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Introduction

The Northeast Proton Therapy Center (NPTC), located on the main hospital campus of the Massachusetts General Hospital (MGH), represents the forefront of technological advancement in radiation therapy. The construction of the facility was jointly funded by the MGH and the National Cancer Institute to meet the increasing medical demand for high precision radiation therapy provided by proton therapy. The program builds on more than forty years of pioneering work and experience gained by MGH physicians, physicists, and clinical support personnel at Harvard University’s Cyclotron Laboratory where more than nine thousand patients were treated with proton therapy from 1961 to it’s closing in 2002.

At the NPTC protons (charged particles) are accelerated with a large magnetic field in a machine called a cyclotron. Large magnets help guide the proton beam to three treatment rooms. Two of the treatment rooms incorporate 110-Ton gantries. These 3 story high gantries can be rotated to aim the proton beam from various directions. In the gantry rooms patients lie on robotic beds that can be adjusted for precise alignment of targets contained throughout the body. The third treatment room contains two specialized “beamlines”. The first beamline is specially designed to treat lesions contained in the eye. The second beamline is dedicated to high precision stereotactic treatments within the head.

At the NPTC there is a large research program aimed at improving current treatment techniques as well as developing new equipment and approaches. The NPTC is proud to be a leader in the revolution of proton therapy.

Layout of the NPTC treatment level showing the FDA approved radiation delivery system, which includes a cyclotron (upper left insert) and an array of over 50 magnets, each weighing between 1,000 and 5,000 pounds (highlighted in orange, blue and green). Protons can be delivered sequentially to any of the 3 treatment rooms by bending the beam using the magnets. Radiation is isolated to individual treatment rooms with 5 feet thick concrete walls.
Principles of Proton Therapy

Irregularly shaped lesions with awkward configurations near critical structures are well suited for proton therapy. Protons have a physical advantage over gamma rays and x-rays when it comes to sparing normal tissues. Protons deposit most of their radiation energy in what is known as the Bragg peak, which occurs at the point of greatest penetration of the protons in tissue. The exact depth to which protons penetrate, and at which the Bragg peak occurs, is dependent on the energy of the beam. This energy can be very precisely controlled to place the Bragg peak within a tumor or other tissues that are targeted to receive the radiation dose. Because the protons are absorbed at this point, normal tissues beyond the target receive very little or no radiation.

Radiation levels from a conventional x-ray therapy unit (Linac) and protons of various energies as they penetrate in tissue or water. X-rays have a maximum dose near the surface followed by a continuously reducing dose with depth. Proton energy can be adjusted to match the depth of the target with a sharp drop in dose beyond the Bragg peak.

A broadened proton beam as well as an x-ray beam adjusted to treat an 8 cm thick target with a maximum depth of 23 cm. The x-ray beam “spills” unnecessary dose beyond the target compared to protons.
The proton Bragg peak is generally narrower than most lesions therefore special equipment is used to combine protons of various energies to broaden the Bragg peak to match the thickness of individual targets. Properly selecting the thickness of the broadened Bragg peak ensures uniform dose coverage of a target with optimal reduction of dose at the entry surface of the beam. Tumors can have very irregular shapes and can be located close to critical organs. Every patient’s tumor shape, size and location are unique. Patient specific hardware, which helps sculpt the proton beam, is customized to maximize the dose to the tumor while minimizing the dose to normal structures. Aiming proton beams, each with customized hardware, from various directions further ensures that the dose to normal tissues is reduced as much as possible therefore reducing the risk of treatment related complications.

Customized dose-shaping devices used for proton therapy. A brass aperture shaped to the outline of a target blocks the proton beam outside a specified safety margin. The penetration depth of the protons that pass through the aperture opening is adjusted to match the shape of the target with a Lucite range compensator. A target is depicted in red on the rightmost figure with the proton radiation dose conforming to its shape and avoiding a critical structure shown in green.
There are many individuals involved in the treatment process. Some of these professionals are directly involved with patients while others work behind the scene to provide the necessary services to treat patients. A multidisciplinary approach often requires coordinating radiation treatments with procedures performed in other departments such as Radiology, Surgery and Medical Oncology. These departments have their own group of professionals to ensure the highest quality medical care. The professionals directly involved with treatments at the NPTC are listed in the sequence of their role in the treatment process.

