CNR-INO
ISTITUTO NAZIONALE DI OTTICA
CONSIGLIO NAZIONALE DELLE RICERCHE

4th European Advanced Accelerator Workshop
15-21 September 2019
Isola d'Elba, Italy

Toward effective applications of laser-driven VHEE in radiotherapy: Dosimetry, multiple-field irradiation and intensity-modulated fields

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The ILIL (*Intense Laser Irradiation* Laboratory) group

PEOPLE

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- Lorenzo **FULGENTINI**
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http://ilil.ino.it

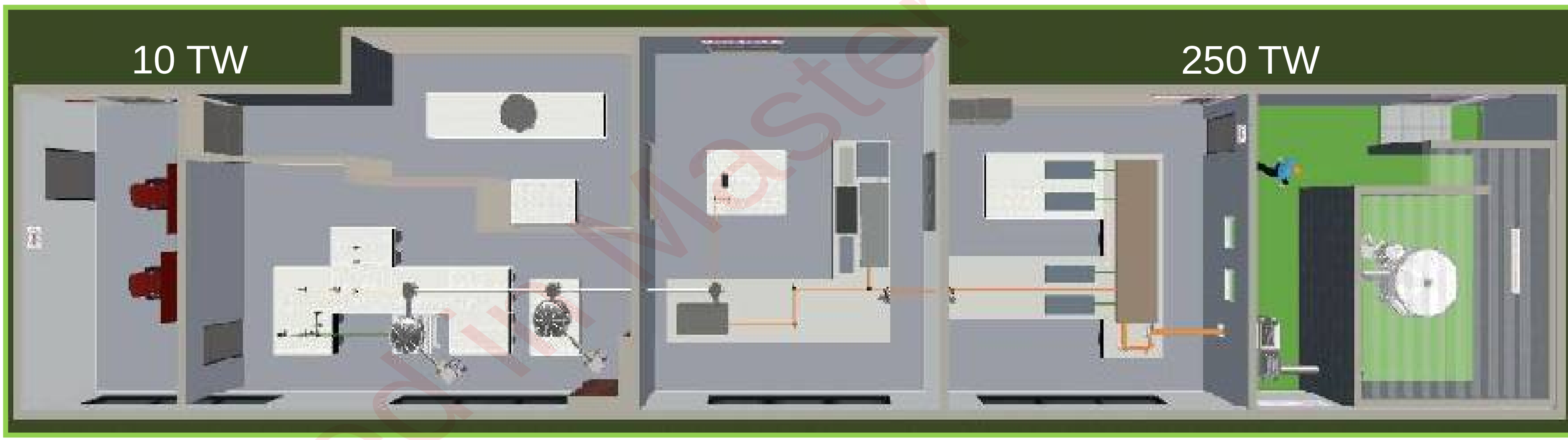
Main activities and lab

Laser-plasma interactions in ICF and Shock ignition*

- Laser-driven instabilities and plasma characterization
- Diagnostics of ICF-relevant plasmas

Laser-driven particle accelerators

- **Electron acceleration** and X-rays radiation sources
- Light Ion acceleration



Control room | TW Target Area | Front end | Power Amplifier | Shielded T.A.

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*Also through LASERLAB access to Laser facilities (RAL-CLF(UK), PALS (CZ) and within EURATOM Collaboration)

The ILIL lasers: 200TW upgrade

Parameter	10TW (2016)	Current (mid 2019)	Final
Final amplifier pump energy	- (final amp: 2J)	15J	20J
Pulse duration	~40 fs	25 fs	25 fs
Energy before compression	0.6 J	6J	7.5J
Energy after compression	0.45 J	>4 J	>5J
Rep rate	10 Hz	1 Hz (up to 2Hz)	1 Hz (up to 2Hz)
Max intensity on target	$2x10^{19}$ W/cm^2	$>10^{20}$ W/cm2	$>4x10^{20}$ W/cm^2
Contrast (ns)	$>10^9$	10^9	10^9

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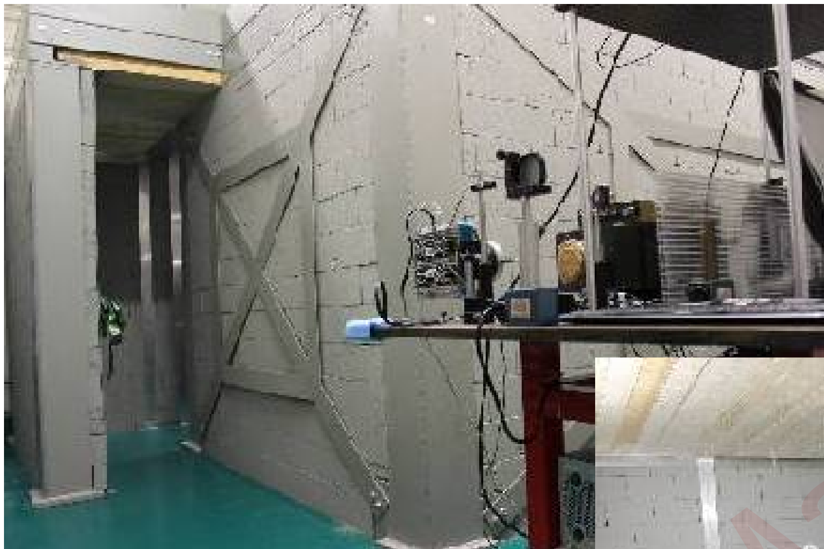
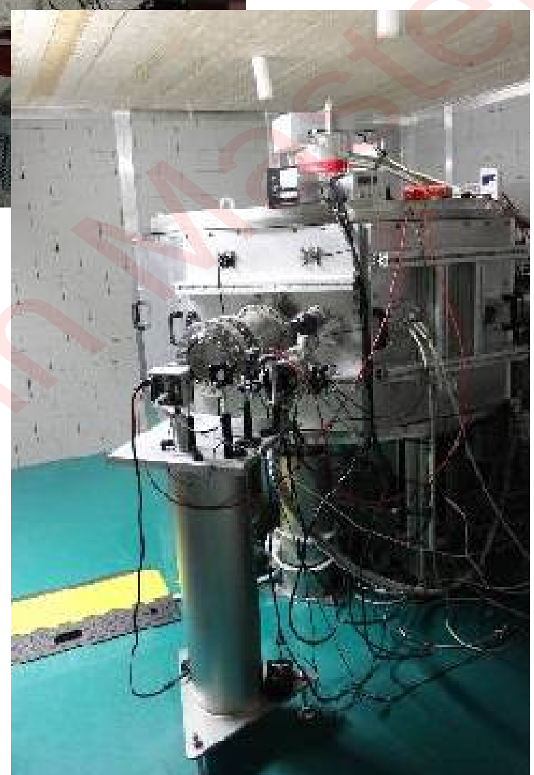
The lab: the 250TW Target Area

Target Area with radiation shielding inaugurated on March 2018





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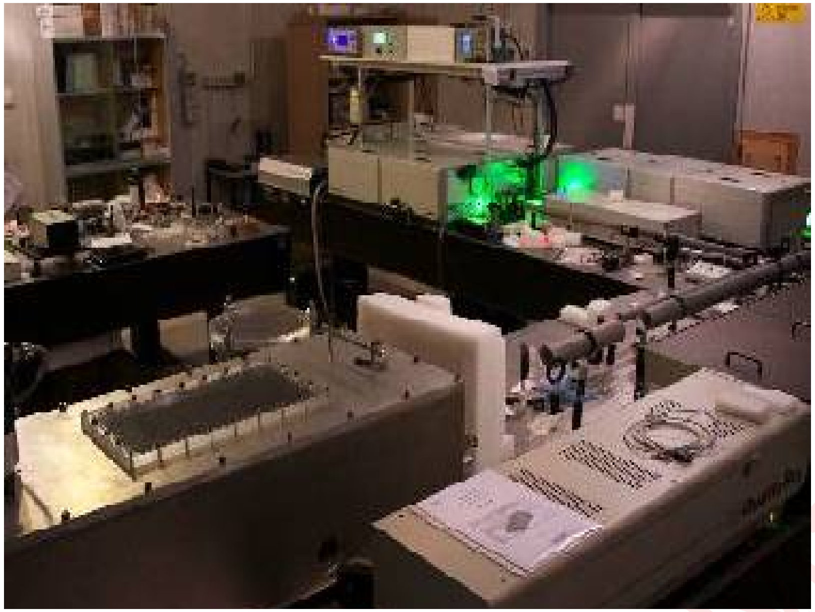
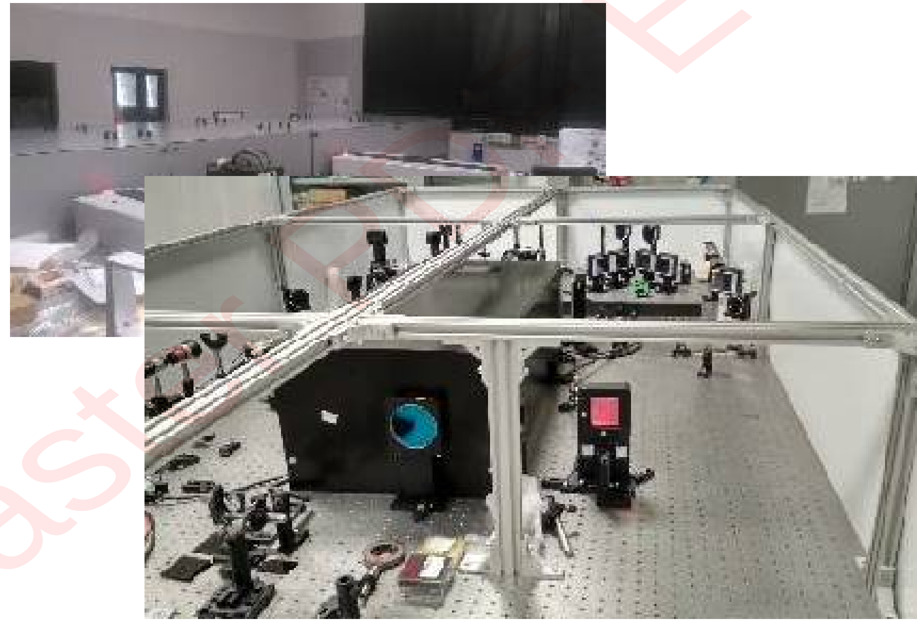
The lab: the laser system

Front-end and 10TW compressor



ILIL 250TW final amplifier (8J)



250TW compressor

Past research on LWFA applications to medicine at the ILIL lab: "low-energy" e- bunches for Intra-Operatory RT

Comparison with "conventional" sources in medicine

Comparable figures as for electron energy, bunch charge, rep rate, average current

Bunch duration (→ peak current) of laser-driven accelerators much shorter
→ Much higher instantaneous dose rate

Parameter	LIAC (Sordina SpA)	Laser-LINAC
Max e^- kinetic energy	12 MeV	Up to 100s MeV
Total charge/bunch(shot)	1.8 nC	1 nC
Repetition rate	5-20 Hz	10 Hz
Average current	18 pA (@10Hz)	10 pA
Bunch duration	1.2 microseconds	~1 ps
Dose/pulse	0.5 – 5 cGy	Up to cGy?
Instantaneous dose rate	$\sim 10^7$ Gy/s	$>\sim 10^{12}$-10^{13} Gy/s

→ *High-current* e^- bunches (with respect to those from RF LINACS): different radiobiological effects?
Novel applications/protocols in perspectives?

