P. Lansonneur et al.,Physica Medica 60 (2019) 50–57, 2019

Simulation and experimental validation of a prototype electron beam linear accelerator for preclinical studies

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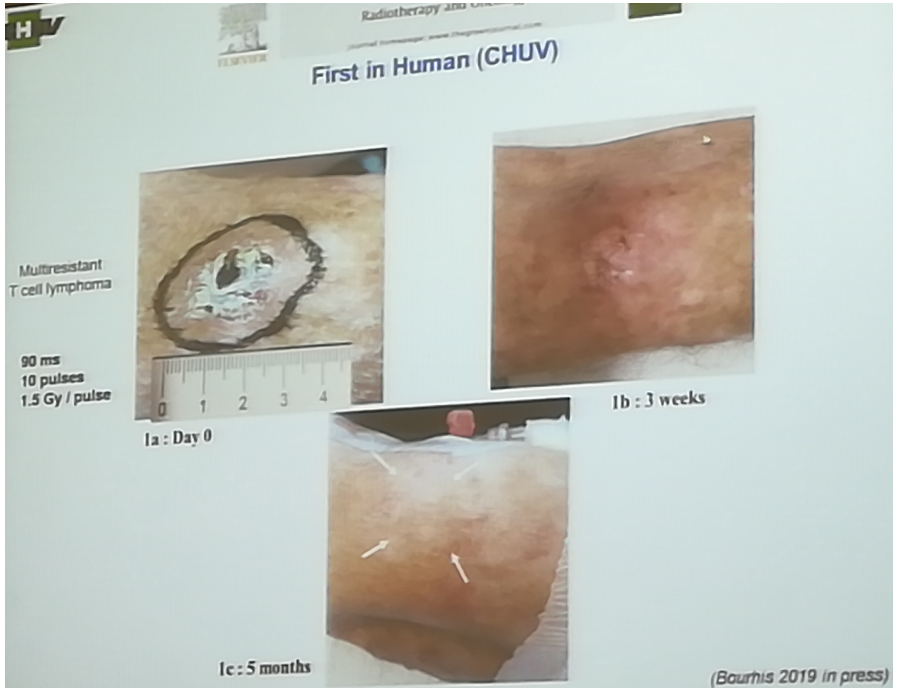
Introduction

FLASH irradiation

- Irradiation at **ultra-high dose-rate (>> 40 Gy/s)**
- may reduce adverse side effects + equally efficient for tumour control as conventional irradiation

- **In vivo studies**: effect verified with photons, electrons and protons
  Lungs, brain, skin Vozenin et al. *Clinical Oncology*, *31*(7), 407-415, 2019.
  rat, cats, pig + human patient (2019)



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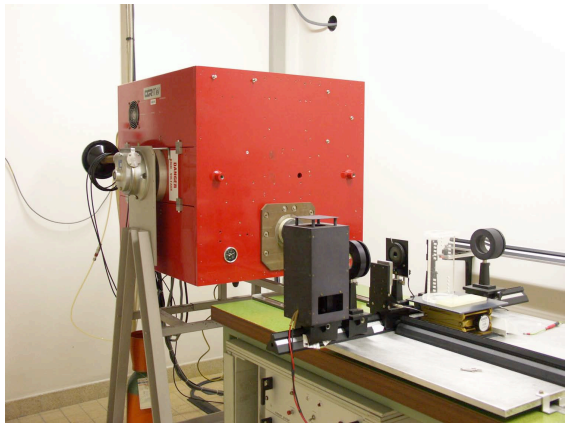
IC Electron LINAC (EuroMeV/PMB-ALCEN)

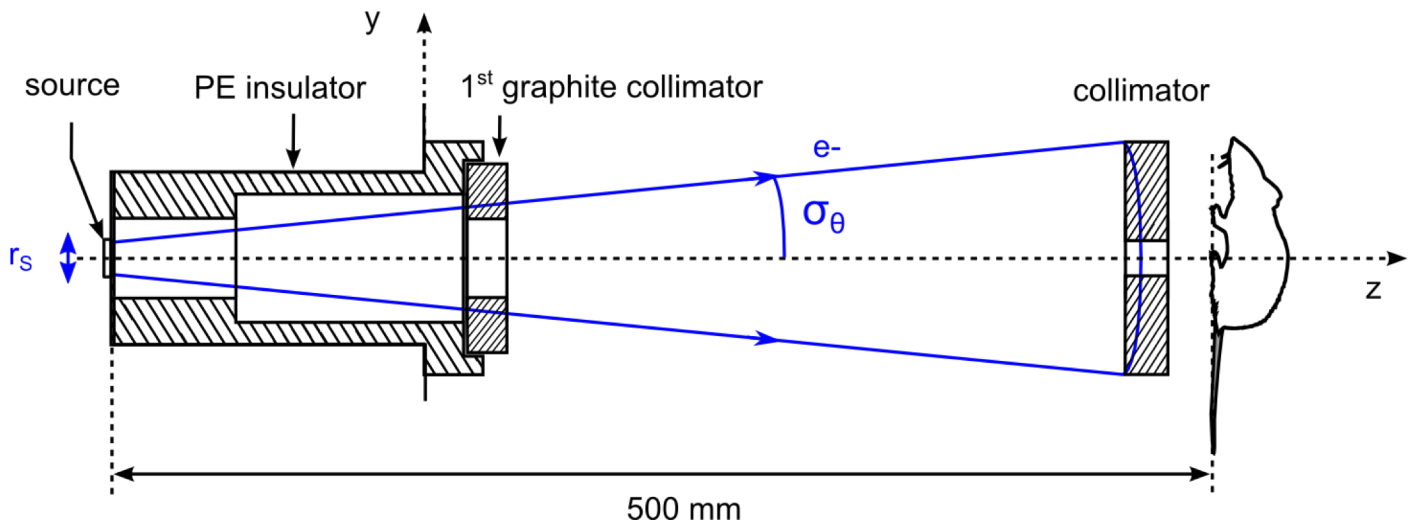


	FLASH mode	CONV mode
Energy	4 - 5 MeV	
Pulses duration	0.1 to 2.2 µs	3 µs
Repetition rate	10 - 200 Hz	
Dose per pulse	**~ 1 Gy**	**~ 1 mGy**
Mean dose rate	**~ 100 Gy/s**	**0.1 Gy/s**
Dose-rate in pulse	~ 10^6 Gy/s	300 Gy/s

