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Proton Therapy Construction Projects in the United States

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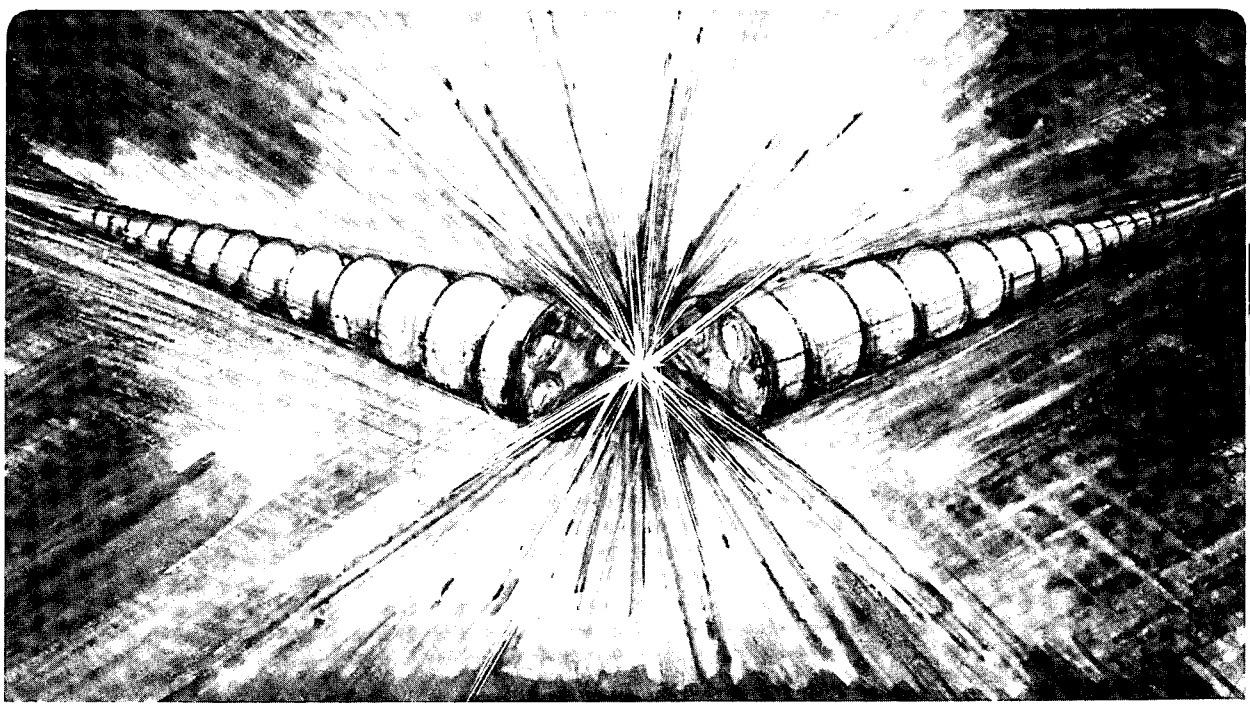
November 1992



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Proton Therapy Construction Projects in the United States*

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Abstract

Proton and heavy-ion radiation therapy has been taking place now for 40 years, at many accelerator laboratories around the world, essentially all of these centers built originally for physics research. The high degree of promise shown for using these particles for treating and curing cancer has stimulated the medical community to look seriously at building dedicated accelerator facilities in a hospital setting, where more rapid progress can be made in clinical research, and development of effective treatments with these beams. In the United States, the first such facility, at the Loma Linda University Medical Center, has been in operation now for two years, and is currently treating a total of 35 to 40 patients per day. Two new projects are being designed at present, one at the Massachusetts General Hospital in Boston, Massachusetts, the second a joint project of the Lawrence Berkeley Laboratory and the University of California at Davis Medical Center in Sacramento, California. This paper will discuss accelerator and beam characteristics relevant to the proton-therapy application, and will present performance and operations characteristics for the Loma Linda facility, as well as details of the plans, process and progress towards construction of the new facilities in Boston and Sacramento.

