Treatment planning & VHEE potential

VHEE are interesting... how to assess their potential?

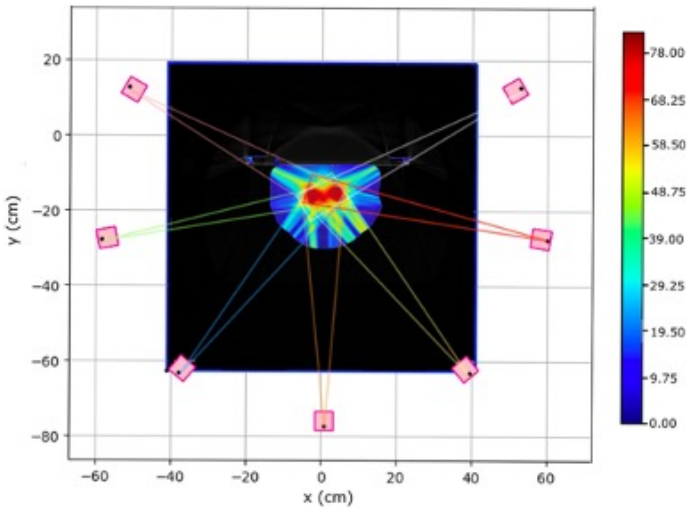
- There are several reasons why VHEE (both in conv and FLASH mode) are interesting as an EBRT alternative to γ and PT.. The only way, for now, to evaluate in a reliable way the gain from this technology proceeds via the following steps:
  - Collect the best knowledge about districts/therapies not yet satisfactory or that could potentially receive benefits from ipo-fractionation of plans [instead of current standard of 2Gy/fraction → 6-8 Gy/fraction] or whose irradiation geometry would favour broader 'Bragg Peaks' but without the large tails characteristics of γ
  - Implement (from scratch!) a VHEE TPS and compare the results with state-of-the-art RT or PT

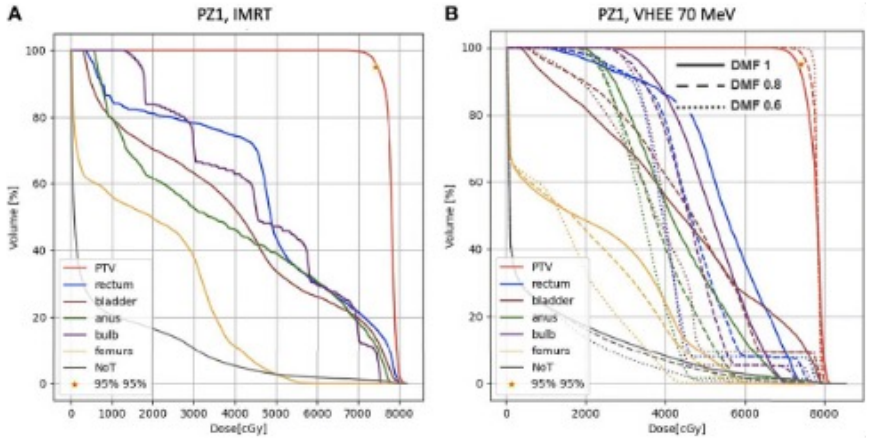
The VHEE TPS

- For now:
  - mimic RT or PT irradiation geometries
  - Implement an ‘active’ scanning tumour coverage strategy (as done in PT)
  - Take into account characteristics of e- interaction with matter → define each pencil beam dimension and energy, maximising the absorbed dose at the PTV centre.
- In the future
  - Develop an automated tool that will explore the possible geometries and irradiation strategies that provide the better tumour control while sparing as much as possible the OARs. [Several ‘parallel’ approaches: Machine Learning, Parallel/quantum computing oriented optimisation algorithms implementation, Fast MC approach]

VHEE plans: current status

- The technique potential has been already tested in:
  - Standard, simple geometry, deep seated tumor case: the prostate treatment. **Comparable results with RT and PT have been demonstrated.**





