Exploring deep in-vivo application of laser-driven very-high, energy, wide spectrum electrons

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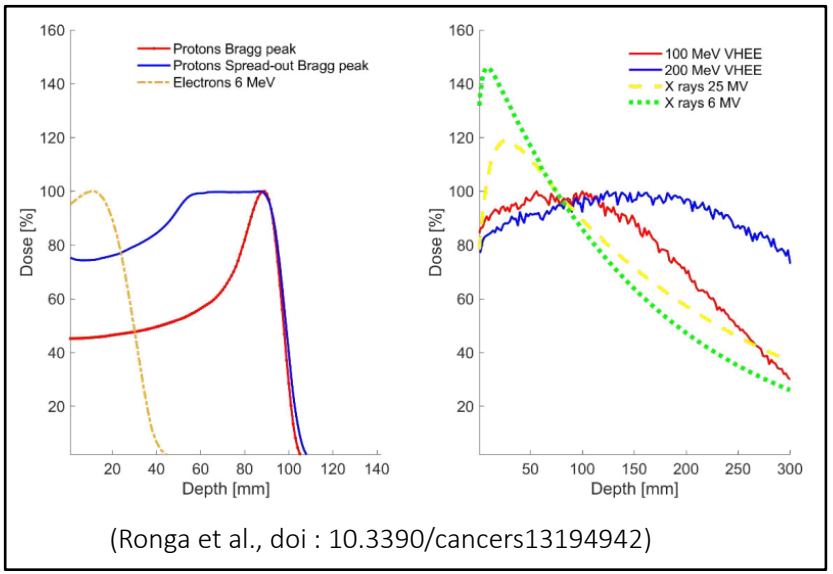
Medical application of energetic electrons (VHEE)

« Comparison of relative depth-dose distributions »



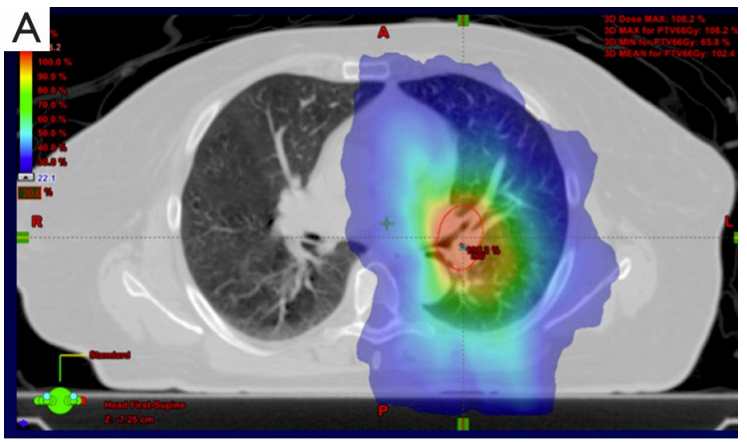
(Ronga et al., doi : 10.3390/cancers13194942)

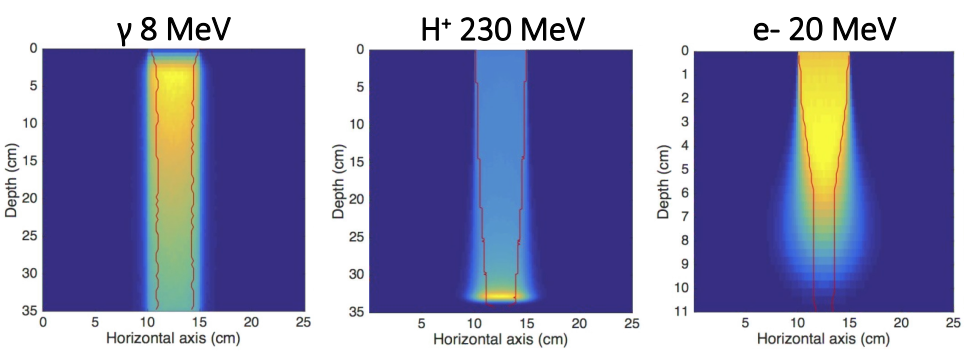
Very High-Energy Electrons : 70 MeV < E < 200 MeV

- Better conformality (resp. photons)
- Lesser sensitivity to density (resp. protons)

- Diffusion
- Difficult acceleration
- Difficult screening

Treatment planning (photons)