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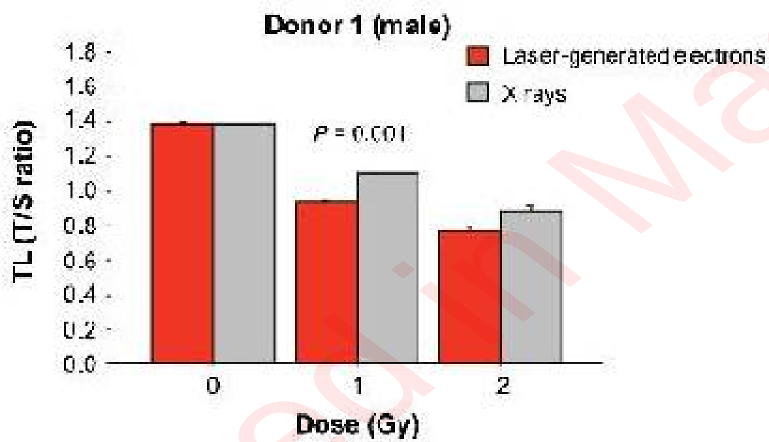
A. Giulietti, Proc. SPIE 10239 (2017); L. Labate, Proc. SPIE 10239 (2017); L. Labate *et al.*, J. Phys. D 49, 274501 (2016)

Past radiobiology experiments at ILIL with “low-energy” e- bunches: Comparative study of cell damage: radiation-induced telomere shortening

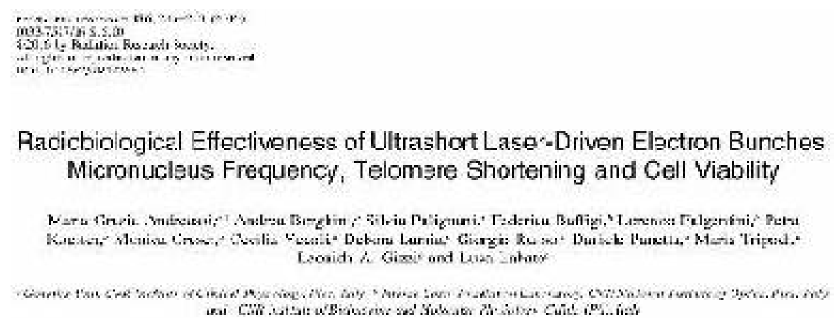
- Telomeres play a vitally important part in preserving the integrity and stability of chromosomes
- Telomere length was studied after irradiation with LWFA electron bunches and X-rays from an X-ray tube (standard in radiation biology)

Irradiations at different dose levels was carried out



Telomeres shorter than baseline from 0.1 Gy (p<0.001)

Results comparable for laser-driven electron bunches and X-rays


Radiobiological Effectiveness of Ultrashort Laser-Driven Electron Bunches: Micronucleus Frequency, Telomere Shortening and Cell Viability

M.G. Andreassi *et al.*, Rad. Res. 186, 245 (2016)

Contents

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Contents

- **Motivations: (laser-driven) VHEE to possibly open up new frontiers in radiotherapy protocols**
- Recent experimental studies of real RT modalities with VHEE at the ILIL laboratory
  - Overview of the LWFA regime and e- bunch dosimetric properties
  - Preliminary steps toward "real" biomedical applications: Demonstration of Intensity Modulation and Multiple-Field irradiation
- Summary and conclusions (current state and perspectives for FLASH-RT)

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Motivations: laser-driven VHEE as a possible new tool for radiotherapy

Most common radiotherapy nowadays use *Bremsstrahlung* X-ray photon beams from MV clinical LINACs

This is historically due to the lack of availability of clinical VHEE LINAC sources

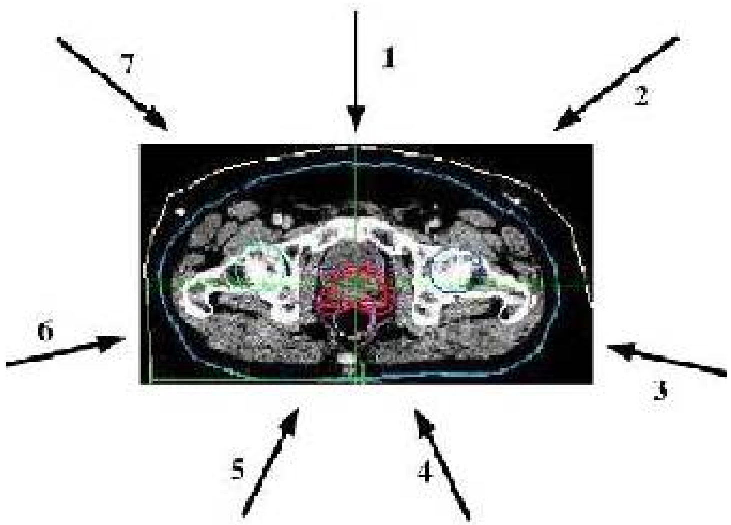
current limit of clinical LINACs: 22 MeV

→ unsuitable to treat deep-seated tumors, due to the steep attenuation profile in human tissues

Notable exception: Intra-Operatory Radiation Therapy (IORT) – 6-12 MeV

Bremsstrahlung photon beams: rather poor directionality, broad spectrum, long attenuation lengths in human tissues

→ "Advanced" X-ray modalities: Intensity-Modulated RadioTherapy (IMRT) coupled to Multi-Field irradiation



Motivations: laser-driven VHEE as a possible new tool for radiotherapy (2)

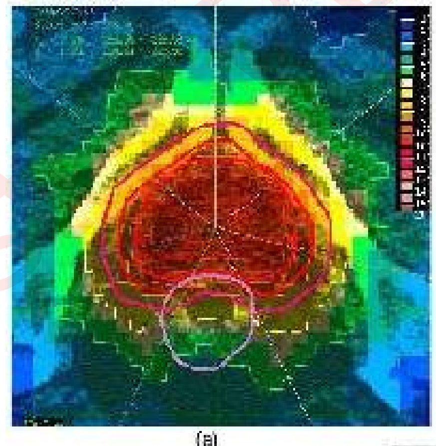
Laser-driven acceleration of electrons to >100MeV (up to ~250MeV) energy (so-called VHEE) have the potential to modify this scenario → revived interest for electron radiotherapy

Possible usage has been investigated over the past 10 years by means of Monte Carlo simulations, showing a potential for good dose conformation, comparable (or exceeding) that of current photon beam modalities

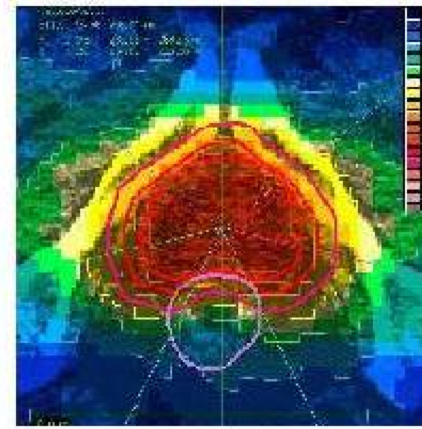
Quality of a prostate treatment plan evaluated for a 6MV IMRT and a VHEE treatment

- Better target coverage achieved
- Extent of the sparing of organs at risk found to be dependent on depth (due to e- exhibiting larger scattering)

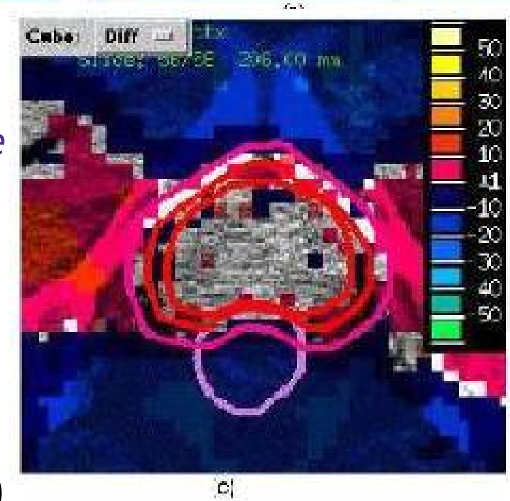
6MV X-rays



150MeV e-



difference



T. Fuchs *et al.*, Phys. Med. Biol. **54**, 3315 (2009)
Des Rosiers *et al.*, Int. J. Radiat. Oncol. Biol. Phys. **72**, S612 (2008)

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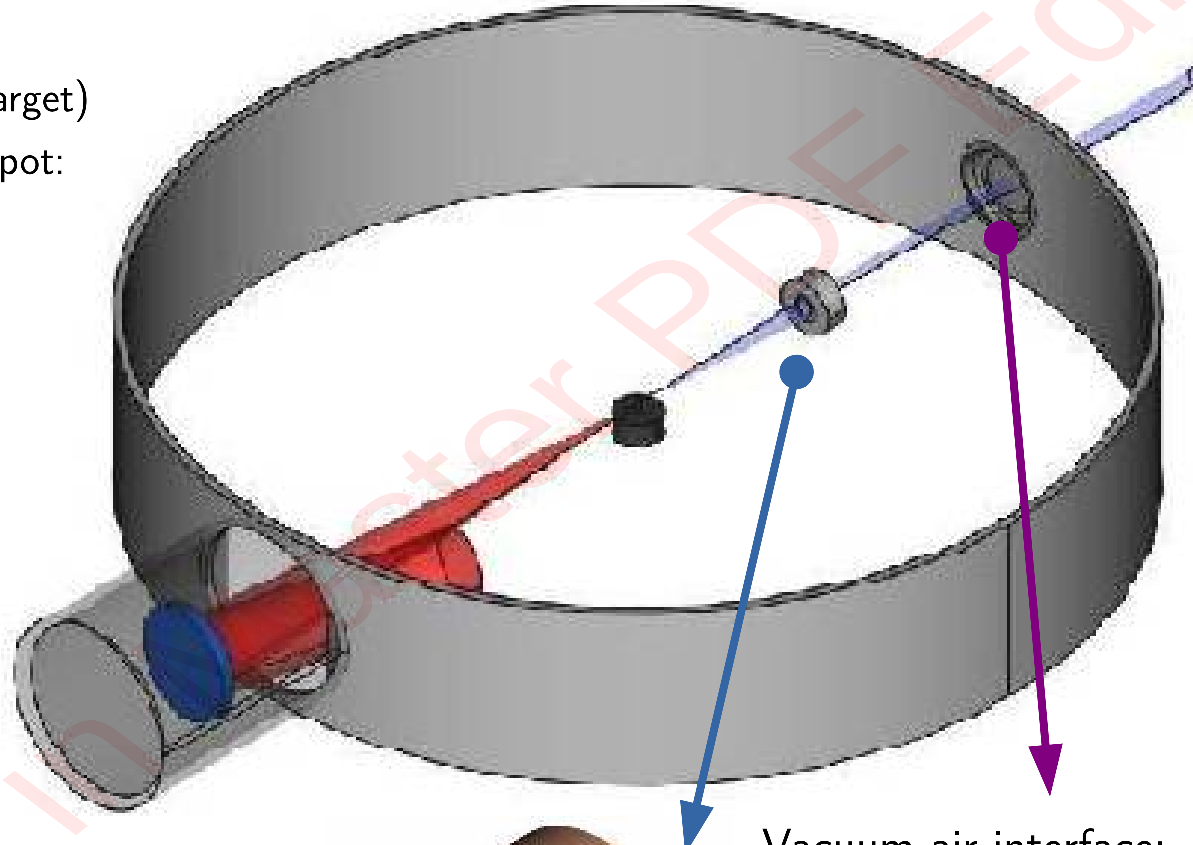
A quick look at the experiment setup/parameters

Laser beam figures

- 150TW beamline (>4J on target)
- beam energy in the central spot: <~ 3J (Strehl ratio ~0.7)
- focused with an f/~20 OAP
- w ~ 31micron
- a_0 ~ 1.7

