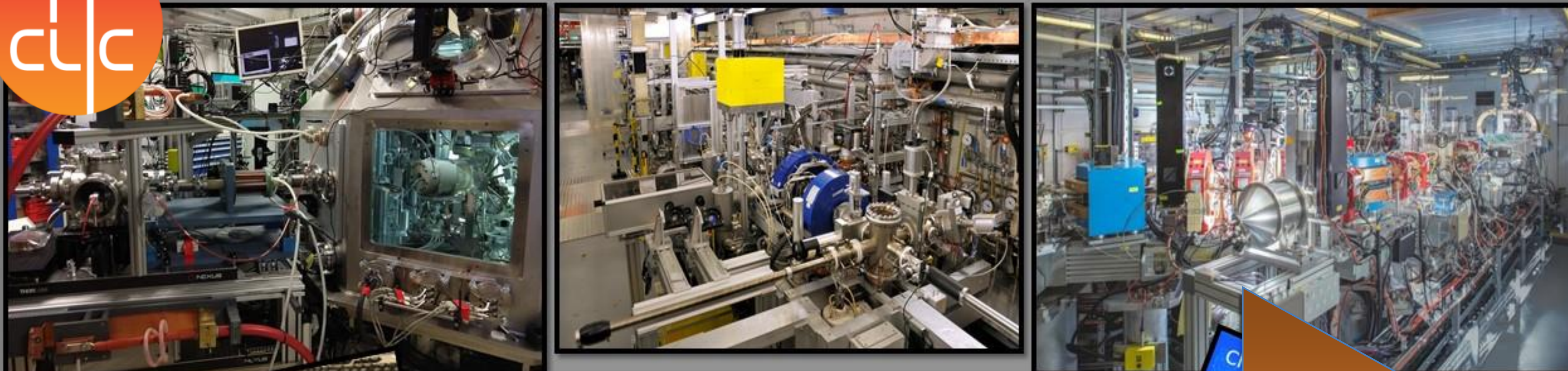
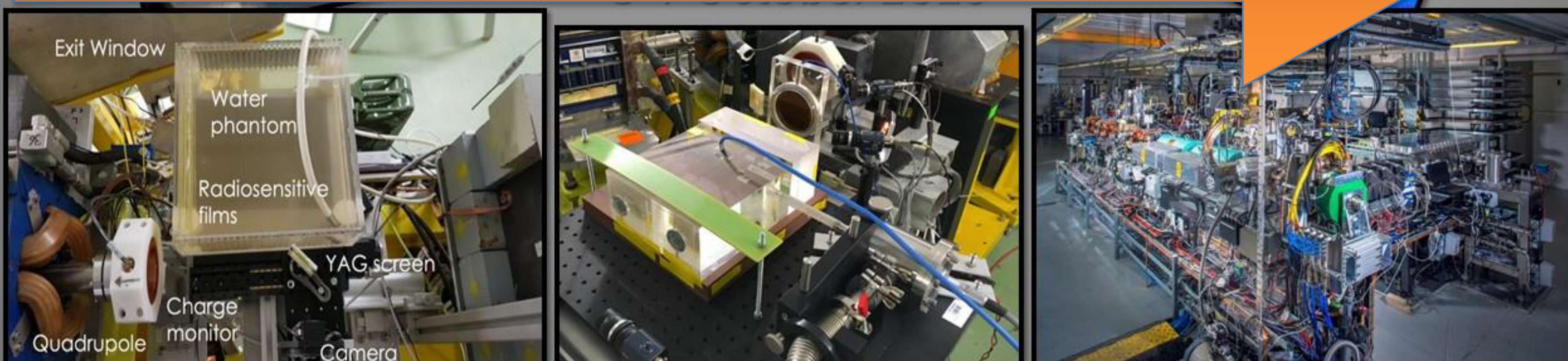
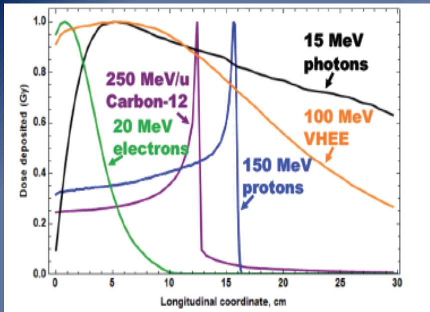


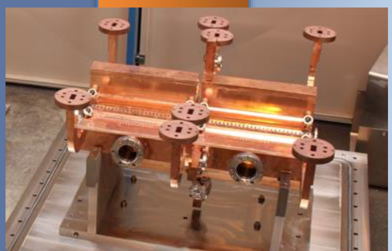
VHEE with High-Gradient linacs

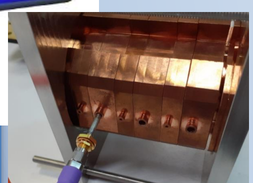


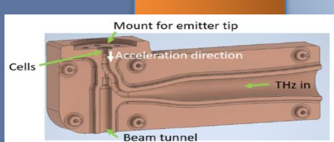
Dr. A. Faus-Golfe



Dose profiles for various particle beams in water (beam widths $r = 0.5$ cm)







OUTLINE

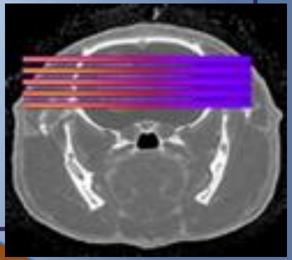
- ***The Challenges of Radiotherapy***
  - *New RT approaches*
    - *VHEE RT*
    - *New delivery doses modalities: FLASH*
- ***Facilities for VHEE R&D***
- ***Technologies for VHEE: HG linacs***
- ***Summary and Future perspectives***

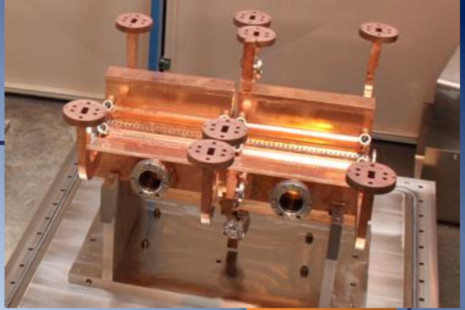
CHALLENGES IN RADIOTHERAPY

New RT approaches

- ***RT treatment of some radio resistant tumours, paediatric cancers and tumours close to a delicate structure (i.e. spinal cord) is currently limited***
- **One of the main challenges is to find approaches to increase the normal tissue resistance**
- **Standard RT is restricted to the few temporal and spatial schemes, dose rates, broad field sizes: mainly photons, 2 Gy/session, 1 session/day, 5 days/week, dose rates ~ 2 Gy/min, field sizes > cm^2, homogeneous dose distributions**

- ***Possible strategies to spare normal tissue***
- **Different particle types: Very High Energy Electrons (VHEE)**
- **Different dose delivery methods: Grid Mini-beam or FLASH RT**

