A Dive into the Experimental Process and Applications of Particle Therapy in Cancer Treatment

Jessica Whitehouse

T00682230

Phys 3500

December 2, 2023

In the modern world of science and healthcare, one would think that we have new and innovative ways to treat various diseases, but the current cancer treatment was invented nearly a century ago. The common cancer treatment of chemotherapy, which is one of the most prominent cancer treatment plans, was initially introduced in 1935, and it's fair to say that in the fast-moving world of science, it is time for something new (DeVita, 2).

Particle therapy via FLASH radiotherapy is a contemporary set of treatment plans that covers a wide range of options. This includes using protons or very high-energy electrons (VHEE) being accelerated with a linear particle accelerator to target cancerous cells in the human body. While these variations are still under development, they are progressing swiftly, with some laboratories already doing mouse and human trials. Both mammal trials have provided promising results, with subjects being seemingly cured of the cancerous cells (ASTRO).

All of the methods of particle therapy include the use of a linear particle accelerator, also called a linac. While a linac can be used with a variety of different particles, including positrons and anti-protons, only electrons and protons have been tested with this treatment. As discussed in class, linacs use electric fields to accelerate charged particles, such as the electron with a negative charge of -e and the proton with a positive charge of +e. Since linacs are, as the name suggests, linear, they do not need to use magnetic fields to bend the particle beams, making the process simpler. By using alternating potentials, the particles will bunch together into pulses, which can be adjusted for an added measurable variable (Matuszak).

FLASH radiotherapy (FLASH-RT) is a specific program of particle therapy that has had successful mammal trials. This program can be altered to accommodate the use of VHEE or protons as the particle of choice, and there's extensive research in both sections of this field. One human case, provided by Lausanne University Hospital, showcased a patient with a skin tumor. Using electrons from an Oriatron eRT6 5.6 MeV microwave LINAC, the skin tumor was removed completely 150 days after starting the treatment (Sampayan).

At the University of Cincinnati Cancer Center, they proceeded with human trials using protons instead, claiming that they can penetrate deeper into the skin compared to electrons. This human study was more in-depth compared to the study at Lausanne University Hospital, as it also recorded the pain levels that each patient experienced during the treatment process. Over the

12 treatment sites, 6 recorded complete pain relief, 2 recorded partial pain relief, and the remaining 4 recorded only temporary pain flares (ASTRO).

To understand the progress of FLASH-RT, it must be taken back to the beginning. The first ever FLASH dose was applied accidentally with electrons when the linac unexpectedly fired an electron beam when a researcher was in the chamber (Sampayan). This sparked the innovative steps that FLASH-RT has gone through. At the CERN lab, specifically the CLEAR department, there is a linac comprised of 40 m metal tubes stuffed with aluminum foil at one end (Larson). This site uses VHEE FLASH with no human trials. At CLEAR, their goal is to upgrade the maximum excitation for an electron in FLASH from the previously used 10 MeV to 200 MeV. This would allow for the electron beam to reach deeper seated tumors that previously only accelerated protons could reach.

The CLEAR facility also researches the best methods for focusing the electron beam. As of June 2021, they found that the use of a large aperture electromagnetic lens could focus the VHEE beam a couple of centimeters into a bucket of water. With that lens, there was also limited scattering, and the beam stayed consistently focused. After more precision checks, human trials are expected to begin at CLEAR in 2025 (Hortala).

An interesting aspect of FLASH-RT is the consensus between different research groups that there is no definitive answer as to how it exactly works compared to conventional radiotherapy. One of the hypotheses is that due to the high-level doses implemented in FLASH-RT, the cells are deprived of oxygen at a different level compared to conventional radiotherapy. The more oxygen-deprived the cell is, the more resistance it has to the radiation. This therefore would cause less damage to the cell, which is an effect shown by FLASH-RT (RO). Another hypothesis is that fewer white blood cells are affected due to the shortened dosage time of FLASH-RT. This in turn leaves the body with more tools to fight the cancerous cells naturally, along with any other bacterium or virus that enters the body (RO).

Each research study has experimented with different accelerator parameters. In the study at the University of Cincinnati Cancer Hospital, they used a burst of 8 Gy of radiation with protons at ≥40 Gy per second (ASTRO). This resulted in a pulse that lasted only 3/10 of a second. Compared to the study at Lausanne University Hospital, proton beams with 276 to 319 Gy per second were used (Sampayan).

Between all of the sources noted it is important to note that they all range in years. Even though the range is only 2020-2022, there was still time for considerable steps forward to be made. When Wilson's article was published in 2020, he had many questions regarding what would happen in human trials. Many of these were answered in the later articles published in 2022, which included human trial results. It is also important to note that while Larson's news article was published later, and on the same journalism site as Hortala's, Hortala's had more specific language. Between the news articles and research articles, there was a considerable jump in vocabulary in base knowledge that was required to understand the research articles compared to the news articles. Even with that barrier, many of the news sites were able to summarize the research in brief terms, only missing the nuanced and small details, but still getting the main points across.

In a collection of the points stated above, not only does FLASH-RT reduce pain during radiotherapy cancer treatments, but also has varying particle options including electrons and protons. By using linacs, these particles can be accelerated to such energies that they can precisely target cancerous cells without harming surrounding cells. Not only have these technologies already been tested on humans successfully, but there are plans for deeper-seated tumor tests to be implemented in 2025. While there is no change in effectiveness between electrons and protons, currently proton beams can reach deeper past skin, but with the new trials at CLEAR, this may be changing soon.

In totality, FLASH-RT is an up-and-coming cancer therapy, that not only reduces patient pain but also expands the limits of linacs for the benefit of humankind.

Bibliography

Chu, Edward, and Vincent DeVita. "The History of Chemotherapy - Yale Cancer Center." *Yale Cancer Center*, 6 July 2008, www.yalecancercenter.org/answers_july_6_08_89594_5_v1.pdf.

Editors of ASTRO. "Flash Radiation Therapy Shows Promise in First-in-Human Trial." American Society for Radiation Oncology, 23 Oct. 2022, www.astro.org/News-and-Publications/News-and-Media-Center/News-Releases/2022/FLASH-radiation-therapy-shows-promise-in-first-in.

Editors of Research Outreach. "Flash Radiotherapy: What, How and Why?" *Research Outreach*, 2 Oct. 2020, researchoutreach.org/articles/flash-radiotherapy-what-how-why/.

Hortala, Thomas. "Clear Study Paves the Way for Novel Electron-Based Cancer Therapy." *Phys.Org*, Phys.org, 10 June 2021, phys.org/news/2021-06-paves-electron-based-cancer-therapy.html.

Larson, Nina. "Particle Physics Pushing Cancer Treatment Boundaries." *Phys.Org*, Phys.org, 22 Oct. 2022, phys.org/news/2022-10-particle-physics-cancer-treatment-boundaries.html.

Matuszak, Natalia, et al. "Flash radiotherapy: An emerging approach in radiation therapy." *Reports of Practical Oncology and Radiotherapy*, vol. 27, no. 2, 19 May 2022, pp. 343–351, https://doi.org/10.5603/rpor.a2022.0038.