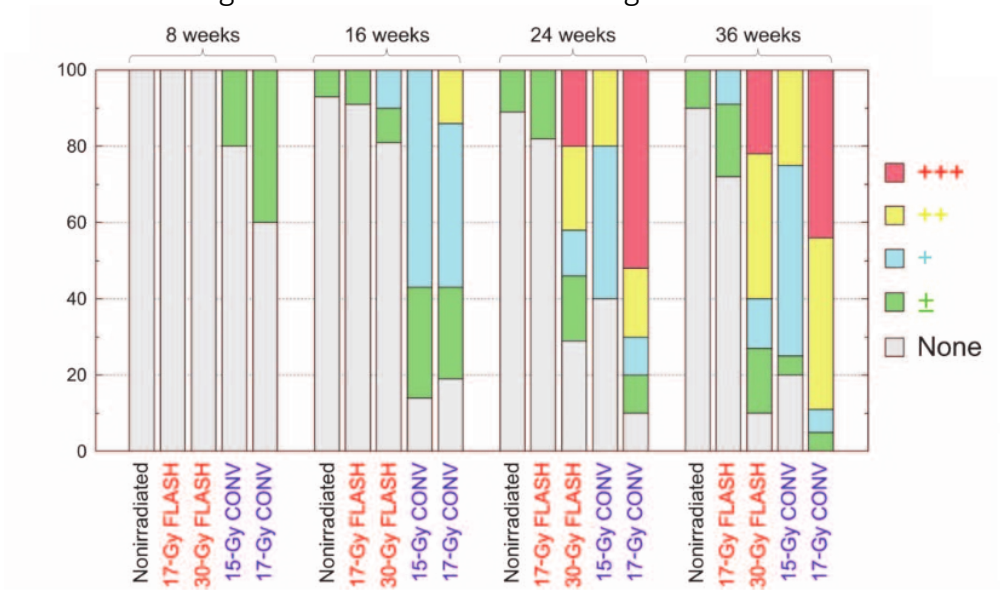


(Credit M. Cavallone)

Temporal effects in toxicity, FLASH

Mice in-vivo bilateral thorax exposure (4.5MeV electrons)

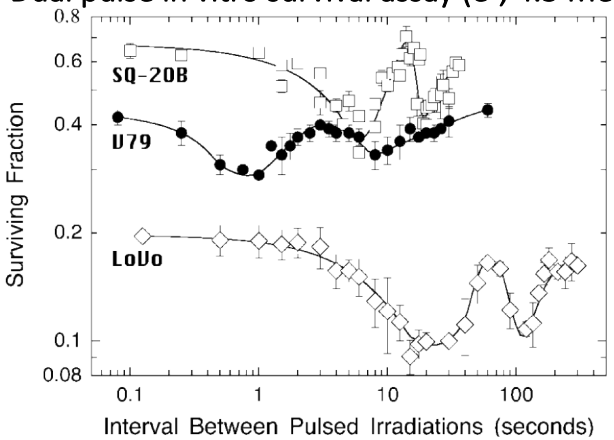
Lung fibrosis occurrence following irradiation



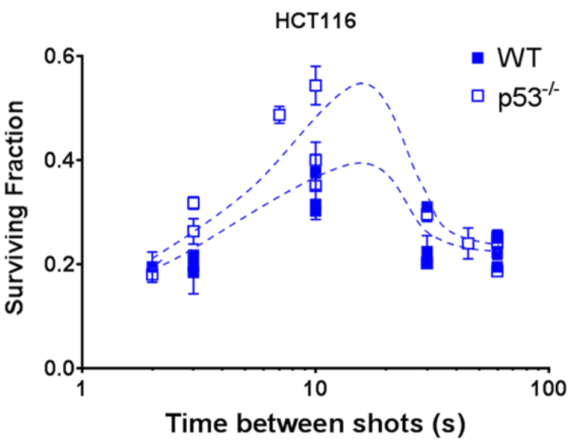
CONV e-: **0.03 Gy/s**

FLASH e-: **60 Gy/s**

Dual pulse in vitro survival assay (e-, 4.5 MeV)



Multiple pulses in vitro survival assay (laser-driven, H+, 10 MeV)