Rationale for Protons in Radiation Therapy

For more than 50 years now, radiation has been known to be effective in the treatment of cancer. In these intervening years techniques have been refined to improve cure rates and decrease the complications associated with radiation therapy. Experience has shown that treatment effectiveness is improved any time that dose to the tumor can be increased while decreasing the integrated dose to normal tissue outside the desired treatment volume. In the early days of treatment with x-ray generators, where the steep attenuation of the lower energies of x-rays available then produced a much higher dose at shallow depths, it was found that dose could be concentrated in the tumor by overlapping fields brought in from many angles. With the advent of higher energy electron accelerators the exponential attenuation of x-rays was greatly decreased, and the overlapping doses at the tumor allow deposition of a therapeutically-effective dose with quite significant sparing of normal tissue surrounding the treatment volume. Still, many types of cancers cannot be treated with x-ray beams because of the inability of these beams to avoid some critical structures in front of or behind the treatment volume.

Beams of "heavy charged particles" (protons, helium, carbon, neon, etc.) offer intrinsically better possibilities for precision radiotherapy, primarily because of the nature of the energy-loss mechanism for these particles. As $dE/dx \approx 1/E$, the rate of energy loss is steepest at the end of the particle range. This so-called "Bragg Peak" (Figure 1) offers the possibility of depositing a large dose of radiation into the region where the beam is made to stop, with significantly less dose delivered to surrounding normal tissue. This fact was first pointed out by R.R. Wilson in 1946 [1].

Heavier ions have another characteristic that may be positive or negative, clinical tests have yet to be completed. As the ionization for each particle depends on Z^2, the biological damage associated with each heavier ion will be quite a bit greater than that for a proton. This will increase the effectiveness of the ions for cell-killing in the tumor: such effects have indeed been clearly seen. However, damage to normal tissue is also increased on the particle's path to the tumor. The response of human tissue to heavier-ion beams has been under intense study at the Bevalac in Berkeley [2], but much more work is needed to fully understand how best to use such beams for effective treatments. With the planned closure of the Bevalac in early 1993, this work will be continued at HIMAC, a large dedicated heavy-ion center nearing completion in Chiba, Japan[3].

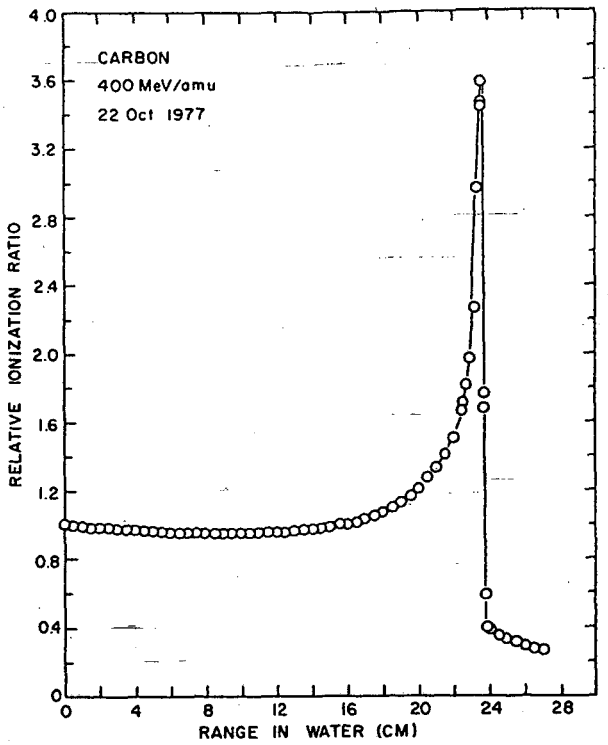

Figure 1: Bragg Peak,
dose deposition of charged particle beam

To reach deep-seated tumors, the range of the beam must be adjustable, up to a maximum depth of around 30 cm. At this depth, multiple scattering and range-straggling of charged-particle beams can be quite significant. Figure 2a shows the dose-deposition for a proton beam penetrating 25 cm into water (essentially equivalent to human tissue, for purposes of beam interactions). A beam entering with a diameter of 4 mm spreads out to over 25 mm at the stopping point. This loss of definition affects the precision possible for dose-placement with proton beams. Figure 2b compares multiple scattering and range straggling of proton beams with heavier ions. It is seen that carbon beams suffer about one-quarter of the beam degradation, and so offer superior dose-localization potential.

