

# Development of C-band electron linacs for FLASH-RT at La Sapienza University & INFN

Luigi Palumbo

Compact Light Workshop November 8,9 2021



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## Flash therapy is revolutionary in the perspective of cancer cure

- it spares healthy tissues from the damage of the ionizing radiation maintaining the tumor control as efficient as in conventional radiotherapy.
- to allow the implementation of the revolutionary FLASH therapy concept into actual clinical use electron linear accelerators are required to deliver very high dose rate ( $> 10^6$  Gy/s) in very short time of irradiation ( $< 100$  ms).



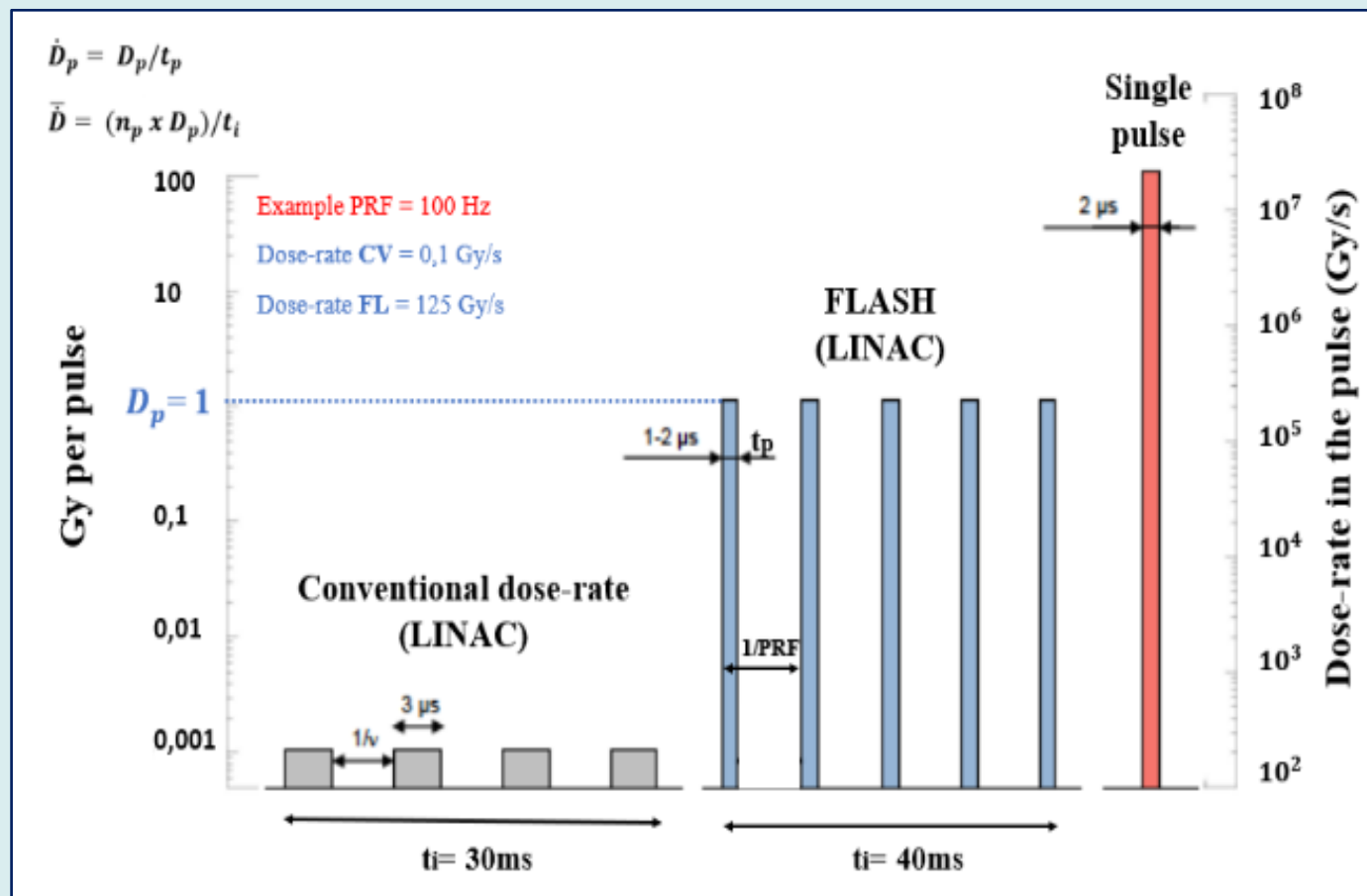
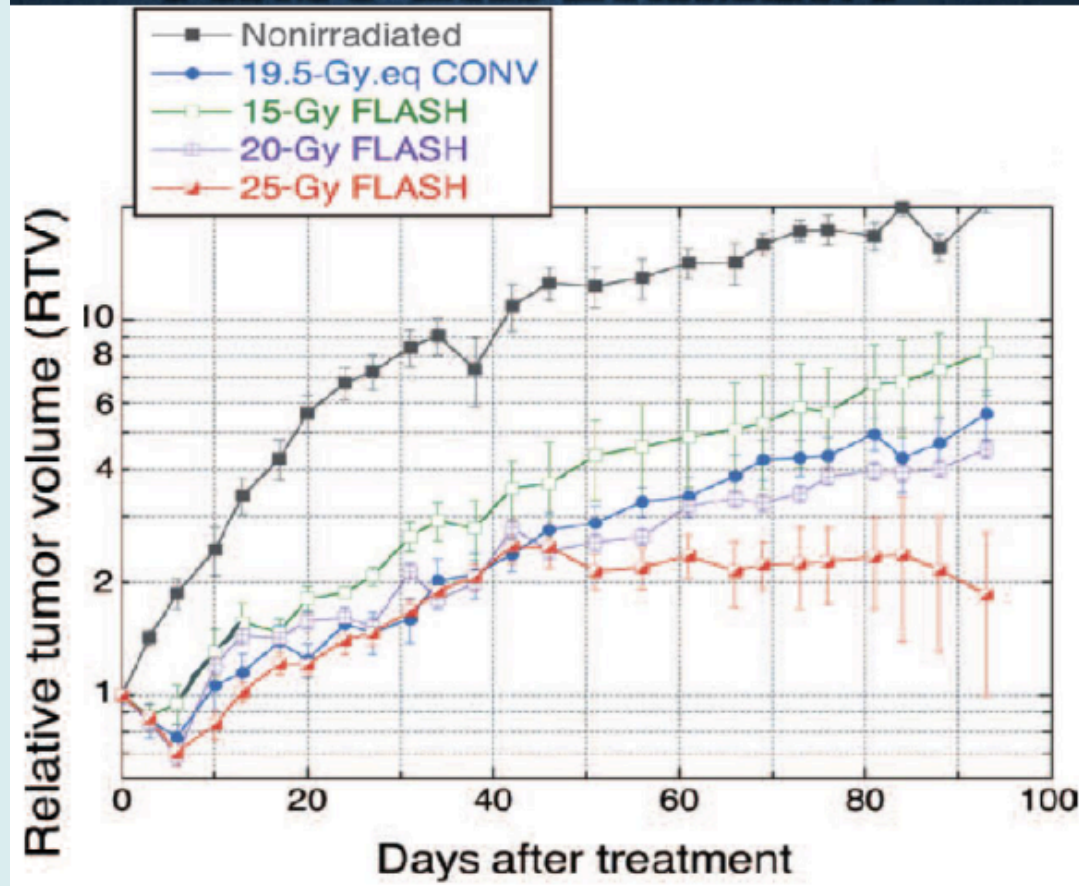


Table 1: Main FLASH parameters for the irradiations.

Parameter	Description	Value
PRF	Pulse repetition frequency	> 100 Hz
$t_p$	Pulse width	0.1-4.0 µs
$t_i$	Total irradiation time	< 100 ms
$\bar{D}$	Time-averaged dose rate	> 100 Gy/s
$\dot{D}_p$	Dose-rate in a single pulse	> 10 <sup>6</sup> Gy/s
$D_p$	Dose in a single pulse	> 1 Gy

# FLASH THERAPY IN MICE: FIRST EXPERIMENT



V. Favaudon et al., *Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice*, *Sci Transl Med.* 6, 245ra293, 2014.

# Is the evidence robust?

First evidence on animals..... Much less damage to standard tissue for same dose release

Mouse skin treated with electron beam

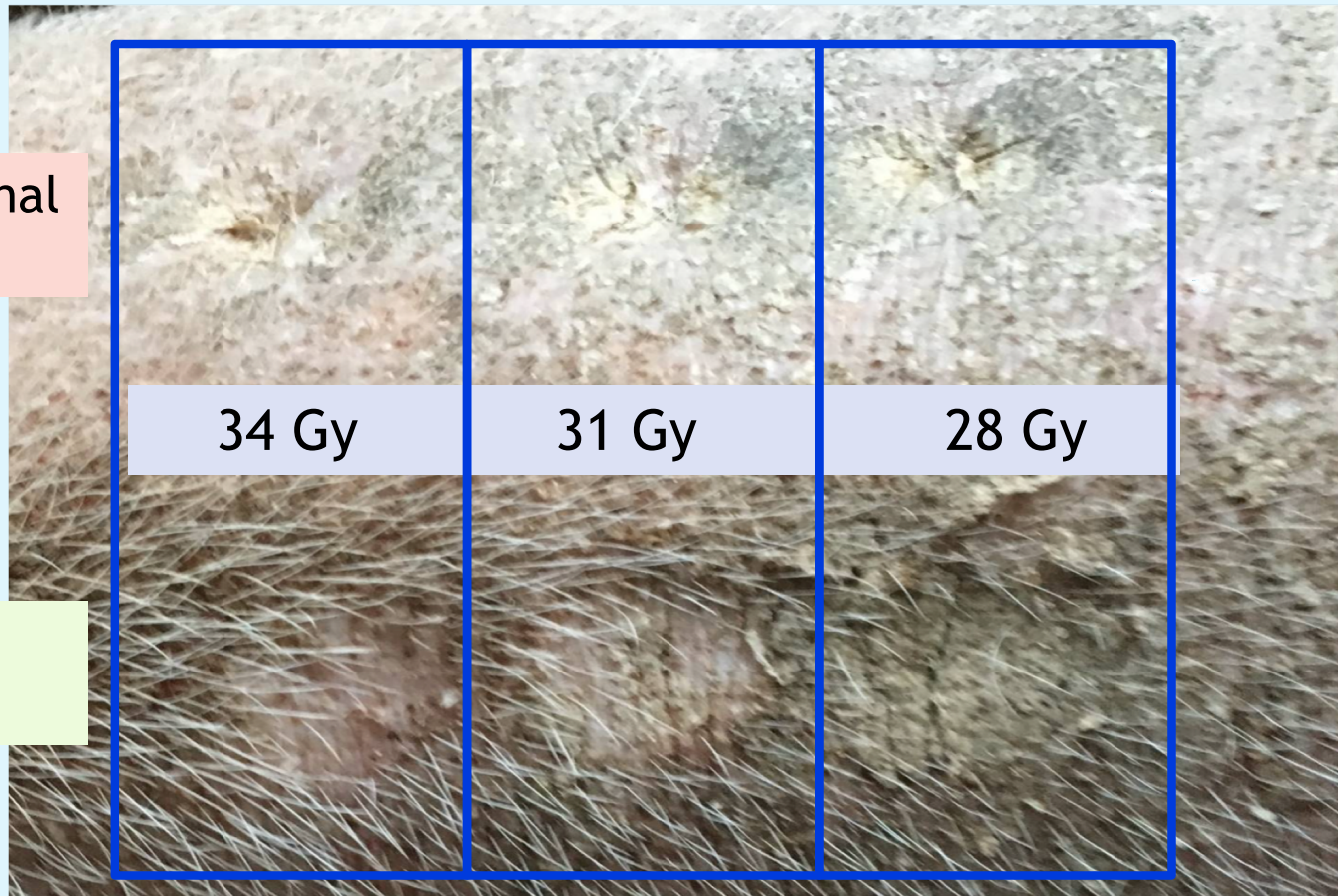
Conventional  
therapy

34 Gy

31 Gy

28 Gy

FLASH  
therapy





# Is the evidence robust?

The evidence seems robust, even if the exact features are yet to be explored.  
The first patients have been already treated!!!