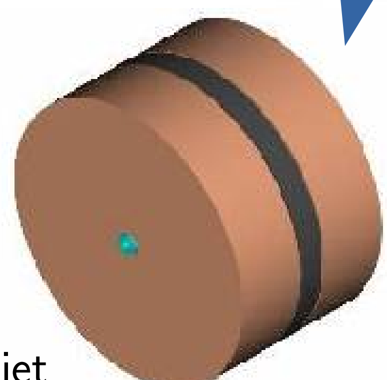


Vacuum-air interface:

70micron thick kapton window

e- bunch collimator:

- multi-layer PVC/Pb/PVC
- total thickness: 7cm
- teflon tube at the center, with a 2mm aperture
- placed 35cm downstream the gas-jet



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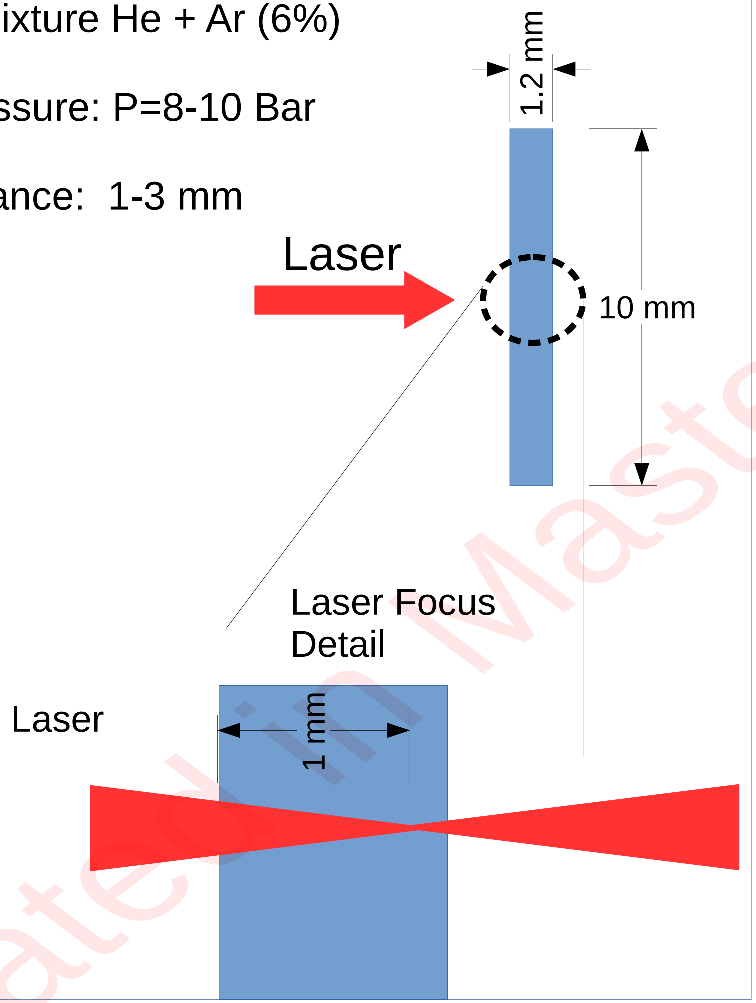
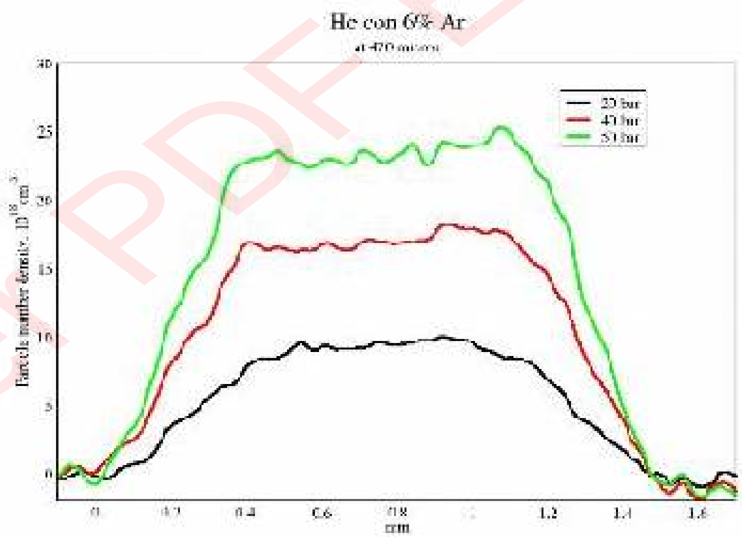
A quick look at the experiment setup/parameters: the gas-jet nozzle

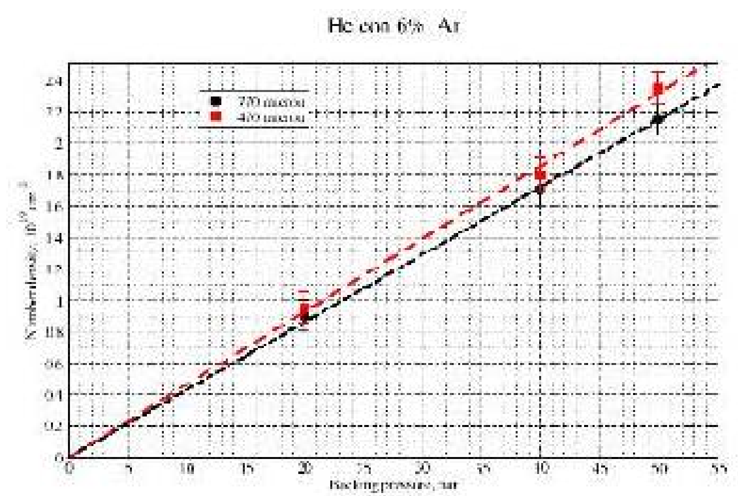
- Gas Type: Mixture He + Ar (6%)
- Backing Pressure: P=8-10 Bar
- Vertical Distance: 1-3 mm

Nozzle (top view)



(Offline) density profile characterization





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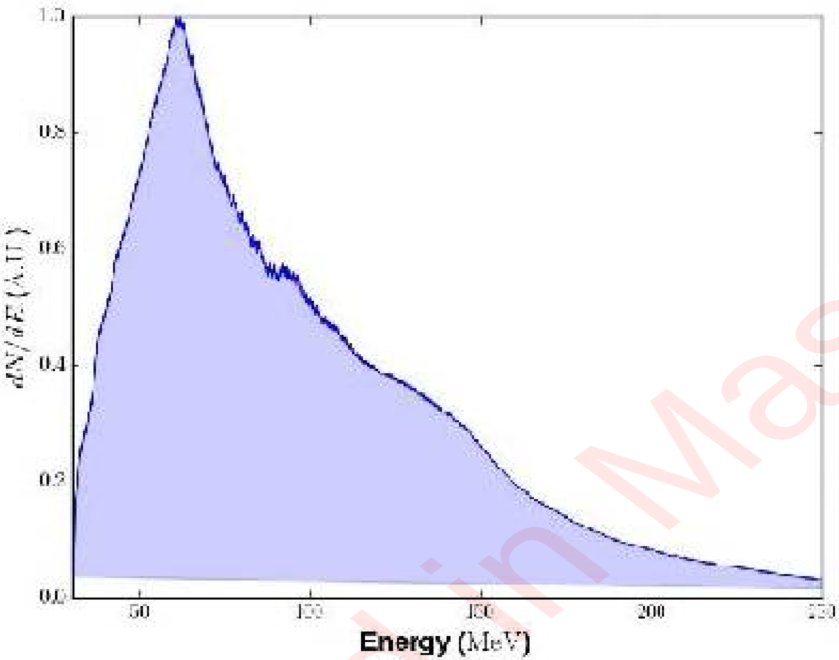
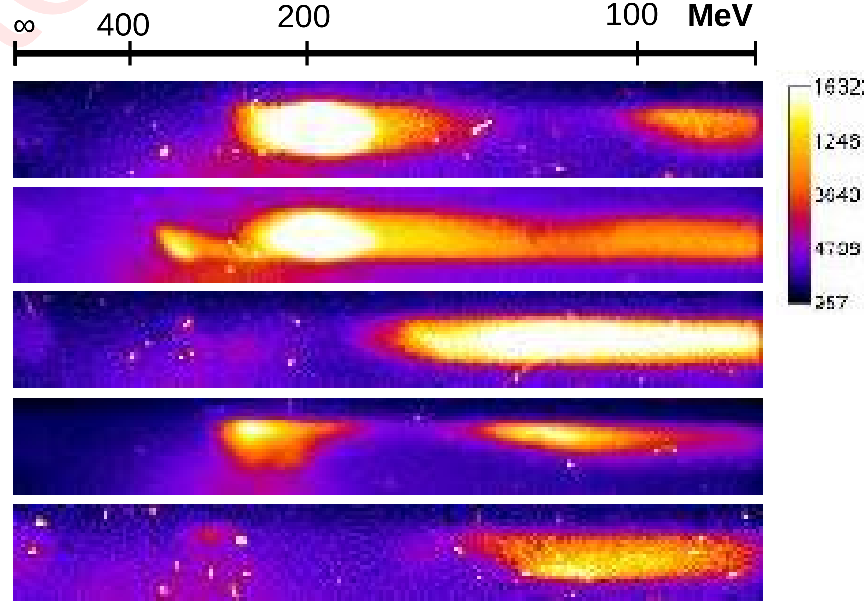
Electron spectra: main features

A LWFA condition delivering e- bunches with energy ~100MeV was seeked for (mainly by (de)tuning laser focus position, backing pressure and density profile)



Most of the charge is contained in an energy interval 80-150 MeV

A few examples of e- spectra



Average spectrum pretty stable when averaged over 20 shots

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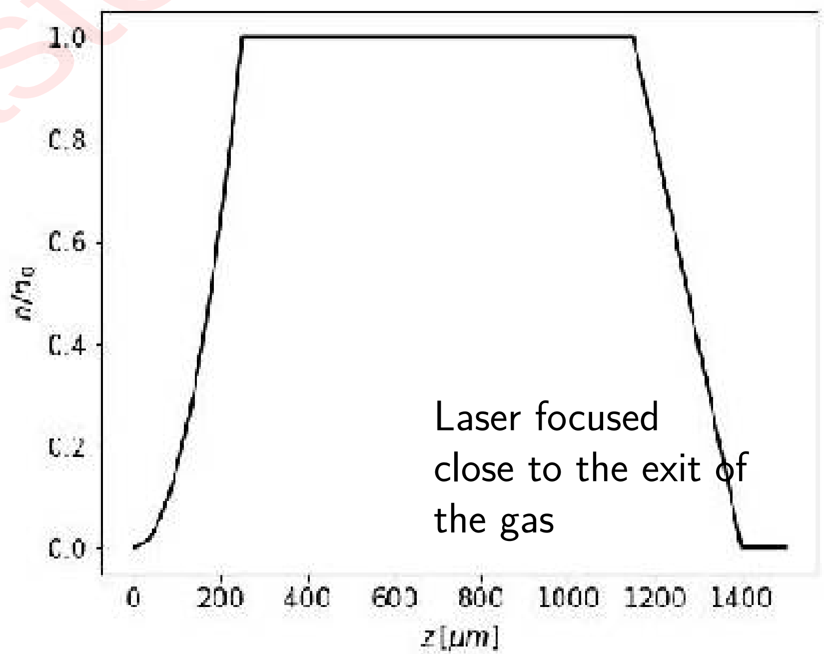
A closer look at the LWFA conditions: Preliminary PIC study

