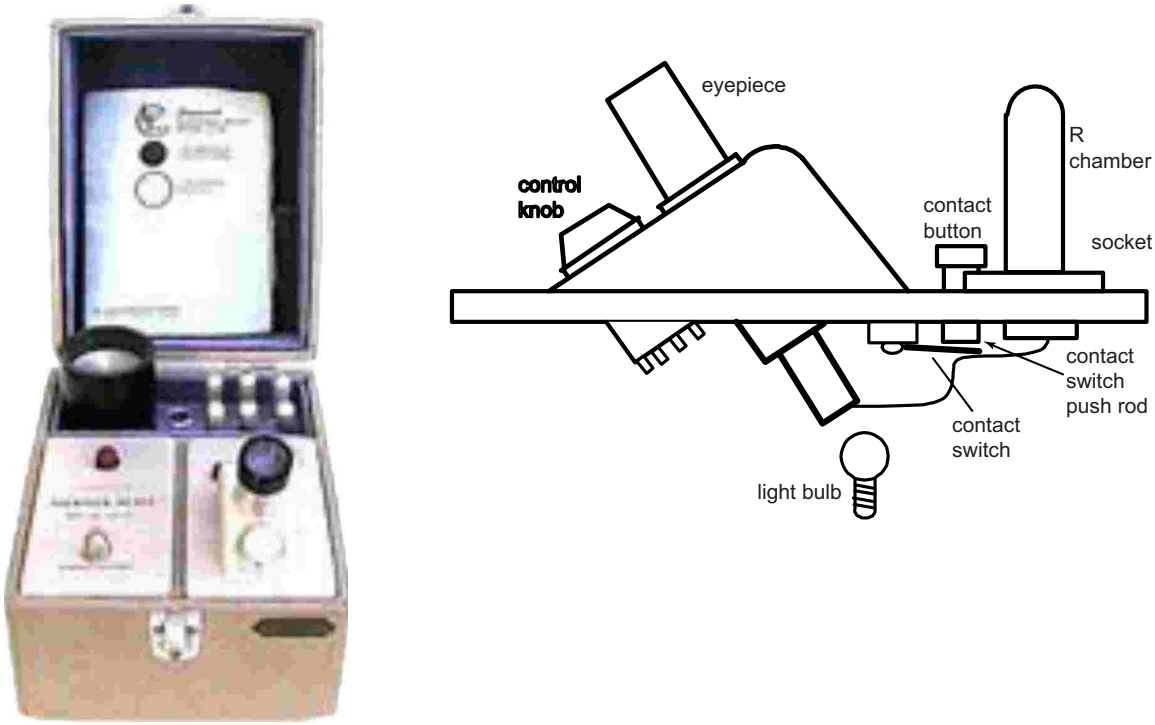


FIG. 5. Lansverk electrostatic dose meter with "miniature" ion chambers. These are charged before used and read after exposure with an electroscope. They were small enough to place in a phantom. (Images from ORNL courtesy of Paul Frame).

ing on energy deposition and biological effects. Clinical neutron accelerators were developed, including systems located within hospitals.

II.B. Calibration and dosimetry

Determining "dose" in radiotherapy was a major research focus of the medical physics community in the 1950s. Areas of concern were determining the activity of a radioactive source, the output of a supervoltage machine, and the distribution of dose within a patient.

The "New York Millicurie" was established by intercomparison of standards between institutions in the region. These interactions between medical physicists contributed to the formation of RAMPS a decade before AAPM. The definition of the activity of a sample was eventually stabilized by the National Bureau of Standards (now NIST).

Because of electron equilibrium issues, the calibration of high-energy machines was limited by the physics of the free-air chamber to photon energies below 3 MeV. Various techniques, including absolute calorimetric measurements and cavity ionization methods, were developed locally to enable calibration at emerging higher energies. Major centers had their favorite high precision methods. Unfortunately, the disagreement between centers often exceeded the claimed precisions. The Scientific Committee on Radiation Dosimetry (SCRAD) was formed to resolve these differences. The 1966 and 1971 SCRAD reports on electron and photon dosimetry[13,14] were fundamental to dosimetric traceability and the intercomparison of clinical results.

Direct measurements of patient dose were essentially impossible in the 1950s. Phantom measurements were tedious and only yielded results under highly defined conditions. Figure 4 illustrates such an experiment using an "advanced" anthromorphic phantom with cork lungs. A few miniature ion chambers (Fig. 5) could be charged, placed within cavities in the phantom, irradiated, and visually read using an electroscope. These measurements were usually used to normalize the dosimetry of films placed between phantom slices. Precision film dosimetry was itself an art. Cameron's introduction of TLD into radiation dosimetry changed the paradigm.[15] As many TLD powder capsules (later chips) as the experimenter had patience to prepare could be put into a phantom and read out at leisure. Of greater importance, TLD could be used for surface or intracavitrary dosimetry during routine examinations or treatments.

