DEVELOPING A CLINICAL PROTON ACCELERATOR FACILITY: CONSORTIUM-ASSISTED TECHNOLOGY TRANSFER

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Abstract

A hospital-based proton accelerator facility has emerged from the efforts of a consortium of physicists, engineers and physicians from several high-energy physics laboratories, industries and universities, working together to develop the requirements and conceptual design for a clinical program. A variable-energy medical synchrotron for accelerating protons to a prescribed energy, intensity and beam quality, has been placed in a hospital setting at Loma Linda University Medical Center for treating patients with localized cancer. Treatments began in October, 1990. Scientists from Fermi National Accelerator Laboratory; Harvard Cyclotron Laboratory; Lawrence Berkeley Laboratories; the Paul Scherrer Institute; Uppsala, Sweden; Argonne, Brookhaven and Los Alamos National Laboratories; and Loma Linda University, all cooperated to produce the conceptual design. Loma Linda University contracted with Fermi National Accelerator Laboratory to design and build a 250 MeV synchrotron and beam transport system, the latter to guide protons into four treatment rooms. Lawrence Berkeley Laboratories consulted with Loma Linda University on the design of the beam delivery system (nozzle). A gantry concept devised by scientists at Harvard Cyclotron Laboratory, was adapted and fabricated by Science Applications International Corporation. The control and safety systems were designed and developed by Loma Linda University Radiation Research Laboratory. Presently, the synchrotron, beam transport system and treatment room hardware have been installed and tested and are operating satisfactorily. The stationary beam has been fully commissioned and is being used to treat patients with tumors and other diseases of those sites. At this time, commissioning is underway for the first of three gantry-delivered beam lines; clinical operations are expected shortly.

The purposes of the program are control of cancer and some benign diseases, and reducing side effects of current treatment. A major aim has been to develop a cost-effective process for exploiting the absorption characteristics of protons in tissue. The design requirements were dictated by the clinical needs of patients, physicians and the medical center environment. These requirements increased the complexity of the system, particularly its beam delivery capability. This complexity necessitated a consortium; no single facility possessed the expertise and equipment to accomplish this massive task.

I. INTRODUCTION

The Proton Treatment Center at Loma Linda University Medical Center began clinical operations on October 23, 1990. This beginning is part of a much larger and longer process. In historical terms, the process is as old as radiation therapy, a continuation of the search for more-precise means of delivering radiation to diseased sites. For Loma Linda University (LLU), the process is at least two decades old. For the Proton Treatment Center itself, the process began in 1985, and illustrates the importance of concentrated effort in transferring technology from the laboratory to the clinic.

II. BRIEF HISTORY: THE SEARCH FOR PRECISION

At its beginning, radiation therapy was characterized by poor understanding of the physical and biological effects of the new phenomenon. Trial and error resulted in improved understanding and, unfortunately, personal injury to patients and involved scientists. The ability to destroy a biologic system by depositing excess energy using x-rays and other forms of newly- discovered ionizing radiation, soon became evident. As the new modality became more widely used for clinical treatment, investigators recognized the need for precision that would allow the physician to place the energy in a three-dimensional locus within any targeted volume. This need has driven the physics, engineering and medical communities toward a variety of radioisotopes, and the development of a variety of x-ray generators and high-energy particle accelerators.

Early particle-accelerator studies occurred at Berkeley, where Lawrence developed the cyclotron [1]. Subsequently, Wilson described the potential clinical advantage of proton beams over x-rays [2]. The absorption characteristics of heavy charged particles provide superior three-dimensional control of energy deposition because of the Bragg peak effect, allowing avoidance of significant injury to normal tissue volumes within the patient. Early, successful trials at Berkeley resulted in investigations at several other facilities. To date, over 9000 patients have been treated with protons (Table 1).

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Table 1. WORLDWIDE CHARGED PARTICLE PATIENT TOTALS, JANUARY, 1991*

LOCATION		BEAM	TREATMENT PERIOD	RECENT TOTAL
Berkeley 184	USA	Proton	1955-57	30
Berkeley 184	USA	Helium	1957-87	899
Uppsala	Sweden	Proton	1957-76	73
Harvard	USA	Proton	1961-->	5120
Dubna	USSR	Proton	1964-74	84
Moscow	USSR	Proton	1969-->	1945
Los Alamos	USA	Pion	1974-82	230
Leningrad	USSR	Proton	1975-->	685
Berkeley Bev.	USA	Heavy Ion	1975-->	1422
Chiba	Japan	Proton	1979-->	65
TRIUMF	Canada	Pion	1979-->	227
PSI (SIN)	Switzerland	Pion	1980-->	478
Tsukuba	Japan	Proton	1983-->	178
PSI (SIN)	Switzerland	Proton	1984-->	913
Dubna	USSR	Proton	1987-->	6
Uppsala	Sweden	Proton	1988-->	13
Clatterbridge	England	Proton	1989-->	114
Loma Linda	USA	Proton	1990-->	3

