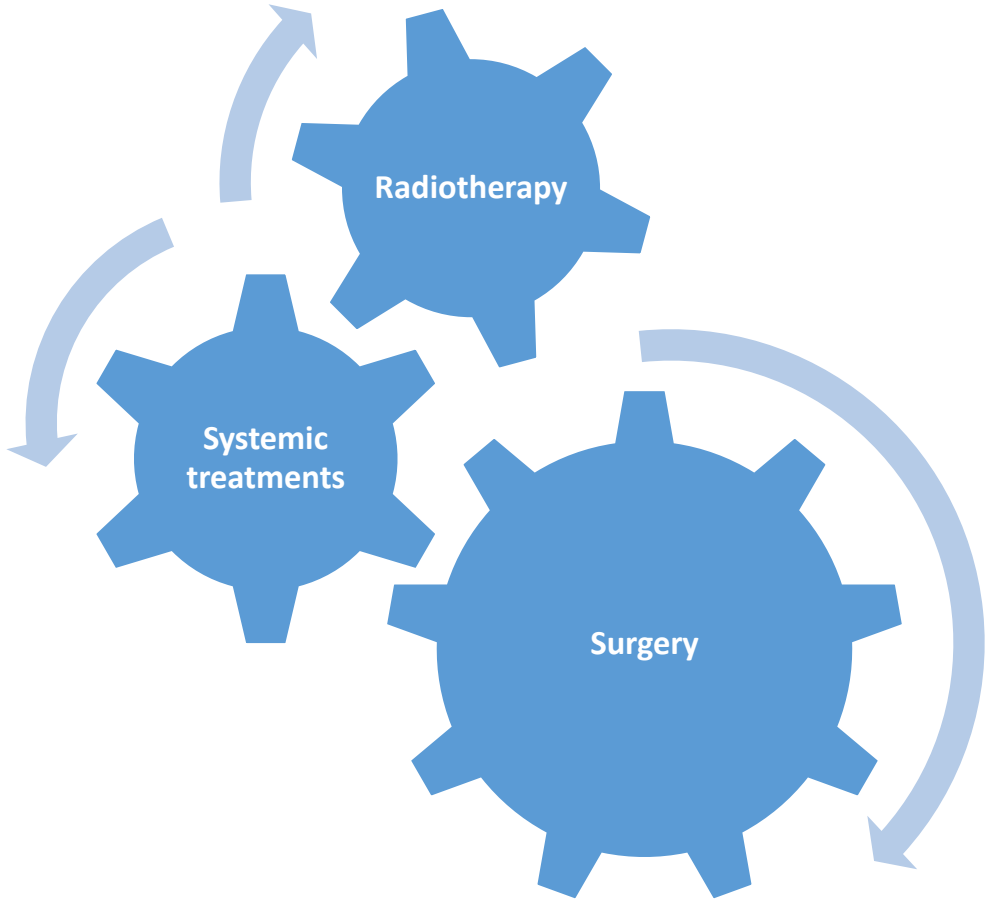
UNIL | Université de Lausanne

RADIO ONCOLOGIE

CHUV

Shaping the future of radiation oncology with CLEAR

Prof. Marie-Catherine Vozenin

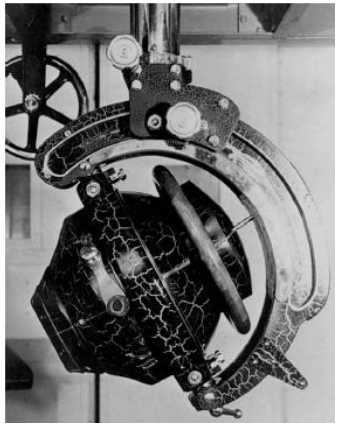


- 50% of cancer patients are treated with RT
- 1/5 person will be treated with RT in a life-time

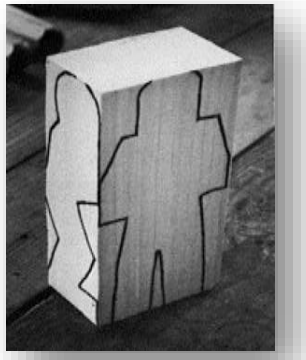
First radiotherapy: July 1896 by Victor Despeignes