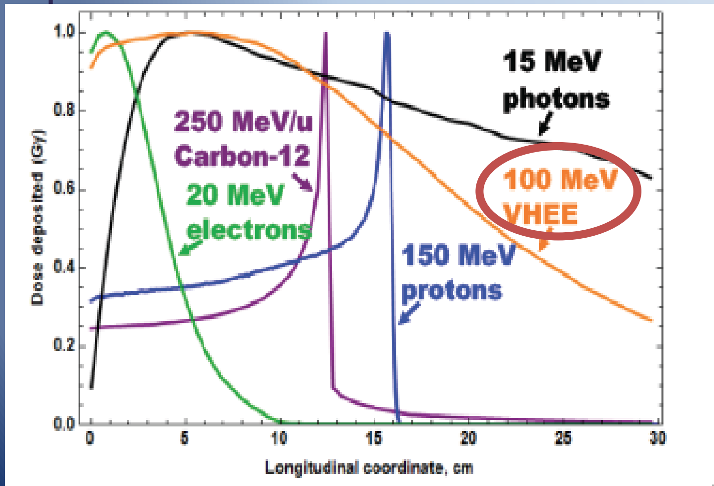




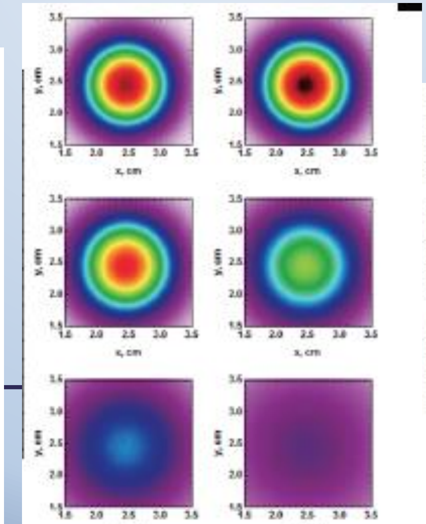
VHEE THERAPY

State of the Art

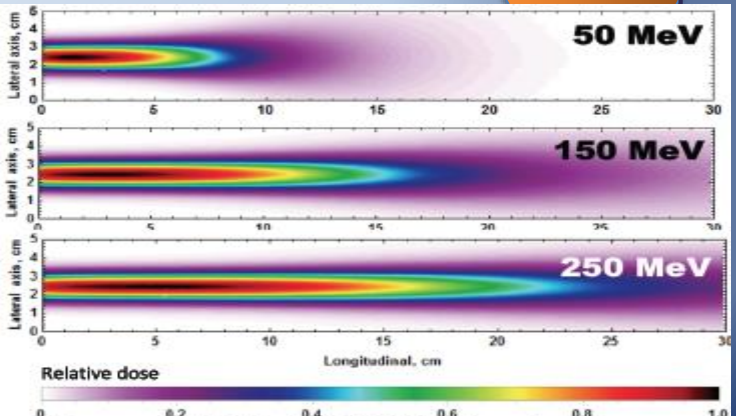
- With recent High-Gradient linac technology developments, Very High Energy Electrons (VHEE) in the range 100–250 MeV offer the promise to be a cost-effective option in anticancer RT and open up innovative treatment modalities (Grid mini-beam, FLASH,..)
- Their ballistic and dosimetric properties can surpass those of photons, which are currently the most commonly used in RT
- Their position compared to protons need to be evaluated, but they can be produced at a reduced cost



Dose profiles for various particle beams in water (beam widths r = 0.5 cm)



Transverse dose maps at 0.5 – 25 cm depths



Dose maps of 50, 150 and 250 MeV VHEE beams in water

NEW DELIVERY DOSE MODALITIES

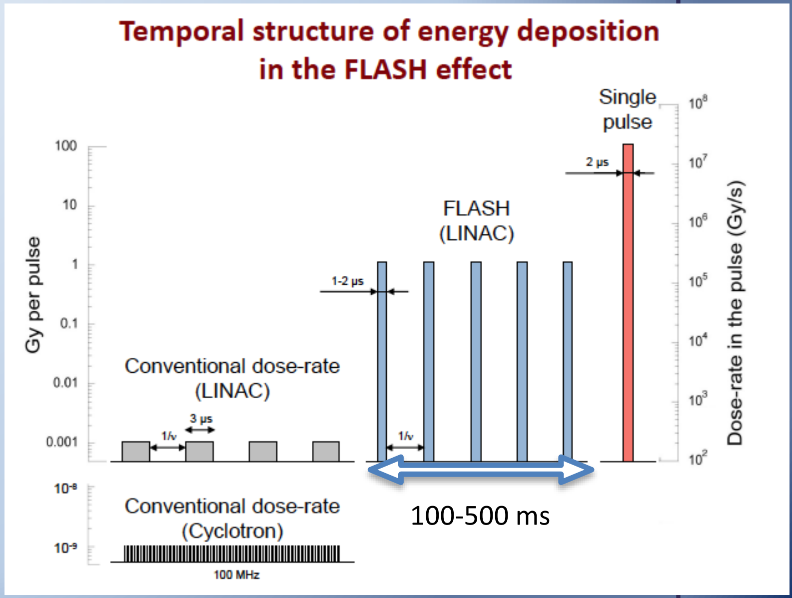
What is FLASH RT?

- New way of dose delivery consisting in ultra short irradiation time or “beam on time” (<500 ms) and very high-dose (60-200 Gy/s)

- No FLASH effect *in vitro* with clonogenic cell death as an endpoint *(Nias et al. Br J Radiol 42: 553, 1969).* The FLASH effect relates to normal, living tissue only.

- The beam-on time, not the dose-rate appears to be the major determinant of the FLASH effect

- Ultrahigh dose-rate pulses (e.g. 10^{13} Gy/s) will NOT provide a FLASH effect as long as the dose per pulse is low and the total length of radiation exposure exceeds 100-500 ms

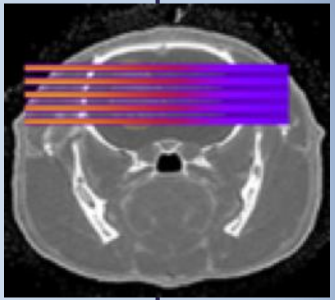


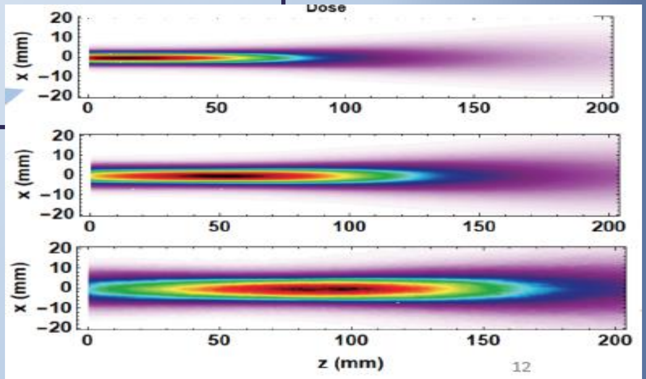
VHEE – FLASH Open questions:

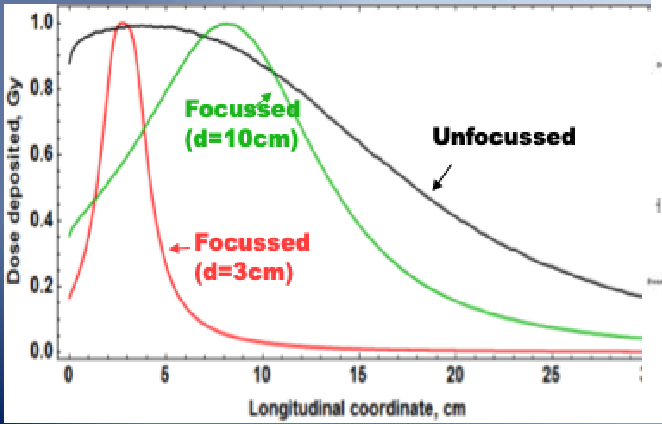
FLASH RT

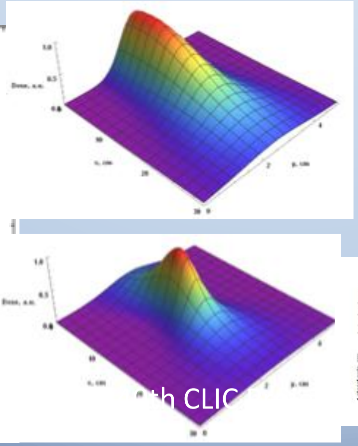
- What High-Energy ?
- Field sizes?
- Inhomogenities?
- Skin/Bone dose ?
- Penumbra?
- Neutrons ?
- Scanning small beams ?
- Focusing and Shaping?
- In vivo experiments for validate FLASH RT?
- Pulse structure impact in FLASH RT?
- ……