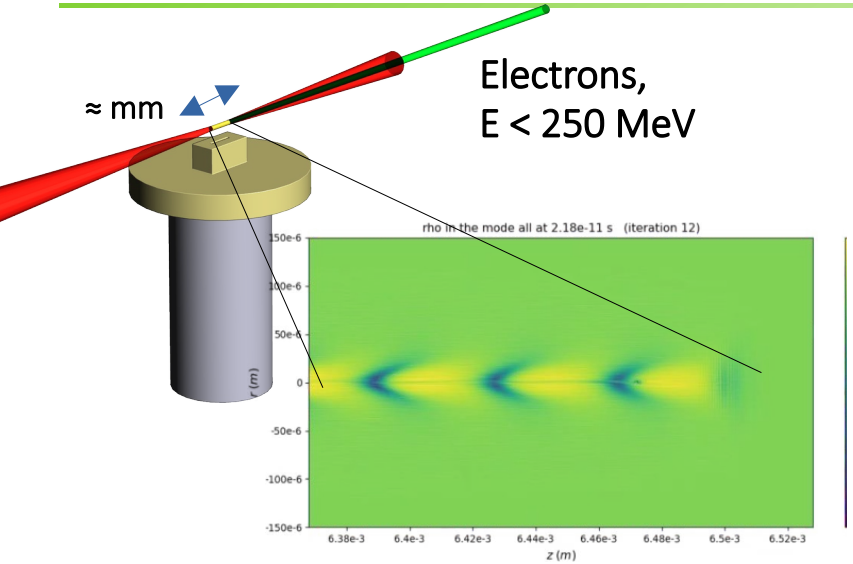


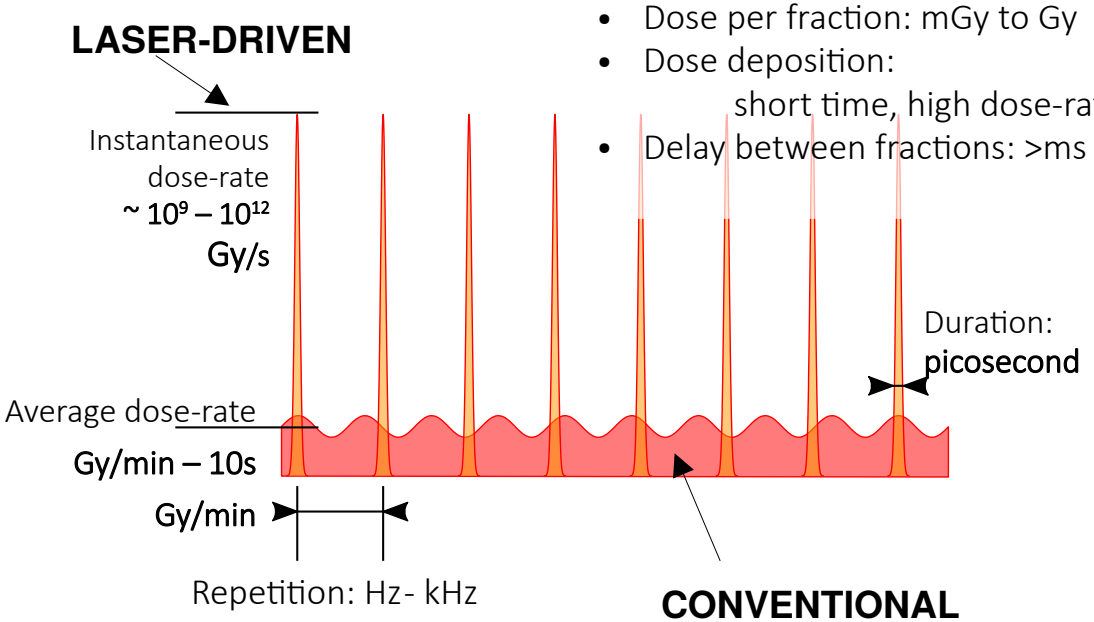
Favaudon et al., DOI: 10.1126/scitranslmed.3008973

Ponette et al. int. j. radiat. biol 2000, vol. 76, no. 9

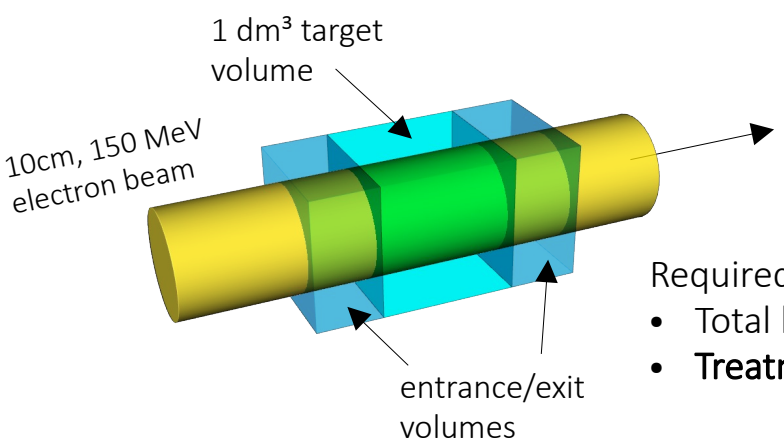
Bayart et al, DOI:10.1038/s41598-019-46512-1

Laser-driven electron beams





- Dose per fraction: mGy to Gy
- Dose deposition: short time, high dose-rate
- Delay between fractions: >ms



Required charge for 10Gy: 500 nC

- Total laser energy: 7.5 kJ (15 J/nC)
- **Treatment time: 75 s (100 W)**

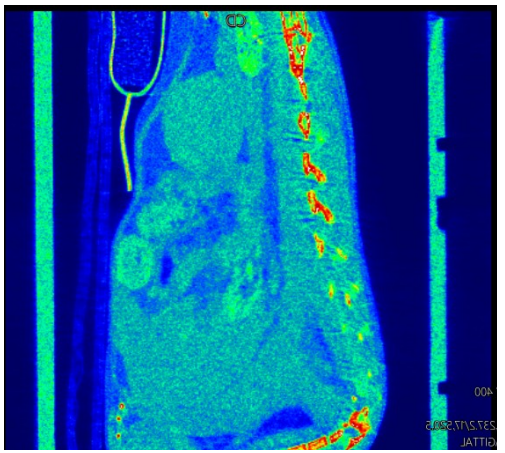
$$\frac{\dot{D}_{inst}}{\dot{D}_{avg}} > 10^9$$

