THE DEEP ELECTRON FLASH THERAPY FACILITY DEFT

C. Rossi on behalf of the DEFT Collaboration

OUTLINE

- INTRODUCTION
- THE MEDICAL BACKGROUND
- EXPERIMENTAL ACTIVITIES AT CLEAR
- COLLABORATION MODEL
- DEFT FACILITY DESIGN
- PRESENT STATUS AND PERSPECTIVES
- CONCLUDING REMARKS

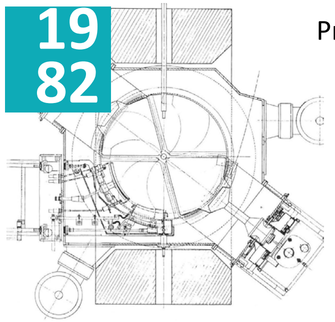
INTRODUCTION

THERYQ FOR HEALTH | CHUV | CERN | CLIC

- Long-time engagement of CERN in the contribution to the development of accelerator-based medical facilities

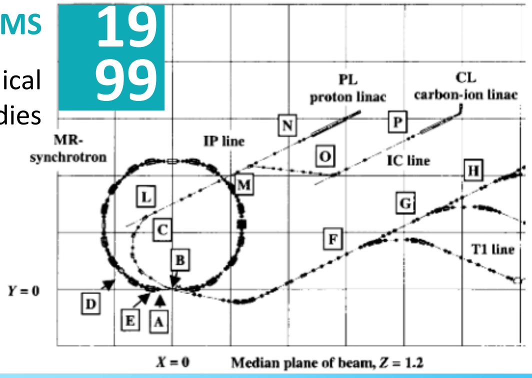
Medicyc & Eulima 19 82

Cyclotrons at Lacassagne center in Nice



PIMMS 19 99

Proton Ion Medical Machine Studies



MedAustron 20 07

Light-ion synchrotron for cancer therapy in Wiener Neustadt (Austria)

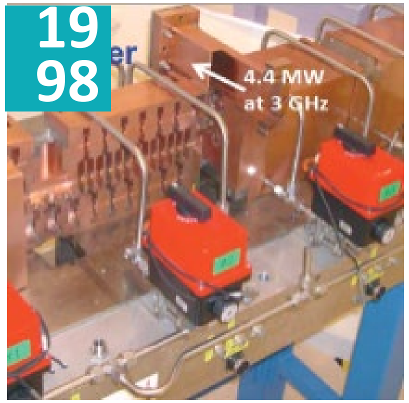
NIMMS 20 18

Next Ion Medical Machine Studies

1980's → *Today*

LIBO 19 98

Linac Booster Built by ADAM/AVO

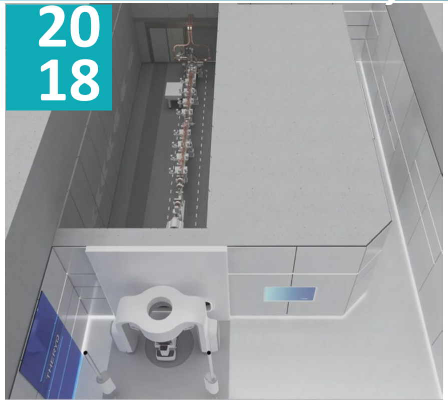


CNAO 20 05

Proton and ion synchrotron for cancer therapy in Pavia (Italy)

DEFT 20 18

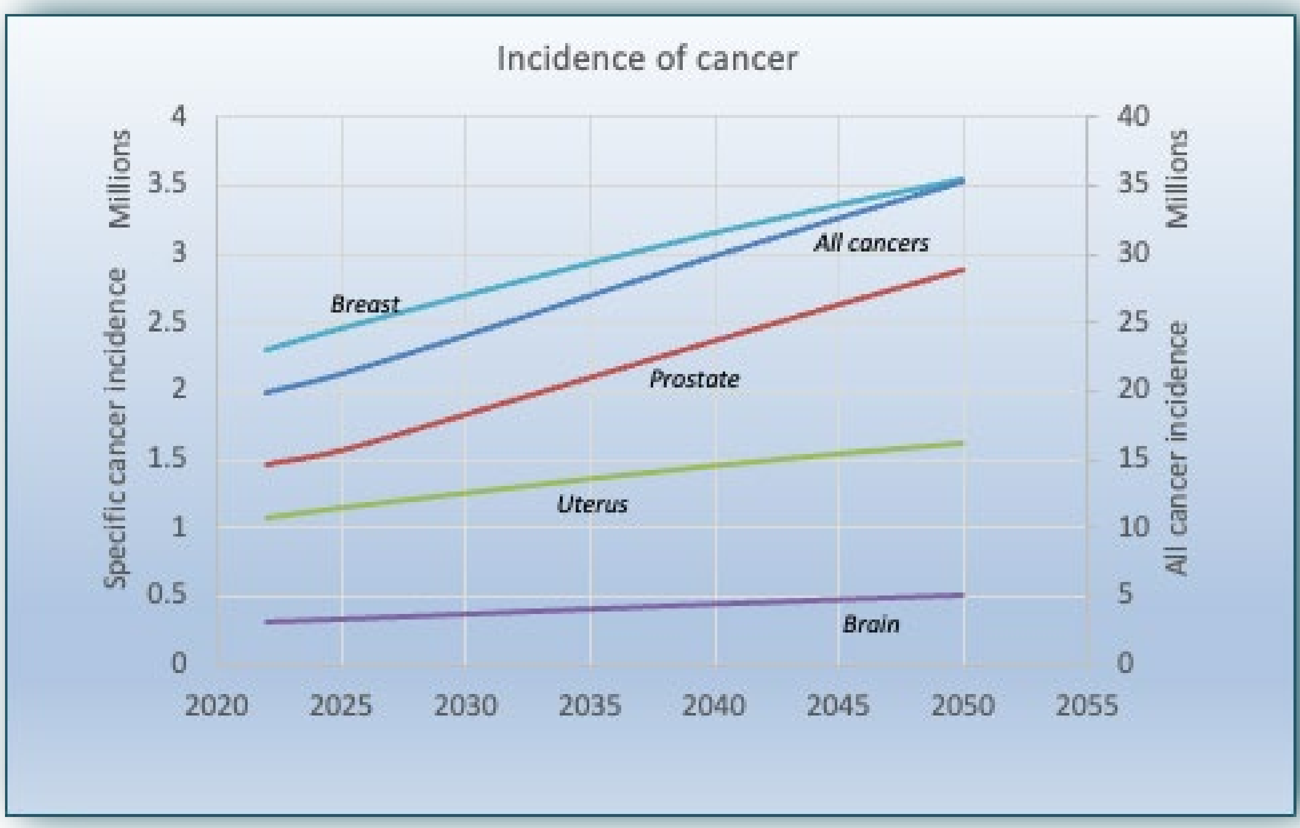
VHEE UHDR Linac in CHUV Lausanne (Switzerland)



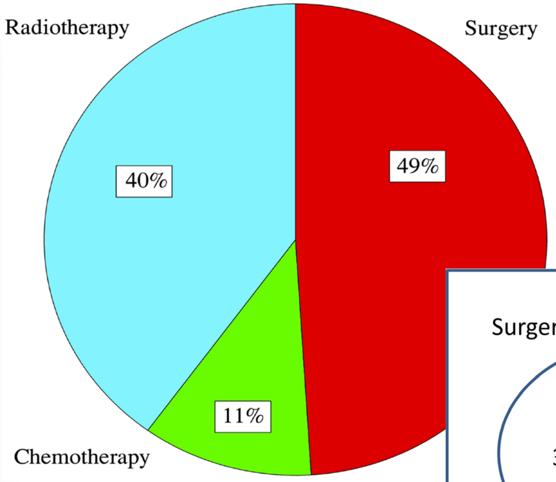
THE MEDICAL BACKGROUND

THERYQ FOR HEALTH · CHUV · CERN · CLIC

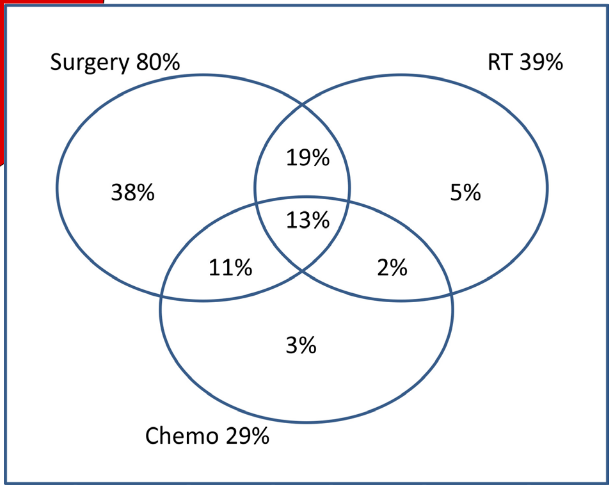
- The World Health Organization announces > 70% incidence increase of cancer until 2050



