Indiana University Cyclotron Facility
2401 Milo B. Sampson Ln.
Bloomington, IN 47408
(812) 855-9365

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**Development of the Midwest Proton Radiation Institute for the Treatment of
Cancer and Other Diseases Using Proton Radiation Therapy**

Final Report

DOE Patent Clearance Granted
MPDR
Mark P. Dvorscak
(630) 252-2393
E-mail: mark.dvorscak@ch.doe.gov
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DOE Chicago Operations Office
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PI: John M. Cameron Ph. D.

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Indiana University
P.O. Box 1847
Bloomington, IN 47402-1847

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Introduction

The Indiana University Cyclotron Facility (IUCF) is a research facility that has been operating since 1975. It houses three research accelerators (a 205 MeV cyclotron, a 240 MeV synchrotron, and a 500 MeV synchrotron) and the requisite space to develop and carry out a broad program of fundamental and applied research. Research activities at IUCF include nuclear and accelerator physics, material science, radiation biology, and proton therapy.

IU is converting 12,000 ft² of research space associated with the 205 MeV cyclotron into a regional proton therapy center that will make use of the natural advantages of proton radiation for research in the treatment of patients. This center, the Midwest Proton Radiotherapy Institute (MPRI), will bring this new modality to within 300 miles of one-quarter of the US population¹. Clinical trials aimed at evaluating the efficacy of new treatments, and research in the development and optimization of new treatments will be conducted at MPRI. MPRI will be a self-supporting radiation treatment facility with income derived from the fees charged for patient treatment and related ancillary activities².

The performance requirements for MPRI are described in the *Clinical Performance Requirements*³. The conversion is being accomplished under the supervision of both the medical director, Allan Thornton, M.D. and the technical director, John Cameron, Ph.D., in consultation with the equity partner hospitals and a regional consortium of referral physicians. The design and construction are being executed primarily by the scientists, engineers, and technicians at IUCF.

Figure 1 shows MPRI in detail. The conversion will result in three patient treatment rooms and an outpatient clinic. The first treatment room contains a fixed horizontal beam delivery system with two treatment lines: a Large Field Line for treating head and neck tumors, primarily, and an Eye Line for treating eye tumors. The second and third treatment rooms will each be equipped with a 360° isocentric rotating gantry. The gantry makes it possible to treat tumors from any angle without having to move the patient, thereby allowing for maximum efficacy in avoiding critical organs, and efficiency in patient set-up and beam delivery⁴. Finally, an outpatient clinic has been constructed for patient care and staff support.

DOE Contribution

This grant was active from July 15, 2000 to July 14, 2002. IUCF/MPRI was awarded \$1,873,000 for salaries for IUCF personnel to develop the first treatment room and its associated beam transport line, including an energy selection system. During the funding period the development included:

1. Construction and commissioning of the T0 Achromat
2. Design, construction, and commissioning of the Trunk Line
3. Design of the Energy Selection Line for all three treatment rooms
4. Construction of the Energy Selection Line to the first treatment room
5. Design of the Dose Delivery System for the Large Field Line

A detailed description of each of these activities follows.

Figure 1. Schematic Representation of MPRI facility

T0 Achromat

Cyclotron operation for proton therapy treatments requires stable beam in the Trunk Line, from which beam is delivered to each treatment room. Therefore, the beam line section immediately following the cyclotron must have achromatic properties to eliminate beam position variation in the Trunk Line due to small energy fluctuations of the cyclotron. This first section, called the T0 achromat, has been designed with flexible optics to allow

- ξ optical matching between the cyclotron and the Trunk Line, and
- ξ compensation of both spatial and angular momentum dispersion of the beam coming out of the cyclotron.

The optics of the beam line is based on a pair of opposite 24-degree bends with four quadrupoles in between. Such a “dog-leg” allows one to tune the beam line for dispersion compensation. The 205 MeV protons extracted from the cyclotron first go through a 5.5 m long straight section, which contains 3 harps for beam emittance measurements and a time-of-flight system for beam energy measurements. The five quadrupoles of the straight section provide optical matching between the cyclotron and the dispersion compensating “dog-leg”. The 45 degree bending dipole and three quadrupoles at the end of the achromat beam line bring the beam to the direction of the Trunk Line and focus the beam to a double focus at the Trunk Line entrance. Achromat beam line has extensive beam diagnostic system for measuring the beam properties extracted from the cyclotron. This facilitates optimal beam line tuning for beam transmission to the Trunk Line. Only the achromat section of the beam handling system should require tuning after each “cold” start of the cyclotron; the settings for the rest of the Trunk Line should be constant.

