

Executive Summary

At the behest of Dr. Jay Hess, Vice-President of University Clinical Affairs and Dean of the Indiana University School of Medicine, this committee was formed to review the current status and future prospects of the Indiana University Health Proton Therapy Center (IUHPTC). In particular, was there a strategy (e.g. investments in new equipment, reorganization, or ways of building patient volume) that would permit this facility to succeed, or should it be closed. The committee was comprised of the following members:

Theodore S. Lawrence, MD, PhD, Committee Chair
Stephen M. Hahn, MD
Patrick J. Loehrer, Sr., MD
Dennis M. Murphy
Anthony L. Zietman, MD
Ellen S. Burton, MPH, CHES, Staff

The information for this report came from detailed written materials as well as a site visit on March 27-28. At the site visit, we heard presentations from attending physicians from the center, referring physicians, resident physicians, physicists, dosimetrists, and administration. We had a full tour of this remarkable facility. In addition, we met with the most senior leadership of Indiana University, including the president, provost, the dean, and CFO (see Appendix 1: Agenda). We had ample opportunity to ask questions at all stages of our review. Therefore, the committee felt that we had obtained a full picture of IUHPTC both from the inside and outside (with the possible exception of finances, as described below), and we feel confident that this is an informed report.

In order to address the current and future status of IUHPTC, we decided to organize our review around the following questions:

- 1) What is the status and future of proton therapy? Who should and should not be treated with proton therapy?
- 2) Can the IUHPTC play a meaningful role in the evaluation of proton therapy? Does IUHPTC have a track record for research and are there opportunities to make unique contributions?
- 3) Is IUHPTC financially viable? What is the current financial condition of IUHPTC and what are the future prospects, given the need to replace the cyclotron in the next few years.
- 4) Is the capability for proton therapy crucial to the mission of IU Health? In other words, would the ability to treat with protons be important enough to mitigate a loss if it were projected based on the analysis from 3) above?

We concluded that proton therapy does have potential value in the treatment of certain cancer patients. However, IUHPTC cannot contribute meaningfully to research in this field. This facility is outdated and requires significant investment to continue to operate. Because of both the expense of these investments and the high operating costs of an aging facility, it does not appear that IUHPTC can ever achieve a positive margin. We did note some potential improvements in financial operations (described in Section 3). Although it would seem reasonable to analyze these suggestions before making a final decision, our high level estimate was that these changes would not bring the facility to a financial break-even point. The presence of IUHPTC is not sufficiently critical to the mission of IU to justify continued financial losses that are likely to continue should the facility remain in operation. Therefore, the committee concluded that the IUHPTC will likely need to be closed.

We wished to note that we were highly impressed with the technical staff and faculty who have done an exceptional job of keeping older and outdated technology in excellent running condition in order to safely treat patients. Their craftsmanship and their dedication to IUHPTC are impressive.

The committee also wished to share some additional thoughts with senior leadership regarding the strategy for winding down the IHUPTC and for IU Health to have a proton facility. These thoughts are presented at the end of the report.

This report was written by the external advisors (Drs. Stephen Hahn, Ted Lawrence (Chair), and Anthony Zietman), with help from the other committee members. There was unanimous agreement on all of the issues described below.

1) What is the Status and Future of proton therapy in the United States

Proton beams generated in physics laboratories were originally used for cancer therapy fifty years ago. The superior distribution of the radiation beam within human tissue made it a potentially attractive alternative to the more standard radiation treatment of the day. Because of technological, computing, and imaging limitations, the concept was regarded as somewhat boutique until the late 1980s and relatively few clinical reports were produced. At this point a confluence of imaging advances and new computing power meant that the ability to realize the 3-dimensional tissue sparing power of proton therapy became possible. Loma Linda University Medical Center opened a patient-focused treatment facility in 1991 and the Massachusetts General Hospital followed in 2000. In recognition of the cost of proton therapy and, in part because its rapid growth was not anticipated, generous billing codes were granted by Medicare with private insurers following suit.

