

The Patient Proton

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This booklet will acquaint the reader, a prospective or current proton therapy patient, with the various aspects of proton radiation treatment of prostate cancer from the **viewpoint of a recent patient**. Understanding what to expect as a patient may help in the difficult decision making process encountered in selecting an appropriate type of treatment. Before listing the topics to be addressed, it should be stated that issues involving insurance coverage and treatment consultation will be left to the appropriate sources. A brief listing of the areas to be addressed includes:

1.Patient specific treatment planning, including immobilization and CT(computed tomography) scan, leading to precise 3-D details of proton beam delivery.

2. The physical aspects of the proton beam that lead to its accurate deposition of energy in the target volume (prostate gland), while largely sparing healthy tissue.

3. A layman's level description of the technology of the synchrotron, and its generation and delivery of the proton beam.

4. A description of the means whereby the proton beam is shaped in three dimensional space (conformed) to precisely fit the irregularly shaped prostate gland (target volume).

5. The radio-biological properties of protons that can lead to the eventual reproductive death of the cancer cells through irreparable damage to the DNA, i.e., the cancer cells may live out their normal life spans but should not be capable of cell division.

6. The patient's experience during the pre-treatment and treatment phases of proton therapy.

7. A comparison of the observed and expected survival and morbidity (side effects) results of proton treatment with other common treatment modalities, e.g., radical prostatectomy and external photon radiation.

8. An introduction to the very efficient and caring support system encountered by the patient. at LLUMC.

Who is this intended audience for this information?

It is probable that the following individuals will derive the most benefit from this presentation:

1. A prospective patient (including family and friends) who wants to assess the likely effectiveness of proton treatment as compared with that of other treatment modalities, e.g., radical prostatectomy, various forms of external photon (x-ray) radiation, brachytherapy (radionuclide seed implants) and cryosurgery (liquid nitrogen probe freezing of the prostate gland), before making a final choice.

2. A newly arrived patient who has fair knowledge of the details of proton therapy and who would like to "round out" his knowledge of certain treatment details. This may very well apply to a spouse or accompanying friend, whose increased understanding will likely lead to more effective support.

3. A "veteran" patient who, through the excellent series of support group presentations, has gained an effective but incomplete comprehension of proton therapy and who would like to have certain of the technical aspects of the treatment brought to the layman's level.

From the eyes of a proton patient

"From the eyes of a proton patient" is a theme that will serve as the common thread throughout this presentation.. It is hoped that the experiences and impressions that are fresh in the mind of a recent proton patient will serve as an effective, yet comforting, guide to the new or prospective patient. As the majority of proton patients come to realize, proton treatment is very well tolerated and becomes a not unpleasant part of the daily routine. This is especially true when one considers the excellent support that exists at LLUMC To avoid unnecessary repetition, the presentation narrative will be aimed at the newly arrived patient. The representations and interpretations contained herein are those of the author alone.

Treatment Planning: immobilization and CT (computed tomography) imaging

As the first step, the new patient undergoes treatment planning with the actual treatment commencing about two weeks later. The objective of treatment planning is to generate proton beam delivery details to effectively







cover the target volume (minimally the

prostate gland plus some margin). This necessitates the generation of a 3-D image of the target volume and surrounding healthy tissue so that effective radiation dosages can be applied. In addition, the patient must be immobilized during planning to insure reproducible positioning during treatment.

Immobilization begins with the patient positioning himself in a "pod", a half cylinder of polyvinyl chloride (PVC), lined with a sheet of polystyrene (Figs. 1 and 2). Before entering the "pod", a rectal balloon (customized condom) is inserted and filled with about 120 mL of water. The expanded balloon pushes much of the rectal wall out of the beam



Fig. 3²



path. Approximately 30 min prior to the start of the planning session, the patient drinks a pint of water. This distends the bladder, resulting in positioning of much of the bladder, plus more of the rectal wall, out of the beam path.

Once the patient is positioned in the "pod", the *in situ* polymerization of a partial body cast composed of polyurethane foam is carried out. Fig. 3 shows the containers of the copolymers and initiating catalyst used in the procedure. Since the polymerization gives off heat (exothermic), the patient experiences a rather comforting warming sensation during the "hardening" process. This immobilization assures a constant distance from the edge of the "pod" to the back edge of the target volume (prostate gland), thereby helping to maintain accuracy of beam delivery during treatment.

When the "pod" has set, the patient is escorted to the CT scanner, where the target volume is scanned at 3 mm intervals (Fig. 4). These CT "slices" are employed in developing a 3-D treatment plan for treatment (Fig 5). At this time, a radiograph (analogous to a film x-ray) is taken, converted to digital form, stored, and finally reconstructed (digital reconstructed radiograph - DRR), at the time of treatment to aid in proper patient alignment. The DRR is compared to a radiograph taken just prior to each treatment and any patient misalignment is immediately corrected.