Bilateral thorax exposure in C57BL/6 mice

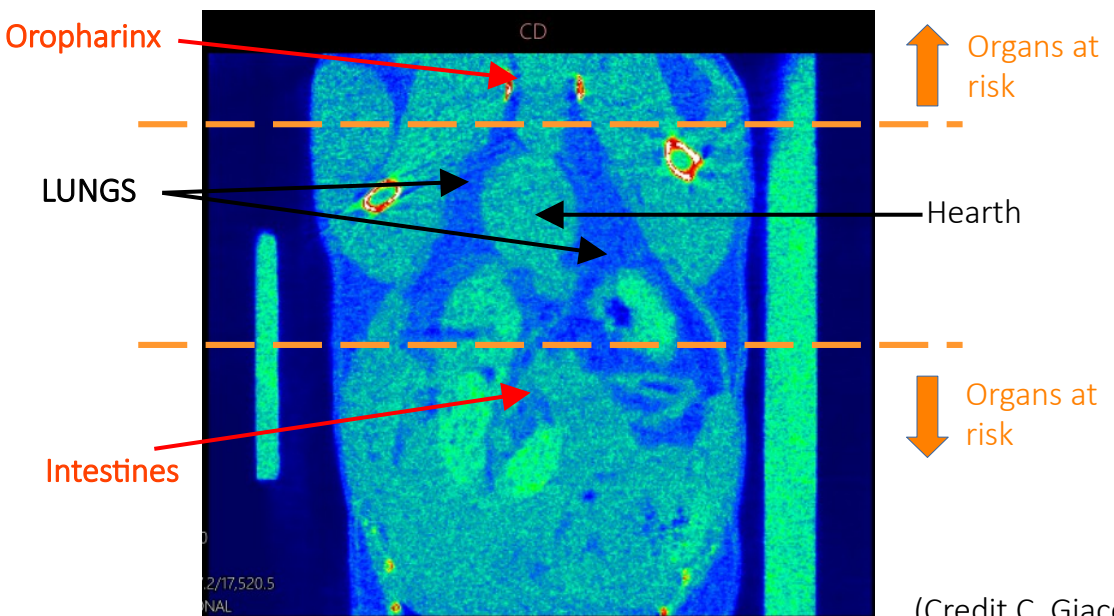
Target dose: 0Gy, 10Gy, 13Gy, 16Gy

Coorte: 24 mice (6 weeks old)

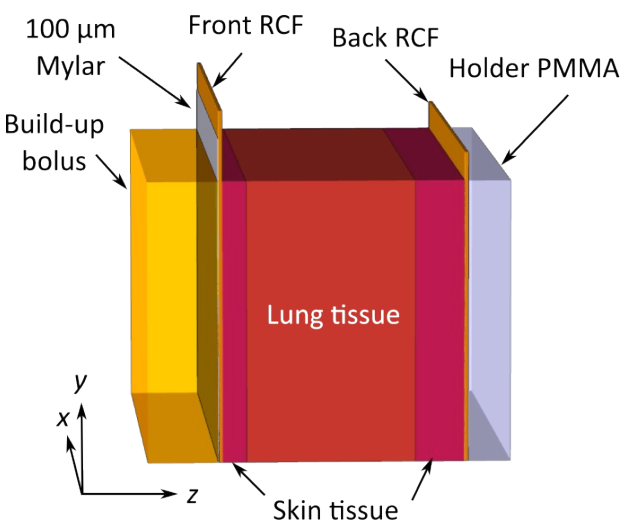
Lateral irradiation size: > 30 mm
Vertical size: limited to 20-25 mm
Dose at intestines < 1 Gy



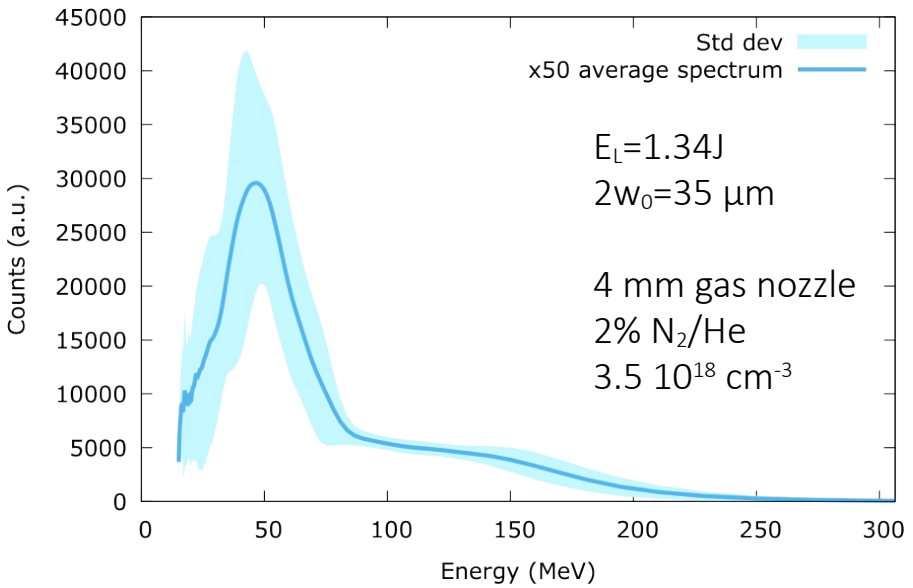
CT scan, C57BL6/J Mouse



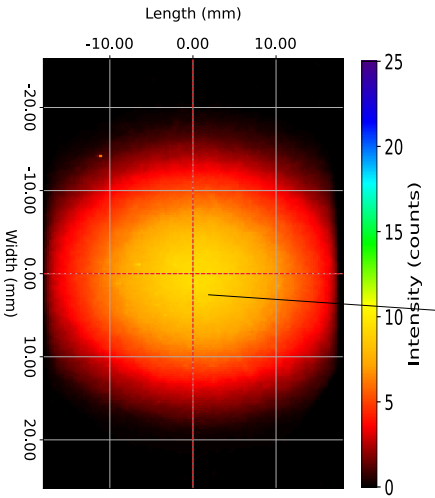
(Credit C. Giaccaglia)