Data from WHO Global Cancer Observatory – 2024 *https://gco.iarc.fr/tomorrow/en*



Prevalence of cancer treatments in the UK (source NHS)



Percentages of patients who survived at least 5 years and who received at least one treatment

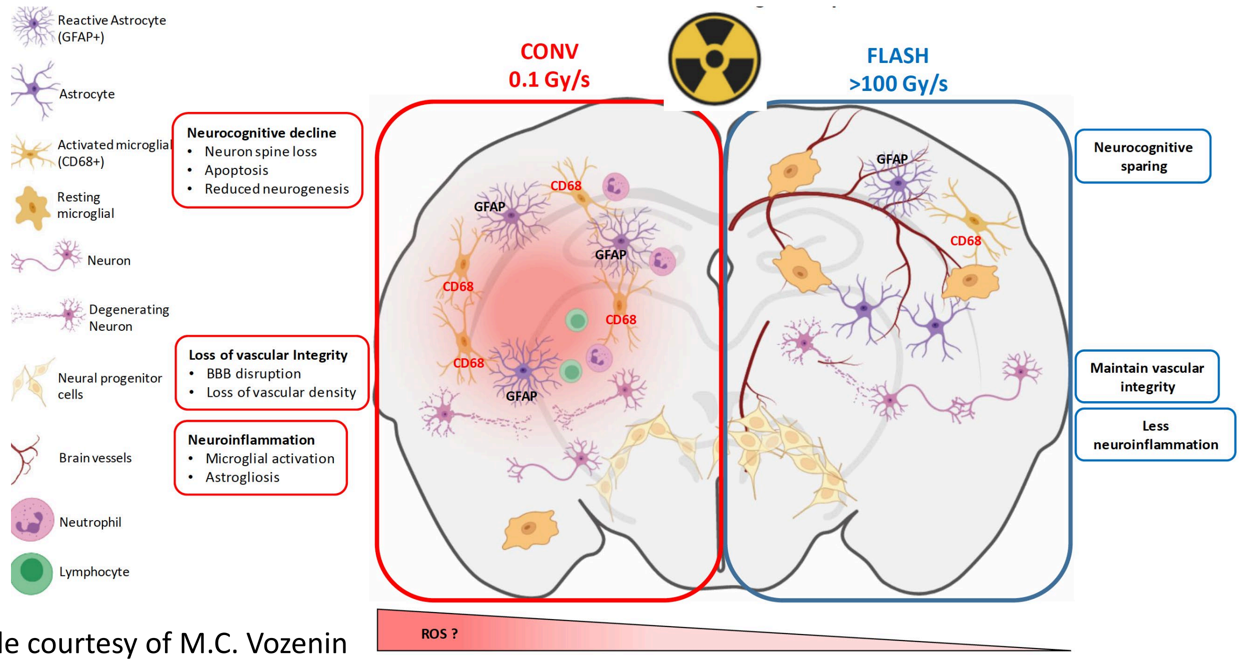
Br J Radiol, Volume 96, Issue 1152, 1 December 2023, 20230334, https://doi.org/10.1259/bjr.20230334

THE MEDICAL BACKGROUND

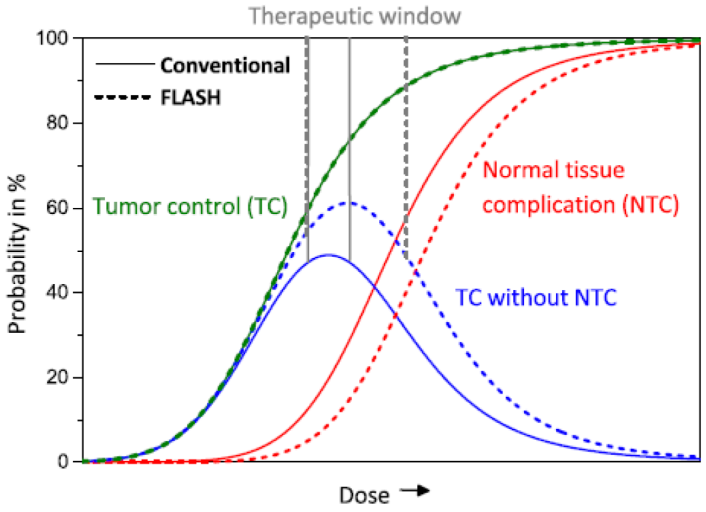
- With equivalent tumor control, FLASH shows reduced normal tissues toxicity wrt CONV (conventional fractionated radiotherapy)

- **The FLASH effect was initially explored in the 1970's and then abandoned. Research restarted in 2014.**
- **The FLASH effect is a biological effect, but not completely understood.**

In vivo experiments on mice brain highlight the biological difference between FLASH and CONV RT (response of normal tissues)



Slide courtesy of M.C. Vozenin



THE MEDICAL BACKGROUND

- First clinical evidence of FLASH effect

ELSEVIER

Radiotherapy and Oncology
Volume 139, October 2019, Pages 18-22

First in Human

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]

1a : Day 0 1b : 3 weeks 1c : 5 months

- **In 2019, 15 Gy** were delivered in **90 ms**, using a **5.6 MeV electron linac**, to a 75-years old patient with a multi-resistant cutaneous lymphoma:
  - **On healthy tissues**: no decrease of the thickness of the epidermis and no disruption at the basal membrane with limited increase of the vascularization.
  - **On Tumor**: Tumor response was rapid, complete, and durable with a short follow-up of 5 months.

Conclusions: This first FLASH-RT treatment was feasible and safe with a favorable outcome both on normal skin and the tumor.

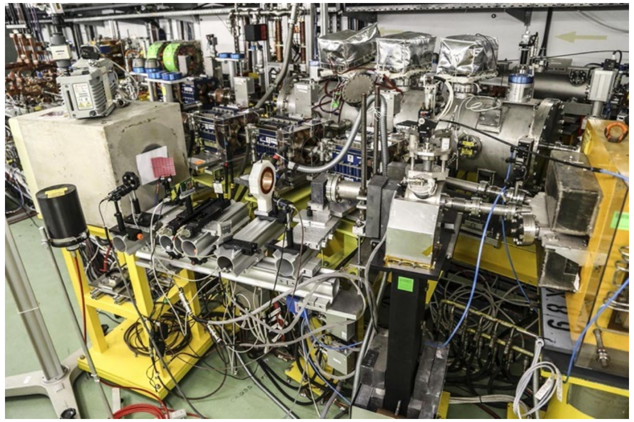
Slide courtesy of prof. J. Bourhis

EXPERIMENTAL ACTIVITIES AT CERN

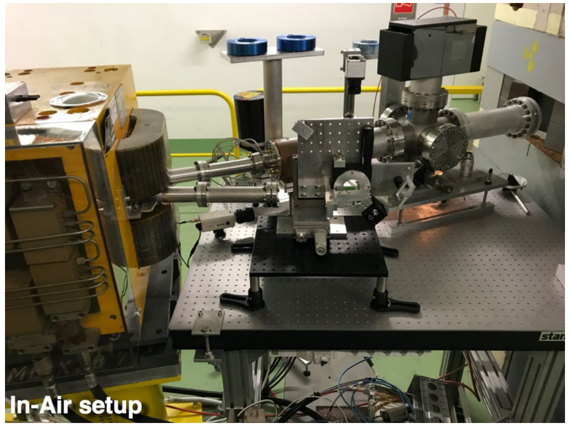
- Extensive and wide spectrum of experimental activities at CLEAR (CERN Linear Electron Accelerator for Research), a 200 MeV electron linac with a photoinjector.