Another important result of the treatment planning system is the fabrication of devices that allow the proton beam to be delivered in a three dimensionally (conformal) precise manner (Fig 6). Treatment apertures, metal castings with irregularly shaped holes matching the target in the beam's eye plane, and boluses, jewelers' wax tissue compensators (blue devices), are customized for each patient. The precise function of these devices will be detailed during a description of the actual proton treatment.

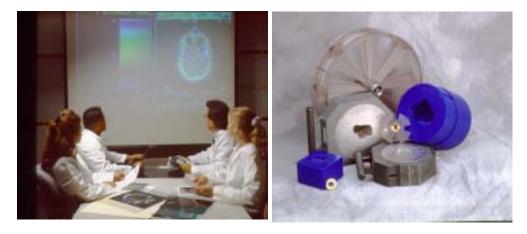


Fig. 5¹

Fig. 6¹

The Proton and its Bragg Peak: precise high energy delivery to an irregularly shaped three dimensional target

What exactly is a proton? The proton is one of the three "classic" fundamental particles of nature - modern particle physics has identified many more. The proton, a positively charged particle, co-inhabits the nuclei of atoms with its neutral cousin the neutron (except for the type of hydrogen nuclei used for proton treatment, which contains only the proton). Extra-nuclear electrons balance the nuclear charge and complete the atom. To obtain the beam of treatment protons, the extra-nuclear electron of each atom must be removed by the input of sufficient energy to overcome the attraction of the nuclear proton. Fig. 7 shows a brief summary of this process for the hydrogen atom, but notice two types of hydrogen atoms are shown! These atoms are isotopes and are distinguished

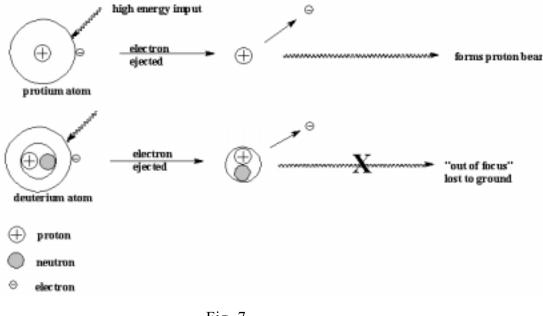
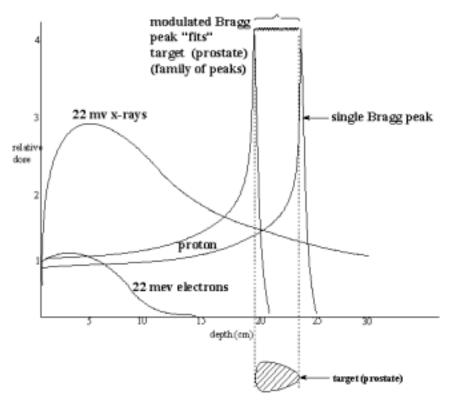


Fig. 7

by different number of neutrons - the number of protons stay the same.

The atom without a neutron is called protium, whereas the atom with one neutron is termed deuterium (there is a third isotope, tritium, which, due to its scarcity and instability, is of no practical concern). Since deuterium is relatively rare (only 15 of 100,000 naturally occurring hydrogen atoms are likely to be deuterium) and since it would not be in focus with the proton beam, its presence does not effect treatment.

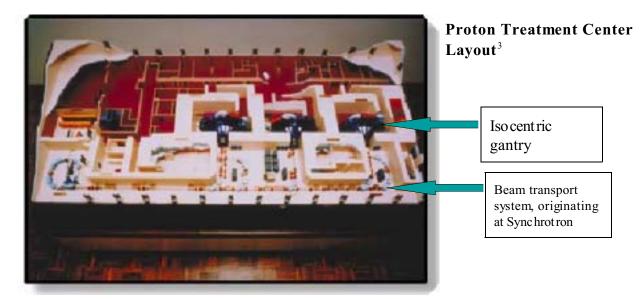
Once a proton beam is formed, two questions may arise. What are the characteristics of the proton beam (approximately 1×10^{11} protons/second) that lead to its choice as an effective treatment modality? Second, how is the beam delivered to the target site in a safe and medically effective manner? Fig. 8 compares the energy deposition characteristics of several radiation treatment modalities. A significant fraction of the total energy of an x-ray beam is deposited within the first 10 cm of body penetration and, also, in the tissue beyond the target, ($\sim 20-25$ cm, is the typical depth of the prostate gland as approached from the side of the body) areas that should be spared from significant energy deposition. It is obvious that an electron beam will fail to reach a target of the depth of the prostate. However, the proton is a particle with sufficient mass (about 1,800 times that of an electron) to develop a Bragg peak, which describes the delivery of energy to a small, well defined target volume while largely sparing neighboring healthy tissue. In fact, the target volume covered by a single Bragg peak is so small that, for practical application, the proton beam must be modulated (spread out in the direction of the beam propagation) (Fig 8). The means of this modulation will be covered in a subsequent section.