PIC simulations carried out with the FBPIC (Fourier-Bessel PIC) code:

- quasi-cylindrical (arbitrary number of angular modes *m*)
- spectral solver for field advance
- particles are moved in real space
- runs most efficiently on GPU

Density profile
(gas jet)

- Cylindrical modes used: m= 0, 1
- $\Delta z = 0.05$ µm
- $\Delta r = 0.13$ µm
- 12 Macroparticles per cell
- ADK ionization ON
- Particle spline: linear



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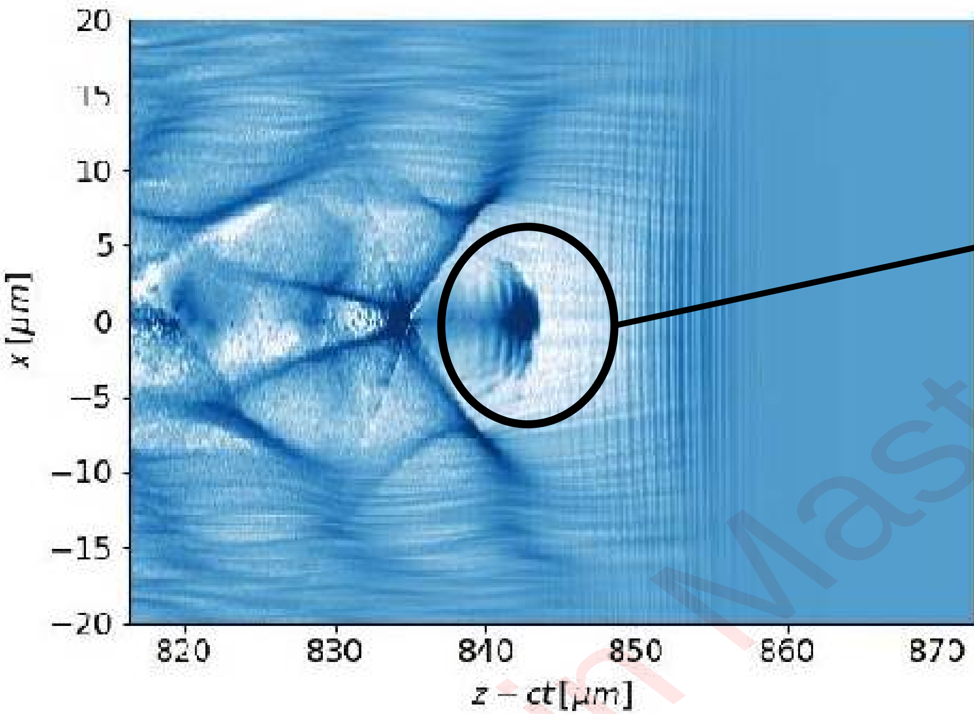
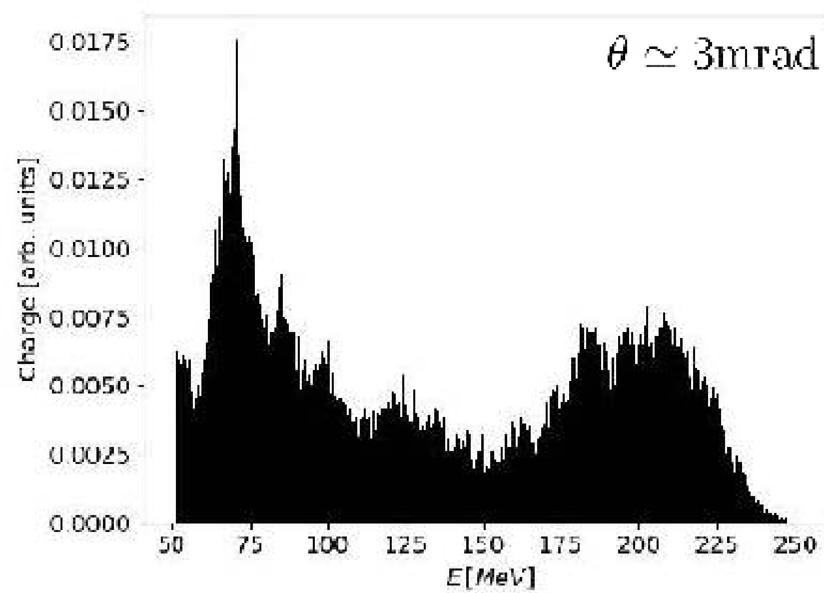
A closer look at the LWFA conditions: Preliminary PIC study (2)

Density log map at ct = 850 µm



Accelerated bunch

Spectrum over the acceptance angle of the collimator



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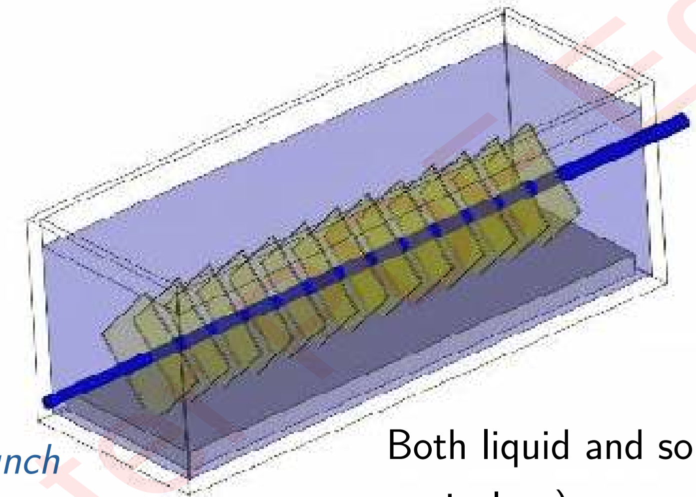
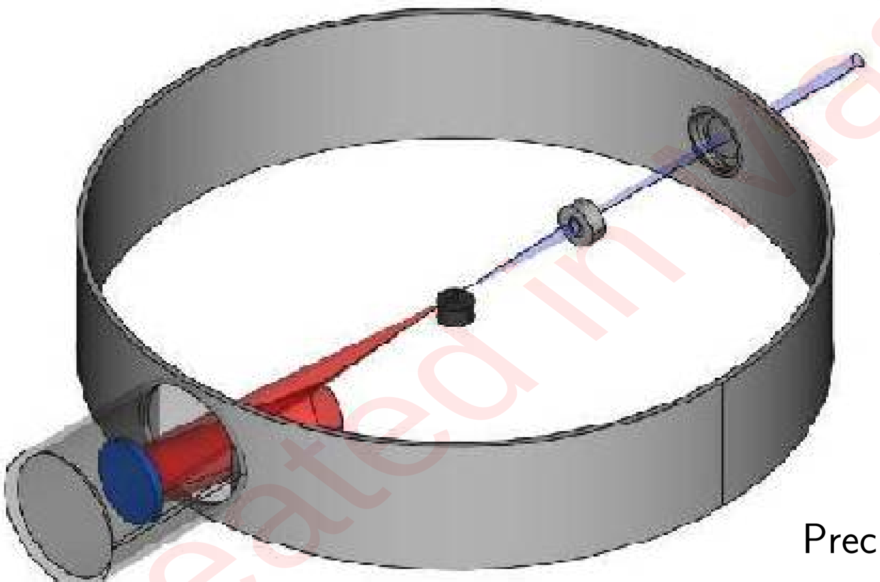
Beam dosimetry

Preliminary to applications relevant for effective RT protocols

"Intrinsic" (charge, divergence,...) beam properties studied w/o the collimator





e- bunch

Both liquid and solid (A150 tissue equivalent) water phantoms used

EBT3 Gafchromic films used as detector (showed* to exhibit energy independent response in the energy range of interest)

e- signal observed on Gaf films up to a depth of ~25cm (integrated over 100 laser shot)

Precise calibration of each EBT3 batch carried out using 6MeV electron bunches from a conventional medical LINAC

*A. Subiel *et al.*, Phys. Med. Biol. **59**, 5811 (2014)

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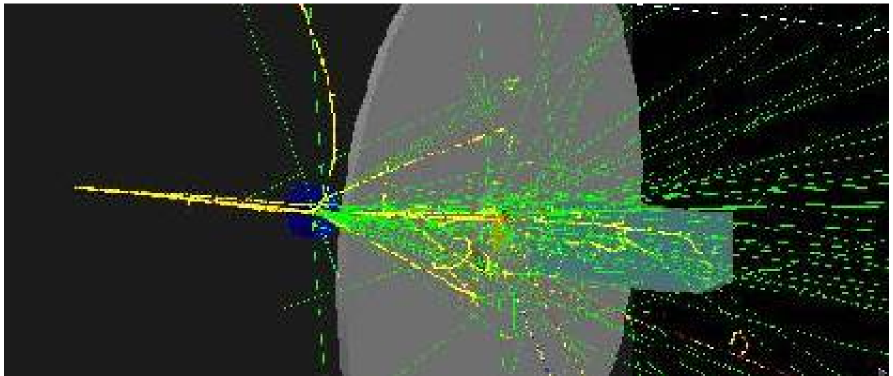
Beam dosimetry: comparison with Monte Carlo simulations

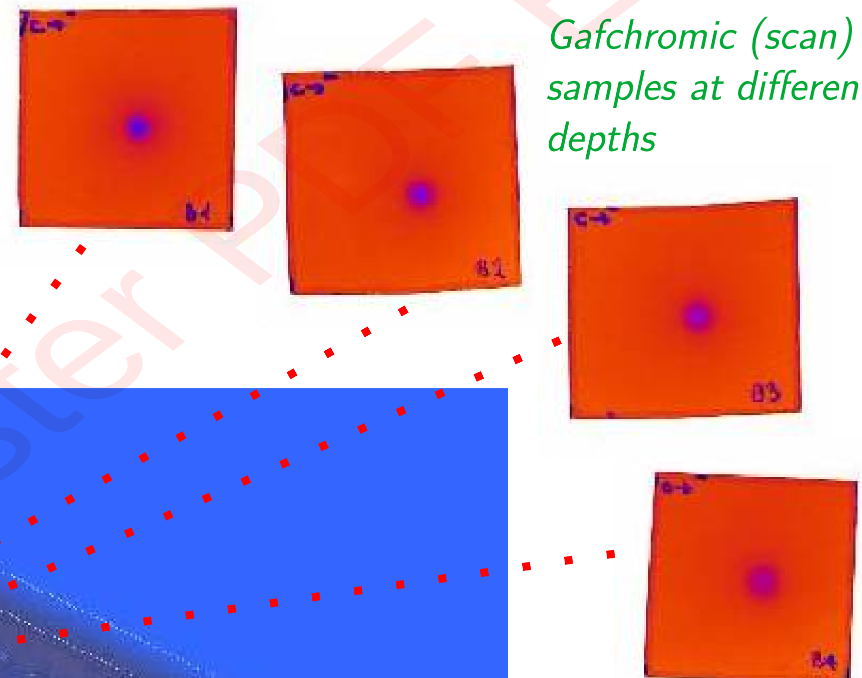
Monte Carlo simulations carried out using the GEANT4 toolkit