Setup overview

Monte Carlo modeling

- **Aim**: . interpret radiobiological experiments
  . create a predictive dosimetry tool



- **Parameters**: energy **E** source radius **r_s**
  energy spread **σ_E** divergence **σ_Θ**

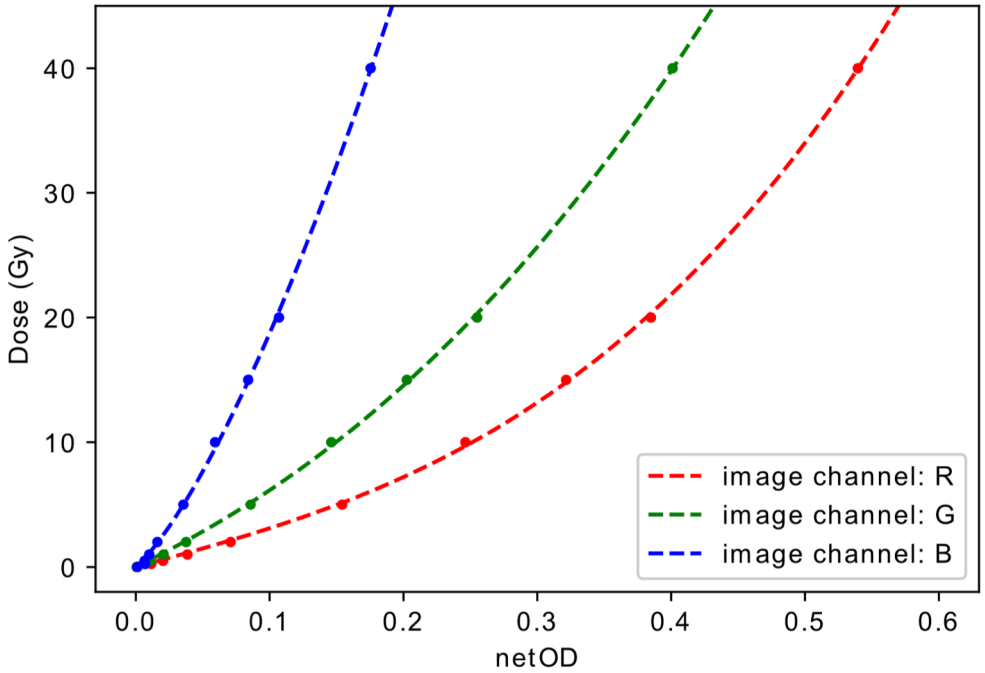
- **Gate 8.0 - Geant4.10.3** Monte-Carlo platform
- Physics builder set "**emstandard_opt3**" for electromagnetic interactions

Dosimetry

EBT-XD Gafchromic films

- active layer (25 µm thick) + 2 x 125 µm polyester sheets
- dose range: 0.4 Gy to 40 Gy
- scanned 36 hours after exposure

- cross-calibrated with a PPC05 ionization chamber:



net optical density:

$$netOD = log_{10}\left(\frac{\langle PV_{unexp}\rangle}{\langle PV_{exp}\rangle}\right)$$

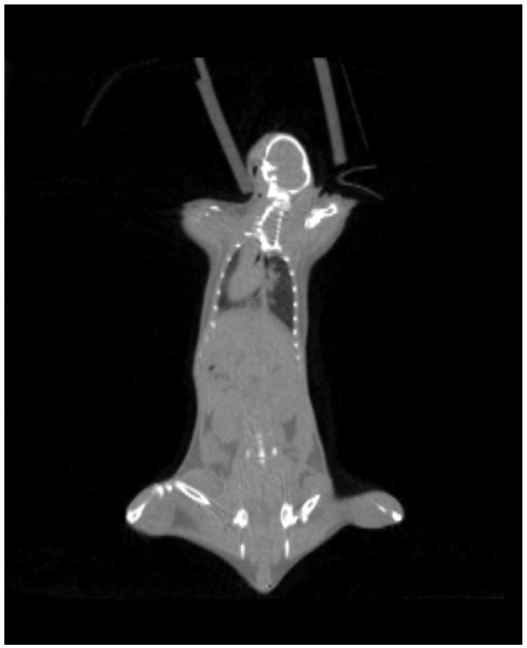
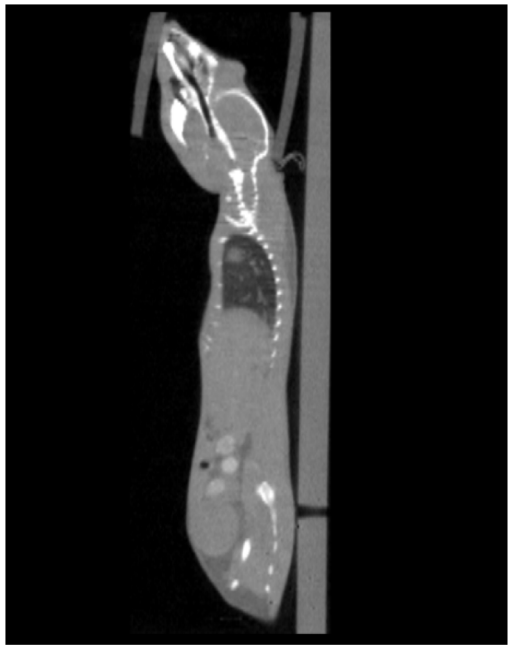
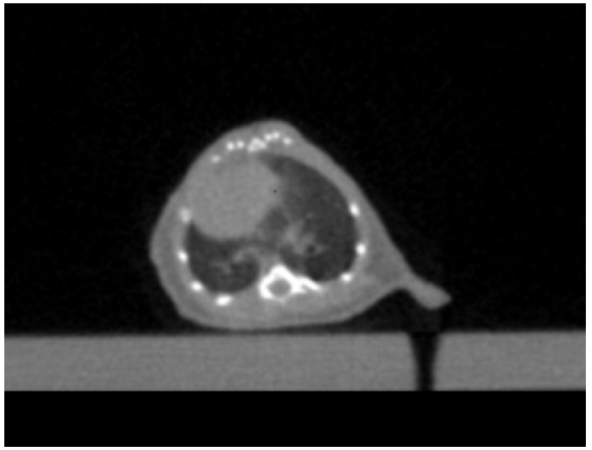
Conversion to dose (D):

$$D = a.netOD + b.netOD^{c}$$

Imaging and HU calibration

- Images acquired on a CBCT (SARRP):