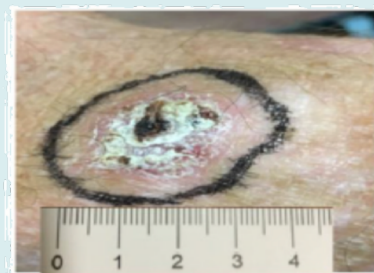
## Treatment of a first patient with FLASH-radiotherapy

Jean Bourhis <sup>a,b,\*</sup>, Wendy Jeanneret Sozzi <sup>a</sup>, Patrik Gonçalves Jorge <sup>a,b,c</sup>, Olivier Gaide <sup>d</sup>, Claude Bailat <sup>c</sup>, Frédéric Duclos <sup>a</sup>, David Patin <sup>a</sup>, Mahmut Ozsahin <sup>a</sup>, François Bochud <sup>c</sup>, Jean-François Germond <sup>c</sup>, Raphaël Moeckli <sup>c,1</sup>, Marie-Catherine Vozenin <sup>a,b,1</sup>

<sup>a</sup>Department of Radiation Oncology, Lausanne University Hospital and University of Lausanne; <sup>b</sup>Radiation Oncology Laboratory, Department of Radiation Oncology, Lausanne University Hospital and University of Lausanne; <sup>c</sup>Institute of Radiation Physics, Lausanne University Hospital and University of Lausanne; and <sup>d</sup>Department of Dermatology, Lausanne University Hospital and University of Lausanne, Switzerland



June 2019



1a : Day 0



1b : 3 weeks



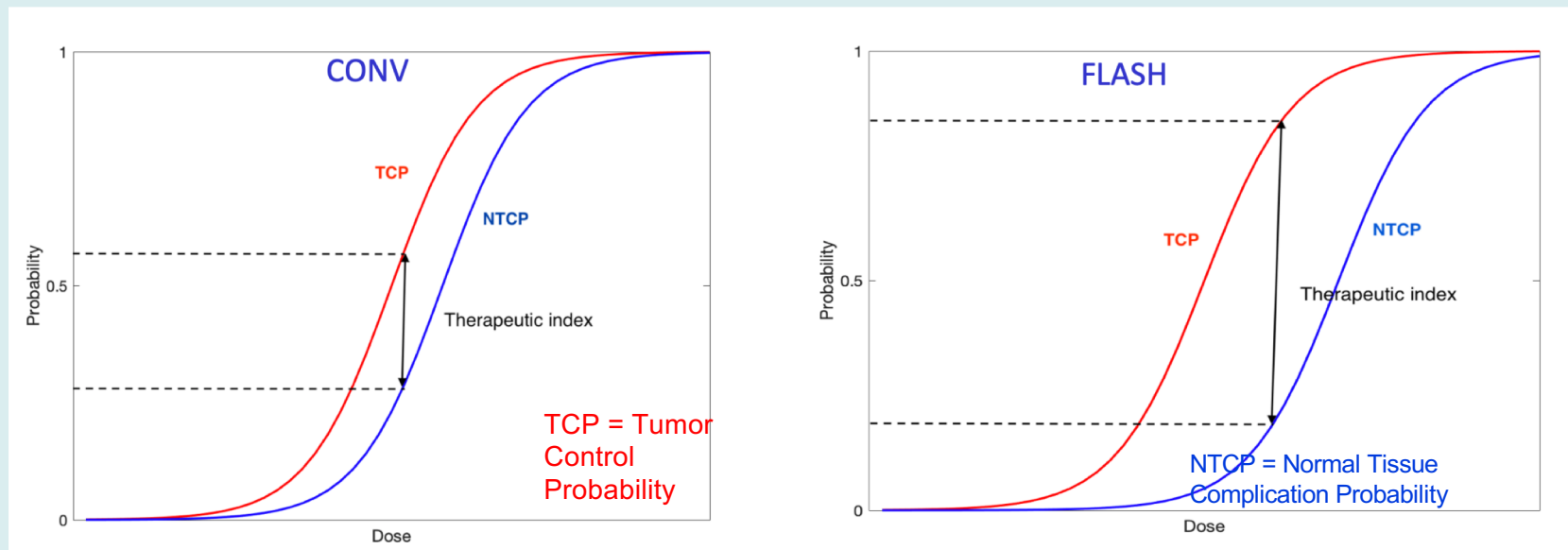
1c : 5 months

- 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.

# FLASH EFFECT

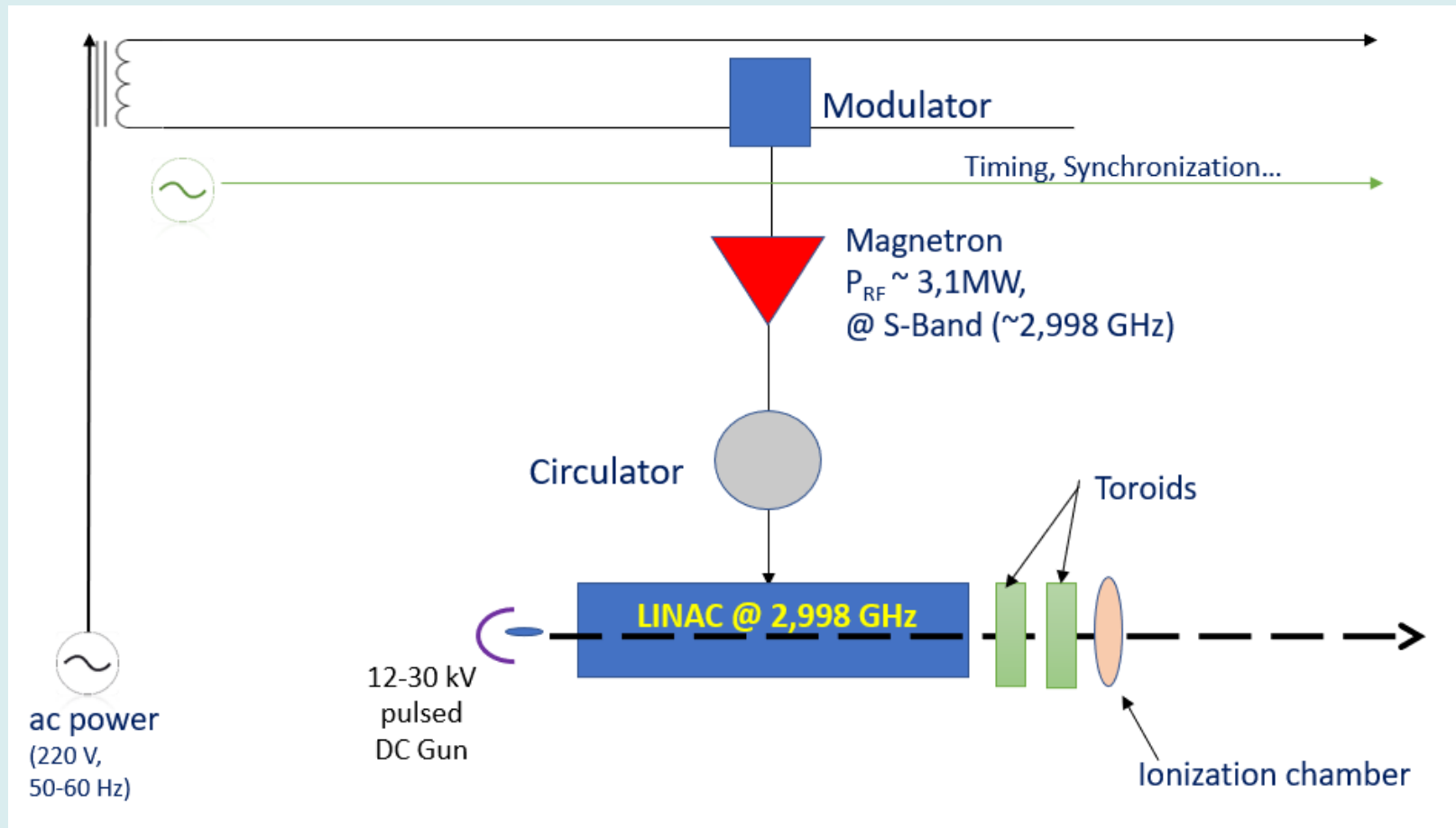
- It has been reported evidence for the sparing effect on healthy tissue if the dose is delivered at very high rate and very short time.
- The effect has been reported (many times) on organs and on animals.
- Many radiobiological models suggested the oxygen concentration plays a crucial role. A huge radiobiology research activity is going on.

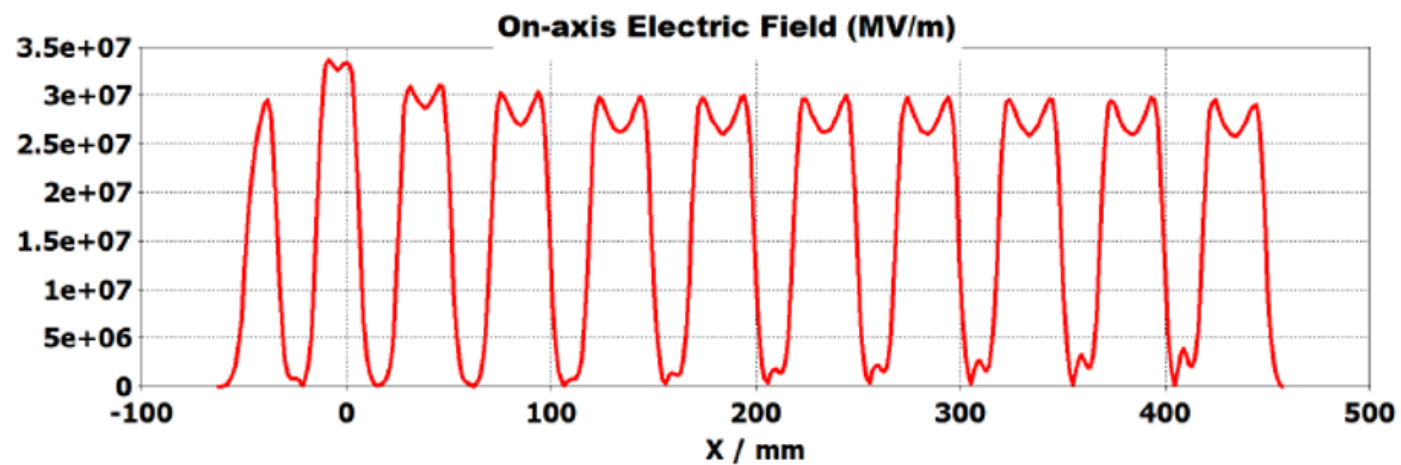
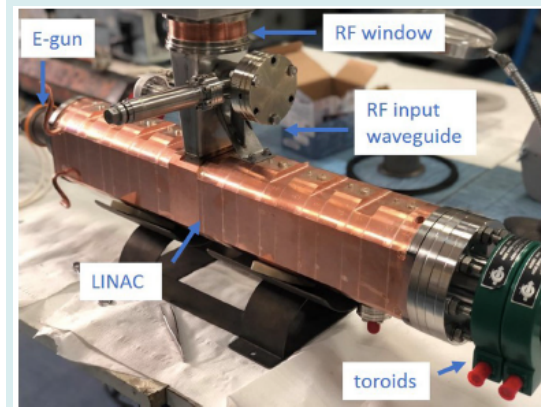
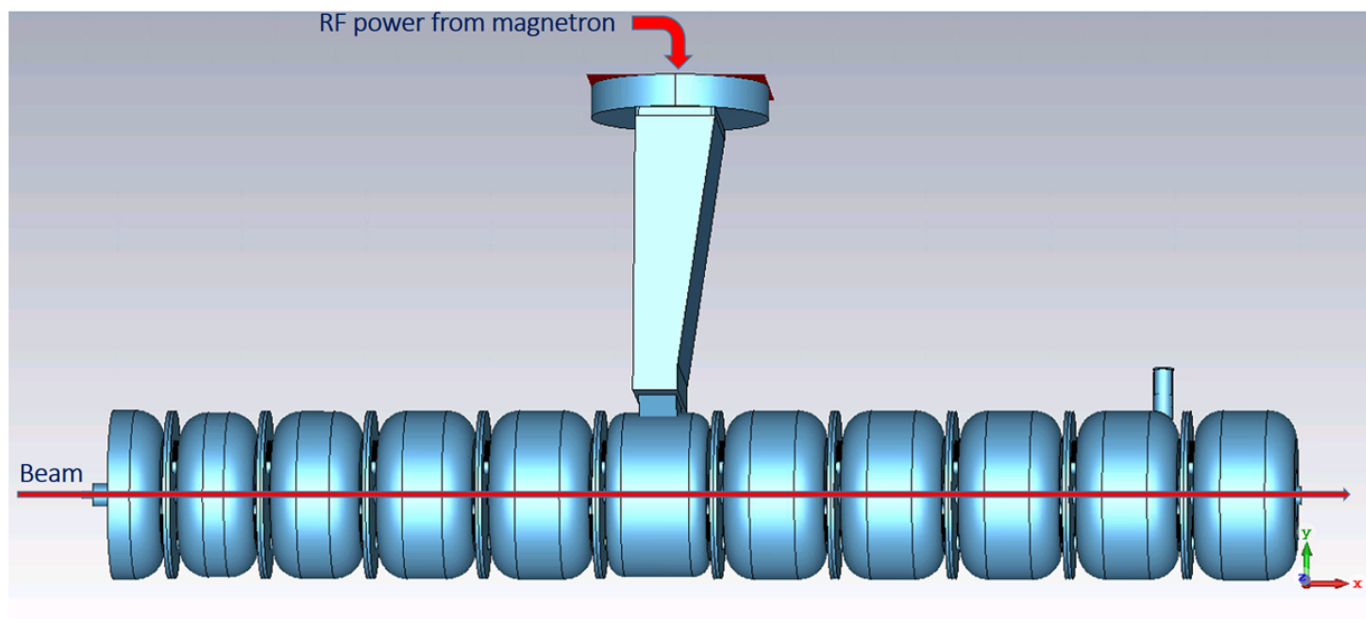


