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Spread Out Carbon Bragg Peak at NSRL

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DISCLAIMER

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Introduction

Charged particles lose energy continuously while traversing non-vacuum medium but have a sharp peak of dE/dx near the end of the path length. This can be very beneficial for cancer radiotherapy where healthy tissues surrounding a tumor are left with little dose compared to traditional therapy methods. However, since the region of high dose is localized to such a small area, it can present challenges when attempting to treat tumors of larger volume. By utilizing a variable thickness degrader system, the treatment area can be expanded during clinical treatment applications. To accommodate these types of radiobiology experiments, NSRL has produced a spread-out Bragg peak degrader wheel which aims to widen the Bragg peak of a 108 MeV/n Carbon beam to deliver a constant linear energy transfer, in water, of 97.7 keV/μm over a range of 36.7 mm.

Background

As charged particles travel through a material, energy is lost according to the Bethe-Bloch equation[1]. For a given velocity, the energy loss rate, or Linear Energy Transfer (LET) is described by the Bragg Curve, as seen in Figure 1. The LET steadily increases as the particle travels through the material, until the particle approaches its stopping point, called the Bragg Peak, where the LET increases rapidly and reaches its maximum. For an incoming particle of speed v, charge z, and energy E, it will travel into a target a distance of x, with an election number density n, and a mean excitation energy I. c is the speed of light, ε_0 is the vacuum permittivity, e is the electron charge, m_e is the electron rest mass, and $\beta = v/c$. The formula can be found below:[2]

$$-\langle\frac{dE}{dx}\rangle = \frac{4\pi}{m_e c^2} * \frac{nz^2}{\beta^2} * \left(\frac{e^2}{4\pi\epsilon_0}\right)^2 * \left[ln\left(\frac{2m_e c^2\beta^2}{I * (1 - \beta^2)}\right) - \beta^2\right]$$

[1] Bethe, H., Ashkin, J., Segré, E. (ed.). *Experimental Nuclear Physics.* New York: J. Wiley. p. 253, (1953).
[2] Sigmund, Peter *Particle Penetration and Radiation Effects. Springer Series in Solid State Sciences, 151.* Berlin Heidelberg: Springer-Verlag. ISBN 3-540-31713-9 (2006).

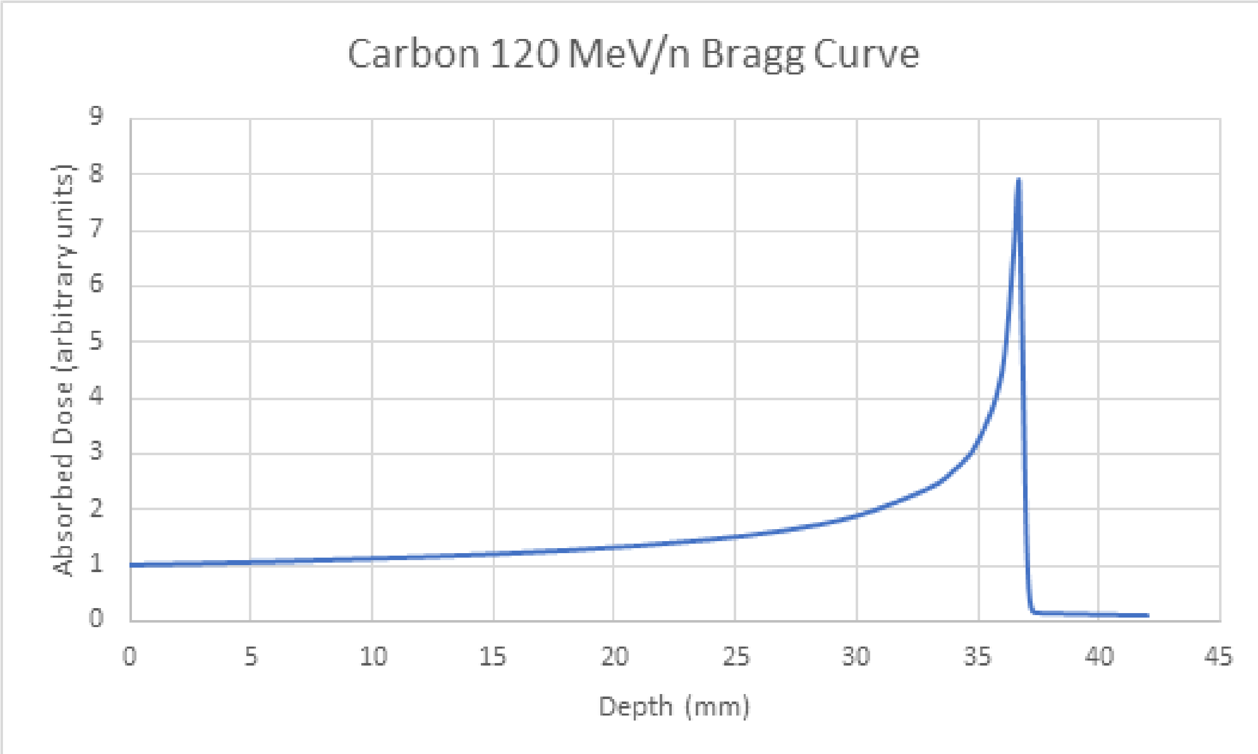

Figure 1: Measured Bragg Curve for a 120 MeV/n carbon beam in polyethylene.

