varian
A Siemens Healthineers Company

Varian FlashForward™ Consortium FLASH Bibliography

Krieger M, van de Water S, Folkerts MM, et al. Med Phys 2022. Varian and Multi-institution.
A quantitative flash effectiveness model to reveal potentials and pitfalls of high dose rate proton therapy.

The authors proposed a phenomenological model, to evaluate and compare treatment plans at ultra-high dose rate. Testing several patient scenarios, they show transmission and single-field treatment typically benefit from the FLASH dose-rate 4- to 5-fold more than Bragg-Peak and multifield plans, at the cost of increased integral dose.

Zhang Y, Ding Z, Perentesis JP, et al. Clin Oncol (R Coll Radiol) 2021. Varian and Cincinnati Children's Hospital Medical Center, USA.
Can rational combination of ultra-high dose rate flash radiotherapy with immunotherapy provide a novel approach to cancer treatment?

The authors reviewed the immune hypothesis as a potential mechanism of action for ultra-high dose rate FLASH radiotherapy by summarizing all the current published studies investigating the immune modulatory effects of FLASH-RT. They concluded that more in-depth studies are necessary to determine how FLASH affects the different immune components of the tumor microenvironment and the surrounding healthy tissues. Pre-clinical studies combining FLASH-RT and immuno-oncology drugs are required for translation of FLASH to clinical trials of immuno-oncology.

van Marlen P, Dahele M, Folkerts M, et al. Cancers (Basel) 2021;13. Amsterdam UMC, Netherlands and Varian.
Ultra-high dose rate transmission beam proton therapy for conventionally fractionated head and neck cancer: Treatment planning and dose rate distributions.

The authors compared simulated proton FLASH transmission plans with VMAT and IMRT plans for conventionally fractionated head and neck treatment. They show proton FLASH transmission would be an acceptable option, and the FLASH effect may apply at standard fraction, which remains to be demonstrated. The rapid delivery of proton FLASH plans may further capitalize on FLASH effects, improve plan quality, facilitate higher patient through-put, and enhance patient comfort.

Singers Sørensen B, Krzysztof Sitarz M, Ankjærgaard C, et al. Radiother Oncol 2021;167:109-115. Aarhus University Hospital, Denmark and DTU Health tech, Denmark.
In vivo validation and tissue sparing factor for acute damage of pencil beam scanning proton flash.

The authors showed, in a novel mouse model of leg acute skin damage, that a 44 to 58% higher dose can be delivered with pencil beam scanning proton FLASH before resulting in the same toxicity as with conventional proton dose rate. These observations suggest that FLASH could widen the therapeutic window in cancer treatments when the same tumor cell cytotoxic effect is observed between proton FLASH and proton conventional dose rate.

Lin Y, Lin B, Fu S, et al. Phys Med Biol 2021;66. Emory University, Atlanta and Multi-institution.
Sddro-joint: Simultaneous dose and dose rate optimization with the joint use of transmission beams and bragg peaks for flash proton therapy.

The authors proposed a new FLASH treatment planning method (SDDRO-Joint) where Bragg peak and transmission beam plans are combined. The showed substantially improved target dose conformality and lower OAR dose while maintaining comparable FLASH dose rate coverage.

Kang M, Wei S, Choi JI, et al. Cancers (Basel) 2021;13. New York Proton Center, USA.
Quantitative assessment of 3d dose rate for proton pencil beam scanning flash radiotherapy and its application for lung hypofractionation treatment planning.

The study developed an in-house Proton Flash planning method to optimize transmission beam treatment for single-fraction and three-fraction SBRT of lung cancer. They described three dose-rate calculation methods: dose-averaged dose rate, average dose rate, and dose threshold dose rate. Especially, the impact of the PB scanning time was evaluated. These planning methods yielded different dosimetry, demonstrating that FLASH planning details require further investigation to explore the correlation between FLASH efficacy and the dose rate metrics.

FLASH therapy is under development and not available for commercial sale.
This bibliography is a representative selection, but not necessarily exhaustive list, of literature pertaining to flash therapy.

Cunningham S, McCauley S, Vairamani K, et al. Cancers (Basel) 2021;13. and Cincinnati Children's Hospital Medical Center, USA and Multi-institutional.
Flash proton pencil beam scanning irradiation minimizes radiation-induced leg contracture and skin toxicity in mice.