* Source: Adapted from *Particles* (Newsletter of the Proton Therapy Co-operative Group), #7, January, 1991

Exploiting the potential of protons and other heavy charged particles was hindered at first, because of: 1) the lack of engineering technology for satisfying the clinical requirements placed upon the entire system; 2) insufficient knowledge of radiation biology and tumor biology; and 3) physicians' in ability to image the tumor with sufficient detail to determine its precise location and extent. By the early 1980s these areas were developed to the extent that exploiting heavy charged particles for clinical uses was possible and practical.

III. THE LLU BACKGROUND

Interest in developing a charged-particle facility for treating patients began at LLU in 1970. A study of the feasibility of such an undertaking indicated the deficiencies (noted above) in developing a system that could fully exploit the potential for treating patients with heavy charged particles. One small but essential missing component was a technology that could accurately guide the external beam of radiation to the unobservable target within the patient. We undertook this task and developed the first computer-assisted radiation simulation techniques using ultrasonograms, followed soon thereafter by a system using CT scanning images of the patient for planning their radiation treatment [3,4,5,6]. This technology is now widely used for conventional and charged-particle treatment planning.

In the mid-1980's, when it was clear that imaging and therapy-planning technologies were sufficiently advanced that precision, highly-conformal proton therapy was clinically feasible, LLU investigators began discussing options for developing proton accelerators. Several meetings were held with physicists and engineers from high-energy physics laboratories, and with other physicians interested in charged-particle therapy. It was evident that widespread interest existed, and that the enormously complex task of designing and building a total clinical system would require a consortium approach.

IV. PTCOG

First meeting at Fermi National Accelerator Laboratory (Fermilab) in January, 1985, a small number of physicians, physicists and engineers interested in developing charged particle treatment capabilities, formed a working group. This group met at regular intervals to define the design requirements for a medically-dedicated accelerator, beam transport system, beam delivery system and facility to house the hardware. The consortium named itself the Proton Therapy Cooperative Group (PTCOG). Herman Suit, MD, Harvard University, was the first chairman of the PTCOG Steering Committee; Michael Goitein, PhD, Harvard, served as secretary. The other members of the Steering Committee were: John Archambeau, MD, Loma Linda; Joseph Castro, MD and Richard Gough, PhD,

Berkeley; Stanley Schriber, PhD, Los Alamos; James Slater, MD, Loma Linda; and Richard Wilson, PhD, Harvard.

Ninety-three scientists attended the initial meeting; most of them, and others, have continued to meet at six-month intervals. No outside support has occurred; each attendee or the attendee's home facility has funded all expenses, indicating a high degree of dedication to the program.

PTCOG divided its tasks into three major categories: a) accelerator design, b) facility design and c) clinical studies. It became clear early on that these categories were interrelated, particularly the first two.

V. Design Requirements

A medically-dedicated heavy-charged-particle accelerator and transport system have considerably different requirements than do similar equipment for basic physics research programs. Reliability is required for both, but the consequences of downtime in patient facilities is extremely serious and may even include fatalities. Costs of construction and operation are important to both, but in the clinical setting, too-high costs can mean patients (and insurers) cannot afford access to the therapy and its lifesaving potential.

Other requirements are critical for a medical machine and facility. Variable energy during treatment, and protracted, uniform beam extraction, provide the physician with the potential to electronically scan the beam as it enters the patient. This capability is needed to deliver a more-conformal high-dose volume without compromising maximum beam penetration or maximum treatment field size. These requirements place increased demands on the control system of the accelerator and transport system.

A. Reliability

Reliability requirements are important for several reasons. Patient safety and convenience can be compromised by excessive downtime. The cost of treatment is affected by unreliable equipment in several ways. Frequent breakdowns require large numbers of maintenance personnel and a large inventory of spare components. Downtime also prevents treatment which, in turn, reduces patient throughput. The repeatability of the equipment affects the frequency and extent of calibration and quality assurance testing. Because the LLUMC proton therapy facility is intended to be reproduced and marketed, reliability is crucial.