While ion treatment for cancer can be extremely beneficial, a monoenergetic beam has a specific defined range, resulting in a very localized treatment. The dose delivered by a monoenergetic beam will vary based on depth within the soft tissue of a target, creating a hotspot at the end of the range of the beam. This can be overcome by creating and delivering a Spread-Out Bragg Peak (SOBP). Multiple energies of the same species beam, each having distinct Bragg peaks and ranges, are delivered upon the target. Doses across the individual Bragg Curves accumulate, delivering a uniform dose throughout the target volume. The SOBP has additional benefits related to cancer treatment such that it can target large or complex volumes within the target.

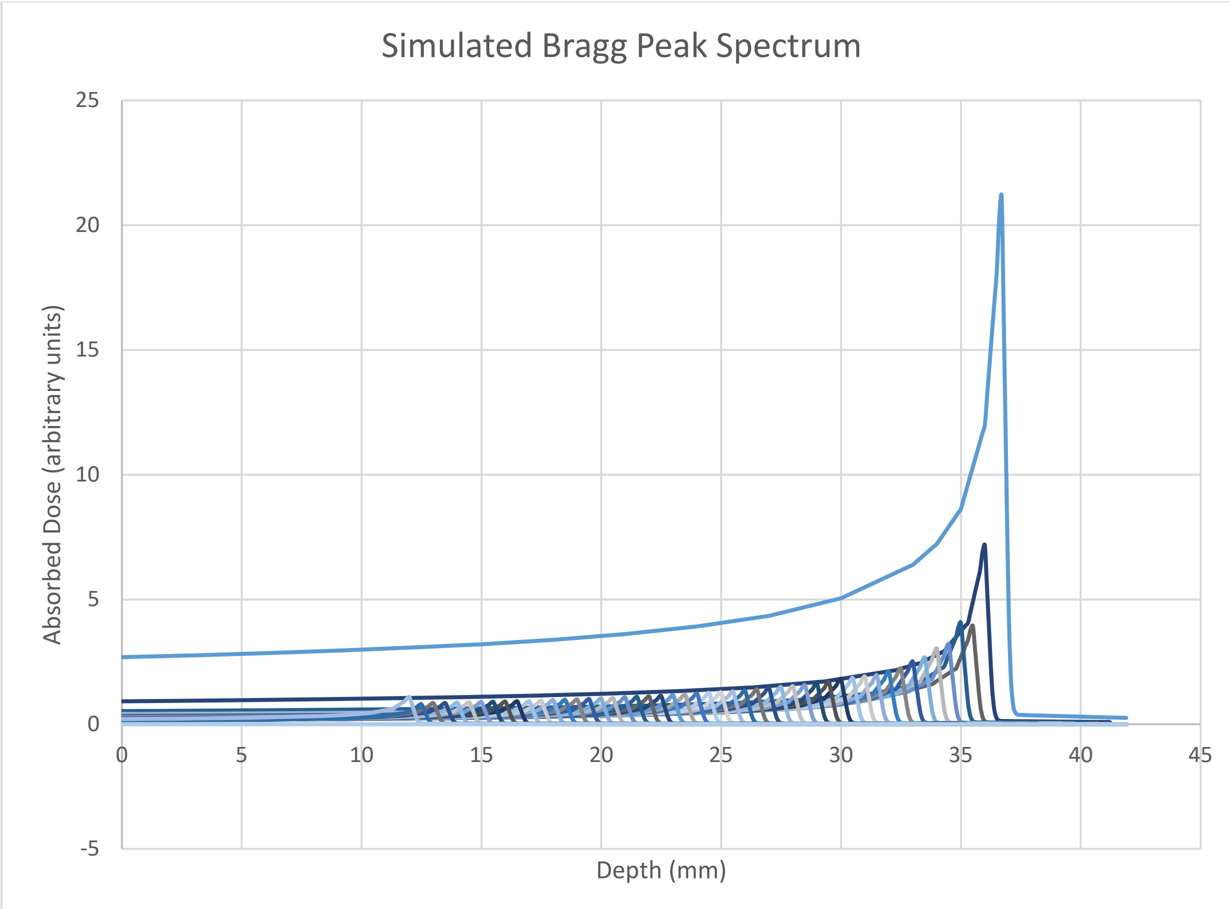

Figure 2: Plot showing 50 Bragg Peaks simulating 50 steps of degrader, in 0.5 mm steps of a measured 120 MeV/n carbon beam.

By utilizing a degrader system with multiple thickness settings, a mono energetic beam can be modified into many different energies. For example, Figure 2 shows a simulation of 50 individual Bragg Peaks, generated by passing a monoenergetic 120 MeV/n carbon beam through varying thicknesses of polyethylene in the degrader wheel. The maximum range is determined by the highest energy, in this case where the beam is not subjected to any degrader. With each subsequent step in degrader thickness, the beam's energy and range and delivered dose is reduced.