Comparison of relative dose (energy deposition) vs body depth for 22 mv x-rays, 22 mev electrons and >200 mev protons

Fig. 8

Proton Treatment System: proton beam generation, transport and delivery



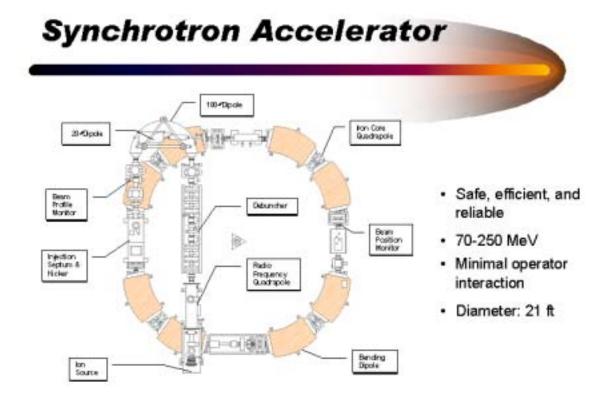
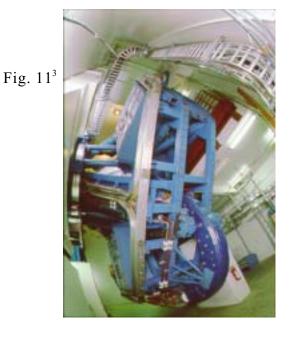


Fig. 9^{3}



Fig. 10³



Hydrogen atoms stripped of their electrons provide the source of protons for the beam (Fig.9). These protons are energized to approximately 2 mev (million electron volts) in the linear accelerator (RFQ - radio frequency quadrupole). Upon injection into the synchrotron, the proton beam can be energized to selected levels in the 70-250 mev range (protons are circulation around the synchrotron at about 10 million revolutions per second). All this "traveling" by the protons is carried out in a tube evacuated to approximately 10⁻⁸ atmospheres (at this strong a vacuum, it is unlikely that protons will collide with air molecules, which would interfere with their flight). Once the proton beam reaches the desired energy there is a "spill" every 2-3 seconds, whereby the beam is either directed to a treatment room or destroyed. Fig 10 shows a portion of the transport system, which carefully "steers" the beam via a series of magnets. Prostate cancer patients are treated in one of three gantry rooms. A gantry, Fig 11 (see also the model of the Proton Treatment Center Layout at the beginning of this section), is a large wheel (it occupies three stories and weighs nearly 90 tons!) which rotates around the "podded" patient, thus allowing treatment from any angle (Fig 12). A series of computers maintain the integrity of the proton beam on its route to the patient. The actual treatment is monitored from a control room, located near the gantry (Fig 13).



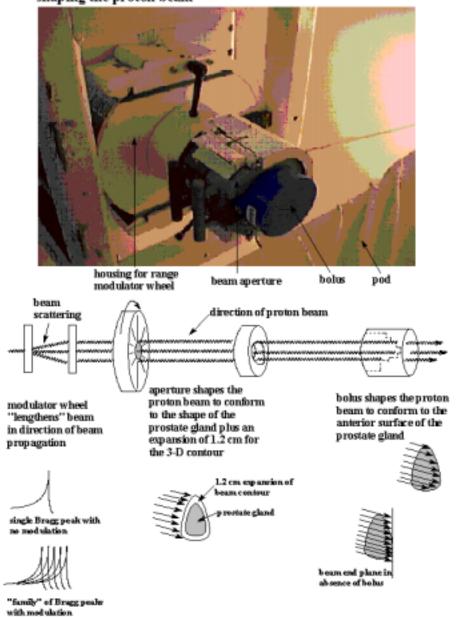
Fig. 12⁻¹



Fig. 13⁻¹

Proton Delivery System: Customized for Each Patient

Upon entering the treatment area (one of the gantries for prostate patients), the patient enters his pod, has the rectal balloon inserted, and undergoes final alignment. This last procedure involves aligning a radiograph taken just prior to treatment to the digitally reconstructed radiograph from the original planning session. Once a radiation oncologist approves the final position adjustments, the technicians in the control room "call the beam". As the proton beam leaves the transport system but before it enters the patient, several adjustments must be made. Fig.14 shows a brief summary of this train of events. As the proton beam enters the treatment area, it undergoes a scattering to increase its cross sectional area in the direction of beam propagation. In essence, the beam's diameter is now large enough to cover the target. At this point the beam would deliver its energy in a single Bragg peak, that is, it would have an effective treatment depth of only a few millimeters. Since the target prostate gland plus a 3-D contour margin of about 1.2 cm has



