FLASH carbon ion irradiation at GANIL

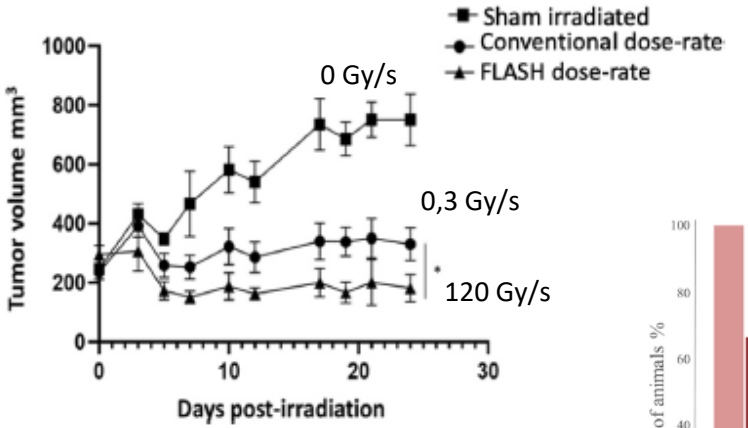
Platform iRiA
irradiations for Radiobiology with Accelarated ions

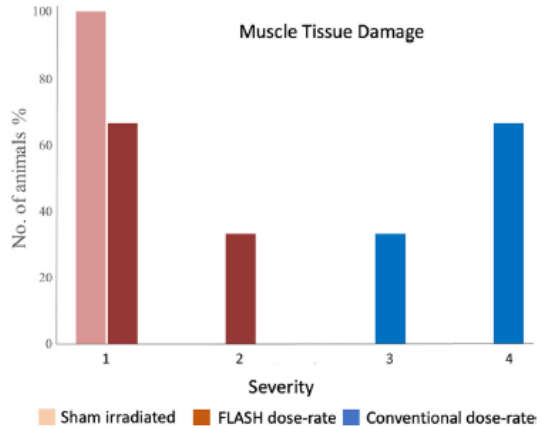
UNIVERSITÉ CAEN NORMANDIE

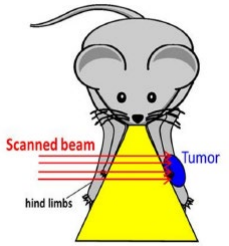
Flash effect in radiobiology

The FLASH effect

- ✓ Ultra high dose rate (> 40 Gy/s)
- ✓ Improved treatment efficiency
  - ✓ Equivalent level of tumor control
  - ✓ Reduced damage to healthy tissue







History

- ✓ 2014 : First demonstration with protons
- ✓ 2018 : First clinical treatment with protons
- ✓ 2020 … : Few studies with carbon ions (GSI, Japan)

FLASH carbon @ GANIL

- ✓ 2023 : First experiment
- ✓ 2024 : First succesfull radiobiology experiment

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Original Article

FLASH with carbon ions: Tumor control, normal tissue sparing, and distal metastasis in a mouse osteosarcoma model

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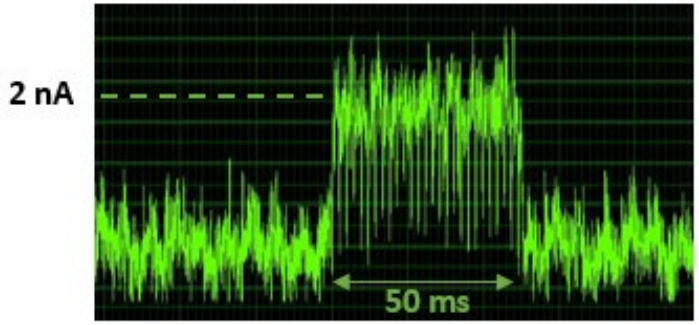
Flash irradiation at GANIL



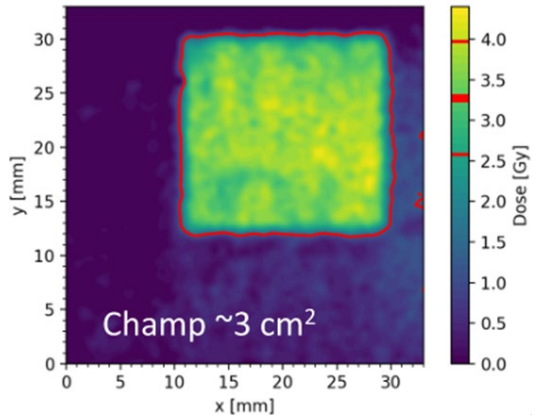
- ✓ High beam intensity / high dose rate
  - ➢ $^{12}C^{6+}$ @ 95 MeV/A
  - ➢ limitation at 23 nA in D1 (2,4 10^{10} pps)
  - ➢ Maximum dose rate 100 Gy/s

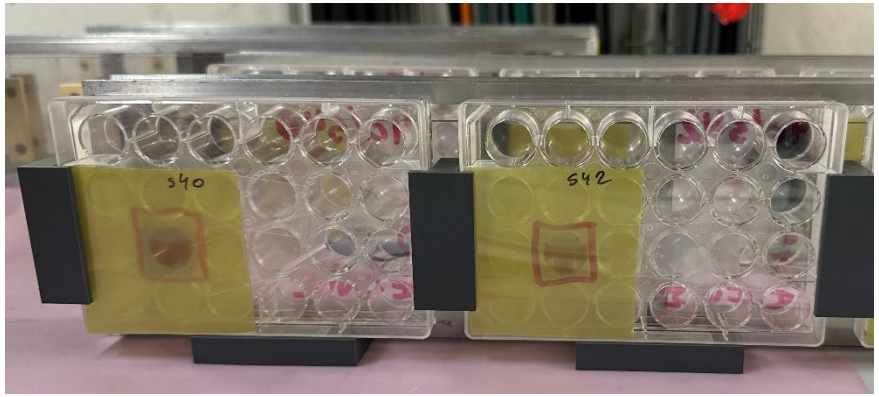
- ✓ Short pulses
  - ➢ Duration : 10 to 100 ms
  - ➢ Rate : 1 pulse every 10 s
  - ➢ « coupe faisc » beam chopper

	Dose rate	Beam intensity	Irradiation time
Conventionnal Dose Rate **CONV**	2 Gy/min	< 1 pA	60 s
Ultra High Dose Rate **FLASH**	100 Gy/s	2 nA	20 ms

calculated for : LET = 70 MeV/µm and S = 3 cm^2

- ✓ Homogeneous irradiation field
  - ➢ field : 1,8 x 1,8 ≈ 3 cm^2
  - ➢ no beam scanning = passive beam
  - ➢ single scattering foil
  - ➢ 90 % beam homogeneity
    ---> 10 % of the incoming intensity