**Radiation Oncologists:**

Physicians who specialize in the use of ionizing radiation to treat various types of cancers and malformations. They determine the most appropriate radiation treatment by defining what needs to be treated (disease) and what needs to be avoided (critical organs and tissues). They prescribe the daily and total radiation dose to be delivered to the disease and the dose limits to critical organs. They determine what radiation delivery methods are most appropriate (protons, x-rays, electrons, brachytherapy) to achieve their treatment goals.
Neurosurgeons:
Physicians who specialize in the treatment and diagnosis of various neurological disorders. Neurosurgeons are involved with high-dose, high-precision radiation treatments (radiosurgery) delivered in one or two sessions. Their services are needed to fit patients with certain stereotactic fixation devices as well as implantation of reference markers used for alignment. They also help radiation oncologists with defining neurological lesions.

Anesthesiologists:
Physicians who administer general and local anesthetics, and manage anesthesiological services. They are responsible for determining the anesthetics to be used, considering such factors as patient's age, weight, and medical condition. They monitor the patient’s vital signs and record observations prior, during and after treatments. Their involvement is usually with pediatric patients.

Radiation Oncology Nurses:
Licensed nurses specializing in the care of patients who receive radiation therapy. They assist physicians with various medical procedures including regular health assessments before, during and following treatments. Their regular contact with patient allows them to coordinate treatments with the various social services offered to patients.

Oncology Social Worker:
There are many aspects to undergoing daily radiation treatments for a period of 1-8 weeks. Some patients are from out of town/country and must find lodging. Some patients are local and are trying to maintain as much as is reasonable their daily routine. The role of the social worker is to help patients by providing them with the resources to manage their life during treatments. These include help with lodging, financial services, nutritional services, psychiatric services, education, health/fitness programs, support groups…

Immobilization Specialists:
The role of radiation therapy is to irradiate diseased areas while sparing adjacent normal tissue. If patients weren’t immobilized it would be necessary to treat a margin, which reflects the motion of the diseased target. This would unnecessarily treat normal tissues surrounding the diseased area. This is especially important when using a high precision approach such as proton therapy. The immobilization specialist understands the treatment requirements so as to customize an appropriate device to be used for both the pre-treatment imaging such as a planning-CT as well as the treatments.

Immobilization devices minimize motion of the diseased target ensuring that the treatment margins are reduced as much as possible. Different approaches are required depending on the treatment area being considered. These include masks, bite molds, body casts, arm and leg rests…
CT technologists RT(R):
Licensed radiological technician operate the CT (Computer Tomography) Scanner that is used for planning most of the proton therapy cases. The CT scanner obtains images as if it were slicing through the body like sliced bread. It allows physicians to see internal as well as external anatomy. The radiological technicians administer contrast material that makes internal body parts more visible. They also make sure patients are ready for the imaging procedure.

The CT scan provides physicians with cross-sectional views of the body. Outlining structures on the individual CT images enables the treatment-planning computer to generate a 3D model of the body. This 3D model is used to determine the optimal directions to aim the proton radiation at the targets while avoiding nearby critical structures. The above images represent a typical case where the targets (red & purple) are near the brainstem (green), optic nerves (yellow), optic chiasm (cyan), eyes (white), lenses (blue), cochlea (blue) and temporal lobes (not shown).

Medical Dosimetrists:
Members of the treatment team who are skilled in calculating and planning doses in radiation therapy. Working closely with the radiation oncologist they generate a treatment plan using sophisticated computer programs. They design special hardware that is used to shape individual proton beams so they conform to the targeted volume while avoiding critical normal structures.

A dosimetrist plans a proton radiation therapy case using sophisticated computer equipment.
Machinists:
Special devices called apertures ensure that only the intended target is irradiated. Compensators further conform the dose to the target shape. Using precision milling equipment the machinists fabricate apertures from brass and the compensators from Lucite for every treatment directions for every patient. The milling coordinates are directly obtained from the treatment-planning computer.

Medical Physicists:
Physicists who specializes in the technical and clinical aspects of radiation therapy. Physicists oversee the technical aspect of the clinical operation of the facility by ensuring that the delivery system, imaging systems, planning systems are functioning properly. They also oversee all aspect of quality assurance and quality control of treatment plans including devices used for patient treatments. In some complicated cases they are directly involved in treatment planning.