  Voltage 60 kV
  Grid resolution 0.245 x 0.245 x 0.245 mm^3

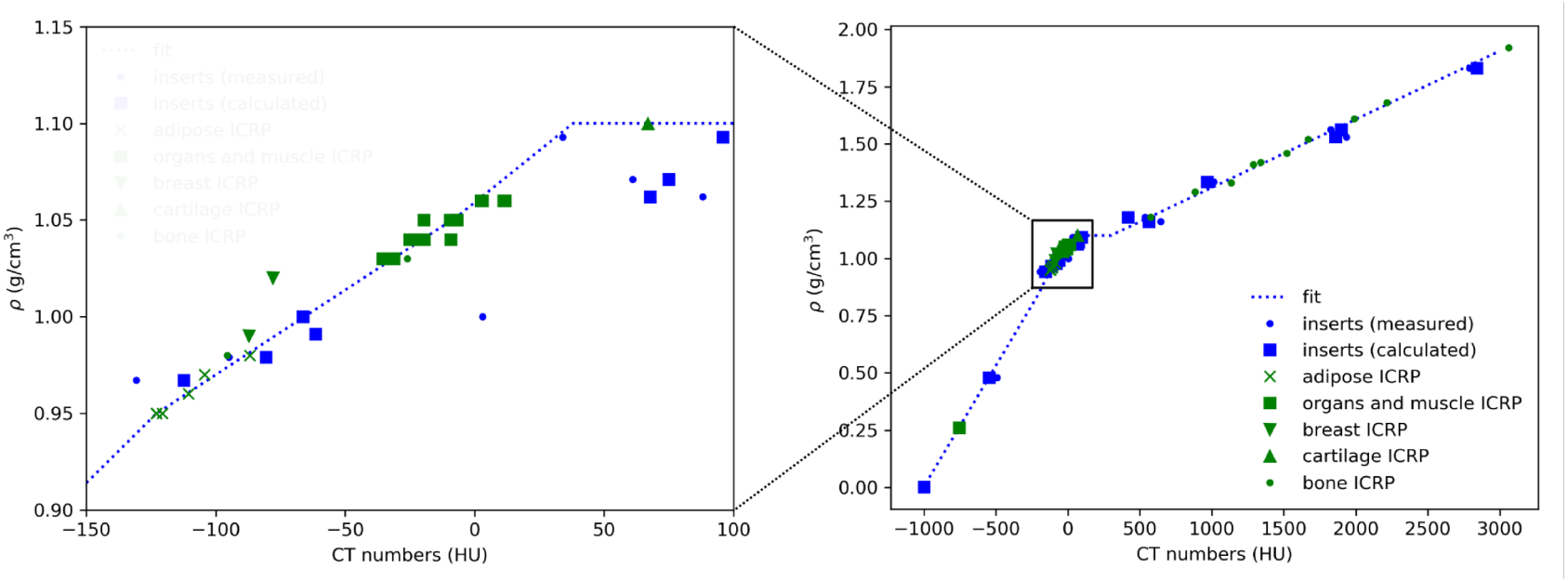




Imaging and HU calibration

- Images acquired on a CBCT (SARRP):

  Voltage 60 kV
  Grid resolution 0.245 x 0.245 x 0.245 mm^3

- stoichiometric calibration (*U. Schneider et al, Physics in Medicine & Biology, 41(1), 111, 1996)* adapted for small animal

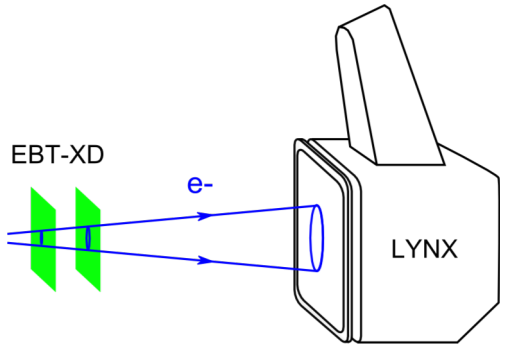


- voxelized digital phantom using the « Hounsfield Material Generator » implemented in GATE

Geometric properties

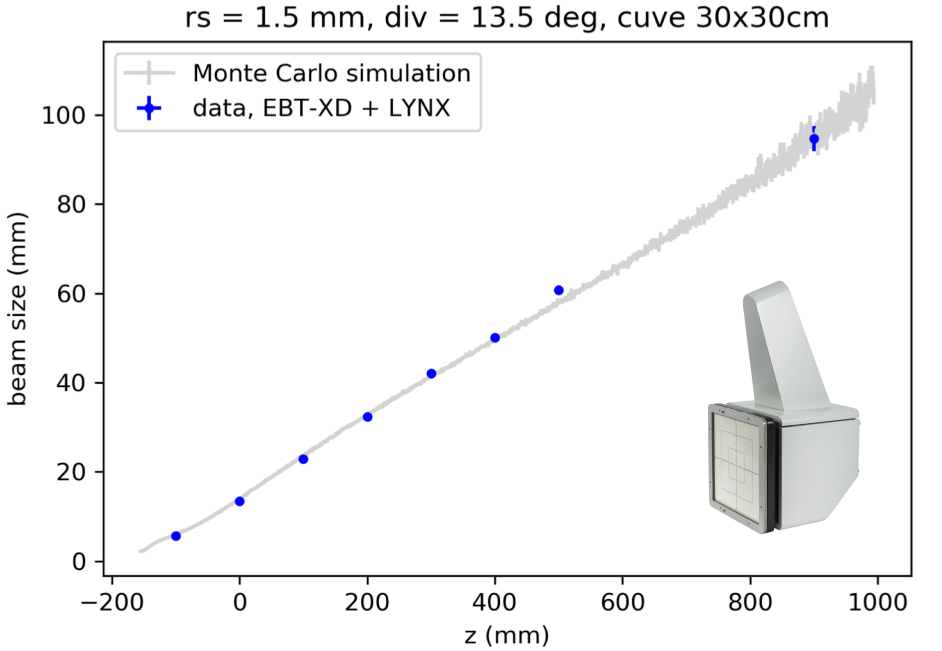
Beam profile (FLASH mode)