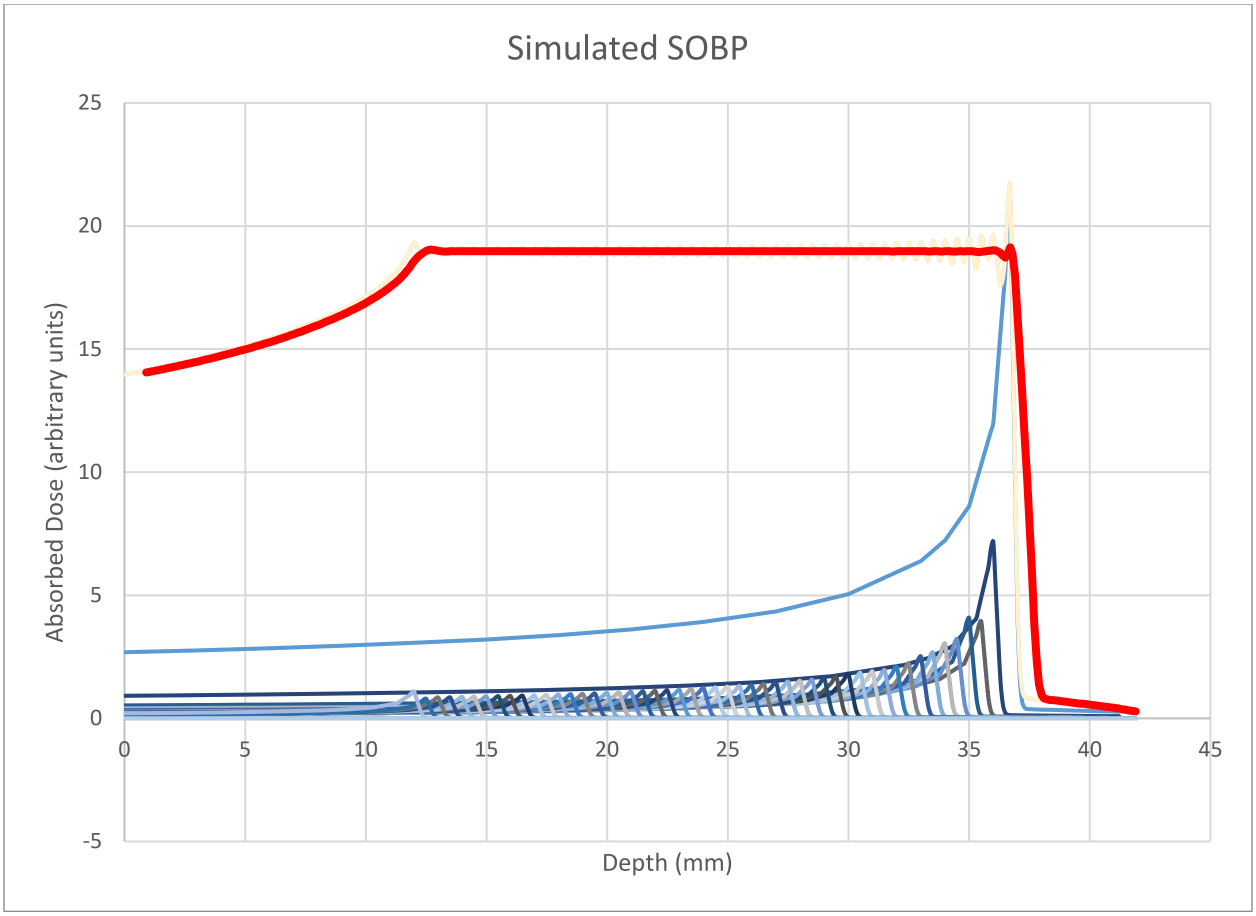

Figure 3: Plot showing the resulting SOBP, consisting of the accumulated doses (red plot), based on appropriate weighting of 30 individual, simulated, Bragg Peaks (blue and grey plots) of a 120 MeV/n carbon beam.

To adjust the weight of each Bragg Peak, a given section of degrader is designed to be a certain fraction of the total area of the wheel. Once proper ratios of degrader are achieved, the contribution from each Bragg Peak to the accumulated dose will flatten out over the range of energies generated. Figure 3 shows the SOBP (red plot), generated from the proper weighing and accumulation of the dose delivered by 50 individual Bragg Peaks. A table describing the relative weights of the degrader thicknesses can be found in Appendix A and detailed photographs of the degrader wheel used to deliver a carbon SOBP are shown in Figure 5. By increasing the number of degrader steps, a more uniform and consistent dose can be delivered within the volume of the target.

By utilizing a SOBP, ion treatment can prove to be highly effective as compared to traditional methods for cancer treatment. Knowing the location and dimensions of a tumor, a treatment can be designed and prescribed to treat a highly localized area, avoiding healthy surrounding tissues. Figure 4 shows the comparison of the dose delivered in two examples as compared to X-ray (XRT) therapy and Carbon Ion Therapy (CIRT). In XRT, a high dose is spread out through a large path, affecting not only the tumor but the surrounding healthy organs and tissues. CIRT on the other hand, while healthy tissues and organs are still receiving some amount of dose, it is significantly less as compared to XRT[3].

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[3] N. Kubo, J. Saitoh, H. Shimada, and K. Shirai, *Dosimetric comparison of carbon ion and X-ray radiotherapy for Stage IIIA non-small cell lung cancer.* Journal of Radiation Research, 57(5): 1-7. May 2016. doi:10.1093/jrr/rrw041