Cyclotron Operators:
The cyclotron operators run and monitor the radiation delivery system during treatments. With mechanical, electrical, software, hardware and controls backgrounds they maintain, upgrade and repair the cyclotron and radiation delivery system.

An operator monitors the status of the radiation delivery system in the facility’s main control room.

Radiation Therapists:
Technologists licensed to deliver therapeutic radiation to patients in accordance to a medical prescription. At the NPTC the radiation therapists use x-ray and ultra-sound imaging to ensure patients are set-up for treatment according to the treatment plan. Corrections are made using a robotic treatment table. Patients become very familiar with the radiation therapists since they see them on a daily basis.

While in the treatment room a radiation therapist compares an x-ray image, obtained just prior to treatment, to an image from the treatment-planning CT. Once the treatment position is confirmed the therapists step out of the treatment room and verify the final proton radiation parameters prior to administering the radiation treatment.
Treatment Options

The NPTC has three broad radiation therapy programs. They are:

- **Proton Stereotactic Radiotherapy (PSRT)**
  Involves treating lesions throughout the body over an extended 1-8 week course (5-40 sessions). PSRT treatment sessions are usually limited to once per day and lasting 20-40 minutes each.

- **Proton Stereotactic Radiosurgery (PSRS)**
  Involves treating lesions, usually contained within the head with a high dose of radiation delivered in 1-2 sessions. PSRS treatment sessions are around one hour.

- **Proton Ocular Radiotherapy (PORT)**
  Treats ocular lesions contained within the eye with the radiation delivered in 2-5 sessions. PORT treatment sessions are usually limited to once per day and lasting 10-20 minutes each.

The leftmost figure shows a patient lying on the robotic bed in one of the two gantry treatment rooms. The gantries are used to treat lesions throughout the body. The middle figure shows a patient sitting in an adjustable chair in preparation for treatment of the eye. The rightmost image shows a patient lying in a high-precision robotic bed used for stereotactic radiosurgery.

Despite having three distinct programs the general pre-treatment process follows a similar course. Prior to treatment the patient’s medical history, including imaging studies are reviewed to ensure that proton therapy is appropriate. It may be necessary to obtain additional tests to update the medical record. Unfortunately, the NPTC is a limited resource and not all patients who would benefit from proton therapy can be accepted. When a patient is accepted for proton therapy he/she will undergo a simulation process to enable proper planning prior to treatment. This process involves making an immobilization device to help the patient maintain a steady body position during the treatment. Using the custom immobilization device, treatment planning x-ray images are obtain to help delineate the lesion(s) or target(s) and map their position within the body. When patients come for their treatments, images are taken using state-of-the-art x-ray or ultra-sound technology. These pre-treatment images are compared to the planning images to ensure high precision alignment.

Massachusetts General Hospital’s Cancer Center offers numerous educational and support services for patients and their families, plus many amenities to make your treatment visits as comfortable as possible. For a complete list, please ask our staff for a copy of “A Patient’s Guide to the Cancer Center”, a booklet filled with information and resources including outpatient pharmacy hours, child care, interpreter services, financial counseling and much more.
Proton Stereotactic Radiotherapy (PSRT)

Fractionated PSRT is used to treat both adult and pediatric patients with a variety of diagnosis. A multi-disciplinary approach may involve combining PSRT with surgery, chemotherapy as well as conventional x-ray therapy. The need for combined-modality treatments depends on the specific disease being treated as well as patient’s medical history. Pediatric and adult patients benefit from proton therapy by sparing normal tissue, which would otherwise be compromised using conventional x-ray therapy alone.

Pediatric protocols include solid tumors such as Rhabdomyosarcoma, Ewing sarcoma, Craniopharyngioma, Ependymoma and Astrocytoma; as well as tumors of the central nervous system (CNS) such as Medulloblastoma. Special care is provided for young children, as they often require administration of general anesthesia for each treatment session. Board certified anesthesiologist provides this service as a regular part of the pediatric care. Pediatric nurses help the transition for parents and child in the induction and recovery process.

Two-year-old patient, Mary Conroy and her mom Mari-Beth with pediatric nurse Rachel Bolton. Pediatric nurses provide extensive care during the induction and recovery process.

Mary and mom say hello to colorful monkeys as they enter the treatment room. The treatment delivery team includes an anesthesiologist who monitors vital signs during sedation and radiation therapists who align the patient and deliver the radiation.

