L'effetto Flash

Fabio Di Martino

UO Fisica Sanitaria

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Pisa

Italy

Sommario

Stato dell'arte: evidenze sperimentali e prospettive cliniche

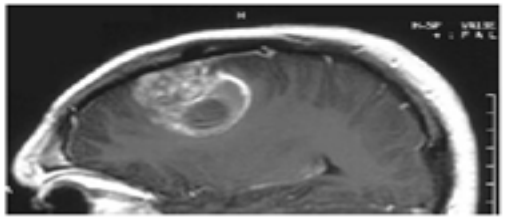
Questioni aperte: limiti dei risultati sperimentali ottenuti e lavoro necessario per l'implementazione clinica della Flash

Cosa possiamo realizzare a Pisa

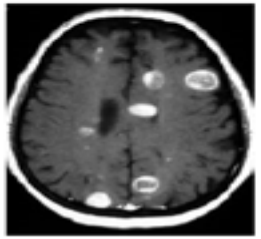
Stato dell'arte della radioterapia e limiti della radioterapia attuale

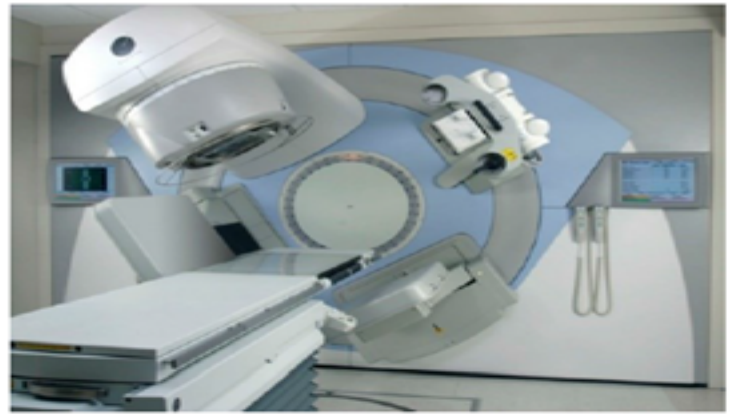
- Limitations of "conventional" radiotherapy

Radioresistant, bulky and diffuse cancers (glioblastomas)

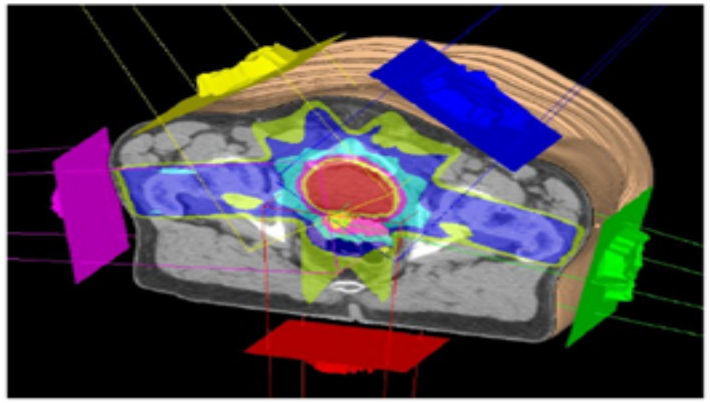


Non-localized tumors (metastases)





Clinical electron accelerator
(X-rays ~6-25 MV)



⟶ La tossicità dei tessuti sani limita la capacità "curativa" del trattamento

Che cos'è l'effetto Flash?

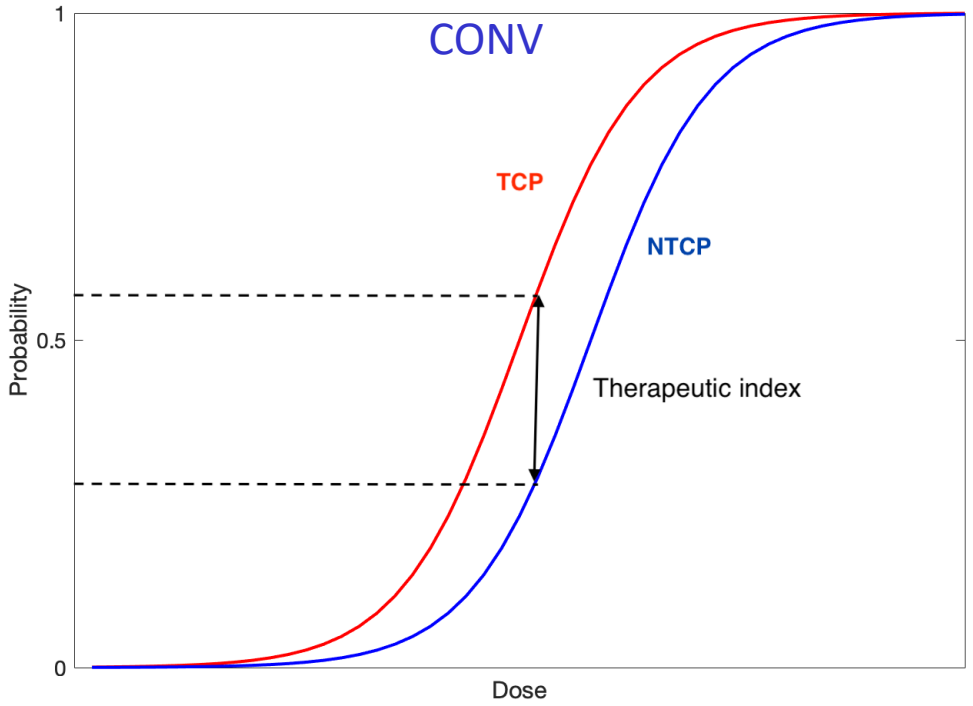
Effetto radiobiologico → Radioterapia/oncologia

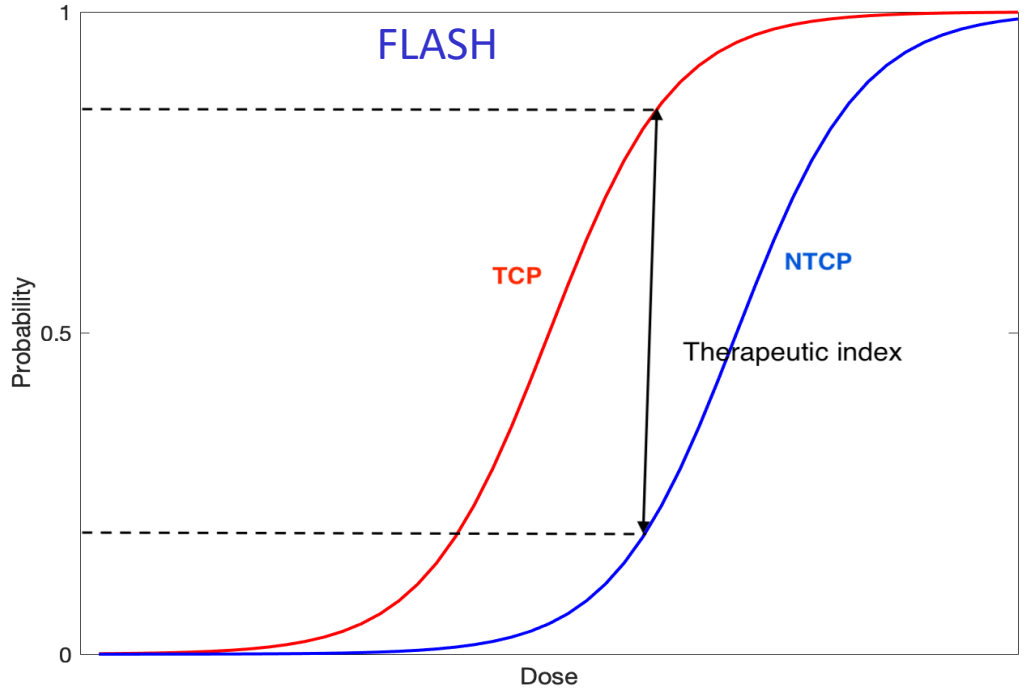
Che consiste in un risparmio delle complicazioni agli organi a rischio mantenendo inalterata l'efficacia terapeutica sul tumore → Enormi possibili implicazioni cliniche

Ottenuta utilizzando fasci di elettroni di E=4-7 MeV
Dose-rate > 40Gy/s
T>200ms → Conoscenze limitate

Effetto osservato sperimentalmente su diversi modelli animali
E su diversi organi → Esistenza dell'effetto

Prospettive cliniche





Allargamento della “finestra terapeutica” → Prospettiva clinica più rivoluzionaria dell’adroterapia