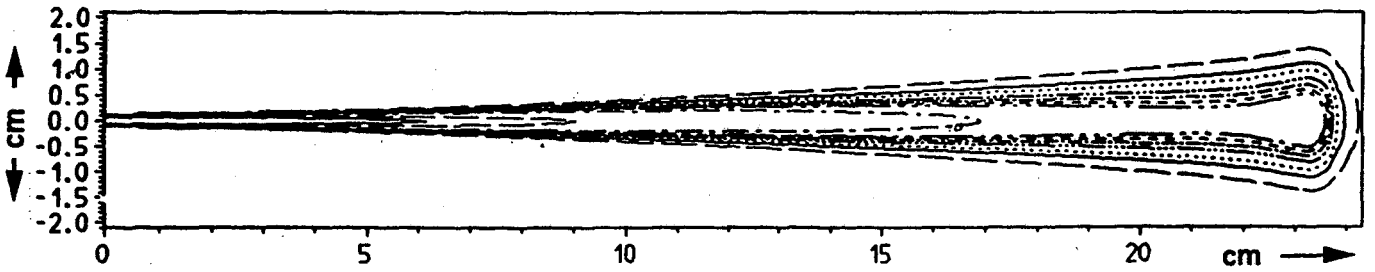

Figure 2a: Proton stopping in water
spreading due to multiple scattering
[calculation of A. Brahme, Uppsala]

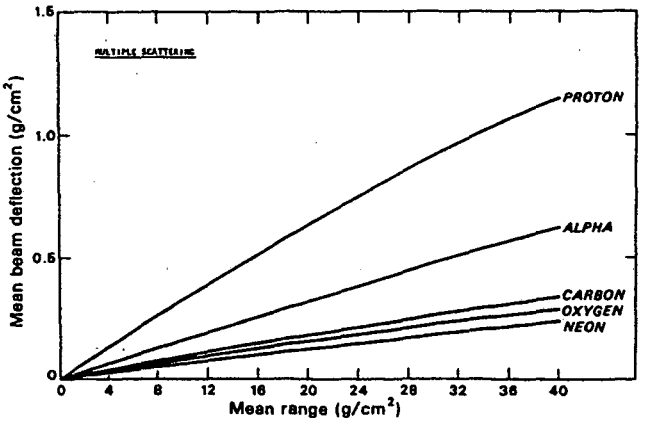

Figure 2b: Multiple scattering for different ions
carbon ions scatter about four times less than protons

For several reasons, then, clinical application of heavy charged particles is focusing on protons. First, dose localization, although not as good as for heavier ions, is still considerably better than x-rays. Second, the biological response of tissue to protons is approximately the same as that for x-rays, is very well studied and understood, so the uncertainties associated with using heavier ions is avoided. Third, the beam energy needed to satisfy clinical requirements, around 250 MeV for protons, is much lower than that needed for heavier ions. (Carbon beams should be around 350 MeV/amu.) The magnetic rigidity ($B\rho$) for protons is around 2.5 Tesla-meters, while for carbon it is around 6 T-m. Thus a carbon machine is about 2.5 times bigger than a proton machine. The accelerator is bigger, but more important, the gantry systems, needed for isocentric delivery, will be much bigger than the already-very-large proton gantry. (At Loma Linda, the only facility with operating gantries, the diameter of the proton gantry is 13 meters.) This point will be addressed further later on.

