Cancer Treatment by Using Flash Radiotherapy Technique

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Abstract—**Flash radiotherapy (RT) is a method that administers radiation at an extremely rapid pace to the intended area. Its purpose is to minimize the harmful effects of radiation on healthy tissues while maintaining the therapeutic impact on cancer cells, as opposed to traditional radiation therapy. This article provides an overview of the published data on FLASH-RT and examines the existing understanding of this innovative approach. Furthermore, we focus on the technical challenges and limitations of FLASH-RT and explain how this modality works physically, specifically how technology helps the transfer of energy by ionizing radiation (looking at things like the beam on/off sequence, pulse-energy load, and gap times). It is important to note that the current preclinical research mostly relies on FLASH electrons, and the practical use of FLASH-RT in clinical settings is extremely restricted. To implement FLASH-RT in regular clinical radiation, it is necessary to create devices that can generate FLASH photon beams.**

Keywords: FLASH RT, radiotherapy, ionizing radiation, ultra-high dose rate, dosimetry parameters, biological effect, FLASH electrons, FLASH photons.

INTRODUCTION

Radiation therapy has been a fundamental aspect of cancer treatment for a long time, and its effectiveness in fighting tumors continues to increase as our knowledge of tumor biology, imaging, and radiation administration advances. By utilizing state-of-the-art technology, it is possible to administer radiation beams with exceptional precision to the intended target, thereby reducing harm to adjacent healthy tissues. due to the hazards However, this is only applicable to radiation side effects that have a significant impact on the likelihood of removing the malignant tissues. Flash radiotherapy (FLASHRT) is an emerging technology that has the potential to overcome the limitations of conventional radiotherapy. It involves delivering radiation at extremely high dose rates, several orders of magnitude greater than those used in conventional radiotherapy (40 Gy/s vs. 0.5–5 Gy/min, respectively). [1] Mechanism of Flash-RT biological

The mechanism of Flash-RT makes it advantageous over radiotherapy in the following ways:

First: Oxygen consumption hypothesis FLASH-RT works at the molecular level by looking at how oxygen metabolism might affect the area around cells [2]. FLASH-RT irradiation causes a reduction in the amount of oxygen in the tissue, resulting in a short period of low oxygen levels and temporary resistance to radiation. Oxygen has a crucial role in influencing the FLASH effect and serves as a physical metric for assessing the FLASH effect. At high dose rates, high doses quickly reduce the amount of oxygen, causing it to spread out in order to maintain sufficient oxygenation levels. As a result, normal tissue reacts similarly to hypoxic tissue. Following FLASH-RT, there is a reduction in the amount of oxygen in the tumor tissue through radiochemical processes, which ultimately results in the tumor being resistant to radiation.

a. Oxygen consumption hypothesis: high-dose transient irradiation decreases oxygen levels, particularly affecting normal cells, leading to increased radiation resistance. The hypothesis suggests that in the presence of low oxygen levels, there is a reduction in the levels of reactive oxygen species (ROS) in normal cells.

b. E Elevated b-ROS levels lead to progressive damage to DNA, RNA, proteins, and lipids over time.

Second: Cell damage caused by reactive oxygen species (ROS) The user's text is "[3]". The electronic irradiation using Con-RT and FLASH-RT had little impact on the morphology of zebrafish embryos.

Third: Hypothesis on the immune system and inflammation [4], The text elucidates that chromatin remodeling is facilitated by poly (adenosine diphosphate ribose) polymerase, and the effectiveness of inflammatory and anti-inflammatory cell signaling may be contingent upon the length of therapy.

Fourth: The relationship between DNA damage, cellular aging, and the development of fibrosis.

Fifth: Significant evidence exists regarding variations in DNA damage in healthy tissues following Con-RT and FLASH irradiation.

Pro FLASH-RT exhibits comparable tumor-killing efficacy to traditional dose-rate radiation while minimizing adverse effects on healthy tissue. The user's text is [5].