Two experimental stations dedicated to medical activities.

vesper



In-air test stand

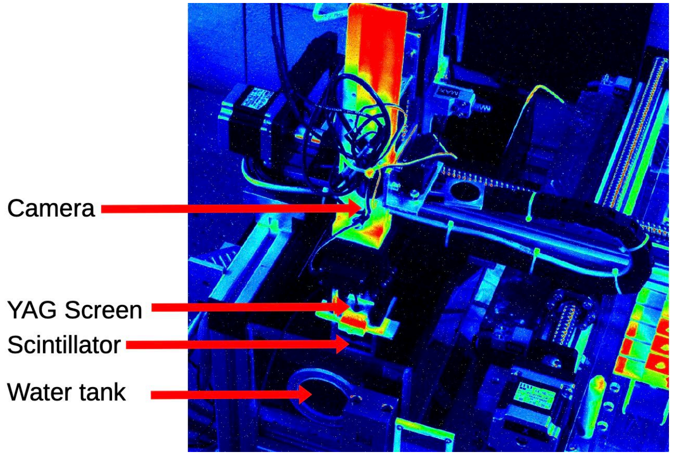


- **14 weeks** of beam dedicated to **medical applications** in **2023.**
- More than **12 conference proceedings** and **9 journal papers** (published or being reviewed) for medical applications, see the full list on: https://clear.cern/content/publications
- **> 13 Medical Application Experiments** planned for **2024**, see the full list on: https://pkorysko.web.cern.ch/CLEAR/Table/CLEAR_experiments_2024.html

More details in R. Corsini: Medical activities in CLEAR: studies towards radiotherapy using Very High Energy Electrons (VHEE) in the FLASH regime - *THPB018 @ LINAC2024*

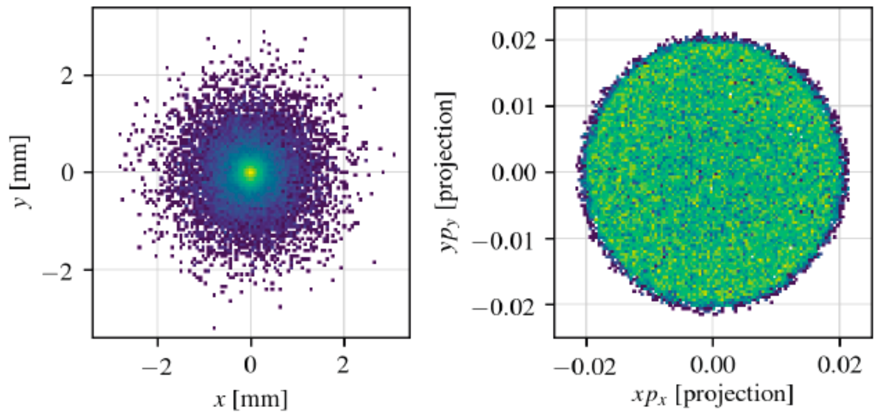
EXPERIMENTAL ACTIVITIES AT CERN

- CLEAR is the ideal facility to study UHDR leading to the FLASH effect with VHEE, interesting for deep seated tumors (NO *in vivo* experiments at CERN).

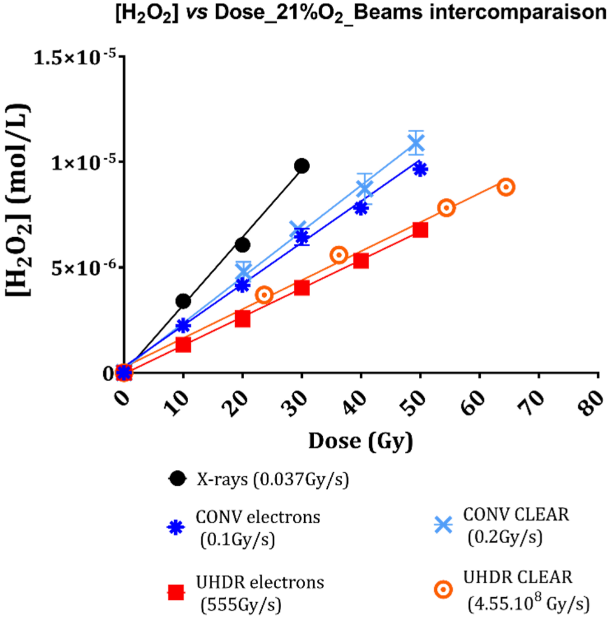


Fibre-optic Monitor for UHDR Real-time Dosimetry

courtesy of R. Corsini and P. Korysko



Transverse and projected beam profile at the CLEAR linac exit.



Real Time dosimetry

Beam Dynamics studies

The FLASH effect

More details in R. Corsini: Medical activities in CLEAR: studies towards radiotherapy using Very High Energy Electrons (VHEE) in the FLASH regime - *THPB018 @ LINAC2024*

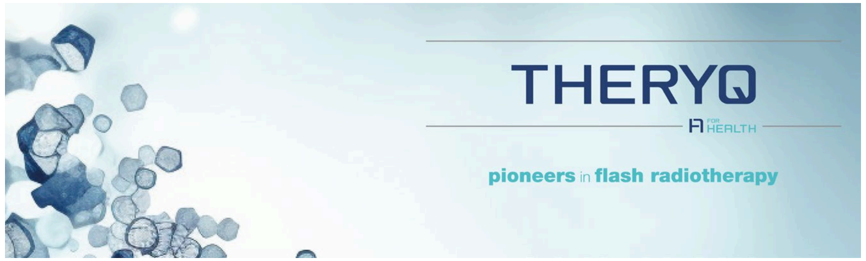
THE PARTNERS

- CERN is the European Center for Nuclear Research

Performs world-class research in fundamental physics

- CHUV is the University Hospital of Vaud in Lausanne

16 Medical Departments, 12 400 collaborators, 1.9BCHF annual budget



- THERYQ is a spin-off of PMB-ALCEN

Created in 2022 to pursue all radiotherapy activities of PMB

THE COLLABORATION

- Initial collaboration agreement signed between CHUV and CERN in 2020, supported by the donation of the Biltema Foundation and by the ISREC Foundation.

  - ➢ Produced a CDR in 2021, followed by a TDR delivered in early 2023

- THERYQ joined CHUV and CERN in the end of 2022

The new partner provided the vision from industry and enabled the possibility of building a certified medical facility FLASHDEEP™.

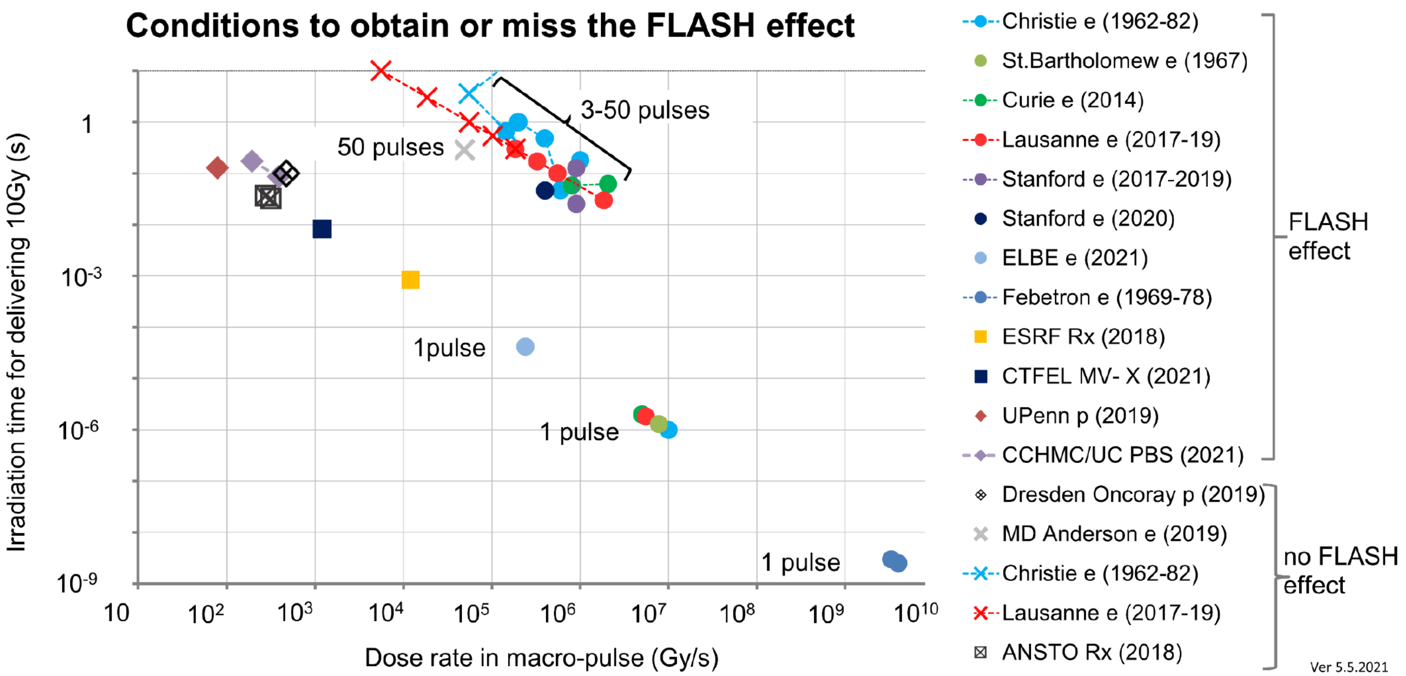
A staged approach soon appeared as a straightforward way of quickly achieving the possibility to explore and validate the FLASH effect and start pre-clinical studies.