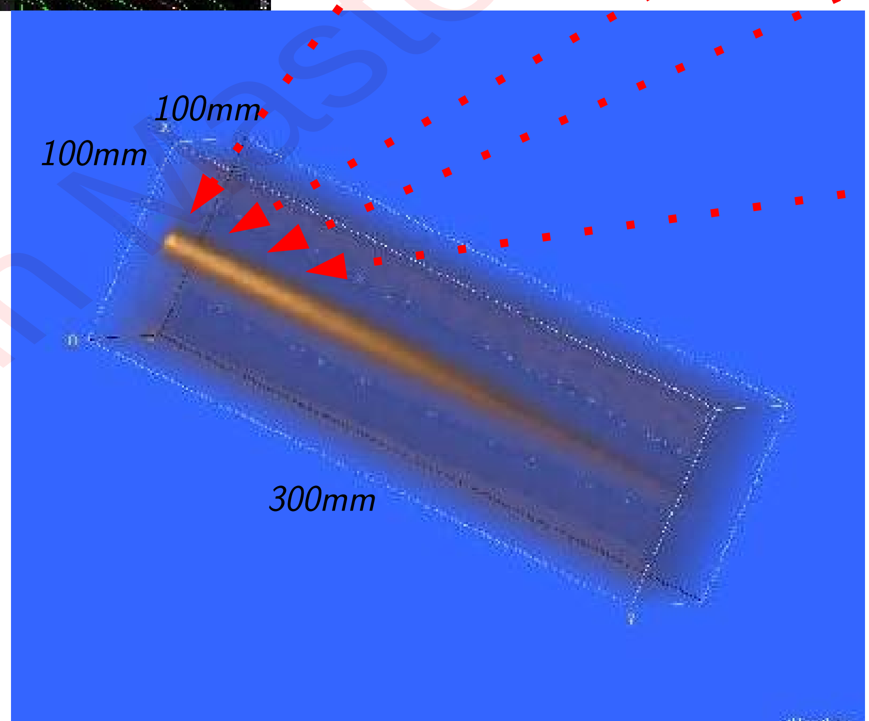
GEANT4 simulation tracking of few primary events

Size of the beam at the entrance ~3.5mm

Estimated bunch charge: ~200pC



Gafchromic (scan) samples at different depths



Rendering of the dose deposition pattern as provided by GEANT4 simulations

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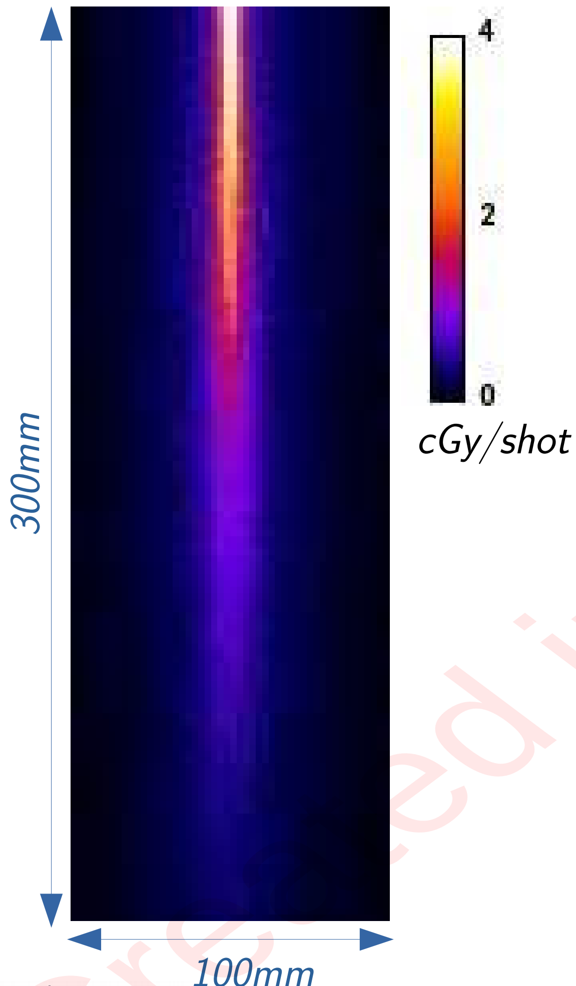
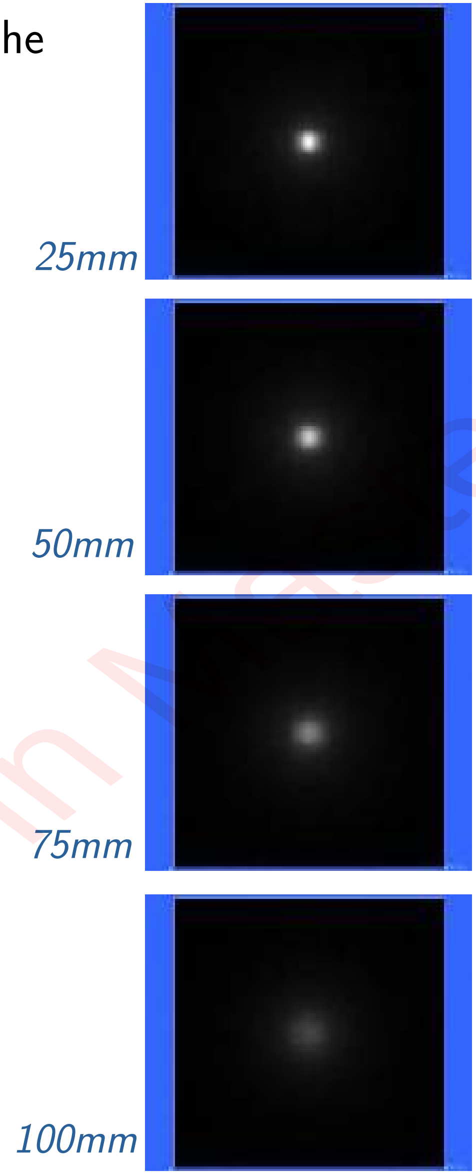
Beam dosimetry: absolute dose and dose depth properties

Dose deposition pattern on the central (axis) plane





Dose/shot: 3-5 cGy (at z_{max})

Percentage Dose Depth:
z_{max} ~35mm
$R_{50\%}$ ~110mm

The dose deposition remains confined to few mm within ~120mm

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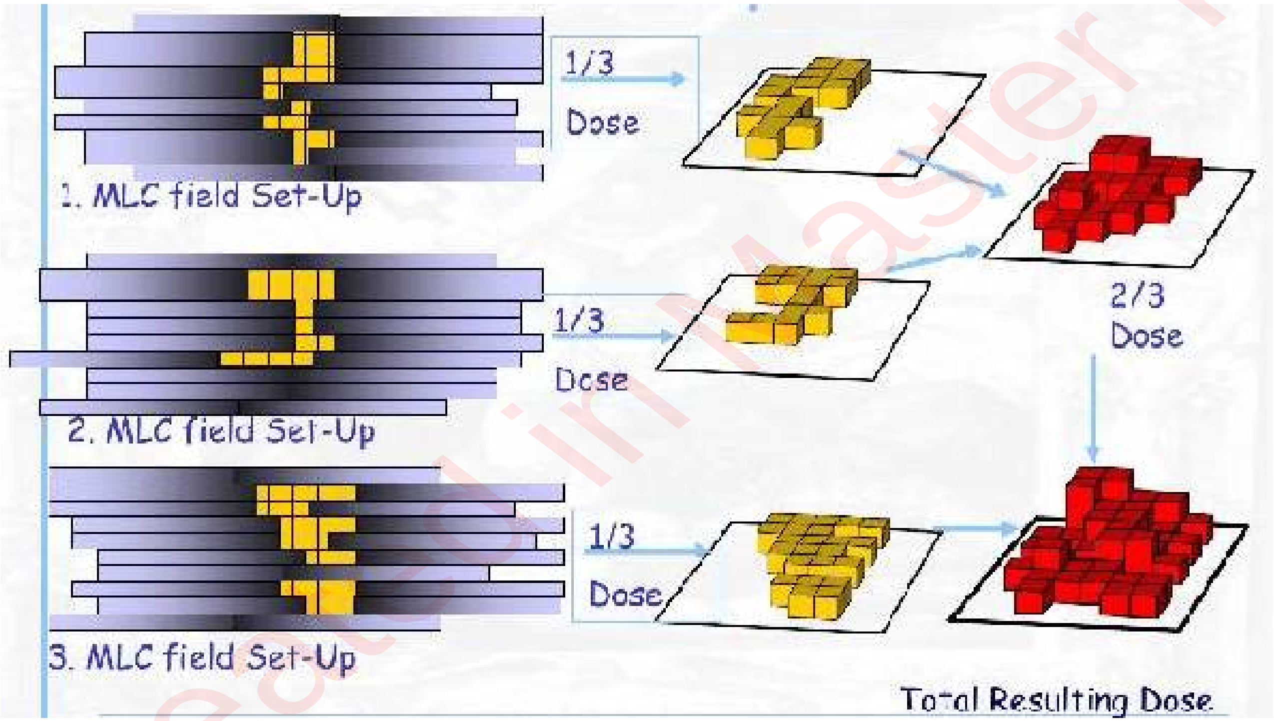
Intensity-Modulated Radiation Therapy

Intensity-modulated radiation therapy is a method of radiation delivery allowing a fine shaped distribution of dose to avoid unsustainable damage to the tumor surrounding structures

It employs (photon) beamlets with 3-4mm size using a *Multi-Leaf Collimator* (a specialized, computer-controlled device made up by many tungsten *leaves* after the accelerator tube and converted)



Routinely delivered coupled to multi-field irradiation

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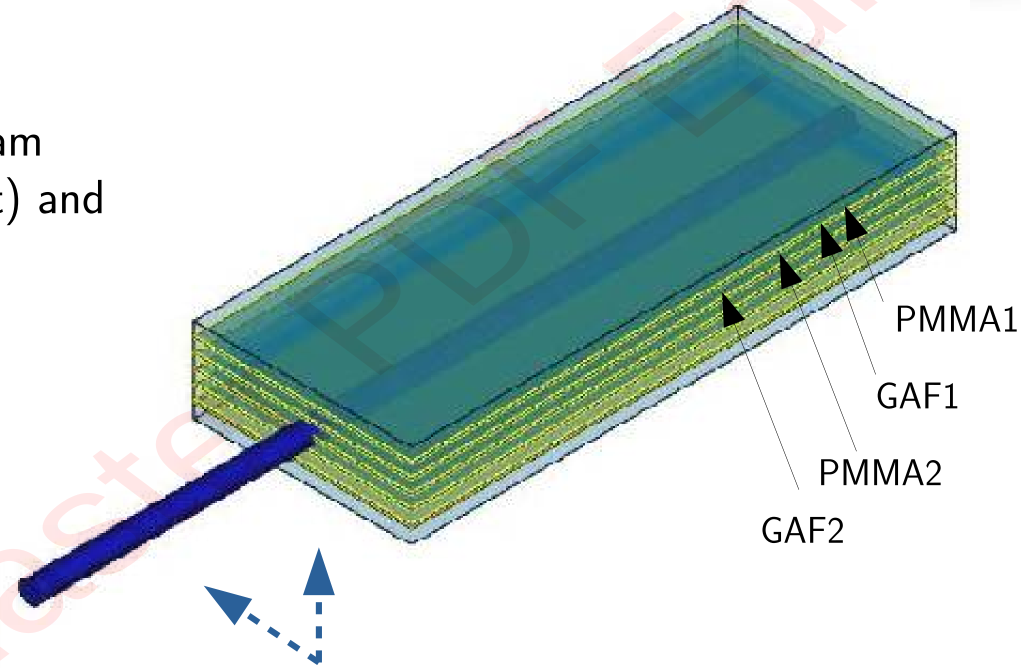
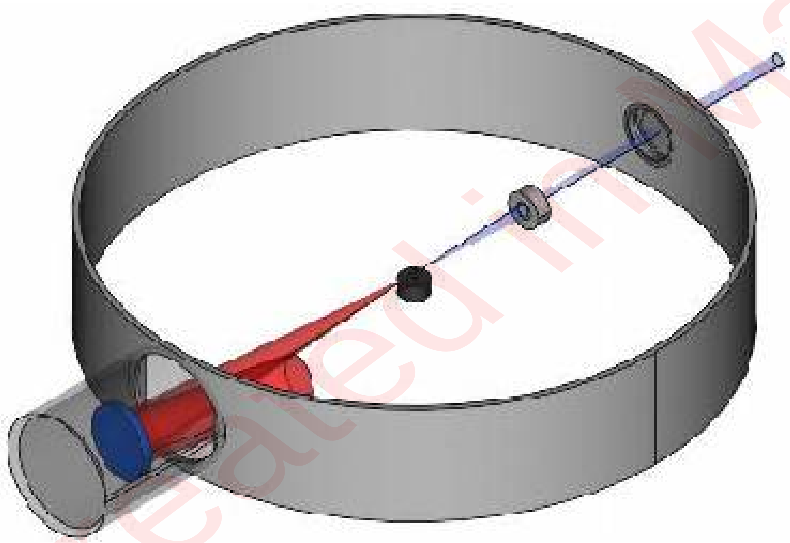
Intensity-modulated RT with laser-driven e-