II.C. Treatment planning (1958–1983)

The era started with manual treatment planning for external beam therapy being done with central axis depth dose tables such as those found in Johns and Cunningham.[16] Two dimensional isodose curves were available and used to prepare 2D treatment plans (Fig. 6). Close inspection of the esophageal treatment plan (Fig. 7) shows typical simplifications used in this era: The isodose distribution is shown without correction for skin curvature and the beams are not perturbed by the spine (shown) or lungs (not shown).

It was always understood that the patient was neither a homogeneous ellipsoid nor a rectangular box. Procedures were available to accommodate external contours (Fig. 8).

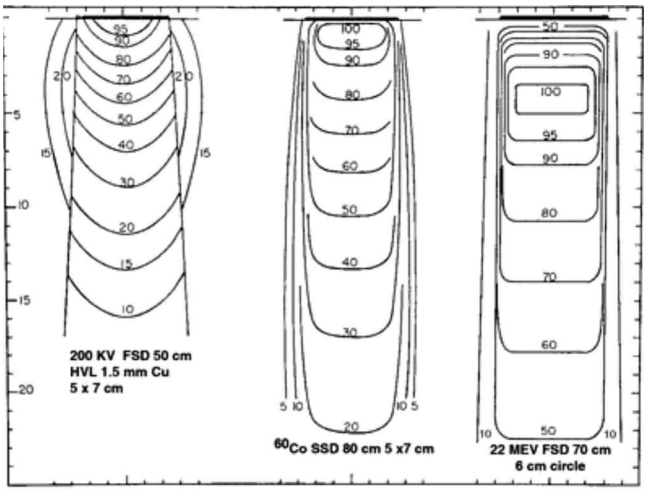


FIG. 6. Isodose curves from typical systems in use in the mid 1960s (Johns and Cunningham).

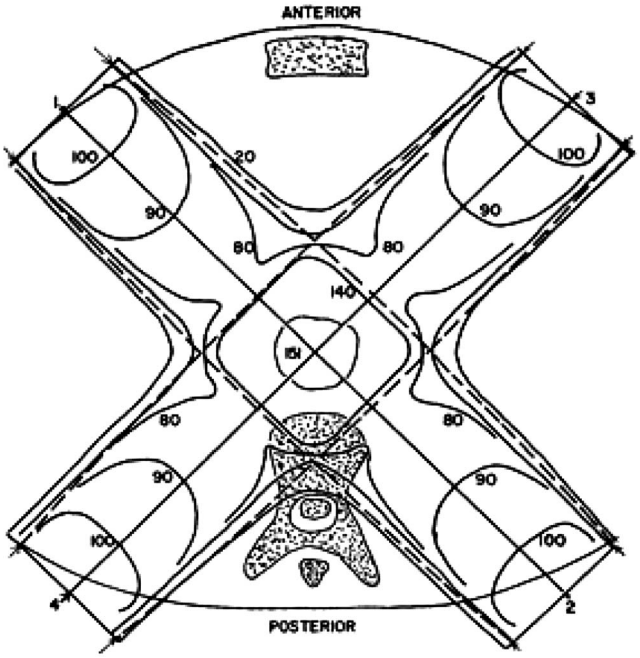


FIG. 7. Manual cobalt treatment plan from the mid 1960s. Note isodose curves in air, sparse anatomy, and the absence of density corrections (Johns and Cunningham).

Eycleshymer and Schoemaker's 1911 cross-sectional atlas was used to estimate the location of internal structures. This atlas was based on the average anatomy of 11 subjects. It was last reprinted in 1970.[17] A typical section is shown in Fig. 9. Such drawings were occasionally optically warped to fit the measured contour.

In the 1960s, there was a commercially available tomography which could image a patient in a supine position (Fig. 10). Diagnostic imaging underwent revolutionary changes in the 1970s. These included the early development of CT, MRI, and PET imaging. The advent of CT in the early 1970s and MRI at the end of this decade provided previously unavailable means for noninvasive delineation of the patient's anatomy and extent of disease. PET was emerging, but was not used in large clinical volumes at this time.

As soon as CT was available, it had an immediate and major impact on treatment planning. For example, Emami *et al.* found chest CT to be essential in 17 of 32 patients. Similar results were found by many other groups.[18] The basic improvements brought by CT were better delineation of target and normal structures, and estimation of tissue density. Figure 11 illustrates an early CT-based plan including tissue density corrections. Although the plan is crude by 2008 standards, it reflects a significant advance over prior dose estimation methods (e.g., in Fig. 7).

Computer based treatment planning was proposed in the 1950s by Tsien.[19] The increasing availability of digital computers provided Stovall and Shalek at Anderson[20] and Balter and Laughlin at Memorial[21] means to develop brachytherapy dosimetry programs in the early sixties. External beam programs soon followed.[22] By today's standards, this first generation of clinical programs were unbelievably slow. The first clinical Memorial brachytherapy program required 100 ms for a single inverse square calculation. Its output was usually presented as points with 1 cm spacing; the isodose curves were drawn by hand (Fig. 12). Within a few years, speeds had increased to the point where computational spacing could be reduced to the size of a single teletype character or to adequately drive a plotter (Fig. 13).