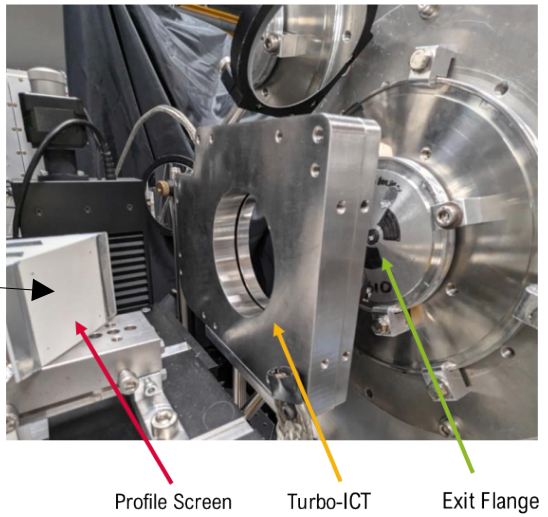


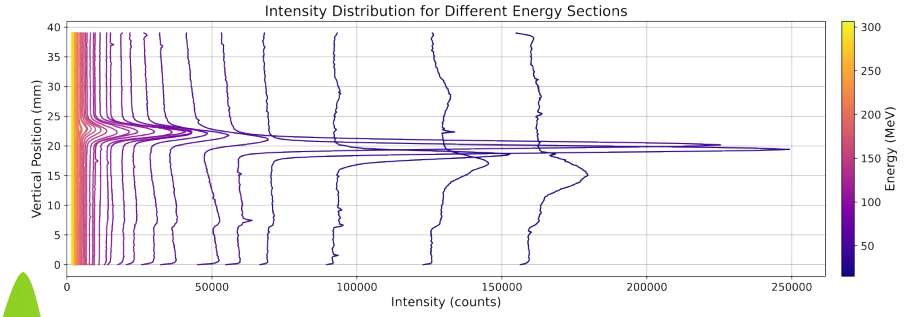
Electron source parameters (Salle Jaune)

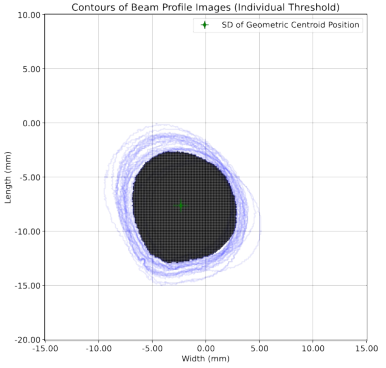


Beam monitor









Average charge: 559.58 pC/shot (1.8%)

