

Weighing Proton Therapy's Clinical Readiness and Costs

We have two comments on the recent article by Michael Goitein, Antony Lomax, and Eros Pedroni ("Treating Cancer with Protons," *PHYSICS TODAY*, September 2002, page 45). First, the 5000 uveal melanoma patients that the authors mention were treated at the Harvard University Cyclotron Laboratory (about 3000 patients) and the Paul Scherrer Institute (about 2000), not Massachusetts General Hospital and PSI as stated. Ian Constable and Evangelos Gragoudas at the Massachusetts Eye and Ear Infirmary developed the technique with HCL staff as part of a strong collaboration with MGH's radiation oncology department. PSI and other proton radiation therapy centers later emulated the technique. The long-term teamwork between physicists and hospital staff, in a small but very coherent group with HCL as its nucleus, led to that and many other developments in proton therapy.¹

Second, and far more important, the authors' statement that "[protons] have moved from the laboratory to the clinic" glosses over the problems that have so far attended that move. The difficulties of technology transfer have been, and are still, seriously underestimated by many in positions of responsibility. Techniques that would be pedestrian in a mature high-energy physics lab are difficult in the clinic or in commercial ventures, in which the resources and technical backup are far smaller. It is no accident, for instance, that the 17-year-old magnetic scanning technique² is currently found only at two large laboratories—PSI and the Laboratory for Heavy-Ion Research (GSI) in Darmstadt, Germany.

A look at the two dedicated proton treatment facilities in the US illus-

trates the problem. Around 1987, the Loma Linda University Medical Center selected Fermilab to furnish a synchrotron and chose Science Application Industrial Corp (SAIC) as an industrial partner to replicate the technology for other customers. LLUMC also began hiring a technical team and forming the Radiation Research Laboratory (RRL) to provide systems engineering, safety systems, and clinical hardware and software for the treatment rooms. In 1990, the year of the first treatment, LLUMC and SAIC ended their business relationship and RRL became responsible for further development and maintenance.

In time, RRL was reconfigured and is now Optivus Technology Inc, housed about two miles from the therapy center. According to Dave Lesyna, current vice president for engineering, the original staff of about 34 has grown to roughly 60 and comprises 24 engineers of various sorts, 8 service technicians, and 28 managerial and support staff. Those numbers do not include the clinical staff (oncologists, radiation therapists, dosimetrists, medical physicists, machine operators, and support staff) who operate the facility. In essence, starting with Fermilab and SAIC and ending with a significant in-house effort, LLUMC has produced, in one decade, a proton radiation therapy facility that has more than 150 treatment sessions per day and treats more than 1000 patients annually. Furthermore, the technical expertise is available for magnetic scanning, intensity modulated therapy, and similar advances. Optivus markets a proton therapy system based on the LLUMC experience and cleared by the Food and Drug Administration.

MGH went the opposite route. Ion Beam Applications (IBA) was selected as the equipment vendor, and is still responsible for completion of the facility, most of the maintenance, and future upgrades. The hospital assumed responsibility for producing some of the equipment, but, by design, the technical staff on the hospital side is limited to around six people. The time from groundbreaking to first treatment (in November 2001) proved to be six years instead of three

because of hardware and software problems. As of March 2003, only half the beam lines shown in figure 2 of the article by Goitein and coauthors were in service. The throughput in the single operational gantry room was about 18 patients per day, less than half the design goal. Overall equipment reliability was about 90%, unacceptably low in a clinical setting. In short, the technical forces demanded by the project were greatly underestimated by both the hospital and the vendor, even though the LLUMC experience was available to them.

Broadly speaking, development of a proton-radiation therapy center can take one of two routes. The hospital can buy major pieces of equipment and retain responsibility for integrating them and procuring additional equipment as needed. Or the hospital can buy a complete turnkey system from a commercial vendor. It is critically important to the future of proton radiation therapy that the personnel requirements be realistically assessed by the responsible party—either the hospital or the turnkey vendor. The next few centers, now on the drawing boards, will be a test.

References

1. B. Gottschalk, A. M. Koehler, J. M. Sisterson, M. S. Wagner, *CERN Courier* **39**, (1999).
2. H. Tsunemoto et al., *Radiat. Res.* **104**, S235 (1985).