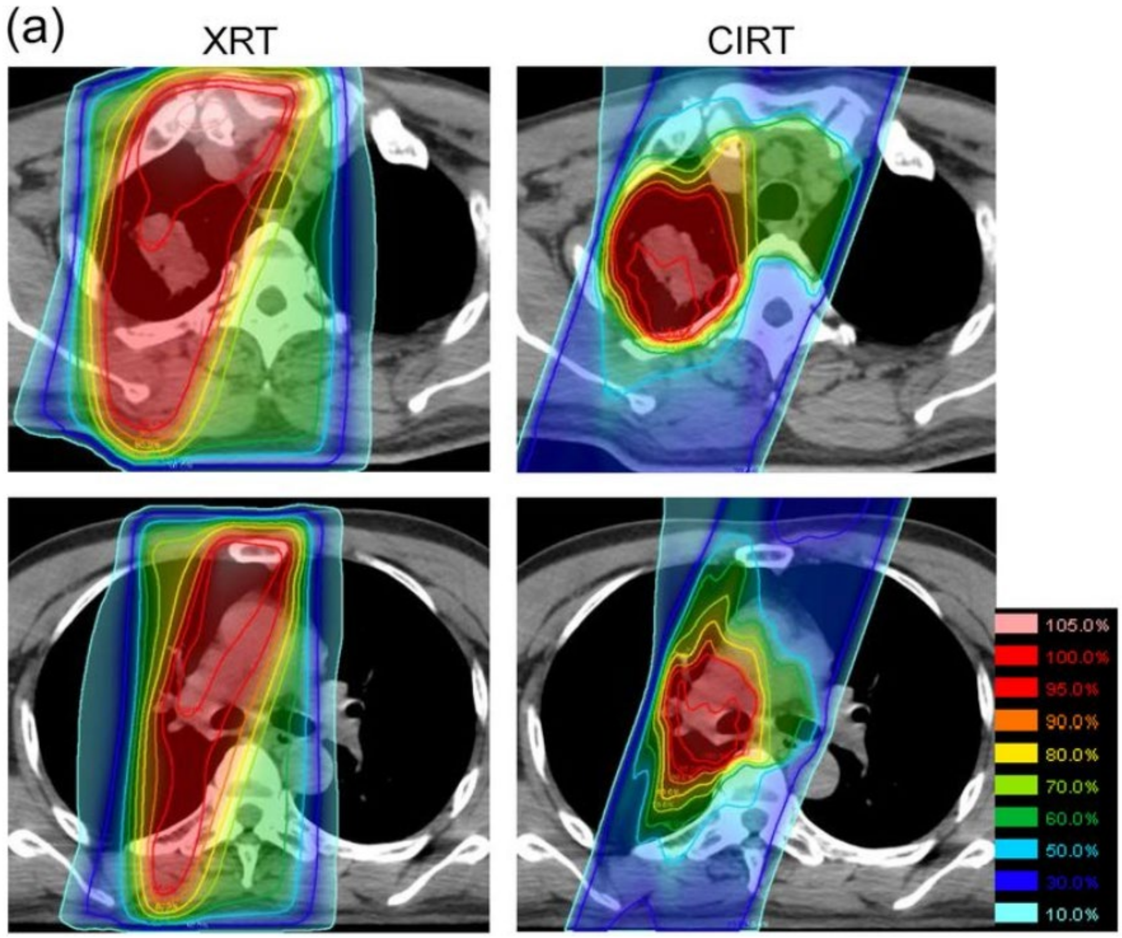

Figure 4: Comparison of doses received along treatment path via X-ray therapy (XRT) versus carbon therapy (CIRT).