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RELATED WORK

Different studies were done regarding the FLASH radiotherapy, in [6] the author gives as brief history and status studies of FLASH RT that focuses on modalities of delivery of FLASH irradiation, primary mechanism of effect of the FLASH, with some Existing prospects and challenges of this original technique were also discussed. While in [7] The author review a FLASH radiotherapy with summarized study that is conducted with the effect of the FLASH thereby, with more focus on the future development therapy of FLASH proton beam potential, finally in [8] shows an emphasize review of the difficulties and efforted In moving FLASH radiotherapy forward, while discussing the difference effected variables and their impacts, also some main topics were analyzed such as FLASH radiotherapy biochemical mechanism, FLASH radiotherapy therapy and many more.

RESULTS AND ANALYSIS:

The primary distinction lies in the time-dose delivery structure employed in conventional and FLASH radiation. In traditional radiation, pulses can be arranged in a sequence with a frequency of 100 Hz, occurring at intervals of 10 ms, and each pulse can have a duration of 4 µs. Assuming a dose rate of 0.02 Gy/s (1.2 Gy/min) recorded under standard conditions in a phantom, a total dosage of 2.4 Gy is administered in 12000 pulses over a 2-minute session. Consequently, the amount of radiation administered in a single pulse is 0.0002 Gy, whereas the rate at which the radiation is supplied inside the pulse is around 50 Gy/s. FLASH radiation assumes a treatment duration of less than 200 ms and an average dose rate greater than 40 Gy/s. Given the literature's reported pulse sequencing method of 100 Hz [9], we may determine the total number of pulses per complete treatment, ranging from a few to 20 (for 200 ms). Various studies provide information on the dose rate inside the pulse, ranging from 105 to 106 Gy/s. Assuming the previously mentioned pulse duration of 1.8–2.0 µs, we can calculate that the dosage delivered during one pulse is 0.2 Gy. This calculation is based on a pulse rate of 105 Gy/s and a pulse duration of 2.0 µs, as shown in table [1]:

TABLE [1]: CALCULATE DOSAGE DELIVERED DURING PULSES

Type of Radiotherapy	Radiant Dose	Pulse	Time
Radiation	2.4-8.4 Gy/ms	1200	2 minutes
FLASH radiotherapy	10-40Gy/ms	105-106	Fewer 200ms

In figure (1) the average dose number was calculated, and result shows in FLASH radiotherapy the dose is higher that Radiation.

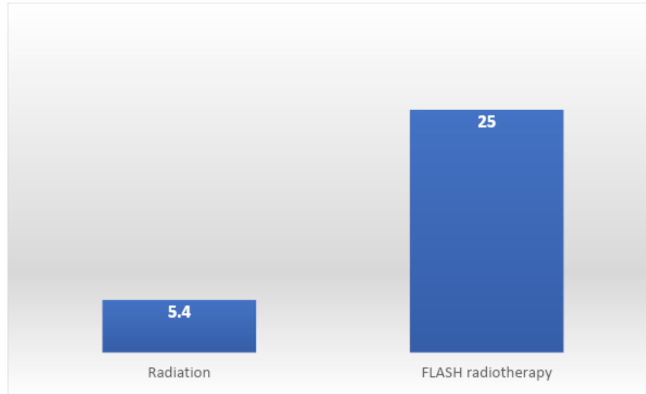

Figure (1): the average dose number

In figure (2) the pulse number was calculated, and result shows in FLASH radiotherapy the pulse number is more than from the Radiation.