Enhanced precision

1930-1970

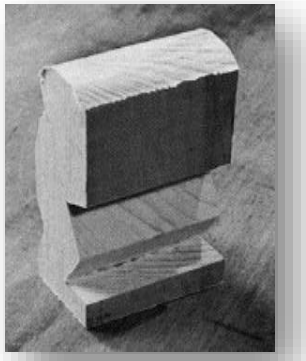


Target volume



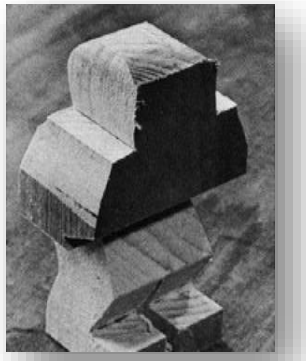
1970-1990

2D planning



1990-2000

3D Conformal



2016

Stereo-RT

High Precision

Modalities of delivery are moving to hypo-fractionation

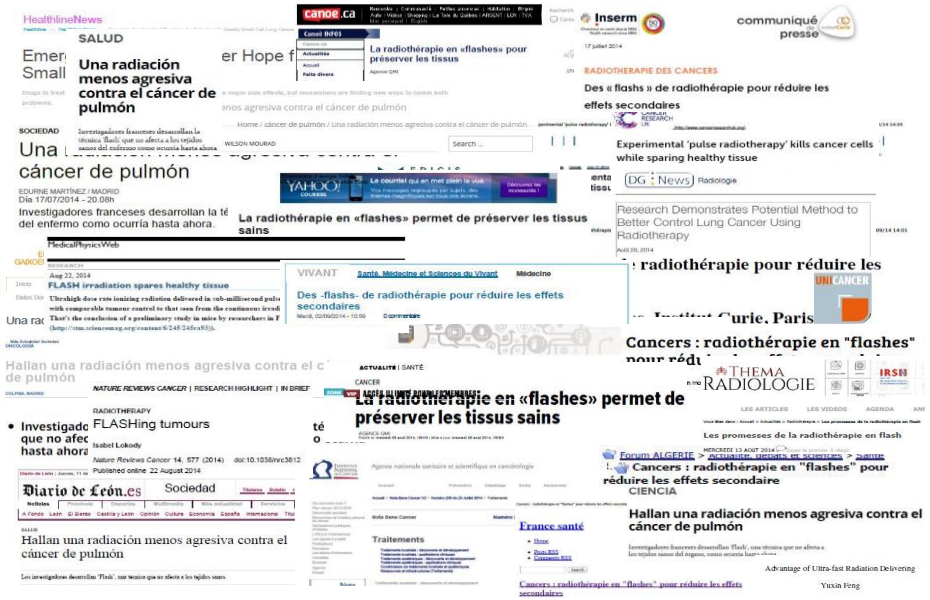
Radiotherapy technology has not really evolved in 50 years

Most Cancers are not cured

Local relapse
Metastasis

V Favaudon

2007/2008 → 2014



RADIATION RESEARCH 92, 172–181 (1982)

Oxygen Depletion in Cells Irradiated at Ultra-high Dose-rates and at Conventional Dose-rates

H. Weiss, E.R. Epp, J.M. Heslin, C.C. Ling & A. Santomasso

To cite this article: H. Weiss, E.R. Epp, J.M. Heslin, C.C. Ling & A. Santomasso (1974) Oxygen Depletion in Cells Irradiated at Ultra-high Dose-rates and at Conventional Dose-rates, International Journal of Radiation Biology and Related Studies in Physics, Chemistry and Medicine, 26:1, 17-29, DOI: 10.1080/09553007414550901

To link to this article: http://dx.doi.org/10.1080/09553007414550901

The Constant Low Oxygen Concentration in All the Target Cells for Mouse Tail Radionecrosis

J. H. HENDRY, J. V. MOORE, B. W. HODGSON, AND J. P. KEENE

Paterson Laboratories, Christie Hospital, and Holt Radium Institute, Manchester, M20 9BX, United Kingdom

HENDRY, J. H., MOORE, J. V., HODGSON, B. W., AND KEENE, J. P., The Constant Low Oxygen Concentration in All the Target Cells for Mouse Tail Radionecrosis. *Radiat. Res.* **92**, 172–181 (1982).