Divergence: ~ mrad

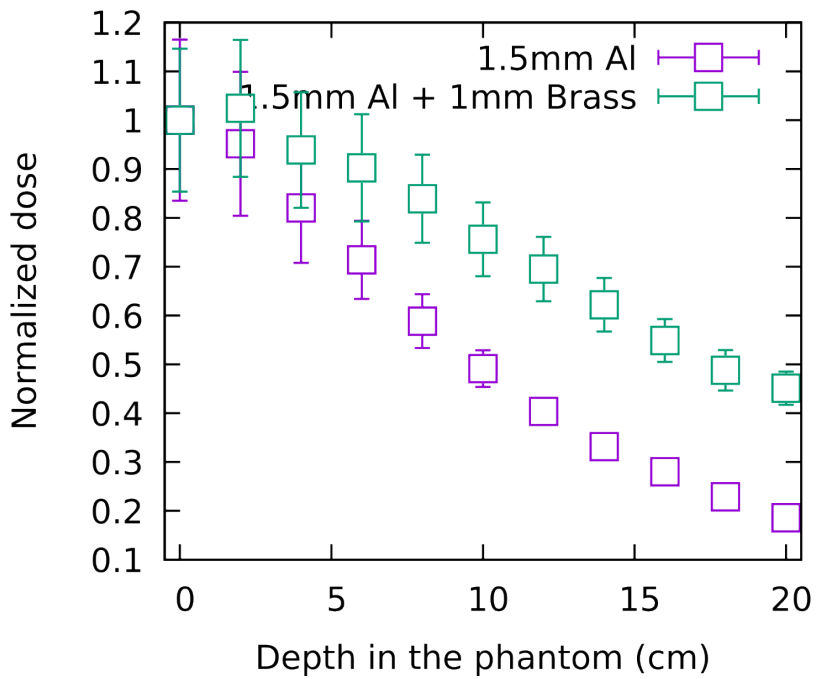
Average centroid motion: 1.6 mrad

Spot surface variation (fixed threshold): 24.6%

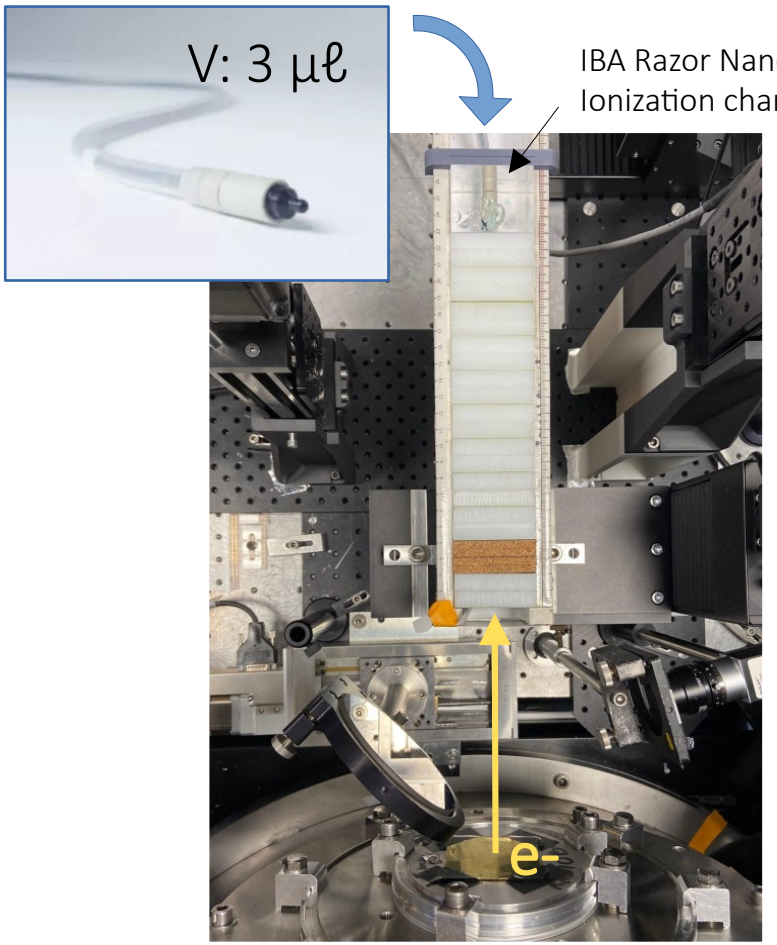
(Credit C. Varma)

Dosimetry in water equivalent phantom

D: 200 – 600 mGy/shot
(2 – 5 cm depth)