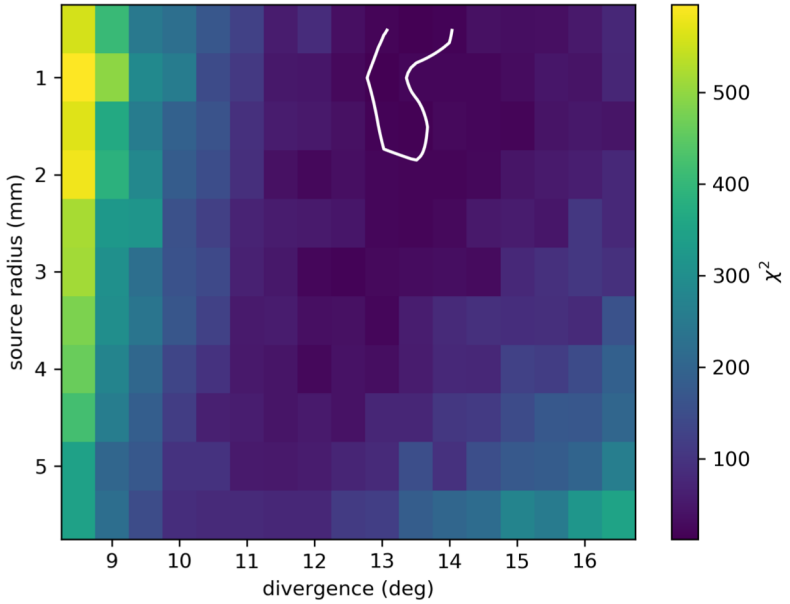
LYNX: scintillating screen + CCD camera



Best fit (95% C.L.):

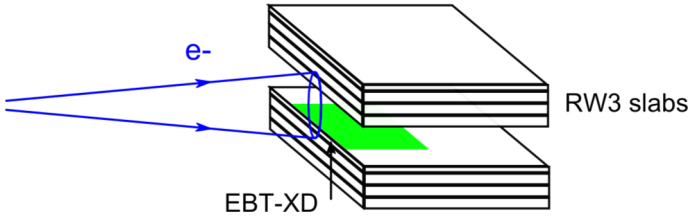
angular spread	13.5 ± 1 deg
source radius	1.5 ± 1 mm





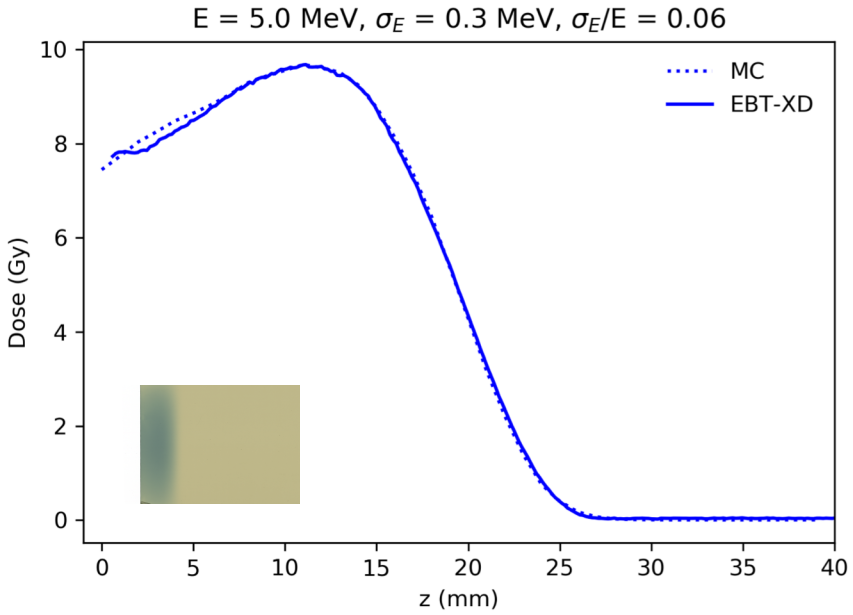
Energy & energy spread

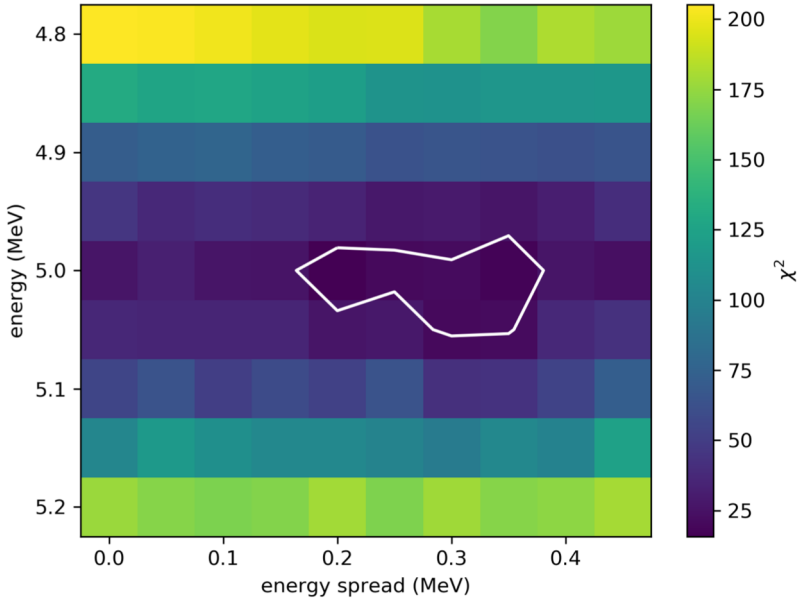
Depth-dose distribution (FLASH mode)



Best fit (95% C.L.):

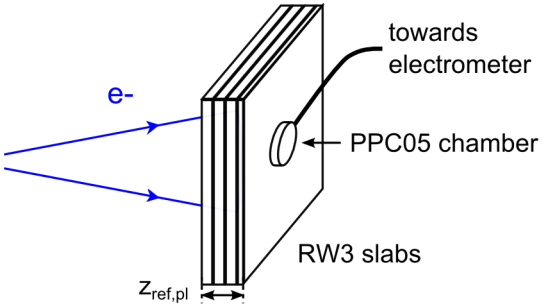
energy	5 ± 0.05 MeV
rel. energy spread	0.06 ± 0.01