DEFT FACILITY DESIGN

- **Requirements for design.**

- In terms of dose: produce very **high dose rates**, deliver full dose or fractions in < 200ms (UHDR ≳ 50 Gy/s average > 10^6 Gy/s intrapulse).
- Provide e- **energy** > 100 MeV, to target deep-seated tumors (VHEE ≳ 20 cm penetration).
- Deliver a **homogeneous dose over a large field**, to treat cancer like brain glioblastomas, where sparing of normal tissues results critical.
- Make the facility **compact** enough to fit into the existing hospital space.

The shorter the better



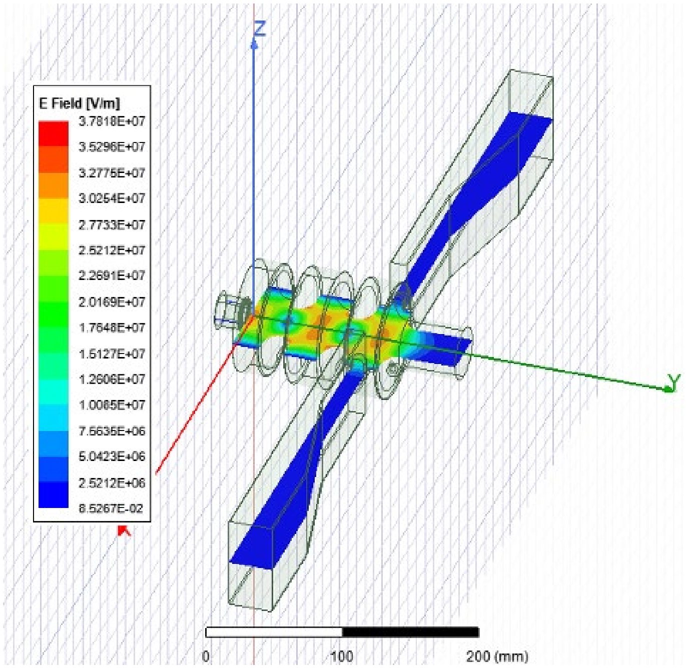
The higher the better

Adapted from Montay-Gruel P et al., CCR, 2020. - courtesy of M.C. Vozenin

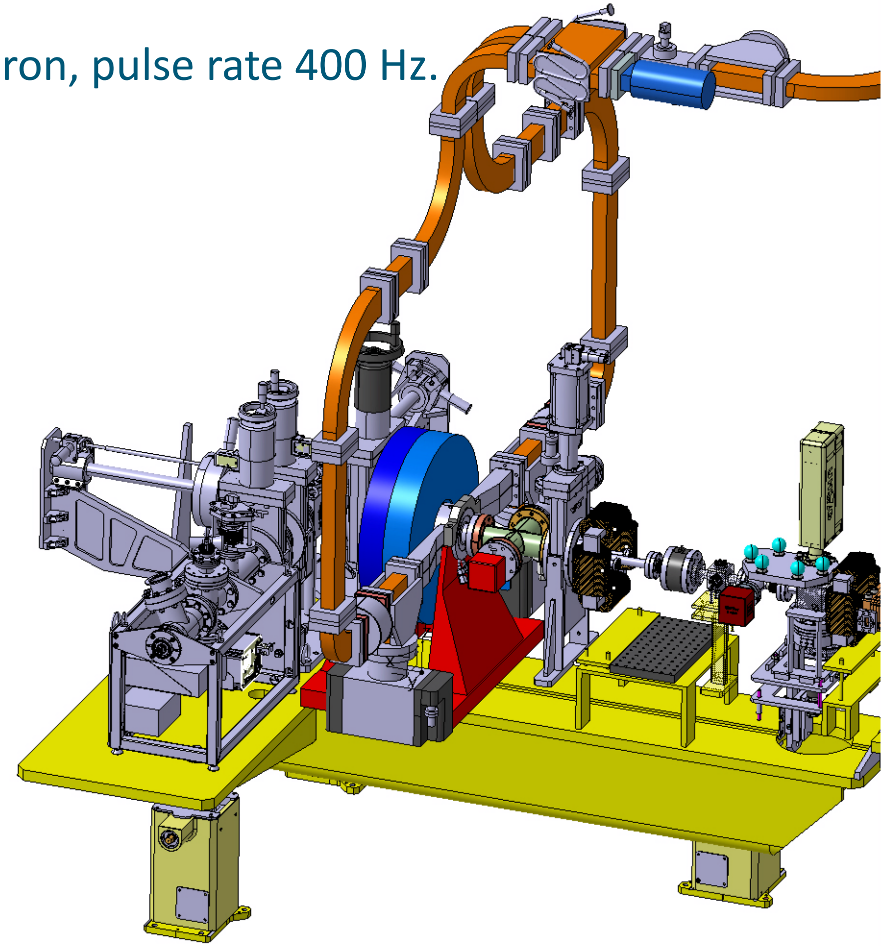
DEFT FACILITY DESIGN

- **The Injector.**

- The 3 GHz photoinjector cavity is fed by an S-band, high power klystron, pulse rate 400 Hz.
- The Gun cavity is a 2.5 cell cavity, max 110 MV/m field gradient.
- The cathode is Cs_2Te coated



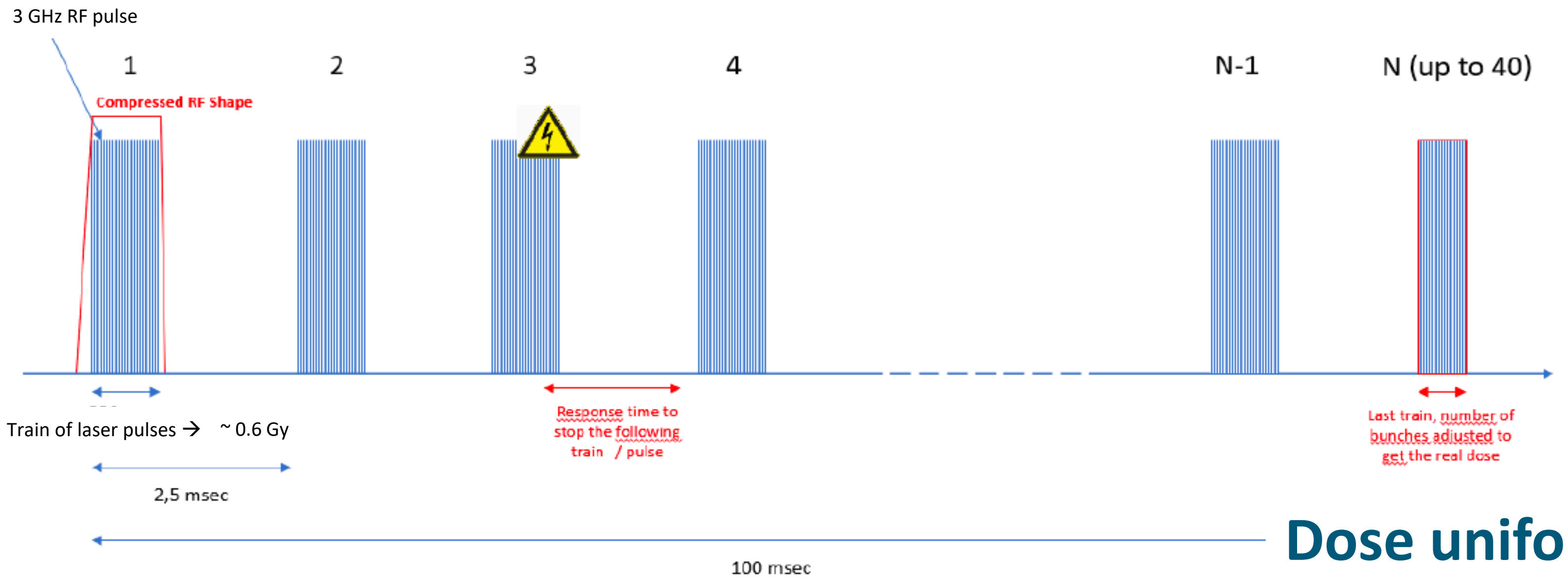
Laser parameter	Value
Laser medium	Nd:YLF
Wavelength	< 270 nm
Typical UV pulse energy	1 uJ
Typical burst energy	1 mJ
Max number of pulses	1000
Burst repetition	400 Hz