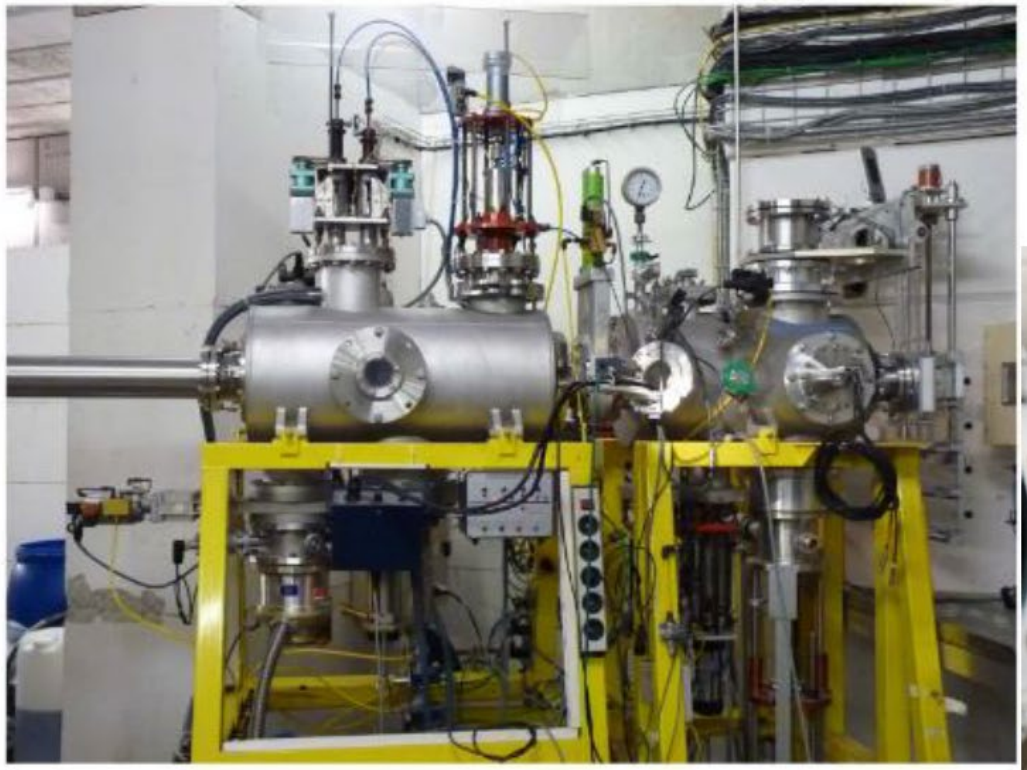


IRABAT beamline in D1

$^{12}C^{6+}$ @ 95 MeV/A

Maximal beam intensity : Imax = 23 nAe

Effective beam intensity : I ≈ 2 nAe



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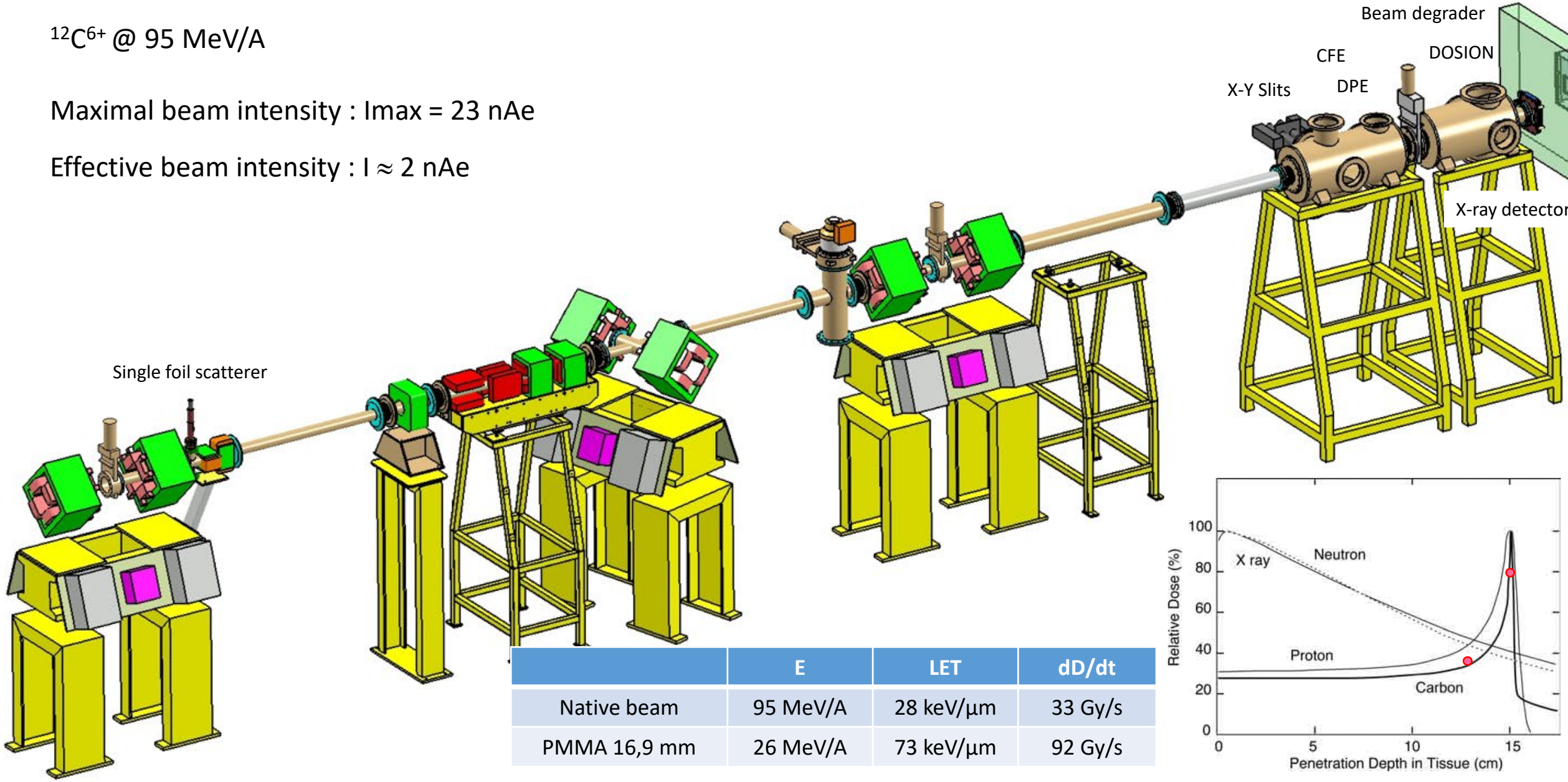
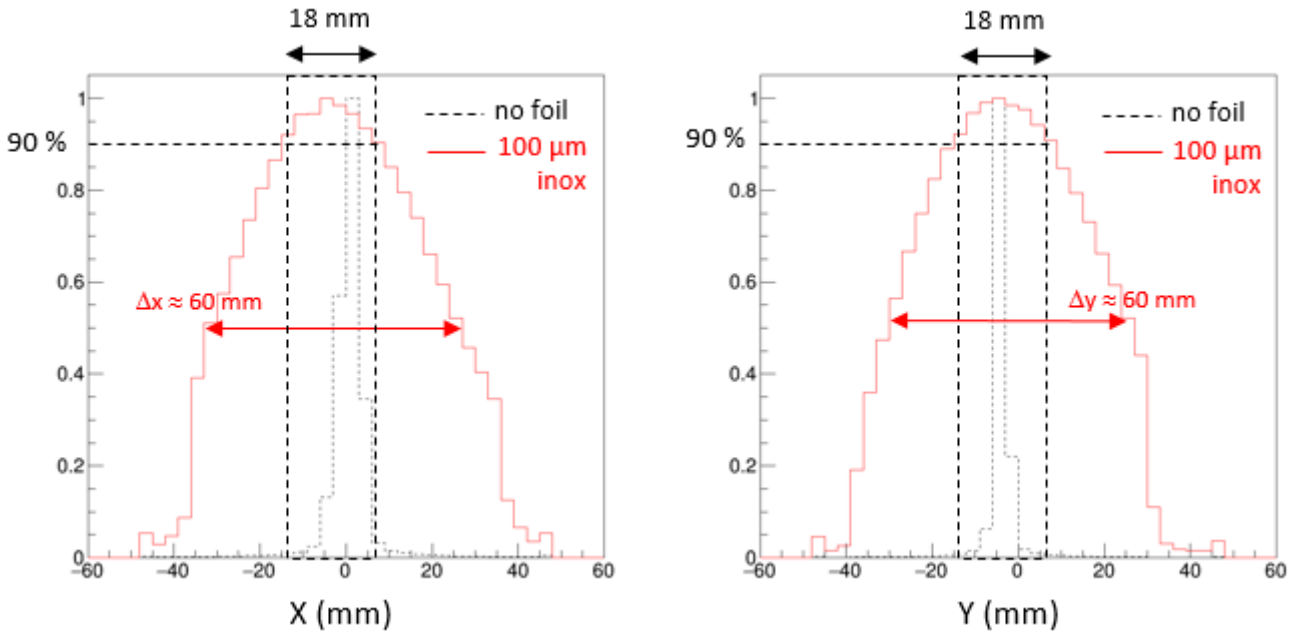