In summary then, although there may be some desirable features for ions heavier than protons, the size, cost and the known biological response of protons are the determining reasons why the medical community is choosing protons as the next-generation radiotherapy modality for new hospital-based facilities.

Experience with Proton and Heavy-Ion Therapy

Protons and heavier ions have been used in therapy for 40 years now. Many laboratories around the world have introduced therapy programs at accelerators whose major function is or was nuclear research. In some cases these programs operate in conjunction with ongoing nuclear research programs, in others the accelerator is dedicated to therapy applications.

The 184" synchrocyclotron at LBL was the site of the first treatments, in the early 1950's. About ten such sites have been or are being used for proton and heavy-ion therapy, including cyclotrons at Uppsala, St. Petersburg, Dubna, Nice, Orsay, Cambridge Massachusetts, Villigen Switzerland, Chiba Japan; and synchrotrons at Berkeley, Tsukuba and Moscow. Most recent addition to the synchrotron list is the facility at Loma Linda, which will be discussed at some length later in this paper. A historical summary of the field is given by Sisterson [4] and Minakova [5].

The strong sentiment of radiotherapists working at laboratory-based accelerators is that the environment at these sites is far from ideal for conducting a clinical program. Many difficulties are mentioned, including problems with patient access, lack of proper resources normally available in hospitals, an intimidating atmosphere for patients, and in many cases great problems in having adequate access to beam time either because of the need to share with other programs, or because the accelerator is scheduled to run only part of the year. Nevertheless, enough research work has been performed at these sites to create enthusiasm for proton therapy within the medical community. This enthusiasm has led to a strong call within the US radiotherapy community for building hospital-based accelerators. As mentioned above, the first of these, at Loma Linda University, is now operating, and two more accelerators, one at the Massachusetts General Hospital, the second at the University of California at Davis, are in the early design stages.

Characteristics of a Hospital-based Proton Therapy Facility

Before describing these projects, the preferred characteristics of a proton therapy facility will be discussed, and an evaluation of available accelerator technologies will be made to determine which, if any, is most suitable for this application. As is well known, there are many sources of protons at the desired energy, however when one looks at the specific requirements for precision of dose delivery, it becomes apparent that some of the technologies are more suitable than others.

First of all, the beam must have enough range to reach any part of the body. The generally accepted figure is around 30 cm, leading to the 250 MeV requirement for the proton beam. Second, the beam intensity should be high enough to treat the average-sized field in about one minute. This translates into around 10^{11} protons per second. The largest field to be irradiated is around 30 x 30 cm, and the desired uniformity of dose deposition is around ±2% across all three dimensions of the treatment field. There is a strong desire to have isocentric delivery of the beam, and that the overall size and cost of the facility be as low as possible.

The call for isocentric delivery adds significantly to the cost and complexity of the facility, but the strong justification for this capability almost demands its inclusion. With an isocentric gantry the patient can be treated in a horizontal, supine position, and beams can be brought in to the patient from any orientation by either changing the gantry angle or rotating the patient couch. Less expensive is treating with a static horizontal beam, but then the patient must be immobilized in a seated or standing position. The advantages of a supine patient are that achieving the required immobilization is a lot easier, and most important is that diagnostic information obtained with commercial CT and MR scanners is directly applicable. Scanning a patient in the actual treatment position is essential for treatment planning and identifying anatomical coordinates for accurately directing the beam; in extreme cases organ motion of up to several centimeters has been observed between seated and supine x-rays.

A critical need for a clinical proton therapy system is extremely good control of the beam; its position, intensity and range must be tightly monitored and controlled. This is absolutely essential for making use of the precise dose-delivery capabilities of charged-particle beams.