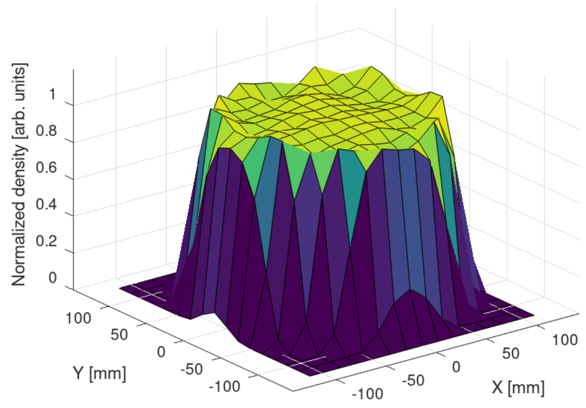


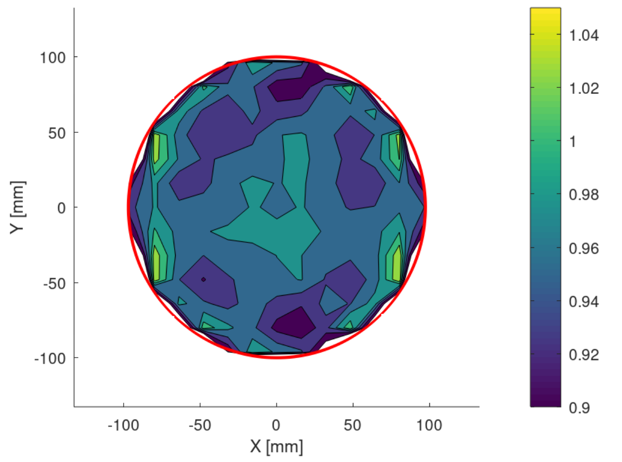
DEFT FACILITY DESIGN

Dose control by Linac pulse modulation

- The RF Gun (3 GHz) is pulsed up to 400 Hz in burst mode → 41 x 3 GHz RF pulses within 100 ms
- The total charge is controlled by controlling the number of RF pulses and of laser train bunches
- Max intrapulse dose rate ~ 0.6 Gy / train → 3.5 10^6 Gy/s
- Max average dose rate over a full treatment > 100 Gy/s





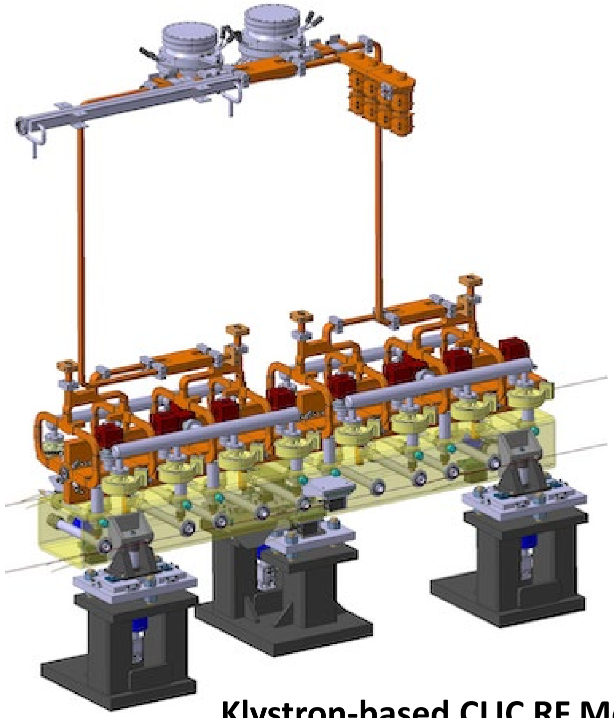


Dose uniformity at the patient position

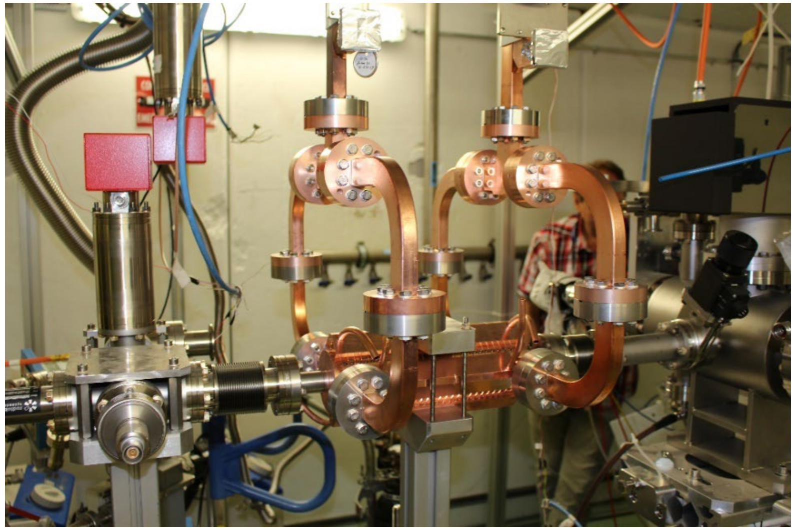
DEFT FACILITY DESIGN

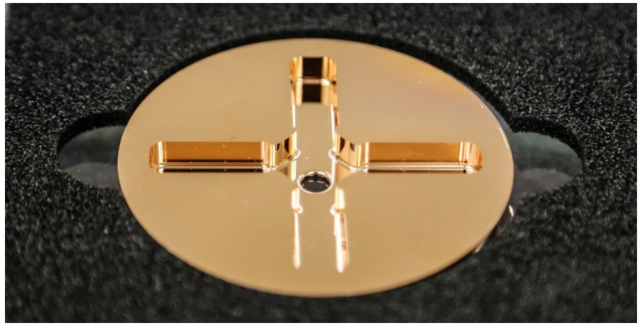
- **The CLIC X-band Technology from CLIC to DEFT.**

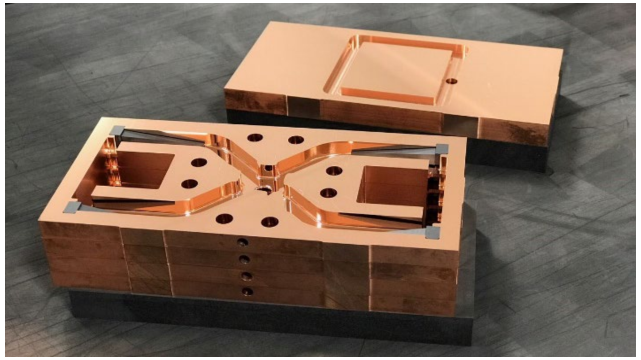
- Two “ RF Modules” accelerate the beam from 7 to > 100 MeV.
- 8 damped accelerating sections, of the CLIC kind, with tapered profile, TW operation.