In 2004 the Midwest Proton Therapy Institute (MPRI, now IUHPTC) became only the third such facility to open in the USA building upon its own solid physics infrastructure rather than choosing to purchase its equipment from a commercial vendor. In the latter part of the decade many new facilities have been opened, briefly slowed by the economic recession, but now accelerating once again. Fifteen are currently functional and at least 20 others are in the construction or planning stages. The recent enthusiasm is derived from a number of advances and opportunities:

- 1) Widespread recognition of the potential of proton beam to reduce late complications of radiation therapy and to increase the chance of eradicating cancer. Developments in imaging and image-guidance of therapy may be folded in with proton beam to create a uniquely accurate form of radiation therapy. This is a natural extension of the current culture of precision therapy that has been developing over the last two decades.
- 2) Emerging data to support the concept of clinical gains at some sites e.g. skull base or eye tumors or in pediatric patients. This has been accompanied by an inference that similar gains can be realized at other sites in the body
- 3) Commercially available “turn-key” proton facilities with creative financing methods that obviate the huge initial financial hurdle with reduced manpower and maintenance needs.

The rise in the number of prostate cancer cases was due to PSA screening coupled with a growing concern about the quality of life consequences of both surgery and the more traditional radiation therapy used for this disease also contributed to this “boom”. Throughout the last decade prostate cancer patients treated by proton therapy became its greatest advocates and their opinion was widely propagated through the Internet generating substantial demand. Proton beam facilities have become

profitable by treating a large number of these rapid throughput cases. Diffusion of this technology has also been spurred by the development of smaller single-room cyclotrons that offer the therapy at a cost in the range of \$30M, as opposed to the \$150-200M for the initial facilities with 4 treatment rooms.

In this era of cost-containment, however, proton beam therapy has come under increasing scrutiny by clinicians, payers, and the media. The fact that any proton facility costs 10-100x as much as the next most expensive medical device has placed it in the center of the debate about value-based medicine and some insurers are starting to balk at the cost and to decline coverage.

The principal issues are:

- 1) A failure of investigators to demonstrate in a scientifically robust fashion the putative benefits of this therapy. There have, to date, been no completed randomized trials at any site demonstrating “proof of principle”. There have been very few prospective quality-of-life studies documenting advantage, even in children. Proton beam does not, therefore, feature in most national guidelines for cancer care.
- 2) A substantial improvement in the alternatives to proton beam. Photon beam (i.e. standard) radiation therapy did not stand still and “intensity-modulated” techniques (which can turn one beam into hundreds of “beamlets”) of external radiation or stereotactic radiation therapy (which uses many relatively low intensity beams focused on the tumor, thus producing an ablative treatment with little toxicity) have closed the gap with proton beam to an unanticipated degree.
- 3) The promulgation of alternatives to radiation therapy such as minimally invasive, robotic surgery, which like proton therapy, have little supporting evidence but much fanfare.
- 4) The changing patterns of care in prostate cancer. The claim of efficacy of screening for prostate cancer has suffered from either negative or ambivalent randomized trials. The number of cases diagnosed per year is now declining and the numbers being managed without active treatment (i.e. observation) is rising fast. The majority of cases are now in the low-risk category and the vast majority of these are being managed by robotic surgical techniques. This is important, as prostate cancer had been the economic driver behind proton therapy in the USA.
- 5) Critical review of payment strategies by CMS specifically for proton therapy but also in the context of wider healthcare and payment reform. It is unknown how new models (medical homes, disease-based payment, bundles) will affect proton therapy but it is unlikely that they will incentivize it.

It is, therefore, quite possible that we are on the verge of a “proton bubble” with the more indebted centers or those without a strong patient supply line closing. Those with less or no debt, or those built around academic institutions, will likely survive and continue to provide the care that pediatric and base of skull tumor patients need. It is hoped that they will develop the data necessary to define the exact role of proton beam therapy in oncology. At present we can say that there are sites where a clinically meaningful advantage likely exists (eye, skull base, pediatrics), those where it likely does not exist (most breast or GI cancers), and those where it needs formal investigation (liver and lung). The future of proton therapy will depend in part upon the demonstration of a meaningful clinical advantage in some, any, or all of these clinical sites, and in part on technological advances that will allow it to “pull away” from the competition once again. Intensity modulated proton therapy is an example of such a technique that is being employed by a few proton centers at present and will likely be adopted by others in the future.