Treatment planning offices in Memorial were overfilled by local physicists who dropped by to run plans for their patients. A remote treatment planning network was developed to give these individuals access at their own institutions.[23] This program ran for several years until semicommercial treatment planning machines such as the programmed console[24] and the fully commercial SHM RAD-8 (Ref. 25) became inexpensive enough to be affordable by most radiotherapy centers. These devices are shown in Figs. 14 and 15.

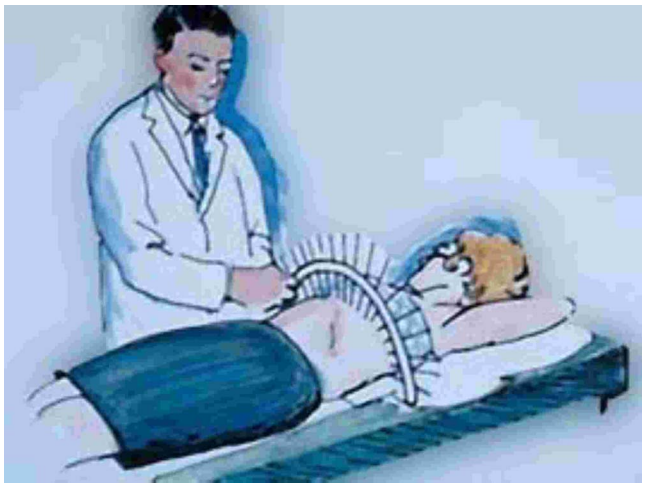


FIG. 8. Mechanical contouring device c 1965 (MSKCC).

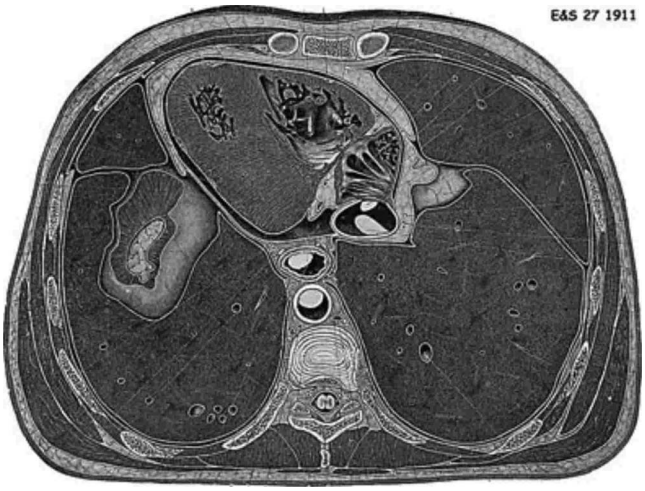


FIG. 9. Page from anatomical cross section atlas often used for pre-CT treatment planning (Eycleshymer and Schoemaker).

The RAD-8 image (Fig. 15) was extracted from an advertisement in Radiology published in the early 1970s. The ad states that the system "gives you the added computational power of a 16 k minicomputer, the PDP-8." The same ad also states that there were 20 000 PDP-8 computers installed worldwide.

CT descriptions of patients and treatment planning computers came together in the late seventies. Internal and external contours were initially input by tracing the photographic output of the CT scanner. The one advantage of this tedious method of data input is that it could work with any CT scanner and any treatment planning computer. Digital versions of CT images were available on 9-track magnetic tape and/or 8-in. floppy disks. Every CT manufacturer had their own proprietary data format. The need for a common format was recognized by the AAPM. Report 10 (Ref. 26) specifies a common interchange format. The basic internal structure of this format was tag-value pairs. This flexible format was adopted by ACR-NEMA for digital data storage and eventually evolved into a key part of DICOM.

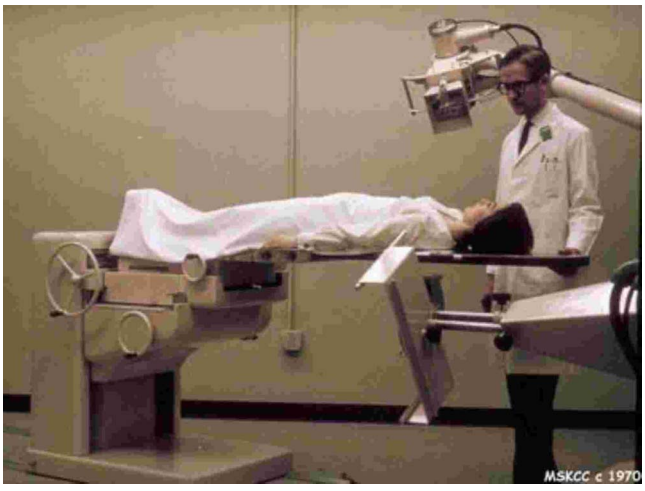


FIG. 10. Mechanical axial tomography (Toshiba) designed for treatment planning. Patient is in the treatment position. Note the film cassette holder.