Struttura temporale del fascio
Dose-rate e dose-per-pulse

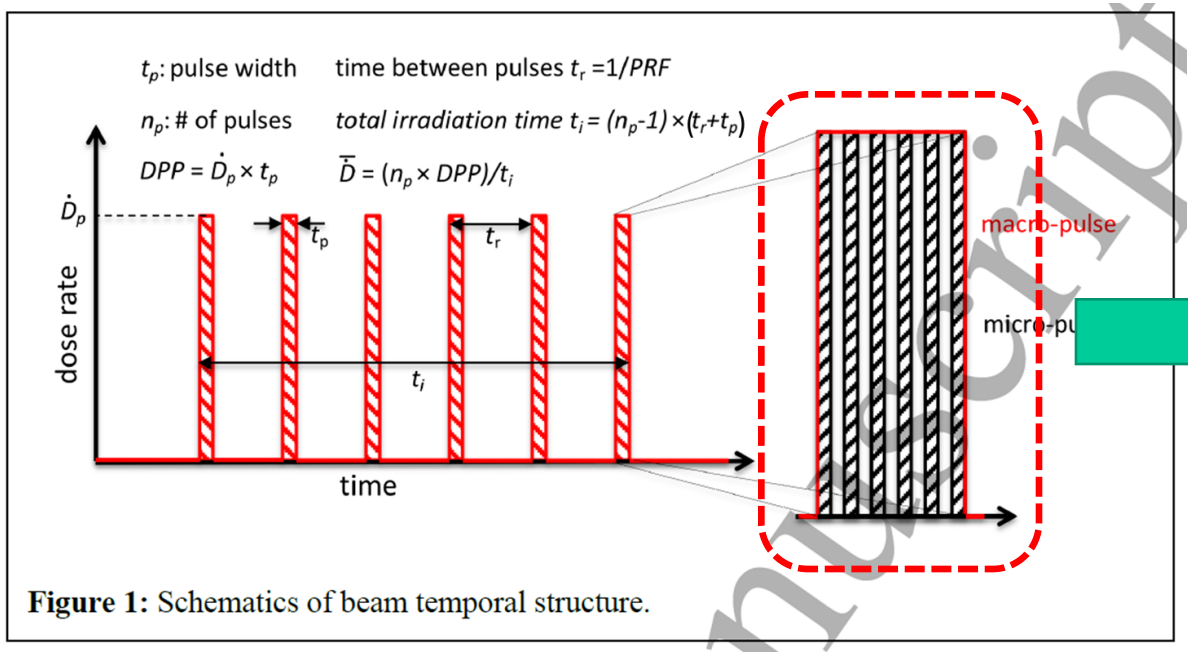
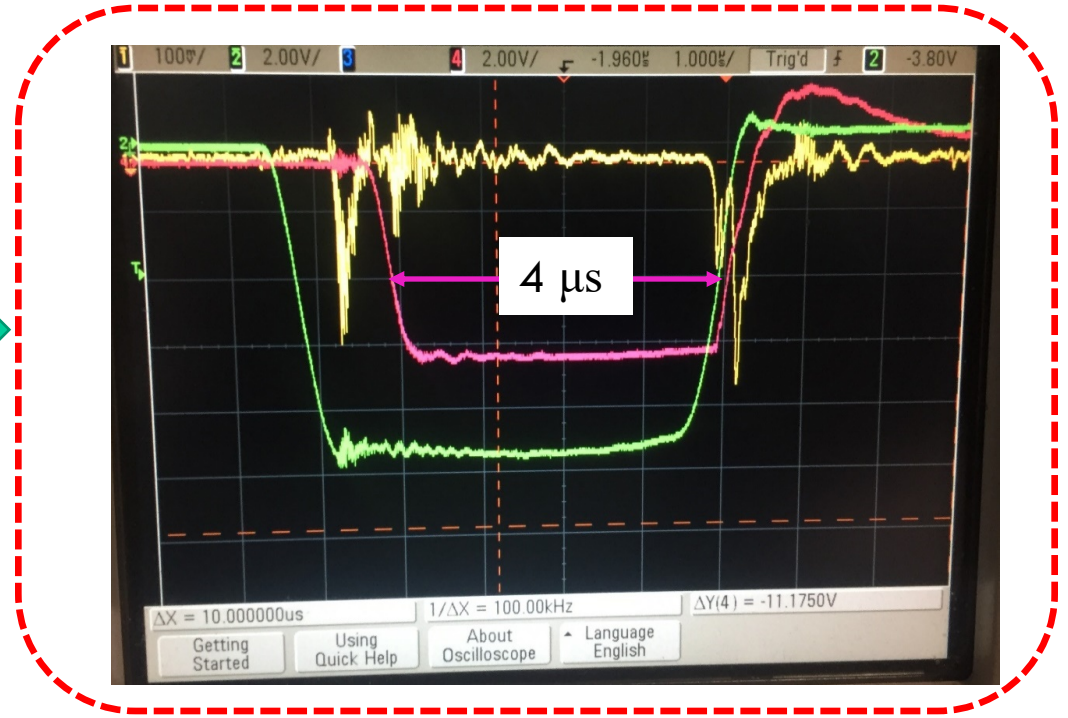


Figure 1: Schematics of beam temporal structure.



$$\begin{cases} t_p & 1-4\ \mu s \\ t_r = \dfrac{1}{PRF};\ PRF_{MAX} = 400\ Hz \rightarrow t_r \geq 2.5\ ms \end{cases}$$

La scala temporale della risposta delle CI è data dal tempo di collezionamento degli ioni. Può variare nel range ~ 4 µs (IBA PPC 05, 300 V) fino a ~ 60 µs (PTW Roos, 200 V). Essendo quindi il tempo di collezione degli ioni << t_r il parametro che determina i problemi di saturazione è il DPP

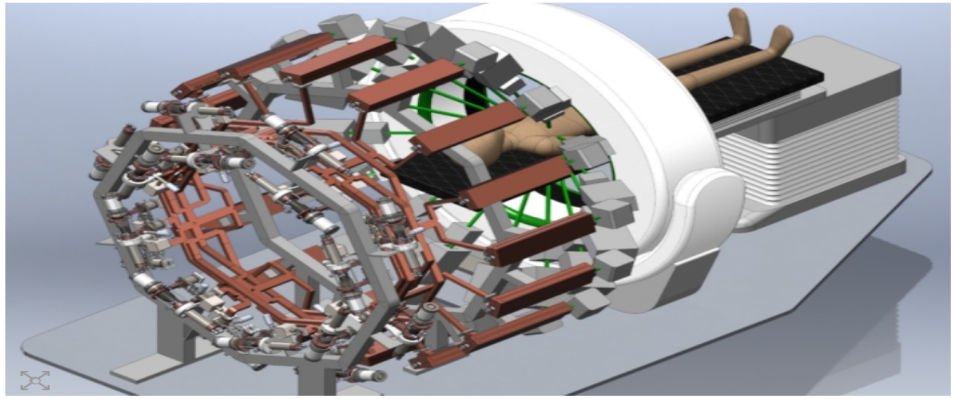
Evoluzione del Dose-per-pulse (DPP)

	CONVENTIONAL RT	IOeRT	FLASH
Mean dose rate	**1 -20 Gy/min ; 0,017 -0,34 Gy/s**	**10 -30 [Gy/min]; 0,17 - 0,5 Gy/s**	**> 40 Gy/s**
dose per pulse D_p	< 0.001 Gy/p (0.1 cGy/p)	0,001 < D_p < 0.15 Gy/p	D_p > 0.5 Gy/p
Models	IAEA TRS 398; AAPM TG 51	Protocols still applies, but a correction for saturation is needed (Di Martino, Laitano)	A new description of the IC behaviour is needed

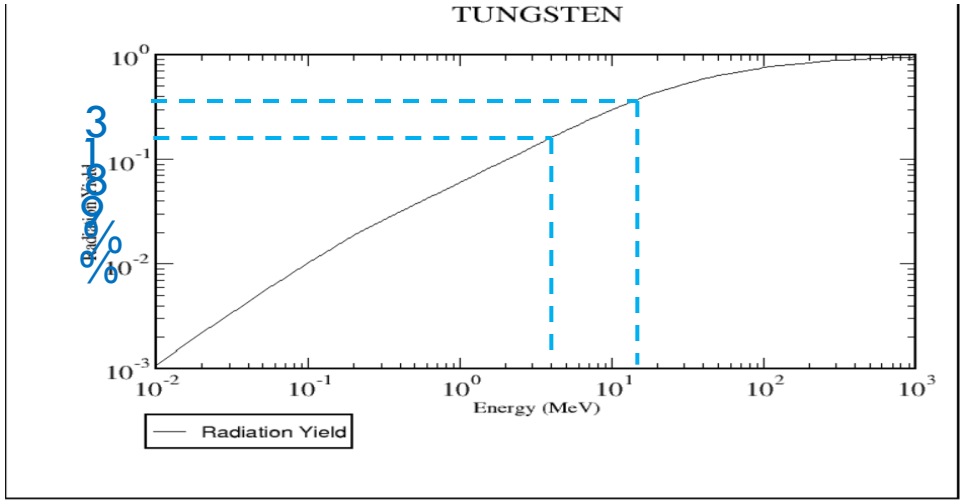
fotoni

PHASER linac will translate FLASH radiotherapy to the clinic

04 Jul 2019 Tami Freeman



Conceptual rendering of the PHASER system. (Courtesy: *Radiother. Oncol.* 10.1016/j.radonc.2019.05.005)