It is against this background of clinical and economic uncertainty that the past contributions, current viability, and future potential of the Bloomington facility must be measured.

2) Can the IUHPTC play a meaningful role in the evaluation of proton therapy?

Meaningful evaluation could take three forms: development of new technology, discovery of new biology, or the conduct of impactful clinical trials. The committee considered the current and potential contribution of IUHPTC to each.

a) Implementation of new technology

With respect to technology, it is important to note that IUHPTC was initially a technology leader. For instance, they were initially leaders in developing a scanned beam to produce a uniform field. Standard technology 10+ years ago used double scattering to turn a small beam into a usable treatment field, which could generate a “neutron bath” that could partially negate the precision of proton therapy. Thus, the scanning technology used by IUHPTC was probably the superior technology 10 years ago.

However, although initially a potential strength, the most important impediment is that the technology has not continued to develop. Although the replacement of the cyclotron would permit the facility to continue to function, it would not permit the development of state of the art technology, which would require multiple other components. For instance, the use of brass mounted compensators, while safe and effective, would no longer be considered “cutting edge” for technology development. Current machines use a multileaf collimator, which is far less time consuming and labor intensive, than the approach used at IUHPTC. Current research in proton delivery is now focused on intensity modulated proton therapy (IMPT) using scanning beam techniques, beam energy switching, and tumor localization using on-board imaging including cone-beam CT scanning. Although the collaboration with industry on nozzle development that was discussed at the site visit might ultimately help, it is still under development, and will not overcome the basic issues of an outdated cyclotron and the aging beamline.

b) Biological research

This topic was minimally covered at the site visit. Some work was performed in the past confirming well-established findings that the relative biological effectiveness (RBE) of protons is about 1.1 compared to photons. Some institutions are testing the hypothesis that the RBE of protons may be much higher than 1.1 in a small region at the end of the Bragg peak. However, there appears to be no active research at IUHPTC on the biology of proton therapy.

c) Clinical Research

There has been only very modest clinical research at IUHPTC. Clinical trial development is severely hampered by the location of the facility in Bloomington for at least three reasons. First, all patients must travel a significant distance to come to the facility. This has limited the overall number of patients treated, which makes it hard to accrue a sufficient number of patients with a single disease to answer a clinical question. Second, it is far from the “nerve center” of IU. Although the physicians at IUHPTC spend a day a week at the University Hospital, it is difficult to have sufficient interaction with other physicians in such a setting to develop novel studies. Third, many clinical trials require both chemotherapy and radiation therapy, which is sometimes given in a rigid schedule (i.e. chemotherapy with radiation therapy 2 hours later). If the patient’s medical or pediatric oncologist is in Indianapolis, it is difficult to carry out such studies. It was noted that there is a medical oncology group that works with IUHPTC in Bloomington, but it was difficult to assess their dedication to prospective clinical trials.

The outcome of this situation is that there is a small research portfolio. There are very few prospective clinical trials, and these trials are accruing few if any patients. Although some of the retrospective

reviews that have been conducted are intriguing (especially the treatment of leptomenigeal disease), there are and will likely continue to be too few patients to answer any question definitively. Other centers with larger patient populations and more advanced technology will answer the important questions first.

In summary, the committee concluded that IUHPTC will not be able to contribute substantially to the technical, biological, or clinical development of proton therapy.

We do wish to add that the quality of clinical care seemed to be high. We were extraordinarily impressed with the dedication and professionalism of the entire team from physician to machinist. We would also note that our interviews with referring physicians showed that they were delighted with the care that their patients received and impressed with the dedication of the physicians and staff. IU can be proud of the level of care delivered by IUHPTC. Furthermore, the residents were pleased with the educational experience and felt that they were more competitive when looking for their first job because of their experience with proton therapy.

3) Is IUHPTC financially viable?

We assessed three areas: current program, proposed revisions of the program by the leadership team and alternatives to evaluate.