	E	LET	dD/dt
Native beam	95 MeV/A	28 keV/µm	33 Gy/s
PMMA 16,9 mm	26 MeV/A	73 keV/µm	92 Gy/s

Single foil beam scatterer

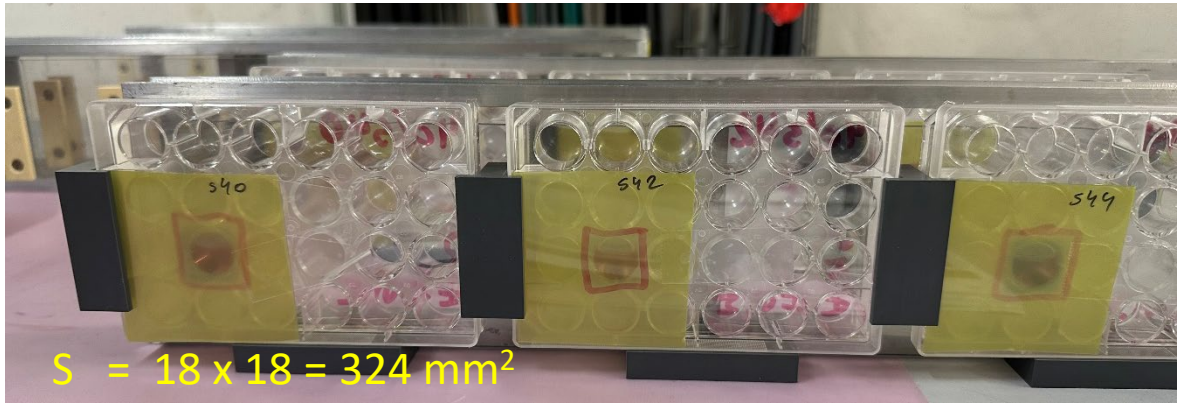


scattering foil

Field homogeneity = 90 %

Effective beam intensity

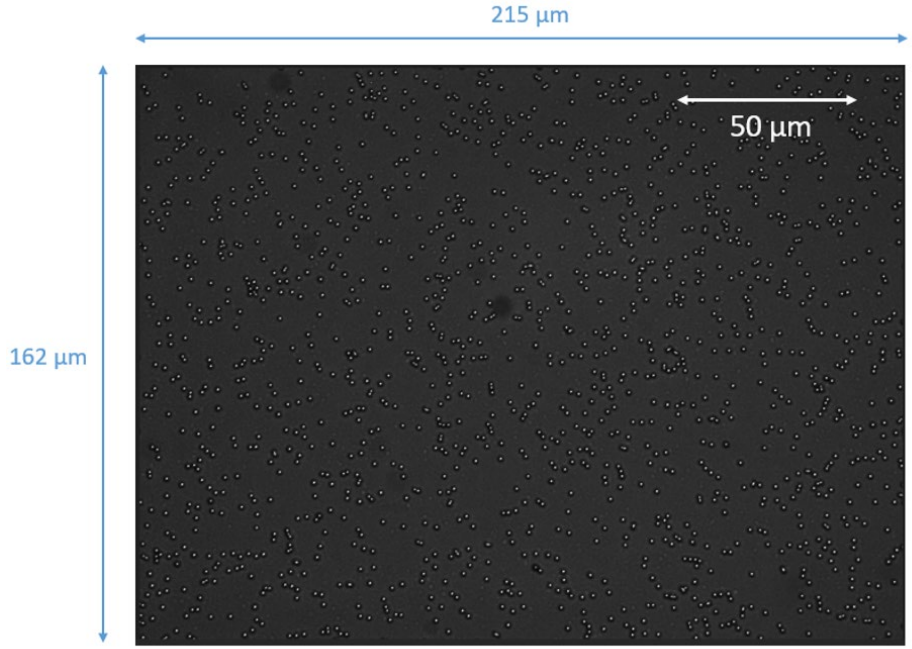
I_S = 10% x Imax = 2,4 10^9 pps = 2,3 nAe



Dosimetry

Dosimetry :

- ✓ Absolute calibration
  - ➢ CR39 ion track detector
  - ➢ LET calculation



- ✓ For each irradiation pulse
  - ➢ total dose
  - ➢ dose rate
  - ➢ 2D dose map

- ✓ Redundant online monitoring systems

	Mode	Dose rate	Dose	2D map
X-ray	CONV	✓	✓	✗
DPE	FLASH	✓	✓	✗
Gafchromic films	CONV + FLASH	✗	✓	✓
DOSION	CONV + FLASH	✓	✓	✓

X-ray detector

- ✓ Beam intensity monitor for CONV mode (<1 pA to 1 nA)