The study demonstrated that Proton FLASH delivered using pencil beam scanning technology reduced skin toxicity and equivalent tumor control in a preclinical mouse model compared to conventional proton therapy. These outcomes demonstrate the value of Proton PBS FLASH radiotherapy and its potential role in minimizing long term side effects from RT.

van Marlen P, Dahele M, Folkerts M, et al. Int J Radiat Oncol Biol Phys 2020;106:621-629. Amsterdam UMC, Netherlands and Varian.
Bringing flash to the clinic: Treatment planning considerations for ultrahigh dose-rate proton beams.

The study demonstrates the framework for evaluating FLASH characteristics of scanning Proton Beam plans in clinic. Sparing of lungs, thoracic wall and heart in FLASH plans was better than in VMAT plans while maintaining tumor coverage.

Folkerts MM, Abel E, Busold S, et al. Med Phys 2020;47:6396-6404. Varian.
A framework for defining flash dose rate for pencil beam scanning.

The authors propose a standardized method for calculating and reporting PBS treatment dose rate which will further advance research and potential applications of PBS FLASH radiotherapy.

Kanouta E, Johansen JG, Kertzscher G, et al. Med Phys 2022. Aarhus University Hospital, Denmark and Multi-institutional.
Time structure of pencil beam scanning proton flash beams measured with scintillator detectors and compared with log files.

The authors developed a new scintillator detector system with sub-millisecond resolution which can used for time structure measurements in PBS proton FLASH treatments. Excellent agreement was found between measured and logged spot durations, indicating high accuracy of spot duration and reliability of the logged durations, but small systematic errors were also noticed. Their small volume makes them feasible for in vivo use in preclinical FLASH studies.

Kang M, Wei S, Choi JI, et al. Int J Radiat Oncol Biol Phys 2022. New York Proton Center, USA.
A universal range shifter and range compensator can enable proton pencil beam scanning single-energy bragg peak flash-rt treatment using current commercially available proton systems.

This is a description of an inverse planning tool to optimize intensity-modulated proton therapy (IMPT) using a single-energy layer for Bragg peak FLASH RT-planning, when combined with universal range shifters (URs) and range compensators (RC) to adapt the dose to the distal target contour. With this method target coverage and uniformity were similar to transmission plans, but OAR sparing was improved because exit dose was eliminated. This method can make Bragg peak FLASH-RT feasible in clinical practice, without significant upgrade to the cyclotron.

FLASH therapy is under development and not available for commercial sale.
This bibliography is a representative selection, but not necessarily exhaustive list, of literature pertaining to flash therapy.

FLASH therapy is under development and not available for commercial sale.

Not all products or features are available for sale in all markets.

This bibliography is a comprehensive selection of articles but is not necessarily an exhaustive list of literature pertaining to flash therapy.

Medical Advice Disclaimer
Varian as a medical device manufacturer cannot and does not recommend specific treatment approaches. Individual treatment results may vary.

Safety Statement
Radiation treatments may cause side effects that can vary depending on the part of the body being treated. The most frequent ones are typically temporary and may include, but are not limited to, irritation to the respiratory, digestive, urinary or reproductive systems, fatigue, nausea, skin irritation, and hair loss. In some patients, they can be severe. Treatment sessions may vary in complexity and time. Radiation treatment is not appropriate for all cancers. Side effects of applicator placement and/or implantation may occur. These side effects may include, but are not limited to, localized discomfort, bleeding, and infection or other localized side effects based on the location the applicator is placed. Side effects may also occur as a result of procedural anesthesia, and may include, but are not limited to, hypotension, bradycardia, respiratory suppression, airway obstruction, bronchospasm, or decreased oxygen saturation. Patients should discuss the treatment and side effects with their physicians before starting treatment sessions. For more information, visit www.varian.com/safety.

varian
A Siemens Healthineers Company

varian.com

USA, Corporate Headquarters
Varian Medical Systems, Inc
3100 Hansen Way
Palo Alto, CA 94304
Tel: 650.424.5700
800.544.4636

Headquarters Europe, Eastern Europe, Middle & Near East, India, Africa
Varian Medical Systems
International AG
Steinhausen, Switzerland
Tel: 41.41.749.8844

Asia Pacific Headquarters
Varian Medical
Systems
Pacific, Inc.
Kowloon, Hong Kong
Tel: 852.2724.2836

Australasian Headquarters
Varian Medical
Systems Australasia
Pty Ltd.
Sydney, Australia
Tel: 61.2.9485.0100

Latin American Headquarters
Varian Medical
Systems
Brasil Ltda.
São Paulo, Brazil
Tel: 55.11.3457.2655

RAD 11003

03/2022