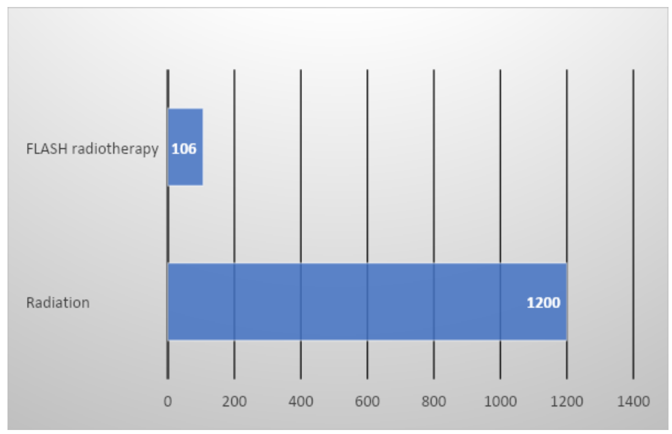

Figure (2): the pulse number

In figure (3) the time was calculated, and result shows in FLASH radiotherapy the time is less than from the Radiation.

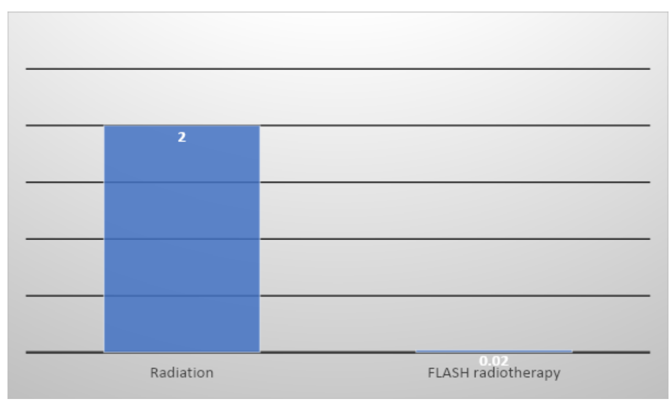

Figure (3): the time

The relation between the Oxygen Consumption Hypothesis and the ROS Hypothesis is that the ROS Hypothesis is a subset of the broader Oxygen Consumption Hypothesis.

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The Oxygen Consumption Hypothesis suggests that the aging process is primarily driven by cumulative damage caused by reactive oxygen species (ROS) generated during normal metabolic processes. It emphasizes that ROS are produced as byproducts of oxygen consumption in cells, particularly in mitochondria.
Within the Oxygen Consumption Hypothesis, the ROS Hypothesis specifically focuses on the role of ROS in the aging process. It suggests that increased levels of ROS, resulting from oxygen consumption, contribute to the aging process by causing oxidative damage to cellular components, such as DNA, proteins, and lipids. The accumulation of this damage is believed to lead to the functional decline of tissues and organs, as well as the manifestation of various age-related diseases.
In essence, the ROS Hypothesis is a more specific aspect of the broader Oxygen Consumption Hypothesis. It emphasizes the role of ROS and their impact on cellular damage and aging-related degenerative changes, within the framework of how oxygen consumption influences the aging process. As seen in figure (4).

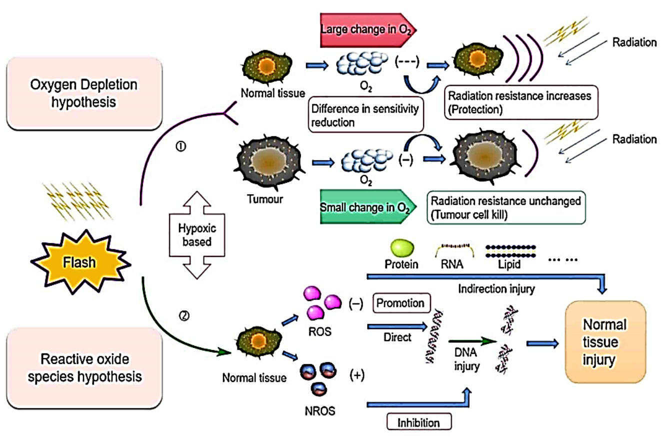

Figure (4): Mechanistic diagram of the oxygen consumption hypothesis and ROS hypothesis [10]