RESEARCH ARTICLE

RADIATION TOXICITY

Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice

Vincent Favaudon,[1,2]* Laura Caplier,[3†] Virginie Monceau,[4,5‡] Frédéric Pouzoulet,[1,2§] Mano Sayarath,[1,2¶] Charles Fouillade,[1,2] Marie-France Poupon,[1,2] Isabel Brito,[6,7] Philippe Hupé,[6,7,8,9] Jean Bourhis,[4,5,10] Janet Hall,[1,2] Jean-Jacques Fontaine,[3] Marie-Catherine Vozenin[4,5,10,11]

RESEARCH HIGHLIGHTS

IN BRIEF

RADIOTHERAPY

FLASHing tumours

A new study in mice suggests that radiation delivered in short pulses at ultrahigh dose rates (FLASH) is as effective against lung tumours as conventional protracted single lower dose rates and has fewer side effects. Using both orthotopic lung tumours in immunocompetent mice and human lung tumour xenografts in nude mice, Favaudon *et al.* showed that FLASH irradiation caused less lung fibrogenesis and less apoptosis in normal tissue than conventional radiation. Although this technique was only tested in one tumour type, it suggests that delivery methods are crucial to minimizing radiation treatment side effects, and it has implications for therapeutic protocols.

ORIGINAL RESEARCH PAPER Favaudon, V. *et al.* Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice. *Sci. Transl Med.* **6**, 245ra93 (2014)

FLASH radiotherapy

Irradiation at ultra high dose rate

Very fast delivery of the dose

Shift from minute of exposure to milli- and even micro-second

Balistic advantage of FLASH-RT

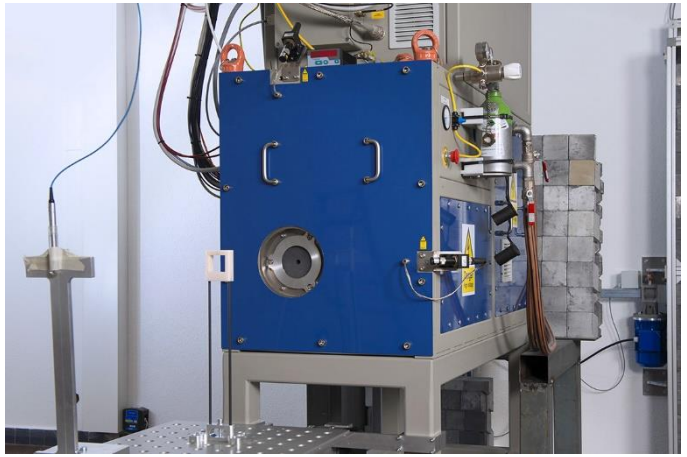
Freeze motion

Radiobiological advantage of FLASH-RT

THE FLASH EFFECT

P Montay-Gruel

eRT6 Oriatron PBM/Alcen
Electron beam, 5.5 MeV energy
Pulsed beam



C Bailat

High dose-per-pulse electron beam dosimetry: Commissioning of the Oriatron eRT6 prototype linear accelerator for preclinical use

Maud Jaccard, Maria Teresa Durán, Kristoffer Petersson, and Jean-François Germond
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Philippe Liger
PMB-Alcen, Peynier, France

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Radio-Oncology Laboratory, DO/CHUV, Lausanne University Hospital, Lausanne, Switzerland

François Bochud and Claude Bailat[a)]
Institute of Radiation Physics, Lausanne University Hospital, Lausanne, Switzerland

High dose-per-pulse electron beam dosimetry — A model to correct for the ion recombination in the Advanced Markus ionization chamber

Kristoffer Petersson,[a)] Maud Jaccard, Jean-François Germond, Thierry Buchillier, and François Bochud
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Claude Bailat
CHUV, Institut de Radiophysique, Rue du Grand-Pré 1, CH-1007 Lausanne, Switzerland

High dose-per-pulse electron beam dosimetry: Usability and dose-rate independence of EBT3 Gafchromic films

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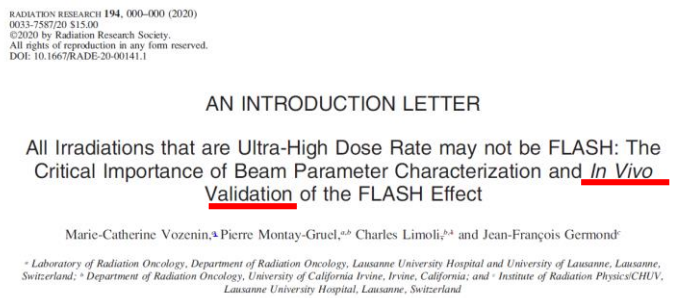
François O. Bochud and Claude Bailat
Institute of Radiation Physics (IRA), Lausanne University Hospital, Lausanne, Switzerland

THE FLASH EFFECT is a biological effect



RADIATION RESEARCH 194, 000–000 (2020)
0033-7587/20 $15.00

DOI: 10.1667/RADE-20-00141.1

AN INTRODUCTION LETTER

All Irradiations that are Ultra-High Dose Rate may not be FLASH: The Critical Importance of Beam Parameter Characterization and *In Vivo* Validation of the FLASH Effect