Our situation: “pencil (electron) beam”

IMRT can be obtained by changing the beam entrance point (2D pattern, at the moment) and varying the number of shots

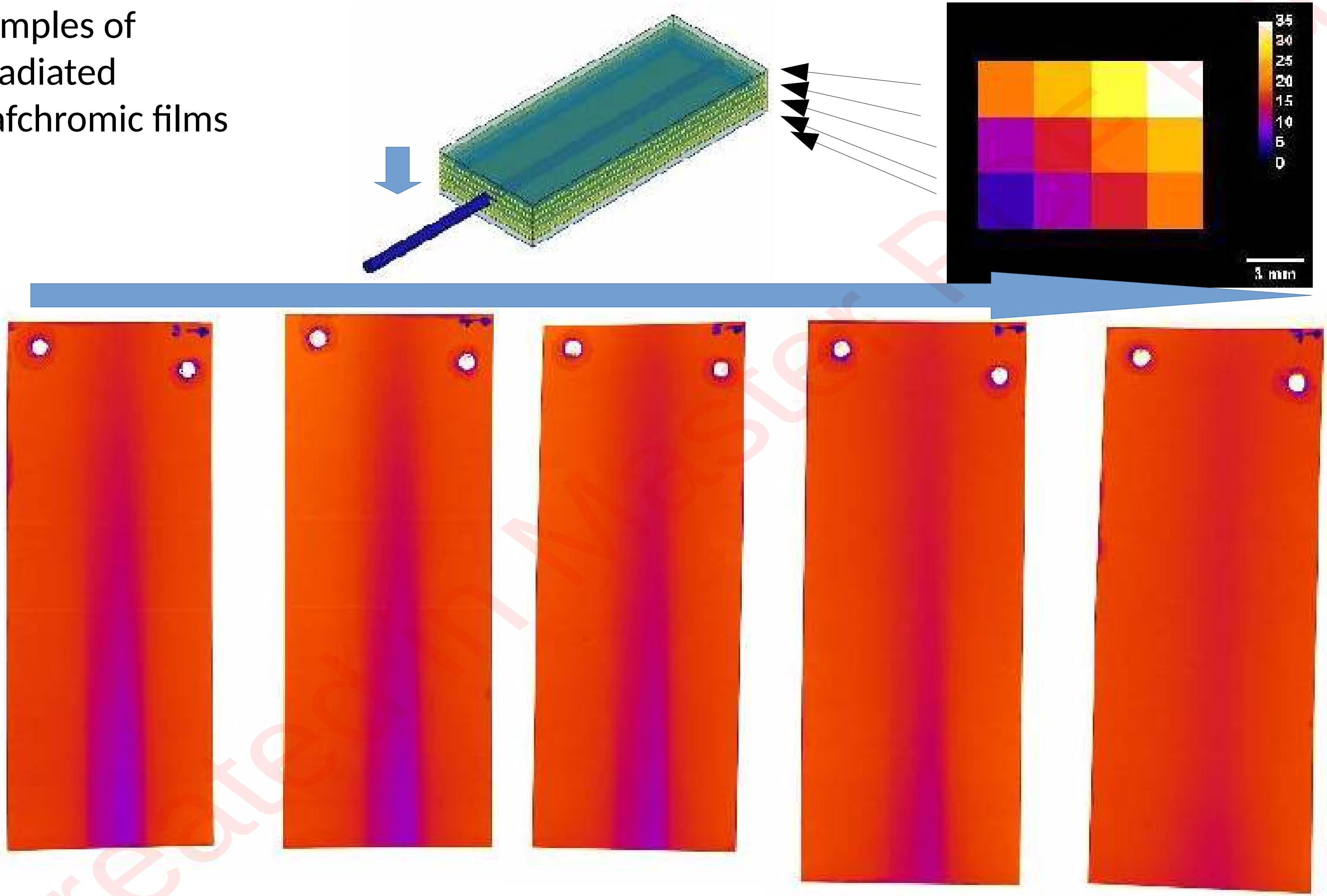




PMMA phantom with Gafchromic films placed with surface parallel to the e- beam direction (“continuous” sampling along the longitudinal direction and one of the transverse direction, discrete sampling in the other transverse direction)

IMRT with laser-driven e- beams

Samples of irradiated Gafchromic films



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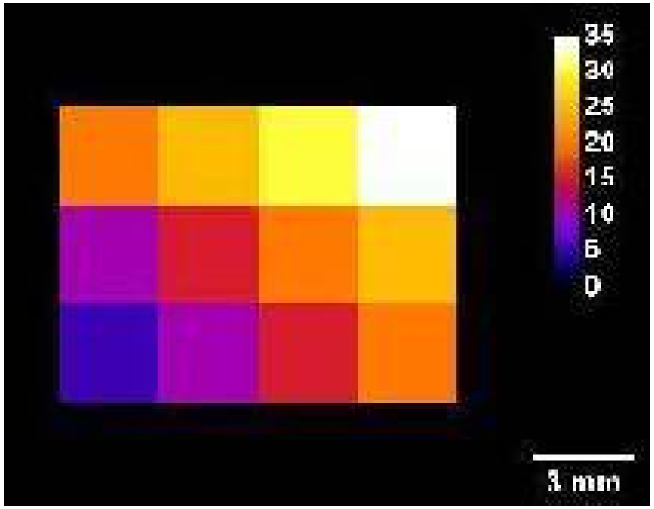
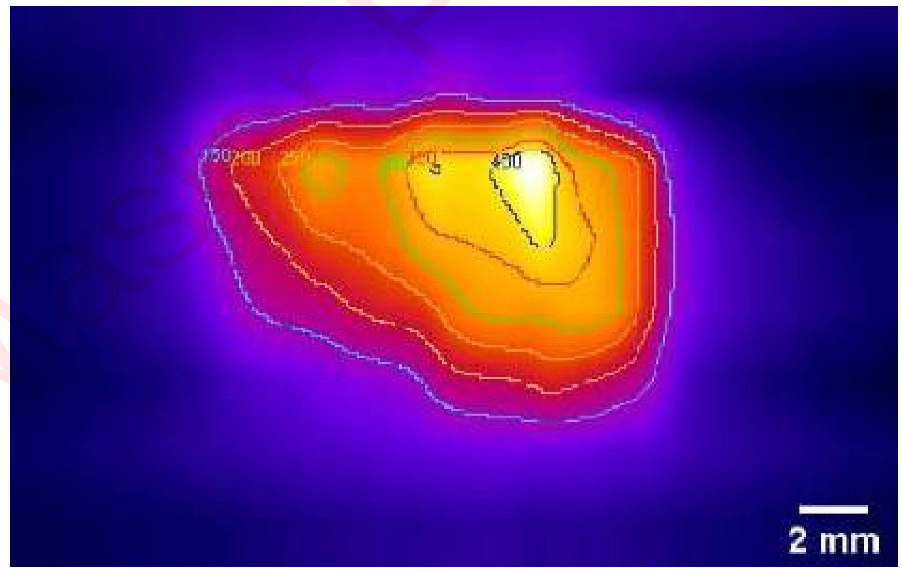
Mimicking a (single-field) IMRT: 2D modulation pattern

Irradiation pattern: (no. of shots on each position)



Experimental dose deposition transverse profile at z_{max}



Dose transverse profile tailoring with mm resolution

Comparison with expected pattern (as predicted by Monte Carlo simulations) still ongoing

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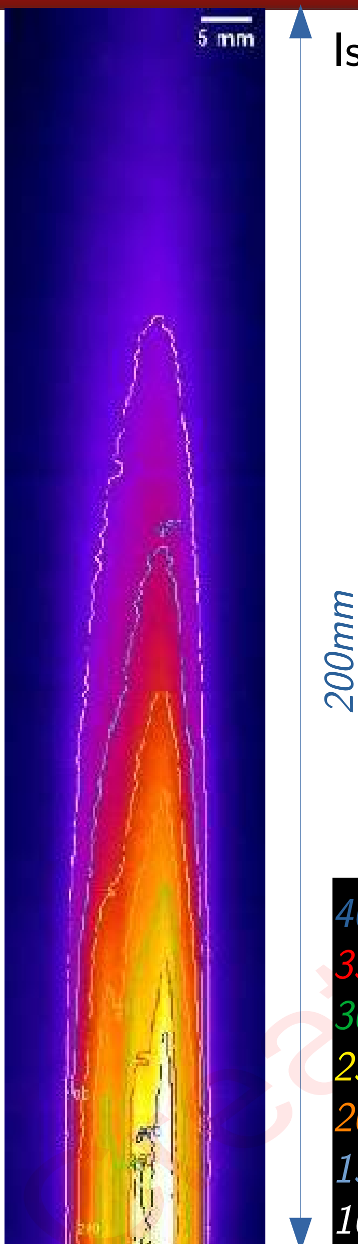
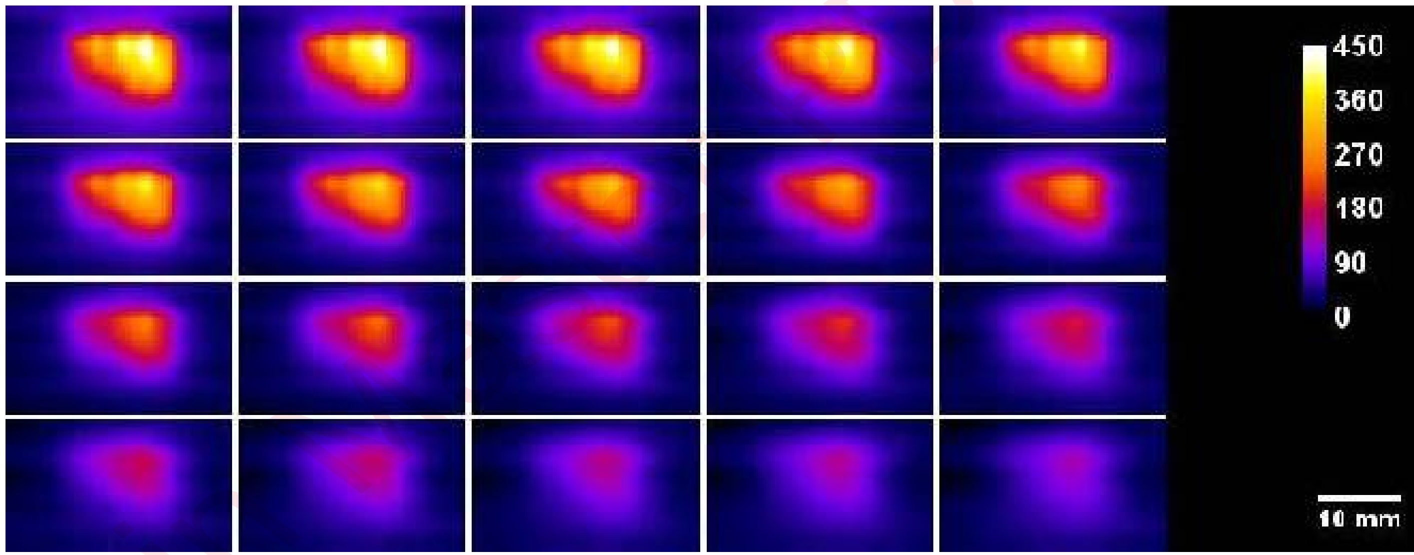
IMRT with laser-driven e- beams: depth dose delivery