Klystron-based CLIC RF Module



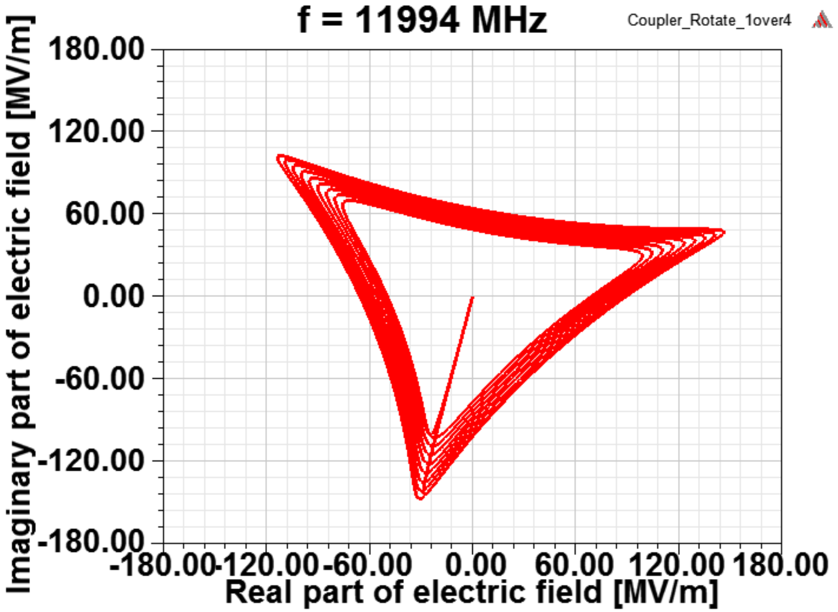




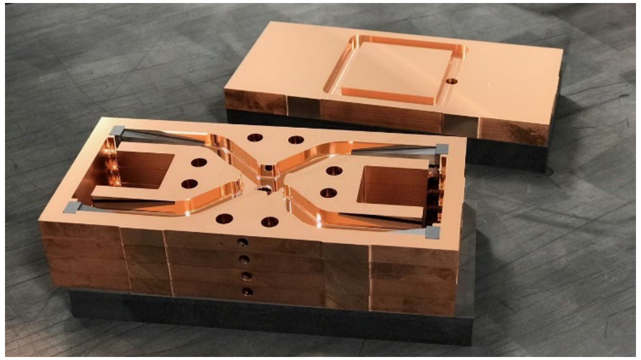
DEFT FACILITY DESIGN

- **The CLIC X-band Technology from CLIC to DEFT.**

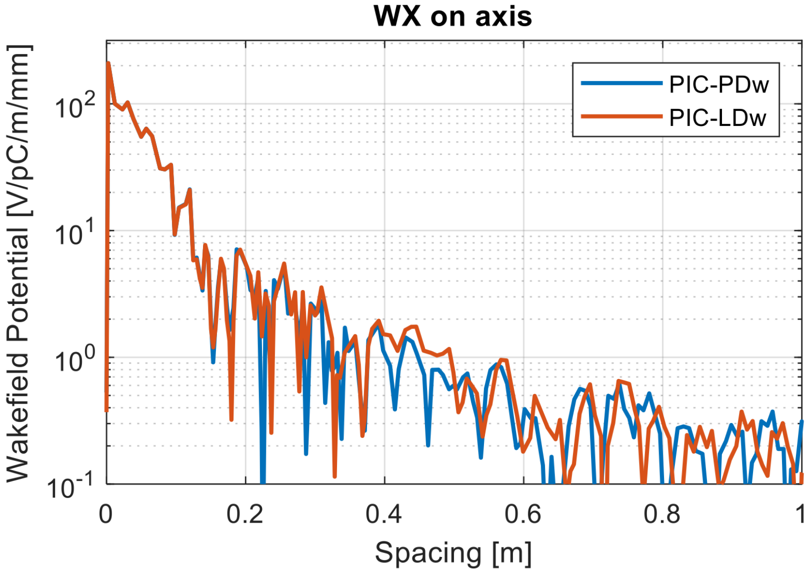
- Each AS is 0.6 m long with two coupling cells at the two ends.
- AS have cell-to-cell phase advance of $2\pi/3$.
- High-order mode damping to suppress long-range wakefields.



Klystron-based CLIC RF Module



Damping of HOM by SiC loads



DEFT FACILITY DESIGN

- **RF power production.**

- Two X-band RF power sources are combined to feed the two modules, following the scheme adopted for the klystron-based CLIC.

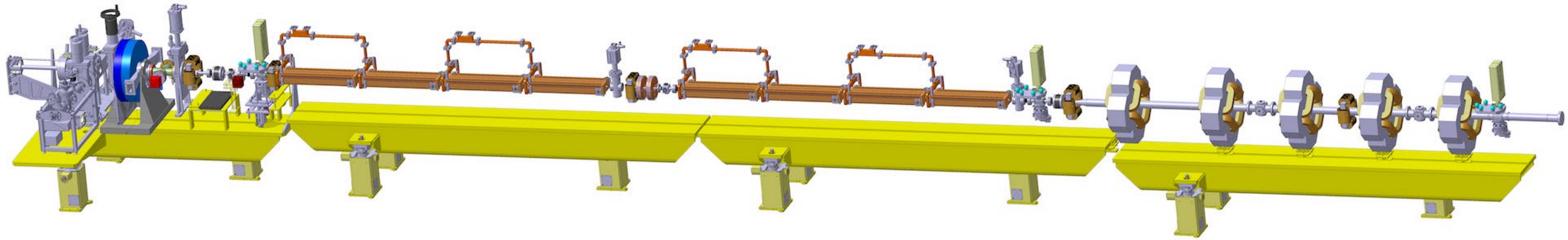
CLIC Klystron modulator

- Klystrons RF peak power is in the 20 – 25 MW range, delivering 2.3 μsec pulses at 400 Hz

- A typical treatment with 25 Gy in 100 ms would deliver 560 J to the patient.
- The corresponding energy provided by the X-band RF system would be 4.2 kJ.
- The RF-to-beam efficiency results to be around 13%.

DEFT FACILITY DESIGN

- **Beam delivery.**
- Beam dynamics simulations performed with the code RF-Track (A. Latina). https://zenodo.org/doi/10.5281/zenodo.3887084
- After acceleration, the beam is guided through a magnetic channel and it expands to reach the required transverse size.
- A Ti window separates the accelerator side from the patient area.
- The Beam Conforming System is followed by the clinical instrumentation for quality assurance, to keep the delivered dose under control.



View of the accelerator and Beam Delivery System (support and alignment system still under development)

DEFT FACILITY DESIGN

- **The patient area.**
- Upright position for the patient and integrated CT scanner. Stereoscopic X-ray imaging system for patient positioning