Marie-Catherine Vozenin,[a] Pierre Montay-Gruel,[a,b] Charles Limoli,[b,1] and Jean-François Germond[c]

[a] Laboratory of Radiation Oncology, Department of Radiation Oncology, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland; [b] Department of Radiation Oncology, University of California Irvine, Irvine, California; and [c] Institute of Radiation Physics/CHUV, Lausanne University Hospital, Lausanne, Switzerland

Normal tissue sparing

FLASH-RT does not induce Normal tissue toxicity When CONV-RT does

Electron
Chabi et al**. IJROBP**2020
Montay-Gruel et al. **Rad Res**, 2020
Allen et al. **Rad Res**, 2020
Alaghban et al. **Cancers**, 2020
Bourhis J et al. **Radiother Oncol.** 2019.
Jorge PG et al. **Radiother Oncol.** 2019 Oct.
Montay-Gruel P et al. **Proc Natl Acad Sci U S A**. 2019.
Vozenin et al. **Clin Can Res**, 2019.
Montay-Gruel P et al. **Radiother&Oncol.**, 2017.
Jaccard M et al. **Med Phys**, 2018.
Favaudon V et al. **Sci Transl Med**. 2014.

X-ray-synchrotron
Montay-Gruel P et al. **Radiother Oncol.** 2018.

Electron
Beyreuther et al., **Radiother Oncol**, 2021
Soto et al. **Rad Res**, 2020.
Fouillade C et al. **CCR,** 2019.
Simmons et al. **Radiother Oncol.** 2019.
Loo B et al. **IJROBP**, 2017, abst.
Hendry et al. **Rad Res**, 1982.

Proton
Cunningham et al., Cancers, 2021
Zhang et al. **Rad Res,** 2020.
Diffenderfer et al. **IJROBP**, 2020.
Girdhani et al. **Can Res**, 2019, abst.

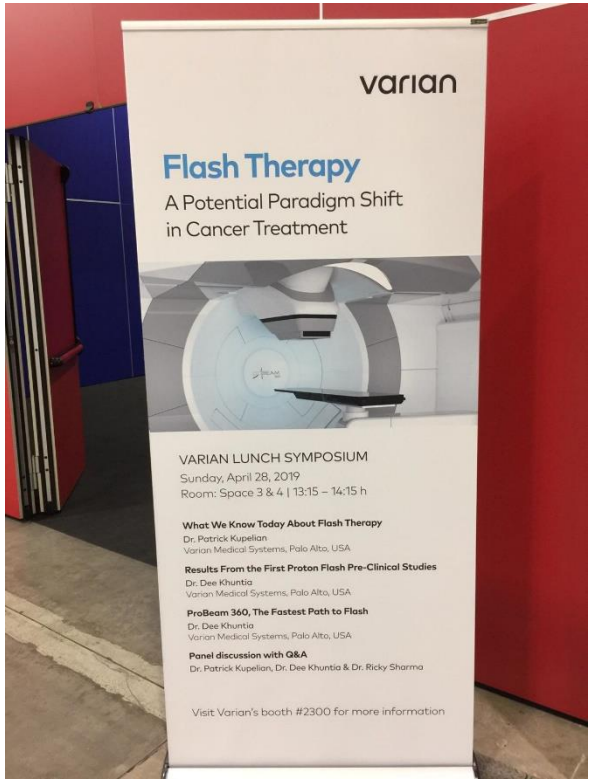
X -ray synchrotron
Smyth et al. **Sci Rep**, 2018.
Proton
Beyreuther et al. **Radiother Oncol.** 2019.
Electron
Venkatesulu at al. **Sc Rep**, 2019.

And FLASH-RT is equally able to eradicate tumors compared to CONV-RT

Electron
Chabi et al. **IJROBP**, 2020.
Montay-Gruel P et al. **CCR**, 2020.
Bourhis J et al. **Radiother Oncol.** 2019.
Jorge PG et al. **Radiother Oncol.** 2019.
Favaudon V et al. **Sci Transl Med**. 2014.

Electron
Kim et al. **IJROBP**, 2020

Proton
Diffenderfer et al. **IJROBP**, 2020.
Girdhani et al. **Can Res**, 2019, abst.