Beam Energy and LET Distribution

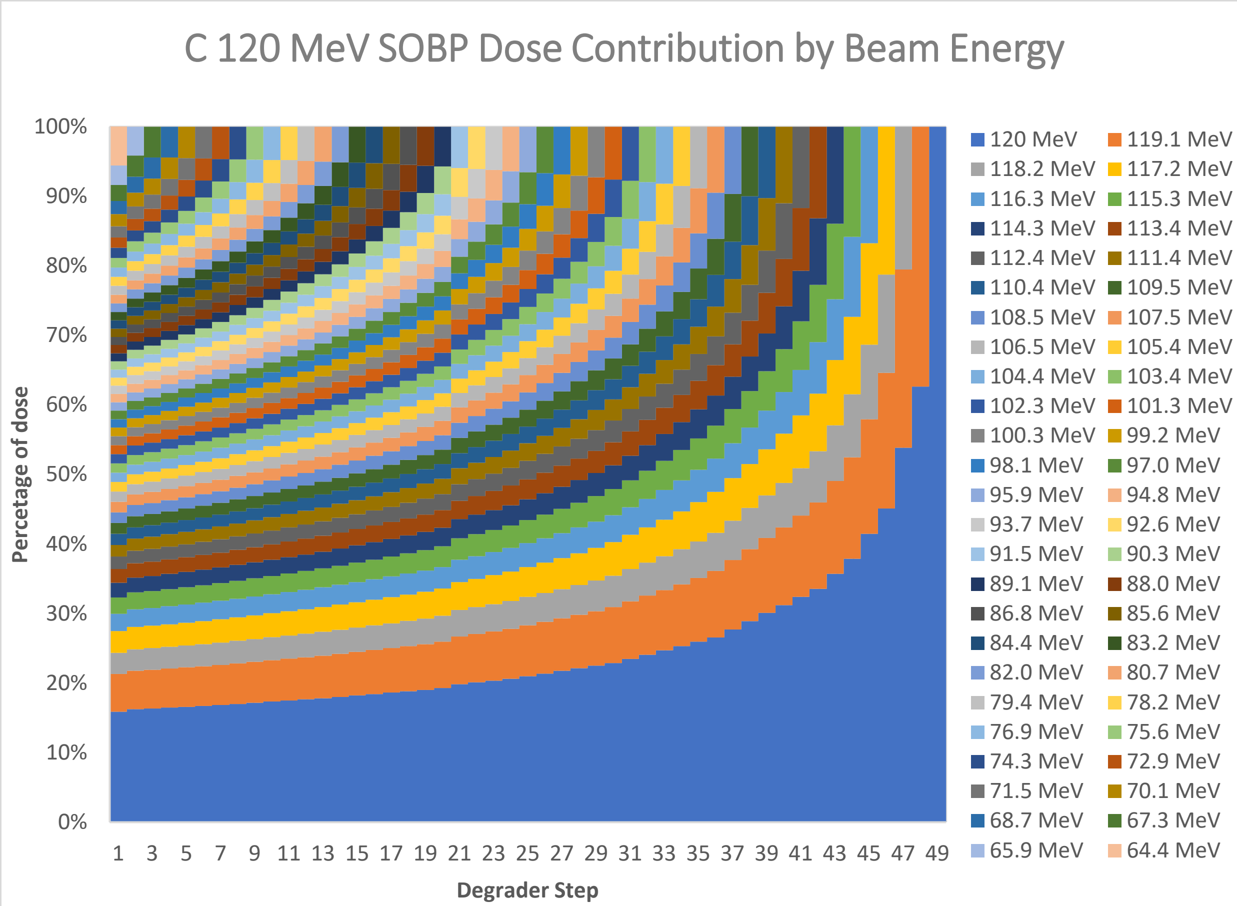

Figure 5: Graph depicting the breakdown of the contribution of dose received in 1 mm increments, generated by the properly weighted degrader steps by the degrader wheel. Each color represents the weighted contribution of one beam and its height is proportional to the fraction of the total dose it has delivered at a given depth.

Biological effects and not only determined by the dose received but also from the LET. Damage from high LET has been documented to have a greater effectiveness on biological systems than low LET. LET dependent damage has been seen on a wide scale, comparing effects seen from multicellular structures down to the DNA scale[4].

While the doses received in a target across the depth of a SOBP are uniform, the beam energies, and resulting LETs, delivering those doses vary as the depth changes. Figure 5 depicts the contributions from the 50 individual beams from the simulation. Each section of degrader generates a beam of progressively lower energy, resulting in increasing LET. Each color represents a distinct beam energy and fraction of the total dose it contributes at a given depth. For example, at the deepest point in the SOBP, the dose is completely delivered by the undegraded 120 MeV beam, with an LET of 2.267 keV/micron, while the

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[4] Goodhead, D.T., *Mechanisms for the biological effectiveness of high-LET radiations*, J. Radiat. Res., (1999) Dec;40 Suppl:1-13. doi:10.1269/jrr.40.s1. PMID: 10804988.

dose is delivered at the most shallow point is comprised of a sum of the doses delivered by all 50 beams, ranging from 120 MeV (2.267 keV/micron) down to 64.4 MeV (3.652 keV/micron).

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Wheel Design and Application

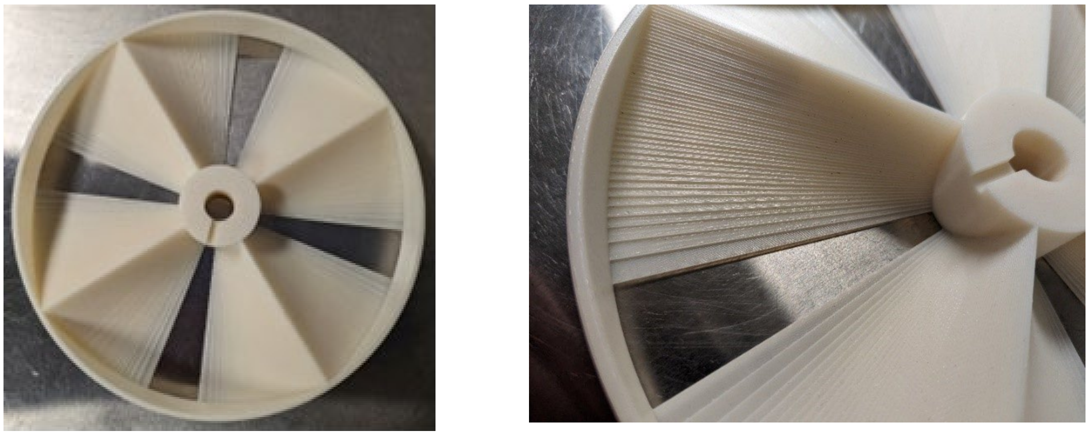


Figure 6: Detailed photographs showing the degrader wheel, spoke step size and distribution, used to generate a SOBP for Carbon 120 MeV/n.

At NSRL, SOBP are delivered by using a 120 MeV/n carbon beam, measured at the target's mounting location. The carbon beam is shaped into a 1 cm diameter pencil beam and aligned through a copper aperture for additional collimation before reaching the target. Finally, the degrader wheel is mounted in front of the aperture and set to rotate at a constant speed of approximately 200 RPM to ensure a fully modulated beam. Through slow extraction from the Booster Synchrotron, NSRL receives beam to the target room in spills. Every spill cycle (typically 4.2 or 6.6 s), beam is received with typical spill length of 0.4 s. At 200 RPM, the wheel will rotate 1.3 times over the course of one spill, sampling 10.4 instances of the 50-step degrader and eliminating any effects from inconsistent start and stop positions from spill to spill.