Construction of the T0 Achromat began in July, 2000 and it was commissioned with 205 MeV protons from the Cyclotron in December, 2000. Construction included installation of the electromagnets, power supplies, vacuum system, beam diagnostics, and the beam transport control system. The beam properties out of the cyclotron have been measured⁵ and the achromatic properties of the beam line have been demonstrated⁶.

Trunk Line

The Trunk Line delivers the beam from the T0 Achromat to the beam dump at the end of the line, providing a continuous beam of protons for any of the three treatment rooms to take when it is ready. The Trunk Line operates at a fixed energy of 205 MeV, which corresponds to a 27 cm proton range in water. To adjust the proton range for each treatment field, each treatment room has an associated energy degrader that is situated at the beginning of the Energy Selection (ES) Line. The optics of the Trunk Line consists of three sections (T1, T2, T3). Each section ends with a beam double focus, which corresponds to the ES Line degrader “location” projection onto the Trunk Line. Consequently, when beam is delivered to the corresponding treatment room, the double focus occurs at the degrader. The second and third sections of the Trunk Line have telescopic properties, i.e. they reproduce the beam optics and provide the same beam focus at the degrader locations for the second and third treatment rooms.

The Trunk Line ion-optical properties are summarized in the following table:

Table 1	
Trunk Line Properties	
Operating beam current (nominal)	200 nA
Nominal beam energy	205 MeV
Vacuum chamber aperture in the Trunk Line	3" (7.62 cm)
Beam spot size at the focal point (degrader locations)	$\zeta_x = 1 \text{ mm}$ $\zeta_y = 1 \text{ mm}$
Beam spot size at the beam dump	$\zeta_x = 2.2 \text{ cm}; \zeta_y = 2 \text{ cm}$
Transmission efficiency (Cyclotron to Dump)	> 99%

Each section consists of 6 quadrupole magnets and a system of beam position monitors and beam steerers that insure beam alignment by monitoring the beam position and correcting for detected position errors. Wire scanners are installed at the Trunk Line double focus locations. They serve as minimally destructive continuous beam spot size monitoring devices.

To monitor the beam stability out of the cyclotron, the beam is regularly delivered to the beam dump at the end of the Trunk Line. The cyclotron beam energy and energy spread is continuously monitored with the Multi-Leaf Faraday cup in the beam dump.

Construction of the Trunk Line, including installation of the electromagnets, power supplies, vacuum system, beam diagnostics, and the beam transport control system, took place from July to November, 2001. Commissioning of the Trunk Line was completed in January, 2002.

Energy Selection Line

To allow for independent setup and operation, each treatment room has its own Energy Selection (ES) beam line⁷ where the beam properties will be set for each treatment.

The main functions of the ES Line are:

- to provide the beam on/off switch to each treatment room
- to set the beam energy and energy spread required for a given treatment, and
- to transport the beam to the treatment room while controlling the beam spot size and position at the entrance to the nozzle.

Each ES line has a kicker dipole and Lambertson magnet pair that provides fast beam switching into that ES line. Each time the kicker is activated, the beam is kicked vertically up into the dipole field region of the Lambertson magnet where it is bent by 12° horizontally to the ES Line. A variable thickness energy degrader in each ES Line sets the beam energy for a given treatment. All ES Line magnets are laminated magnets to allow for reproducible energy changes.

After the beam energy is degraded to the required treatment energy, the beam is transported through two 63-degree bending magnets and 8 quadrupoles, optically configured into a double achromat, as shown in Figure 2. The ES Line optics are designed to produce significant momentum dispersion between the dipoles, which allows momentum band cutting, while at the entrance to the treatment room (or gantry), momentum dispersion is completely canceled⁸. The 63-degree bending magnets also eliminate transmission of neutron radiation created by the degradation process. The detailed design specifications for the magnetic elements are described in the ES Line design report⁹.