US 20190022411A1

(19) United States

(12) Patent Application Publication (10) Pub. No.: US 2019/0022411 A1

Parry et al. (43) Pub. Date: Jan. 24, 2019

(54) METHODS OF USE OF ULTRA-HIGH DOSE RATE RADIATION AND THERAPEUTIC AGENT

(71) Applicant: VARIAN MEDICAL SYSTEMS, INC., Palo Alto, CA (US)

8 Mars 2019

Press Release

Flash Irradiation Delivered in a Clinical Treatment Room

Successful Flash Irradiation at Isocenter in IBA's Proteus® Solution Gantry Room

J Bourhis

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

Treatment of a first patient with FLASH-radiotherapy

Jean Bourhis [a,b,*], Wendy Jeanneret Sozzi [a], Patrik Gonçalves Jorge [a,b,c], Olivier Gaide [d], Claude Bailat [c], Fréderic Duclos [a], David Patin [a], Mahmut Ozsahin [a], François Bochud [c], Jean-François Germond [c], Raphaël Moeckli [c,1], Marie-Catherine Vozenin [a,b,1]

[a] Department of Radiation Oncology, Lausanne University Hospital and University of Lausanne; [b] Radiation Oncology Laboratory, Department of Radiation Oncology. Lausanne University Hospital and University of Lausanne; [c] Institute of Radiation Physics, Lausanne University Hospital and University of Lausanne; and [d] Department of Dermatology, Lausanne University Hospital and University of Lausanne, Switzerland

Varian and the Cincinnati Children's/UC Health Proton Therapy Center Announce Initial Patient Treated in the FAST-01 First Human Clinical Trial of FLASH Therapy for Cancer