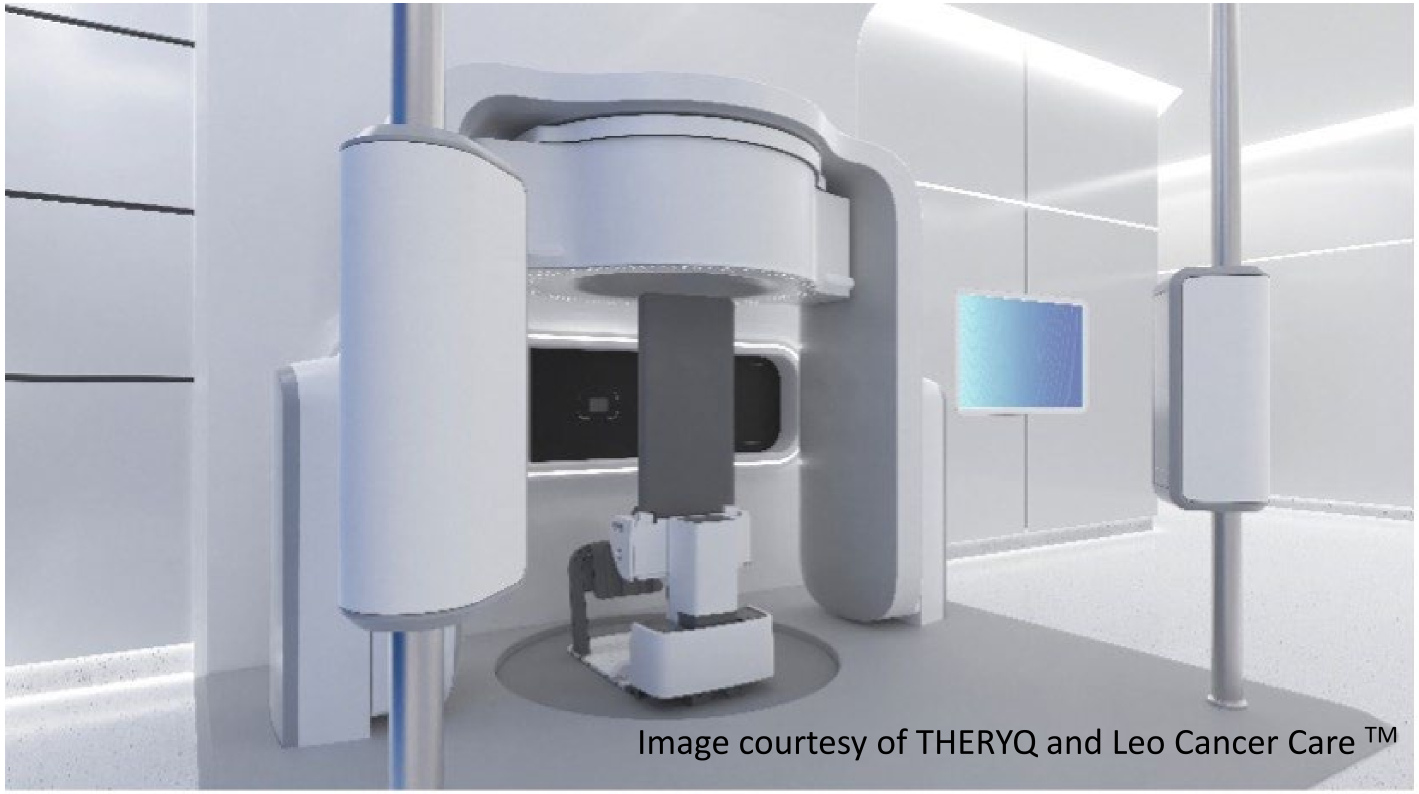
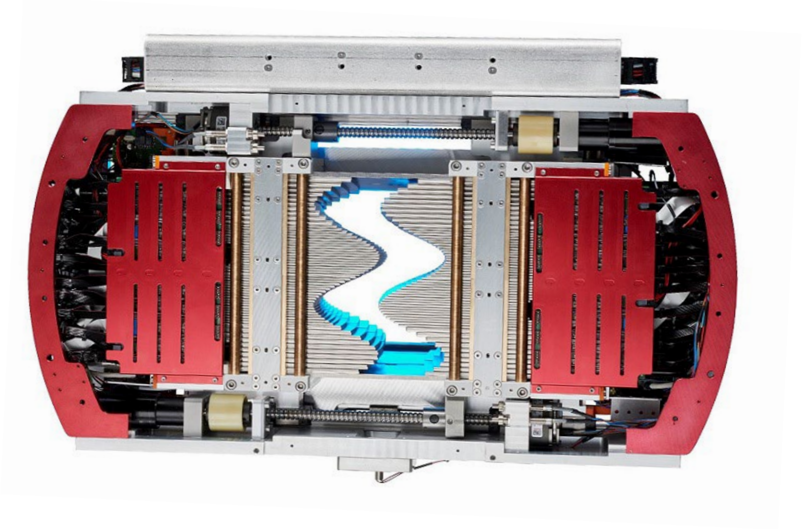
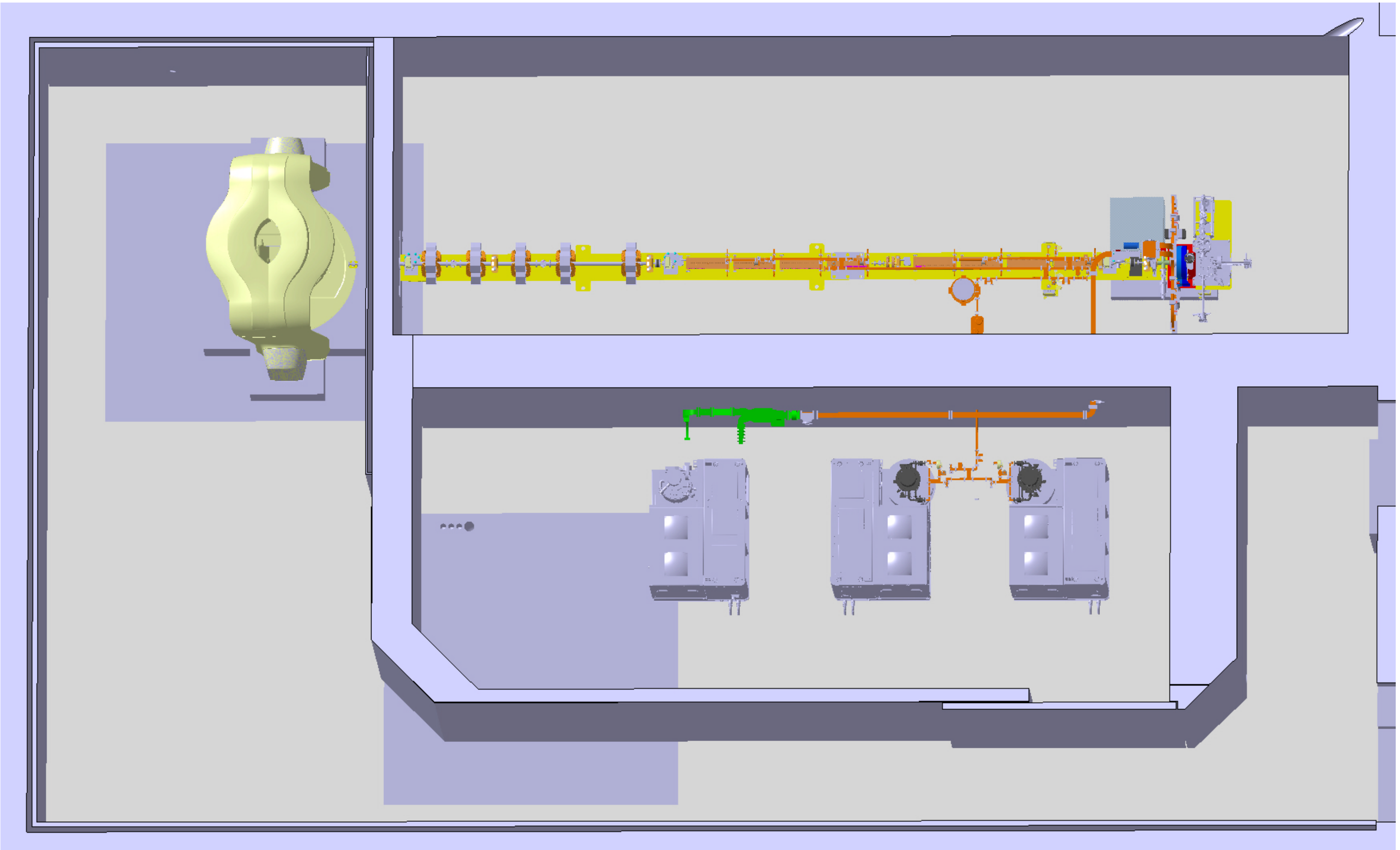


Image courtesy of THERYQ and Leo Cancer Care ™



- A multi-leaf collimator enables dose conformality at the patient position

DEFT FACILITY DESIGN



Stage 1 is single beam, with the option for a scanning beam.

The multi-beam option is still compatible with the existing building.