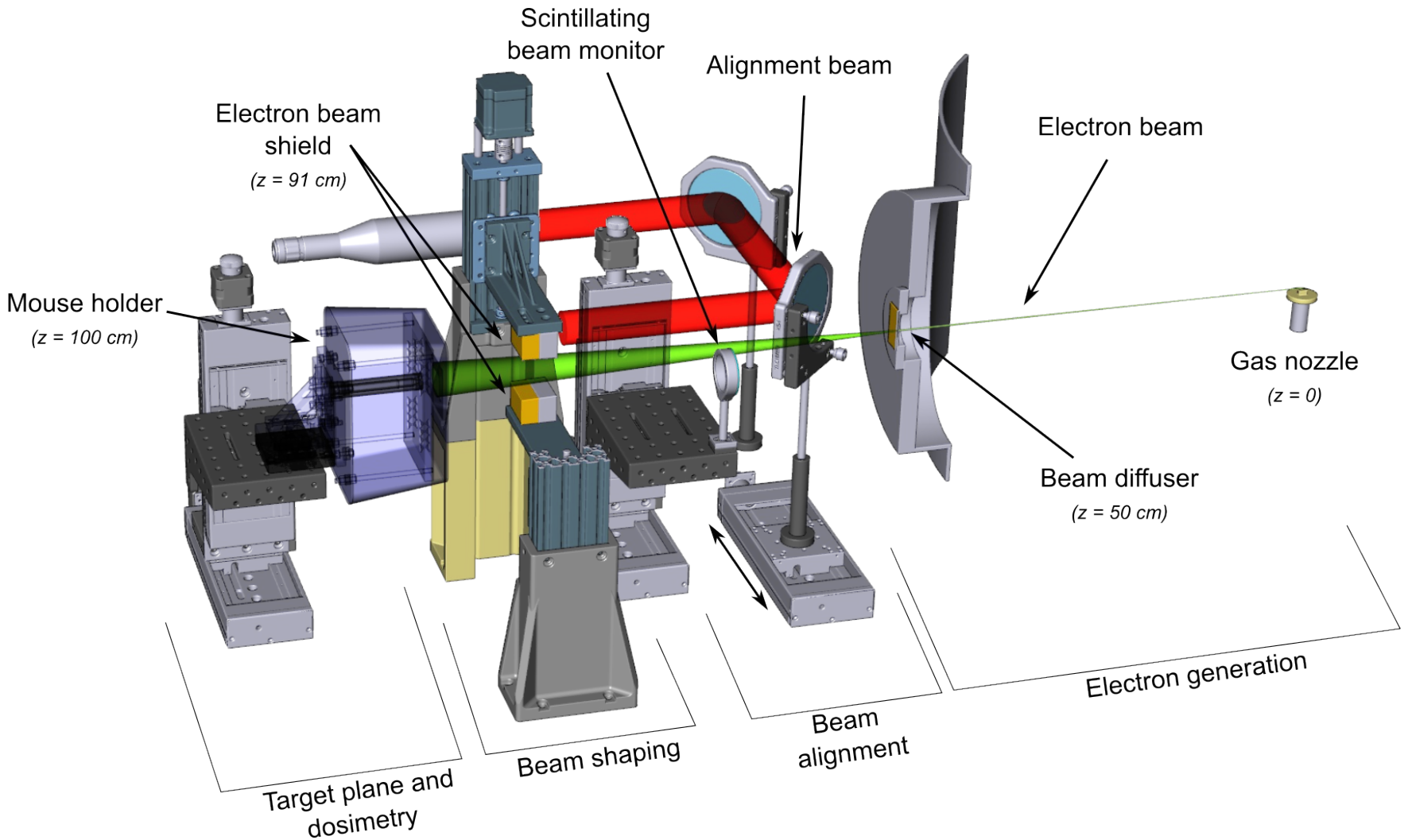


ROI: 10 mm diameter
Δz: 16cm

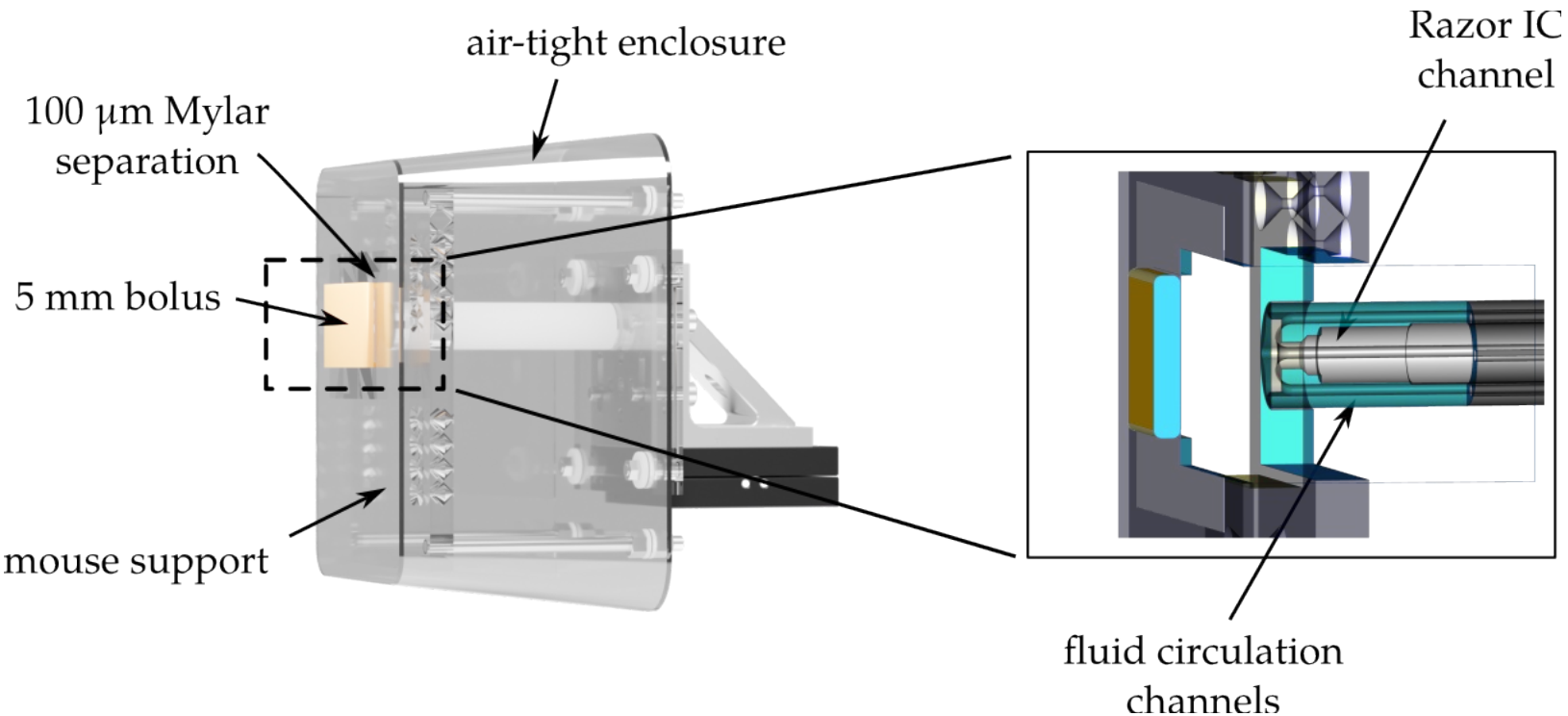


Penetration test phantom
(Credit C. Giaccaglia)