# Sapienza & INFN on Flash-RT

- A Sapienza-INFN group has invested on the e-FLASH technology. The group is centered at the SBAI Department and has a twofold interest on FLASH RT.
- realization of Linacs for FLASH-RT
  1. S-Band 7 MeV with SIT Company
  2. C-Band 12 MeV with SIT Company
  3. C-band compact VHEE demonstrator
- development of a new TPS software based on MC dose evaluation, able to treat electron, photon and protons and to run on GPU

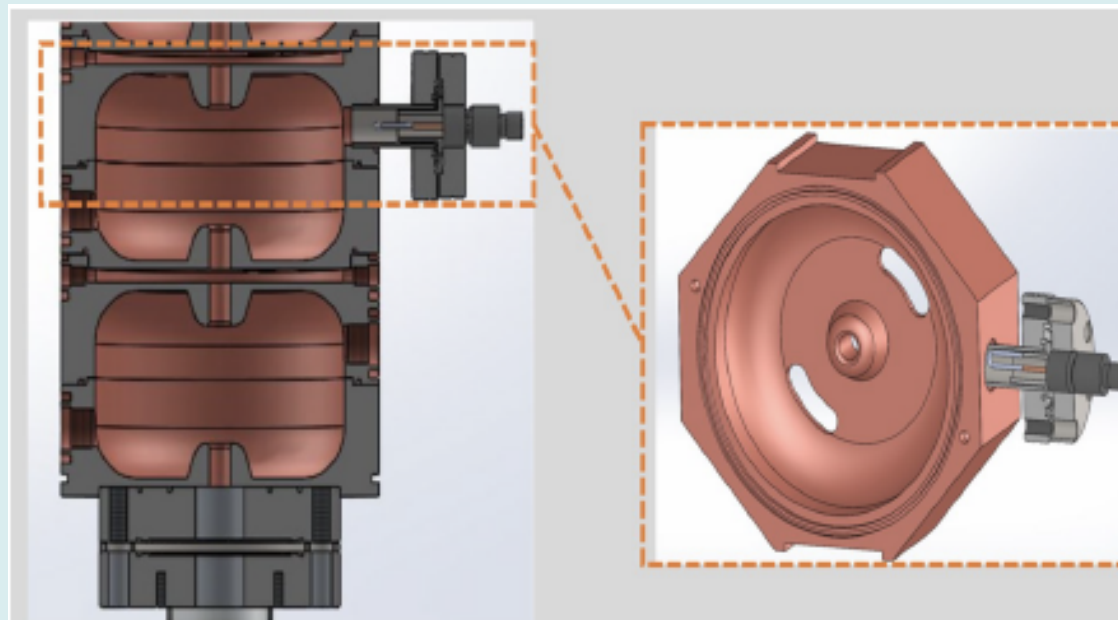
# 1. S-Band 7 MeV e-Linac for Flash-RT (with SIT )





Biperiodic structure  $\sim 3$  GHz  
 Accelerating mode  $\pi/2$   
 Magnetic coupling





PHYSICAL REVIEW ACCELERATORS AND BEAMS **24**, 050102 (2021)

**Compact S-band linear accelerator system for ultrafast,  
ultrahigh dose-rate radiotherapy**

L. Faillace<sup>1,6,\*</sup> S. Barone,<sup>2</sup> G. Battistoni<sup>3</sup> M. Di Francesco,<sup>2</sup> G. Felici<sup>2</sup> L. Ficcadenti,<sup>4</sup>  
G. Franciosini,<sup>4,5</sup> F. Galante,<sup>2</sup> L. Giuliano<sup>1,4</sup> L. Grasso,<sup>2</sup> A. Mostacci,<sup>1,4</sup> S. Muraro,<sup>3</sup> M. Pacitti,<sup>2</sup>  
L. Palumbo,<sup>1,4</sup> V. Patera<sup>1,4</sup> and M. Migliorati<sup>1,4</sup>

## Electron LINAC-FLASH 7 MeV – constructed by SIT Company



**Machine delivered to**

- CURIE Institute (Orsay)
- University of Antwerp, Belgium.
- CPFR, Pisa, Italy.

Table 2: Main characteristics of the EF4000

Characteristics EF4000	Value
Output energy	5 - 7 MeV
Pulse repetition frequency	1 - 250 Hz
Pulse width	0.5 - 4 $\mu$ s
Maximum peak beam current	120 mA
Dose rate per pulse	$> 10^6$ Gy/s
Mean Dose rate	1000 Gy/s
Max Dose per pulse	30 Gy in a surface of $\varnothing$ 10 mm

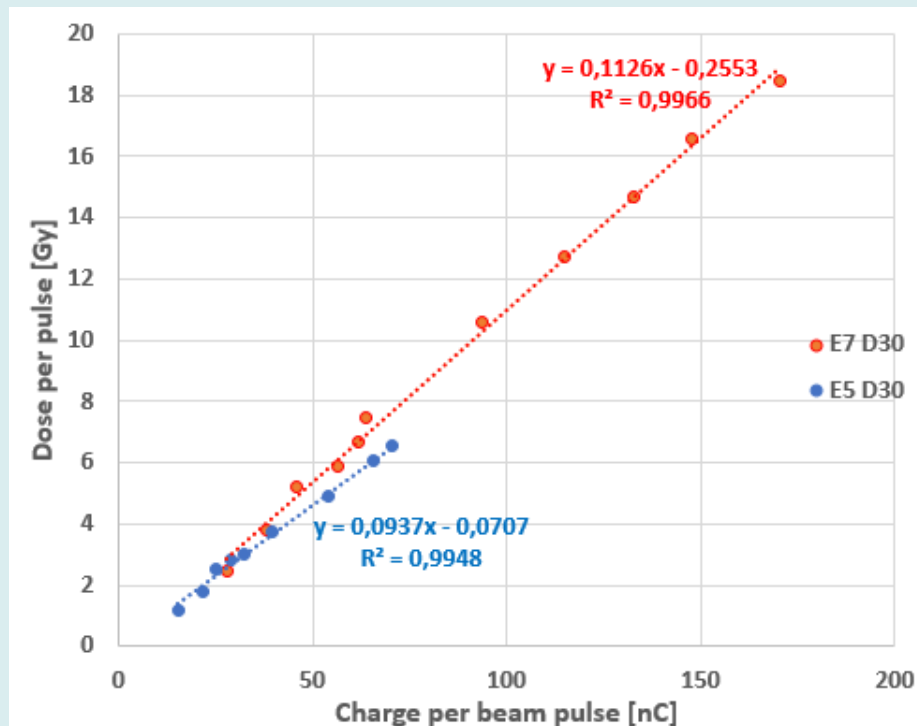
## DOSE MEASUREMENTS AT CURIE INSTITUTE (Orsay)

Diameter applicator mm	7 MeV dose per pulse at 4 $\mu$ s		5 MeV dose per pulse at 4 $\mu$ s	
	Conventional [Gy]	FLASH [Gy]	Conventional [Gy]	FLASH [Gy]
120	0.04	3	0.004	2
100	0.06	5	0.007	3
50	0.15	13	0.014	9
40	0.19	16	0.018	10
35	0.23	19	0.021	12
30	0.24	19	0.022	12
10	0.21	30	0.024	15

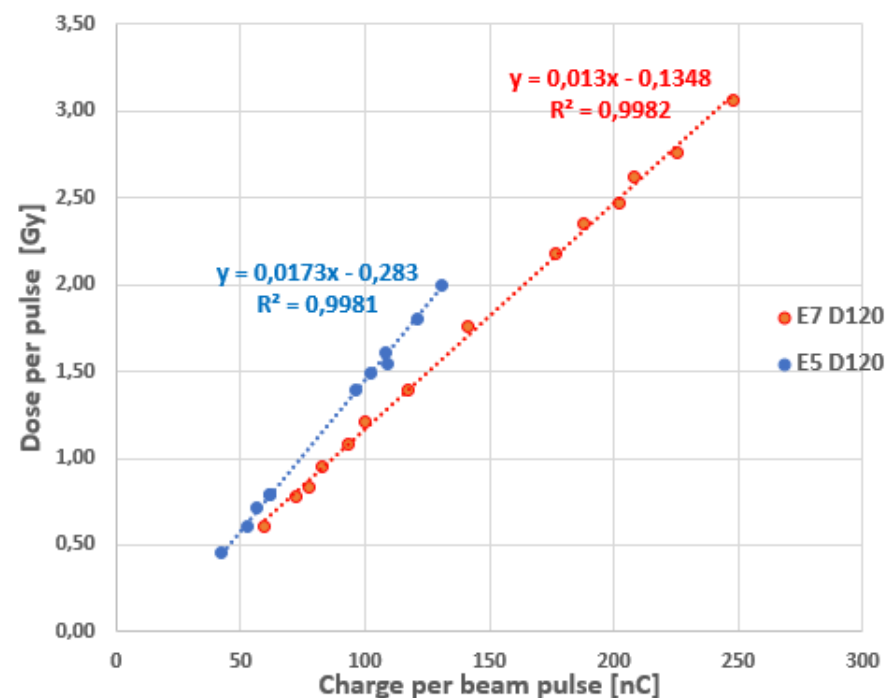
*BEAM PARAMETERS AND DOSE RATES MEASUREMENTS OF THE ELECTRON FLASH LINAC AT CURIE INSTITUTE (Paper in prep.)*

*L.Giuliano, G.Franciosini, L. Faillace, M.Migliorati, L.Palumbo G. Felici, F.Galante A. Patriarca M. Dutreix, V.Favaudon and S. Heinrich*