protoni

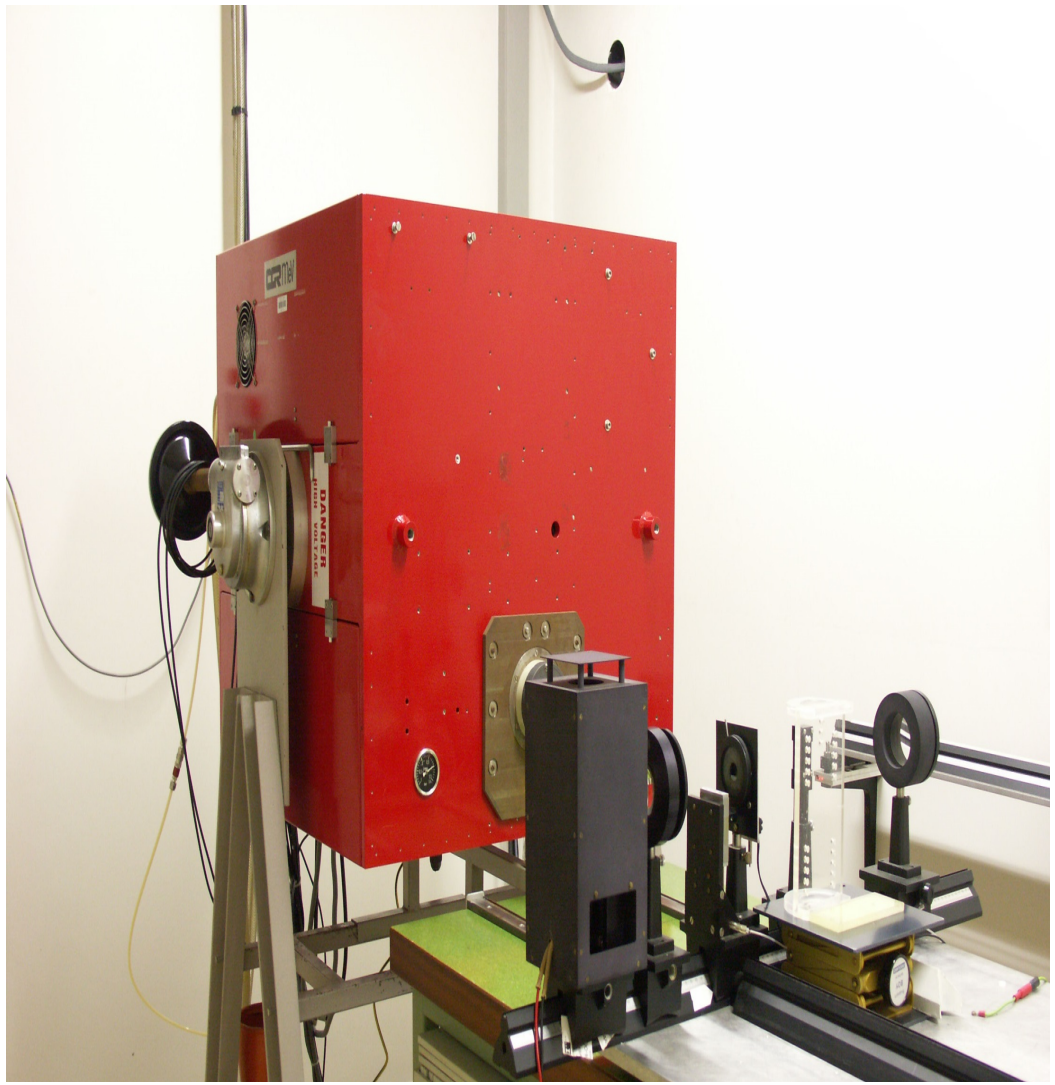
Technical Challenges for FLASH Proton Therapy

Simon Jolly[a,*], Hywel Owen[b,c], Marco Schippers[d], Carsten Welsch[b,e]

[a]*University College London, United Kingdom*
[b]*Cockcroft Institute of Accelerator Science and Technology*
[c]*University of Manchester, United Kingdom*
[d]*Paul Scherrer Institute, Switzerland*
[e]*University of Liverpool, United Kingdom*

Interesse e investimenti ma non ancora fasci Flash!

Elettroni a bassa energia (4-7MeV)



Linac indistriali

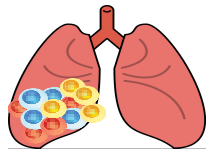
Dati sperimentali

RESEARCH ARTICLE

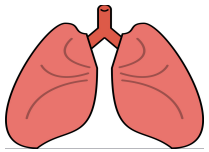
RADIATION TOXICITY

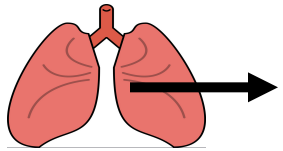
Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice

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]



FLASH





RT

Toxicity evaluation

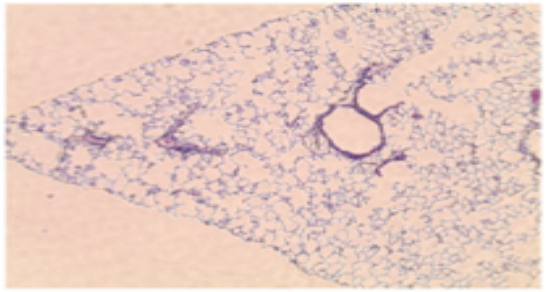
Anti-tumor efficacy

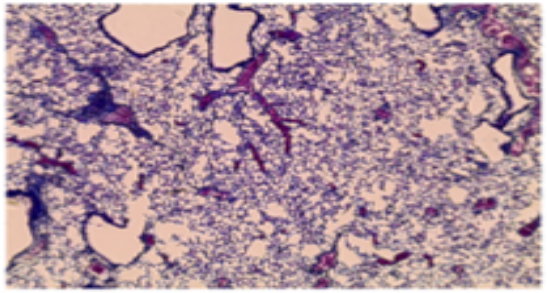
FLASH EFFECT

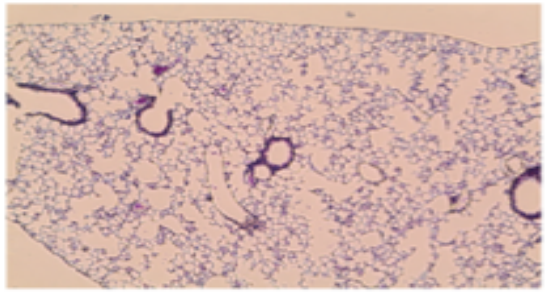
Contrôle non irradié

17 Gy CONV

17 Gy FLASH







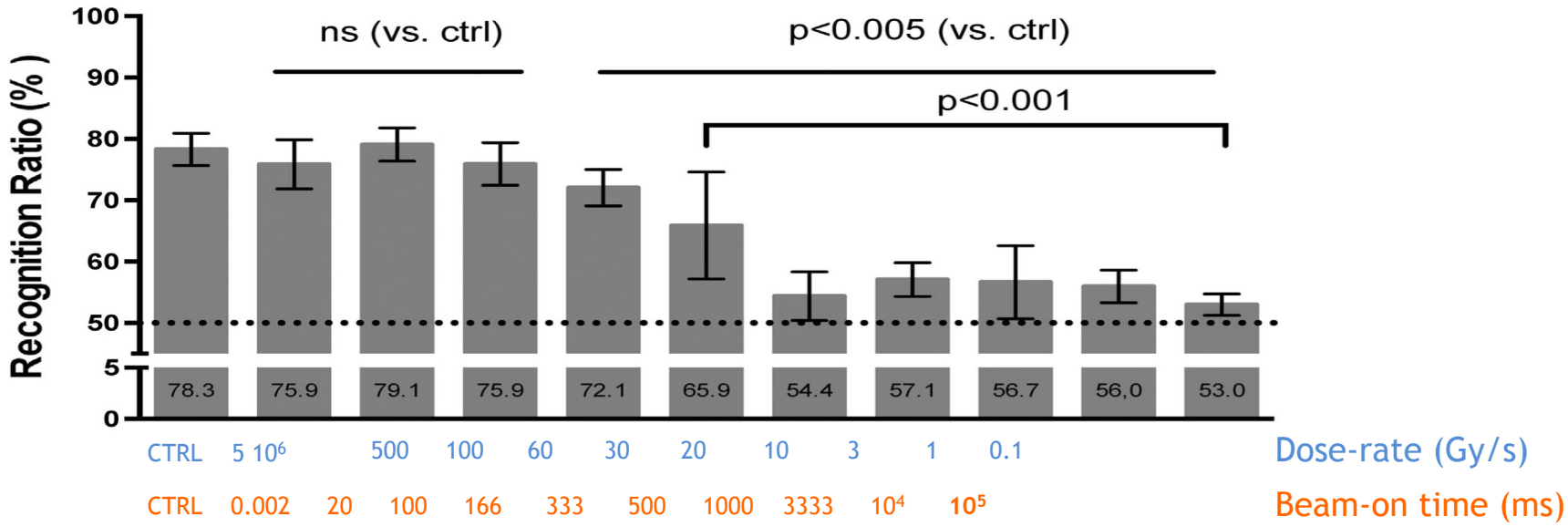
HEALTHY

FIBROTIC

HEALTHY

absence of radiation-induced toxicity in the normal lung

Whole brain irradiation - 10 Gy in single dose 6MV e^-



Montay-Gruel et al. Radiother Oncol 124: 365-9, 2017

skin

CONV

FLASH

Localmente avanzato T2/T3N0M0 squamoso

The advantage of FLASH radiotherapy confirmed in mini-pig and cat-cancer patients

Marie-Catherine Vozenin[1&], Pauline De Fornel [2&], Kristoffer Petersson[1,3 &], Vincent Favaudon[4], Maud Jaccard[1,3], Jean-François Germond[3], Benoit Petit[1], Marco Burki[5], Gisèle Ferrand[6], David Patin[3], Hanan Bouchaab[1], Mahmut Ozsahin[1], François Bochud[3], Claude Bailat[3], Patrick Devauchelle[2*] and Jean Bourhis[1, 6*]

[1]Radio-Oncology Laboratory, Department of Radiation Oncology, Lausanne University Hospital, Lausanne, Switzerland.
[2] Micen-vet, Créteil, France.
[3] Institute of Radiation Physics (IRA), Lausanne University Hospital, Switzerland.
[4] Institut Curie, INSERM U1021/CNRS UMR3347, Université Paris-Sud, 91405 Orsay, France.
[5] Service de Chirurgie Expérimentale, Département de chirurgie et anesthésie, Lausanne University Hospital, Lausanne, Switzerland.
[6] UNIL, Lausanne, Switzerland.