Oncology

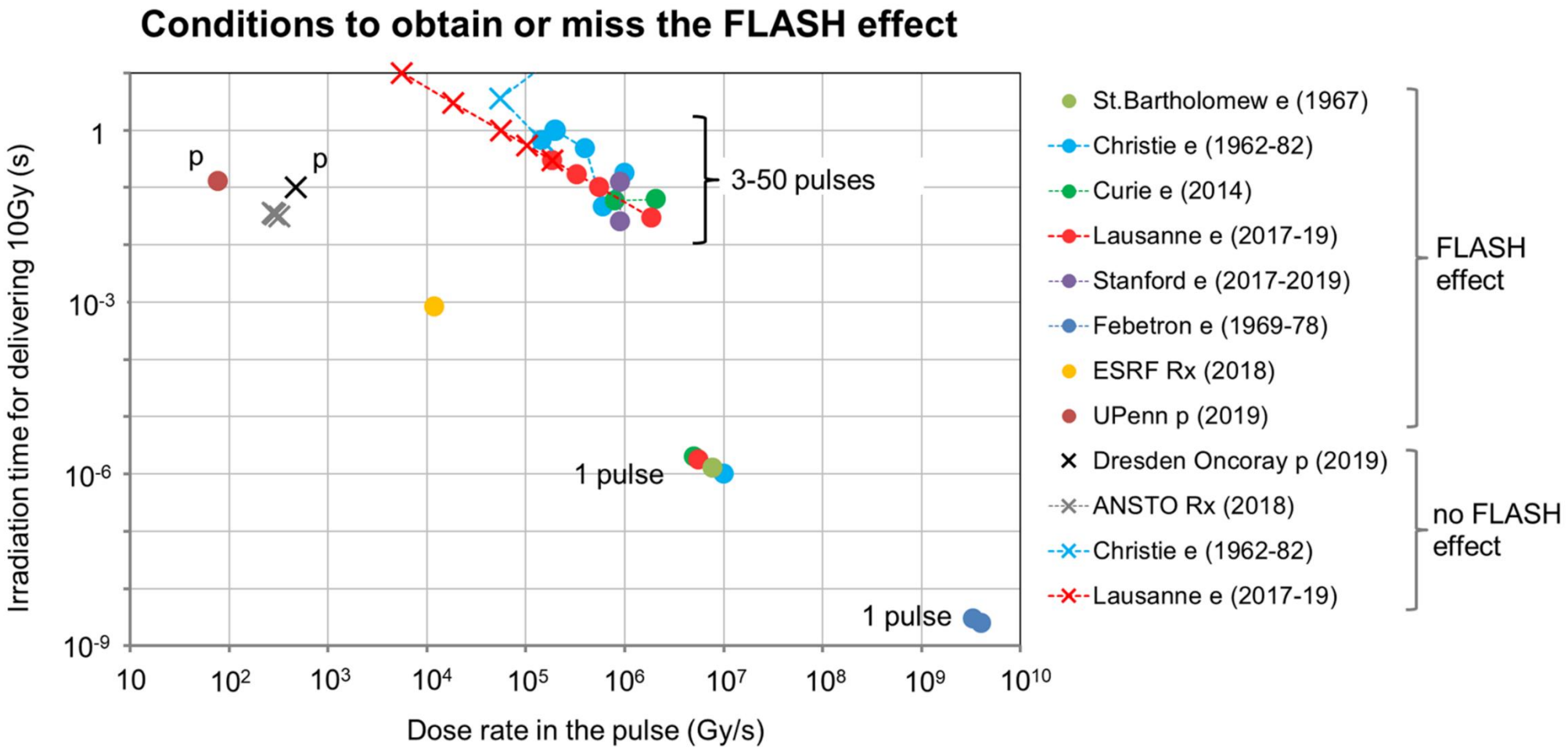
November 19, 2020

PALO ALTO, Calif., and CINCINNATI, Ohio, Nov. 19, 2020 /PRNewswire/ -- Varian (NYSE: VAR) and the Cincinnati Children's/UC Health Proton Therapy Center today announce the start of the first clinical trial of FLASH therapy as part of the recently opened FAST-01 study (**Fe**A**S**ibility **S**tudy of FLASH Radiotherapy for the **T**reatment of Symptomatic Bone Metastases). The clinical trial involves the investigational use of Varian's ProBeam® particle accelerator modified to enable radiation therapy delivery at ultra-high dose rates (dose delivered in less than 1 second) and is being conducted at the Cincinnati Children's/UC Health Proton Therapy Center with John C. Breneman M.D., Medical Director of the center, serving as principal investigator.

The first clinical trial patient was treated this week. The FAST-01 study is expected to enroll up to 10 patients with bone metastases to evaluate clinical workflow feasibility, treatment-related side effects, and efficacy of treatment as assessed by measuring pain relief of trial participants. The clinical trial, informed by years of preclinical work, was designed by experts at Varian and multiple centers in the FlashForward™ Consortium, including Cincinnati's Children's/UC Health Proton Therapy Center and the New York Proton Center.

JF Germond

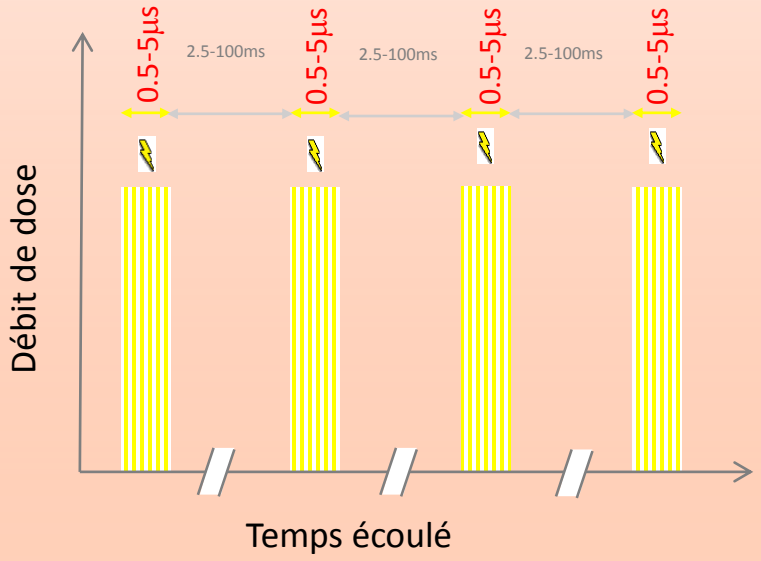
Figure 1



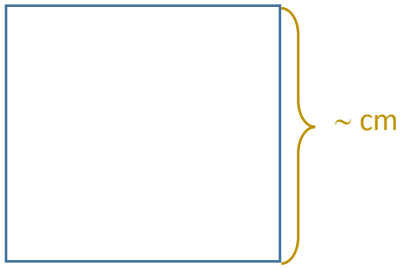
Montay-Gruel P et al., CCR, 2020.