I. Current Program

a. Structural Issues within the program

There are three fiscally related entities/activities that comprise the total activities of the proton facility: the entity which provides the core infrastructure and beam for the programs in the facility (IU Cyclotron Operations), the entity which provides patient care utilizing the proton beam facility (IU Health Proton Therapy Center), and a set of contracted research or industry based research (NASA as one of the most prominent examples). While all of these activities are closely linked, the structure obscures the overall performance of the program because there is no single accounting for overall operating performance. Using the financial statements provided, the FY13 revenues and expenses (excluding transfers from or to related entities) for the programs are approximately as follows:

Revenues

Cyclotron Operations/ Revenue from Outside contracts/IU Budget allotment	2,918,000
IUHPTC	<u>16,294,000</u>
Total Revenue	19,212,000

Costs

Cyclotron Operations	8,460,000
IUHPTC (exclusive of contribution to Cyclotron Operations of \$4.4M for beam and supplemental payment \$1.7M)	<u>14,271,000</u>
Total Costs	24,344,000

Combined Operating Performance	-\$3,519,000
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This very broad combination of the overall fiscal performance is conservative and not likely to change in the near future with the existing structure.

In lieu of a consistent overall economic overview of the program, there should be a formalized way to allocate the true costs of the program to each of the entities. There are no defined cost allocation methodologies to appropriately charge the core infrastructure costs to the two revenue-generating

activities (IUHPTC and contracted research activities). The costs charged to the Proton Therapy facility are allocated by “What IUHPTC can afford to pay”, according to the Proton Therapy Program COO/CFO. The lack of a formal cost allocation process fundamentally understates the costs of IUHPTC and overstates their performance. In addition to obscuring the ongoing operating losses (when viewed as one entity), this approach has created the perception amongst the staff that the enterprise is performing well economically. The perception was communicated to the site visit committee as well, as it was repeatedly stated during the presentation that IUHPTC was “solvent” and “reducing its debt”.

b. Structural issues of program within IU and IU Health entities

As a stand-alone entity, there are numerous fiscal activities of IUHPTC that are fiscally suboptimal:

- 1) The Center approaches managed care payers such as Anthem and United Healthcare individually versus utilizing the negotiating strength of the IU Health. As a result they have not seen any increases in their rates for multiple years from their largest commercial payers.
- 2) The Center is not receiving optimal payments from governmental payers (Medicare and Medicaid) because it does not take advantage of hospital based facility rates. These rates are significantly higher and commonly received by other proton facilities nationally.
- 3) Personnel and other costs related to administrative functions (Finance, HR, IT, and Marketing functions) seem to be duplicative. Between the two organizations, there are 20 roles that could be part of larger corporate functions. Additional savings could be achieved with the consolidation of the dosimetrists and physicists with members of the AHC clinical operations.

Even if all of these changes were implemented, it would not overcome the issues described above and below of an aging facility that will require substantial investment and overcapacity for the projected number of patients.

c. Core Operating Cost Structure

The Proton program is based on technology that is over twenty-five years old and is highly dependent on higher labor costs to overcome the age of the base technology platform. Within the Cyclotron Operations, there are 63 people required to create and maintain the cyclotron. Overall, the review group perceived they were seeing a custom manufacturing facility that provided a very high quality product in an industry that has become significantly automated. This leads to very high labor costs to create the beam for treatment. The members of the review team with modern facilities felt that newer equipment required substantially fewer staff to run the core run the facility (potentially less than 10% of the IU facility staffing if the facility was new and contained to one or two rooms).

The volumes and the current capacity of the facility do not support the overhead of the facility for the clinical program. The facility is currently only running 2 rooms clinically and 1 additional room for research or industry based activities. The program is seeing a decline in the number of treatments and although some reductions in force have occurred, they have not kept up with the rates of the volume decline.

There are a series of purchased services agreements with physicians, specifically with the IU Radiation Oncology Department and with Bloomington Anesthesia group. IUHPTC provides over \$1.75M in support payments to the Radiation Oncology Department for support of payments to 4 MDs who provide medical coverage for the patients. If this program is discontinued or substantially downsized, the economic implication for those faculty will need to be recognized. Additionally, there is a coverage contract with Bloomington Anesthesiologists involved in the treatment of pediatric patients. This

coverage is provided at a fixed rate regardless of the number patients and the Anesthesiologists provide other billable clinical services when volumes are low. This contract is viewed as a largely unfavorable agreement for IUHPTC but there may be an impact to Bloomington Hospital if it is discontinued.