## Dose vs. pulse charge

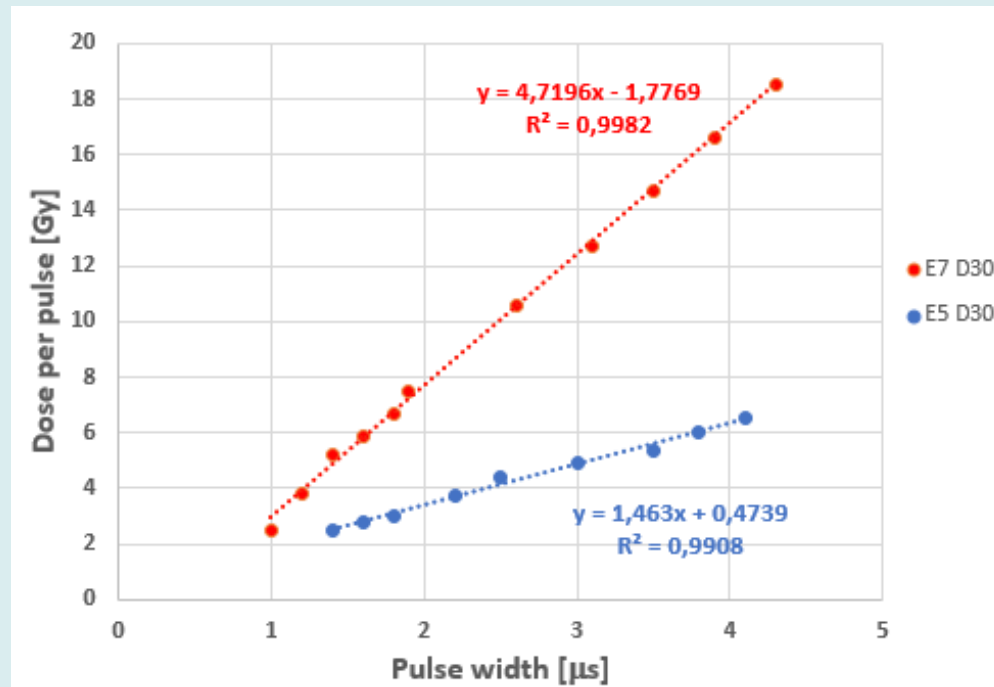


Applicator diameter 30 mm

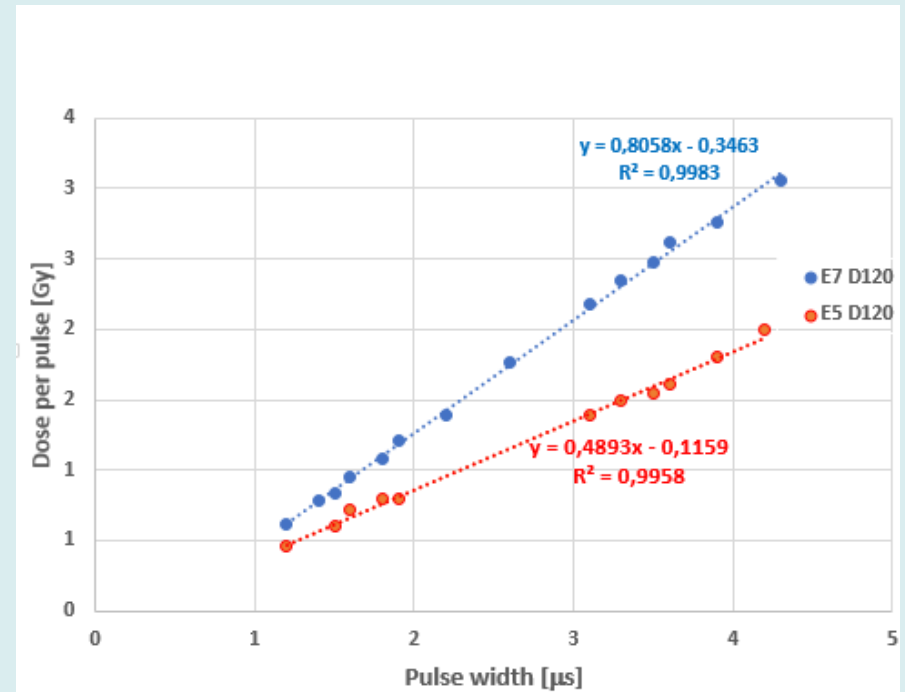


Applicator diameter 120 mm

## Dose vs. pulse width $\mu s$

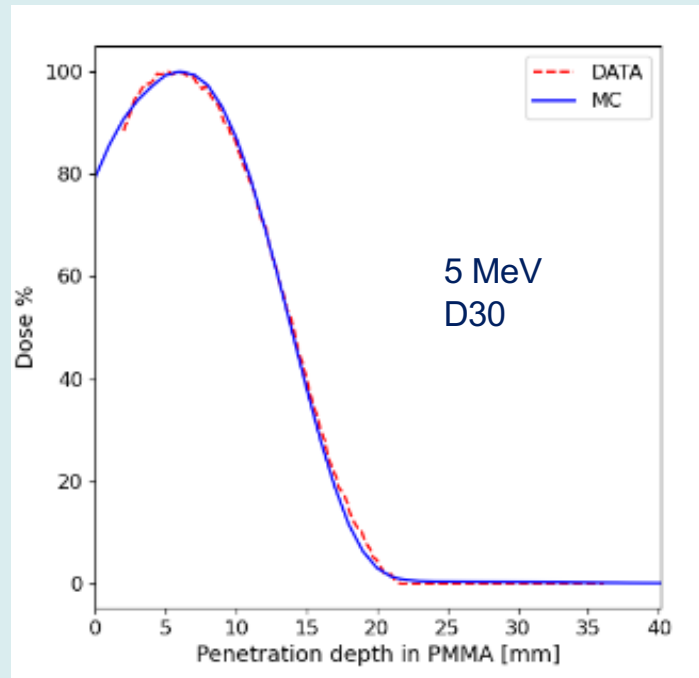


Applicator diameter 30 mm



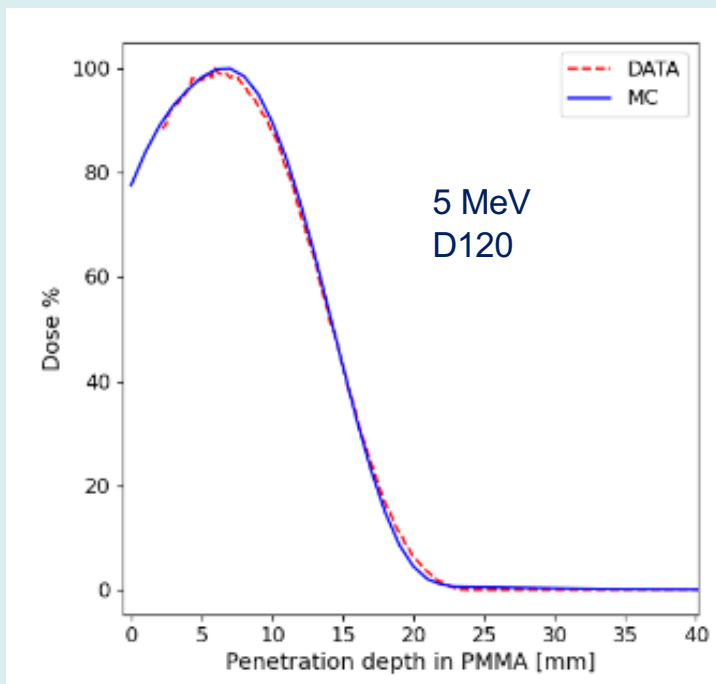
Applicator diameter 120 mm

## Dosimetric analysis - 5 MeV - PDD

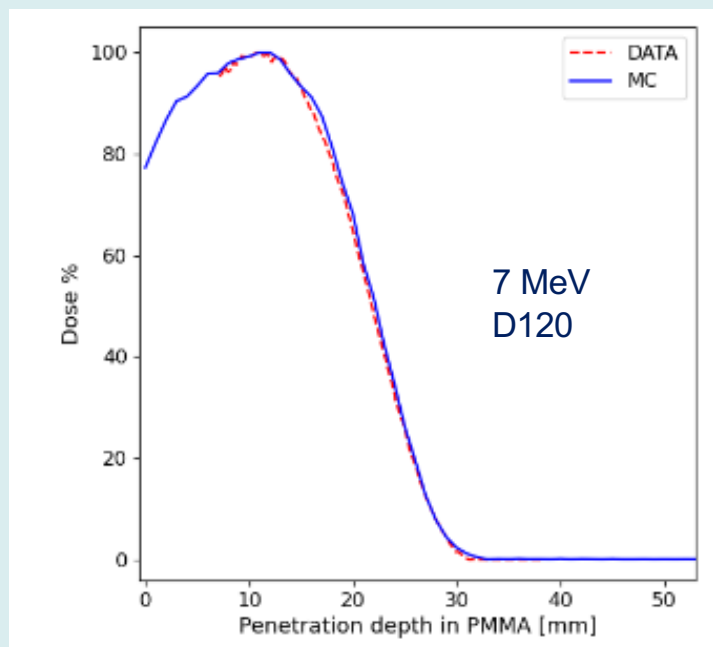


The dosimetric quantities to be compared to experimental measurements are evaluated by means of the FLUKA Monte Carlo software.  
(G. Franciosini- blue curves)

The Percent Depth Dose (PDD) and beam transverse profile were investigated using Gafchromics films at different depth in a poly-methyl methacrylate (PMMA) phantom  
(L. Giuliano data: dashed-red curves)

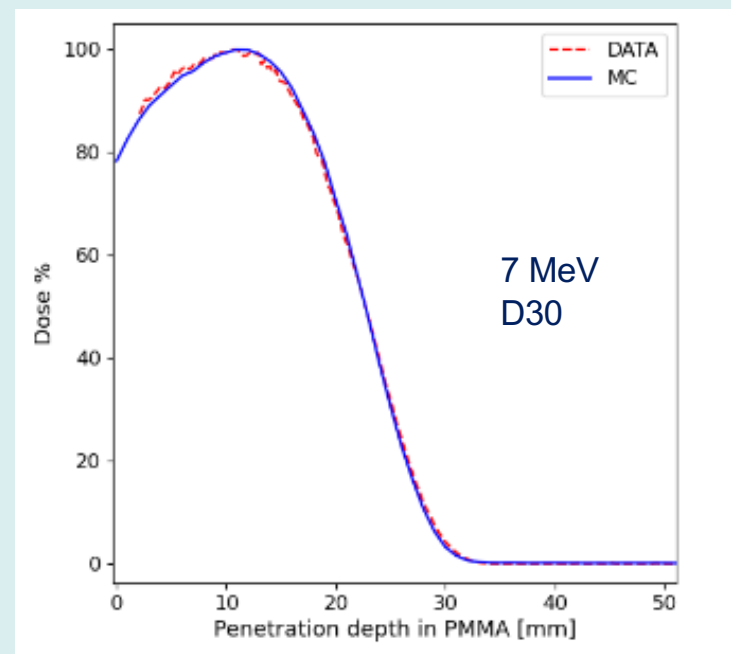


## Dosimetric analysis - 7 MeV - PDD



The dosimetric quantities to be compared to experimental measurements are evaluated by means of the FLUKA Monte Carlo software. (blu curves)

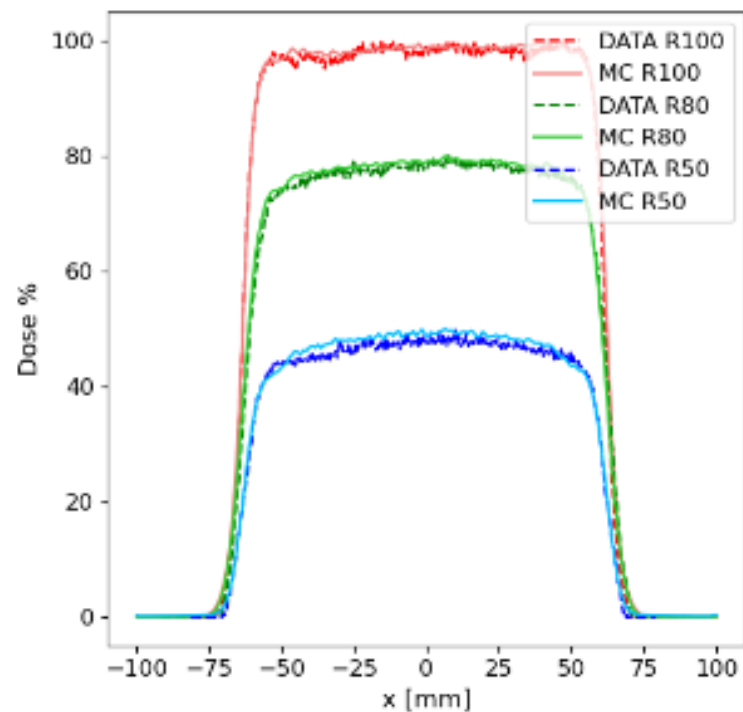
The Percent Depth Dose (PDD) and beam transverse profile were investigated using Gafchromics films at different depth in a poly-methyl methacrylate (PMMA) phantom (dashed-red curve)



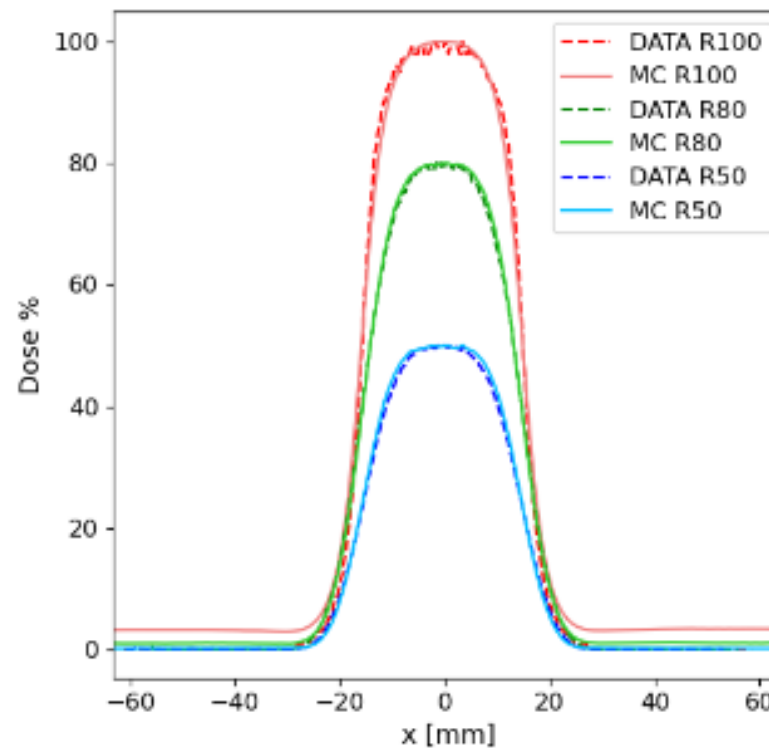
# TRAVERSE DOSE PROFILE AT 100% - 80 % and 50 % of the PDD (7MeV)