Adult protocols include base of skull tumors such as Chordoma and Chondrosarcoma; bone and soft tissue sarcomas including sacral, spinal and paraspinal sarcomas; Nasopharyngeal and Paranasal Sinus Carcinoma; and Prostate Adenocarcinoma.

The series of images that follow demonstrate the radiation dose conformality obtained with proton therapy in many areas of the body. In all cases the red area designates the high dose region and the blue area designates the low dose region. Some of the cases have two targets; the first target includes the area of obvious disease and is prescribed to receive a high dose of radiation; the second target with a lower prescription dose includes regions that are at risk of disease.

Please note that the list of protocols and examples presented in this document is not complete and other protocols are being considered and implemented.
A: **Adenocystic Carcinoma of the Lacrimal Gland**: Proton radiation minimizes the dose to the adjacent brain, brain stem and spares some of the orbit.

B: **Paranasal Sinus Tumor**: Proton radiation minimizes the dose to the adjacent brain as well as some of the optic structures including the eyes.

**Skull Base Chordoma**: Proton radiation minimizes the dose to the adjacent brain, brainstem and some of the auditory structures.
Early Stage Prostate Adenocarcinoma: Proton radiation minimizes the dose to the adjacent femurs, bladder and rectum.

Lumbar Spine Chordoma: Proton radiation minimizes the dose to the adjacent kidneys and bowel.

Hepatoma: Proton radiation minimizes the dose to the adjacent liver.
**Medulloblastoma** is the most common malignant pediatric brain tumor. It develops in the part of the brain that controls balance and coordination. It is also a fast-growing cancer that often spreads to the central nervous system. By using Proton Beam radiation in these cases allows the special radiation to be targeted to the tumor while minimizing radiation to healthy tissue and other critical structures in the brain and spine. As with all other proton therapy treatments the goal is to minimize the dose to adjacent normal structures minimizing treatment related complications. Pediatric patients may benefit the most from such treatments because of the potential harm to growing organs and bones from receiving conventional radiation therapy alone.

As with all other proton therapy treatments the goal is to minimize the dose to adjacent normal structures minimizing treatment related complications. Pediatric patients may benefit the most from such treatments because of the potential harm to growing organs and bones from receiving conventional radiation therapy alone.

Proton radiation ensures that no dose reaches the anterior pelvic and thoracic structures when treating the entire spinal column. The dose to the whole brain is very uniform preventing regions of unwanted high doses. The base of skull is irradiated to a higher dose while avoiding the cochlea (blue outline) as much as possible.

**Radiation Therapy with Standard X-Rays and Protons for Medulloblastoma**

For certain tumors of the brain, radiation is given to the back of the brain (posterior fossa). With standard radiation there is incidental dose given to healthy brain tissue surrounding the tumor. An example of this is the cochlea, the organ in the middle ear that is responsible for bringing sound into the ear through the nerves. Injury to the cochlea can have the potential long-term effect of hearing loss. One benefit of proton therapy is the ability to shape the radiation so that less dose is delivered to the cochlea. Clinical studies are under way to determine the long term affects in children.
**Retinoblastoma**
Proton beam therapy can be used to minimize the radiation dose to bones surrounding the eye. Radiation to young growing bones affects their rate of growth and ultimately their final size. Cosmetic appearance can be very obvious when normal and irradiated bones are next to each other. The unusual retinoblastoma case depicted in these figures shows a proton radiation plan that treats a portion of the eye while sparing much of the surrounding bones, which would otherwise be irradiated if x-ray therapy were used. The red color-wash overlaid on the CT images represents regions receiving high doses of proton radiation whereas the blue represents regions receiving low doses of proton radiation.

**Rhabdomyosarcoma** occurs in every part of the body. Proton beam therapy can be used to minimize the radiation dose to bones and other critical structures surrounding the particular disease area. The case depicted in these figures shows a proton radiation plan that treats obvious disease and surrounding areas at risk of disease. Avoiding the cochlea with the proton beam ensures that hearing will be preserved. The chance of maintaining vision in the nearby eye can be increased by minimizing the dose to the eye and optic structures. Avoiding nearby brain also reduces the potential damage caused by high doses of radiation. The red color-wash overlaid on the CT images represents regions receiving high doses of proton radiation whereas the blue represents regions receiving low doses of proton radiation.
Planning & Treatment Process (PSRT)

Once a patient is accepted for proton therapy they will need to go through a planning process prior to undergoing treatment. One of the first steps is the fabrication of a custom immobilization device. The purpose of the device is to ensure that patients remain as still as possible during the treatment enabling us to aim the protons to a targeted area that has very little motion, thereby minimizing the need to treat a larger area which encompasses both the planned target and its motion.