B. Safety

Since the proton beam is intended to be used on humans, patient safety is a paramount design consideration. All characteristics of the beam must be monitored throughout the calibration and treatment process, including beam energy, intensity, position, focus, treatment uniformity, and dosage. Several devices used to shape or position the proton beam for each patient's treatment are independently verified by a bar-coding system. Each component of the beam delivery system must be correctly configured before the safety system will allow the proton beam to enter the treatment room. All beam delivery system devices that move via the control system are redundantly interlocked to the proton beam delivery.

Personnel safety considerations are similar to, but more comprehensive than, those employed in research laboratories. Machine safety, in turn, is considered crucial to keeping the entire facility operating in a reliable manner.

C. Flexibility

In addition to being made maneuverable, to allow physicians to manipulate the beam to conform with patient-treatment parameters, the system was designed to be adaptable to changing concepts and ideas, allowing LLUMC to research and develop new technology. Consequently, a fundamental design requirement is flexibility. This requirement has its greatest impact in the design and implementation of technology. The treatment area is one where many new ideas are expected to occur. As a result, the nozzle and control system are highly modular and contain well-defined, simple interfaces. Further, because the facility is intended to be reproduced and marketed, different configurations and technology may be required to facilitate adaptations in other geographic sites.

D. Cost

An overall goal has been to make the benefits of proton beam treatments generally available by developing an affordable system. Hence, the facility has been designed for high patient throughput, conventionally-trained radiotherapy technologists, and low maintenance costs.

Patient alignment typically consumes the majority of time in radiation therapy. The LLUMC facility was designed to expedite this by locating preparation rooms adjacent to the therapy rooms, for pre-aligning patients and allowing pipelining of patient treatments. Complete body molds are used for each patient. These have the benefit of precise positioning as well as rapid alignment capabilities.

Laboratories in which proton therapy has heretofore been performed, typically require many personnel to operate the treatment process. Conventional radiotherapy, in contrast, uses two treatment technologists to operate the machine and manage the treatment. The LLUMC facility was designed to permit operation by a conventional staff, thus restraining costs. The accelerator, transport system and attendant operating software, make this possible.

Maintenance costs are held to a reasonable level by a strong preventive maintenance program, and by

identifying component weaknesses so that problem devices may be upgraded.

E. Proton Beam Requirements

The LLUMC medical beam has many unique requirements, differing it from a high-energy research tool. For example, very high beam intensities can be dangerous and are undesirable. For clinical use we require very stable beam intensity, precise energy, very stable beam position, and extraction duration. In addition, the system must provide a proton beam of a given energy, intensity, and extraction duration each machine cycle, placing very rigorous demands on the control and safety systems.

The energy range requirements are 70 to 250 MeV. The cycle time requirement is 2 seconds nominal, with extraction duration varying from 0.05 to 5.0 seconds. Extracted proton beam intensity requirements are 0.2 to 10 nA in beam current. The intensity stability is to be within +/- 2.5% at a 1kHz sampling rate. Extraction efficiency must be greater than 95%.

VI. DISCUSSION

A serious need exists to improve the control of localized cancer; an equally serious need exists to reduce the undesirable side effects of cancer treatment. These needs must be fulfilled using cost-effective techniques that can be utilized for the benefit of the population at large. Also, to meet the treatment challenge cancer presents, more-effective control of disseminated disease must become available. The use of heavy-charged-particle radiation addresses both the need for improving the local control of cancer and the need to reduce treatment morbidity. In many cases, reduced dissemination of disease will follow improved local cancer control [7].

The joint efforts of scientists, donating their time and talents to help develop the design requirements and conceptual designs of systems needed for producing a clinical proton therapy facility, have been extremely successful and represent an unusual international cooperative effort. It is unlikely that a facility design such as described herein would have been done successfully, or even have been undertaken, given the complexity of the undertaking, had any one institution attempted the effort. It required a marriage of the expertise of physicists and engineers familiar with particle accelerators and transport systems, and the clinical realities known to radiation oncologists, for a facility such as Loma Linda's to be developed. Through the efforts of personnel from Fermi National Accelerator Laboratory, Lawrence Berkeley Laboratory, Harvard Cyclotron Laboratory, the Paul Scherrer Institute, Science Applications International Corporation and many others, the Loma Linda University Medical Center Proton Treatment Center has become a medical-care reality. Many other proton or ion facilities are in the planning stages, as noted in Table 2.