Treating a 3-Dimensional Target Volume

The goal is to treat an irregularly-shaped 3-dimensional target volume, conforming the areas of highest dose to this irregular shape and thus minimizing the exposure to healthy tissue outside of this volume. Achieving this is very difficult, and in fact is not being done on a routine basis for patient treatments in any of today's operating facilities. Although it is possible to shape the lateral outline of the treatment field with a complex-shaped collimator, the range modulation of the beam is uniform across the full treatment field. Stated differently, the volume containing stopping particles is a cylindrical section with a constant height (z) across the entire (x,y) transverse extent of the treatment field. A "bolus compensator" is typically fabricated and placed in front of the patient to tailor the back side (distal end) of the field, but that only increases the exposure of normal tissue upstream of the target volume. This concept is illustrated in Figure 3a.

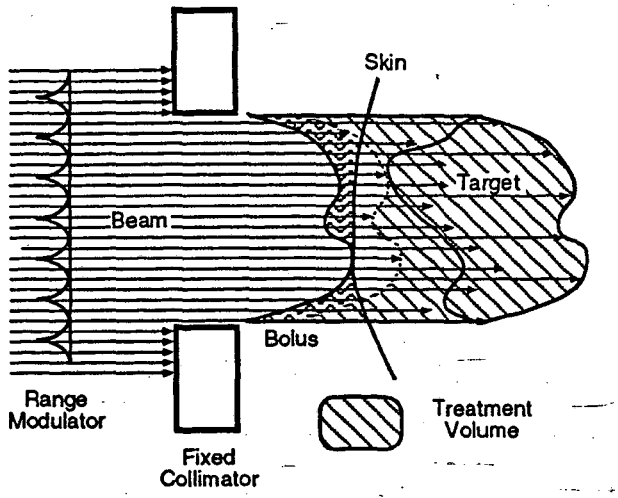

Figure 3a: 2-Dimensional Treatment System

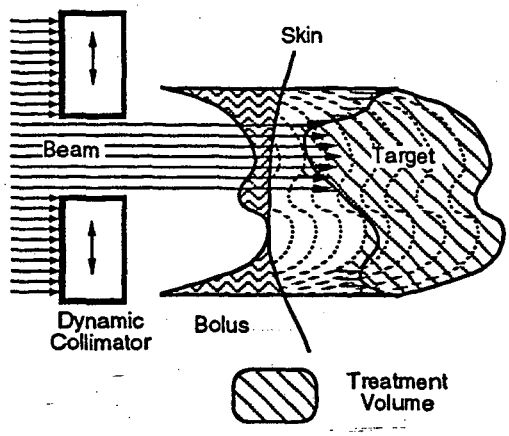

Figure 3b: 3-Dimensional Treatment System, conforming to shape of target volume

Various schemes are being developed for achieving this goal of 3-dimensional treatments, including range-stacking with a variable collimator [6] (shown schematically in Figure 3b), voxel scanning [7] and raster scanning [6], and it is anticipated that within the next 5 years this technology will be in actual clinical use. All of these schemes, however, require highly-accurate control over beam parameters.

Lateral beam spreading can be achieved either by "passive" means, using appropriately-shaped scattering foils [8] or by "active" magnetic scanning [6,7]. The former places less demands on intensity control of the beam, as the entire field is receiving dose at the same time. For "active" systems, beam intensity control must be very tight as the small beam-spot is moved across the treatment field by a scanning system. Quality of the treatment beam is not as good for scattered beams, edge-definition is lower, higher beam energy is needed to compensate for energy-loss in the scattering system, and a higher neutron dose is generated because of nuclear interactions in the scattering foils and the heavy collimators needed to stop the high percentage of the beam (in excess of 60%) not in the suitably-uniform treatment field. Although the "active" delivery systems require substantially more control over the beam parameters, their flexibility and higher precision of treatment delivery clearly point to these techniques as superior.

The depth of penetration of the beam must be adjustable independently for each (x,y) coordinate. Regardless of how the beam is painted over the volume, this independence requires that the beam energy entering the patient must be adjusted to correspond to the desired range for each element of the treatment volume. Energy adjustment can be performed by degrading the beam upstream of the patient or by varying the energy at which the beam is extracted from the accelerator. Although simpler, degrading the beam reduces the beam quality and increases the neutron dose to the patient. On the other hand, variable energy extraction introduces complexity into the accelerator design and places a further constraint on accelerator technologies that can be used. Nevertheless, because of the flexibility and higher precision, variable energy extraction is in fact preferred.