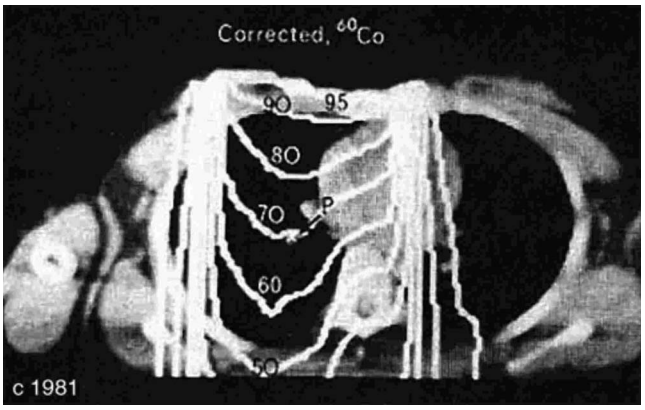


FIG. 11. Betatron treatment plan c 1980. CT cross-sectional image of anatomy. Plan is corrected for tissue density (courtesy of J. Cunningham).

There was (and is) a real need to verify the adequacy of the treatment plan. Portal films, taken on the treatment machine itself, had been employed for a long time. These images are adequate when the plan consists of a few static fields. The process was increasingly inefficient as the number of fields increased and almost unusable for moving fields. Physical radiation therapy simulators were introduced in the late 1960s.[27–30] These simulators replicated the geometry and mechanical movements of the treatment machine with the

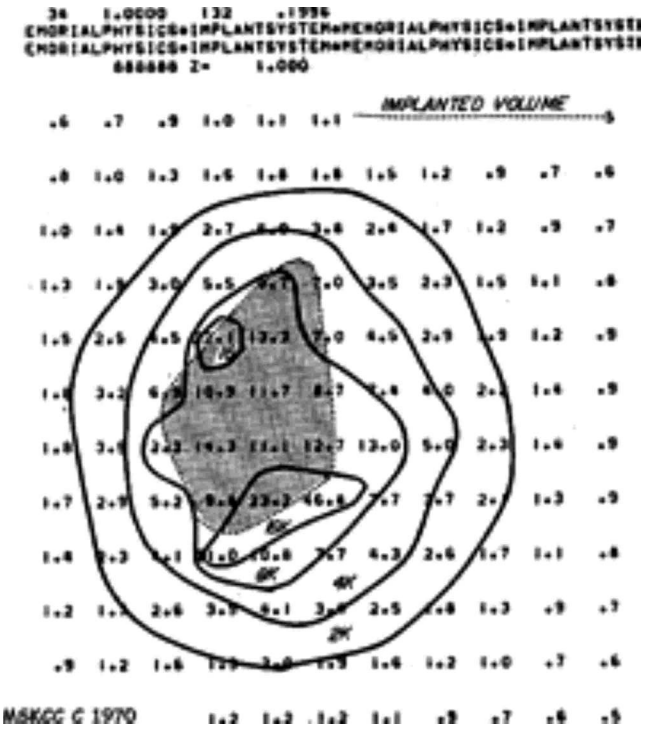


FIG. 12. One plane of the output of a seed implant calculation. The isodose curves were drawn manually. The implanted volume was defined by calculating the intersection lines between each seed and every other seed. The high-dose region outside the implant was due to close seeds in a different plane (MSKCC).

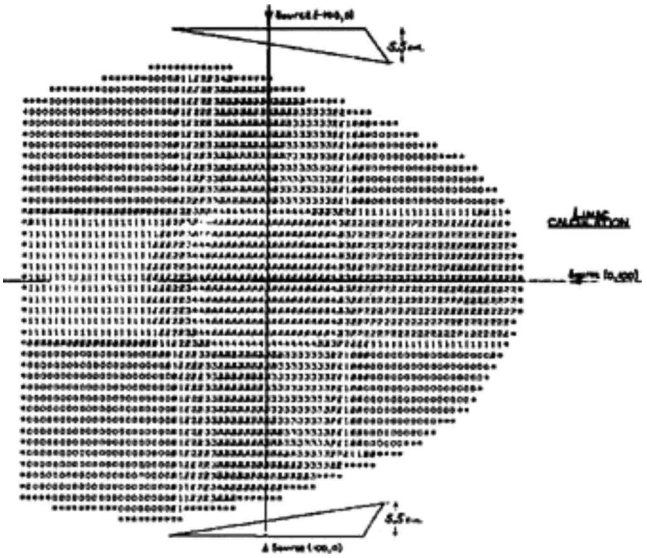


FIG. 13. Output for a three field treatment plan sent by teletype from the Memorial Dose Distribution Computation Service. The beam information and wedges were hand drawn later. The percentage depth dose was calculated for each character position. The character coded its value (Holt).

improved imaging associated with a diagnostic fluoroscope (kV beam) and image intensifier (Fig. 16).

