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*Technology in Cancer Research and Treatment*  
ISSN 1533-0346  
Volume 6, Number 4 Supplement, August 2007  
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## **Developing and Understanding a Hospital-based Proton Facility: Bringing Physics into Medicine**

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From October 18 to 20, 2006, a symposium, Developing and Understanding a Hospital-based Proton Facility: Bringing Physics Into Medicine, was held at the Renaissance Esmeralda Resort and Spa, Indian Wells, California. The event was offered by the Department of Radiation Medicine at Loma Linda University (LLU), supported by the Telemedicine and Advanced Technology Research Center (TATRC) and the United States Army Medical Research and Materiel Command (USAMRMC). The meeting was intended to discuss factors involved in planning, developing, and operating a hospital-based proton treatment center. It brought together some of the most distinguished physicists, radiation biologists, and radiation oncologists in the world, and more than 100 individuals participated in the three-day educational offering. This overview reports on the event and introduces several papers written by many of the speakers from their presentations, for publication in this issue of *Technology in Cancer Research and Treatment*. Both the symposium and the papers are appropriate for this journal: exploitation of technology was one of the underlying themes of the symposium.

Key words: Proton therapy; Physics; Hospital; Treatment facility

The primary foci of the symposium were on the physics underlying proton radiation treatment and the practical applications thereof. A major concern was to present information useful to individuals and institutions seeking to establish a hospital-based proton treatment facility. Speakers at the symposium represented many of the institutions that have played a leading role in the use of protons and heavy charged particles for therapy: Fermi National Accelerator Laboratory (Fermilab), where the world's first synchrotron designed for medical treatments was built; Lawrence Berkeley Laboratory, where the first proton treatment for cancer was performed (in 1954) and which has played a leading role in clinical investigation of heavy charged particles for therapy; the Paul Scherrer Institute, which has long conducted pion and proton investigations, and is a pioneer in the technique of scanned beams; Massachusetts General Hospital, which, in association with Harvard Cyclotron Laboratory, began investigations of proton therapy in the early 1960s and continues to do so at the Francis H. Burr Proton Therapy Center; and Loma Linda University Medical Center (LLUMC), which pioneered the hospital-based employment of proton radiation therapy. Presentations also were made by distinguished scientists from Johns Hopkins University, Columbia University, the University of Southern California, and the National Aeronautics and Space Administration. Attendees at the symposium also heard from representatives of institutions that have recently begun or are planning hospital- or clinic-based proton radiation therapy facilities, including M.D. Anderson Cancer Center and Tumor Institute, the University of Florida, Indiana University, and the University of Pennsylvania in association with Walter Reed Army Medical Center.

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The initial address was given by **Dr. Leon Lederman**, Director Emeritus of Fermilab and Pritzker Professor of Science at Illinois Institute of Technology. It was Dr. Lederman's decision that permitted Fermilab to engage in partnership with LLU to develop the world's first hospital-based proton synchrotron. In his highly successful career, Dr. Lederman has conducted experiments that provided major advances in the understanding of particles and interactions, thus contributing significantly to the "standard model." Among his many awards are the National Medal of Science, the Elliot Cresson Medal, the Nobel Prize in Physics, and the Enrico Fermi Prize. Dr. Lederman's presentation surveyed a variety of particles and sub-particles that make up the universe; he described some of the physics research that has been done at Fermilab and will be done at CERN, in Geneva, Switzerland, to study the basic nature of these particles. He over-viewed such basic matters as what a particle is and what an electron volt is, and described the most elemental particles and the high-energy machines, such as those at Fermilab and CERN, that are needed to reveal and study them. Dr. Lederman is a teacher in the most profound sense of the word; his presentation, given with the good humor and didactic clarity for which he is famous, was a true educational experience for all who heard it. In this issue Dr. Lederman offers his message almost exactly as he gave it at the symposium, so that our readers may share the same wonder and delight that attendees experienced. The paper reminds us again of the manifold debt that physicians and other scientists owe to discoveries made by physicists.