The emerging approach of Flash radiotherapy in radiation therapy is a novel technique that delivers extremely high doses of radiation in a very short amount of time, typically within a few milliseconds. Traditional radiation therapy involves delivering the radiation dose over a longer period, typically several minutes.
Flash radiotherapy utilizes a highly intense beam of electrons or protons to administer the treatment. The delivery of such high doses at ultra-high dose rates is made possible by advanced technological developments, such as high-powered linear accelerators and specialized beam delivery systems.
The potential advantages of Flash radiotherapy are still being studied, but early preclinical and clinical data suggest several potential benefits. One advantage is the sparing of normal tissues during treatment, potentially reducing side effects and complications. This is because the rapid delivery of radiation triggers certain biological responses that appear to protect healthy tissues. Additionally, Flash radiotherapy may allow for shorter treatment sessions, improving patient comfort and convenience.
Furthermore, Flash radiotherapy has shown promise in enhancing the effectiveness of radiation therapy against tumors. Preclinical studies have indicated increased tumor cell kill rates, potentially improving treatment outcomes. However, further research is needed to determine the optimal application of Flash radiotherapy in various cancer types and clinical scenarios.
It is important to note that Flash radiotherapy is still in the experimental and early clinical investigation stage. Ongoing research aims to refine the technique, understand its mechanisms of action, evaluate its safety and effectiveness, and explore potential combinations with other treatment modalities. As seen in figure (5).

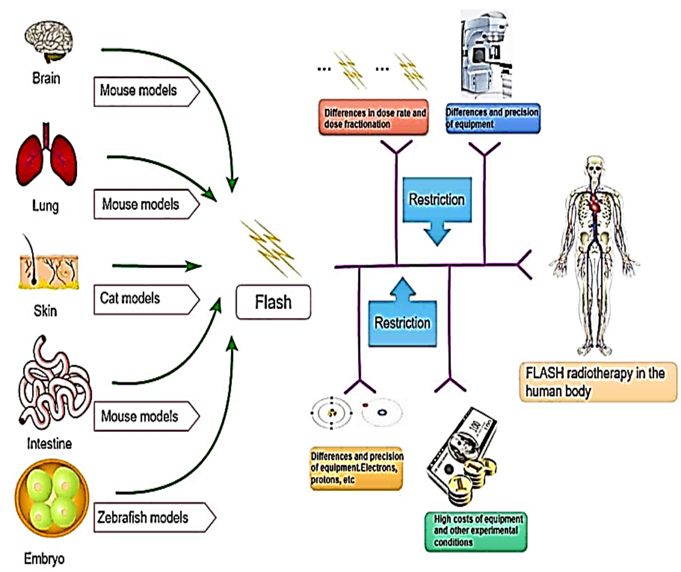

Figure (5): Shows an emerging approach of Flash radiotherapy: in radiation therapy [11].

Conclusion

The treatment strategy of FLASH radiotherapy is an exciting new method that is now very important and has big potential to change clinical cancer treatment future, the FLASH-RT is a specific radiation technique that has been under research for approximately 60 years, the modality has been examined across various levels, ranging from bacteria and cells in a controlled laboratory setting, to mice and other small animals, and finally in human patients, the FLASH-RT project originated from the implementation of UHDR radiation, during which the FLASH effect was serendipitously observed, and the main fundamental characteristic of FLASH-RT is its strong ability to effectively control tumors while also providing targeted protection to normal tissues.
FLASH-RT has the potential to play a crucial role in treating a range of liver, pancreatic, and colon cancers in the future, also it has the potential to replace specific surgical procedures,

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resulting in a significant decrease in both pain and economic burden, enhancing the rates of patient survival and minimizing the adverse effects of radiation. FLASH-RT exhibits substantial promise for the treatment of tumors, also it can revolutionize the existing theoretical framework of radiation in the future.

Radiation causes a reduction in the amount of oxygen by radiochemical processes, especially when the dosage rate is high. It can be inferred with confidence that the FLASH effect is, to some extent, attributable to oxygen consumption, therefore the FLASH-RT possesses theoretical benefits compared to traditional radiation. Preclinical investigations provide evidence for the efficacy of FLASH-RT, albeit their scope was limited to depths of only a few millimeters.

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