Coordinated role of the modulator, aperture and bolus in shaping the proton beam

Fig. 14²



Fig. 15²

considerable depth in the direction of the beam, a family of Bragg peaks must be created. This is accomplished by a modulator wheel, whose precise role will be covered in the next paragraph. The elongated beam now passes through a metal aperture ring, which shapes the beam to fit the cross sectional area of the target (beam's eye view). Finally, the beam passes through a tissue compensator device, a bolus, which conforms the beam to the rear surface of the target.

Further details of the operation of each of these proton modifying devices will now be addressed. The modulator wheel is composed of polycarbonate, a material whose properties can change the energy of a proton beam as it passes through the wheel. As Figs. 15 and 16 show, the wheel contains absorber sectors (spokes) of varying thicknesses. As the wheel rotates, the proton beam will pass through the various sectors as well as empty space, on a proportionate basis. The result is a family of Bragg peaks that have sufficient depth to include the target.

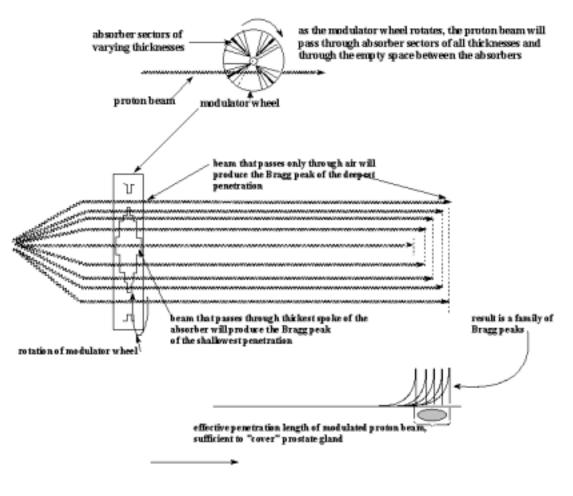
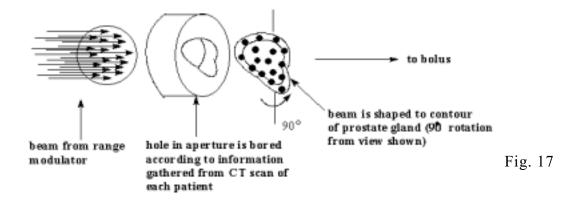


Fig. 16

Now that the proton beam has the requisite depth, it must be shaped to the cross sectional outline of the prostate plus margin (this is the view from the perspective of the traveling beam). The aperture is specific to each patient and is molded according to information gathered at the initial planning session. Fig.17 shows the aperture shaping of the proton beam to the target as a 90° rotation from the direction of the beam.



The final shaping process occurs in the bolus, the last device between the proton source and the patient. Fig. 19 shows a photo of the bolus, which is composed of jeweler's wax whose composition effects, in a known way, the energy of a penetrating proton beam. As Fig. 18 illustrates, the greater the depth of penetration by the proton beam, the less the depth in the target will be the development of the Bragg Peak.

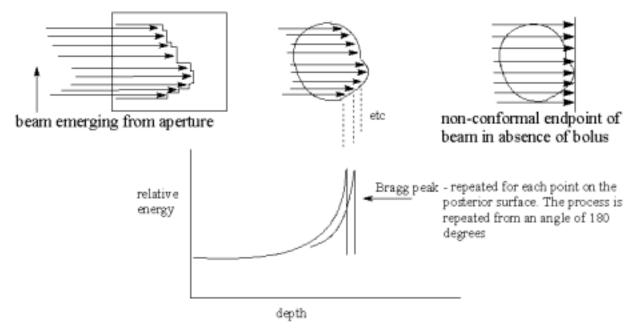
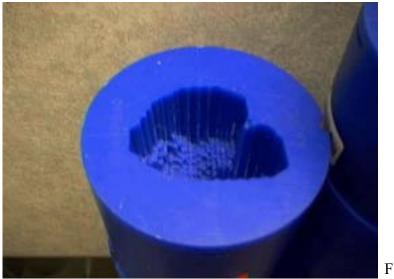