Dr. Lederman's presentation was followed by that of Dr. Alope Chatterjee, Senior Staff Biophysicist in the Life Sciences Division at Lawrence Berkeley National Laboratory. For 37 years, Dr. Chatterjee has conducted research in theoretical modeling involving energetic protons and heavy charged particles and their damaging effects on cells and tissues; in conducting this work, he has done research in radiation physics, radiation chemistry, and radiation biology. His presentation discussed the physical processes in the track structure of heavy ions and protons for applications in biology. He noted that protons and heavy ions have significant physical and biological advantages in the radiation treatment of cancer patients: about 90% of the total radiation dose can be concentrated on tumor volumes, while only about 10% is deposited in surrounding normal tissue. This, the Bragg peak phenomenon, is well understood on the basis of physical processes. He presented comparisons of Bragg curves for protons available at the Loma Linda facility and carbon ions available in Japan and Germany and demonstrated that, for a given depth of a tumor volume in a cancer patient, protons deposit much less energy in the surrounding normal tissue than carbon ions do. He observed that, in order to understand damages to DNA at the molecular level, the inclusion of track structure as well as chromosome structure have been

very useful. He presented results based on computer simulations of interaction between tracks and chromosomes, showing that, in the region of Bragg peak, the molecular damages are excessive compared to the region in the plateau.

The next speaker at the symposium dealt with dosimetry at the macro level. **Dr. Baldev Patyal**, Chief Medical Physicist in the Department of Radiation Medicine, LLUMC, offers in this issue a paper that encapsulates his presentation. He observes that high-energy photons and high-energy protons differ in the ways they interact with matter, and that these differences lead to distinct advantages of protons over photons for treatment of cancer, an observation first elucidated by Robert R. Wilson in his seminal 1946 paper (1). He reports that some aspects of proton interactions with tissue that make this modality superior for treating cancer are: (i) a low entrance dose and low doses to the normal tissues proximal to the tumor; (ii) near the end of their range, protons lose energy very rapidly and deposit all their energy over a very small volume, before coming to rest; and (iii) beyond the Bragg peak, the energy deposited by the protons is almost zero. These are ideal properties of a radiation modality to treat cancer; high-energy proton interactions intrinsically exhibit these properties, and thus provide a superior modality for treatment of cancer. Dr. Patyal observes that one advantage of protons over photons is the ease with which the tumor target can be irradiated conformally to a high dose, and at the same time the normal structures in the vicinity of the tumor can be protected conformally from that high dose. Given the same dose to the tumor *via* photons and protons, protons inherently deliver less integral dose and thus lead to far fewer normal-tissue complications. In addition, proton interactions also offer distinct radiobiological advantages over photons. Superior physical and radiobiological proton interactions lead naturally to the concepts of dose escalation and hypofractionation. He demonstrates the superiority of treatment delivery with protons by showing proton plans on actual patients, and comparing them with photon plans.

**Dr. John F. Dicello**, Professor of Radiation Medicine at LLU and Professor Emeritus, Department of Radiation Oncology and Molecular Radiation Sciences, Johns Hopkins University School of Medicine, followed Dr. Patyal at the symposium. His paper, published herein, reviews the radiation quality of protons and other energetic ion beams, dealing with relevant physical properties, other than dose, of the different types of radiations that can contribute to differences in absorption characteristics in various tissues and the corresponding clinical outcomes. He notes that early clinical studies of protons, neutrons, pions, and heavy ions proceeded on the presumption that these particles might have a therapeutic advantage owing to greater relative biological effectiveness (RBE). During the last three decades, however, advantages from protons and light ions have resulted largely from the better

dose delivery and localization that these ions made possible, in conjunction with improved imaging. Protons or light ions differ significantly in comparison with photon or electron beams in how they interact with tissue atoms and molecules, and in how they transfer energy to those tissues. They tend to travel in straight lines and produce long tracks, with the energy concentrated closer to the track of the primary particle, whereas photons or electrons tend to scatter more easily and produce a more uniform distribution of energy transfers. As hadrons, protons and similar ions are more likely to produce long-range nuclear secondaries with higher masses. This higher concentration of energy associated with the heavier particle beams and the more massive secondaries result in differences in dose localization, clinically and microscopically, and, therefore, potential differences in short-term and long term chemical and biological processes. Although protons tend to have the least differences in clinical response in comparison with photons and electrons, biological differences have nonetheless been observed and it is incumbent upon researchers to understand these different mechanisms and exploit their benefits. Dr. Dicello's article reviews the physical properties of these different particles in terms of microdosimetric distributions of energy deposition in order to compare protons with photons and heavy ions.