Applicator 120 mm

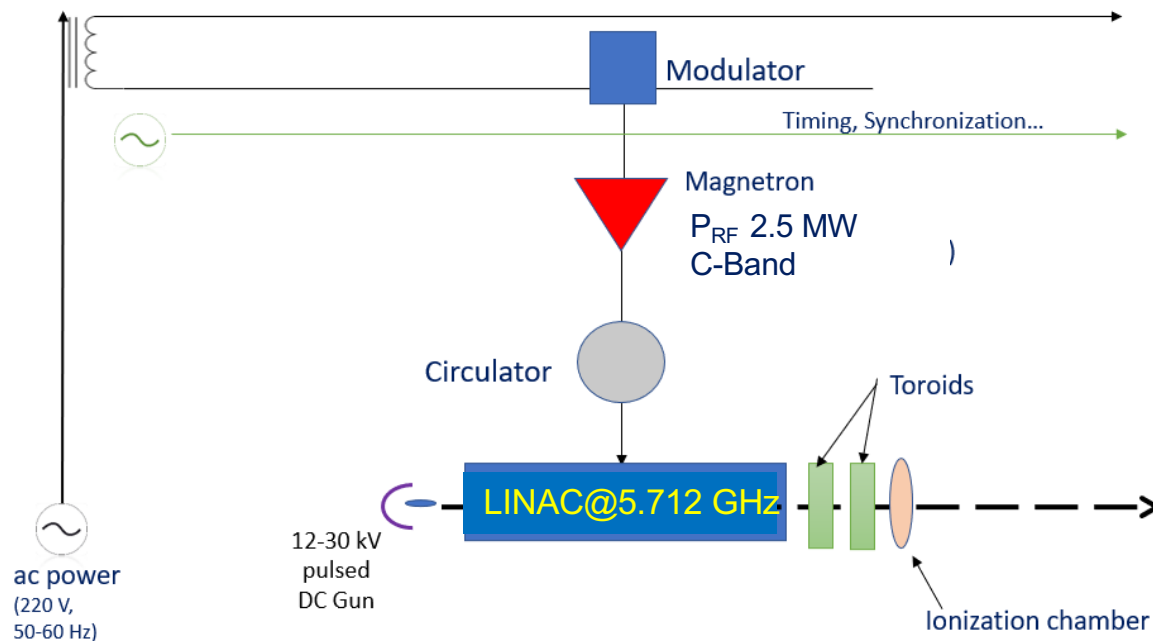


Applicator 30 mm



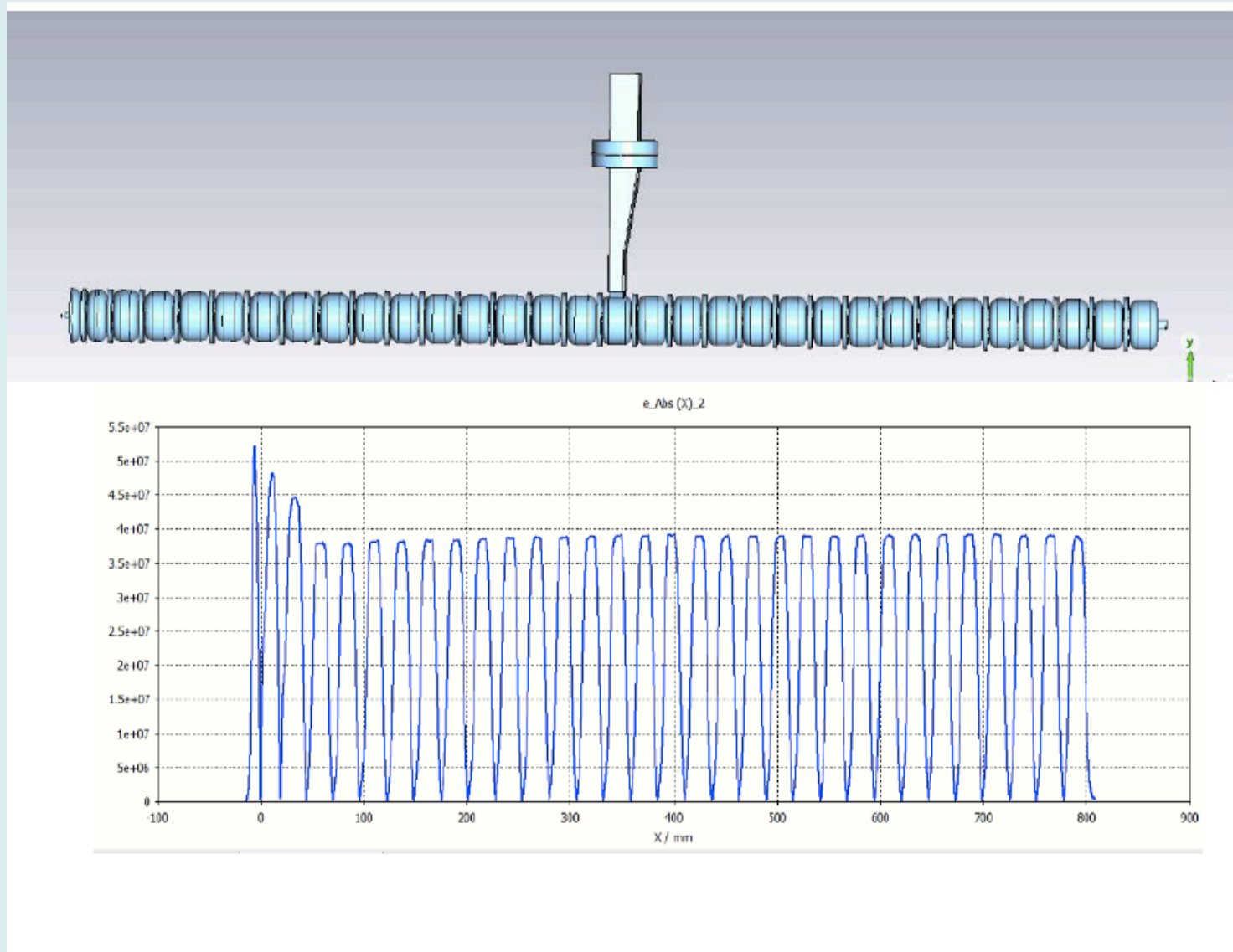


## 2. C-Band Linac 12 MeV, for Flash-RT (SIT Company)

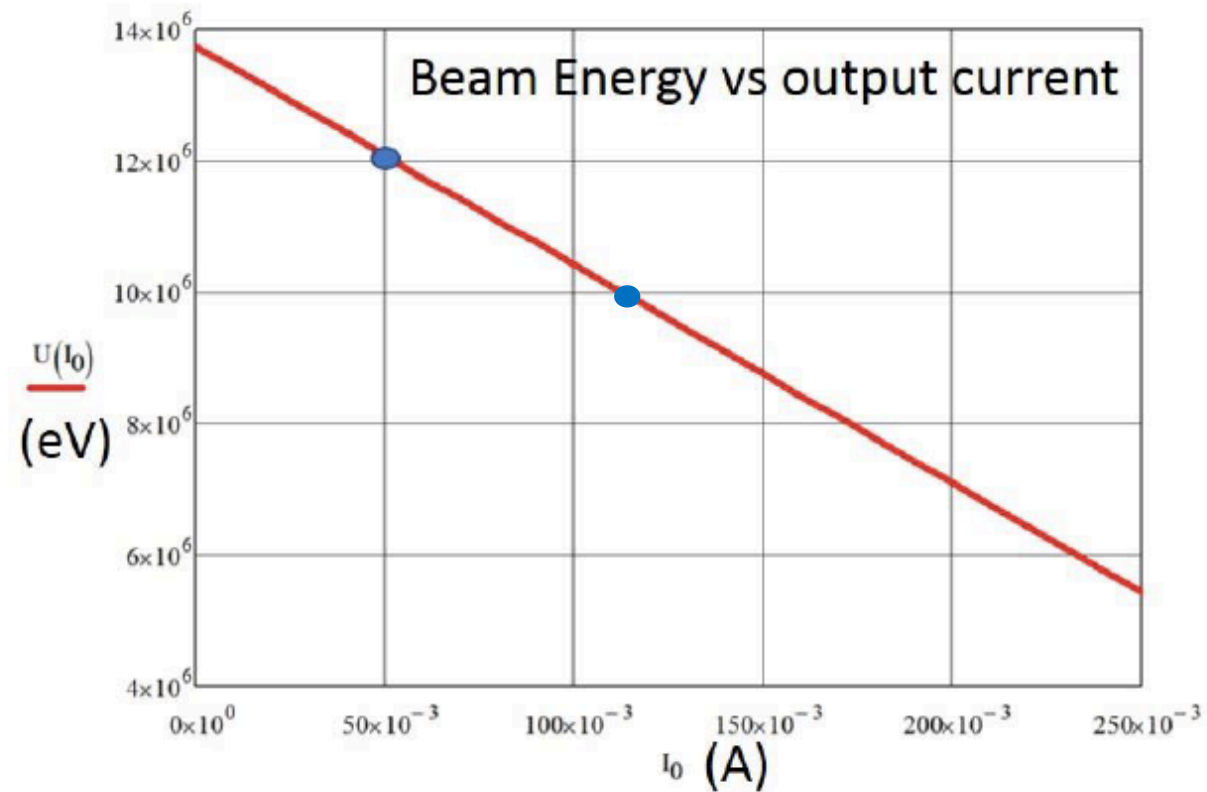


Parameter	Value
Frequency	5.712 GHz
Magnetron Power	2.5 MW
Number of accelerating cells	32
Linac length	~82 cm
Output Energy	12 MeV
Output Beam Current	50 mA

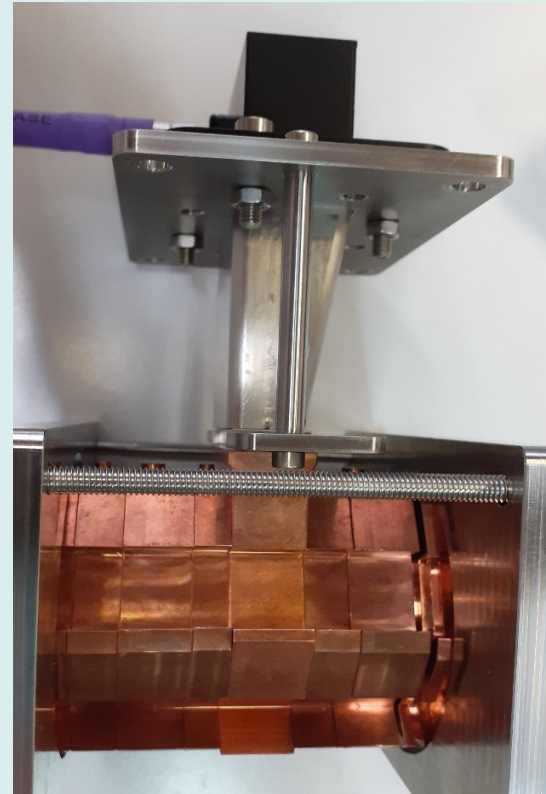
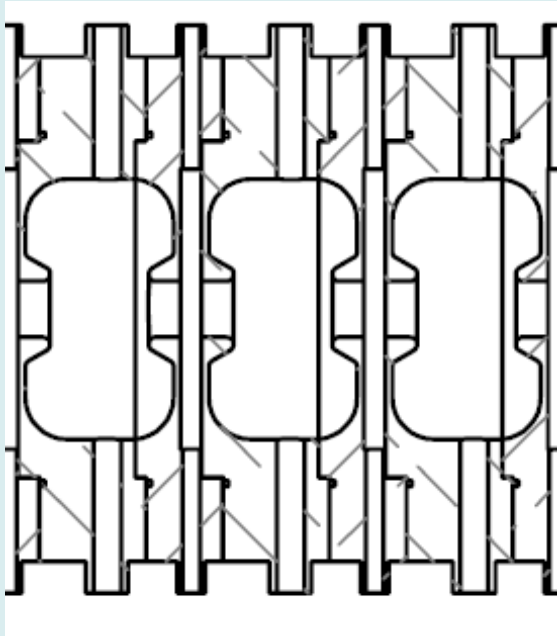
## 3D MODEL AND ON AXIS ELECTRIC FIELD