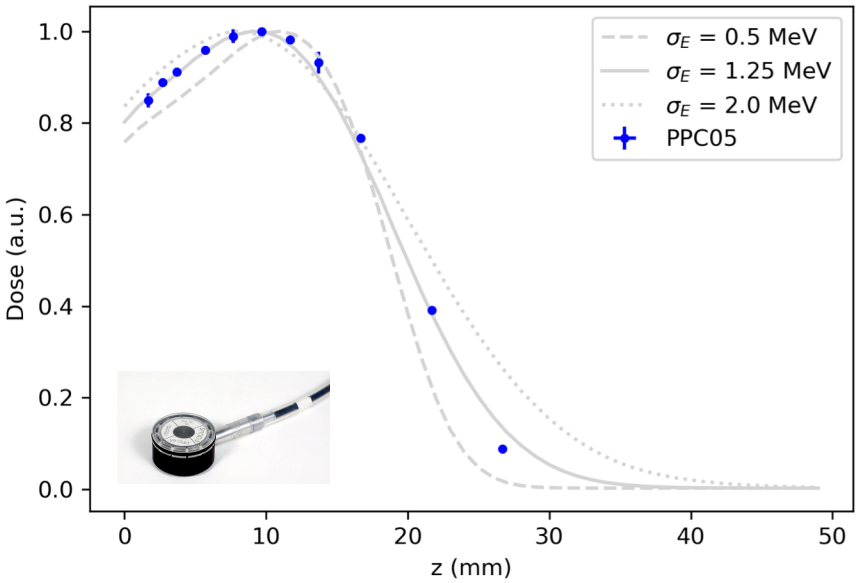
Energy & energy spread

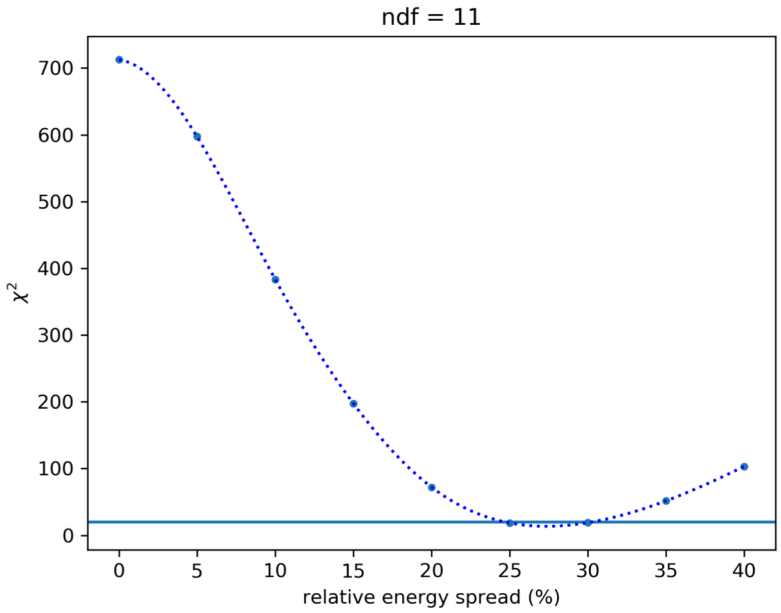
Depth-dose distribution (CONV mode)



Best fit (95% C.L.):

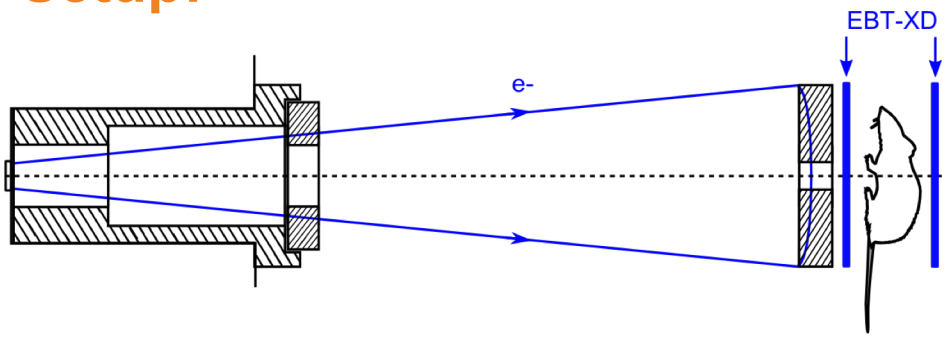
rel. energy spread 0.27 ± 0.03





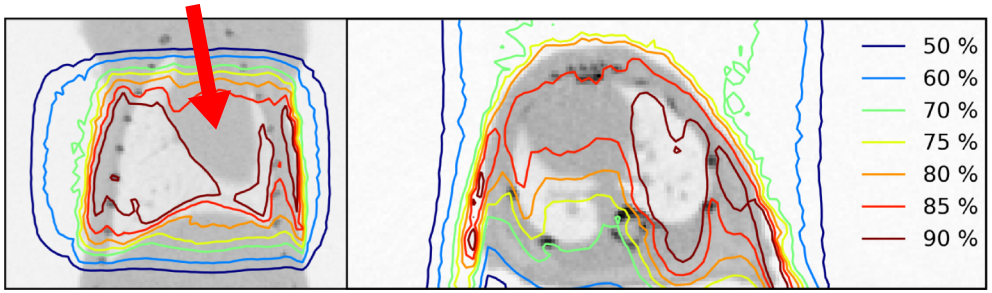
Lungs irradiation

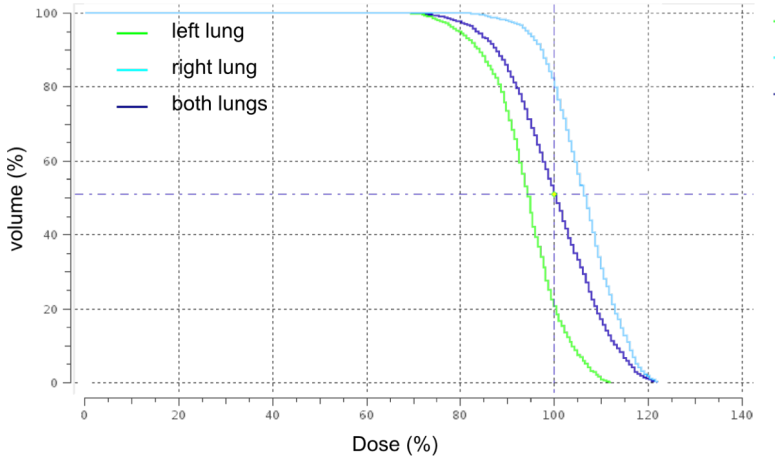
Setup:



Sequence:

1) Mouse scanner (CBCT)
2) irradiation





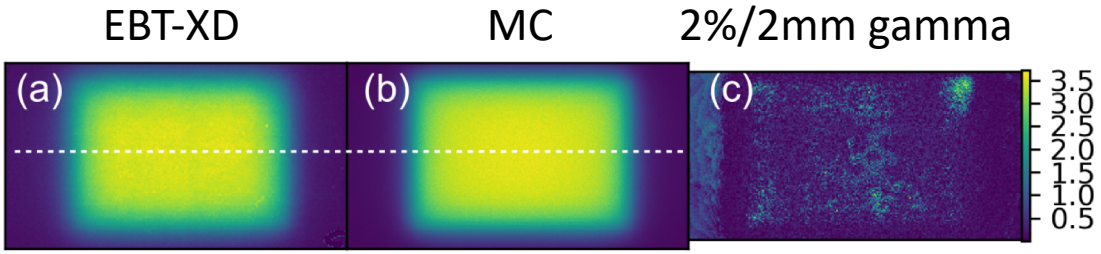
Heart «screening effect »: → ≠ doses left/right lungs
→ difference up to **10%!**

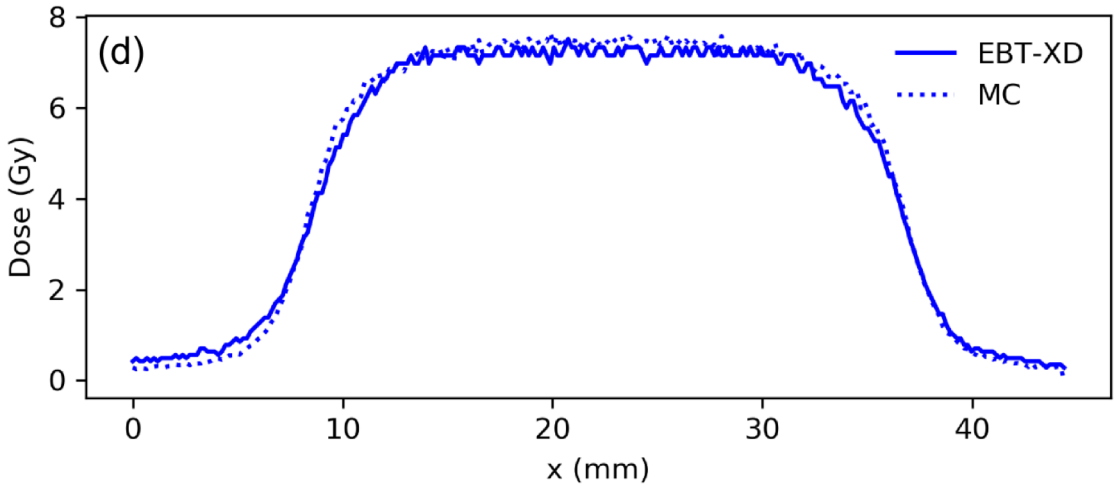
Lungs irradiation

Dose distribution (CONV mode):

- **validate** the MC in a **complex geometry** (dose heterogeneity in the lungs)
- 2D dose distribution images **registration**

Film placed upstream:





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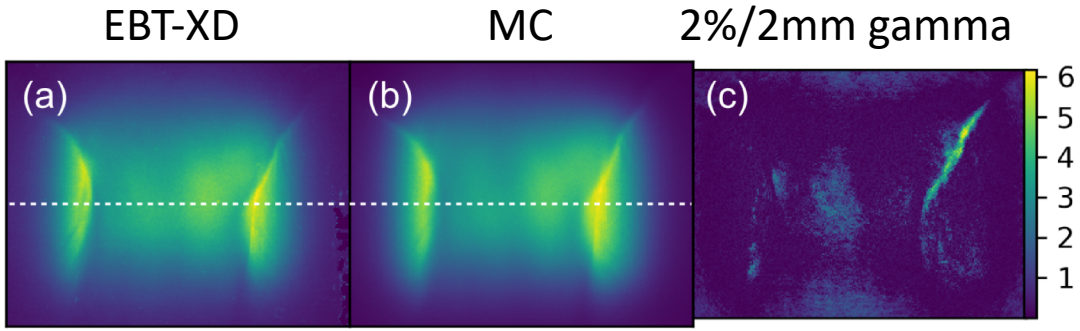
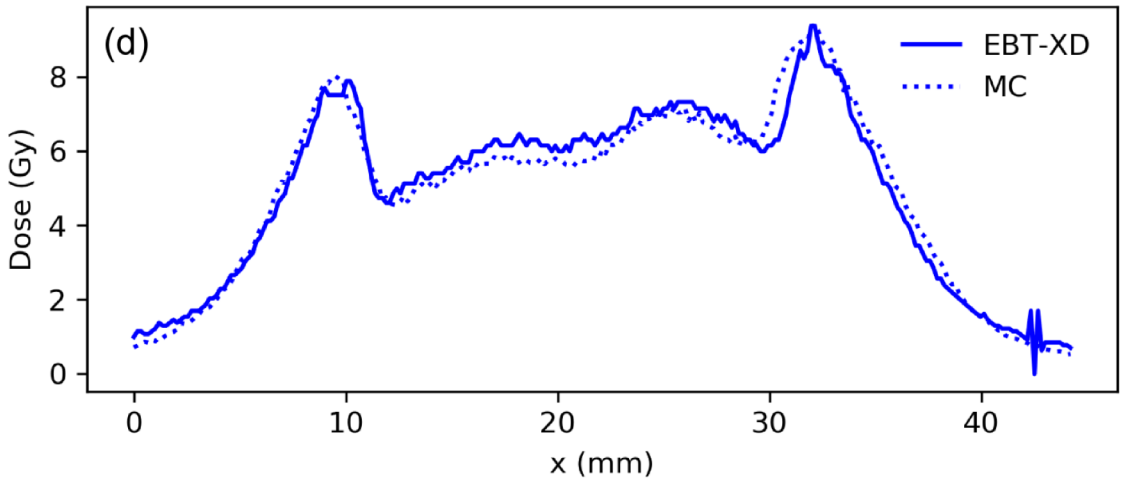