Using the patient specific immobilization device a CT imaging study is obtained. A CT scanner obtains images as if it were slicing through the body like sliced bread. It allows physicians to see internal as well as external anatomy. Contrast material that makes internal body parts more visible is often administered during the study.

The planning process involves outlining the targeted area as well as those normal body structures, which might be of concern if irradiated. An example might be a lesion located near the eyes. In such a case the lesion and any other suspicious tissue would be outlined as a target and the optic structures would also be outlined as critical structures. Once physicians have outlined all structures of interest they define the radiation doses to be delivered. Using the above example the plan would involve delivering the prescribed dose to the target while keeping the dose to the optic structures below a predefined value. At this stage dosimetrists or physicists generate a 3D treatment plan, which models the radiation onto the planning CT according to the dose prescription. Plans are customized to the specific shape and location of the targets being considered. Plan reflects the various directions from which the radiation is aimed.

Once a plan is finalized and reviewed by physicians special hardware is fabricated for each treatment direction to be used. A thorough quality assurance process ensures that every device being made adheres to the intended specifications. Before devices are used for treatment, measurements ensure that the computer plan is properly modeled.

The whole pre-planning process from immobilization to the first treatment typically takes a few days to a week.

Depending on the complexity of the cases treatment sessions usually last between 20 and 40 minutes. As the treatment session starts the patient is greeted by radiation therapists. The therapists assist the patients onto the treatment bed and into their immobilization device. Once in position the therapists verify the patient’s position by taking x-ray images or using a 3D ultrasound machine. Adjustments are made based on the images and when necessary new images are acquired to confirm the final treatment position. With the patient in the treatment position the therapists request for radiation from the delivery system. Radiation is delivered to one of three treatment rooms sequentially therefore small delays are possible from the time radiation is requested to the time it is ready to be delivered. Only when the delivery system is ready to deliver radiation will the therapists leave the treatment room. Final radiation parameters are confirmed and the radiation is delivered while the therapists monitor the patient via closed circuit video cameras.

Each treatment session may be slightly different since the proton radiation may be delivered from different directions. X-ray treatments may also be incorporated into the treatment plan. In such cases a different machine called a linear accelerator is used to deliver the radiation. Receiving a limited number of high-energy x-ray treatments in combination with proton therapy does not compromise the overall treatment plan and is sometimes advantageous. X-ray treatments are provided within the same department and are generally quicker than proton treatments.

Physicians and nurses regularly examine patients throughout the treatment course to monitor progress and address any concerns patient may have. Follow-up instructions are provided to monitor patient progress following the treatment course.
Proton Stereotactic Radiosurgery (PSRS)

Small targets that tend to be spherical can be effectively treated using gamma or x-ray radiosurgery. However, with larger and more irregularly shaped targets, it becomes increasingly difficult to deliver a uniform dose of radiation within the target and spare surrounding normal tissues. In this circumstance, the unique characteristics of proton radiation are a significant advantage for performing radiosurgery.

Proton radiosurgery is offered for the treatment of a variety of tumors and malformations. Some of these include pituitary adenomas, meningiomas, acoustic neuromas, cavernous sinus tumors and arterial venous malformations (AVM). The dose uniformity of protons is especially attractive for the treatment of AVMs as these malformations are not solid tumors but rather a tangle of vessels and normal brain. This means that when targeting an AVM it is impossible to avoid the normal brain contained within the malformation. A uniform dose means that there are no “spikes” of excessively high dose within the target. In some limited circumstances proton radiosurgery can be used for lesions that are not contained within the head.

An example of a treatment plan for a large AVM. The PSRS treatment is delivered in two sessions using a total of six treatment directions to provide a conformal proton dose distribution.
Planning & Treatment Process (PSRS)

Upon referral to our center, a senior neurosurgeon and radiation oncologist reviews each case, assessing the medical and treatment history, medications and prior imaging studies to determine the best treatment course for the particular condition. Further diagnostic imaging such as MRI or angiography may be required. An opportunity to meet with the physicians to discuss their treatment recommendations is part of the process.