Beam position monitors in the quadrupoles monitor the beam position. Three vertical steerers along with trim coils on the bending magnets are available to correct for detected position errors.

A momentum selection slit together with a Multi-Leaf Faraday Cup select and verify the energy and energy spread of the degraded beam. Beam collimators at the beginning of each ES Line minimize the beam losses in the beam line elements. The beam will be transmitted in vacuum in each ES Line.

Figure 2: Layout of the components for the ES 1 beam line

A Secondary-electron Emission Monitor (SEM) and Gas Harp at the end of each ES Line monitor the beam current and the beam spot size and position at the entrance to the Nozzle.

The ES Line for the Fixed Beam Treatment Room includes a switching magnet, so the beam can be directed to either the Large Field Line or the Eye Line.

Construction of the ES Line to the Fixed Beam Treatment Room was completed in July, 2002 and commissioning began in August. Test results so far indicate that the ES Line performance meets or exceeds all specifications.

Dose Delivery System for the Large Field Line

The Fixed Beam Dose Delivery System (DDS)¹⁰ oversees the application of the proton beam to the patient via either the Large Field Line or the Eye Line in Treatment Room One. Since these two treatment lines are installed in the same treatment room, they cannot operate simultaneously. Each line has its own nozzle to facilitate the dose delivery process. The proton beam will be directed into one nozzle or the other by means of a ± 10 degree switch magnet, and its position will be measured with gas harps installed in each of the nozzles. The switch magnet and gas harps are part of the ES Line described above. The responsibilities of the DDS with respect to delivering the beam to a patient, starts beyond the gas harps. This is illustrated schematically in Figure 3.

Figure 3: The Fixed Beam Treatment Room beam line configuration showing the border between the BDS (ES Line) and DDS. The angle between the two beam lines is 20 degrees.

The dose delivery process includes spreading, modulating, and collimating (shaping) the beam, monitoring the properties of the dose being delivered, and stopping the treatment when either a) the dose has been successfully delivered, or b) the system detects a parameter that is out of tolerance.

A schematic illustration of the beam delivery nozzle for large field treatments is shown in Figure 4. The large field nozzle contains the devices required to modify the incident proton beam to the required shape and size. This includes a scan magnet and passive scattering elements, a beam energy modulator (ridge filter), several anti-scatter collimators, several ionization chambers and a retractable snout system to mount the patient-specific apertures and compensators as close as possible to the patient. Parallel plate ionization chambers are the primary dose measuring devices while segmented ionization chambers are used to measure beam symmetry and flatness.

Figure 4: A schematic illustration of the configuration for a typical beam delivery nozzle for large field treatments.

Control and monitoring of the DDS functions are carried out by the Dose Delivery System Control Computer (DDSCC), its software, and the electronics required to control and monitor the nozzle components. The user communicates with the DDSCC via the Treatment Room Control System (TRCS). The DDS control system has three separate control processes, as illustrated in Figure 5. They are (1) to monitor the dose delivered to the patient, (2) to spread the beam using either the scanning magnet or the passive scattering system and (3) to modify the beam shape and energy distribution using several patient and beam-specific devices such as ridge filters, apertures and compensators.

Figure 5: A functional flow diagram of the DDS control processes.

The dose monitoring function (upper trace in Figure 5) is facilitated by two electronic units called Dose Terminators (DTs) and manages the dose delivery process, which includes validating several beam parameters. The dose monitoring function involves three feedback loops to ensure that (1) the dose delivered to the patient does not exceed the prescribed dose, (2) the beam flatness and symmetry meet the specifications, and (3) the appropriate high voltages are applied to the ionization chambers.

The beam spreading function (lower trace in Figure 5) involves spreading the beam in two dimensions to cover the maximum lateral dimensions of the treatment target. Two methods will be employed to spread the beam. The first method will use two passive scatterers to spread the beam for field sizes up to a maximum diameter of 120 mm. A single control loop is required for passive scattering to verify the longitudinal position of the first scatterer, which is motorized. The second method actively spreads the beam using a scanning magnet that sweeps the beam in two dimensions across the treatment area. The scanning magnet will be employed at a later stage.