Isodose curves

400 cGy ---
350 cGy ---
300 cGy ---
250 cGy ---
200 cGy ---
150 cGy ---
100 cGy ---

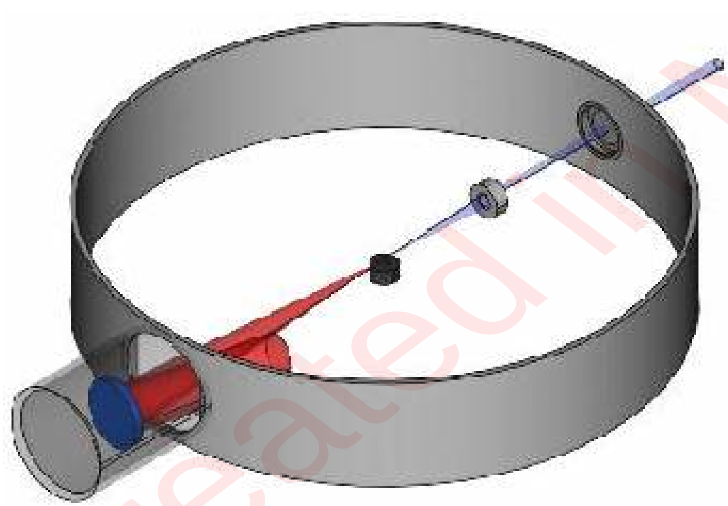
Transverse dose maps at different depths

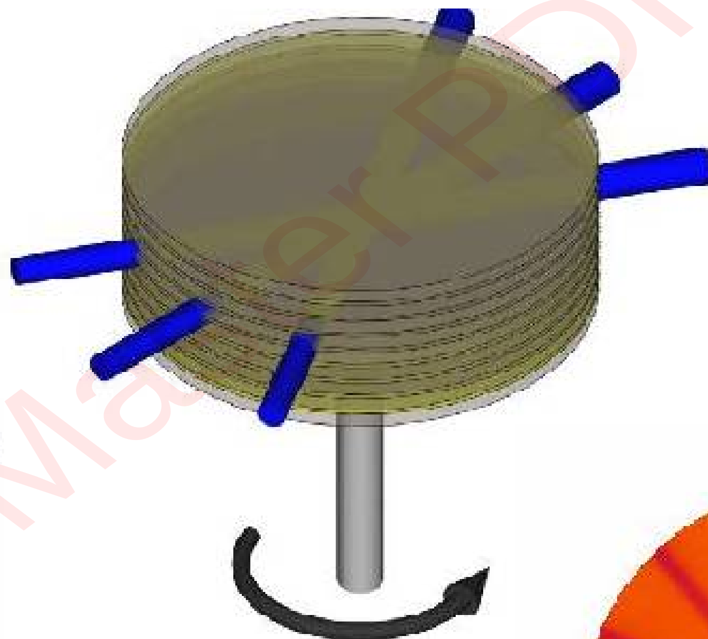


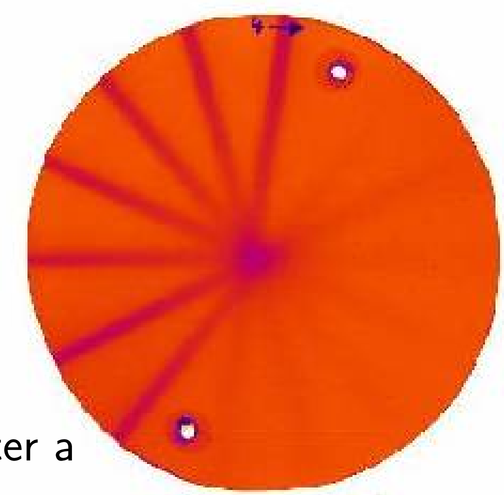
Transverse dose deposition pattern retains its (given) pattern within <1mm along the whole depth – good direction stability

Multifield irradiation: the experimental scheme

PMMA cylindrical phantom, made up by thin cylinders interleaved with round Gaf films







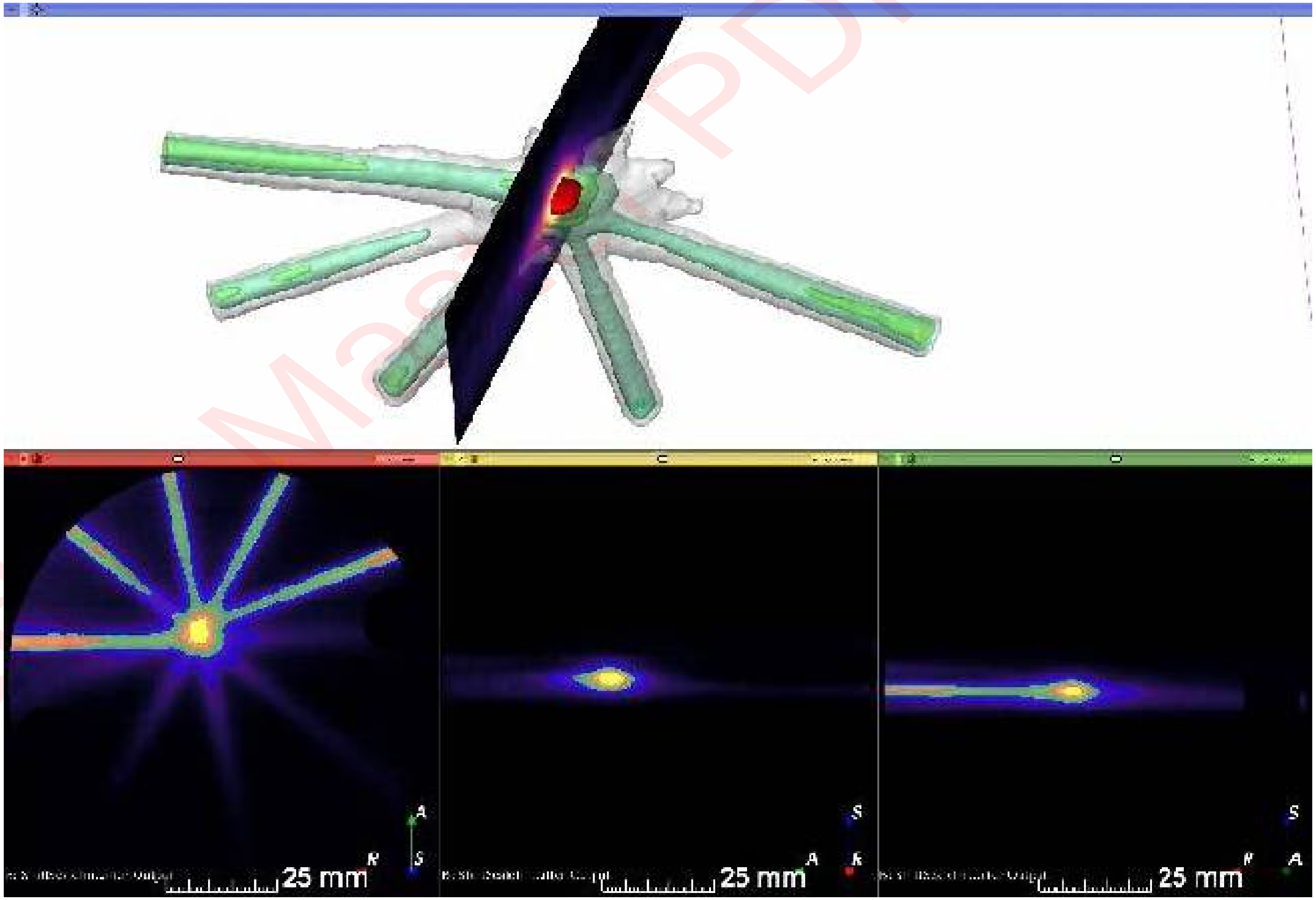
Example of irradiated Gaf after a 7 field (7 angles) irradiation

Multifield irradiation: 5-fields results

First irradiation scheme: 5 fields (at 40degree to each other), each irradiated with 40 laser shots

Up to ~2.5Gy reached on a small volume (~5mm size) at the (rotation) center

<20cGy distributed over a volume with ~15-20mm typical size surrounding this volume



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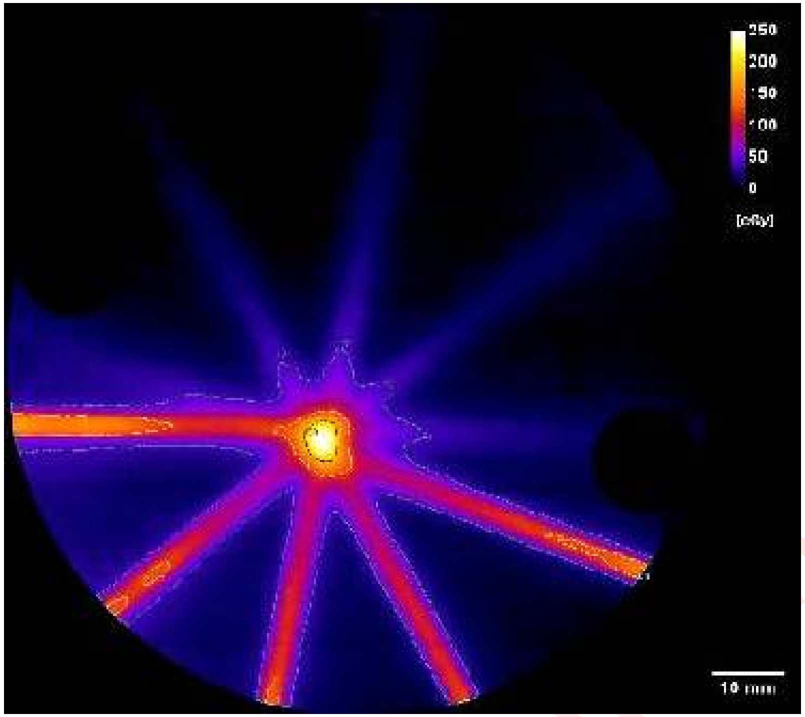
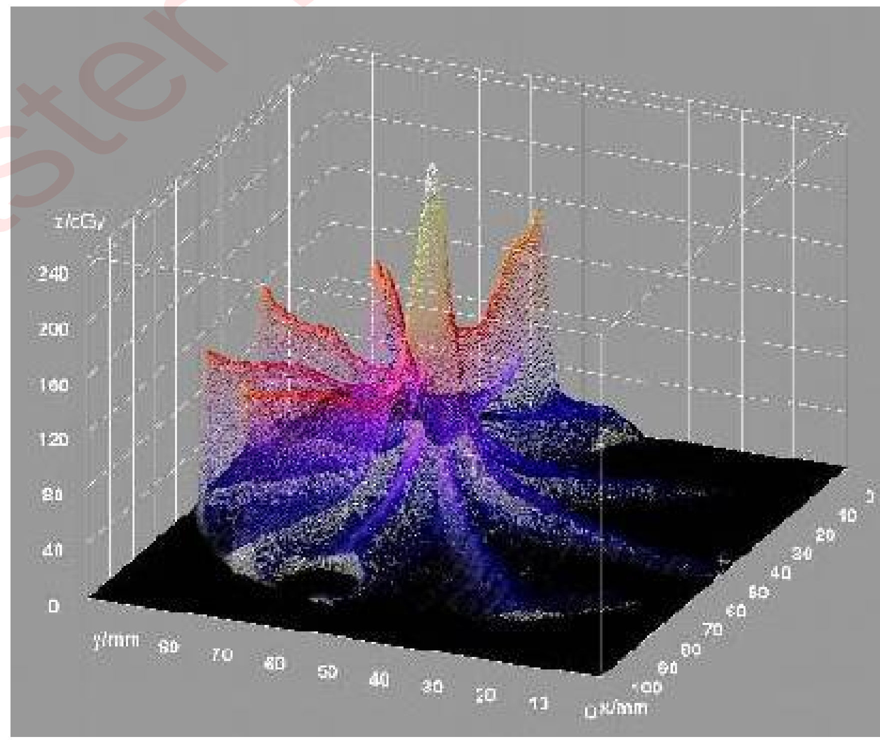
Multifield irradiation: 5-fields results