Brachytherapy planning requires knowledge of the source positions. The mathematics of reconstructing the location of a metallic object in a patient were well described in the first volumes of most of the major radiological journals. The major problems needed to extend the mathematics to the automatic description of seed implants are the identification of the same seed on each of the radiographs used for the reconstruction and information on the location of the x-ray tube focal spot relative to each image. A rigid frame provided the solution (Fig. 17). Fixed tube positions and fiducials in the cassette trays define the geometry, and thus lines can be traced from each seed image back to the focal spot. The intersections (or closest approaches within a specified tolerance) of the lines from two or three films uniquely identify individual sources.[31] This method seems to be independently

FIG. 14. Programmed Console c 1967 software and data resided on the magnetic striped cards. Note the graphic input device used for entering contours (Cunningham).

FIG. 15. Rad-8 treatment planning system c 1973 (from *Radiology*, reprinted with permission).

reinvented every decade for one treatment purpose or another.[32] A variant is currently used for HDR reconstructions. Here, two sets of fiducial markers are used to construct the location of the focal spot relative to the film. Individual source positions are unambiguously identified by the shapes of targets on continuous dummy ribbons.

II.D. Multileaf collimation

The need to spare normal tissues has been apparent from an early stage of radiotherapy. While beam quality is one factor in tissue sparing, field shaping can arguably be considered most critical to this process. Various forms of field shaping devices have been developed over the past 5 decades, but the multileaf collimator (MLC) is clearly an invention that has proven critical to the advancement of precise radiation delivery.

Takahashi described the MLC in 1965 as part of a system to aid in rotational therapy.[33] In 1979, Sofia reported on a computer-controlled MLC, paving the way for modern MLC design and implementation.[34]

III. 1983: AAPM SILVER ANNIVERSARY

The AAPM's first quarter century was a golden era for medical physics and the radiological sciences. The funda-

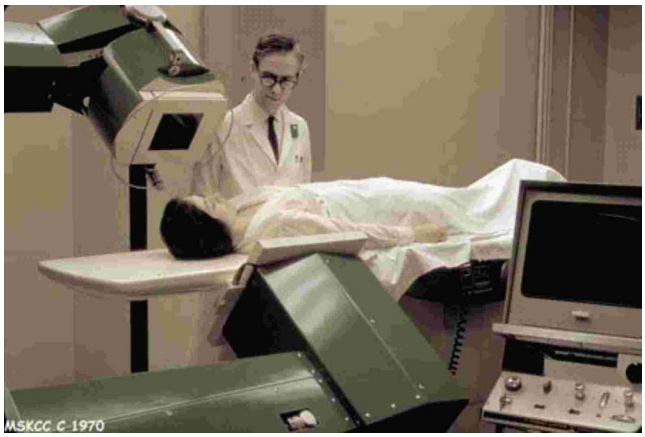


FIG. 16. Radiation therapy simulator for an 80 cm cobalt machine c 1970. Note that the results were documented by placing a cassette in front of the image intensifier (MSKCC).

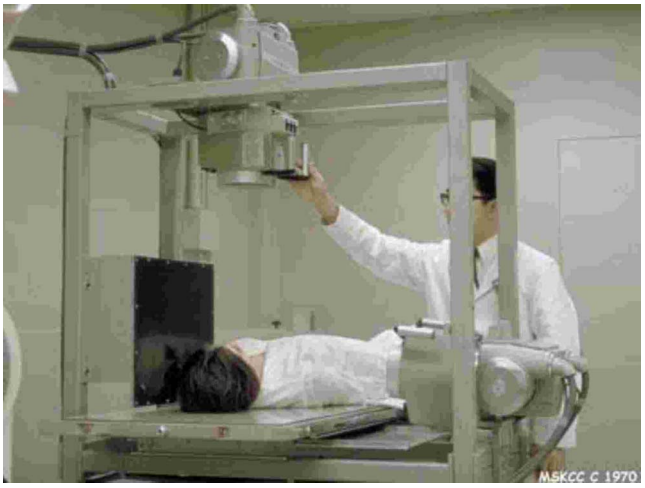


FIG. 17. Apparatus for the automatic localization of implanted seeds c 1970 (MSKCC).

mental discoveries of this era laid the groundwork for dramatic advances in the precision of treatment planning, deliver, and verification that have been realized in the past quarter century. As the 1980s unfolded, the pancreas and metastatic foci could generally be seen using a combination of CT, MRI, and PET imaging. Radiotherapy was generally delivered using megavoltage photon and electron beams. Treatments were planned with the aid of CT-determined anatomy of individual patients, but not in general fully utilizing the three-dimensional data for planning and dose calculation. Treatment delivery was verified using portal films. CT brought with it the virtual elimination of exploratory surgery, and as a consequence ad hoc seed brachytherapy sharply declined. The treatment of a pancreatic cancer patient was in general very simple and low dose, due to toxicity risk.