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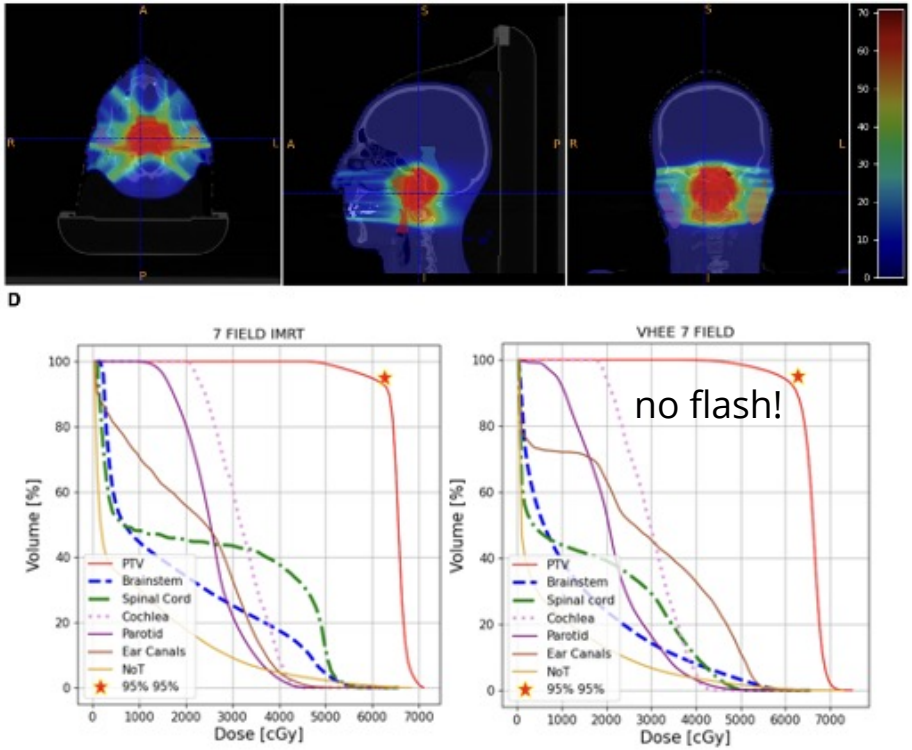
  - Standard, difficult, irradiation geometry: the treatment of intra-cranial lesions. Once again, **comparable results with RT and PT have been demonstrated**

Chordoma patient, VHEE with 7 fields



VHEE plans: current status

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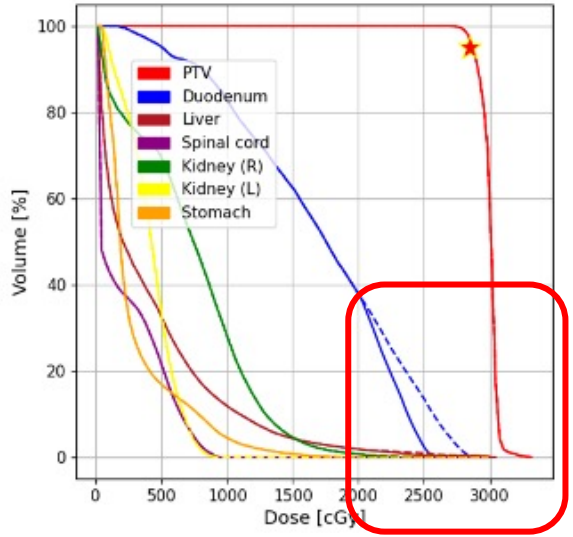
  - FLASH-oriented studies: pancreas / lung where ipo-fractionation is a real option..

Pancreatic cancer where constraints on duodenum are limiting the maximal dose to the PTV
NO FLASH → VHEE & RT similar results… But with FLASH:



Assuming the FLASH effect 'kicks in' in each fraction above 4Gy..

Dose @ PTV could be increased!

→ promising results obtained in terms of a possible dose escalation!

The next steps

- A real ‘revolution’ in the VHEE planning field would be to have a fully automated approach capable of exploring different field origins, field energies and pencil beam dimensions. For now the VHEE plans have been obtained mimicking the geometry of PT and IMRT plans, and the energies identified ‘by hand’, centering the e^- BP on the PTV. It is op paramount importance to go beyond this approach to fully exploit the VHEE power. For that we need:
  - **Machine Learning based solution** for the quick (instantaneous) evaluation of the expected absorbed dose in a given configuration (beam direction, size, energy) [Collaboration with C. M .Terracciano & Sapienza / INFN RM1 group]
  - **Quantum computing optimisation solutions**: the problem of exploring the phase space parameters in which all the fields have energy, origin/direction, size and fluence left ‘free to vary’ cannot be handled with standard computing approaches! Quantum algorithms can help speeding up the problem solution & **Parallel tempering approaches** can be implemented to gain additional speed. [https://learn.microsoft.com/it-it/azure/quantum/optimization-overview-introduction]