June 2018 · Clinical Cancer Research
DOI: 10.1158/1078-0432.CCR-17-3375

Before RT

@ 7 months

@ 14 months

Cute – Intestino – Polmoni - Cervello

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]

Contents lists available at ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com

Irradiation in a flash: Unique sparing of memory in mice after whole brain irradiation with dose rates above 100 Gy/s

Pierre Montay-Gruel[a,b,1], Kristoffer Petersson[c,1], Maud Jaccard[c], Gaël Boivin[a], Jean-François Germond[c], Benoit Petit[a], Raphaël Doenlen[d], Vincent Favaudon[b], François Bochud[c], Claude Bailat[c], Jean Bourhis[a,1], Marie-Catherine Vozenin[a,e,1]

Contents lists available at ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com

Original article

X-rays can trigger the FLASH effect: Ultra-high dose-rate synchrotron light source prevents normal brain injury after whole brain irradiation in mice

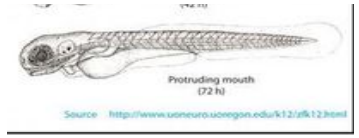
Pierre Montay-Gruel[a], Audrey Bouchet[b], Maud Jaccard[c], David Patin[c], Raphael Serduc[b,e], Warren Aim[b], Kristoffer Petersson[a,c], Benoit Petit[a], Claude Bailat[c], Jean Bourhis[a], Elke Bräuer-Krisch[d,1], Marie-Catherine Vozenin[a,1]

Clinical Trial Brief Report

Clinical Cancer Research

The Advantage of FLASH Radiotherapy Confirmed in Mini-pig and Cat-cancer Patients

Marie-Catherine Vozenin[1], Pauline De Fornel[2], Kristoffer Petersson[1,3], Vincent Favaudon[4], Maud Jaccard[1,3], Jean-François Germond[5], Benoit Petit[1], Marco Burki[5], Gisèle Ferrand[6], David Patin[3], Hanan Bouchaab[1], Mahmut Ozsahin[1,6], François Bochud[3], Claude Bailat[3], Patrick Devauchelle[2], and Jean Bourhis[1,6]



(P003) Delivery of Ultra-Rapid Flash Radiation Therapy and Demonstration of Normal Tissue Sparing After Abdominal Irradiation of Mice

Billy W. Loo, MD, PhD, Emil Schuler, PhD, Frederick M. Lartey, PhD, Marjan Rafat, PhD, Gregory J. King, PhD, Stefania Trovati, PhD, Albert C. Koong, MD, PhD, and Peter G. Maxim, PhD; *Stanford University*

CCR Translations

Clinical Cancer Research

Ultrahigh Dose-rate Radiotherapy: Next Steps for FLASH-RT

Kevin J. Harrington

Long-term neurocognitive benefits of FLASH radiotherapy driven by reduced reactive oxygen species

Pierre Montay-Gruel[a,b,1], Munjal M. Acharya[c,1], Kristoffer Petersson[a,b,d], Leila Alikhani[c], Chakradhar Yakkala[a,b], Barrett D. Allen[c], Jonathan Ollivier[a,b], Benoit Petit[a,b], Patrik Gonçalves Jorge[a,b,d], Amber R. Syage[c], Thuan A. Nguyen[c], Al Anoud D. Baddour[c], Celine Lu[c], Paramvir Singh[c], Raphael Moeckli[d], François Bochud[d], Jean-François Germond[d], Pascal Froidevaux[d], Claude Bailat[d], Jean Bourhis[a,b], Marie-Catherine Vozenin[a,b,2,3], and Charles L. Limoli[c,2,3]

[a]Laboratory of Radiation Oncology, Lausanne University Hospital, University of Lausanne, Lausanne VD-1011, Switzerland; [b]Department of Radiation Oncology, Lausanne University Hospital, University of Lausanne, Lausanne VD-1011, Switzerland; [c]Department of Radiation Oncology, University of California, Irvine, CA 92697-2695; and [d]Institute of Radiation Physics, Lausanne University Hospital, University of Lausanne, Lausanne VD-1011, Switzerland

Edited by James E. Cleaver, University of California, San Francisco, CA, and approved April 18, 2019 (received for review February 12, 2019)

Contents lists available at ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com

Original Article

Reduced cognitive deficits after FLASH irradiation of whole mouse brain are associated with less hippocampal dendritic spine loss and neuroinflammation

Danielle A. Simmons[a,#], Frederick M. Lartey[b,c,#], Emil Schüler[b], Marjan Rafat[b,d], Gregory King[b], Anna Kim[b], Ryan Ko[b], Sarah Semaan[a], Selena Gonzalez[a], Melissa Jenkins[b], Pooja Pradhan[b], Zion Shih[b], Jinghui Wang[b], Rie von Eyben[b], Edward E. Graves[b,e], Peter G. Maxim[b,f,*], Frank M. Longo[a,*], Billy W. Loo Jr.[b,e,*]

[a]Department of Neurology and Neurological Sciences, [b]Department of Radiation Oncology, Stanford University School of Medicine; [c]The Jackson Laboratory, Sacramento; [d]Department of Chemical and Biomolecular Engineering, Vanderbilt University, Nashville; [e]Stanford Cancer Institute, Stanford University School of Medicine; and [f]Department of Radiation Oncology, Indiana University School of Medicine, Indianapolis, United States

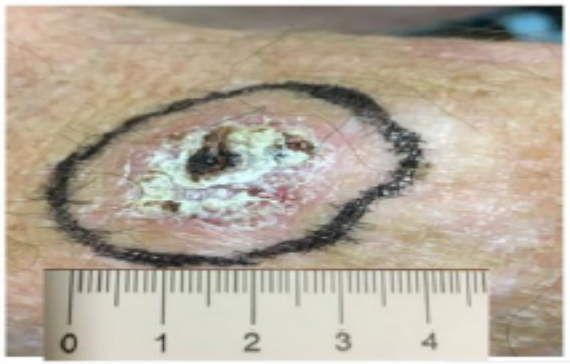
Per la prima volta su un paziente!

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

June 2019



1a : Day 0

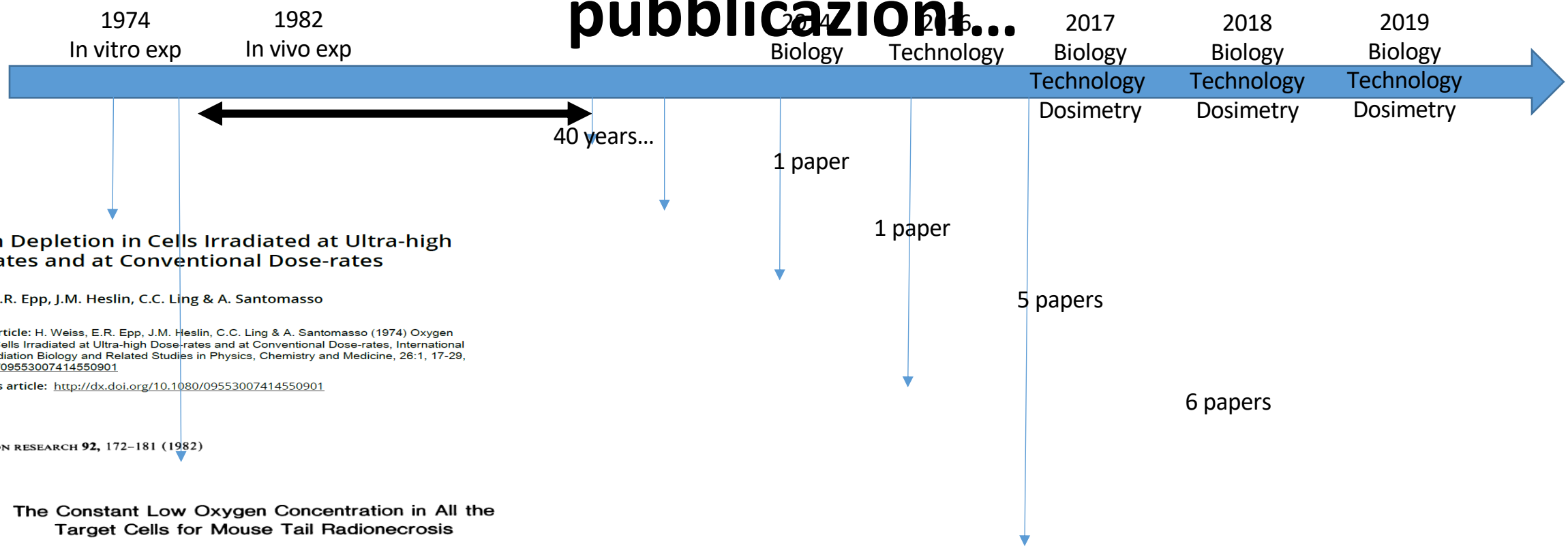
1b : 3 weeks

1c : 5 months

- Paziente 75-enne con linfoma cutaneo multi-resistente
- 15 Gy in 90 ms con un fascio di elettroni di 5.6 MeV
- Nei tessuti sani si è osservato solo un leggero aumento della vascolarizzazione
- Risposta completa (regressione macroscopica completa) sul tumore a 5 mesi

Atun R, et al. Lancet Oncol 2015;16:1153-86.

Nonostante la crescita esponenziale di investimenti e pubblicazioni…



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

RADIATION RESEARCH **92,** 172–181 (1982)

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, M2O 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).