III.A. Treatment planning (1983–2008)

The improvements in power of computers available for treatment planning helped spur investigations into more sophisticated dose calculation algorithms. A significant number of innovations in three-dimensional dose calculation occurred in the last 25 years. Included in these are improvements in empirical models of dose deposition,[35] and the advent of Monte Carlo methods for modeling radiation transport in medical linear accelerators.[36,37] The introduction of convolution methods for dose modeling has led to widespread improvements in dose modeling accuracy for commercially available treatment planning systems.[38–41]

In relation to improved calculation methods, visualization tools have also dramatically improved our ability to plan treatments conformally. The beam's eye view concept[42] was a critical step in understanding the relationship between beam orientation, field shaping, and normal organ sparing (Fig. 18).

A critical element for improving our understanding of anatomy and ability to optimize plans is the development of the patient model from multiple sources of information.

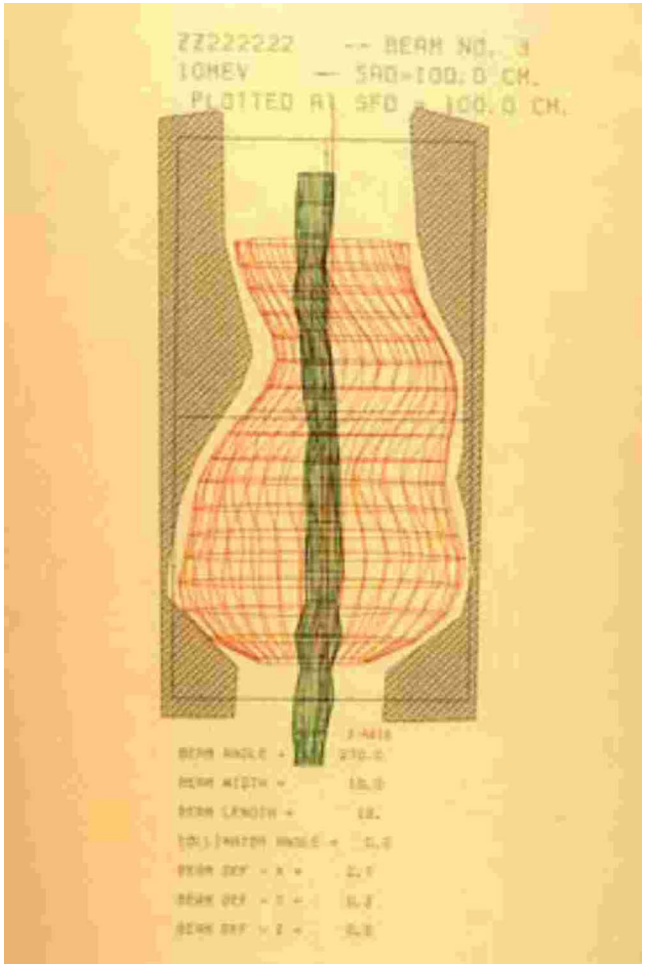


FIG. 18. Early beam's eye view projection (courtesy of D. McShan).

Three-dimensional image alignment techniques have been pioneered by medical physicists, notably with the introduction of surface fitting for aligning MRI, CT, and PET images of the brain,[43] and continuing through a series of innovations over subsequent years.

III.B. CT simulation

The advances in three-dimensional treatment planning mentioned above provided a true paradigm shift in radiation oncology. The intrinsic volumetric representation of the patient moved from the imagination of the physician and a few related measurements to a more palpable three-dimensional model of the patient from which more direct visualizations of the influence of treatment geometry could be appreciated. This digital patient model could be extended to more eloquent applications and could even serve as the reference model for the patient as a basis for setup verification. The generation of the digitally reconstructed radiograph[44] allowed for treatment geometry to be viewed as if an x-ray image was acquired through the patient along the beam path. This tool, combined with advanced three-dimensional visualization methods, allowed for the evolution of virtual, or CT-based, simulation.[45,46] The ability to replace the conventional simulator with a patient model derived from CT scans

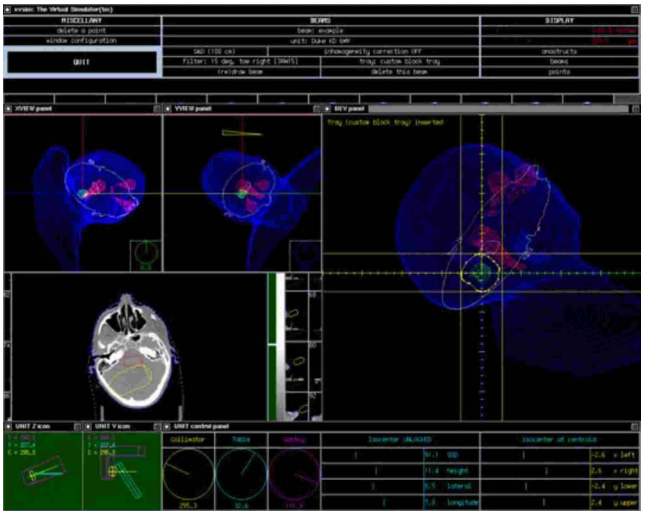


FIG. 19. Screen capture from an early use of a virtual simulator at the University of North Carolina (courtesy of G. Sherouse).