Conclusion

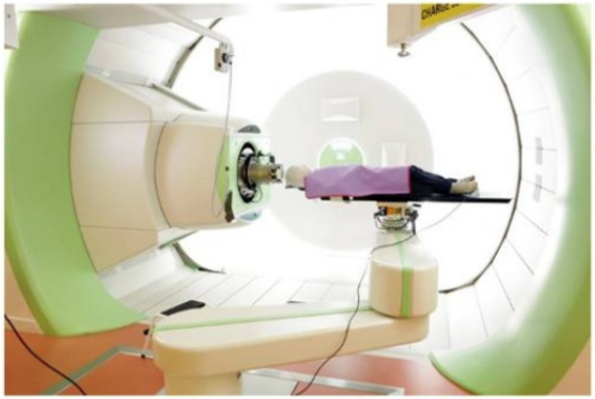
- We have modeled a prototype electron beam linear accelerator
- We have computed the 3D dose distributions and dose-volume histograms in lungs on small animals.
- Important dose difference between the lungs when irradiating from the front side
- Results applicable to many particle accelerators
- support the analysis of radiobiological experiments for pre-clinical research with very high dose-rate electron beams.
- serve as an input for microdosimetry studies (Geant4-DNA)

Backup

Advertisement

Protontherapy center

Y1 Room – 201 MeV



Isocentric Gantry – 230 MeV

Y2 Room – 76 MeV

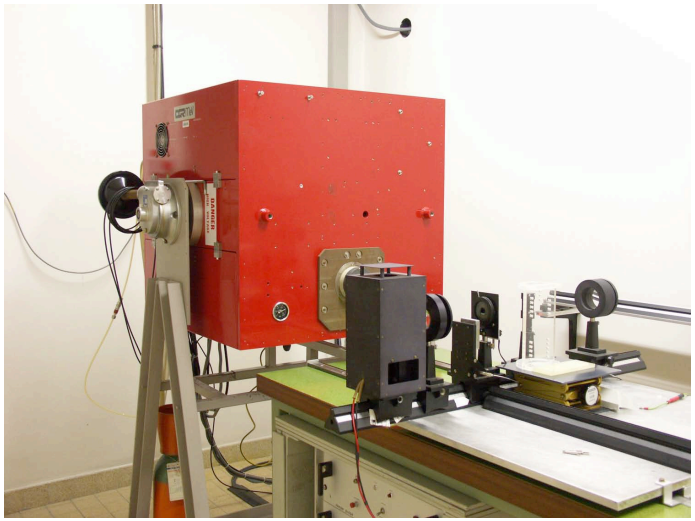
Contact: comex.cpo@curie.fr

The Orsay RadExp facilities

Protontherapy center

Small Animal CBCT (SARRP)

Electron LINAC
(EuroMeV/PMB-ALCEN)



Dosimetry

EBT-XD Gafchromic films

- active layer (25 µm thick), sandwiched between two 125 µm matte-polyester sheets
- dose range: 0.4 Gy to 40 Gy
- scanned 36 hours after exposure
- cross-calibrated with a PPC05 ionization chamber

PPC05 Ionization chamber

Rated energy	2 to 50 MeV
Min. dose rate	50 µGy/s
Max. dose rate	15 Gy/pulse (pulsed)

Scintillating screen + CCD camera (LYNX)

- Beam profile measurements
- field of view: 300 x 300 mm²
- spatial resolution : 0.5 mm

Lungs irradiation

Dose distribution (FLASH mode):

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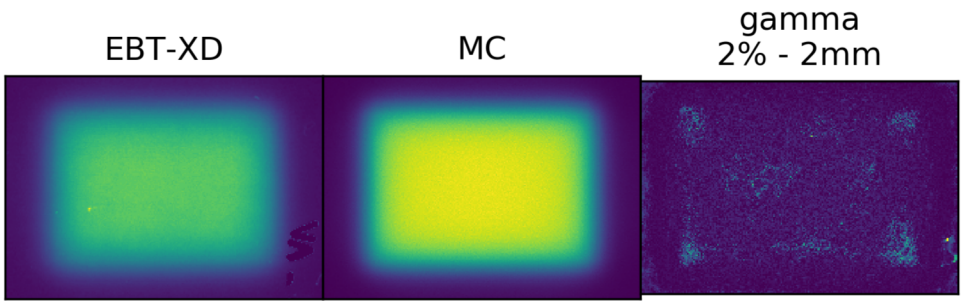