On the treatment day, a member of the proton therapy team greets the patients making them comfortable, providing them with an overview of the treatment day and answering any questions they may have.

For patients with lesions contained within the head, the treatment plan will require that several tiny beads, known as fiducials, be implanted in the surface of the skull. During the proton therapy session, the fiducials help to insure that the proton beam is very precisely aimed at the target. Using a small needle, a neurosurgeon puts the fiducials in place. Performed with a local anesthetic, the procedure is very simple and the patient should only feel a slight pressure from the needle. This procedure is only applicable if lesions are located within the head.

For both a CT scan and later during the actual proton therapy treatment, it is crucial that patients remain absolutely still. To insure this, we will need to fit the patient with an immobilization device. Some circumstances require a stereotactic head frame to remain in place from the time of the CT to the end of the treatment. If this is the type of immobilization that is indicated the physician will secure the frame to the patients head. While the head frame is a bit awkward, wearing it is not painful. Patients should feel only a slight pressure as the frame is attached. Patients fitted with this type of frame are planned and treated on the same day. If a different type of frame is used the process may be separated so that the planning occurs on a different day from the treatment.

Two different types of immobilization devices used for proton radiosurgery. The device on the left is a stereotactic frame, which requires that the planning and treatment be done on the same day. The device on the right enables treatments to be delivered on a different day than the planning CT study. This frame is useful for patients who require more than one treatment session. Many factors are considered in determining the most appropriate frame for treatment.

When the frame is securely in place, IV contrast is injected in preparation for a CT scan. The CT scan creates a precise three-dimensional picture of the area to be treated. This becomes the framework for calculating the radiation dose and designing the treatment. For the CT scan, patients lie on a treatment bed with the immobilization device secured to prevent motion.

Physicians use the CT scan, in addition to other studies to outline the target(s) and important normal structures. The size of the target, as well as its relationship to these structures, is critical in calculating the prescribed radiation dose. It also determines the directions from which the proton beam is aimed through the body to the target.
Once the treatment plan is finalized, customized equipment is fabricated to shape the proton beam so that the radiation dose matches as closely as possible the shape of the target. This equipment is designed for each direction from which the beam is aimed.

The total time required for treatment is around one hour. This time varies depending on the number of directions the proton beam is aimed. The proton beam is typically aimed from 3 to 6 directions. Treatments may be done using the gantry system or using the dedicated stereotactic “beamline”. Many factors are considered in determining the most appropriate treatment room.

A model poses to show how the proton beam devices are brought near the patient in preparation for treatment. In this picture the beam is rotated using the gantry system for a treatment from the front and left of the patient. In the dedicated stereotactic system the proton beam is fixed and patients are rotated to achieve the same directions.

As the treatment session starts the patient is greeted by radiation therapists. The therapists assist the patients onto the treatment bed and into their immobilization device. Once in position the therapists verify the patient’s position by taking x-ray images. Adjustments are made based on the images and when necessary new images are acquired to confirm the final treatment position. Prior to treatment a medical physicist reviews the x-ray images. With the patient in the treatment position the therapists request for radiation from the delivery system. The radiation is delivered to one of three treatment rooms sequentially therefore small delays are possible from the time the radiation is requested to the time it is ready to be delivered. When the delivery system is ready to deliver radiation the therapists leave the treatment room. Final radiation parameters are confirmed and the radiation is delivered while the therapists monitor the patient via closed circuit video cameras.

As soon as the treatment is over, the immobilization device is removed. After treatment, the physician discusses further care with the patient, including any immediate precautions, follow-up recommendations and instructions in the event of further symptoms related to the illness and/or treatment. After a brief observation period patients are free to go home.
Proton Ocular Radiotherapy (PORT)

Conventional treatments for choroidal melanoma are enucleation (removal of the eye) and radiation therapy using eye plaques. Eye plaque therapy uses a radioactive cup sutured to the surface of the eye (over the tumor) and kept in place for up to a week before it is removed. Proton ocular radiation therapy is an alternative to enucleation and conventional eye plaque therapy. It is used to treat ocular melanomas, angiomas, hemangiomas and metastatic lesions contained within the eye. Tumors located in the very back of the eye and under orbital muscles are very difficult to treat with plaque therapy because it is not possible to suture the plaque over the tumor without causing significant damage to the muscles or nerves. Proton therapy does not require covering the tumor with a solid plaque and therefore its application is much less flexible.