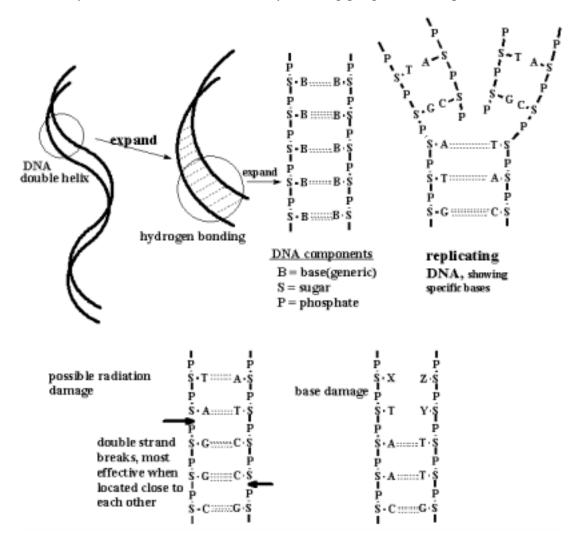
Fig 18 Effect of bolus in shaping proton beam to "fit" posterior surface (beam's eye view) of the prostate gland





Proton Beam Damage to Cellular DNA

How is proton therapy of benefit to the prostate cancer patient? The most significant effect of proton radiation is likely damage to cellular chromosomes. In particular, it is damage to the DNA component of the chromosomes that has the greatest effect. Two modes of lethal damage have been identified. But first, an introduction to DNA structure and function is in order (Fig.20). From the top, left to right, the figure depicts the double stranded nature of DNA, an expanded portion showing the approximate location of hydrogen bonding (relatively weak interactions that hold the two strands together), a further expansion showing the molecular components and more detailed nature of hydrogen bonding of DNA, and, finally, a simple representation of the process whereby DNA duplication occurs during cell division. Clearly, if radiation caused structural changes to DNA can be induced, there is the chance of disrupting its duplication and hence the ability of the cell to divide, thereby causing programmed reproductive death.



The bottom of Fig. 20, left to right, shows two molecular events whereby DNA damage occurs, formation of breaks along the individual strands and changes in the chemical nature of the bases. While single strand breaks are readily repaired, double strand breaks often produce an irreparable and, hence, lethal situation for the cell (as long as the breaks are separated by only a few base-pairs). Changing the nature of the bases (shown as letter changes, e.g., A to Y), can disrupt the delicate positioning required for successful hydrogen bonding and hence the maintenance of the molecular integrity of the DNA. Taken together and in sufficient numbers, these two modes of damage result in multiply damaged sites, MDS, and are thought to be quite lethal to the cancer cells.

Proton Therapy and Patient Survival

What is the curative effect of proton therapy? What are the side effects? How does it compare in effectiveness to other treatment modalities? These are important questions if one is seriously considering any treatment modality. This section will deal with the first question. What is meant by survival and how can it be "measured"? This is a complex question requiring the knowledge of a number of important terms - some of which the reader will likely already be familiar. Therefore, the following information will briefly define prognostic and post treatment factors, and two important definitions of survival.

Important Prostate Cancer Terms (a useful site for details of these terms: <u>www.prostateinfo.com</u>)

Prognostic Factors - Determined at Time of Diagnosis

<u>PSA</u>: prostate-specific antigen, ng/mL (ng=nanogram, 10⁻⁹ gram) A protein (enzyme) in the blood whose increase can often indicate the presence of prostate cancer or other prostate problems. Two types are recognized - free and bound - with a high proportion of the latter associated with possible cancer. Only total PSA will be referenced so as to be consistent with the literature herein cited.

TNM Staging System - A clinical grading system that indicates the size (T) of the primary tumor, the extent of any lymph node involvement (N), and the presence or absence of distant metastases (M).

- Each staging factor ranges from a value of 0 to some integer (often with subcategories, see the above website for details), with a higher value signifying a more worrisome situation in each category.
- For example, a staging of **T2aN0M0** would indicate a tumor confined to less than one half of the prostate, with no indication of spread to regional lymph nodes or distant metastasis.

Gleason Scoring System - Indicates Aggressiveness of Tumor

A pathologist's evaluation of the aggressiveness (likely rate of advancement) of a tumor based on a score derived from a histological examination of prostate tissue from a biopsy. The pathologist looks for the two most prevalent **patterns of abnormal cells** on the slide. Each cell pattern is assigned a number from 1 to 5, with the higher number signifying a more likely aggressive tumor. The two scores are summed to give a total score. For example, a score of 1 + 1 = 2 would indicate cells just slightly different from normal cells (they are well differentiated), whereas a score of 4 + 3 = 7 would indicate a more aggressive tumor (they are less differentiated). Original sketches drawn by Dr. Gleason, a pathologist, to define his system are presented to the right. Due to the inherent subjective

nature of the Gleason system (a reproducibility of ± 1 by the same pathologist is considered the limit of confidence), many pathologists recommend that more than one pathologist review the slides. Despite its subjective nature, recall that the Gleason score is a significant prognostic predictor of bNED survival. Present research is aimed at identifying possible biochemical markers that would produce a more quantitatively significant scoring system.