The next two presentations at the symposium were devoted to cell and tissue biologic effects of protons. The presenters were Andrew Wroe, a doctoral student from the Centre for Medical Radiation Physics (CMRP) at the University of Wollongong, Australia, and **Dr. Eric Hall**, an eminent radiation biologist from Columbia University who has received numerous honors and awards from societies in the United Kingdom and the United States, including gold medals from the American Society for Therapeutic Radiology and Oncology and the Radiological Society of North America. Dr. Hall is the long-time author of one of the definitive texts for students of radiation biology (2). Both presentations centered around the issue of neutron exposure in tissues as a by-product of proton irradiation by scattering techniques. At the symposium, their findings differed and generated spirited discussion.

Mr. Wroe recounted studies that have been done to determine the dose equivalent external to therapeutic proton fields in order to assess additional risk to the patient. To compliment this work, he reported on measurements that were performed to assess the dose equivalent outside a typical passively scattered and modulated prostate treatment field, using a Silicon-On-Insulator (SOI) microdosimeter, a technique that allows for determining the dose equivalent directly from the energy deposition spectra. Measurements were completed both at the surface of an anthropomorphic phantom and within a homogeneous polystyrene phantom, with the dose equivalent determined at various positions external to the incident proton field. He reported that the dose equivalent at the surface

of the anthropomorphic phantom decreases from 3.9 to 0.18 mSv/Gy when the lateral distance from the proton field edge increases from 2.5 to 60 cm. Measurements along the proton depth dose distribution at a constant depth of 5 cm from the primary field edge indicate a decrease in dose equivalent as a function of depth, with a 38% decrease relative to the surface dose at a depth of 5 cm in polystyrene. Measurements completed as a function of lateral distance from the primary field at two separate depths within polystyrene illustrate a convergence of the dose equivalent at approximately 20 cm from the primary field edge. Past the distal edge of the spread-out Bragg peak, measured dose equivalents decrease exponentially for increasing distance, with an initial measured value of 1.6 mSv/Gy at 0.6 cm from the distal edge. He concluded that the reported study showed the applicability of the SOI microdosimeter in measuring the dose equivalent outside proton treatment fields, and has provided valuable information of the dose equivalent experienced by prostate cancer patients treated with protons. Secondary neutrons were present, but many secondary particles produced within the passive scattering and collimation system were of low penetrating power and did not penetrate to a great depth within the phantom.

Dr. Hall's paper in this issue, on the other hand, notes that, while protons represent a logical step forward as a modality for radiotherapy because it is possible to concentrate dose in the tumor region and minimize dose to normal tissue, the pencil beam emerging from a cyclotron or synchrotron needs to be broadened to cover typical tumor volumes. Ideally, he observes, this should be accomplished by scanning the pencil beam using magnetic fields. Given that this technically challenging, a simpler method is to use passive modulation; however, that method produces neutrons in the scattering foil, resulting in a total body dose to the patient. Inasmuch as neutrons are highly effective at inducing second cancers, spot scanning is essential for the full potential of protons to be realized.

**Dr. James M. Slater** spoke on selecting the optimum particle for routine radiation medicine. In his paper, adapted from his presentation, he notes that cancer cells, along with their uncontrolled growth, invade into surrounding normal tissues, thus making it necessary to require that the selected beam of radiation be capable of selective cell destruction. Malignant cells do have some features that work in favor of radiation treatment: they are less able to repair radiation injury than are normal cells. This offers a potential advantage to radiation therapy: one can treat tissues that contain both normal cells and cancer cells with some confidence that the normal cells will survive and the cancer cells will not survive as their inferior repair mechanisms fail to repair the resulting damage. Even so, radiation oncologists must avoid injuring normal cells as much as possible. Selecting the optimal particle, then, is an exercise in identifying a par-

ticle that can be so controlled that its beam can be made to avoid normal cells as much as possible, yet will permit normal-cell repair in those instances where radiation exposure is unavoidable. Protons are able to do both, making them highly suitable as a mainstream therapeutic particle.

Dr. Francis Cucinotta, Chief Scientist in the Space Radiation Program, NASA Johnson Space Center, Houston, was the next speaker at the symposium. His talk, on the role of non-targeted effects as mediators in the biological effects of proton irradiation, dealt with radiation-induced cell damage from another perspective. He noted that, in recent years, the hypothesis that non-DNA targets are primary initiators and mediators of the biological effects of ionizing radiation, such as that from proton beams and heavy ions, has gained much interest. These phenomena have been called bystander effects, to distinguish them from the more traditionally studied model that focuses on direct damage to DNA. His presentation reviewed cellular and extra-cellular structures and signal transduction pathways that have been implemented in recent studies of this mechanism. Non-targeted effects of interest include oxidative damage to the cytoplasm and mitochondria, disruption of the extra-cellular matrix, and modification of cytokine signaling including transforming growth factor- $\beta$  (TGF- $\beta$ ), and gap junction communication. His talk introduced these targets and pathways, and contrasted their role with DNA damage pathways.