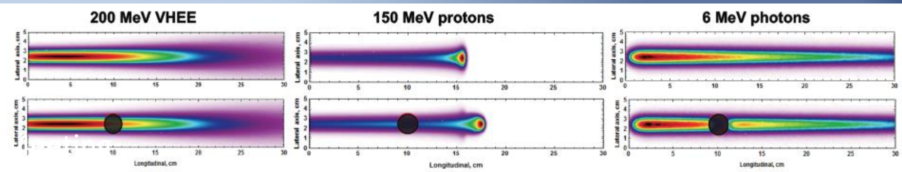
Mini-beams









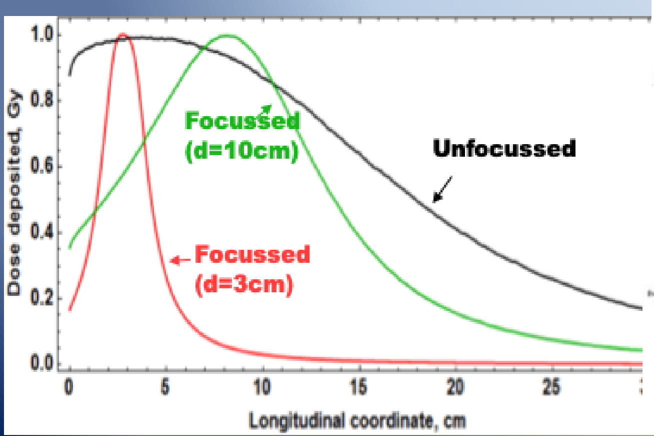


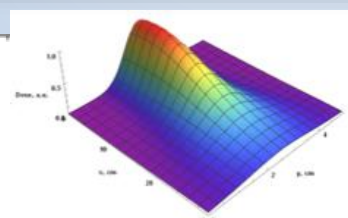
VHEE – FLASH Open questions:

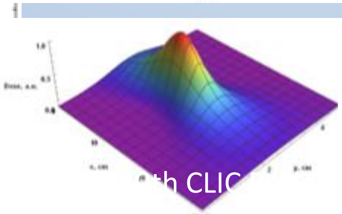
FLASH RT

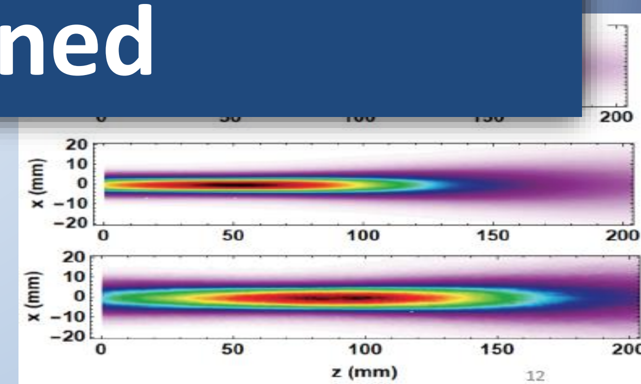
- What High-Energy ?
- Field sizes?
- Inhomogenities??
- Skin
- -Per
- -Ne
- Sca
- Focu
- In vi
- Puls
- ......

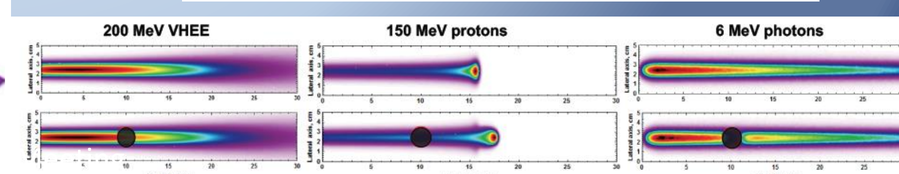
To answer these questions, a lot of experiments are being performed and new facilities are been designed