Post Treatment Factor

PSA nadir: the lowest PSA value occurring during the post treatment period The PSA nadir commonly occurs during the first 18-24 months after treatment, and is a significant predictor of survival chances.

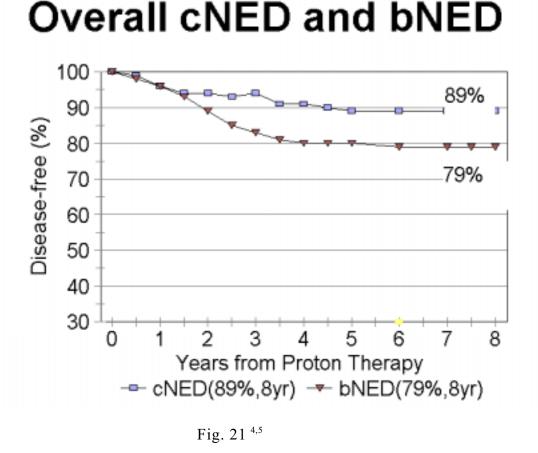
Clinical versus Biochemical Survival

<u>Clinical survival</u>: **no clinical evidence of disease (cNED)**: post treatment clinical examination reveals no evidence of the disease.

<u>Biochemical survival</u>: **no biochemical evidence of disease (bNED)**: indicates a non-rising post treatment PSA. One accepted definition specifies a PSA that increases by no more than 10% in three consecutive determinations, or one large increase requiring some medical intervention, e.g., hormone treatment.

Survival Results for LLUMC Proton Treatment Patients

What can the proton treatment patient expect in terms of long term survival. Eight year overall clinical and biochemical disease-free survival rates were 89% and 79% respectively (Fig. 21). An immediately question may arise, "How does this compare to other treatment results?"; this question will be addressed in the next section.



Are there prognostic factors that will allow the patient to assess his likely bNED, or the failure thereof? All three prognostic factors, initial PSA, Gleason score and clinical staging, are significant predictors of bNED.

As post-therapy time increases, is there a post treatment factor whose determination predicts bNED survival? Yes, the PSA nadir is such a predictor (Fig. 22). Recall that the PSA nadir normally occurs during the first 18-24 months following treatment. Thus, the patient has a reliable predictor of survival whose determination commences shortly after (typically 4 months) the termination of treatment. For example, a PSA nadir of less than 0.51ng/mL would predict a bNED of 90% at 7 years (top curve on Fig. 22).

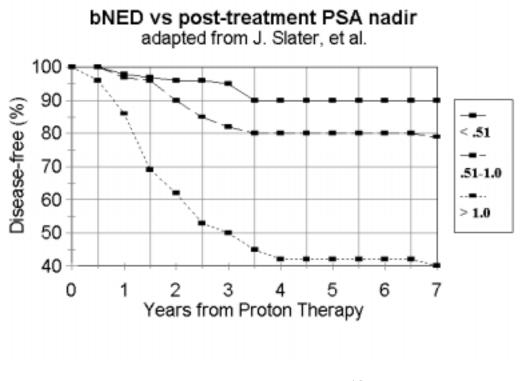


Fig. 22 4,5

Can the Results of Proton Therapy be Meaningfully Compared to Those of Other Treatment Modalities?

The answer to this question is yes, however, the means to the answer are a bit involved. These comparisons should ideally be conducted under the umbrella of a large randomized study, where individuals with known prognostic factors can be divided between the treatment modalities of interest. While this has not occurred, and is not likely to occur, the prognostic factors mentioned above, i.e., initial PSA, Gleason score and clinical staging, have also proven significant predictors of survival for radical prostatectomy and external photon radiation. The commonality of these prognostic factors makes it possible to calculate reliable estimations of 5 year bNED rates for LLUMC proton patients assuming they had undergone either of the other treatment modalities (assume a LLUMC proton patient was placed in the "shoes" of a surgery or photon patient with nearly identical prognostic values) (Fig. 23). The survival benefits of proton treatment for all patient-categories are summarized on the bottom line (**Total**). The advantage of proton therapy is also seen within each of the three prognostic categories.