Le uniche evidenze sperimentali certe e quantitative sono…

L'effetto c'è!

Durata totale irraggiamento < **200ms**

Elettroni di energia 4-7 MeV

Dose-rate > **40 Gy/s**

Applicazione clinica diretta solo al trattamento di lesioni superficiali e alla IOERT (radioterapia intraoperatoria)!

Perchè così poche informazioni quantitative?

- Esperimenti radiobiologici eseguiti sostanzialmente da **2 soli centri**
- Effetto Flash visto solo in **vivo**
- Linac utilizzati **non dedicati** e privi di un sistema di **beam monitoring**
- Problemi relativi all'utilizzo dei dosimetri attivi a valori di **dose-per-pulse** Flash

↓

Difficoltà a realizzare esperimenti quantitativi

Questioni aperte fondamentali per un ampio utilizzo clinico della Flash e la sua ottimizzazione

teoriche

Capire i meccanismi
Radiobiologici
Alla base dell'effetto

quantitative

Risposta **organi seriali**

Effetto **volume**

Dipendenza dalla **dose**, **dose-rate**, **dose-per-pulse** e **instantaneous dose-per-pulse**

Dipendenza dal **LET (Linear Energy Transfert)**

Campi adiacenti

tecnologiche

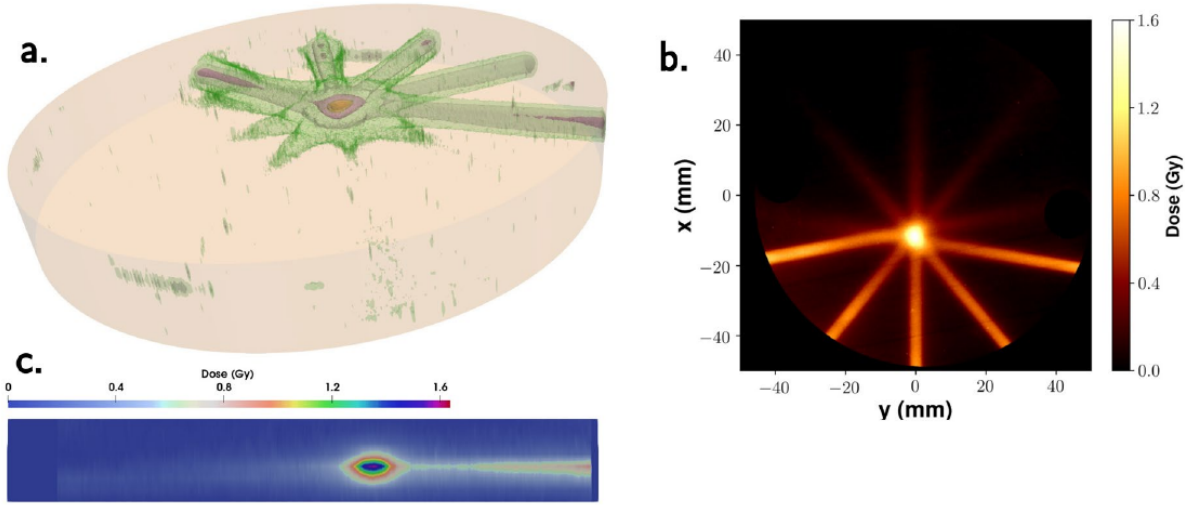
Realizzazione di Linac di elettroni
Ad alta energia (100-250 MeV)
VHEE (very high energy electrons)

VHEE(very high energy electron)

Linac a RF → Limiti nel raggiungere alte energie in spazi limitati

Laser-driven → Limiti di stabilità in fluenza ed energia

↓ See L. Labate *et al.*, Sci. Rep. **10**, 17307 (2020)



Per capire i problemi teorici e le dipendenze quantitative cosa serve?

Linac dedicato

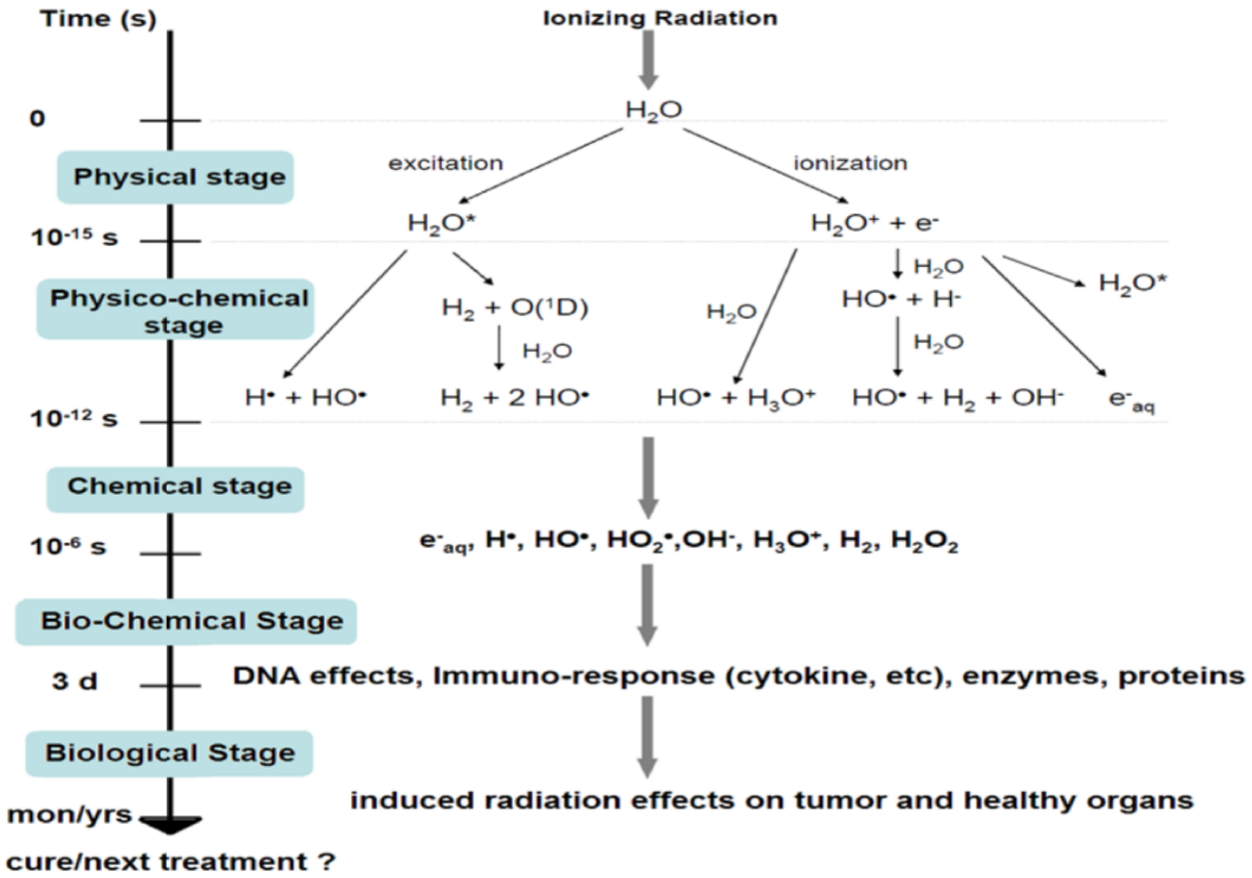
Dosimetria

Esperimenti radiobiologici quantitativi

Multidisciplinarietà

radiobiologia

La scala temporale



Le ipotesi

Oxygen depletion

Inflammation/Immune system

↓

Oxygen depletion analyzed on chemical track structure level does not explain FLASH effect

Daria Boscolo et al

Radiother Oncol

Storia dei problemi dosimetrici
Su elettroni ad alto DPP

dosimetria

Problemi dosimetrici
Introdotti dalla FLASH

Ion recombination correction for very high dose-per-pulse high-energy electron beams

F. Di Martino,[a)] M. Giannelli, A. C. Traino, and M. Lazzeri[b)]
U.O. Fisica Sanitaria–Sezione di Fisica Medica, Azienda Ospedaliera Universitaria Pisana, via Roma 67, 56126 Pisa, Italy

Med. Phys. 2005

Charge collection efficiency in ionization chambers exposed to electron beams with high dose per pulse

Phys. Med. Biol. 2006

R F Laitano[1], A S Guerra[1], M Pimpinella[1], C Caporali[1] and A Petrucci[2]

Dosimetric characteristics of electron beams produced by two mobile accelerators, Novac7 and Liac, for intraoperative radiation therapy through Monte Carlo simulation

J. Appl. Clin. Med. Phys. 2013

Sergio Righi,[1] Evis Karaj,[2] Giuseppe Felici,[3] Fabio Di Martino[4a]

Characterization of a microDiamond detector in high-dose-per-pulse electron beams for intra operative radiation therapy

Phys. Med. 2015

C. Di Venanzio [a], Marco Marinelli [a], A. Tonnetti [a], G. Verona-Rinati [a], M.D. Falco [b,*], M. Pimpinella [c], A. Ciccotelli [d], S. De Stefano [d], G. Felici [d], F. Marangoni [d]

Use of parallel-plate ionization chambers in reference dosimetry of NOVAC and LIAC® mobile electron linear accelerators for intraoperative radiotherapy: a multi-center survey

Med. Phys. 44 (1), January 2017

Paolo Scalchi[a)]
Department of Medical Physics, Azienda U.L.S.S. 8, Vicenza 36100, Italy