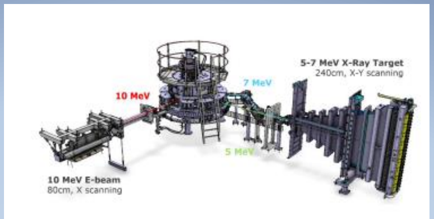












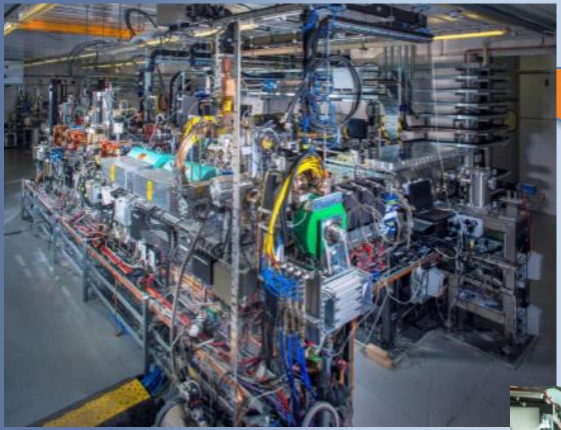
FEERIX/ AERIAL

FLASH IC

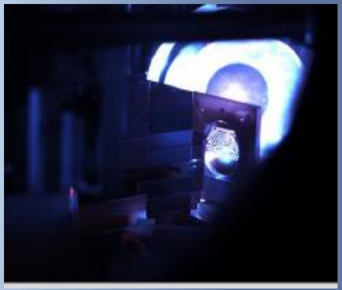
CLEAR CERN

ORIATRON CHUV

Operating Facilities



ELBE HZDR

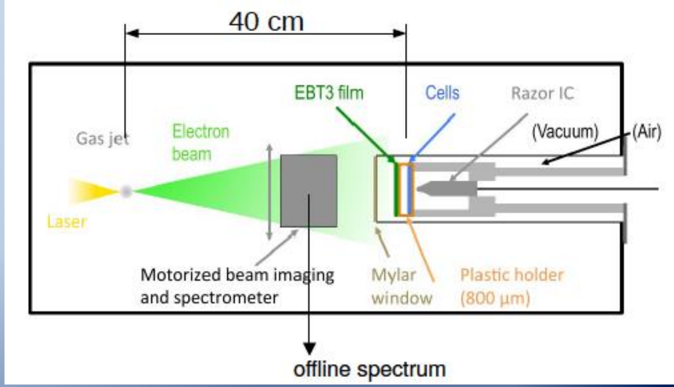


CLARA STFC CI

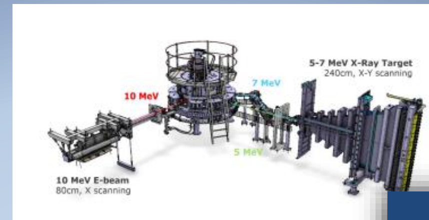
LOA Salle Noire IPP

PTB Berlin

AWA Argonne



CLEAR CERN

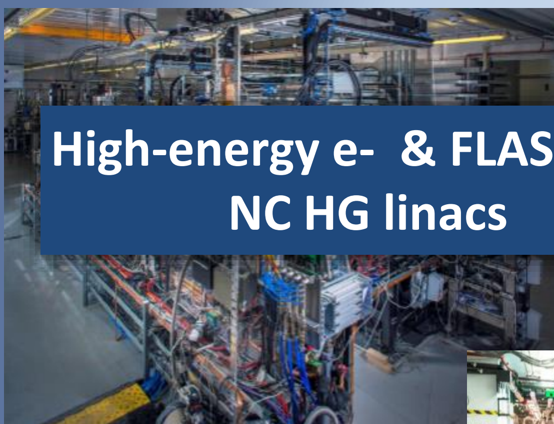


FEERIX/ AERIA

Low-energy e- & FLASH
Cyclos & linacs

FLASH IC

ORIATRON CHUV



High-energy e- & FLASH
NC HG linacs

Operating Facilities

ELBE HZDR

High-energy e- & FLASH
SC linacs

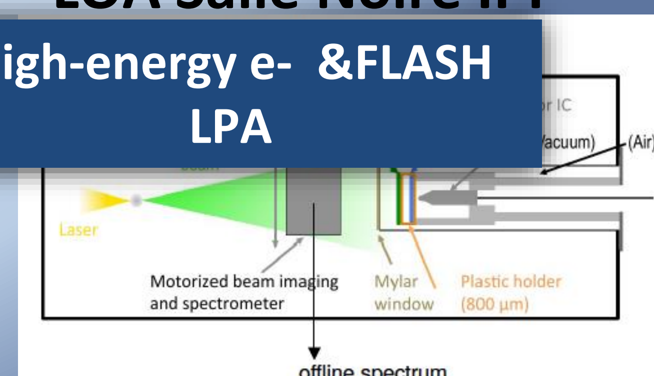
CLARA STFC CI

PTB Berlin

AWA Argonne

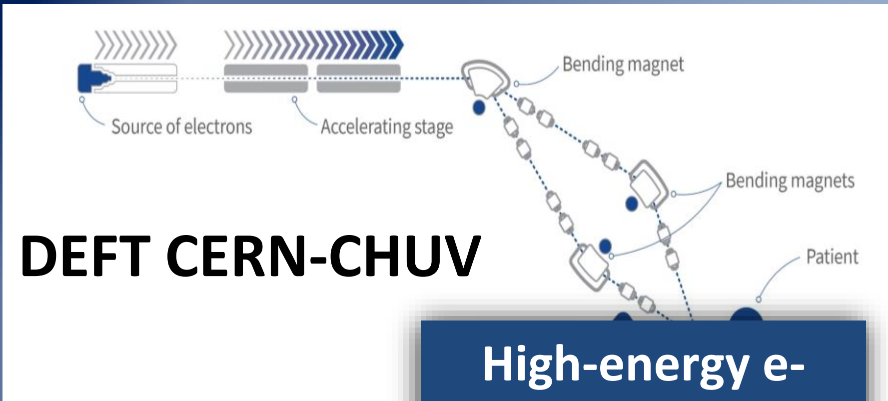
LOA Salle Noire IPP

High-energy e- &FLASH
LPA



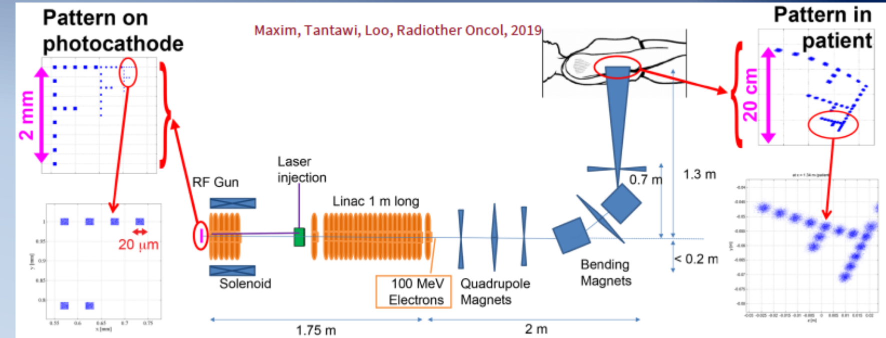
On design Facilities

DEFT CERN-CHUV

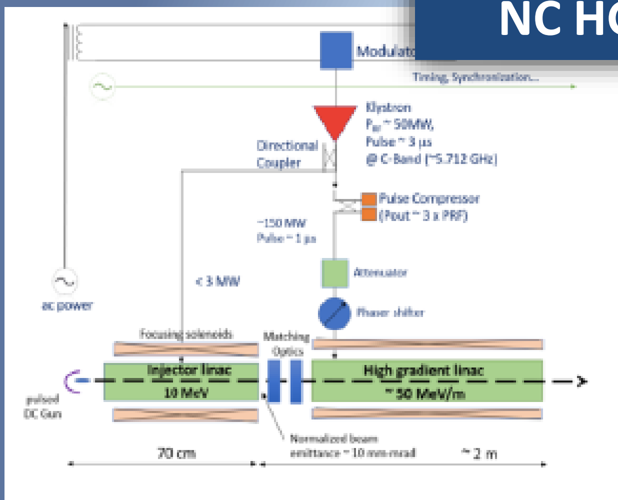


High-energy e- NC HG linacs

e-beam PHASER

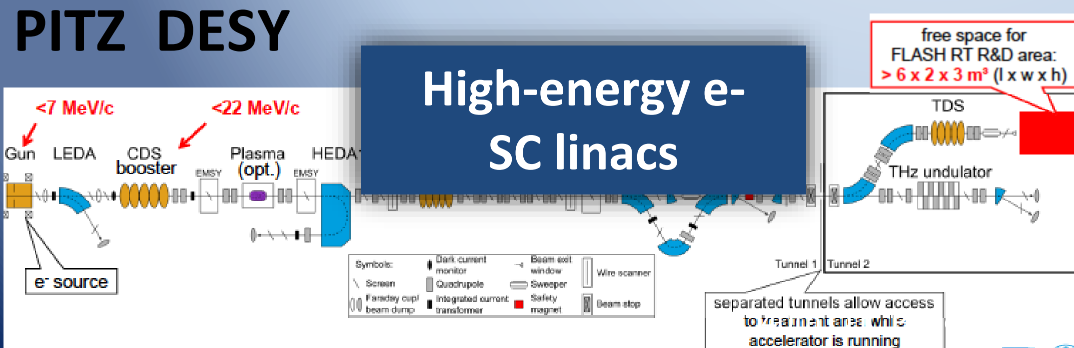


FRIDA Sapienza-INFN



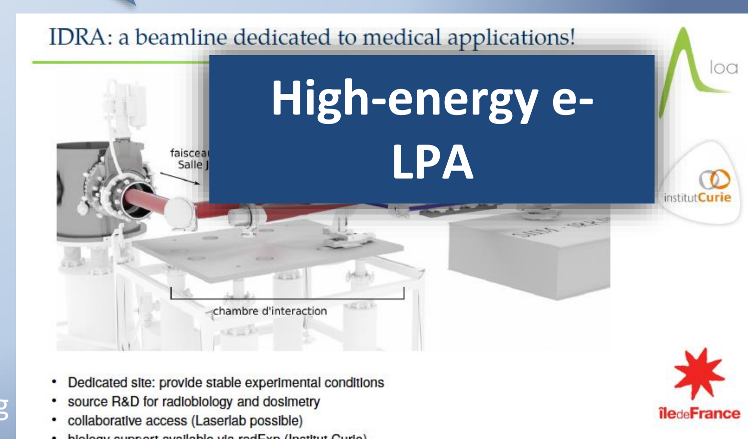
PITZ DESY

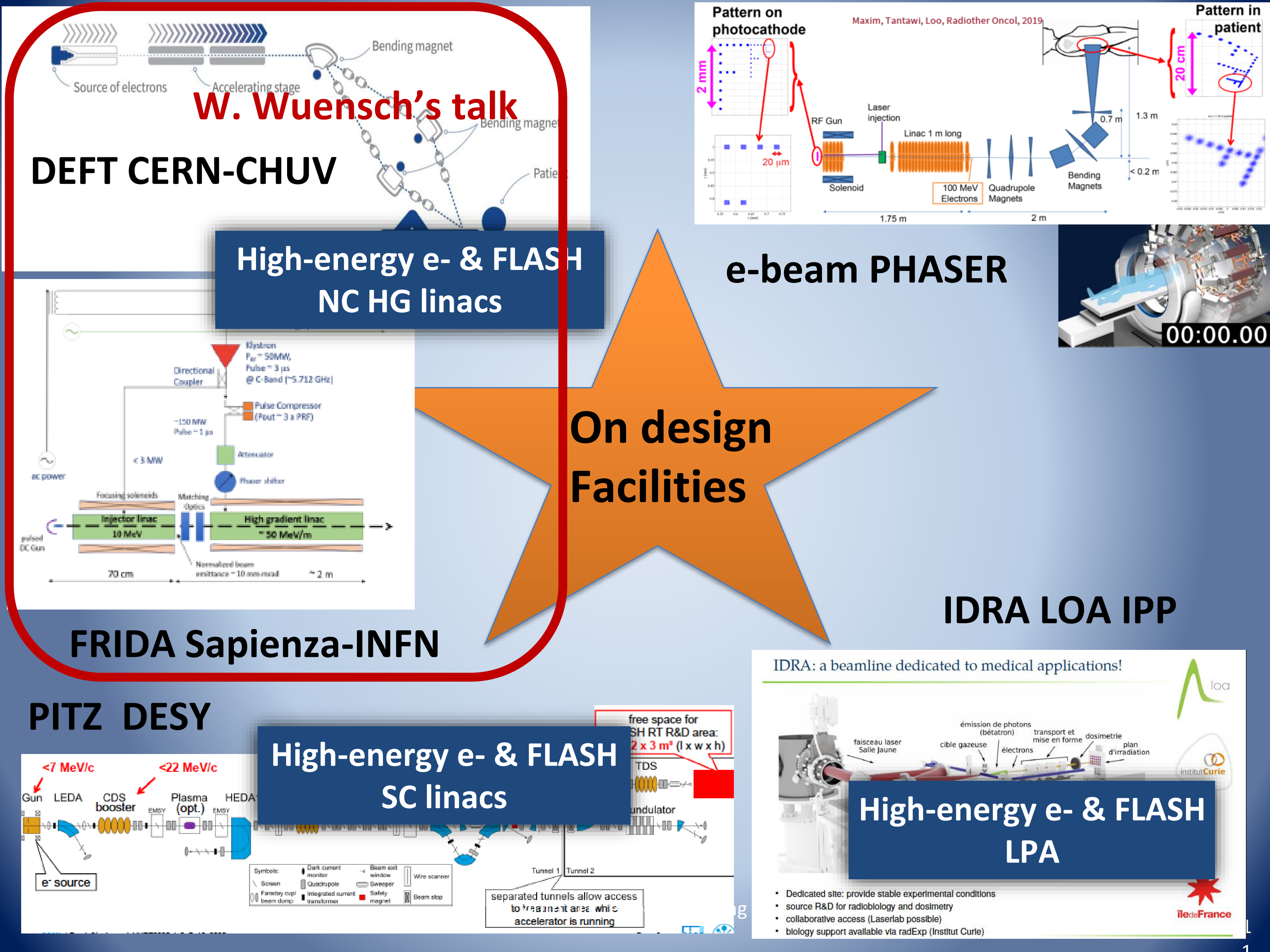
High-energy e- SC linacs



IDRA LOA IPP

High-energy e- LPA

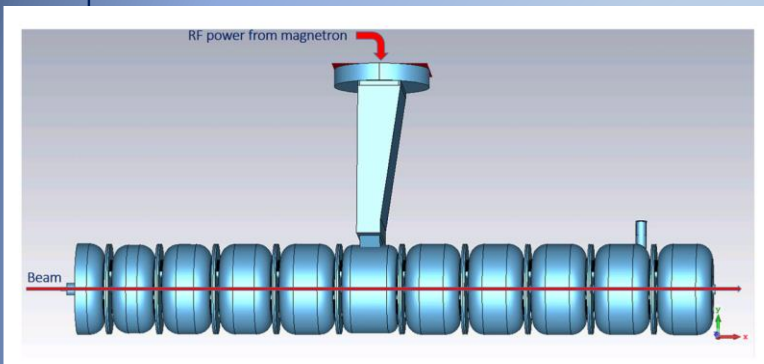




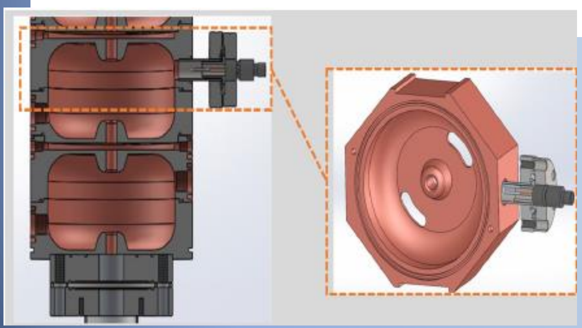
On design
Facilities
DEFT CERN-CHUV
W. Wuensch's talk
Source of electrons
Accelerating stage
Bending magnet
High-energy e- & FLASH