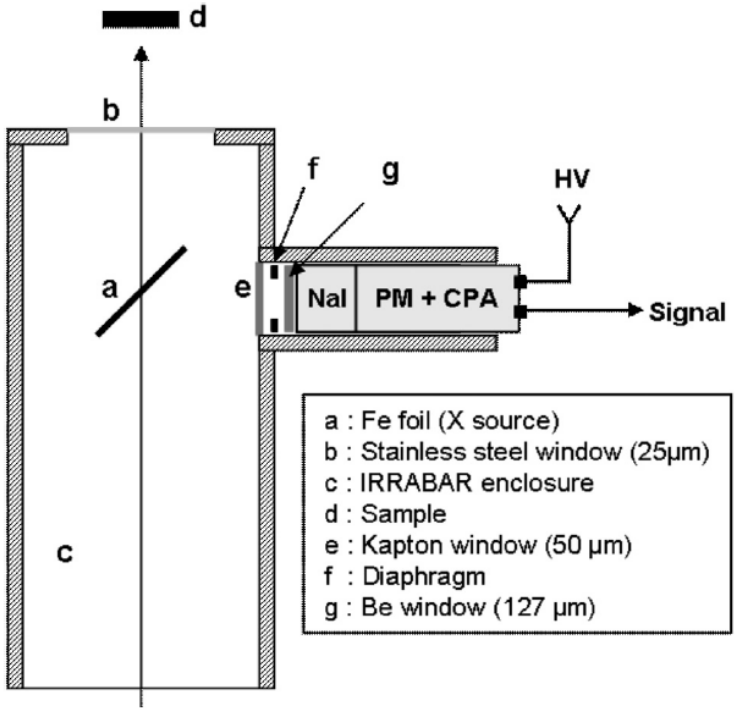
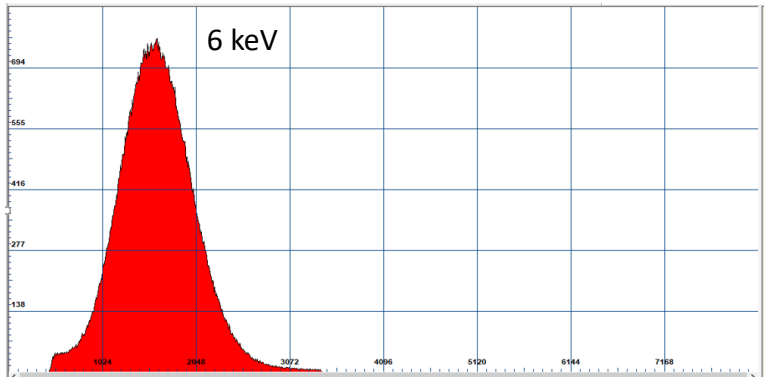
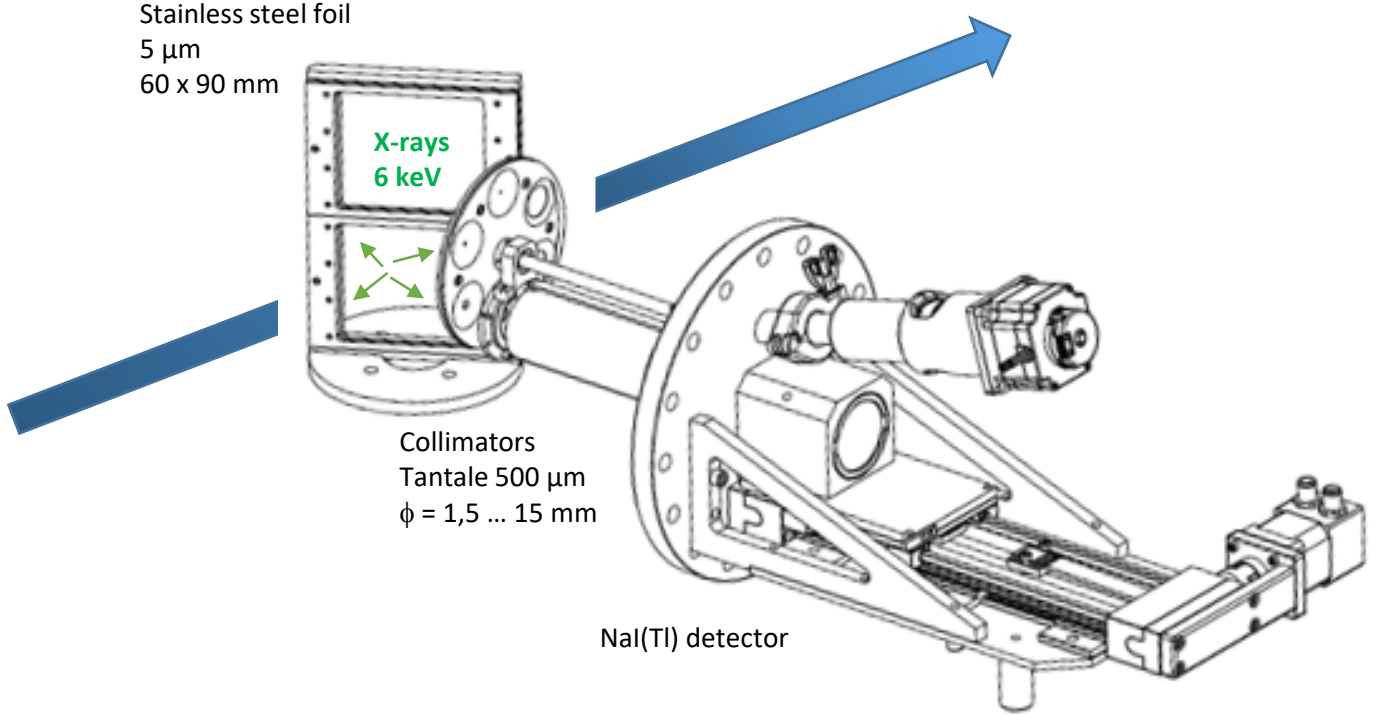


Fig. 3. IRRABAT chamber and X detector.



Stainless steel foil
5 µm
60 x 90 mm

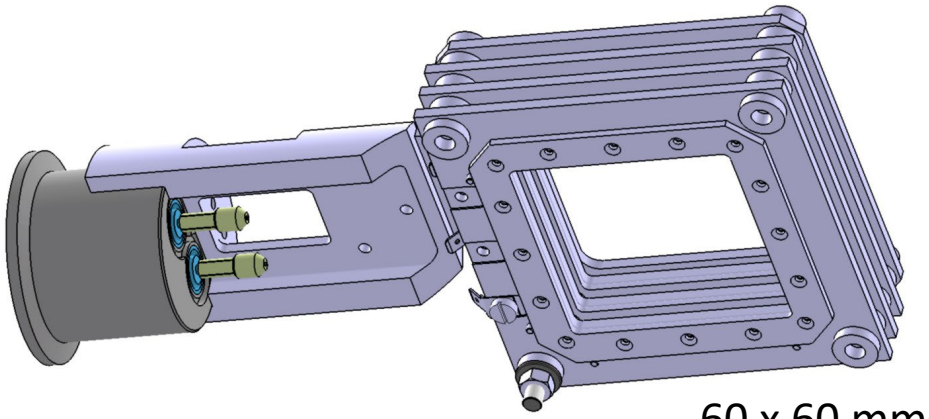


Collimators
Tantale 500 µm
ϕ = 1,5 … 15 mm

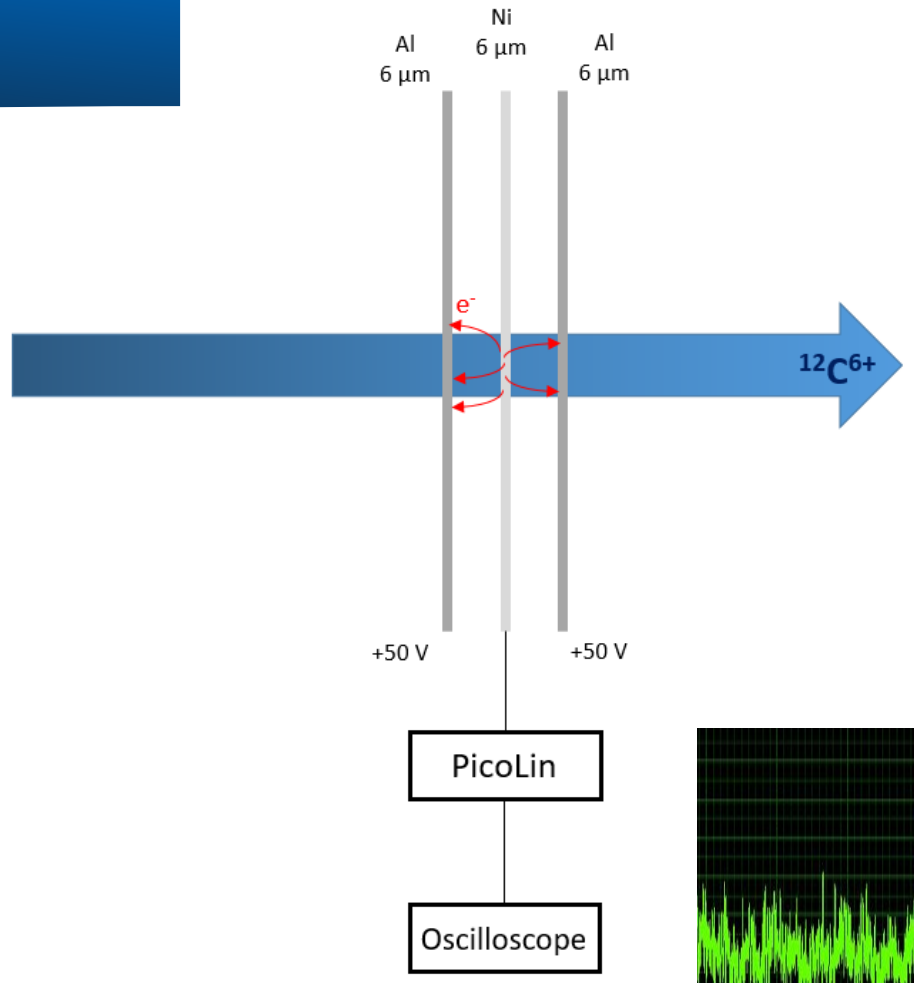
NaI(Tl) detector

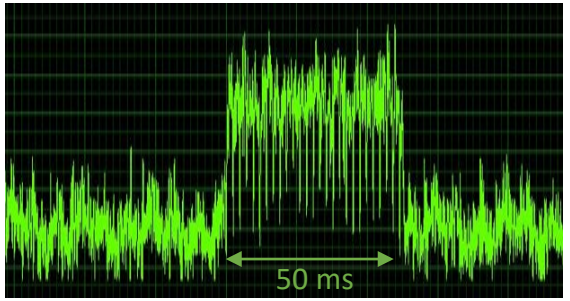
Transparent beam monitor DPE

✓ Beam intensity monitor for FLASH mode (> 1 nA)