Table 2. FUTURE SITES*

Institution	Expected Opening
Louvain-la-Neuve, Belgium	1991
Nice, France	1991
Orsay, France	1991
N.A.C., South Africa	1991
P.S.I., Switzerland	1992
G.S.I., Germany	1992
Chiba, Japan	1994
A.P.D.C., USA	1994
Harvard, USA	1995
Novosibirsk, USSR	1995
TRIUMF, Canada	?
EULIMA, Europe	?
Indiana, USA	?
Berkeley, USA	?
Tsukuba, Japan	?
Chicago, USA	?
Antwerp, Belgium	?

* Source: Adapted from *Particles* (Newsletter of the Proton Therapy Co-operative Group), #7, January, 1991

At present, the synchrotron, the beam transport system and the treatment room hardware have been installed and are operating satisfactorily. The stationary beam, which has two branches for treating patients with eye and with head and neck tumors, has been fully commissioned and is being employed as it was designed. Commissioning is nearly complete on the first of the three gantry-delivered treatment systems, and treatments will begin shortly. The remaining gantry systems will be placed in operation in the coming months, incorporating, where necessary, refinements generated by operation of the first gantry. A schematic overview of the treatment level of the facility is provided in Figure 1.

The necessary technology and radiobiological data are now in place to enable physicians to exploit proton irradiation for desired clinical objectives. This new capability would not have occurred without the knowledge, expertise and commitment of scientists and engineers in several disciplines. The transfer of technology that made the Loma Linda accelerator possible is a salient example of science at its best.

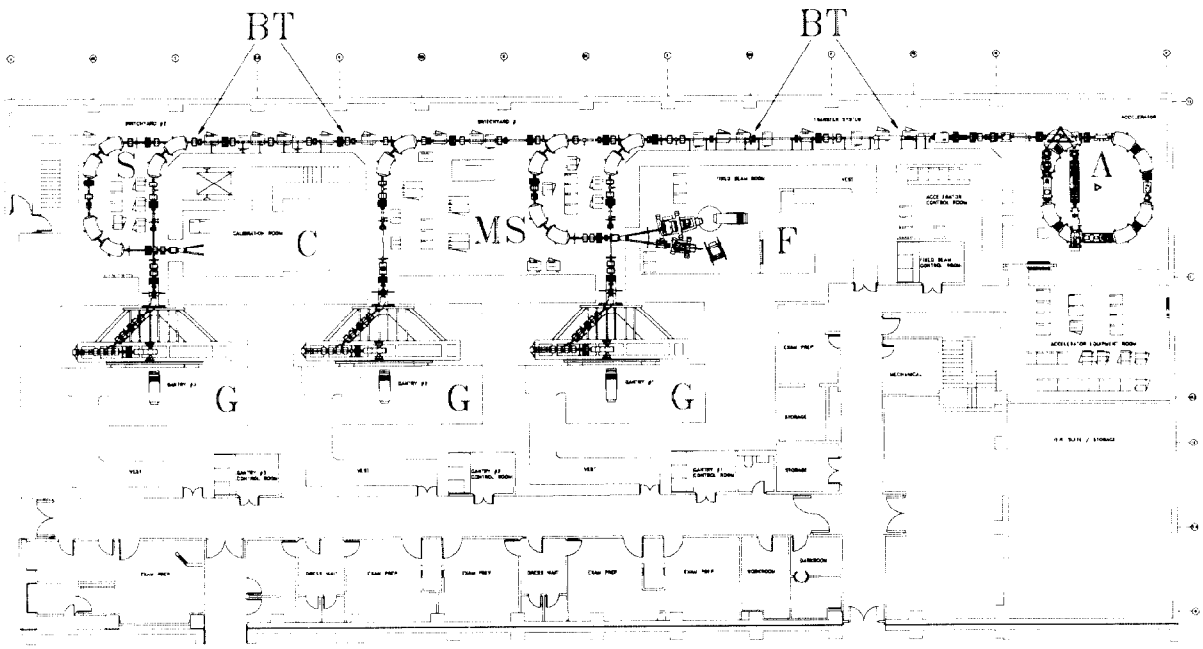

Figure 1. Plan of treatment level (level B), Loma Linda University Medical Center. Beam is generated in the proton accelerator (A, upper left). It is extracted as per the patient's dose prescription and travels via the beam transport system (BT, top) to the appropriate treatment room. It is routed to the appropriate room at the main switchyard (MS), which sends beam to the fixed-beam room (F) or to either of two gantries (G). Beam directed to the remaining gantry or to the calibration room (C) passes through a second switchyard (S).

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