The degrader wheel is divided into four quadrants with varying thicknesses of polyethene, spanning from 0 mm up to 25 mm in 50 steps. The amount of polyethylene encountered by the incoming beam will induce an energy loss, primarily through ionization, degrade the energy, decrease the range and ultimately, shift the location of the Bragg Peak within the target. 50 individual steps of degrader will generate 50 discrete beams, each with a unique energy, range, and Bragg Curve. The resulting LET delivered by a SOBP is equivalent to the maximum LET for that ion species, linearly spread over the maximum and minimum ranges of the modified Carbon beam. For example, while delivering a SOBP via Carbon 108 MeV/n beam, the LET delivered would be 97.7 keV/µm.

Calibration and Alignment

To ensure the proper dose is delivered, prior to the experiment, the SOBP will be calibrated using a large ion chamber at the exit of the vacuum window, a permanent fixture of the NSRL target room, and a small ionization chamber (EGG chamber), temporarily mounted at the target location, as seen in Figure 7.

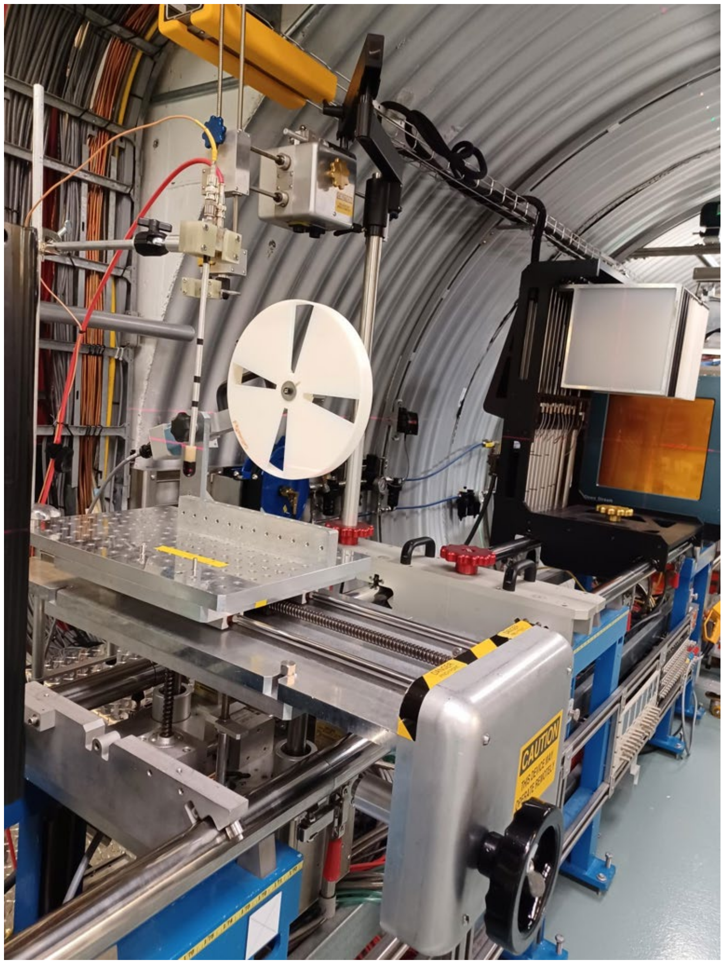


Figure 7: SOBP module mounted in the NSRL target room with EGG chamber mounted at the target location and the large ion chamber seen upstream (amber window), preparing to begin a calibration measurement. Image source: Sally Amundsen, "EGG chamber & Delran wheel setup face", 2023.

The copper collimator will be removed, and the degrader wheel is lifted out of the beam path. A carbon beam is delivered, and the ratio of the dose received by the EGG chamber to the counts on the large ion chamber is calculated and saved in a setup file. Next, the degrader wheel, remaining stationary, will be lowered into position and aligned such that the beam will pass through a section with no degrader. The calibration number determined in the previous step will be verified. Confidence in proper alignment is achieved if the calibration number remains constant throughout this process. Next, the degrader wheel will be set to rotate at approximately 200 RPM. With the EGG chamber still mounted in the target location, one final calibration will take place and will be recorded in a setup file, representing the SOBP.

The EGG chamber will be removed, and the copper collimator is installed, verifying its final location with the alignment lasers, as seen in Figure 8, where the green and red lasers are used for the *x-axis* and *y-axis* alignment, respectively.

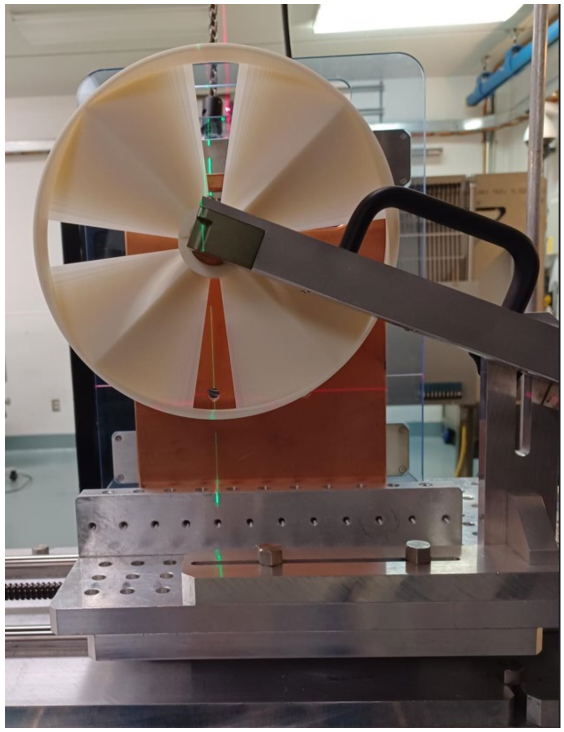


Figure 8: SOBP module with copper collimator installed and aligned with x and y axis alignment lasers. Image source: Sally Amundson, "Setup laser alignment for wheel collimator & holder", 2023.