NC HG linacs
Klystron
Directional Coupler
Pulse Compressor
Attenuator
Phase shifter
ac power
< 3 MW
Focusing solenoids
Matching Optics
Injector linac
10 MeV
High gradient linac
~ 50 MeV/m
pulsed DC Gun
70 cm
~ 2 m
FRIDA Sapienza-INFN
Pattern on photocathode
Maxim, Tantawi, Loo, Radiother Oncol, 2019
Pattern in patient
2 mm
20 cm
20 µm
RF Gun
Laser injection
Linac 1 m long
Solenoid
100 MeV Electrons
Quadrupole Magnets
Bending Magnets
0.7 m
1.3 m
< 0.2 m
1.75 m
2 m
e-beam PHASER
00:00.00
IDRA LOA IPP
IDRA: a beamline dedicated to medical applications!
loa
faisceau laser Salle Jaune
cible gazeuse
émission de photons (bétatron)
électrons
transport et mise en forme
dosimetrie
plan d'irradiation
institutCurie
High-energy e- & FLASH
LPA
Dedicated site: provide stable experimental conditions
source R&D for radiobiology and dosimetry
collaborative access (Laserlab possible)
biology support available via radExp (Institut Curie)
îledeFrance
PITZ DESY
<7 MeV/c
<22 MeV/c
Gun
LEDA
CDS booster
Plasma (opt.)
HEDA
e⁻ source
free space for SH RT R&D area: 2 x 3 m³ (l x w x h)
TDS
undulator
High-energy e- & FLASH
SC linacs
Tunnel 1
Tunnel 2
separated tunnels allow access to treatment area while accelerator is running

Sapienza & INFN on Flash-RT

- Development of 5-7 MeV S-Band e-Linac for Flash-RT with industrial partnership (SIT), nowadays installed at IC Orsay