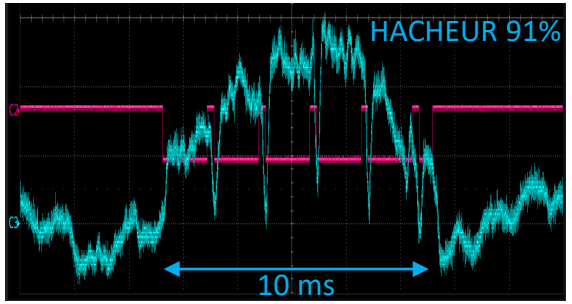
60 x 60 mm^2





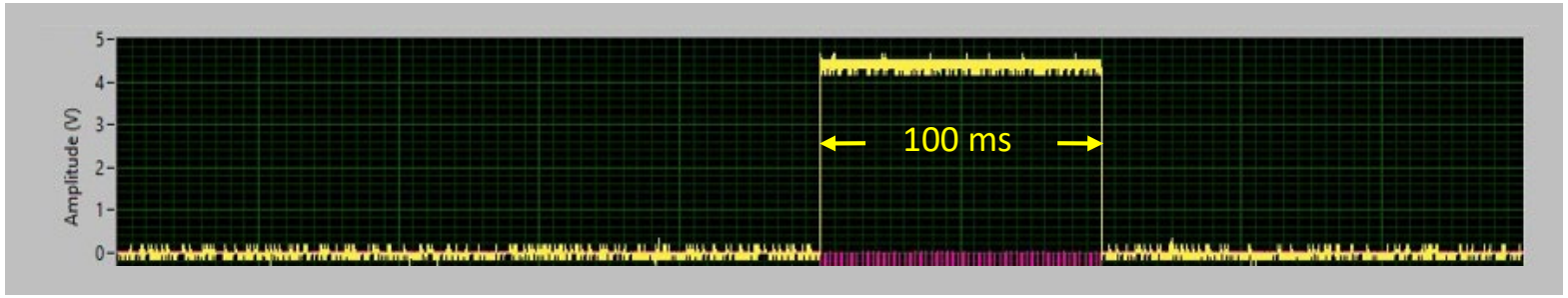
Calibration with Faraday Cup

--> $I_{DPE} \approx I_S \approx$ 2-3 nAe (~6 e^- per incoming ion)