Appropriate Accelerator Technologies

Summarizing the above discussion, the relative importance of the various accelerator characteristics can be listed. Very important are: adequate intensity (above 10^{11} protons/sec), excellent control of intensity over a large dynamic range (1:100 typical) in both a macroscopic and microscopic (sub-millisecond) time scale, a long duty factor (greater than 25%), a well-developed, integrated control system with a strong emphasis on safety and reliability. Important, but not as critical as the above: energy variability (70 to 250 MeV), compactness, efficiency of beam utilization and cost (both construction and operations). These factors can be translated into an intercomparison between linac, cyclotron and synchrotron technologies for appropriateness in this proton therapy application. The Table below summarizes this intercomparison.

	Linac	Cyclotron	Synchrotron
Intensity	+ (problem, too much)	++	+ (needs care in design)
Intensity control	+ (H^- linac, laser stripping)	++	0 (Needs care in design)
Duty factor	- - (very poor)	++	++
Controls	0	+	0
Safety, reliability	-	+	+
Energy variability	- (in discrete steps)	- -	++
Compactness	- -	++	+
Beam utilization	- -	-	+
Cost	- -	0	0
Technological risk	- -	-	++

{++ excellent} {+ OK} {0 average} {- poor} {- - very poor}

It is clear that linacs are less desirable, due largely to their very short duty factor, difficulties in intensity control and energy variability. Cyclotrons offer many advantages in areas of intensity, beam control and duty factor, but suffer in lack of energy variability. Synchrotrons are more complex, larger in size than cyclotrons and require great care in design for adequate intensity control, but offer a level of flexibility that is not available with the other technologies. This flexibility is viewed as most important to allow for upgrading of the accelerator as new developments occur in beam-delivery techniques, such as refinements in scanning systems. The "Technological Risk" category refers to specific application in the proton therapy area, the extension in design required for a therapy machine over the current demonstrated state of the art.

Proton Therapy Facilities: Loma Linda, California

Located 60 kilometers east of Los Angeles, the Loma Linda University Medical Center has been operating a proton-therapy facility now for over one year [9]. The facility layout, shown in Figure 4, is driven by a 250 MeV weak-focusing synchrotron designed by a Fermilab team headed by Lee Teng. A duoplasmatron source feeds a 2 MeV RFQ which single-turn injects the synchrotron. Operating at 0.5 Hz, beam is extracted over a 400 msec flattop via half-integer resonant extraction. A large switchyard sends beam to one of five irradiation areas, one fixed beam room with two ports (a dedicated eye-treatment line and a large-field station), a fixed-beam room designated as a test area, and three gantry rooms. The gantries are of the "cork-screw" design developed by Andreas Koehler of the Harvard Cyclotron Laboratory [10].

Overall gantry diameter is 13 meters, with a drift distance from the last magnet to the patient isocenter of 3 meters. The gantry design, installation and commissioning of the entire facility was performed by SAIC. The Loma Linda facility commenced patient treatments in October 1990, and are now treating between 35 and 40 patients per day in the two rooms that have been completed. Magnets are being installed in the remaining two gantries, so these two rooms as well as the fixed-beam test-area will be operational in early 1993.