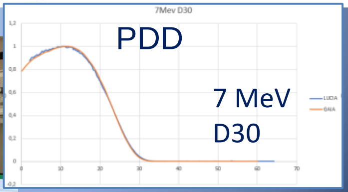
Characteristics EF4000	Value
Output energy	5 - 7 MeV
Pulse repetition frequency	1 - 250 Hz
Pulse width	0.5 - 4 μs
Maximum peak beam current	120 mA
Dose rate per pulse	$> 10^6$ Gy/s
Mean Dose rate	1000 Gy/s
Max Dose per pulse	30 Gy in a surface of ⌀ 10 mm

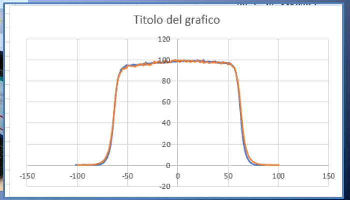


Biperiodic structure ~ 3 GHz
Accelerting mode $\pi/2$
Magneting coupling

FLASH IORT machine

Dosimetric analysis - 7 MeV – Measurements vs Fluka





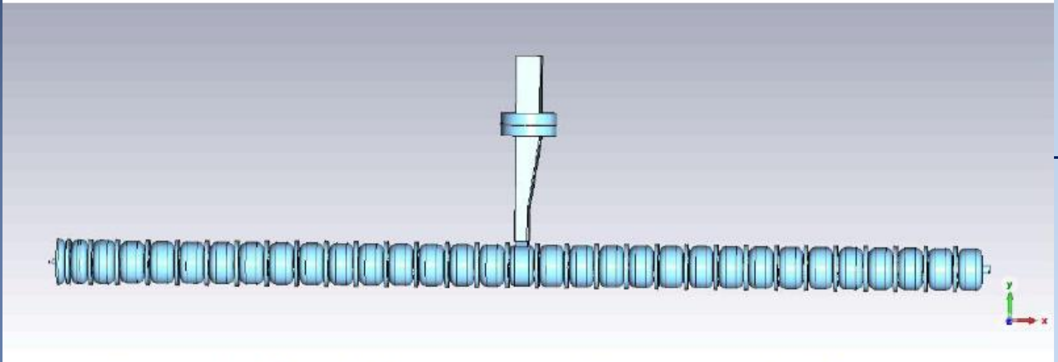
PHYSICAL REVIEW ACCELERATORS AND BEAMS 24, 050102 (2021)

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

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

Sapienza & INFN on Flash-RT

➢ **Development of a C-Band Linac 12 MeV – SIT Company**

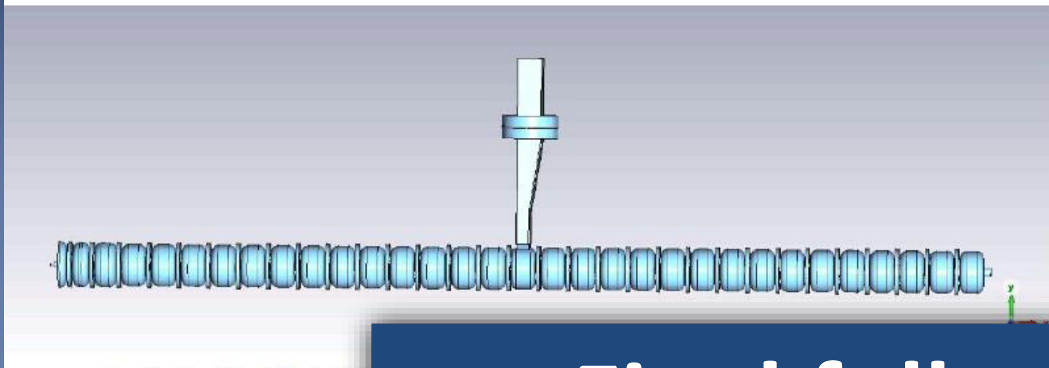


32 biperiodics cells structure

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

Sapienza & INFN on Flash-RT

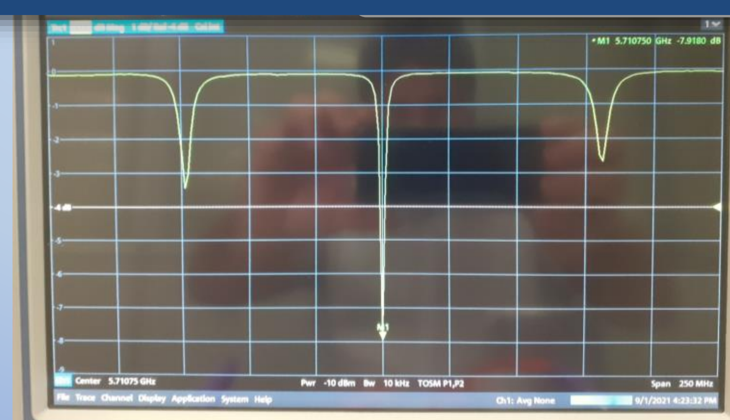
➤ **Development of a C-Band Linac 12 MeV – SIT Company**



32 b

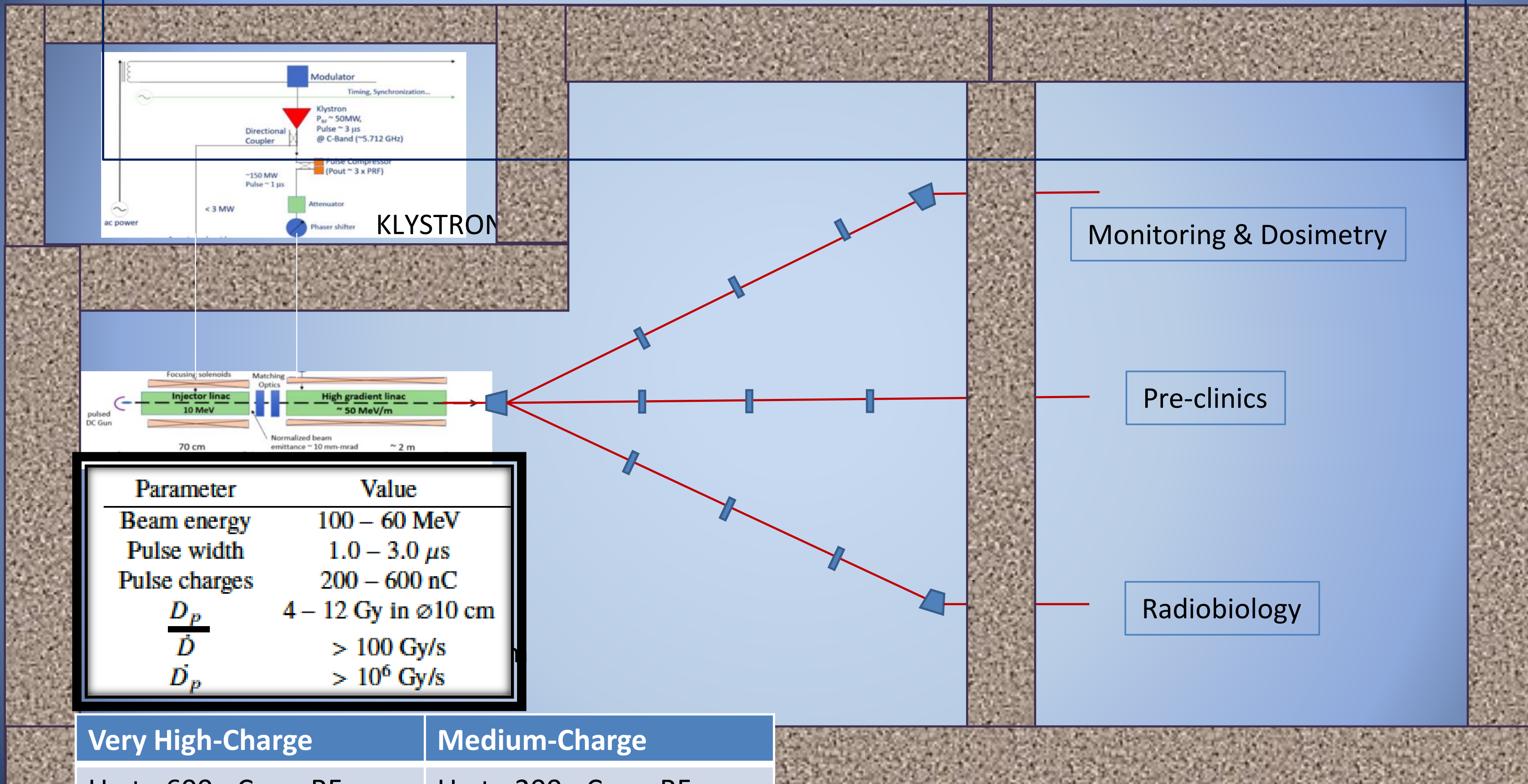
Parameter	Value
Frequency	5.712 GHz
Magnetron Power	2.5 MW
Number of accelerating cells	32
	2 cm
	MeV
	mA