## ENERGY vs CURRENT

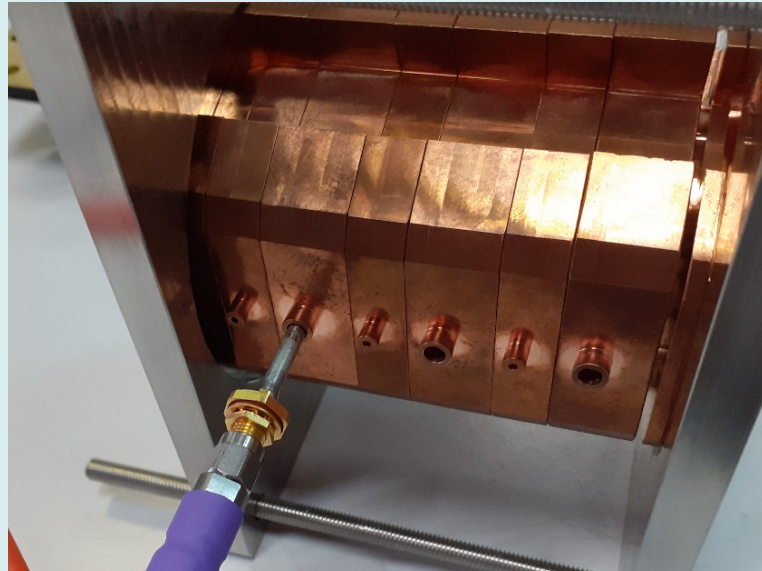


## ACCELERATOR CELLS PROTOTYPING



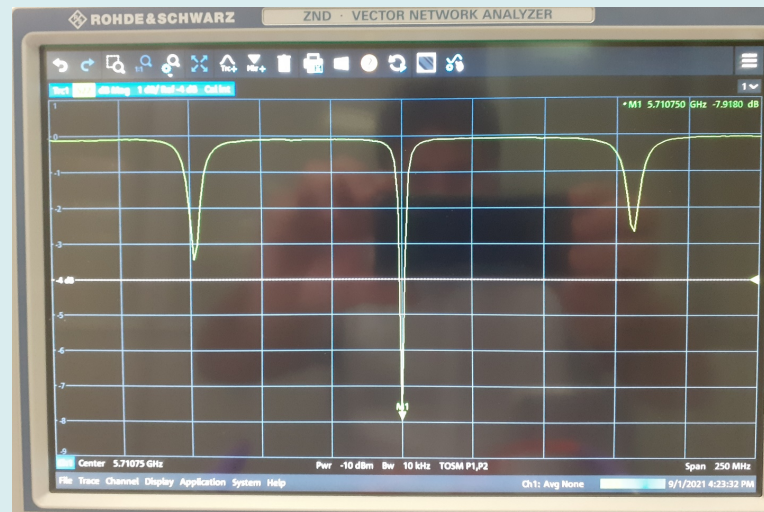
*Courtesy SIT company*





## FIRST TESTS

*Courtesy SIT company*



### 3. C-Band Linac 50-130 MeV, (VHEE)

To treat deep tumors the electron energy must be increased.  
Never introduced such VHEE in clinical RT till now!

The electron beams with  $E > 50$  MeV are suitable to this scope.

Standard LINACs can easily provide the needed beam:  
transverse spot size of  $\sim$  mm and angular divergence below  
tenth of degree.

Very High Energy Electron Radiotherapy Workshop (VHEE'2020)

5-7 October 2020  
CERN  
Europe/Zurich timezone

Search...

Overview

Timetable

Contribution List

Registration

Scientific Advisory Committee

Local Organising Committee

Videoconference instructions

VHEE 2017

CLIC Project Office  
✉ [clic.project.office@cern.ch](mailto:clic.project.office@cern.ch)



VHEE2020  
5-7 October 2020

Establishing innovative treatment modalities for cancer is a major 21st century health challenge. Although accelerated electrons are widely used to generate X-rays for radiotherapy, electrons are less frequently used directly because low energy electrons have limited penetration range and are mostly for the treatment of superficial tumours and thus limiting their clinical applicability.

The discovery of FLASH effect and the technology innovation in accelerator physics are fostering interest and activities on VHEE-Flash-RT





# SAPIENZA & INFN EFFORT for VHEE-FLASH-RT

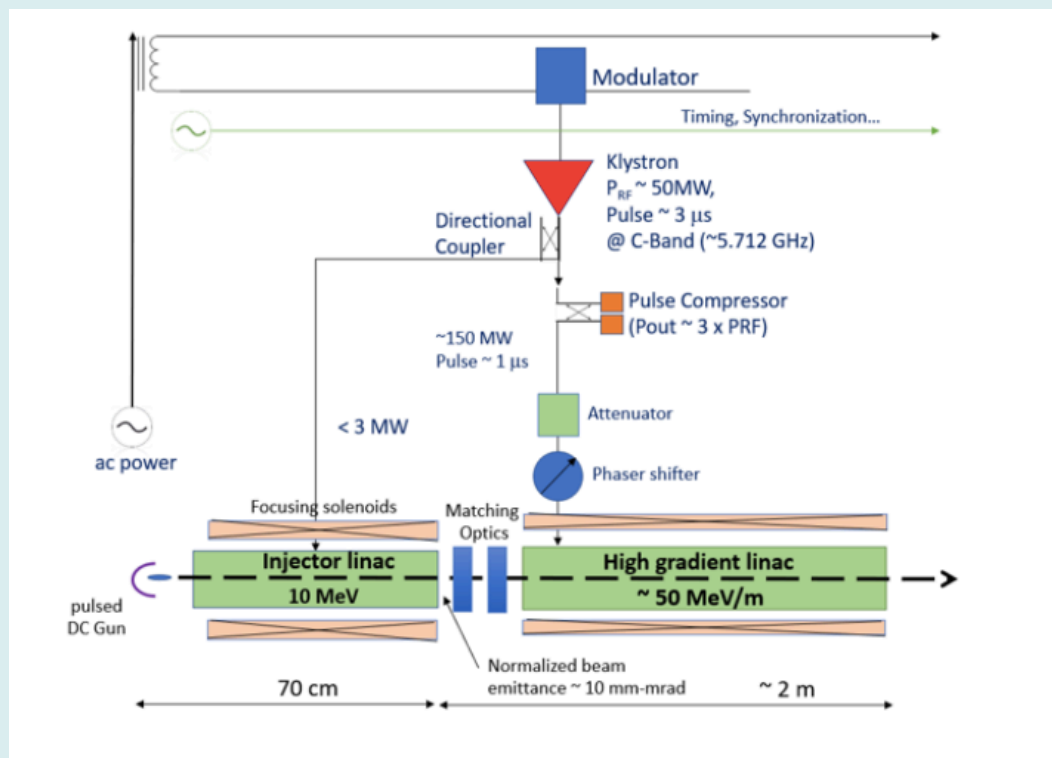


Table 5: Dose parameters for VHEE FLASH LINAC

Parameter	Value
Beam energy	100 – 60 MeV
Pulse width	1.0 – 3.0 μs
Pulse charges	200 – 600 nC
$\frac{D_p}{\dot{D}}$	4 – 12 Gy in Ø10 cm
$\frac{\dot{D}}{D_p}$	> 100 Gy/s
$\frac{\dot{D}_p}{D_p}$	> 10 <sup>6</sup> Gy/s

## PRELIMINARY STUDY OF A COMPACT LINAC VHEE-FLASH 60-100 MeV (Sapienza, INFN & CURIE)

### PRELIMINARY STUDIES OF A COMPACT VHEE LINEAR ACCELERATOR SYSTEM FOR FLASH RADIOTHERAPY

L. Giuliano <sup>\*1,2</sup>, D. Alesini<sup>3</sup>, M. Behtouei<sup>3</sup>, F. Bosco<sup>1,2</sup>, M. Carillo<sup>1,2</sup>, G. Cuttone<sup>4</sup>  
D. De Arcangelis<sup>1,2</sup>, V. Favaudon<sup>5</sup>, L. Ficcadenti<sup>1,2</sup>, S. Heinrich<sup>5</sup>, M. Migliorati<sup>1,2</sup>, A. Mostacci<sup>1,2</sup>  
L. Palumbo<sup>1,2</sup>, A. Patriarca <sup>5</sup>, B. Spataro <sup>3</sup>, G. Torrisi<sup>4</sup>, L. Faillace<sup>1,3</sup>

<sup>1</sup>Sapienza University, Rome, Italy

<sup>2</sup>INFN/Roma1, Rome, Italy

<sup>3</sup>INFN/LNF, Frascati, Italy

<sup>4</sup>INFN/LNS, Catania, Italy

<sup>5</sup>Curie Institute, Orsay, France

IPAC Conference, May 2021



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# INFN FRIDA: FLASH Radiotherapy with high Dose-rate particle beams

*A community of 80 researchers distributed in 7 INFN sections & Labs: CT, LNS, Milano, Pisa, Roma1, TIFPA, Torino.*

- CT: Amato, Bartolotta, Borgese, D'Oca, Italiano, Marrale, Romano, Tomarchio (3.8 FTE)
- LNS: Bravatà, Calvaruso, Cammarata, Catalano, Cirrone, Cuttone, Forte, Guarrera, Mauro, Ficarra, Milluzzo, Minafra, Petringa, Russo, Sorbello, Torrisi (FTE: 4.7)
- Milano: Bortolussi - Bacci - Dong - Drebot - Giove - Mattei - Muraro - Massa - Mattei - Mettiver - Russo - Sarnu - Serafini (2 FTE)
- Pisa: Belcari, Bisogni, Costa, Del Sarto, Di Martino, Gizzi, Kraan, Labate, Marasciulli, Morrocchi, Paiar, Rosso, Sportelli, Stretto, Ursino, Vannini, Zancacchi (2.8 FTE)
- Roma1: Faillace, Ficcadenti, Franciosini, Giuliano, Marafini, Migliorati, Mostacci, Palumbo, Patera, Sarti, Schiavi, Toppi, Traini, Trigilio (2.5 FTE)
- TIFPA: Attili, Bellinzona, Bisio, Boscolo, Cordoni, Croci, Fuss, Manghi, La Tessa, Scifoni, Schwarz, Tommasino (4.0 FTE)
- Torino : Abujami, Aprà, Cirio, Martì Villarreal, Monti, Picollo, Vignati (4.3 FTE)





# INFN FRIDA project

**FRIDA is interdisciplinary project addressing crucial areas related with FLASH therapy.**

**4 work-packages:**

- ✓ **mechanism modelling & radio-biology experiments;**
  - ✓ **beam delivery techniques (VHEE);**
  - ✓ **Detectors for beam monitoring;**
  - ✓ **treatment planning development**
- ✓ **Explore the time scales at which the FLASH effect occurs**
  - ✓ **Develop compact, high intensity sources and delivery solutions for EBRT with e and p**
  - ✓ **Explore novel detection strategies both for dosimetry and beam monitoring applications**
  - ✓ **Explore clinical potential of FLASH EBRT**

**Budget ~1 ME, Project Approved - 2022/2024**



# A study case: prostate cancer

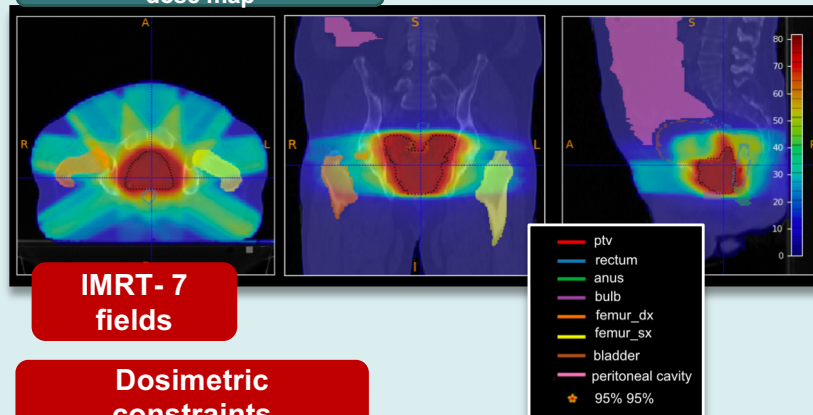
IMRT

PROTONS

VHEE

RESULTS

Pinnacle TPS optimized dose map



IMRT- 7 fields

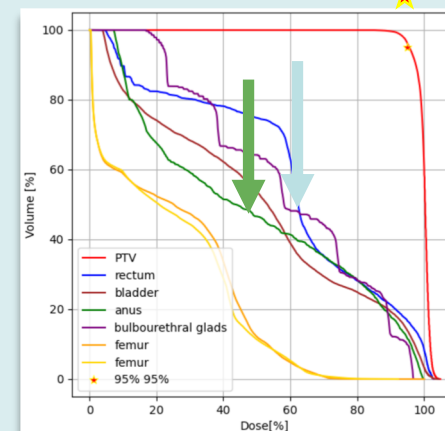
Dosimetric constraints

Organ	dosimetric constraints			
Target volume	V <sub>95%</sub> > 95% never above 107%			
Rectum	V <sub>50</sub> < 50%	V <sub>60</sub> < 35%	V <sub>65</sub> < 25%	V <sub>70</sub> < 20%, V <sub>75</sub> < 15%
Anus	V <sub>30</sub> < 50%			
Bulbourethral Glands	D < 50 Gy			
Femurs	D̄ < 52 Gy, V <sub>60</sub> < 5%			
Bladder	D̄ < 65 Gy, V <sub>65</sub> < 50%, V <sub>70</sub> < 35%, V <sub>75</sub> < 25%, V <sub>80</sub> < 15%			