The success of PORT treatments is very impressive with approximately 3,500 patients treated with a 5-year local control of 98% and 95% for small/medium and large ocular melanomas, respectively. The overall 5-year metastases-free survival is 80% with a better outcome for smaller lesions (95%) and a worst outcome (60%) for larger lesions. Improvement of vision depends on the original condition of the eye, tumor size and location and whether there is retinal detachment.

Planning & Treatment Process (PORT)

Most patients are referred in collaboration with the Massachusetts Eye and Ear Infirmary (MEEI). Pre-treatment assessments involve a series of ophthalmologic studies including but not limited to fluorescein angiography and ultrasound imaging. In the angiography study an ophthalmologist injects a dye (fluorescein) into the veins of the arm. As the dye travels through the vessels of the eye a camera equipped with special filters is used to photograph the back of the eye. In the ultrasound imaging study mild anesthetic eye drops are used so that a probe coated with a sterile gel can be pressed against the eye. Sound waves are generated from the probe and reflected from the eye. The reflected signal is then fed to a computer, which generates images of the internal topography of the eye.

A: A wide-angle photograph of the eye showing a tumor at the left of the image. The light colored circle located on the right side of the image is the optic nerve with a diameter around 2-3mm.

B: Fluorescein angiography images combined to create a composite view of the back of the eye. The optic nerve is the circular structure at the top left of the image where much of the vasculature originates. The tumor is located at the bottom right of the image.

C: An ultrasound image showing a cross-sectional view of a choroids melanoma measuring approximately 8x12mm.

Once accepted for proton therapy patients are scheduled at MEEI for a surgical procedure that involves suturing tiny tantalum clips on the surface of the eye. During the surgery the ophthalmologist illuminates the front of the eye. Because the tumor is less opaque then the eye it creates a shadow on the outer surface of the eye. Four clips are sutured along the periphery of the tumor. Measurements describing the location of the clips with respect to various reference points are obtained by the MEEI ophthalmologist and recorded by a dosimetrist or physicists from the
NPTC. Depending on the diagnosis and location of the tumor some patients may not require surgical implantation of the tantalum markers.

A few days following the surgery patients are seen by a radiation oncologist at MGH. A customized mask and bite mold are then fabricated in preparation for the proton radiation planning process. The purpose of the mask and bite mold is to ensure that patients remain as still as possible during the treatment enabling the protons to be targeted to an area that has very little motion, thereby minimizing the need to treat a larger area which encompasses both the planned target and its motion.

![The mask and bite mold minimize motion of the head ensuring that the treatment margins are reduced as much as possible.](image)

Patients who have had the tantalum implants undergo a treatment-planning simulation. The simulation involves sitting in the treatment chair and staring at a blinking red light that is fixed in space. Orthogonal (at right angles) x-rays are obtained for three fixation positions. The x-ray images show the tantalum clips very well.

A: An x-ray image of an eye with tantalum clips. The image is taken from the front of the eye. Three of the clips look flat because they are at the side edge of the eye. Each tic-marks represent 1 mm.

B: An x-ray image of the same eye as above with tantalum clips. The image is taken from the side of the eye with the eye unmoved from the first image (A). Three of the clips look flat because they are at the side edge of the eye.

Using a 3D eye model and the coordinates of the clips obtained from a few pairs of x-ray images ensures that they eye is tracking reliably.
The planning process involves combining information from the x-ray, ultrasound and angiography images to model the tumor and its location on the eye. The radiation oncologist in collaboration with the ophthalmologist, the dosimetrists, physicists and ophthalmologic technician outlines the tumor and determine the optimal direction for the proton treatment. The radiation oncologist then defines the dose to be delivered.

Once a plan is finalized and approved by the radiation oncologist and the ophthalmologist special hardware is fabricated for each treatment direction to be used. A thorough quality assurance process ensures that every device being made adheres to the intended specifications. Before devices are used for treatment, measurements ensure that the computer plan is properly modeled.

The whole pre-planning process from surgery, immobilization to the first treatment typically takes a few days to a week.