Final full prototype expected end 2021



Sapienza & INFN on Flash-RT

➢ **Proposal of a VHEE-LINAC- FLASH RT Research Laboratory (Concept)**

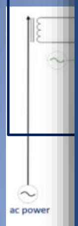


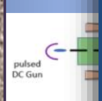
Parameter	Value
Beam energy	100 – 60 MeV
Pulse width	1.0 – 3.0 μs
Pulse charges	200 – 600 nC
D_p	4 – 12 Gy in ⌀10 cm
$\dot{D}$	> 100 Gy/s
$\dot{D}_p$	> 10^6 Gy/s

Very High-Charge	Medium-Charge
Up to 600 nC per RF pulse	Up to 200 nC per RF pulse

IPAC Conference, 2021

Sapienza & INFN on Flash-RT





FRIDA Project INFN

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.***
- ***Main Objectives:***
  - *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***

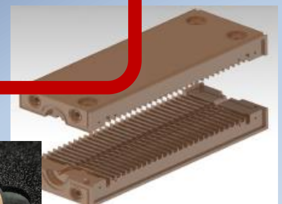
Up to 600 nC per RF pulse	Up to 200 nC per RF pulse

IPAC Conference, 2021

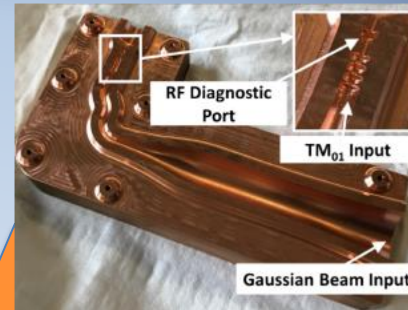
Normal Conducting RF

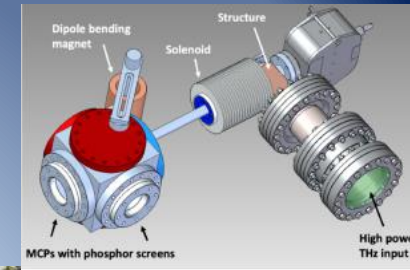
>100 MeV/m is now achievable in labs

12 GHz RF structure

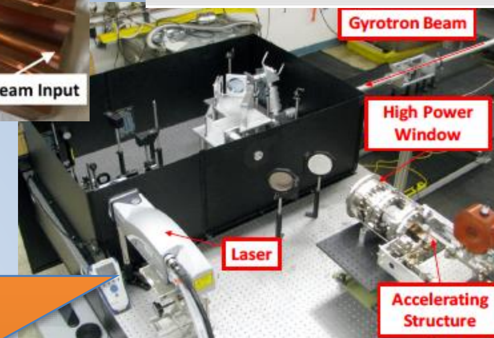


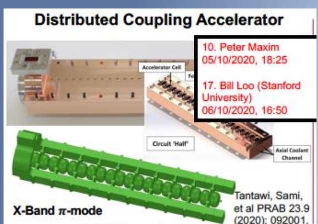
110 GHz RF structure

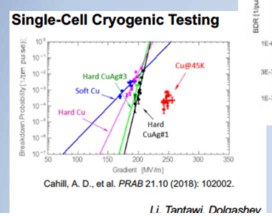


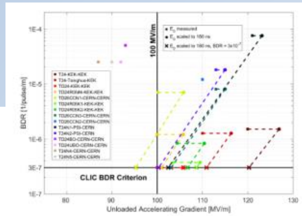


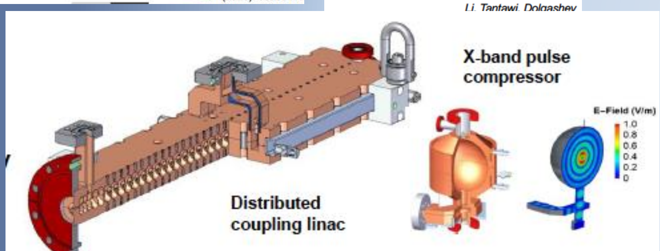
Short tunable pulse length Laser





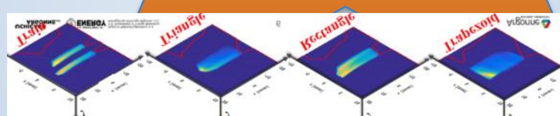


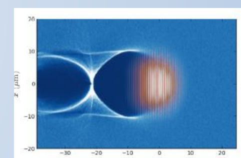


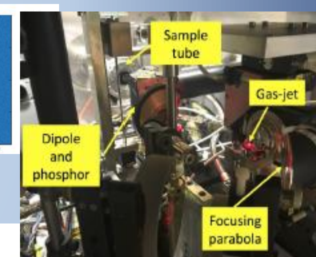


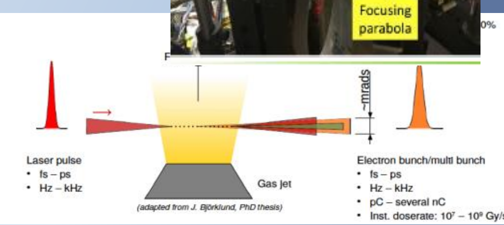
Technologies

Laser-Driven e⁻

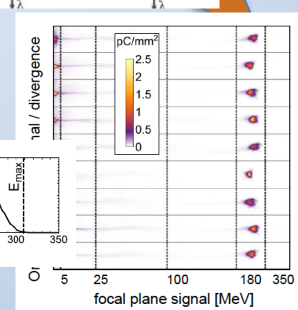


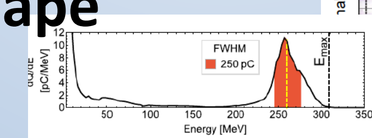




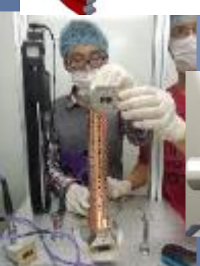


Longitudinal shape





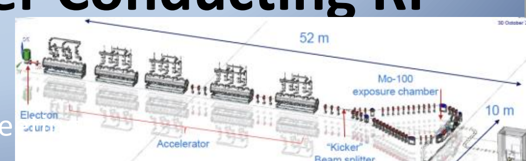
Rhodotrons



5.712 GHz RF structure

2.998 GHz RF structure

Super Conducting RF



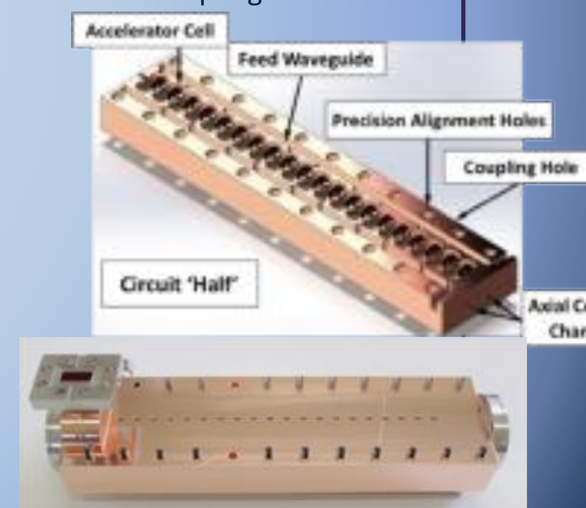
NOVEL ACCELERATOR TECHNOLOGIES FOR VHEE – FLASH Applications

VHEE RT requires beam energies between 50-200 MeV, an improved dose conformity and scale to higher doses rates, in the case of the FLASH-RT until 50 Gy/s are needed.