Bernard Gottschalk
(gottschalk@huhepl.harvard.edu)

Andreas M. Koehler
(koehler@huhepl.harvard.edu)

Richard Wilson
(wilson5@fas.harvard.edu)
Harvard University
Cambridge, Massachusetts

In their article, Michael Goitein, Antony Lomax, and Eros Pedroni describe how beams of 250-MeV protons can produce radiation dose distributions that conform to the shapes of tumors much more precisely than those from 6- to 10-MeV x rays. The authors also describe how, due to the sharply defined depths of penetration, the doses to normal organs surrounding the tumor may be kept well below tolerance levels. As a result, the reader is led to believe that proton-beam installations dedicated to radiation

Letters and opinions are encouraged and should be sent to Letters, *PHYSICS TODAY*, American Center for Physics, One Physics Ellipse, College Park, MD 20740-3842 or by e-mail to pletter@aip.org (using your surname as "Subject"). Please include your affiliation, mailing address, and daytime phone number. We reserve the right to edit submissions.

therapy could significantly affect a cancer patient's life expectancy and quality of life. Several clinical considerations throw this hypothesis into doubt, to say nothing of the economics. But first, permit us to point out the fundamental flaw in the authors' argument.

Surgery is the primary treatment for more than 80% of all cancers at most hospitals, and for good reasons. For example, when treating esophageal cancer, it is standard practice for a surgeon to resect several centimeters of apparently normal tissue above and below the cancerous region to assure that microscopic disease has not been left behind. Subsequent pathological staging provides guidelines about the likely course of the disease and whether follow-up treatments will be required. Despite what would appear to be an aggressive and definitive approach, the five-year survival rate for esophageal cancer patients is around 15%. The results for other, more common cancers are not so dismal: about 60% for the colon and 80% for the bladder. In the context of surgical experience, one must wonder how the millimeter precision of proton-beam dose distributions will benefit the patient.

Albeit more traumatic than radiation therapy, surgery presents the family physician with the status of the patient's cancer in a matter of days, and the need for adjuvant therapies can be decided early on. The authors suggest that the results of well-established clinical protocols, many of which include radiation, can be improved by the precisely defined dose distributions provided by proton beams. However, before this highly complex and expensive modality receives widespread adoption, clinical data must show marked and statistically significant improvements in the life expectancies of most cancer patients.

Radiation therapy plays a primary or competing treatment role in at least six cancers that make up more than 23% of all new cases; it also is used in supportive therapy for many others. Along with surgery and chemotherapy, radiation therapy is a critical component in the current armamentarium for the treatment of cancer. As for the future of the therapeutic applications of ionizing radiation, clinical trials over the past decade suggest that a plateau has been reached and that the impact of new modalities such as proton beams and intensity-modulated

radiation therapy (IMRT) on overall cancer mortality will be difficult to detect. As the cost of health care continues to rise at an alarming rate, consideration of the cost/benefit ratios for newly introduced technologies increases in importance. Are 250-MeV proton-beam facilities likely to show a favorable reduction in this ratio for cancer patients? Based on the results of more than 20 years of proton-beam therapy compared with those achieved by conventional x rays, we think not.

Goitein and his colleagues present some data on clinical experience that are difficult to interpret in the context of their article. However, the reader should appreciate that, whether by prostatectomy or conventional x-ray therapy, the 5- and 10-year relative survival rates (relative to age-matched men who die of other causes) for early-stage prostate cancer are 90–98% and 80%–90%, respectively. The authors present a sketchy overview and some results unrelated to those obtained by more conventional treatments. Except for prostate and lung, the other disease sites mentioned make up but a small percentage of all new cases. How can the authors justify the expenditure of tens of millions of dollars for equip-

SPECTROSCOPIC ELLIPSOMETERS

FOR MATERIALS CHARACTERIZATION

Determine Refractive Index and Film Thickness

VERSATILE FOR APPLICATIONS INCLUDING:

Semiconductor

Photoresists, AR coatings, low-k, poly, SiGe, III-Vs and II-VIs....

Telecommunications

AR for lasers, VCSELs, DWDM films....

Optical Coating

AR films, hi-lo stacks, hard coatings....

Data Storage

Head and disk structures, phase-change media



J.A. Woollam Co., Inc.