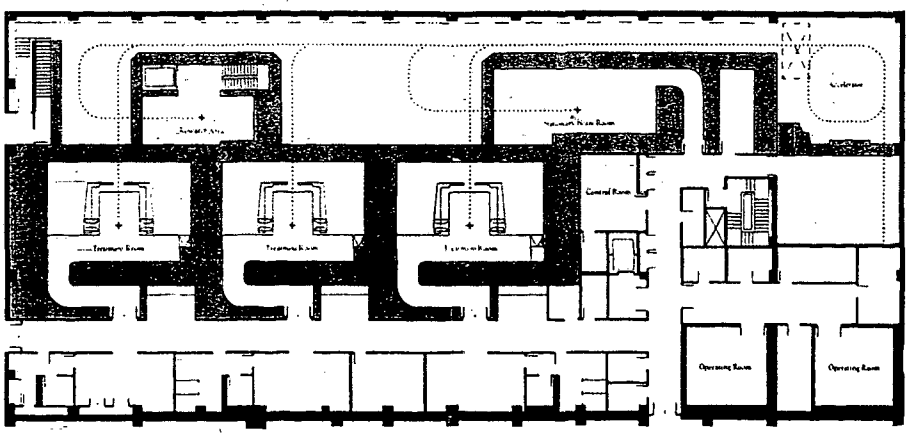

Figure 4: Layout of Loma Linda Proton Therapy Facility
Synchrotron (in upper right corner) feeds three gantry rooms and two fixed-beam rooms

Performance of the Loma Linda accelerator has been for the most part excellent, although some of the original design specifications have not yet been met. The beam intensity is 2 x 10^{10} protons/sec, about a factor of 5 below the original specification. Time structure of the extracted beam is very pronounced, scanning is not now possible because of inadequate control over this spill structure. The accelerator control system does not allow for rapid pulse-to-pulse energy variation, although nothing in the accelerator design prevents this from being accomplished. On the positive side, reliability, stability and operational reproducibility of the accelerator have been excellent. Upgrade efforts are now underway to correct the above-listed problems, and no impediments are seen from this facility accomplishing all of its design and performance objectives.

The Next Generation: Proton Therapy Facilities at the Massachusetts General Hospital and the University of California, Davis

The National Cancer Institute of the US National Institutes of Health has been funding design studies for the "next generation" of hospital-based proton therapy facilities. Two sites have been selected for these studies, the Massachusetts General Hospital (MGH) in Boston, MA, and the University of California, Davis Medical Center (UCDMC), in Sacramento, CA (in conjunction with the Lawrence Berkeley Laboratory). Both facilities will be located on hospital campuses. MGH is located in the center of a very crowded urban area, an exercise yard of a historical prison building has been identified as the actual construction site for the NorthEast Proton Therapy Center. The restricted space, as well as the poor soil conditions (high water table, thick mud layer with a long distance to bedrock) make for expensive civil construction, however this site provides excellent access to the main hospital complex. The UCDMC is

located about 2 km from the center of Sacramento, a large (population base ≈ 3 million) metropolitan center 160 km east of San Francisco. The hospital is located in a residential area, and has a considerable amount of undeveloped land. The Proton Therapy Facility is to be built adjacent to a recently-commissioned Cancer Center with a state-of-the-art radiotherapy department.

The process for designing and fabricating the accelerator and technical components for these two new centers is rather different from the traditional one. The "customers," MGH and UCDMC, with the assistance of LBL, are developing detailed specifications for the desired facilities, and are requesting of Industry designs that will meet the published specifications. Design and fabrication will be done entirely by private industry, the national laboratories, where the expertise resides, will be involved only in providing consultation to the selected industrial firms. This is in compliance with the US Government mandate that the role of National Laboratories is to support and assist in the development of industrial capability, and not to compete with private firms.

At this time, the specification writing phase is almost complete, and approaches to Industry are beginning to identify firms willing to participate in the design and construction process. We anticipate that contracts will be awarded in the next several months, and that construction will start before the end of 1993. The facilities should be ready for patient treatment in 1997.

Summary

Proton therapy is now ready to move from the research laboratory into the clinical arena. With the commissioning of the facility at Loma Linda, this initiative has begun. The plans for new facilities in Boston and Sacramento will further this move, and indications are that before the end of the century many more centers will be in construction or operational around the world. With this large number of particle-therapy facilities, developments should proceed very rapidly to fully-realize the potential of this modality for effective treatment of human cancers.

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