The target fixture, show in Figure 9, is comprised of two components, the mounting fixture and the bite bar "sled". NSRL is equipped with two variations of this fixture with different vertical positions of the through hole, depending on the target treatment location. The target will be prepared on the sled in advance and can be easily attached to the target fixture by two embedded magnets. Multiple sleds are available for use, allowing the user to prepare the next sample while an exposure is in progress.

Figure 9: Target fixture for SOBP. Target can be mounted, via bite bar, and attached to vertical surface by two magnets.

The target fixture is installed behind the copper collimator on the SOBP module, shown in Figure 10, via the guide pins, allowing for efficient and reproducible target swaps in between exposures.

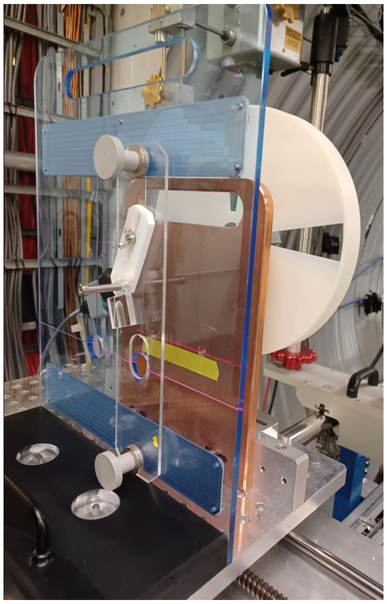


Figure 10: Aligned SOBP module with target fixture mounted in place. Image source: Sally Amundson, "Setup-Sample placement behind Cu collimator & wheel", 2023

Delivering Beam

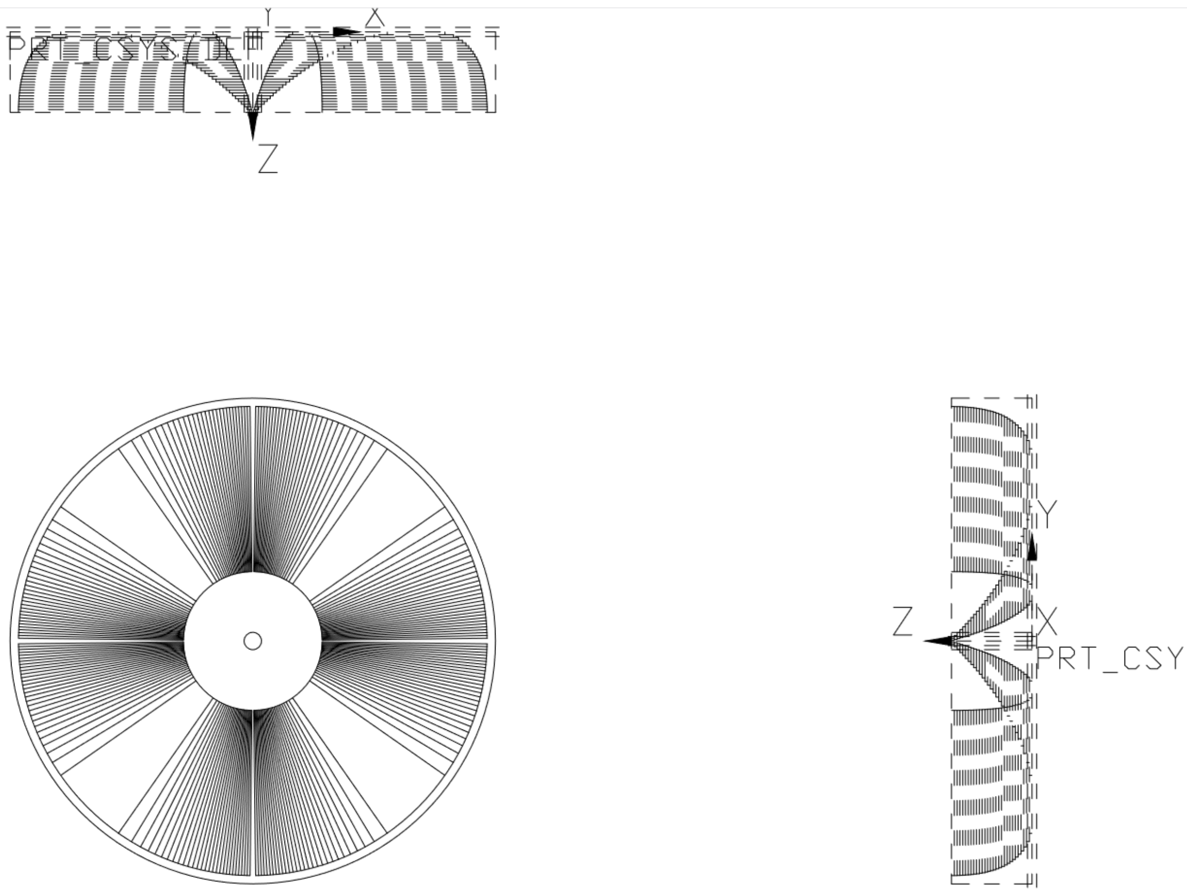
Once the exposure begins, the calibration number will be recalled and applied to the upstream ion chamber. It will continue to accumulate counts with each spill until the target dose is achieved and finally a cutoff signal is sent out. With a sufficient number of properly weighted degrader steps, similar performance is measured compared to the simulated plots in Figure 3, the absorbed dose is accumulated and flattened over the full range of the unmodified 120 MeV/n carbon beam.