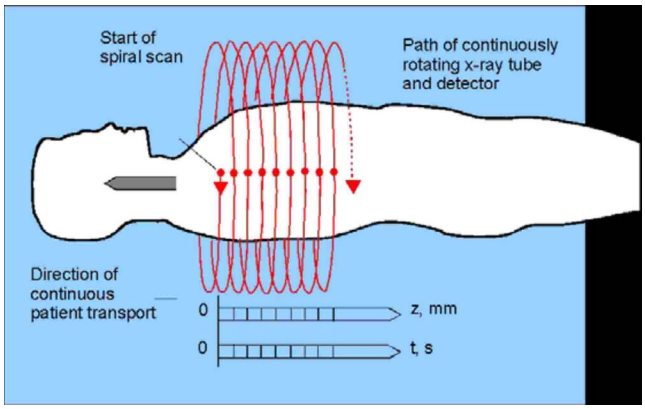


FIG. 20. The helical ("spiral") scanning CT process described in 1989 (courtesy of W. Kalender).

has been one of the most dramatic advances in radiotherapy, both reducing the complexity of simulation, and expanding the routine use of complex beam geometries for more advanced sparing of normal tissues and target coverage. Figure 19 shows an early picture from the virtual simulation system invented by Sherouse and colleagues at the University of North Carolina.

The second half of the modern history of the AAPM saw the growth of dedicated clinical particle therapy centers. The first clinical center in the United States was established at Loma Linda University Medical Center in 1990. The Northeast Proton Center opened in 2002, shifting the clinical operation from the Harvard Cyclotron laboratory. While physics research facilities still continue to treat some patients with their beam lines, additional dedicated medical proton facilities opened in Texas and Florida, and a number of additional private centers are in various phases of planning and construction in the United States.

III.C. Intensity modulated radiation therapy

From early on, it was understood that the precise delivery of radiation involves consideration of a very large number of parameters (modality, energy dose rate, orientation, field shape), and in fact early papers point to the considerations of "optimal" methods of configuring radiation treatments.[47,48] The introduction of computer-controlled, dynamic field shaping, however, was one of two key components that led to the development of intensity modulated radiotherapy (IMRT).

A critical development in the generation of IMRT was the suggestion by Brahme that alteration of the radiation fluence pattern as a beam rotates around the patient can spare central critical structures.[49] Brahme further went on to speculate that dynamic field shaping devices could potentially deliver the complex fluence patterns needed to achieve organ sparing and target dose coverage.[50,51] Subsequent innovations in treatment plan optimization looked at reconstruction algorithms,[52] linear programming methods,[53] and eventually iterative optimization methods, which are still being actively improved.

While these concepts presented a very exciting paradigm, the planning and delivery of such treatments was still pending. Carol, a neurosurgeon, conceived and developed the first practical method of delivering non-uniform fluence patterns during gantry rotation. His company, NOMOS, introduced a binary MLC system which, in combination with linear accelerators operating in arc mode, became the first commercial IMRT device.[54]

The invention of helical CT by Kalender in 1989 (Ref. 55) provided another breakthrough in imaging as well as IMRT (Fig. 20). In addition to paving the way for slip-ring scanners with dramatic improvements in speed, this method of transporting radiation to a patient paved the way for helical tomotherapy, as envisioned and developed by Mackie and colleagues[56,57] (Fig. 21).

III.D. Image guided radiotherapy

The use of portal films demonstrated the importance of anatomically based treatment verification. Early film-based verifications took significant time and resources, and typically required a great deal of skill and time for visual interpretation of field shapes and sizes, as well as their relationship to (skeletal) anatomy visible in these fairly low contrast megavoltage projection radiographs. The advent of electronic portal imaging[58–62] played a key role in advancing this paradigm, and showed the wide array of clever approaches to a technological problem advanced primarily by medical physicists. Digital portal images, while initially of fairly poor quality, were immediately amenable to digital manipulation, including filtering to improve visual interpretation of information,[63–66] manual and automated field shape verification,[67–72] and most importantly image and feature alignment to validate patient positioning.[73–78] Such advances are at the core of the modern era of image guided radiation therapy.

A major technological breakthrough in digital imaging had significant influence from the needs of improved portal

FIG. 21. Benchtop tomotherapy prototype system incorporating a NOMOS collimator (courtesy of T. Mackie).

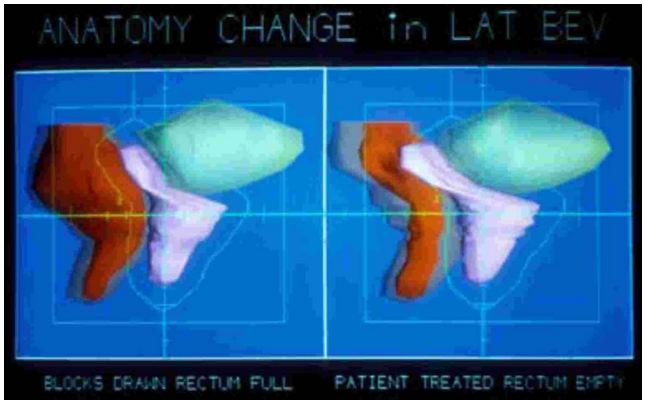


FIG. 23. Prostate movement due to rectal filling state (courtesy of R. Ten Haken).