DEFT FACILITY DESIGN

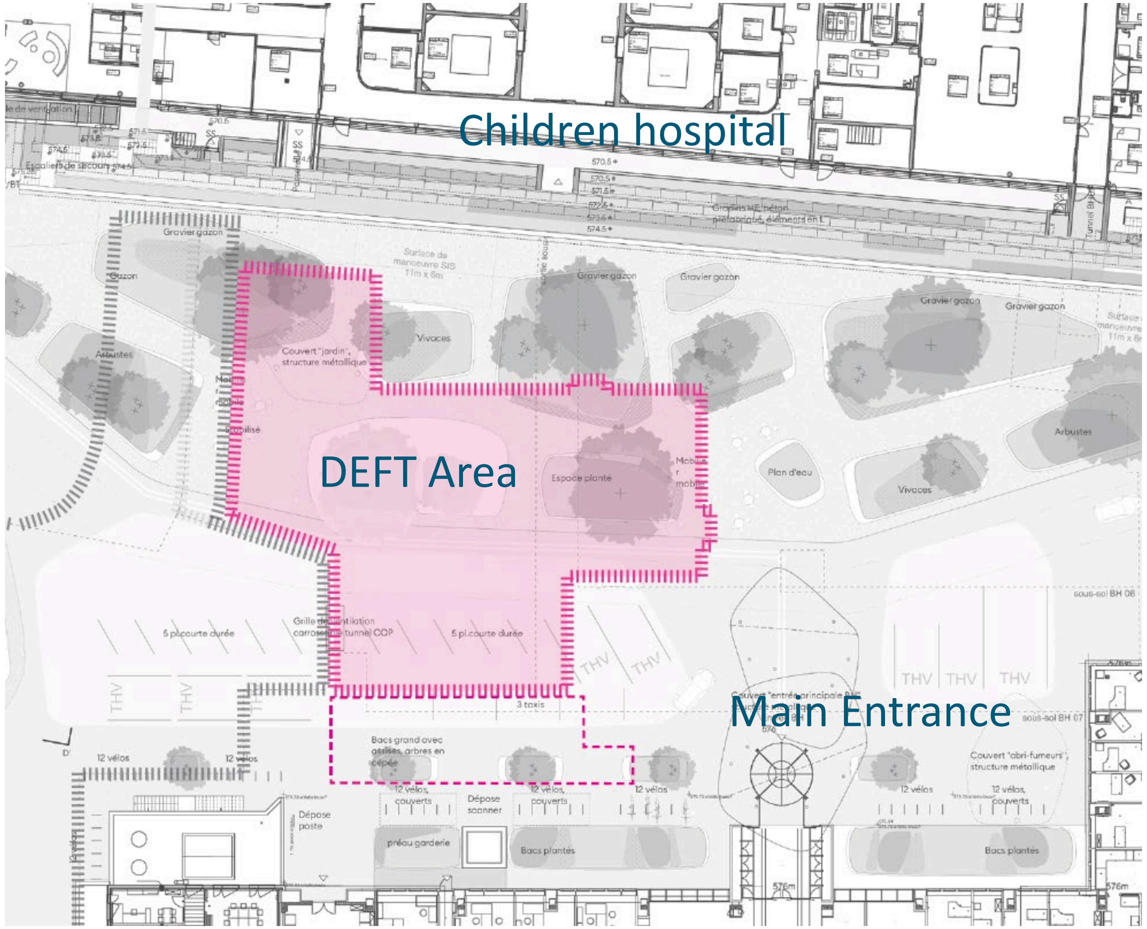
THERYQ
FOR HEALTH
CHUV CERN CLIC

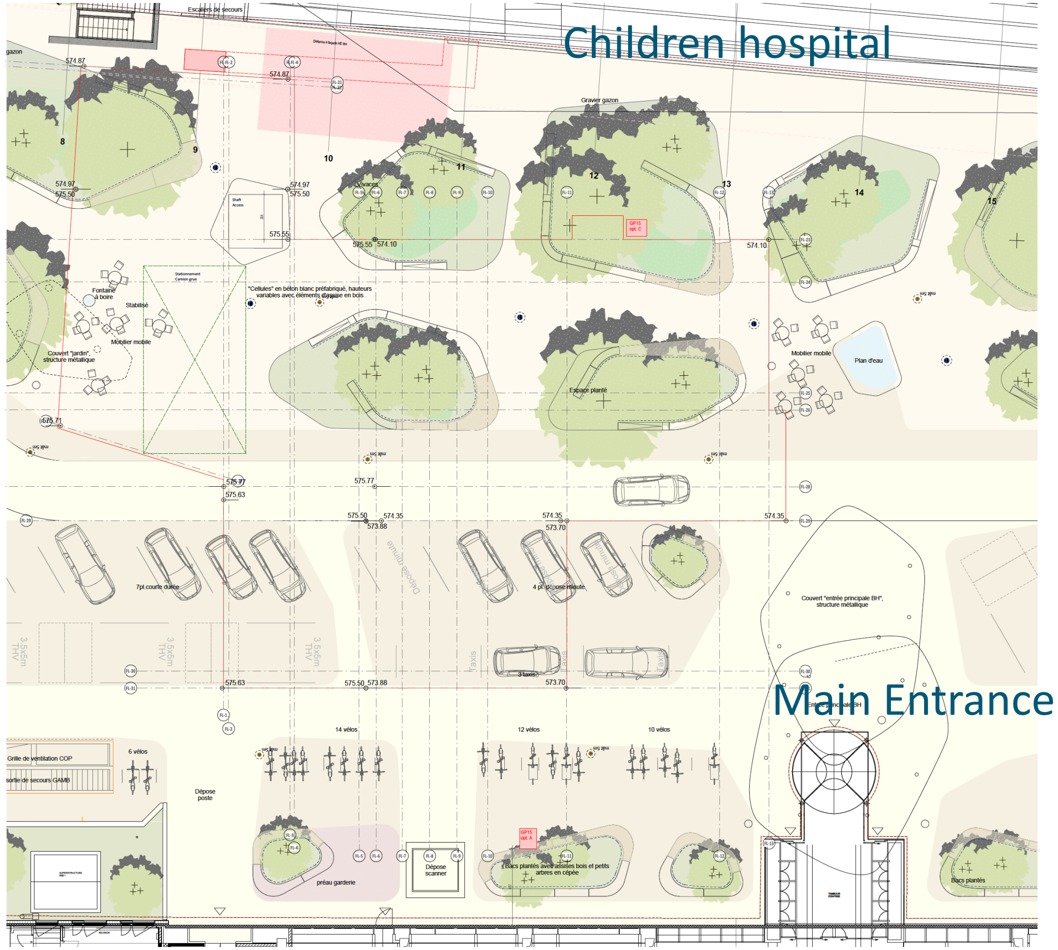
- The integration of the facility into the existing area was not a simple task.

DEFT FACILITY DESIGN

THERYQ FOR HEALTH

CHUV CERN CLIC





Compactness was a clear requirement for this project.

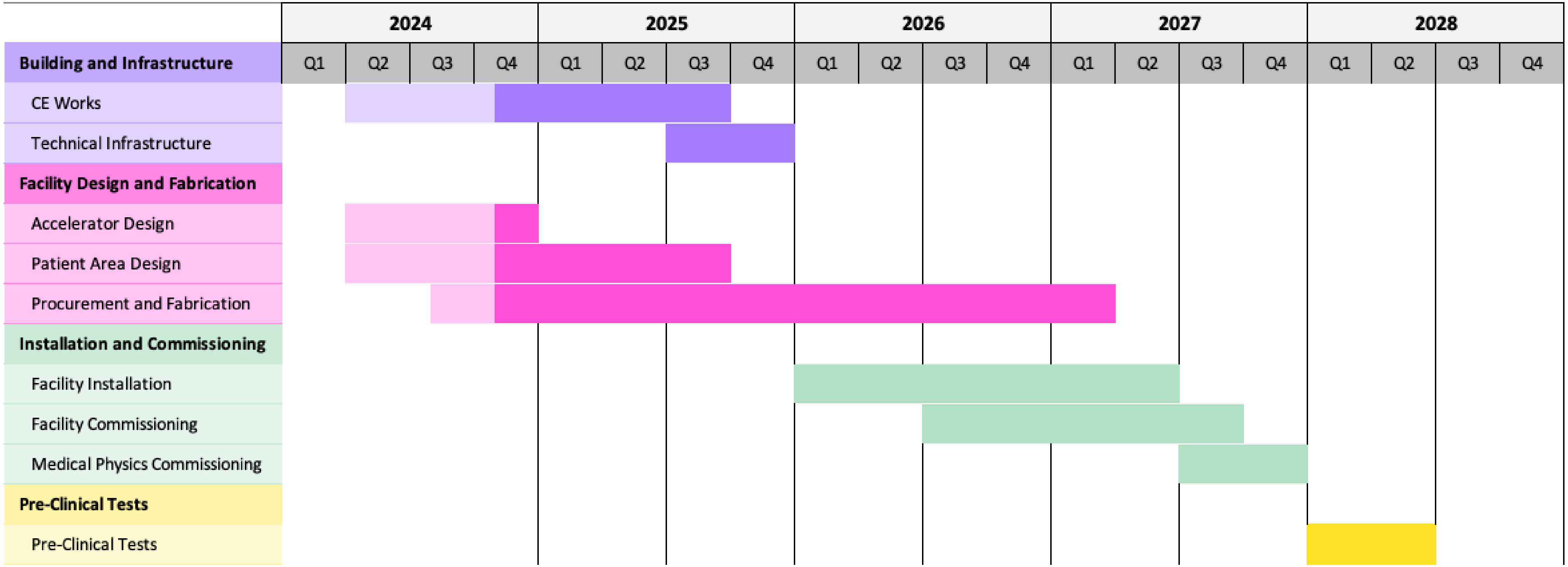
PRESENT STATUS

CHUV hospital

DEFT Area

CE works are quickly progressing in Lausanne.

… AND PERSPECTIVES



CONCLUDING REMARKS

- The DEFT Collaboration is progressing in the realization of a facility based at CHUV, in Lausanne, to study conditions for the FLASH effect and treat patients, in the longer term.
- The facility adopts the X-band technology developed by the CLIC study.
- An industry approach is implemented, so to enable the design of a medically certifiable device, FLASHDEEP^{TM}, suitable for production and commercialisation.
- The option remains to extend the facility operational modes to include a scanning beam and, in the end, a three-beam delivery system, so to enhance the conformality under FLASH-compatible conditions.

Thank you for your attention