$V_{xx} < YY\%$ : YY% of the referred organ or region must absorb less than XX Gy  
D is the mean dose absorbed by a given organ

Real IMRT prostate treatment at Policlinico Umberto I hospital, Rome

- Patient with intermediate-risk prostate cancer, was treated with conventionally fractionated IMRT of **78 Gy in 39 fractions**;
- **7 photons fields** (6 MV-ONCOR Linear Accelerator);



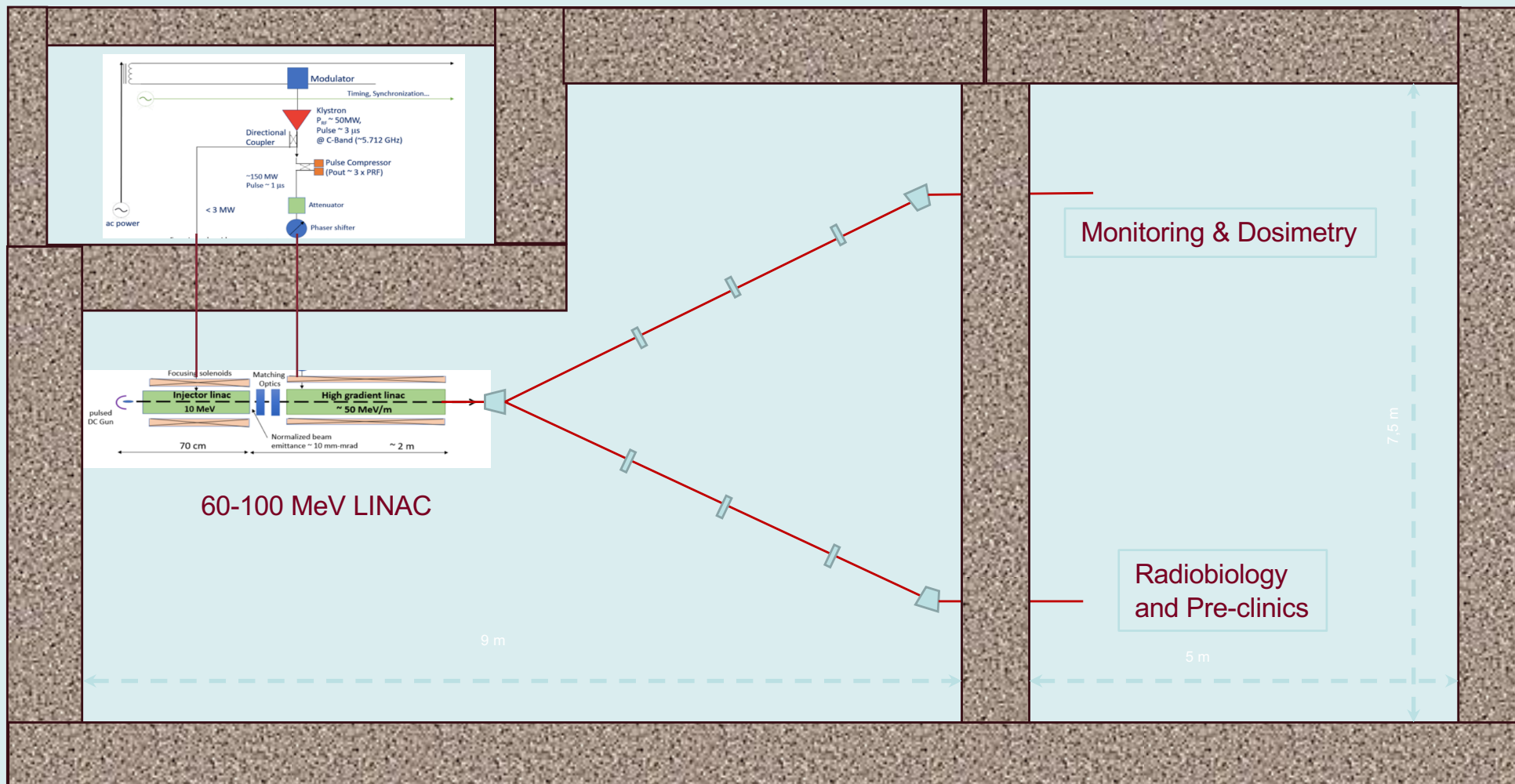
Dose Volume Histograms (DVH)

**SAFEST project**  
**(SapienzaA InFn Electron flaSh facility)**  
**MOU SAPIENZA-INFN (November 2021)**



# VHEE-LINAC- FLASH RT Research Laboratory (Concept)

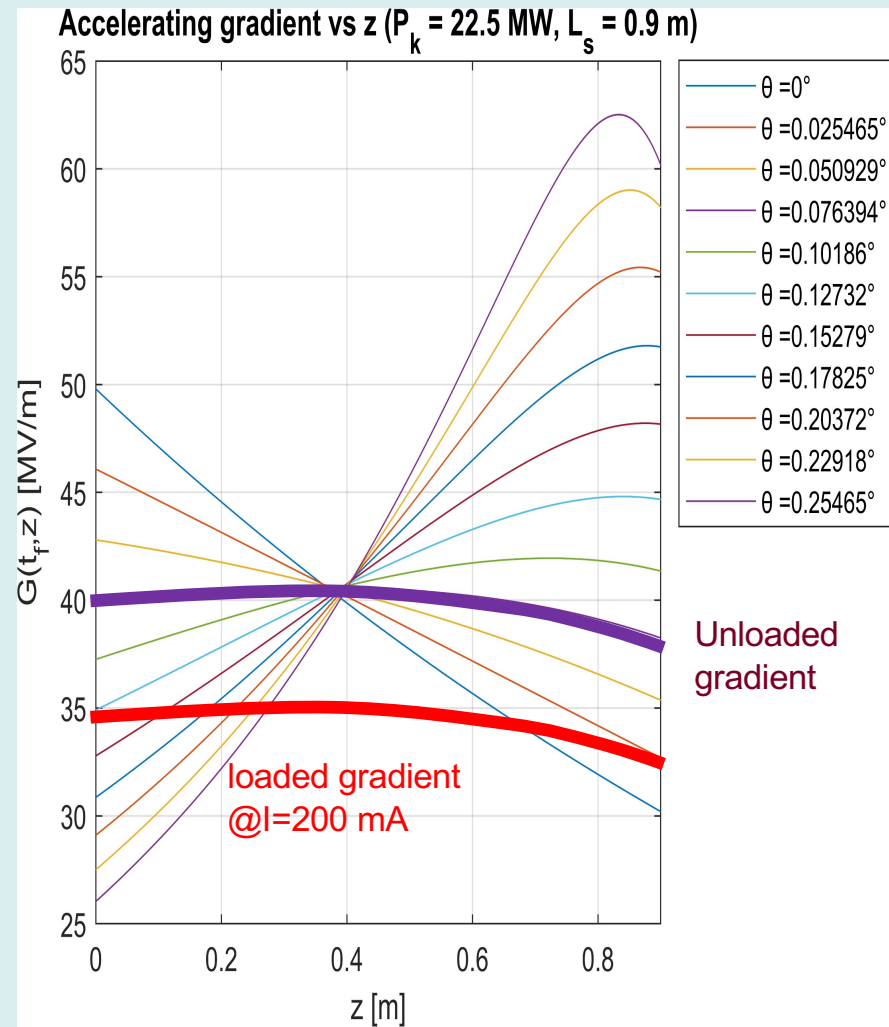
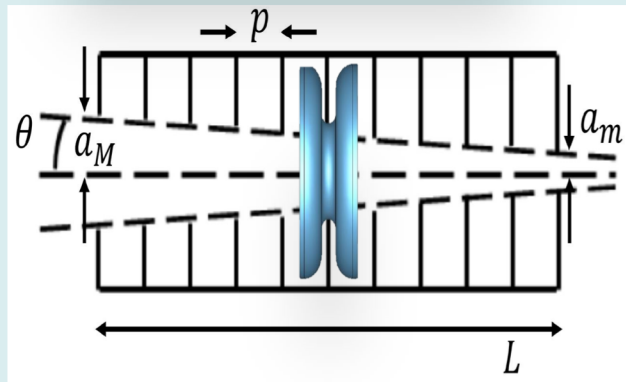
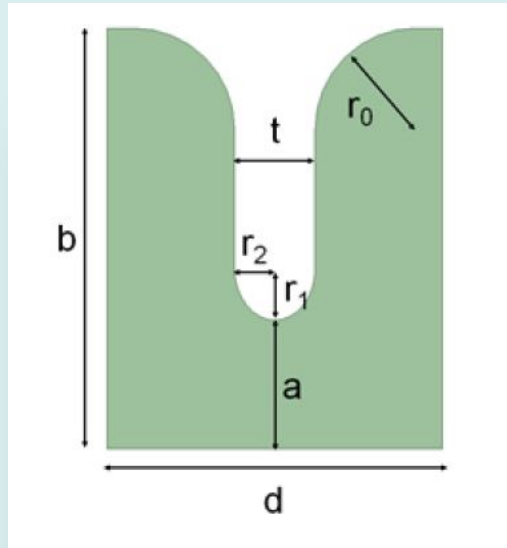
Proposed installation site at La Sapienza



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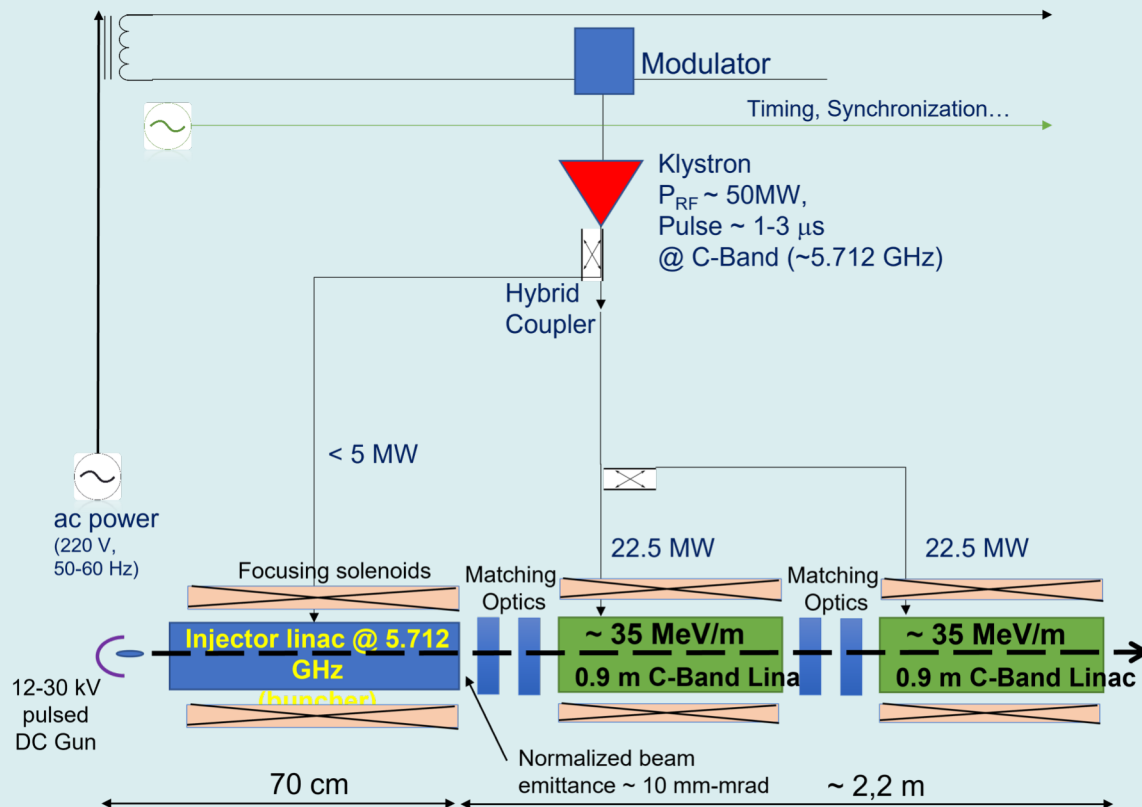