The next two papers, developed from presentations at the symposium, deal with equipment concepts for heavy-charged-particle therapy. The first is offered by **David Lesyna**, Vice President of Engineering, Optivus Proton Therapy, Inc., San Bernardino, California. He notes that a hospital-based proton beam treatment center comprises many systems that must be integrated to form a single medical device, one that is simple to operate and maintain. Using the LLUMC proton treatment delivery system as an example, he indicates the types of automation needed to achieve a high-capacity proton treatment system. His paper notes the work ongoing at LLUMC to continually improve proton radiation therapy and maintain it as a state-of-the-science modality at that institution; developments such as a robotic positioning system and a scanning beam are discussed. The following paper, by **Dr. George Coutrakon**, chief accelerator physicist at LLUMC, offers a status report of charged-particle accelerators for radiation therapy, focusing on current and future designs of medical hadron accelerators for treating cancer and other diseases. He notes that four hospitals and one clinic in the United States offer proton treatments, and other such facilities exist in Japan. Most of these facilities use accelerators designed explicitly for cancer treatments. Dr. Coutrakon also discusses several advanced features that are being incorporated for medical accelerators in new facilities.

The next paper, by **Dr. Reinhard Schulte**, Assistant Profes-

sor of Radiation Medicine at LLUMC, surveys treatment-room concepts for a proton therapy facility. Dr. Schulte's paper emphasizes that targeting of the tumor or other anatomical targets, and avoiding critical structures within the patient, must be very accurate to achieve desired therapeutic results with proton radiation. He overviews treatment room concepts designed to ensure accurate and precise proton beam delivery and promote efficient patient throughput. He emphasizes that, in addition to the technical armamentarium, the interaction between radiation oncologist, radiotherapist, and medical and accelerator physicists is important for effective operation of a proton facility.

At the symposium, several speakers followed Dr. Schulte, all offering reports on clinical experience and future directions at all of the clinical proton treatment centers in the United States and one in Switzerland. Some of those presentations have been reported as papers in this issue.

**Dr. Thomas F. DeLaney**, Medical Director of the Francis H. Burr Proton Therapy Center at Massachusetts General Hospital (MGH), Boston, reported on the relatively recent experience at that center. The MGH effort is unique, however, in that it is the direct descendant of one of the oldest experiences with laboratory-based proton therapy in the world, that of Harvard Cyclotron Laboratory (HCL). His paper in this issue concerns clinical proton radiation therapy research at the Francis H. Burr facility, the hospital-based successor to HCL. The current center has a 230-MeV cyclotron from which proton beams are directed to two isocentric gantries, a stereotactic intracranial beam line, and an eye line. At that institution, clinical treatment protocols have been grouped into two categories: in the first, dose is escalated for anatomic sites where local control with conventional radiation doses has been suboptimal; in the second, the normal tissue sparing with protons is designed to minimize acute and late toxicity to normal tissue. The facility currently treats 60 patients per day, including up to six children daily under anesthesia. Dose-escalation studies have been completed for early stage prostate cancer (in conjunction with LLUMC) and sarcomas of the cervical spine/base of skull and thoracolumbosacral spine. Protocols are in progress or development for patients with carcinoma of the nasopharynx, paranasal sinus carcinoma, non-small-cell lung cancer, locally advanced carcinoma of the prostate, hepatocellular carcinoma, and pancreatic cancer. Studies evaluating the use of protons for morbidity reduction include protocols for craniospinal irradiation in conjunction with systemic chemotherapy for medulloblastoma, retinoblastoma, pediatric rhabdomyosarcoma, other pediatric sarcomas, and accelerated, hypofractionated partial breast irradiation for early-stage breast cancers. For pediatric patients, protons have also been accepted as an alternative to photons for children enrolled in Children's Oncology Group protocols. Treatment of patients on these studies has

often required the development of new treatment techniques, respiratory gating, and development of appropriate clinical infrastructure support such as increased availability of pediatric anesthesia. In addition, a clinical research infrastructure for protocol development and data management is required. He concluded that proton radiation offers potential treatment advantages that can be studied in clinical trials, and noted that accrual to selected studies has been favorable.