As satisfying as these predictions are, a direct comparison between surgery and proton patients is desirable. Since a great deal of prognostic PSA data is available, a reasonably accurate 7-year bNED comparison can be made Fig 24. A similar presentation, Fig 25, can be made of information (ignoring photon data) extracted from Fig 23. Both approaches point to the same conclusion; there is an advantage to proton therapy.

		5-year bNED		
Prognostic Categories	Number of Patients	Observed (proton)	Predicted after surgery	Predicted after external photon irradiation
Initial PSA ng/mL				
<10	505		82	79
10.1-20 >20	242 70	77 58	58 41	66 43
Clinical Stage				
<u>T1</u> T1a/b	<u>228</u> 24		69	<u>78</u>
T1c <u>T2</u>	204 <u>616</u>		84	<u>69</u>
T2a	212	91	83	
T2b T2c	203 201	78 77	58 60	
<u>T3</u>	<u>40</u>	<u>58</u>	<u>38</u>	
Gleason score				
2-4	129	88	82	77
5-6	421	88	75	76
'7-10	239	70	51	61
Total	901	82	70	71

Fig Adapted from

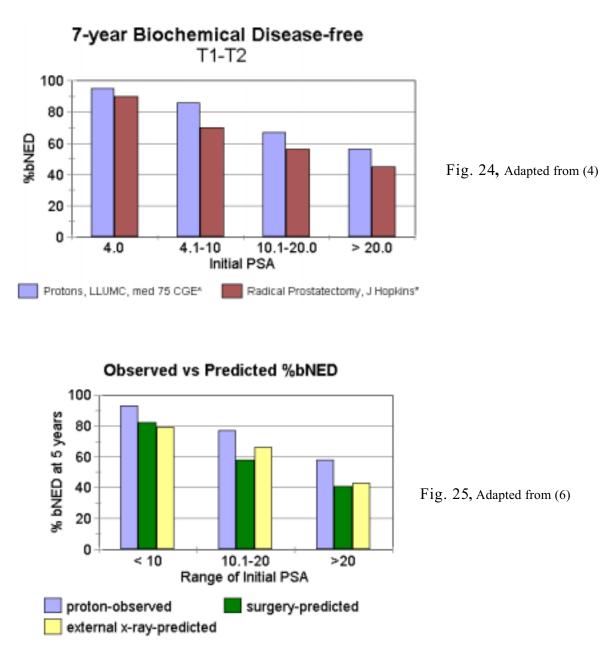
Schulte, et al

What are the Side Effects (Morbidity) of Proton Therapy and How do They Compare to Those of Other Treatment Modalities?

At issue here are problems that develop primarily with the genitourinary (GU) and gastrointestinal (GI) tracts, and that appear within several months to several years following treatment. A morbidity (side effects) grading scale (RTOG - Radiation Therapists Oncology Group) exists which is reasonably self explanatory.

RTOG Morbidity Grading Scale

- 1. Minor symptoms requiring no treatment
- 2. Symptoms responding to simple outpatient care.
- 3. Distressing symptoms that alter life style, and may require hospitalization.
- 4. Symptoms requiring major surgical intervention.
- 5. Fatal complications



For proton patients, one primarily considers grades 2 and 3 morbidity. Fig. 26 reveals 3year morbidity results for LLUMC proton patients. The results were essentially identical for proton alone or proton-photon patients. It is noteworthy that most of the grade 2 occurrences were isolated episodes of rectal bleeding that were assigned to Grade 1 in an earlier version of the scale.

Proton Treatment Side Effects (3 year)						
	Grade 2 (%)	Grade 3 (%)				
GI	21	0	primarily isolated rectal bleeding			
GU	5.4	0.3				
Total	26.4	0.3				

In contrast to radical prostatectomy, incontinence and impotency are seldom at issue.

Fig. 26 ⁵

But, what about a comparison of complications between proton and external photon treatments? Such a comparison suffers from the same lack of randomized data that is experienced by comparisons of survival for various treatment modalities; however, once again the commonality in prognostic factors makes a reliable comparison of GI complications possible (Fig. 27).

Treatment Side Effects (observed vs predicted)					
GI	Grade 2 (%) Grade 3 (%)				
observed (proton: 74-75 Gy)	21	0			
predicted (photon: 75.5 Gy)	37	5			

Fig. 27, Adapted from (6)

Treatment aspects aside, what do I do with my time? Exercise, volunteer, become proactive in "getting " the word out about proton therapy!

It doesn't take long for the new patient to realize there is more to treatment than rapidly moving protons and photons. The pass that is available to the Drayson center is essentially a free membership to a "country club"! Even if you are only capable of the most primitive type of locomotion, there is something there for you. Remember, while the good cells of the body are busy repairing the temporary damage sustained from your last treatment, the rest of **you** requires exercise; you won't hurt a thing!