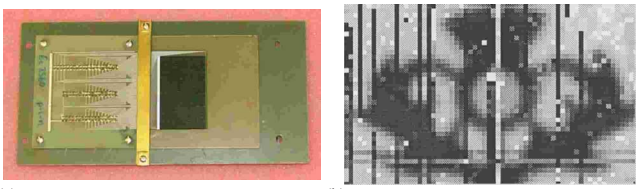
imaging. Antonuk and Street, working with the emerging technology of hydrogenated amorphous silicon arrays, introduced active matrix flat panel imagers to radiography. Such technology has revolutionized digital radiography,[79] and has become a staple for setup verification in radiation oncology. Figure 22 shows a prototype imager and early radiograph.

Early measurements of precision of treatment clearly demonstrated the importance of verification as a critical element in effective radiotherapy. Early in-room megavoltage CT technology was developed at the same time as portal imaging.[80] In the 1990s, two concepts of in-room diagnostic CT imaging emerged. While some groups experimented with placing CT scanners in the treatment room, others, most notably Jaffray and colleagues at William Beaumont Hospital, applied cone beam reconstruction methods to the area detectors used for portal (and prototype gantry-mounted diagnostic) imaging, thus introducing kilovoltage cone beam CT.[81–84] This technology is now spreading very rapidly through the radiotherapy community, providing significant detailed information of the patient at treatment that we are still learning how to optimally utilize.

III.E. "4D" radiotherapy—Managing motion

The same factors that motivated improvements in localization methods for precision therapy led to initial studies of organ movement, perhaps one of the most active areas of research and development in the field of radiotherapy today. One of the earliest studies of organ movement was the demonstration of prostate movement under differential bladder and rectal filling[85] (Fig. 23). Studies such as this were heavily influenced by medical physicists, who developed image analysis tools, models of organ movement, and interventions[86] to minimize the impact of physiological movement on treatment accuracy.

Investigations led by medical physicists included early observations of the effects of breathing on CT models of anatomy as well as delivered dose and necessary treatment margins.[87–90] In the process of determining various ways of optimally managing breathing motions, innovations such as active breathing control,[91] gated radiotherapy,[90,92] tracking systems,[93] and breathing-sorted (4D) CT (Ref. 94 and 95) followed in rapid succession.



(a) (b)

FIG. 22. Photo of an early prototype, active matrix flat-panel imager employing a 64×40 pixel, indirect detection array with a 900 μm pixel pitch. (b) Image from this prototype, obtained on October 24, 1990 at 100 kVp and 1.1 mA, of a "Scottish Thistle" tie pin, representing the national flower of Scotland. Courtesy of Larry Antonuk, Dept. of Radiation Oncology, University of Michigan.

IV. 2008: AAPM GOLDEN ANNIVERSARY

In 2008, dynamic imaging permits appreciation of motion in the pancreas. Deformable image registration promises to better describe the relationship between MRI and CT patient models, as well as different states of the patient during breathing. A breathing gated (or breath held), intensity modulated, treatment can be delivered, with potential increases in pancreas tumor dose at acceptable toxicity (assessed to some extent by models of normal tissue toxicity integrated within the treatment planning framework). Individual metastases are potentially treated with very high precision stereotactic techniques. Intensity modulation may enhance the delivery of particle therapy, with the potential to dramatically change the expected precision of planned dose conformance.

V. THE CURRENT AND EMERGING ERA OF NOVEL TECHNOLOGY IN RADIATION THERAPY

As we approach the present and future, we can look back at an impressive legacy of skill and ingenuity on the part of medical physicists in radiation oncology. Physicists have been able to adapt their education and skills to address complex needs in the medical field. The concepts applied to the

innovative developments have varied widely, including developing and applying fundamental physical theories to produce new methods of delivering and detecting radiation, applying advanced mathematical and practical models to map radiation deposition, model and measure variations in treatment and patient configuration, and improve our understanding of radiation effects on tumor and normal tissues, and ways to optimize treatment planning and delivery based on modeled responses.

We can already see some hints of the future. A major current initiative is the further integration of soft tissue imaging (especially MRI) (Ref. 96 and 97) into the treatment unit. Advances in functional imaging of various forms[98,99] are being applied to better understand patient-specific radiation effects in attempts to better individualize treatment. Molecular targeted therapy is reemerging, with nanotechnology offering significant potential for local enhancement of imaging as well as treatment delivery.

We can only imagine the roles that physicists will play in the future of radiation oncology. It is critical that we keep the skill set and interests of physicists high, as the environment and technology that will lead to the next generation of innovations is not predetermined. We should simultaneously welcome and encourage collaboration with medical, biological, and engineering sciences, as our past and current efforts clearly point towards significant developments in enhancing human health through multidisciplinary approaches in these very complex and rapidly advancing areas.

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