**Dr. Jerry D. Slater**, Chairman of the Department of Radiation Medicine at Loma Linda University, gave the next presentation, and offers a paper in this issue. He reports that the Proton Treatment Center at LLUMC, the world's first hospital-based proton facility, opened in 1990. It has had a long history of development, stretching back to 1970. The facility's early years were marked by a deliberately cautious approach in clinical utilization of protons, with intent to establish hospital-based proton therapy on a scientific basis. More than 50 anatomic sites currently are treated with protons, either as sole treatment or in combination with photon radiation or other modalities. The LLUMC facility was designed to be upgradeable, and development since 1990 has proceeded in three distinct phases of upgrades, both in technology and clinical applications. Upgrades continue, all of them based on an underlying program of basic and clinical research; future new applications of proton radiation therapy, such as employment of protons for larger-volume tumors, are expected to follow owing to the facility's ongoing commitment to employ the latest technology and conduct clinical studies based on a foundation of basic-science research. Dr. Slater's paper offers insights into the development and operation of a hospital-based proton treatment facility. Of special note is his contention that, from the standpoint of the patient and largely from the standpoint of the radiation oncologist also, there is little difference between a "proton patient" and a "photon patient" as practiced at LLUMC. He notes further the absolute necessity for a proton treatment facility to be so designed that it can adapt to advances in technology.

Dr. Nancy Price Mendenhall, Medical Director of the University of Florida Proton Therapy Institute and Professor in the Department of Radiation Oncology at the University of Florida College of Medicine, offered a presentation describing the start-up experience at that facility, which commenced clinical operations at Jacksonville, Florida, in 2006. She described a developmental history extending back to 1998, when the concept for a proton center at Shands Hospital was first presented. The next four years were devoted to feasibility and planning studies, including securing financing, which was a major undertaking for the University of Florida, a state university. The hospital-based facility was conceived of as being a center for patient care and research; the developers felt strongly that it should be a comprehensive radiation therapy service, not protons in isolation from conventional radiation.

A high degree of efficiency was sought, while maintaining a culture of compassion and including a research mission to assist radiation oncologists in understanding how best to use this new modality. Finally, the facility was conceived of as a state and regional resource for the southeastern United States. Dr. Mendenhall offered a perspective from the standpoint of a facility that is just commencing operations. She opined that starting a proton facility differs greatly from a conventional facility; although proton therapy has proved to be beneficial, much remains to be learned about its best use. Most of systems on the market today are not turnkey, in her opinion, so most new programs will need to learn much on their own; it is easy, she observed, to underestimate the complexity of the undertaking. Further, developing and operating a proton facility is a team effort: physicians, physicists, and administrators need to function well together. Strong leadership must be backed up with the authority to make decisions about objectives and operations, manifested in a partnership attitude with architects, constructors, vendors, and the community. Treatments should be done according to protocols, and extra physician time should be allocated for their development. Finally, proton facilities throughout the world should be collaborative and not competitive in their relationships with other programs.

Dr. James D. Cox, Professor of Radiation Oncology and Head of the Division of Radiation Oncology at M.D. Anderson Cancer Center, Houston, Texas, gave the next presentation, in which he described the University of Texas M.D. Anderson Proton Therapy Center. The University of Texas M.D. Anderson Hospital began to develop their center in 1999; groundbreaking took place in May 2003; treatment of patients started on May 2006 on Gantry 1. In July, the facility opened its horizontal fixed-beam room for patient care as well. Clinical commissioning was proceeding on Gantry 2 at the time of the symposium, and was anticipated that it would be available for patient care in September 2006. Hitachi, Ltd. supplies all of the proton-specific hardware and software at the M.D. Anderson center, including the accelerator and beam transport systems. The facility uses Varian Eclipse as the treatment planning system for its passive scattering treatment plans; development is ongoing with Varian for a treatment planning system for pencil beam therapy. An IMPAC data management system is used for the interface of the Hitachi control system. The facility operates a General Electric CT simulator for patient simulation and is upgrading the CT scanner to a 16-slice system. Clinical teams at M.D. Anderson Cancer Center are developing treatment protocols, immobilization devices, and clinical procedures to gain efficiencies in patient care. All individuals under treatment at the facility are registered on clinical protocols to ensure that data are collected on all patients. The proton therapy system combines the multidisciplinary care environment of the M.D. Anderson Cancer Center; the advanced technology,

high-throughput system of radiation treatment delivery of the Department of Radiation Oncology, with its teams of specialized physicians, physicists, and dosimetrists; and the proton treatment facility itself. Dr. Cox noted that the entire system, including the proton component, is intended to bring multidisciplinary care to cancer patients in a unique way.