Simple math convinces one that even a simple majority of those undergoing treatment do not visit the Wednesday evening support group gatherings nor the Thursday evening gastronomical extravaganzas lead by our own "galloping gourmet", Gerry Troy. The

benefits of both are realized only by participation (I am not referring to the "benefit" of adipose tissue deposition resulting from the latter activity!). While on the subject of nutritional intake, don't neglect to consult with Stella, the Center's nutritionist (even if you don't follow all of her advice). A slight alteration in diet has helped many an individual.

There is something quite reassuring about the weekly Wednesday recitation of the "Psalm of Reality", my PSA, my Gleason, my clinical staging. If that doesn't create a bond of mutual support and respect, then I don't know where to send you! Everyone of us deals differently with our own "reality", and the act of sharing gives us all new ways of dealing with our cancer. In December 2000 a remarkable organization first saw the light of day. A group of proton patients, realizing that they did not want to just leave Loma Linda at the end of their treatments founded (with Bob Marckini as the spearhead) the Brotherhood of the Balloon (BOB) so that communication with all involved could be maintained. The BOB has blossomed and has served as an information exchange organization for patients and prospective patients alike. Details about the BOB can be found on its newly launched website: protonbob.com.

As each patient nears the end of his (of course possibly her, in the case of a non-prostate patient) treatment, a farewell of sorts is generally offered, which, in my experience, provides an intimate reflection and summation of personal responses to their Loma Linda stay. One after another, virtually without exception, individuals offer insights that **must** be shared in some manner with those just receiving the familiar news, "I'm sorry to inform you, but your biopsy was positive - you have prostate cancer. However, it appears to be localized and therefore should respond well to treatment." While our experiences, in terms of what support and treatment options were offered, were all somewhat different at that moment, we all could have benefitted from the advice of a recent patient, especially a proton patient! We, therefore, all need to think about how we can provide this comforting and useful information upon our return home. If you would like a copy of the CD Powerpoint version of the Patient Proton, please e-mail me at <u>butler@norwich.edu</u>. There is no cost.

Because of our prostate cancer, we are all of an age to have experienced a bit of life's realities in terms of dealing with various institutions, and I, in particular, have never been associated with any institution (medical or otherwise) where I have been treated with such comprehensive "good will". Physicians, nurses, technicians, social workers, receptionists and other staff members, have all approached me in the most professional and caring manor. I'm sure you reflect my feelings. Is there any doubt why we would want to "give something back"? I suspect that each of us possesses at least one talent that can be applied toward spreading the word about the availability and viability of proton treatment at LLUMC, and, in the not too distant future, elsewhere. However, even before you leave, there is a real possibility of providing your talents here at LLUMC through the office of Volunteer Services. Felicia Beasley, coordinator, would be happy to discuss

with you the possibility of volunteer service. My wife and I found our volunteer activities to be most satisfying!

As an example of how good things can arise from misfortune, my stay at LLUMC has lead to a year's appointment as a visiting professor of chemistry at the University of Redlands, which will also allow me to continue volunteering at LLUMC, and especially to continue to explore new gastronomical "finds" under Gerry Troy's leadership

As a final note, I will share with you an encounter I had near the end of my eight weeks of treatment. While walking to the photon treatment area, I encountered a new "podded" patient in the hallway, returning from his CT scan, and I quite spontaneously leaned over and told him that I hoped he realized how fortunate he was. Well, they wheeled him by so quickly that I had neither time to explain my remarks nor see if he had any idea what this "nut" had just said - but, I think you all know, or will soon know, what I meant!

References

While I have referenced the primary sources employed herein, some of the information and much of the interpretation is the result of casual conversations with many individuals (physicians, technicians, nurses, etc) and is therefore nearly impossible to properly cite. However, I can cite lectures given by both Drs Jerry and James Slater and the symposium given at LLUMC for alumni physicians in early March, 2000.

1. <u>www.protons.llu.edu</u> LLUMC website

AND Visit the proton patient organization's (BOB or Brotherhood of the Balloon) website for useful information concerning proton treatment at LLUMC. There is a secure section for members of the BOB and an open section for those seeking information: www.protonbob.com

2. Author's photograph (Special thanks to Felicia Beasley, Coordinator, of the Department of Volunteer Services for the loan of a digital camera and much encouragement).

3. Optivus, Inc., especially John Blignaut

4. LLUMC Proton Treatment Center, personal communications

5. J. D. Slater, et al, Int. J. Radiation Oncology Biol. Phys., Vol. 42, No 2, 299, 1998.

6. R. W. Schulte, et al, Strahlentherapie und Onkologie, 2000; 176 (Nr. 1)