An international R&D global effort is being made by labs such as CERN, INFN, KEK, MIT, UCLA, LANL, SLAC and industry partners and focused towards the:

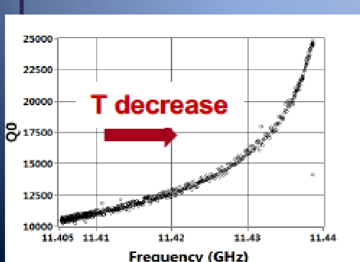
- **Material origin and purity, surface treatments, manufacturing technology**
- **Consistency and reproducibility of test results.**

X-band p-mode Distributed Coupling RF *structures*

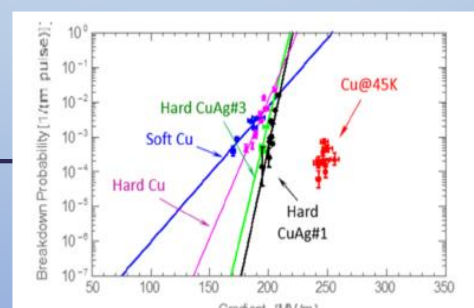


Some promising R&D are:

- **The distributed coupling accelerator (SLAC)**
- **The use of cryogenic copper**



Quality factor for cryogenic copper accelerator structures



Breakdown probability measurement in a single cell cryogenic test

NOVEL ACCELERATOR TECHNOLOGIES FOR VHEE – FLASH Applications II

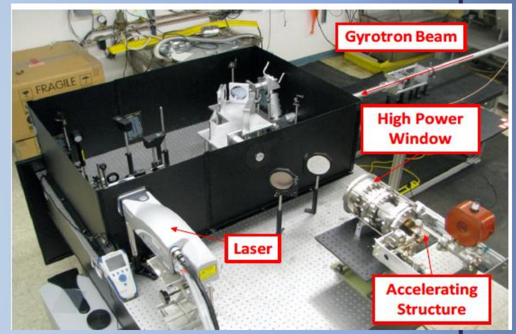
Another approach for the next generation of compact, efficient and high-performance VHEE accelerator is the use of:

- **Higher frequencies millimetric waves (~100 GHz)**
- **Higher repetition rates using THz sources**

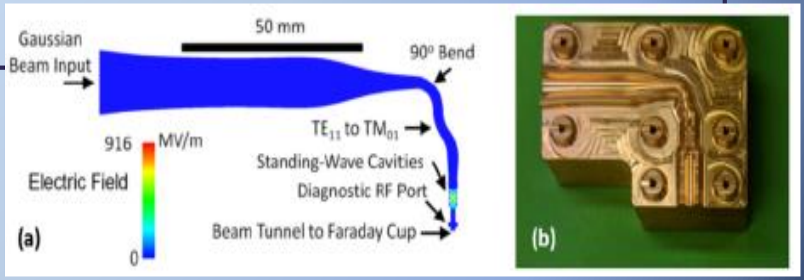
	X-band linac	mm-Wave linac
Frequency	11.424 GHz	100 GHz
Shunt impedance	430 MΩ/m	1 GΩ/m
Structure length	1.16 m	0.5 m

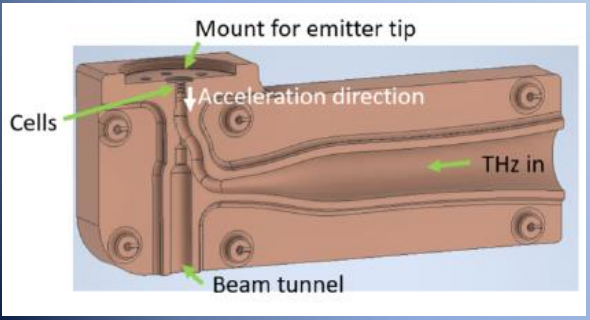
Comparison of X-band and mm-wave linac parameters

Laser-triggered semiconductor switch for pulse shaping (MIT)



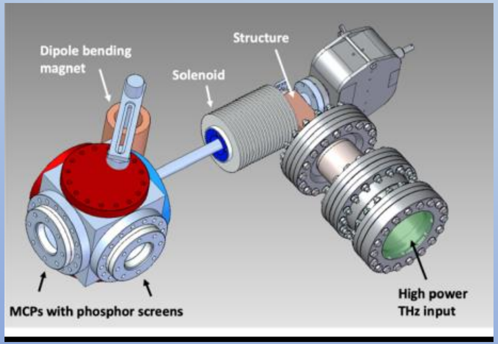
Built and tested structures at 110 GHz to 230 MeV (SLAC)





Relativistic electron source

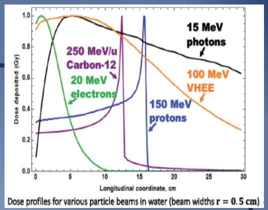
Commissioning device for relativistic electron source



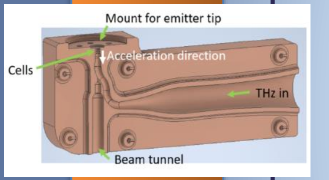
Relativistic electron sources with charges of 160 nC delivered in 1 second, with high repetition rate (ultimately 400Hz) utilizing field emission (100 fC per bunch, 40 ns pulse) (SLAC-NSF)

Detailed information in:
https://indico.cern.ch/event/939012/

SUMMARY and FUTURE PERSPECTIVES



- ➢ **Challenge** in RT is to find possible strategies to **spare normal tissue**
  - ➢ Different particle types: Very High Energy Electrons (VHEE)
  - ➢ Different dose delivery methods: Grid mini-beam or FLASH RT



- ➢ **FLASH** consists of **ultra short** irradiation time or "beam on time" (<**500 ms**) and very **high-dose** (**60-200 Gy/s**), that spare normal tissues from radiation-induced toxicities
  - ➢ **Understanding** the FLASH-RT **limits (min/max dose/time)**
    - ➢ Minimum beam on-time: ms => μm=> ns ? Bunching structure?
    - ➢ Maximun dose > 200 Gy/s ?
  - ➢ **Understanding** the FLASH-RT **underlying mechanism:**
    - ➢ Biological studies
    - ➢ Chemical and kinetic: role of the oxygen
  - ➢ **Extending** to other species: **p, ^{12}C**

- ➢ **Dosimetry** for **ultra-high dose rate** is a key stone, development of dosimeters is mandatory for a clinical application (EURAMET - EMPIR 2018)

- ➢ Which **Accelerator** is the most suitable to cope the necessary **performances**?