EMPIR project UHDpulse

Type:	Joint Research Project
Duration:	2019-2022
Start:	1. Sept. 2019
Funding:	2.1 M €
Coordinator:	Andreas Schüller
Topic:	tools for traceable dose measurements for:

- **FLASH radiotherapy**
- VHEE radiotherapy
- laser driven medical accelerators

http://uhdpulse-empir.eu/

EMPIR EURAMET

The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

The European Metrology Programme for Innovation and Research (EMPIR):

- metrology-focused programme of coordinated R&D
- enables European metrology institutes, industrial and medical organisations, and academia to collaborate

Physikalisch-Technische Bundesanstalt ■ Braunschweig and Berlin

National Metrology Institute

SCIENTIFIC REPORTS

nature research

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OPEN

The challenge of ionisation chamber dosimetry in ultra-short pulsed high dose-rate Very High Energy Electron beams

M. McManus[1,2], F. Romano[5,1], N. D. Lee[1], W. Farabolini[4,6], A. Gilardi[4], G. Royle[2], H. Palmans[3,1] & A. Subiel[1]

High dose-rate radiotherapy, known as FLASH, has been shown to increase the differential response between healthy and tumour tissue. Moreover, Very High Energy Electrons (VHEEs) provide more favourable dose distributions than conventional radiotherapy electron and photon beams. Plane-parallel ionisation chambers are the recommended secondary standard systems for clinical reference dosimetry of electrons, therefore chamber response to these high energy and high dose-per-pulse beams must be well understood. Graphite calorimetry, the UK primary standard, has been employed to measure the dose delivered from a 200 MeV pulsed electron beam. This was compared to the charge

Ricapitolando…

Linac non dedicati → Instabilità dell'output e mancanza di beam monitoring

Risultati sperimentali ottenuti solamente in vivo → Esperimenti meno controllati rispetto a quelli in vitro

Altissimi valori di dose-per-pulse → Problemi di saturazione per I dosimetri attivi

↓

Ancora non si hanno certezze sui meccanismi radiobiologici alla base dell'effetto

Le conoscenza delle dipendenze dell'effetto dai parametri del fascio sono molto limitate

↓

Si può prevedere l'impiego clinico della Flash solo per quanto riguarda la sua applicazione IORT, tantissimo lavoro deve essere fatto per capire e ottimizzare altri sviluppi clinici dell'effetto

Cosa abbiamo fatto: realizzazione e caratterizzazione dosimetrica in fascio FLASH di elettroni

frontiers in Physics

ORIGINAL RESEARCH
published: 11 September 2020
doi: 10.3389/fphy.2020.00374

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Transforming an IORT Linac Into a FLASH Research Machine: Procedure and Dosimetric Characterization

Giuseppe Felici[1], Patrizio Barca[2], Salvatore Barone[1], Eleonora Bortoli[2], Rita Borgheresi[2], Silvia De Stefano[1], Massimo Di Francesco[1], Luigi Grasso[1], Stefania Linsalata[2], Daniela Marfisi[2], Matteo Pacitti[1] and Fabio Di Martino[2]**

[1] R&D Department, Sordina IORT Technologies, Aprilia, Italy, [2] U.O. Fisica Sanitaria, Azienda Universitaria Ospedaliera Pisana, Pisa, Italy

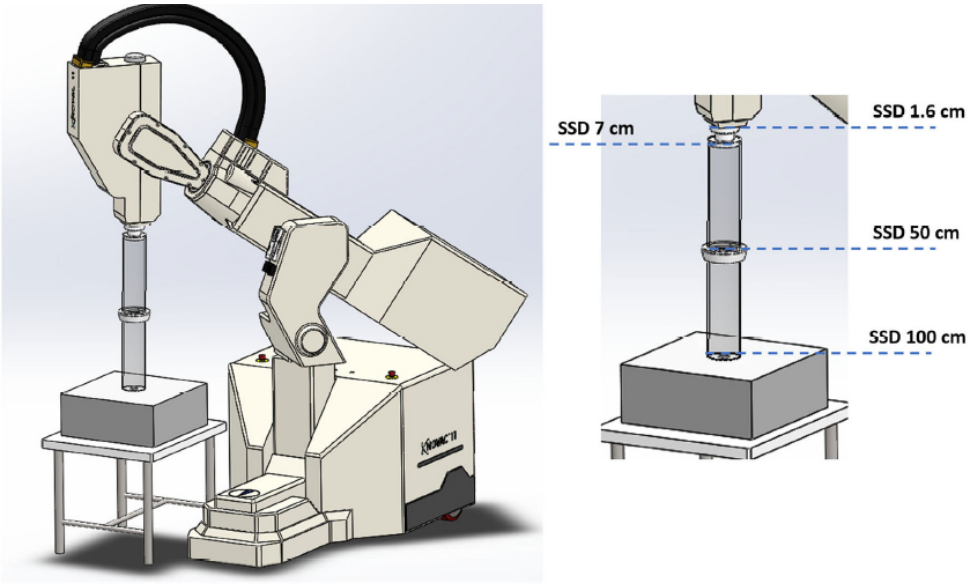
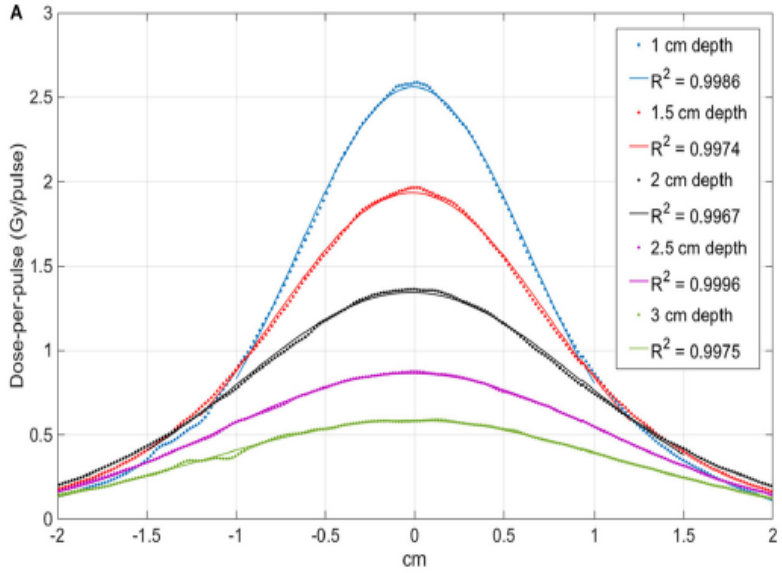
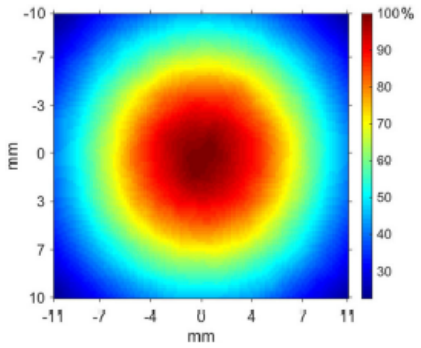
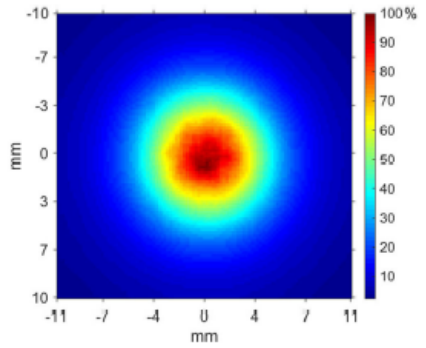


FIGURE 1 | Four collimation configurations obtained acting on Novac7 collimation system architecture.


A
Dose-per-pulse (Gy/pulse)
cm
1 cm depth
R2 = 0.9986
1.5 cm depth
R2 = 0.9974
2 cm depth
R2 = 0.9967
2.5 cm depth
R2 = 0.9996
3 cm depth
R2 = 0.9975