Technology

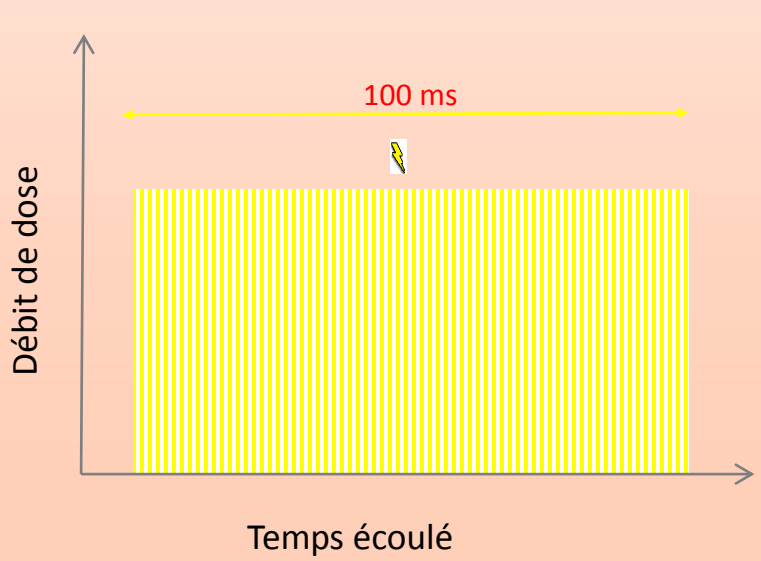
Structure pulsée d'un faisceau électron



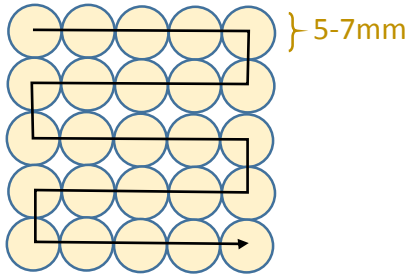
- 1 – 10 pulses
- Microstructure: 5000 bunches
- Pulse repetition frequency 10-250Hz



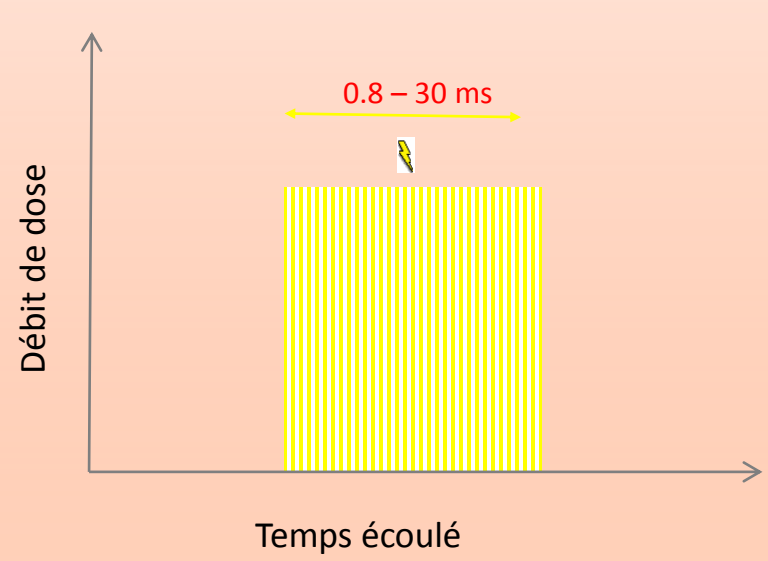
Structure d'un faisceau proton



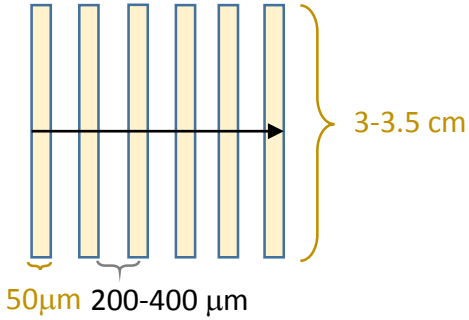
- 1 pulse
- Microstructure: 10^7 bunches
- Spot scanning (@1000Hz)



Structure d'un faisceau RX synchrotron



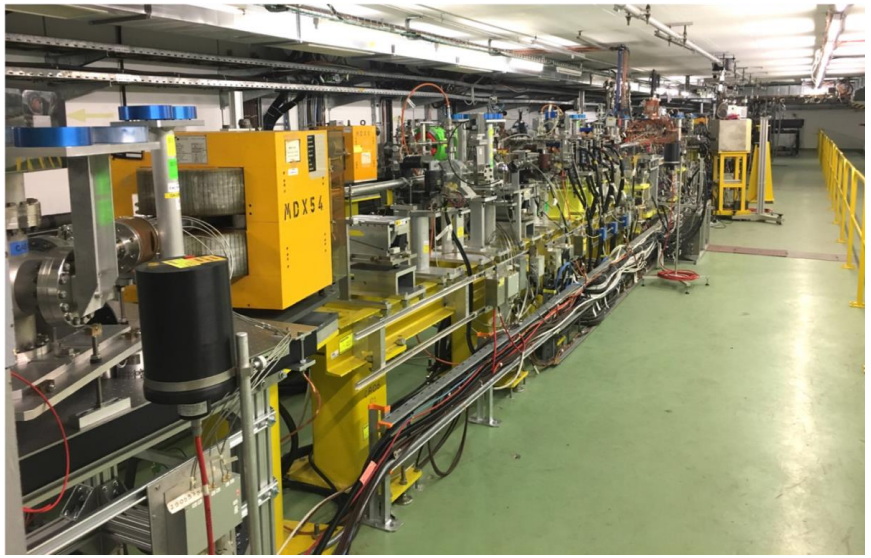
- 1 pulse = 1 stripe
- Microstructure: 10^7 bunches
- Stripe scanning (60mm/s)