645 M St., Suite 102, Lincoln, NE 68508

Ph 402-477-7501 Fax 402-477-8214

www.jawoollam.com

ment, to say nothing of high operating costs, for the treatment of these rare tumors? (Perhaps by the establishment of a few national referral centers, but that is another issue.) In their one-sentence discussion of disease-free survival for lung cancer (83%) at Loma Linda University Medical Center, the authors failed to mention the time period involved. Surgical management of stage-I non-small-cell lung cancer currently achieves five-year survival rates of 50–60%. It is difficult to understand why radiation would be so strikingly superior to surgery for this highly malignant disease. Perhaps the time elapsed since treatment at Loma Linda is considerably shorter than five years.

The authors are to be commended for a clear and comprehensive description of how cyclotrons, originally used to study nuclear structure and interactions, were redeployed to treat cancer. Goitein and his coauthors show how radiation dose distributions can be made to conform to the complex shapes of tumors and thereby permit delivery of higher doses. We wish that these refinements were all it would take to reduce cancer mortality. Unfortunately, the majority of cancer deaths are due to metastases from malignant cells that have stealthily diffused into adjacent tissues and into organs far from the primary. Radiation therapy has been researched and developed for nearly a century, and improvements in radiation source technology have most certainly contributed to the increased life expectancy of cancer patients over that time. Two questions remain: How much more can we reasonably expect from further improvements in dose distributions? And how much are we willing to pay for them?

R. J. Schulz
(schulz@pshift.com)
Yale University

New Haven, Connecticut

A. Robert Kagan
Southern California Permanente
Medical Group
Los Angeles, California

Goitein, Lomax, and Pedroni **reply:** We deeply regret having failed to acknowledge the roles of the Harvard Cyclotron Laboratory and the Massachusetts Eye and Ear Infirmary in developing the proton treatment of ocular tumors. We know better than most how central and vital those roles were to that highly successful program. By April 2002, when the HCL stopped operations, it and the Paul Scherrer Institute were neck and neck

in the number of eye tumors treated: HCL had 3466 and PSI had 3538.

Bernard Gottschalk, Andreas Koehler, and Richard Wilson take the view that proton therapy has not yet achieved the efficiencies and the reliability to justify the claim that it is a routine clinical option—and that we “glossed over” the problems that remain. In just what state proton therapy now finds itself is a matter of judgment. At Loma Linda University Medical Center, 7176 patients had been treated with protons as of April 2002, and LLUMC now treats more than 1000 patients per year. The new

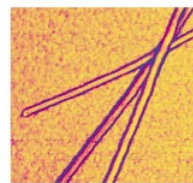
Massachusetts General Hospital facility treated 228 patients in its first full year of operation. Given that only one of MGH's two gantries was in operation, that figure does not compare badly with the current throughput at LLUMC with its three gantries and 10 years' experience.

In addition to LLUMC and MGH, two hospital-based proton centers are operating in Japan; worldwide, several clinical facilities are under construction and others are in mature planning stages. So our opinion that the “move to the clinic” has taken place seems quite reasonable.

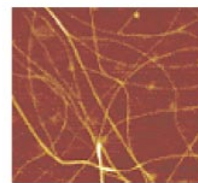
Achieve Control over Nanotube Synthesis

EASYTUBE™
System

- Turnkey System
- Safe
- Flexible
- Reliable
- Repeatable



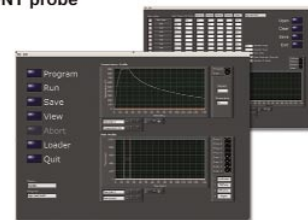
300nm AFM phase
contrast image of
SWNT ropes imaged
with a SWNT probe



High yield SWNT
synthesis process

Achieve control and repeatability with the **EasyTube System**, designed specifically for carbon nanotube synthesis.

The **EasyTube System** integrates advanced catalyzed chemical vapor deposition process with precise computer control, intuitive software interfaces, and process monitoring for safe operation.



Contact Us!

Toll Free Call in USA

1-800-715-8440

International Call

1-805-696-9002

info@nanodevices.com
www.nanodevices.com



NANO DEVICES

5571 Ekwill Street, Santa Barbara, CA 93111, USA
805-696-9002 fax: 805-696-9003