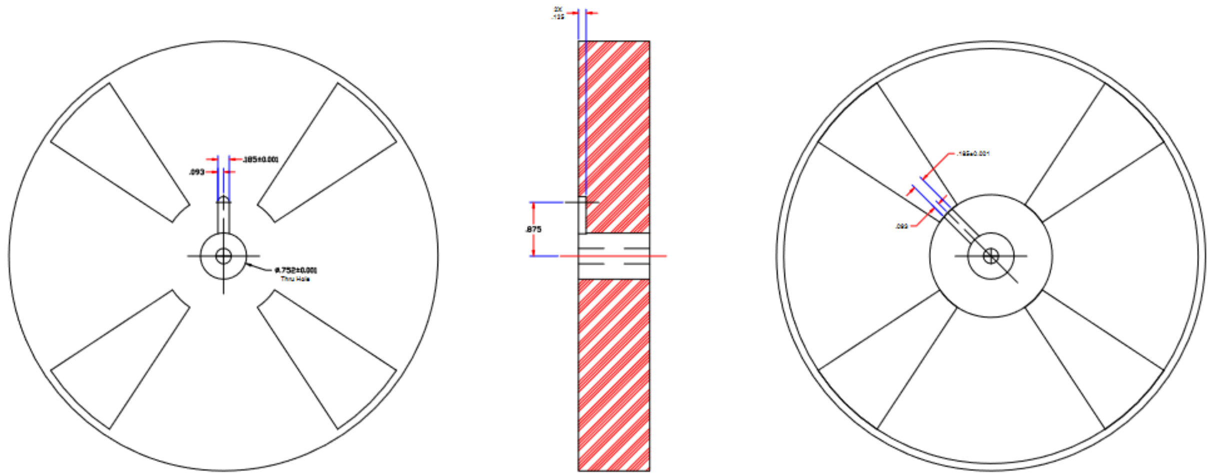
Once the target is mounted and the NSRL target room is secured, the NSRL Operator and Biology Liaison will administer the dose. Four remotely controlled cameras in the target room and a shared screen of the NSRL dosimetry program will provide users with spill-by-spill updates during the exposure. At the conclusion of the run, NSRL will provide the users with a run report containing run times and actual delivered dose.

Appendix A: Table of Degrader Weight Values Used in 50 Bragg Peak Simulation

Degrader (mm)	Percent of Wheel	Degrader (mm)	Percent of Wheel
0	21.13	12.5	1.22
0.5	7.17	13	1.18
1	3.93	13.5	1.15
1.5	4.07	14	1.13
2	3.20	14.5	1.11
2.5	3.03	15	1.09
3	2.66	15.5	1.07
3.5	2.51	16	1.04
4	2.23	16.5	1.02
4.5	2.09	17	1.00
5	1.96	17.5	0.98
5.5	1.90	18	0.97
6	1.84	18.5	0.96
6.5	1.80	19	0.93
7	1.68	19.5	0.91
7.5	1.62	20	0.91
8	1.56	20.5	0.90
8.5	1.52	21	0.89
9	1.48	21.5	0.89
9.5	1.45	22	0.87
10	1.38	22.5	0.86
10.5	1.34	23	0.84
11	1.30	23.5	0.84
11.5	1.27	24	0.80
12	1.24	24.5	1.08

Appendix B: Technical Drawings of the Degrader Wheel

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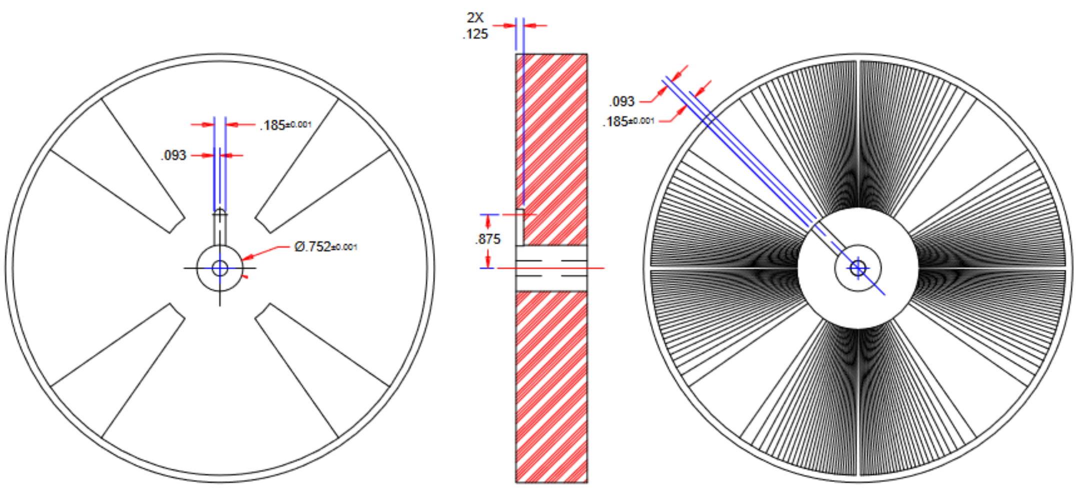
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