II. Proposed Changes to the Facility

The overall sense of the group was that the reinvestment proposal was overly optimistic because it understates the capital investment, overstates the volumes, and appears to understate the ongoing structural operating cost disadvantage required to maintain this type of operation. The capital reinvestment proposed will only deal with one section of the facility's infrastructure, the cyclotron. It will not upgrade the beam delivery system or the treatment facilities. These other components of the infrastructure will be at risk because they are also part of the aged technology. There is a strong sense that there will be significant additional capital investments in the future to maintain the other elements of the facility. The volumes and the revenue growth assumptions are straight-line growth projections of 2% per year of the term of the plan. These seem very difficult to achieve given the current proposed development of over 30 new facilities, particularly in current key referral markets like Ohio (Ohio State University) and Minnesota (The Mayo Clinic) where this facility draws the majority of its out of state referrals, and declining payer reimbursement rates. Most importantly, the investment in the cyclotron does not change the beam delivery technology at the point of patient care. This is a key driver of higher direct operating costs versus other current facilities. The proposed upgrade would reduce the costs of electricity, but that cannot decrease costs sufficiently to reach even a "break even" condition.

The decommissioning plan seems overly expensive and other alternatives may need to be considered. The group felt that the facility could potentially be closed and, pending some safety and security investments, be allowed to decontaminate over a long period of time to substantially reduce the decommissioning costs.

Is the capability for proton therapy crucial to the mission of IU Health?

In our discussions with the leadership of the IU Health system, it became clear that there is no overriding drive to maintain this facility in the face of mounting losses and required investment to maintain operation. As described above, given the lack of a plan to permit the facility to break even, it is difficult to visualize a scenario of continuing to operate IUHPTC.

Thus, although it would be worth considering if operational improvements could save costs, the committee was unanimous that this facility should be closed.

The committee wished to make 2 additional points, which, though perhaps somewhat out of scope of our initial charge, we felt were important to communicate.

- 1) Great sensitivity will be required in closing this facility. The staff seemed completely unaware that this facility is in jeopardy. This feeling has been compounded by the repeated assertions by the IUHPTC leadership that the clinical facility is close to being financially solvent. They feel that they could become solvent if they were purchased by Bloomington Hospital so that they could bill at hospital rates. Thus the sense of the committee is that our report will be received with surprise and consternation, and we would hope that leadership anticipate this reaction and be prepared accordingly.
- 2) We recommend that IU Health evaluates building a new single room proton facility attached to the Riley Children's Hospital for several reasons.

- a) The committee feels that there is emerging evidence that the late toxicity of treatment of children is likely to be significantly less than photon therapy, particularly in the case of pediatric brain tumors. If IU wishes to be considered among the top pediatric oncology programs it should consider having a proton facility. (This argument does not justify maintaining the current facility, which has much more capacity (and expense) than would be required for pediatric patients.)
- b) There are significant strengths at IUHPTC, which would facilitate a future role in the evaluation of proton therapy. The technical staff and faculty at IUHPTC are strengths of the current facility and could contribute to the development of new technologies and operational models in proton therapy.
- c) There is education value to a proton facility. The radiation oncology residents at IU are intelligent, motivated and interested in contributing to the evaluation of proton therapy. With appropriate mentoring and leadership, these residents could become future leaders in the proton therapy community.
- d) Radiation oncology is currently searching for a new chair. A proton facility would likely increase the attractiveness of the department and increase the likelihood of recruiting the top candidate.
- e) A new facility accompanied by a more efficient operational model and realistic business plan could permit IU to participate meaningfully in current evidence generation efforts. The proposal to look at a one-room facility will need the development of a business plan that contains a significantly different operating cost structure because of the use of different technology. There are other core assumptions that need to be reassessed like patient volumes, reimbursement rates, and capital costs. The members of the review team with proton facilities reported that they were fiscally viable with the use of newer technology, better contracting, and lower overall operating costs if the program is carried out at a different location. The committee recognizes that this expenditure would need to be viewed in the context of other capital needs and the overall strategic plan of the IU Health.