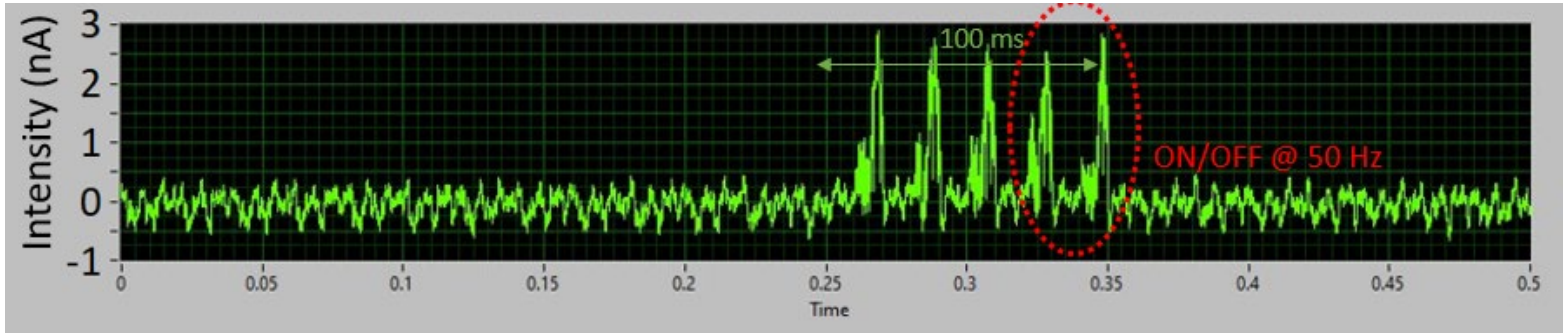


rise time = 150 µs

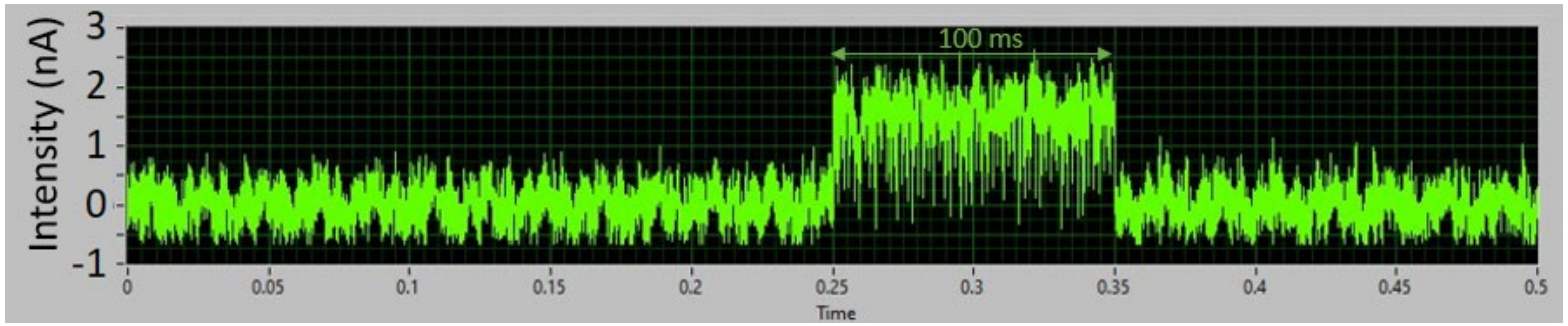
Beam intensity modulation @ 50 Hz



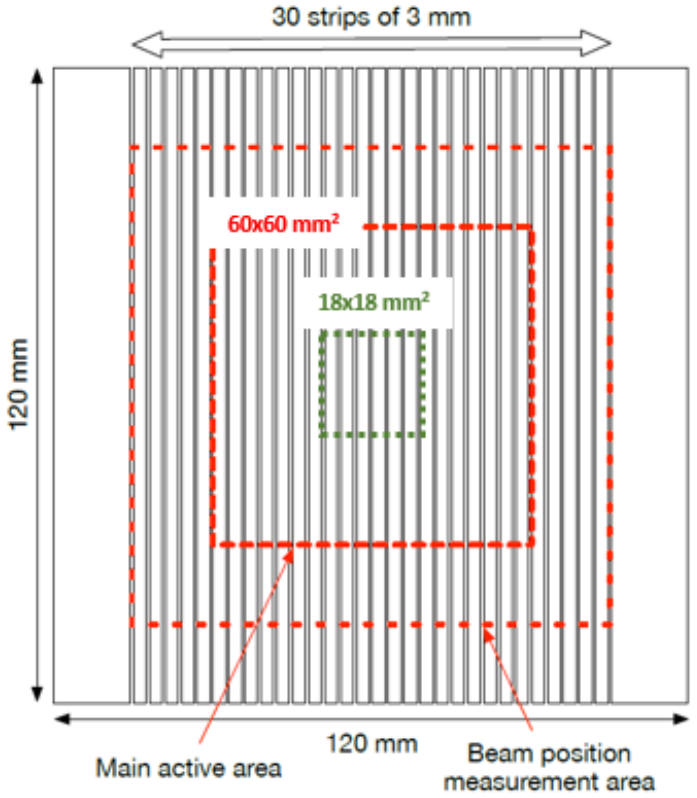
July 2023

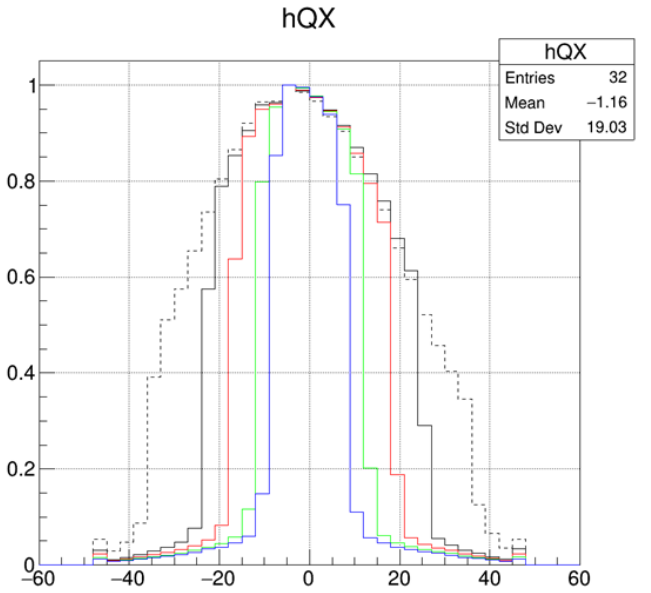


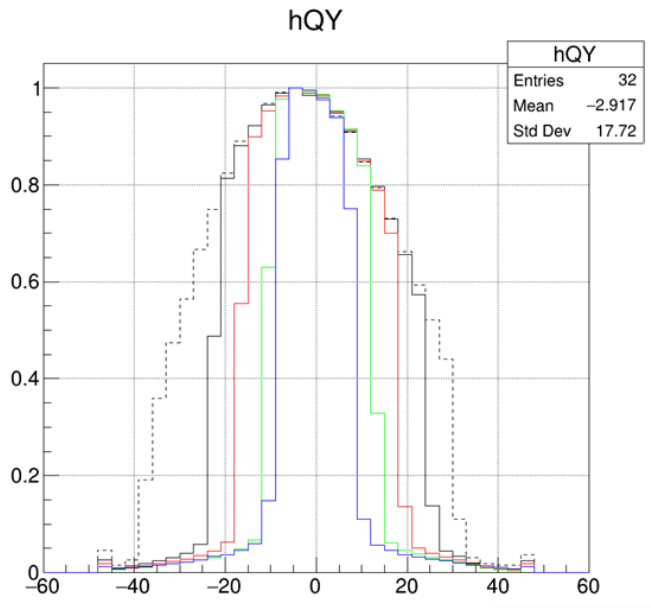
April 2024



DOSION



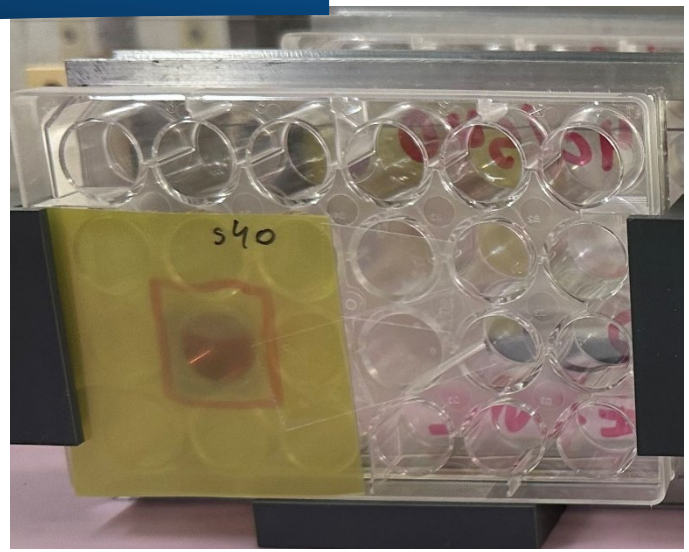


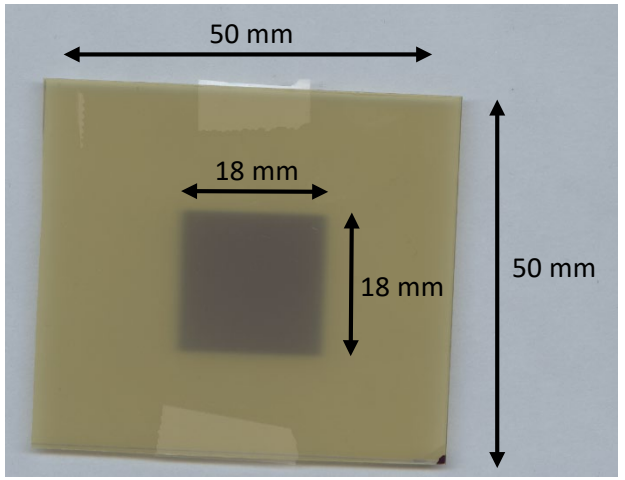


- ✓ Horizontal and Vertical beam profiles
- ✓ Limitations:
  - spatial resolution
  - high dose rates

Gafchromic films - EBT4

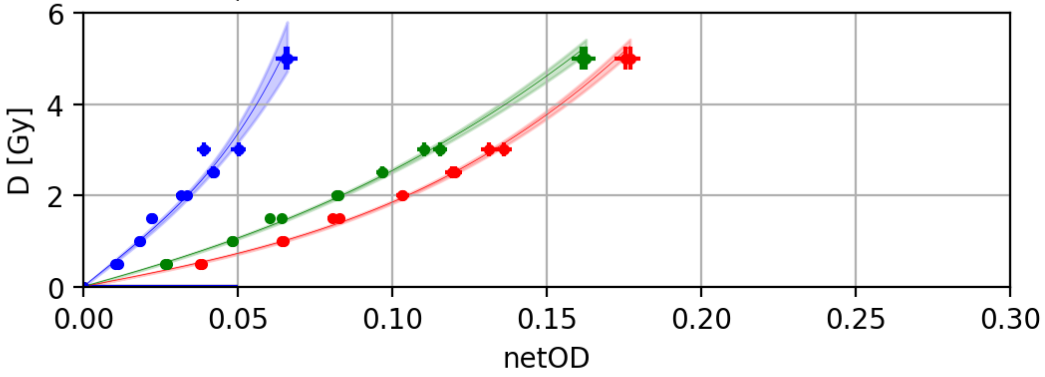
- ✓ 2D dose map
- ✓ Two calibrations : CONV and FLASH





EBT-4, Lot#: 0912301, Calib. date: 23.04.2024

^{13}C 73keV/µm CONV scanned: Red, Green, Blue channels (1 C.I. bands)



$D[Gy] = (13.2 \pm 0.4) * netOD + (529.3 \pm 33.9) * netOD^{3.0}$

$\sigma_D[Gy] = \sqrt{0.1 * netOD^2 + 1148 * netOD^{6.0} + (13 + 1588 * netOD^{2.0})^2 * \sigma^2_{netOD}}$