Dr. Allan F. Thornton, Medical Director of the Midwest Proton Radiotherapy Institute (MPRI) at the Indiana University Cyclotron Facility (IUCF), Bloomington, offered a presentation describing the progress at that Institute. Dr. Thornton described a facility that is being reborn, in a sense; the Indiana experience is several years old but has been restricted to a limited, albeit catholic, corpus of treatments. He described a facility that has had a single horizontal beam line but is in the process of commissioning one gantry beam-delivery unit and constructing another while establishing a new relationship with the School of Medicine at Indiana University. The facility has employed a passive scattering beam-delivery system for its horizontal beam, but will use a system called uniform scanning, described as a "halfway house" between passive scattering and full spot scanning, for its first gantry. The decision about beam delivery in the second gantry will await experience with the first, but a full scanning system is anticipated. The design of the second gantry room also awaits analysis of the experience with the first; development of each room is staged, to permit exploitation of new technology or modifications based on experience. Robotics are used for patient positioning, and an observation area has been included in the room design to permit observation of children who receive general anesthesia in preparation for treatment. MPRI is not a dedicated medical facility; it employs the same 203-MeV cyclotron as does IUCF. The clinical operation's "uptime" is less, therefore, but the facility, including its upgrades, has been less expensive to fabricate than a completely new facility because some of the plant is shared and established construction techniques have been used to create the treatment section.

Dr. Gudrun Goitein, Head of the Division of Radiation Medicine at the Paul Scherrer Institute, Villigen, Switzerland, offered a presentation on the Institute's experience performing radiation therapy with spot scanning proton beams. She recounted some of the Institute's history as a setting for her discussion. The Paul Scherrer Institute (PSI) is Switzerland's largest national research institution (CERN is an international institute). This physics research institute has nonetheless offered particle radiation therapy for more than 20 years, beginning with pion treatments in the 1980s. At that time there was great hope in the pion beam because one thought that the high-linear-energy transfer (high-LET) radiation would be the ideal weapon against relatively radioresistant tumors. Dr. Goitein noted, however, that, over time, the greatest impact arose from the physical dose distribution, whereas PSI

physicians could not show definitely that the RBE effect accounted for a great difference. Also, in 1984, PSI introduced a horizontal proton beam line for treatment of ocular melanomas; more than 4,500 patients have been treated, with excellent results. Spot scanning at PSI was an attempt to employ a pencil beam to treat large volumes, thus reducing penumbra effects from a broadened beam. This helped to maintain the low toxicity associated with proton beams, and Dr. Goitein observed that low toxicity of itself helps make protons useful not only as primary treatment for, say, pediatric tumors, but also as a component in combination regimens with non-radiotherapeutic modalities. Another advantage of beam scanning, according to Dr. Goitein, is that scanned beams often reduce the number of beam angles, in itself leading to less normal tissue irradiated. If intensity modulation is applied to protons, the beam angles remain fewer than obtains with intensity-modulated photon beams. The PSI experience has validated the concept that spot scanning is feasible, safe, reliable, and comfortable for the patient. Regarding the fact that PSI is not a hospital-based facility, Dr. Goitein observed that the facility has less control over referrals and depends on the understanding and cooperation of colleagues at other centers. It is important, therefore, that outside clinics and physicians be made partners and not competitors. The Swiss Proton Users Group was formed to foster this; all clinics and radiation oncologists in Switzerland are represented, as are European colleagues. This atmosphere of cooperation, she observed, should prevail generally.