Time does matter

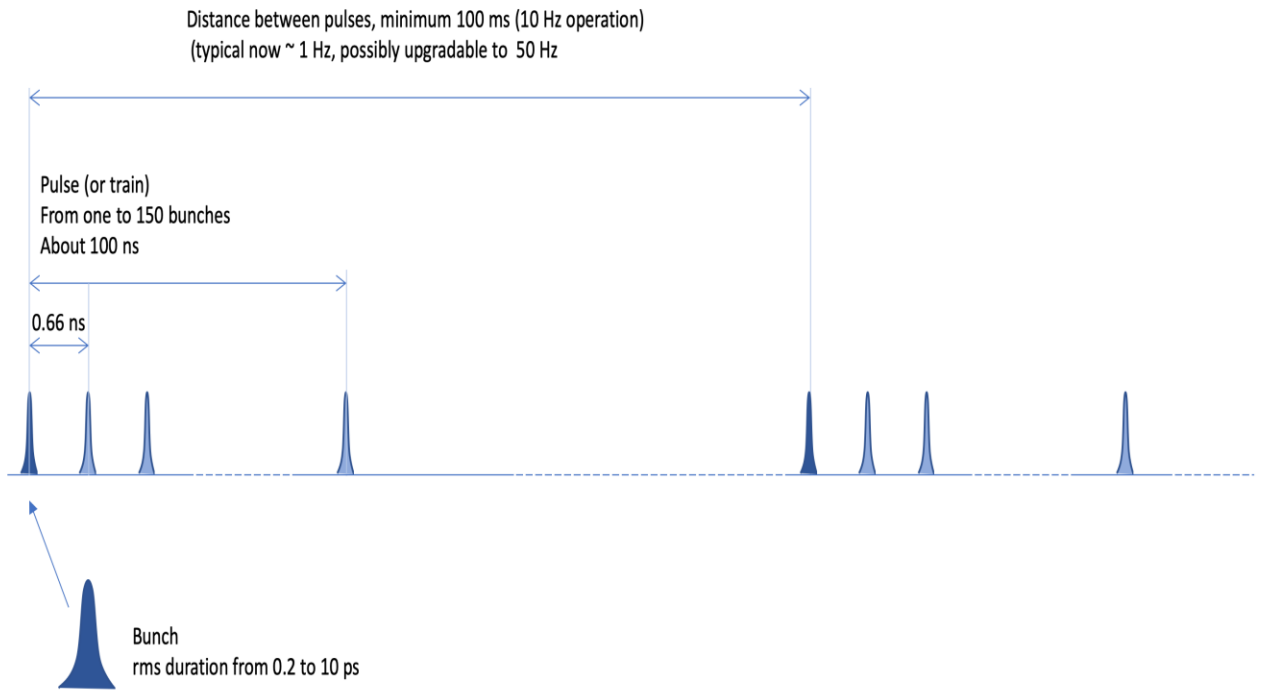
The shorter the better

What CLEAR has



It can shorten the time of exposure like no other beam

Time structure of CLEAR



Focusing and scanning

Medical applications

Accelerators
Models
Radio-Chemistry
Radio-Biology

FLASH «dream» team

Biology team

P Montay-Gruel
B Petit
J Ollivier
I Petridis
R Leavitt
P Barrera
C Romero
G Boivin
H Kacem
N Cherbuin
V To
A Almeida
C Godfroid
A Martinotti

Physics team

F Bochud
C Bailat
JF Germond
P Froidevaux
L Desorgher
P Jorge Goncalves
V Grilj
F Chappuis
D Patin
R Moeckli
T Buchillier
M Gondre
K Petersson
M Jaccard

Clinical team

Radiation-Oncology
J Bourhis
W Jeanneret
M Oszahin
F Herrera

Surgery
N Demartines
D Clerc
C Simon
K Lambercy

Fond'action
FNS N°31003A_156892
FNS/ANR CR32I3L_156924
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