[Sapienza SAFEST] Elenco Partecipanti

Supporto da **39 partecipanti** : 16 PO, 16 PA, 9 RI

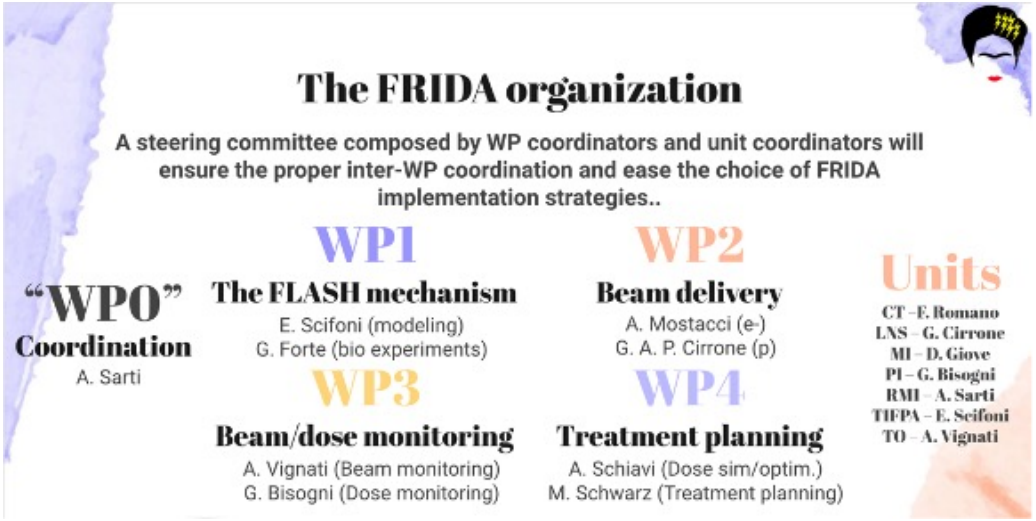
9 Dipartimenti: 4 di area medica, 3 di area ingegneristica, 2 di Scienze, **22 SSD**

1. **Biologia e Biotecnologie**: G. Cenci, R. Negri
2. **Fisica**: R. Faccini, C. Mancini Terracciano
3. **D.I.E.T.**: M. Liberti, F. Palma
4. **Medicina Molecolare**: G. Canettieri, G. Pozzi
5. **Scienze Anatomiche, Istologiche,..**: D.Alvaro, A. Casini, A. Filippini, E. Gaudio, R. Mancinelli, P.Onori, R. Vaccaro
6. **Scienze Statistiche e Attuariali**: L. Passalacqua

1. **S.B.A.I.**: S. Atzeni, S. Carillo, E. Chiadroni, A. Dell'Era, M. Feroci, L. Mattiello, M. Migliorati, A. Mostacci, M. Pasquali, V. Patera, M. Petrarca, R. Petrucci, F. Pitolli, A. Sarti, F. Scaramuzzo, A. Schiavi, A. Sciubba, M. Toppi, S. Vecchio Ciprioti
2. **Scienze e Biotecnologie Mediche**..: R. Pani
3. **Scienze Radiologiche, Oncologiche**, .. : F. De Felice, G. De Vincentis, V. Tombolini

The Sapienza - INFN effort & synergies with FRIDA

- The INFN CSN5 funded (~ 1 M€, call project, for three years, 2022-2024) the FRIDA initiative that is directly related to the study of FLASH potential of VHEE. Having ‘in hand’ a research facility capable of delivering FLASH beams of high energy would provide to the scientific community another tool to study the FLASH effect and the conditions to ‘trigger’ it: dose and dose rate thresholds, irradiation strategies, impact on sparing of healthy tissues…



https://web.infn.it/FRIDA/index.php/it/

FRIDA & VHEE

Within FRIDA there are several research lines that are deeply interconnected with VHEE:

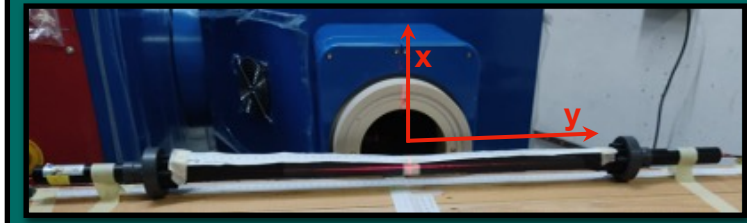
- FLASH therapy with e- is being explored both at RF & plasma acceleration level. The C-band solution for high energy (up to 130 MeV) acceleration is one of the deliverable expected from FRIDA WP2.
- The planning tasks already presented share with FRIDA the interest in understanding the FLASH potential of VHEE irradiations. In this respect, the dose rate studies (that will provide valuable feedback to the beam delivery technology that will have to be implemented) and the lung and pancreatic cancer cases are nicely matching the research program of frida WP4.
- The characterisation and explanation of the FLASH effect needs to proceed via a precise monitoring and assessment of the Dose and Dose rates achieved during irradiation. So far the standard monitoring technologies show severe limitations when applied to FLASH regimes. WP3 in FRIDA aims to address the lack of a monitoring technology suitable for FLASH applications: **one interesting possibility is to exploit the air fluorescence (see next slide)**