# HIGH GRADIENT STRUCTURE STUDIES



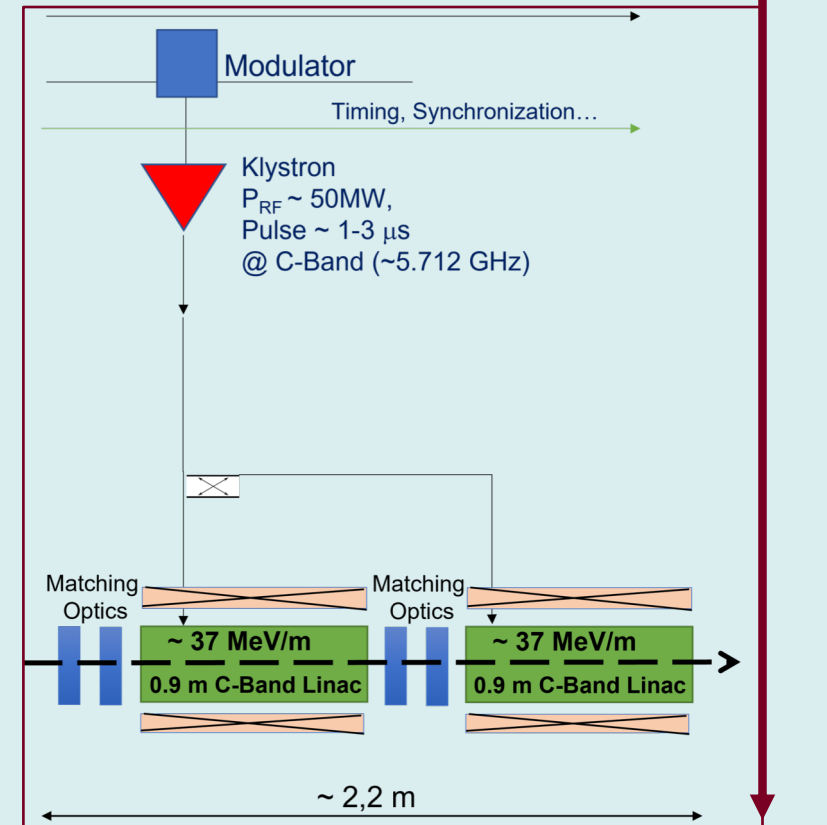
# LINAC VHEE – Phase 1

## Modular layout



60-70 MeV

# Phase 2



120-130 MeV



## ***Electron Beam Parameters with VHEE Linac to investigate FLASH effect***

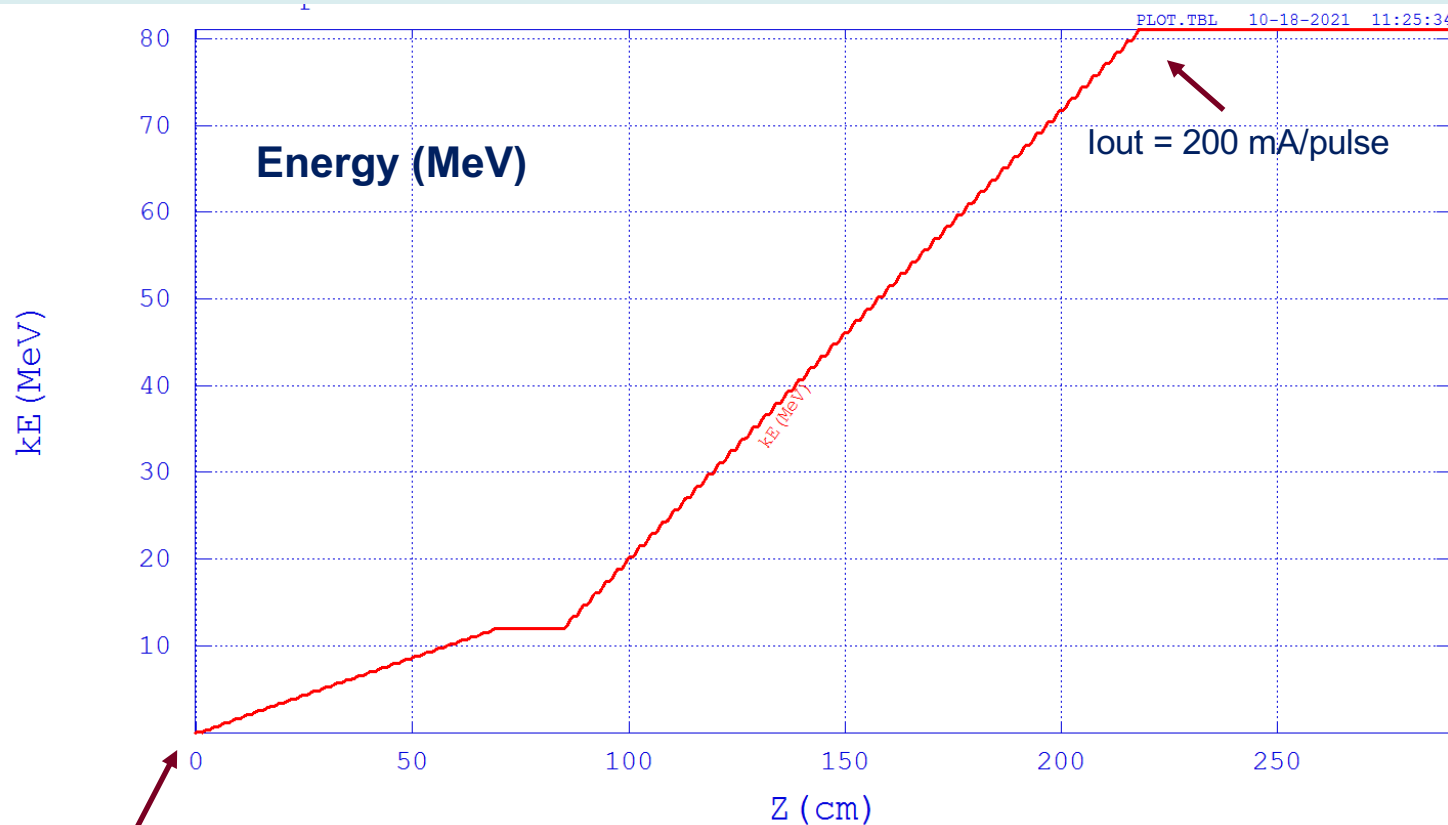
<i>Symbol</i>	Description	Value
<i>E</i>	Beam Energy	60 – 100 – 130 MeV
<i>PRF</i>	Pulse repetition frequency	> 100 Hz
<i>t<sub>p</sub></i>	Pulse width	1 - 3 μs
<i>Q<sub>p</sub></i>	Pulse Charge	200 – 600 nC (higher?)
<i>I<sub>p</sub></i>	Pulse Current	200 mA (higher?)





## Beam Dynamics

**80 MeV** and **200 mA** output e-beam  
Preliminary Results



Input current = 600 mA

Output current = 200 mA

Pulse Length = 3  $\mu\text{s}$

$I_{inj} = 600 \text{ mA}$   
Energy = 15 keV

- Wake-fields effects and BBU study are in progress!

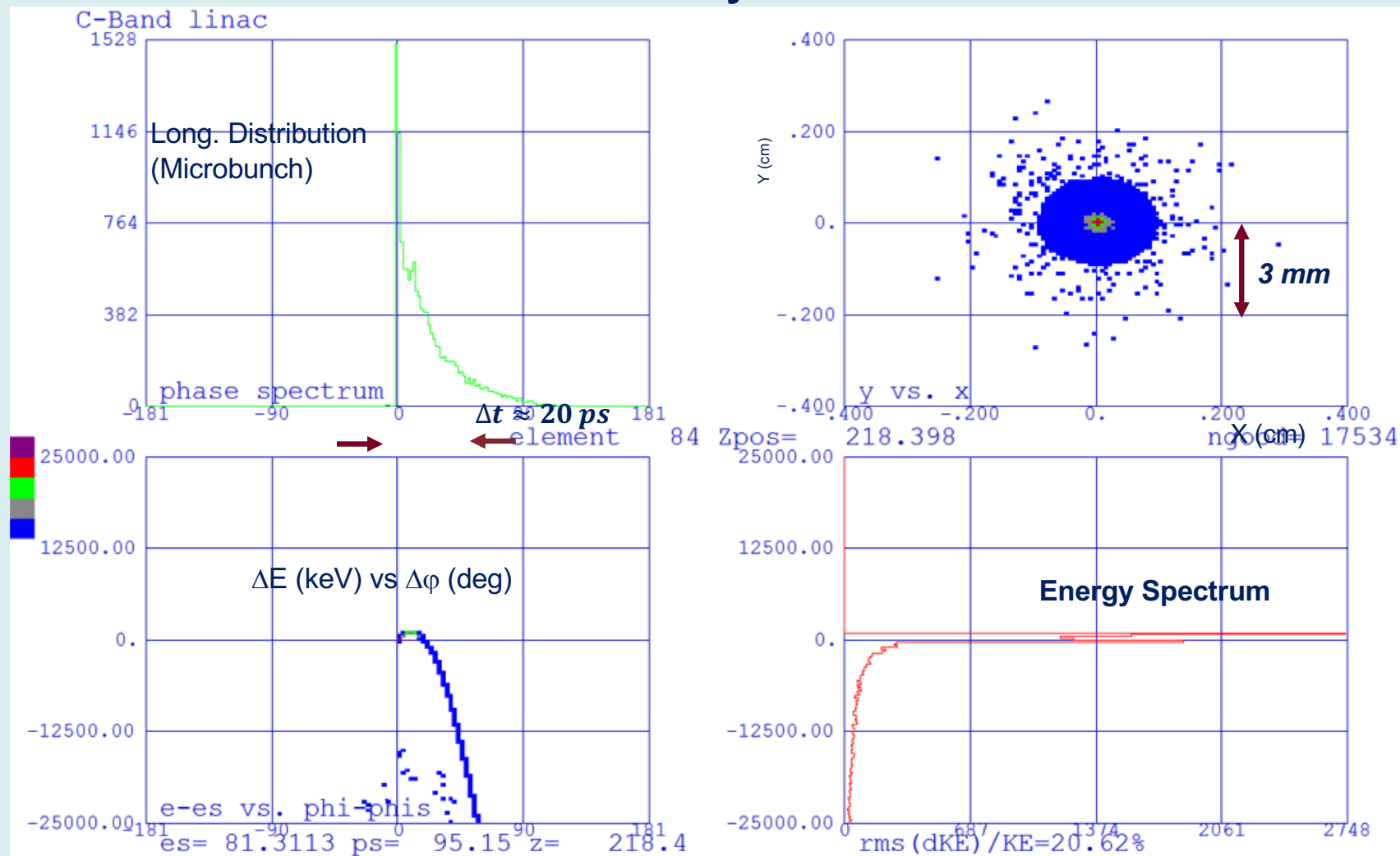


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# Output Phase-Space (Electron beam) Preliminary Results



a) the longitudinal phase distribution in degrees; b) the beam transverse spot size in cm; c) the beam longitudinal phase-space (energy vs. phase); d) the beam energy spectrum in keV

# **NATIONAL RESEARCH INFRASTRUCTURE**

**EU Recovery and Resilience Facility  
National PNRR Funds**

36



# CONCLUSIONS

- FLASH-RT WITH ELECTRON IS A REVOLUTIONARY PROMISING NEW TECHNIQUE
- THERE IS AN EXPONENTIALLY GROWING RESEARCH ON RADIOBIOLOGY
- MORE CLINIC RESEARCH CENTERS ARE BEING INVOLVED
- THERE IS STRONG INDUSTRIAL INTEREST DUE TO A POTENTIAL HUGE MARKET
- KNOW-HOW IS AVAILABLE IN ITALY (UNIVERSITIES AND RESEARCH INSTITUTES)
- A FIRST S-BAND 5-7 MeV FLASH LINAC HAS BEEN DEVELOPED FOR SIT COMPANY
- SECOND PROTOTYPE C-BAND 12 MeV IS IN CONSTRUCTION
- FLASH-RT OPENS NEW OPPORTUNITIES TO THE CURE OF DEEP TUMORS
- MonteCarlo STUDIES CONFIRM THE ADVANTAGES OF FLASH-VHEE vs CONVENTIONAL TRATMENTS.
- A LARGE COMMUNITY OF RESEARCHERS IS PROPOSING RESEARCH PROJECTS (INFN-FRISA)
- SAFEST PROJECT: A JOINT GROUP SAPIENZA-INFN IS BEING DEVELOPING A FEASIBILITY STUDY OF A VHEE FLASH-LINAC AT THE ENERGY 50-130 MeV (MOU November 2021)



**THANK YOU**



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