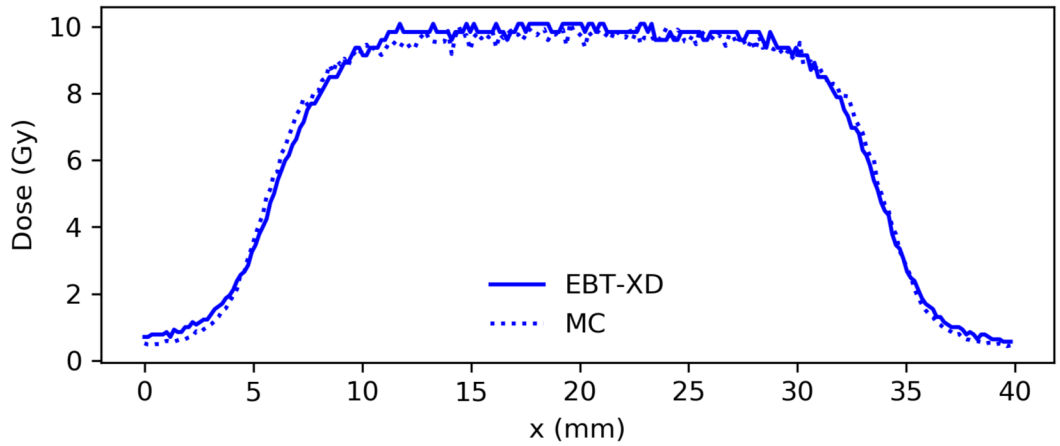

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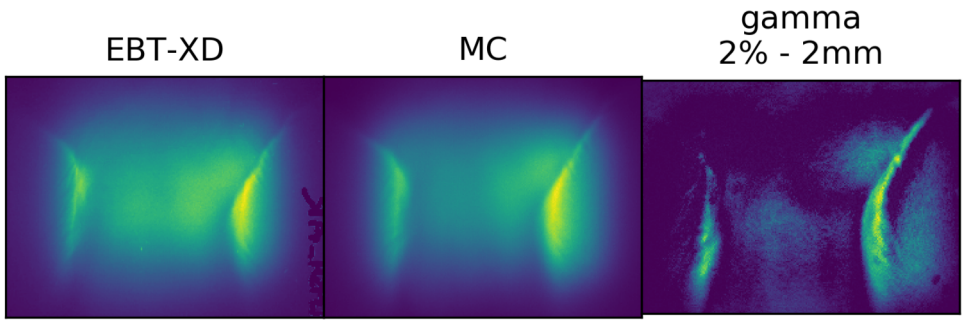
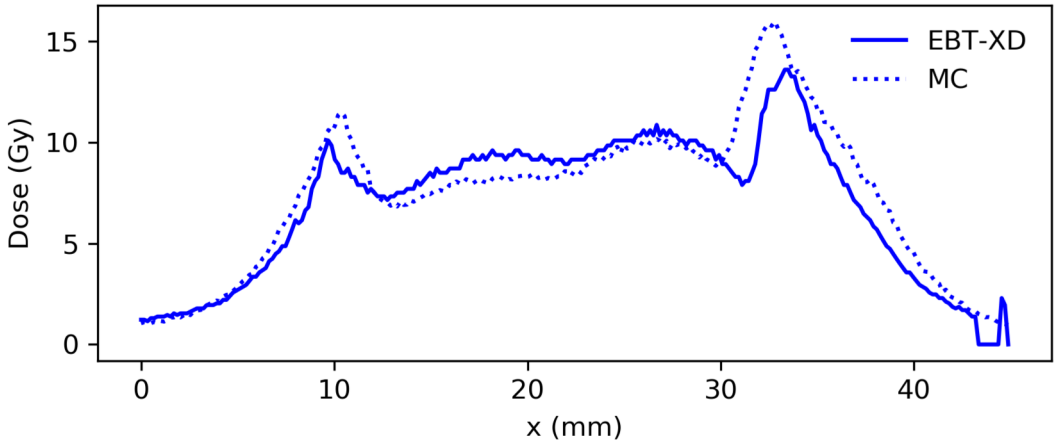
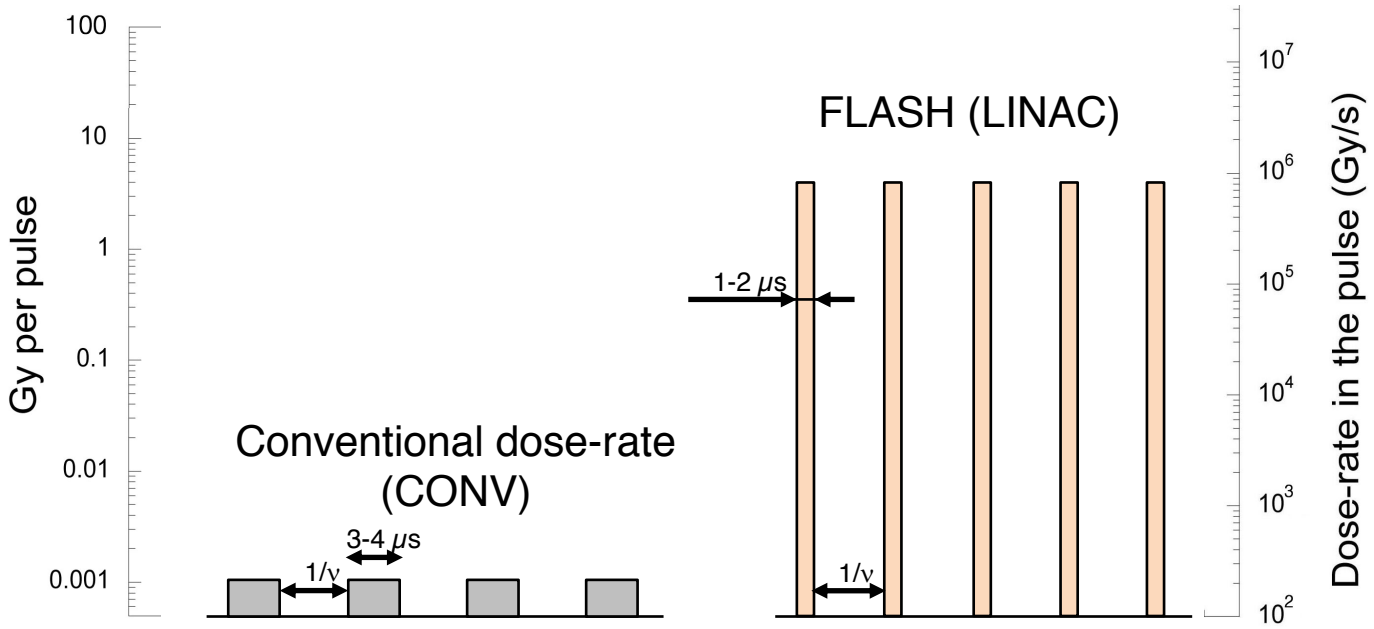




FLASH irradiation

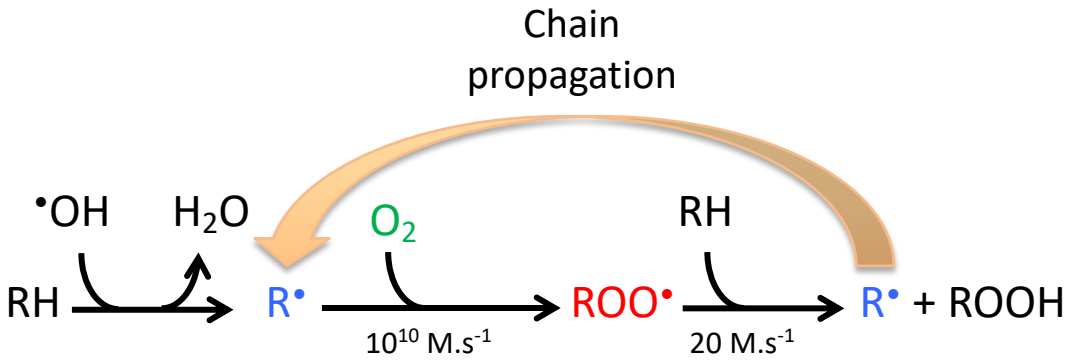
- Irradiation at **ultra-high dose-rate (> 40 Gy/s)**
- reduce adverse side effects in healthy tissues
- equally efficient as conventional irradiation for tumour control

• **temporal structure:**



FLASH chemistry

- strongly depends on oxygen presence:



Chain termination:

$R^{\bullet} + R^{\bullet}$ → Dimerization

$ROO^{\bullet} + ROO^{\bullet}$ → ROOR + O_2

$ROO^{\bullet} + R^{\bullet}$ → ROOR