The beam modifying function (lower trace in Figure 5) involves shaping the beam according to the beams eye view of the target and modifying the energy distribution (energy modulation) to conform precisely to the treatment volume while maintaining other specified beam properties. The beam energy modulation is done by means of ridge filters. Modulating the beam energy in a predetermined manner allows for spreading out the Bragg peak by a desired length, creating a Spread Out Bragg Peak (SOBP). Beam shaping is achieved by means of patient-specific

apertures and patient-specific range modifying compensators. Although all these are passive devices, a control loop is required to read the interlocks from each device to verify that the correct devices are installed in the proper places for a specific treatment field.

Design of the Dose Delivery System for the Large Field Line, including the nozzle devices, control electronics and software was ongoing from June 2001 to July 2002.

Conclusion

This grant funded engineering and technical staff who were designing, constructing, and commissioning the beam and dose delivery systems for the first treatment room for MPRI. During the funding period, the first three construction milestones were met, as shown in Table 2 below. As of this writing, the project is still on track to meet all of the milestones.

Table 2
MPRI Construction Milestones

T0 Achromat Beam Commissioning Begins:	Nov, 2000
Trunk Line Beam Commissioning Begins:	Dec, 2001
Energy Selection Line Commissioning Begins:	Aug, 2002
Fixed Beam Treatment Room Commissioning begins:	Oct, 2002
ES1 & Treatment Room Ready for Patient Treatment:	May, 2003
ES2 & Gantry Installed & Ready for Beam Commissioning:	July, 2004
ES2 Room Ready for Patient Treatment.	July, 2005

This grant represented approximately 40% of the total salary expenditures for all MPRI development activities through 2002.

Publications

The following are IUCF publications associated with the development of MPRI during the funding period:

1. Anferov, V, "Energy Degradation Optimization for Medical Beam Lines," Nuclear Instruments and Methods in Physics Research A496 (2003) 222-227.
2. Klein, S.B, "Status of the Proton Therapy Project at IUCF and the Midwest Proton Radiotherapy Institute" *Proc. CAARI 2002*, Denton TX, Nov. (2002), in press.
3. Katuin, J., Schreuder, N, "The Use of Industrial Robot Arms for High Precision patient Positioning," *Proc. CAARI 2002*, Denton TX, Nov. (2002), in press.
4. V. Anferov, B. Broderick, J.C. Collins, D.L. Friesel, D. Jenner, W.P. Jones, J. Katuin, S.B. Klein, W. Starks, J. Self, N. Schreuder, "The Midwest Proton Radiation Institute Project at the Indiana University Cyclotron Facility" *Proc. CAARI 2002*, Denton TX, Nov (2000).
5. Friesel, D.L., Anferov, V., Hamm, R.W., "A CW RFQ Injector for the IUCF Cyclotron," *Proc CAARI 2000*, Denton TX, Nov. (2000) pp. 651-654.

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- ¹ Cameron, J., Reece, D.M., Nelson, S.R. (eds.). Midwest Proton Radiation Institute: A proton beam cancer therapy facility - Feasibility Study, prepared in collaboration with Meridian Consulting Group, Indianapolis, IN (1997)
 - ² IBID
 - ³ Klein S. "Clinical Performance Requirements", IUCF DOC# 100041.
 - ⁴ Flanz JB, "Large Medical Gantries", Proceedings of the IEEE 1995 Particle Accelerator Conference.
 - ⁵ Anferov VA *et al*, "Dispersion suppression in the MPRI achromat beam line", in Proc. of 2001 Part. Accel. Conf. (PAC-2001), Chicago, (2001).
 - ⁶ Anferov VA, "Dispersion measurement at the end of achromat beam line", IUCF Doc # 100135.
 - ⁷ Anferov VA, "Beam Delivery System Design Proposal", IUCF Doc #100130
 - ⁸ Jones, WP and G.P.A. Berg, "Design of a beam transport system for a proton radiation therapy facility", in Proc. of PAC-99, New York, 2519 (2000).
 - ⁹ Anferov VA, "Energy selection beam line optics design report", IUCF Doc #100132.
 - ¹⁰ Schreuder, AN, "Fixed Beam Treatment Room Dose Delivery System Design Proposal," IUCF Doc #100123