$\chi 2/DoF = 0.740$

residuals normality = 62.58%

$D[Gy] = (19.0 \pm 0.5) * netOD + (203.1 \pm 19.6) * netOD^{2.5}$

$\sigma_D[Gy] = \sqrt{0.3 * netOD^2 + 384 * netOD^{5.0} + (19 + 508 * netOD^{1.5})^2 * \sigma^2_{netOD}}$

$\chi 2/DoF = 0.814$

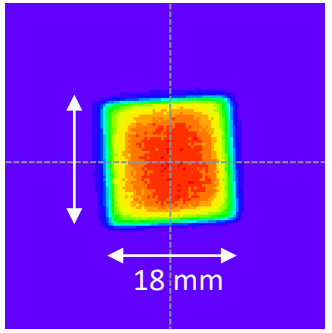
residuals normality = 35.13%

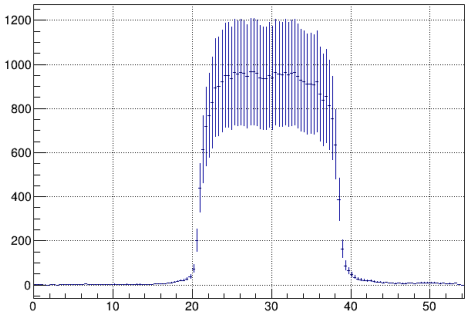
$D[Gy] = (54.3 \pm 2.7) * netOD + (22681.8 \pm 8346.2) * netOD^{3.5}$

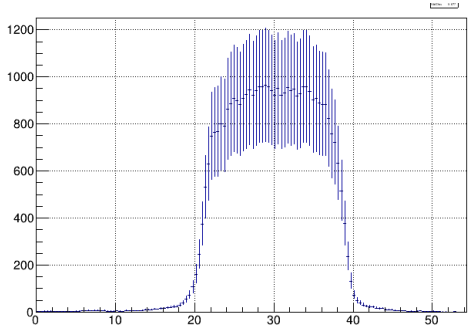
$\sigma_D[Gy] = \sqrt{7.0 * netOD^2 + 69659340 * netOD^{7.0} + (54 + 79386 * netOD^{2.5})^2 * \sigma^2_{netOD}}$

$\chi 2/DoF = 2.633$

residuals normality = 14.04%



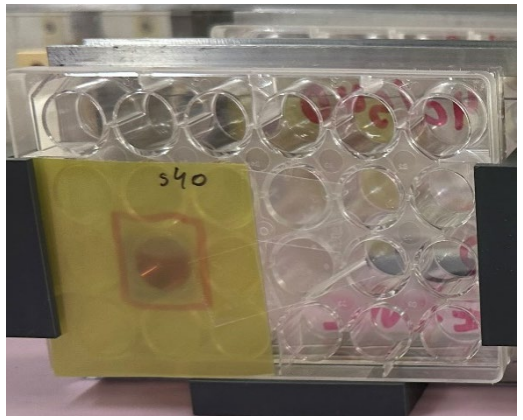


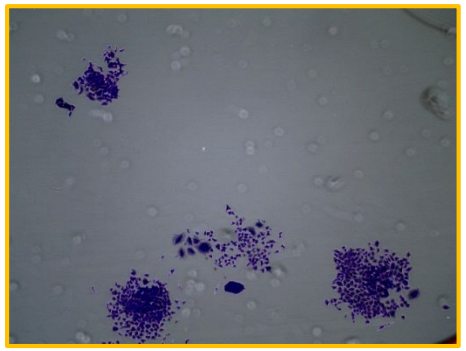


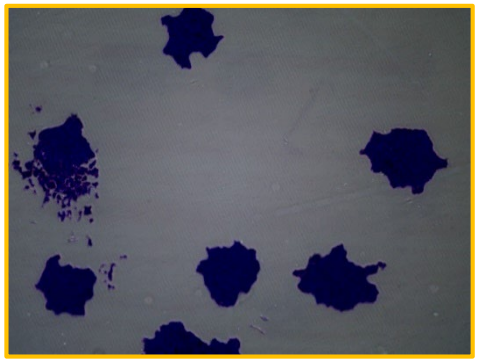
First results

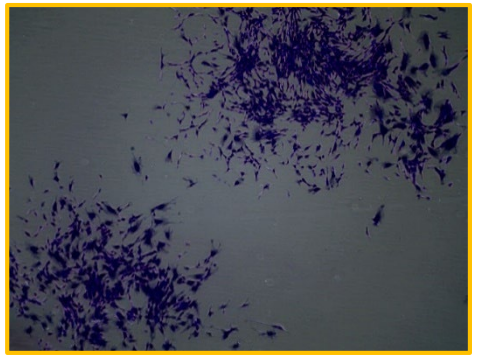
April 2024 P1338 - P1360

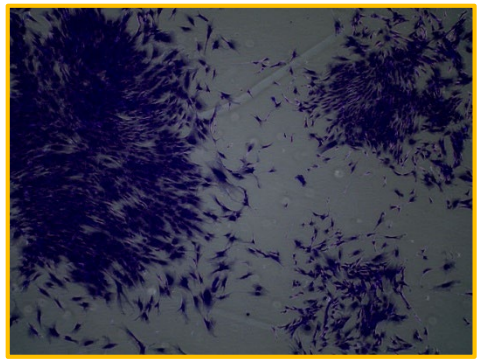
- ✓ Irradiation of in vitro 2D models
  - ➢ normal cells : fibroblast AG1522
  - ➢ tumor cells : lung cancer A549
- ✓ Oxygen conditions
  - ➢ Normoxia 21 %
  - ➢ Hypoxia 2 %
- ✓ Dose rates
  - ➢ CONV 2 Gy/min
  - ➢ FLASH 50 Gy/s
- ✓ Survival fraction