**Dr. James McDonough**, Assistant Professor in the Medical Physics Division of the Department of Radiation Oncology at the University of Pennsylvania, Philadelphia, and **Captain Brent A. Tinnel, M.D.**, Staff Radiation Oncologist, Walter Reed Army Medical Center, Washington D.C., offered separate but complementary presentations on the forthcoming University of Pennsylvania/Walter Reed Army Medical Center Proton Therapy Program. In their co-authored report in this issue, they note that the design of this new proton therapy center, being constructed in Philadelphia, is based on several principles that distinguish it from other proton facilities. Among these is the recognition that advances in imaging, notably functional imaging, will have a large impact on radiotherapy in the future, and that the conformation of proton dose distributions can use that information to a larger degree than can other treatment techniques. Accordingly, the Philadelphia facility will contain four-dimensional CT simulators, an MR simulator capable of spectroscopy, and a PET-CT scanner. A second principle that will be applied to the facility design is to incorporate into proton radiotherapy the recent progress in conventional radiotherapy, including imaging and monitoring of patients during treatment; imaging of soft tissue; accounting for respiratory motion, and expanding the use of intensity-modulated treatments. Thirdly, the facility is being designed to be operated efficiently; to

that end, specifications for equipment have included requirements for high beam intensity, fast switching times between treatment rooms, a multileaf collimator to permit multiple fields to be treated quickly, and plans for an intelligent beam scheduler to determine where the beam can be best used at any given time. The facility will feature “universal” nozzles, which can switch rapidly from scattering to scanning mode, and a set-up room will be used on the patient’s first day of treatment to verify alignment, rather than using up valuable time in a gantry room. The authors note that several of the aforementioned ideas require development, including the applications of existing radiotherapy techniques to proton gantries; accordingly, a series of research and development projects address these issues. Walter Reed Army Medical Center, which will provide a portal through which military personnel and their dependants can receive proton radiotherapy, is involved in several of these development projects as well as the creation of processes to perform treatment planning remotely for military patients being treated at the Philadelphia center.

The final presentation of the symposium was offered by **Dr. Brent J. Liu**, Assistant Professor in the Department of Radiology, Keck School of Medicine, and the Department of Biomedical Engineering, Viterbi School of Engineering, University of Southern California, Los Angeles. Dr. Liu’s paper based on that presentation, published in this issue, describes a knowledge-based imaging informatics approach to managing proton beam therapy of cancer patients. Dr. Liu notes that the need for a unified patient-oriented information system to handle complex proton therapy imaging and informatics data is becoming steadily apparent. Currently, this information is scattered throughout each of the different treatment and information systems in a radiation oncology department, and failure to employ standardized methods makes it difficult and time-consuming to process data, resulting in challenges during patient treatment planning. He presents a methodology to develop an electronic patient record system based on DICOM standards and perform knowledge-based medical imaging informatics research on specific clinical scenarios where patients are treated with protons. Treatment planning is similar in workflow to traditional radiation therapy methods, which utilize prior knowledge to drive the treatment plan in an inverse manner. In March 2006, two new radiotherapy objects were drafted in a DICOM-RT Supplement 102 specifically for ion therapy, including proton therapy. Dr. Liu’s paper presents the initial steps of this imaging and informatics methodology, which lays the foundation for developing future decision-support tools tailored to cancer patients treated with protons.

Several of the presenters touched on common themes. Precision, along with efficiency, seemed to be a consensus, indicating that a clinical proton treatment facility needs to be operated in a highly effective and efficient manner for quality,

economic, and logistical reasons. Associated with this was the theme of reliability: the facility should have very little “downtime,” to achieve these goals. Another point raised by many presenters, both at the symposium and in the papers in this issue, is the special advantage that proton therapy has for treating pediatric tumors. Dr. Goitein perhaps best expressed the potential power of protons in the pediatric milieu when she observed that “the entire child is one critical organ.” A third theme voiced over and over again was the need for cooperation and collaboration, not competition, among the various proton and heavy-charged-particle facilities. Dr. Goitein again expressed the point most succinctly: “Protons are not the way to make money, they are a way to spend money for the improvement of cancer therapy and for the sake of our patients. They trust in us, not in our shareholder mentality.”

The symposium and the scope of the papers published in this issue testify to the intellectual ferment surrounding proton radiation therapy today. Though it is in many ways a mainstream therapeutic procedure that has made a notable impact on the practice of radiation oncology, it is also an evolving therapeutic discipline. Physics is its bedrock, and the many advances being contemplated for the future, such as scanning beams, rely on a profound understanding of physics principles for their realization. These principles extend not only to better understanding of means of delivery, which can be realized through engineering, but also to better understanding of the physical and biological effects of protons as they interact with sub-cellular components. The opportunities for further study are almost infinite.

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