Treatment sessions usually last between 10 and 15 minutes. As the treatment session starts the patient is greeted by radiation therapists. Mild anesthetic eye drops are inserted into the eye. The therapists assist the patients into the treatment chair and into their mask and bite mold, which is attached to the treatment apparatus. The patient is positioned in the treatment position. Eyelid retractors are used to minimize their irradiation as much as possible. With the retractors in place the patient is asked to stare at a fixed blinking red light. X-ray images are acquired and adjustments are made to correct any misalignment. With the patient in the treatment position the therapists request for radiation from the delivery system. Radiation is delivered to one of three treatment rooms sequentially therefore small delays are possible from the time radiation is requested to the time it is ready to be delivered. Only when the delivery system is ready to deliver radiation will the therapists take a final confirming x-ray and leave the treatment room. Final radiation parameters are confirmed and the radiation is delivered while the therapists monitor the patient’s eye position via closed circuit video cameras.

Physicians and nurses regularly examine patients throughout the treatment course to monitor progress and address any concerns patient may have. Follow-up instructions are provided to monitor patient progress following the treatment course.
Frequently Asked Questions

How do I contact the Northeast Proton Therapy Center (NPTC) to have my case evaluated for proton therapy?
We encourage potential patients to seek referrals through their primary care provider (PCP) or local radiation oncology specialists. If these individuals are not familiar with proton therapy an inquiry line (617) 724-1680 and e-mail address InformationRadOnc@Partners.org can be used to directly seek specific contact information.

Why are there so few proton therapy centers if the treatment is so good?
As of summer 2005 there are 23 clinical proton radiotherapy facilities worldwide. Nine new facilities are proposed over the next four years. The upfront cost, around $100M, as well as the operational costs are the primary reason why there are so few proton facilities. In the US reimbursement rates from insurance providers is only slightly higher than conventional radiation therapy making it difficult for centers to recover their investment.

Do I need special approval from my insurance provider to receive proton therapy?
Pre-approval from your insurance provider is required since not all insurance providers cover proton radiation therapy. Many insurance providers will only covers proton therapy for specific diagnosis therefore it’s important that it covers the specific diagnosis being considered.

What are some of the side effects from proton therapy?
Side effects will depend on the patient’s age, medical history, diagnosis, disease size and location. Some patients may receive chemotherapy in conjunction with proton therapy; some will receive much lower radiation doses than others and therefore symptoms will vary significantly. Common symptoms include temporary hair loss and skin reactions in the direct path of the radiation. Fatigue is also associated treatment to large areas.

Once accepted for proton therapy how do I find lodging and how do I coordinate transportation if I am from out of town or country?
The NPTC provides resources to help patients and family find lodging. Some lodging is within walking distance to the NPTC while others require transportation. Subsidized housing may also be available. Some of the lodging options also provide transportation for hospital appointments.

How do I coordinate my proton treatment appointments?
The first few treatments are generally assigned based on available openings. At the time of the first few treatments you should let inform the radiation therapists of any treatment time preferences. However, you should be aware that scheduling is often limited by technical factors such as the need to use specific configurations of the treatment machine. Also, appointments are scheduled for many other patients with their own desires for treatment appointment times. An example of limited scheduling on one of the gantry rooms is the need to treat pediatric patients under anesthesia. A block is reserved in the morning where anesthesiologists and their equipment are available and it would be unfeasible to intersperse these treatments with others.

Why does it take longer to treat me with the proton therapy compared to conventional radiation therapy?
In order to ensure a minimal amount of radiation to normal structures we conform the proton beam very tightly to the target. Diagnostic quality pre-treatment x-ray and ultrasound imaging allows us to keep the margins very tight. This level of imaging is generally not done for conventional therapy. The actual treatment time, when the radiation is turned on, is similar for proton therapy and conventional x-ray therapy.
Why do some patients receive both conventional x-ray therapy as well as proton therapy?

The NPTC provides a limited resource. Managing the potential benefits from proton therapy is done on an individual case basis. In some circumstances it is advantageous to combine these therapies just like it is sometime advantageous to combine radiation therapy with surgery and/or chemotherapy. The goal of the NPTC is to provide the optimal access to patients who would benefit from proton radiation therapy. With experience using both high-quality x-ray and proton therapy, our physicians are well equipped to determine the appropriate combination, which is optimal for patient’s individual treatments.