Isodose curves on a longitudinal plane



Close to 1Gy delivered at the beam entrance on each field (angle)



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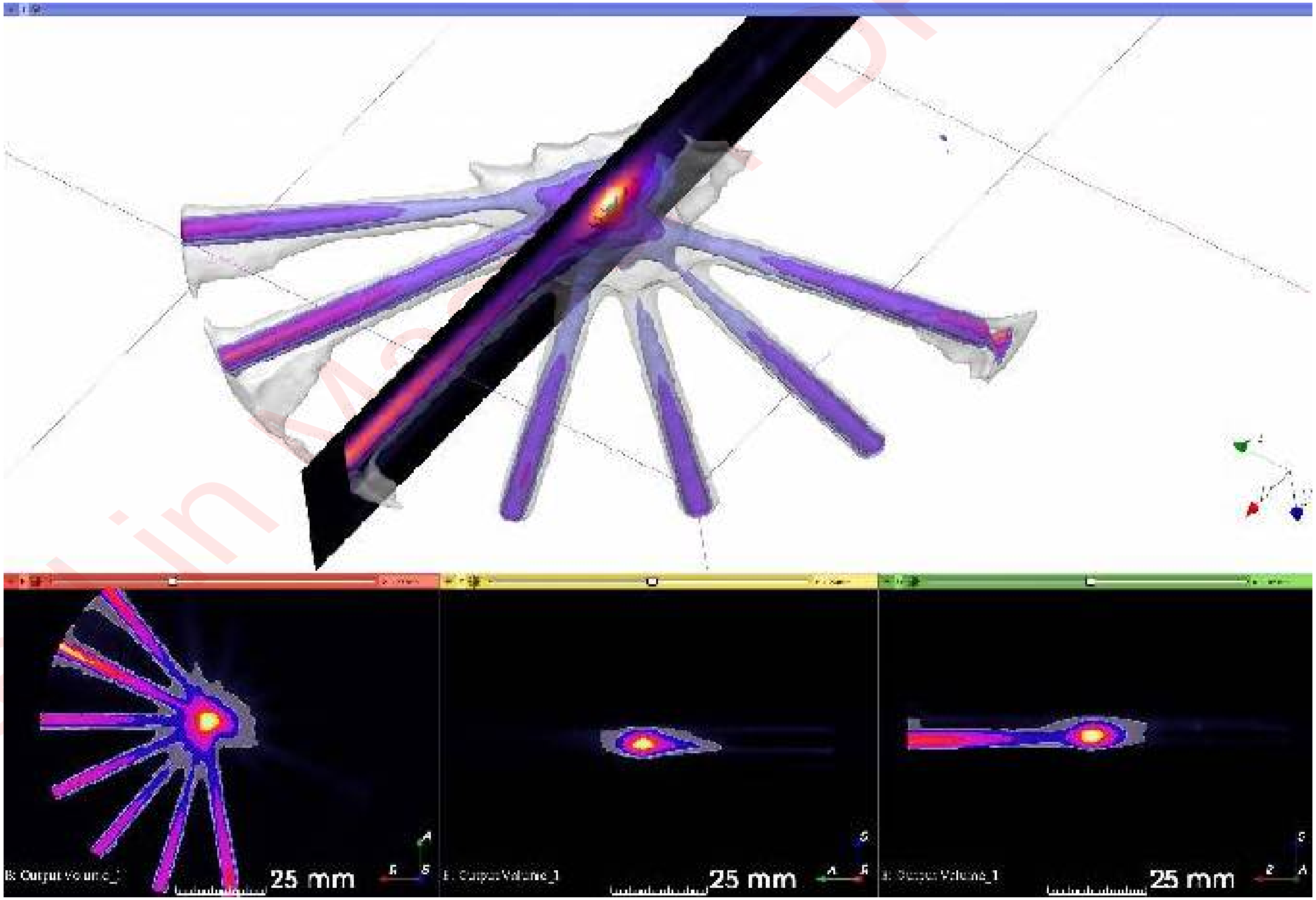
Multifield irradiation: 7-fields results

Improved irradiation scheme: 7 fields (at 25degree to each other), each irradiated with 30 laser shots



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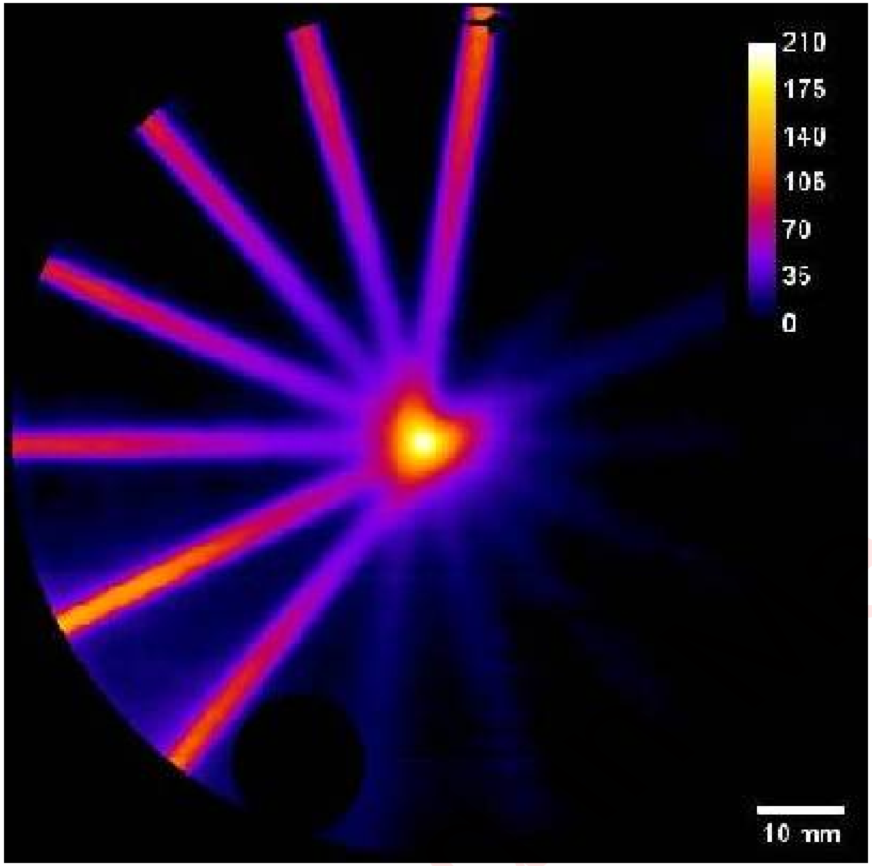
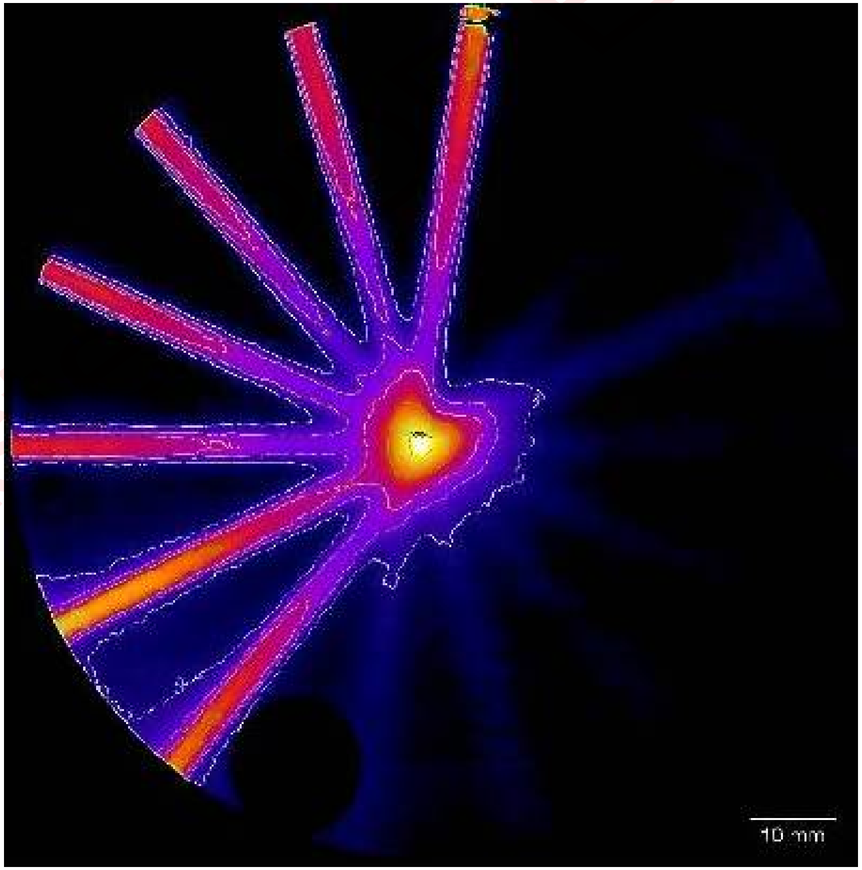


Isodose curves on a longitudinal plane



20 cGy ---	40 cGy ---
60 cGy ---	100 cGy ---
140 cGy ---	180 cGy ---

Improved dose deposition localization

Not negligible (accumulated) dose fluctuations (~20%) between different fields (i.e., shot series)

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Summary and conclusions

- First demonstration experiment of advanced RT modalities with laser-driven e- bunches
- Accurate dosimetry first performed: PDD z_{max}~35mm, $z_{50\%}$>100mm, D at z_{max} ~3-5cGy/shot (relevance for pediatric or head/neck tumors)
- Advanced RT modalities with LWFA "pencil" beams: Intensity Modulated RT and multi-field irradiation
- Dose up to ~2.5Gy (using ~200 laser shots) delivered to a 5mm size volume at ~50mm depth
  Dose goes to ~0.1 of the maximum a few mm away from the target volume
- Demonstration of transverse dose tailoring with mm resolution
- Issues: improve e- spectral features (get rid of low-energy components) to enhance ratio of doses to the target volume to dose to the entrance volumes, stability issues, ...

- Relevance for so-called FLASH-RT
  "FLASH regime": >40Gy/s
  Demonstrated (so far) with e- bunches

  (need for 1kHz rep rate)

Cite this article as:
Durante M, Bräuer-Krisch E, Hill M. Faster and safer? FLASH [illegible] radiotherapy [illegible] 91: 20170628

COMMENTARY

Faster and safer? FLASH ultra-high dose rate in radiotherapy

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