mm
100%


mm
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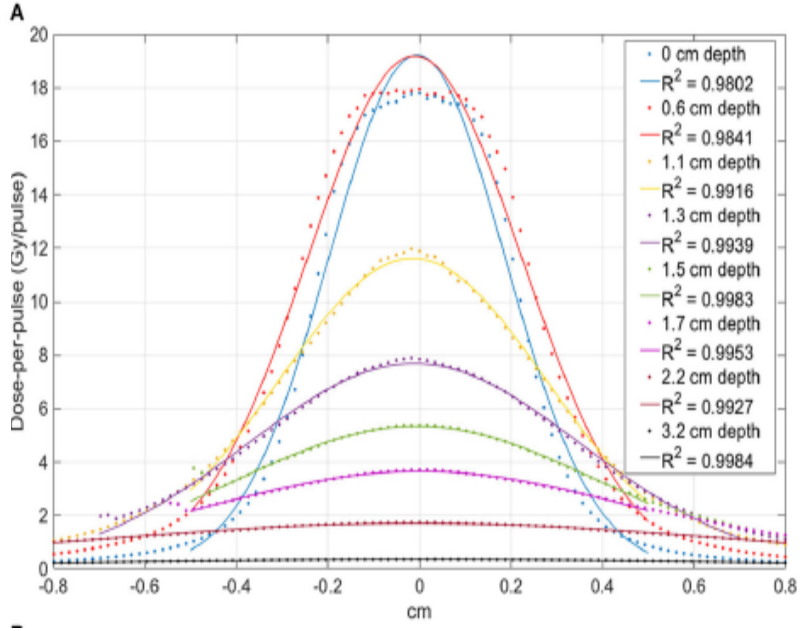
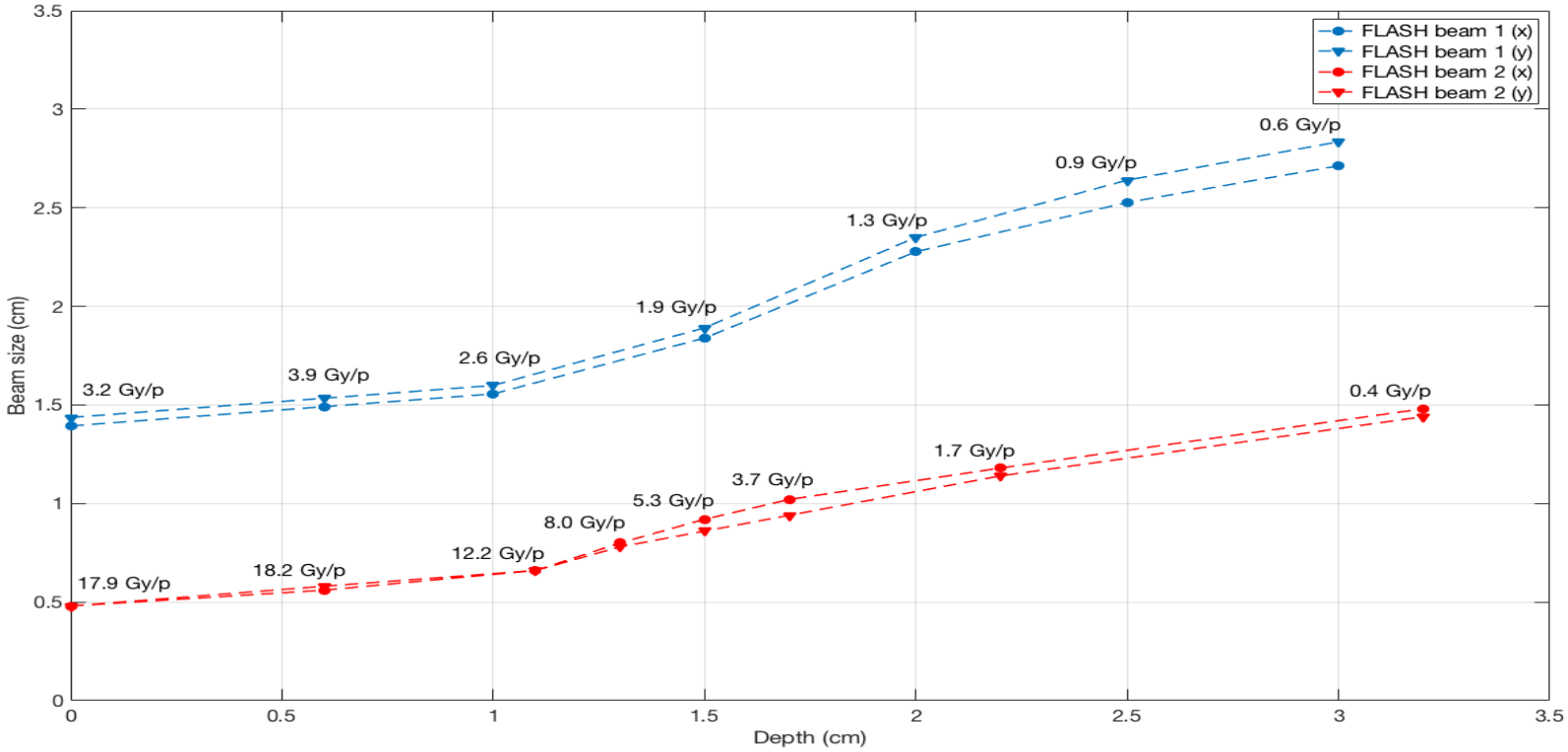

A
Dose-per-pulse (Gy/pulse)
cm
0 cm depth
R2 = 0.9802
0.6 cm depth
R2 = 0.9841
1.1 cm depth
R2 = 0.9916
1.3 cm depth
R2 = 0.9939
1.5 cm depth
R2 = 0.9983
1.7 cm depth
R2 = 0.9953
2.2 cm depth
R2 = 0.9927
3.2 cm depth
R2 = 0.9984


Beam size (cm)
Depth (cm)
FLASH beam 1 (x)
FLASH beam 1 (y)
FLASH beam 2 (x)
FLASH beam 2 (y)
3.2 Gy/p
3.9 Gy/p
2.6 Gy/p
1.9 Gy/p
1.3 Gy/p
0.9 Gy/p
0.6 Gy/p
17.9 Gy/p
18.2 Gy/p
12.2 Gy/p
8.0 Gy/p
5.3 Gy/p
3.7 Gy/p
1.7 Gy/p
0.4 Gy/p

Cosa abbiamo fatto: dosimetria

ORIGINAL RESEARCH ARTICLE

Front. Phys. | doi: 10.3389/fphy.2020.570697

FLASH Radiotherapy with electrons: issues related to the production, monitoring and dosimetric characterization of the beam

Provisionally accepted We'll notify you at publication.

Fabio Di Martino[1*], Patrizio Barca[1], Salvatore Barone[2], Eleonora Bortoli[1], Rita Borgheresi[1], Silvia De Stefano[2], Massimo Di Francesco[2], Luigi Grasso[2], Stefania Linsalata[1], Daniela Marfisi[1], Matteo Pacitti[2] and Giuseppe Felici[2]

[1]U.O. Fisica Sanitaria, Pisana University Hospital, Italy
[2]Other, Italy

The classical theory of recombination in ionization chambers [30] neglects the effect of the electri field generated by the charges in motion after the ionization event. Such hypothesis is no longer tru when dealing with a FLASH beam due to the extremely high ionization density. The simple analysi hereinafter reported clarifies this point. Charge distribution inside a plane parallel chamber is shown in *Figure 11*.

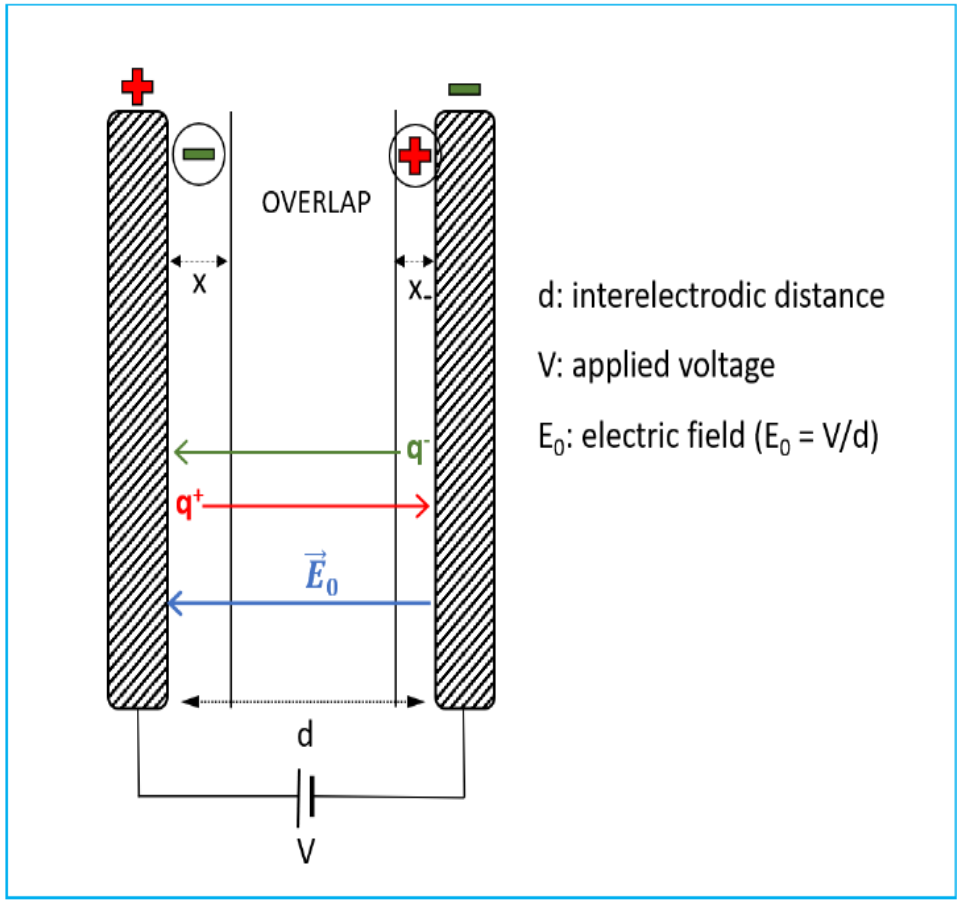


Figure 11: ionization chamber modelling.