Beam Monitor with Air Fluorescence

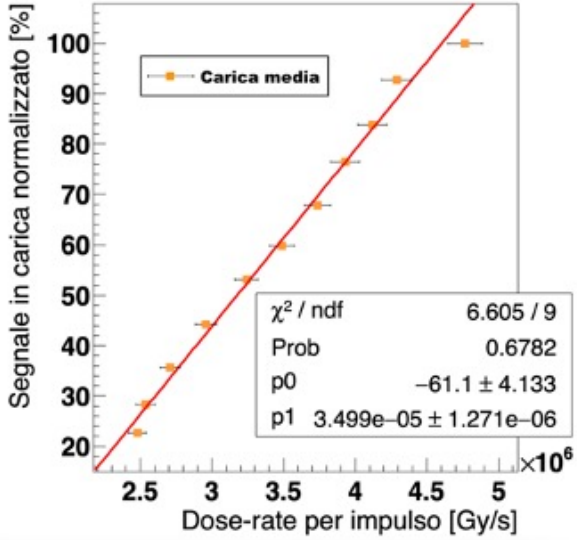
Preliminary measurements have been performed at SIT with LIAC and E-Flash.

Exploiting Fluorescence for beam monitoring purposes does not implies any beam degradation.

- Within FRIDA WP3 there have been built several prototypes, changed shapes and readout systems; tested the prototype as function of beam position (x, y) in order to study the background; characterised the detector proof of principle response as a function of beam intensity (current). The results are promising;



Up to now the detector shows the expected linear response.. Still more tests are needed



- A new test is planned at PISA electron beam [CPFR] in order to better characterise the detector performances and highlight critical aspects;
- An optimised geometry and readout system is under development:
  - A MC simulation with FLUKA of the new design has been developed.. it is an ongoing job (next meeting results!)
  - Part of the readout system is under acquisition
  - An optimised design will be completed during 2023.

The international landscape (quickly evolving)

- VHEE delivery (both in conv and FLASH modes) is being explored world-wide: facilities are under development @ CERN, DESY, SLAC..

Likely to be greatly enlarged with the new facility !!!!!

The proponents **already** have an extended national and international network of collaboration focused on the FLASH RT research

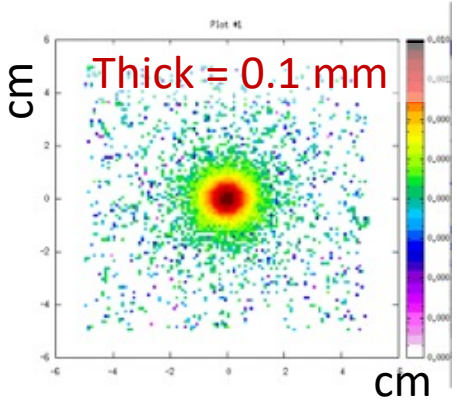
The network is of paramount importance for exchanging ideas, standardizing procedures and acquiring more data

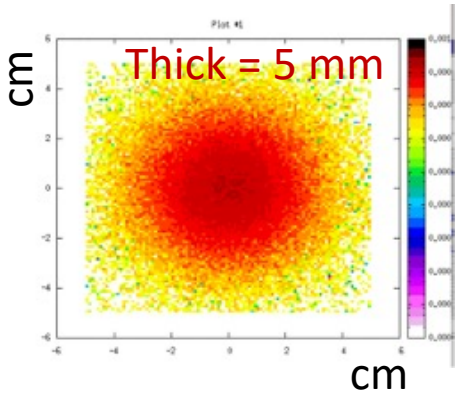
Marie Curie Institute (Parigi) Iridium Network (Anversa)
GSI (Darmstadt)
CPRF (Pisa)
Campus Biomedico (Roma)
Centro Proton terapia (Trento)
Universita'di Trento
University of Washington (USA)

The 'FLASH' e^- irradiation strategy

Line 1 dedicated to 'large' fields Scattering filter:

- few mm of aluminum + 50 cm of air already provide a coverage for 5x5 cm^2 (quads really needed??)
- Enough current to go flash on 10x10cm^2 field in 1 few μs pulse (IORT mode)





Line 2 dedicated to Active scanning system

- magnetic bending from fast scanning dipole (design from INFN-LNF).
- Pulse charge can be modulated->IMeRT (How much accuracy?)
- Low current needed in pbs to go FLASH