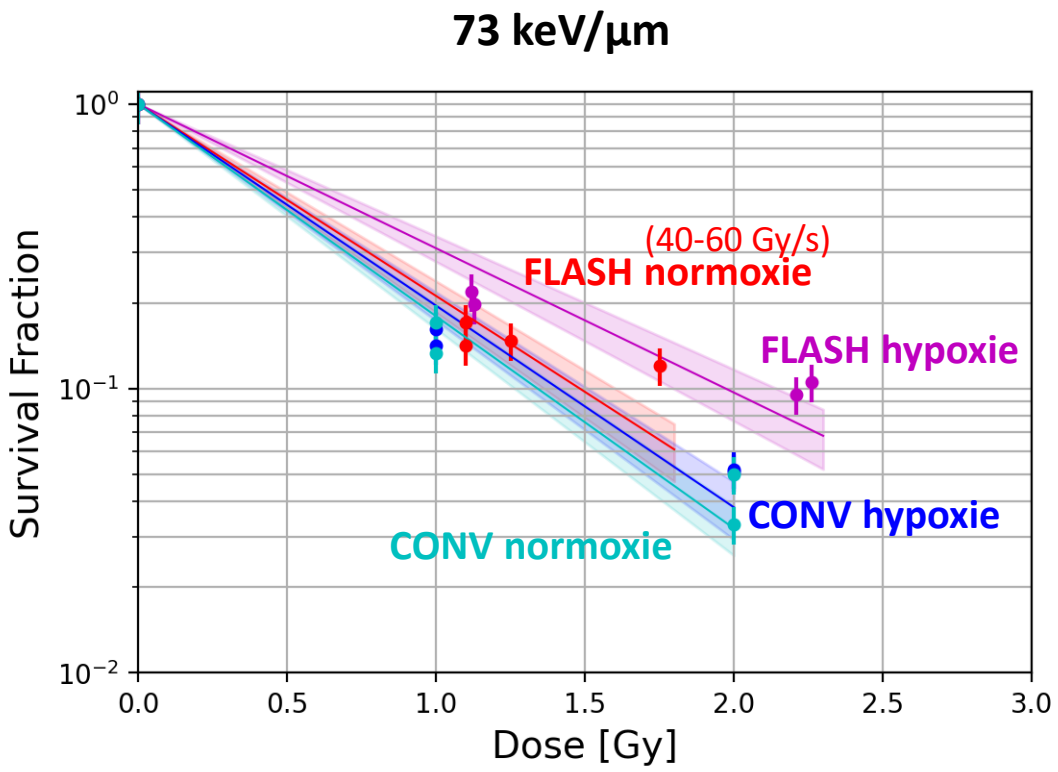




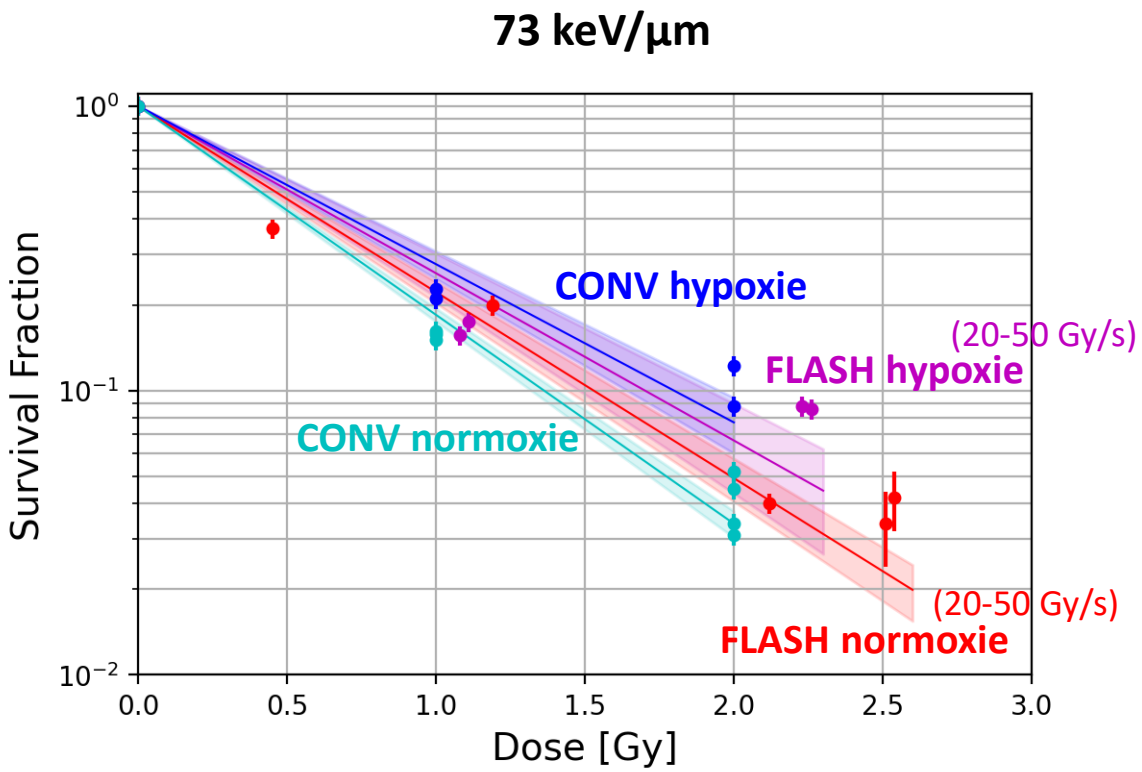


First results

Fibroblast (AG01522)



Lung cancer (A549)

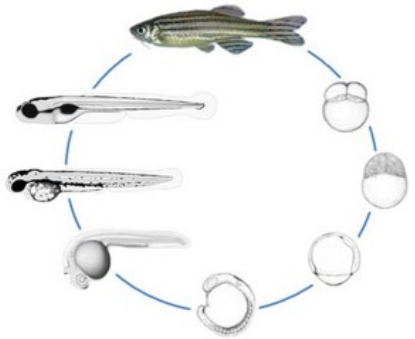


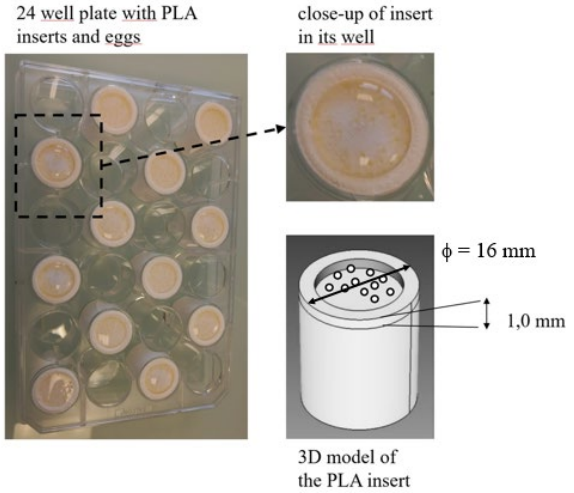
- ✓ FLASH effect in hypoxia conditions :
  - ➢ Less damage to normal cells
  - ➢ Similar damage to cancer cells
- ✓ radiolytic oxygen depletion ?

Future

Radiobiology

- ✓ Confirm results for in vitro 2D models
- ✓ Zebrafish eggs as an animal model
- ✓ Irradiation with ^{16}O ions



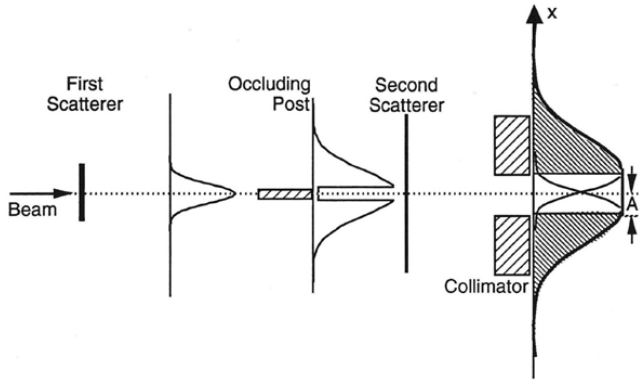


Beam intensity limitation in D1

- ✓ higher dose rates + better field homogeneity
- ✓ new SPR dosimeter with shorter response time ?

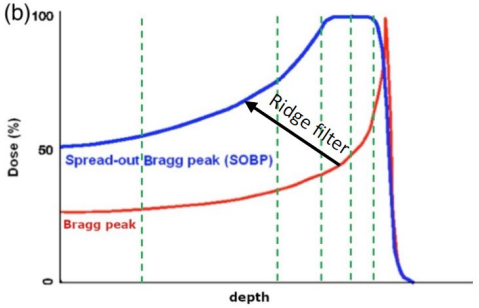
Double scattering method

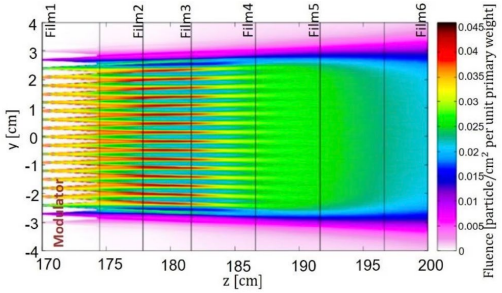
- ✓ larger irradiation field + better field homogeneity
- ✓ beam efficiency up to 40 %



Ridge filter

- ✓ spread out Bragg peak (few mm)
- ✓ in vitro 3D models





DOSION with 1 mm strips

Beamline modelisation in GEANT4

Platform
iRiA
irradiations for Radiobiology
with Accelarated ions

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