Risposta delle principali tipologie di dosimetri utilizzati in radioterapia

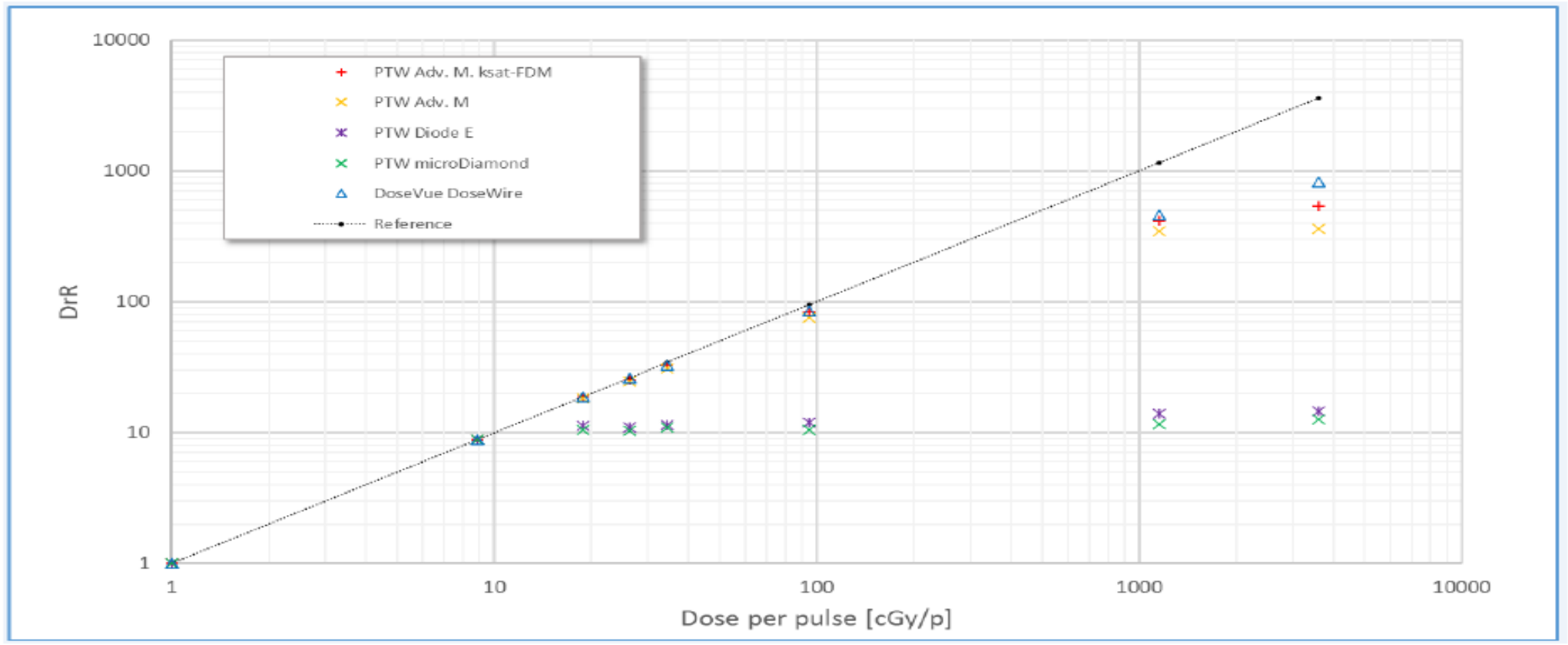


Figure 9: DrR vs. dose per pulse.

Cosa stiamo facendo

Esperimento sulle retine (organo seriale)

PRIN sulla Flash

UO Fisica Sanitaria, Università (Fisica, Radioterapia, Radiodiagnostica),CNR (Neuroscienze)

Sviluppo di scintillazioni come dosimetri FLASH

Call gruppo5 INFN

Sviluppo e realizzazione di una CI FLASH → Collaborazione con Sordina IORT technology

Realizzazione di uno standard per il commissionig di un Linac FLASH dedicato → Collaborazione con L'università di Anversa

↓

ELECTRONFLASH

Linac dedicato: ELECTRONFLASH

3 modelli con energie disponibili:

- 5 MeV and 7 MeV
- 7 MeV and 9 MeV
- 10 MeV and 12 MeV

Dimensione dei campi variabili tra Ø12 cm e Ø 1cm, di forma circolare e quadrata

Dose rate variabile tra 0.1 – 1500 Gy/s con campo di Ø10 cm

Dose per pulse superiore a 20 Gy/pulse and Dose rate superiore a 5000 Gy/s with Ø 4 cm

Dose per pulse up to 40 Gy/pulse and Dose rate up to 10000 Gy/s with Ø 1 cm

Real-time control dell'energie e la fluenza del fascio

Set-up di irraggiamento ottimizzati per gli esperiementi in vivo

ELECTRONFLASH NEL MONDO

Istituto Marie Curie (Parigi) – installato a settembre 2020

V. Favadoun (“scopritore dell’effetto Flash”)

GZA Hospital (Iridium Network) – università di Anversa – acquistato e in programma l’installazione entro questa estate

F. Poortmans – Former President ESTRO (Società Europea radioterapia&Oncologia)

Il progetto: cosa abbiamo?

Esperienza, lavori fatti e lavori che stiamo facendo sulla **dosimetria**

I nostri **radioterapisti** da tempo sono stati coinvolti e sono diventati un riferimento a livello nazionale sugli **aspetti clinici della Flash**

All'interno del nostro ospedale abbiamo una lunga e vasta esperienza clinica sulla **IORT**

Abbiamo un rapporto di lunga collaborazione scientifica con **Sordina**, azienda produttrice di Electronflash

Abbiamo già, all'interno della nostra **Radioterapia**, un **bunker** già perfettamente dimensionato e con tutte le autorizzazioni pronte per installarci il Linac

Nella nostra città abbiamo una rete di **eccellenze scientifiche** tali da coprire in modo ottimale tutte le **competenze multidisciplinari** necessarie

Abbiamo la possibilità di creare nella nostra città un centro di assoluta eccellenza su un argomento che potrebbe rivoluzionare la radio-oncologia. Ma lo dobbiamo fare ora!

Il Progetto: argomenti trattati e professionalità coinvolte

Radiobiologia
- Esperimenti in vitro (organoidi…)
- Esperimenti in vivo
- Studi teorico-computazionali (Monte Carlo code EGS4-DNA…)

Dosimetria
- Studi sugli effetti di saturazione dei dosimetri attuali
- Sviluppo di nuovi dosimetri (scintillatori,nuove CI,…)

Tecnologia
- Sviluppo e ottimizzazione del sistema di erogazione del fascio
- Sviluppo e ottimizzazione del sistema di collimazione del fascio

Pre-clinica → Valutazione aspetti clinici, trials pre-clinici IOERT Flash, interazione con altre terapie oncologiche…

Fisici Medici
Radioterapisti
Radiologi
Oncologi
Fisici teorico-computazionali
Biologi
Biofisici
Fisici alte energie

Il nostro sogno!

Grazie dell'attenzione e speriamo di poter andar avanti!

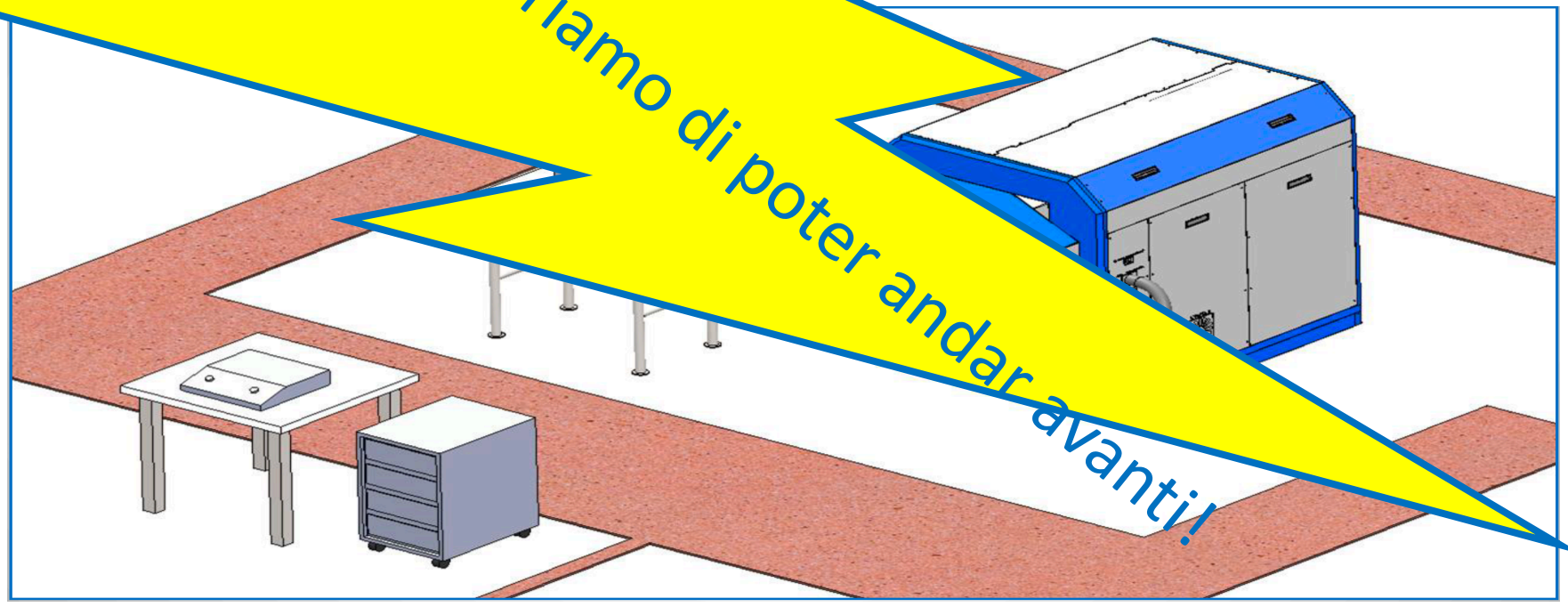
<u>NFLASH 4000</u>

ctrons

*10 cm² @ SSD 100 cm

dose rate 0.1 – 1000 Gy/s; max 4000 Gy/1

energy & output



particle beams with ultra-high pulse dose rates

electrons, protons

ultra-high dose per pulse,
ultra-short pulse duration
or both