In vivo irradiation setup



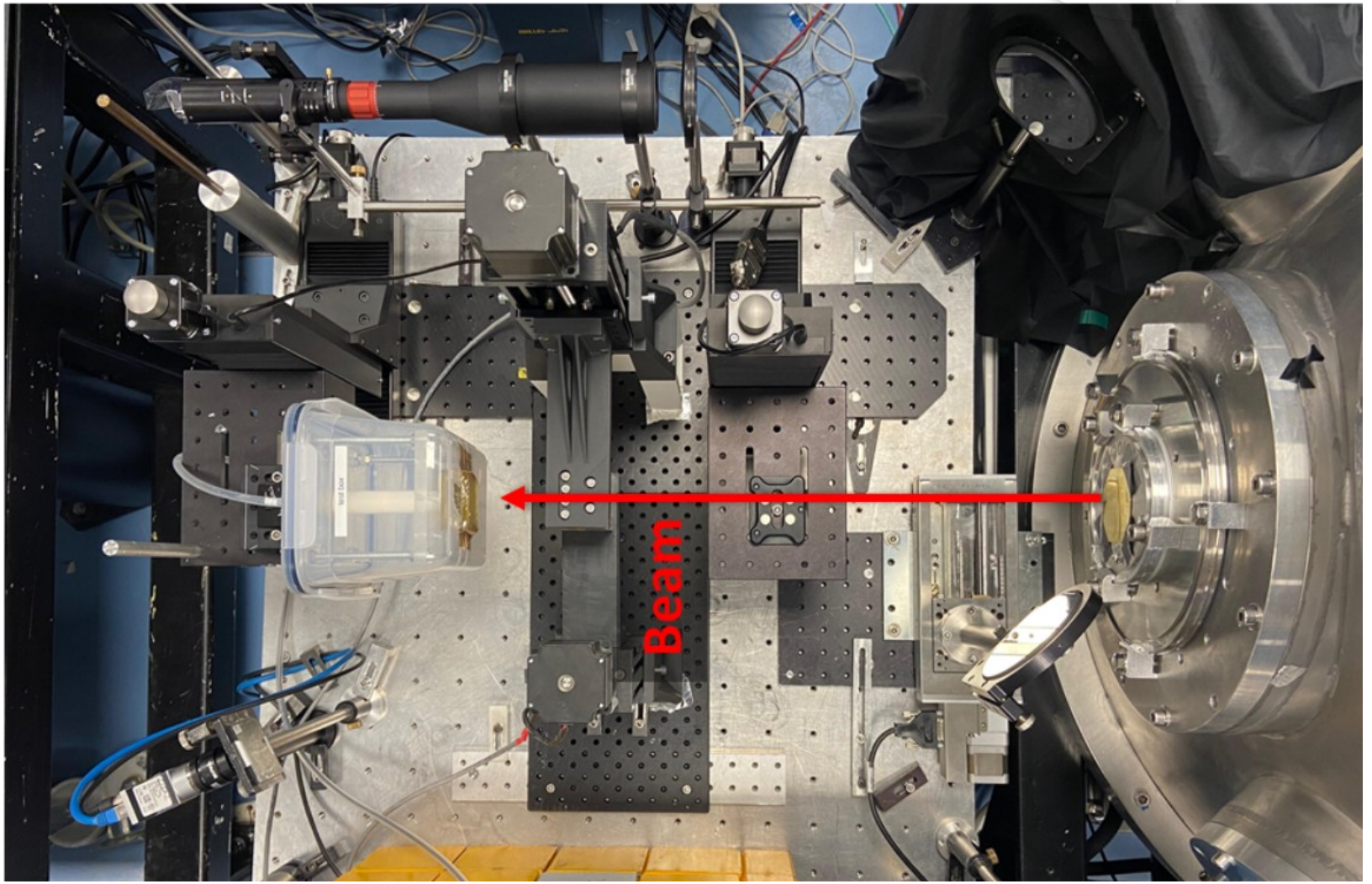
Biological holder and dosimetry



Exposure conditions:

- **30-50 mGy/shot** @ 0.5Hz
- Dose rate: **0.9 – 1.5 Gy/min**
- Current: **250 pA**

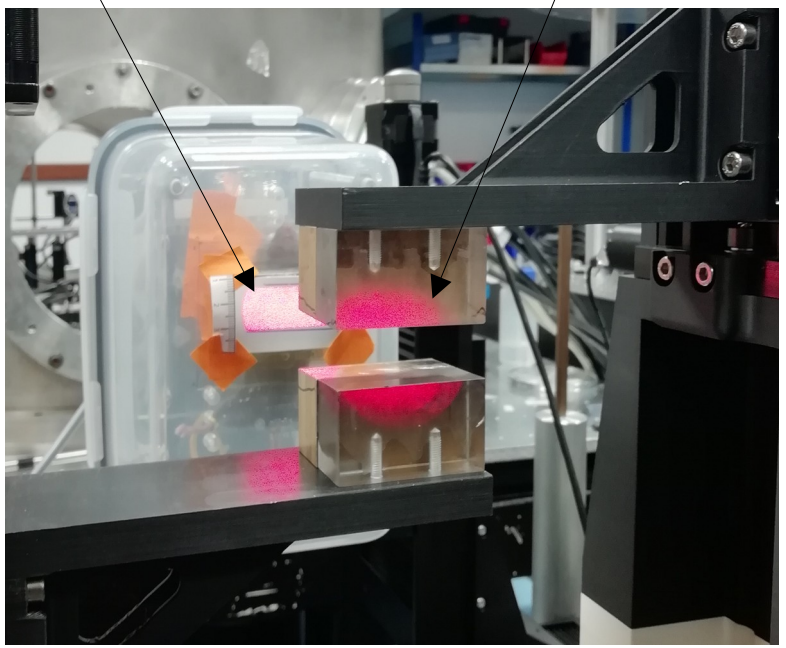
Experimental setup

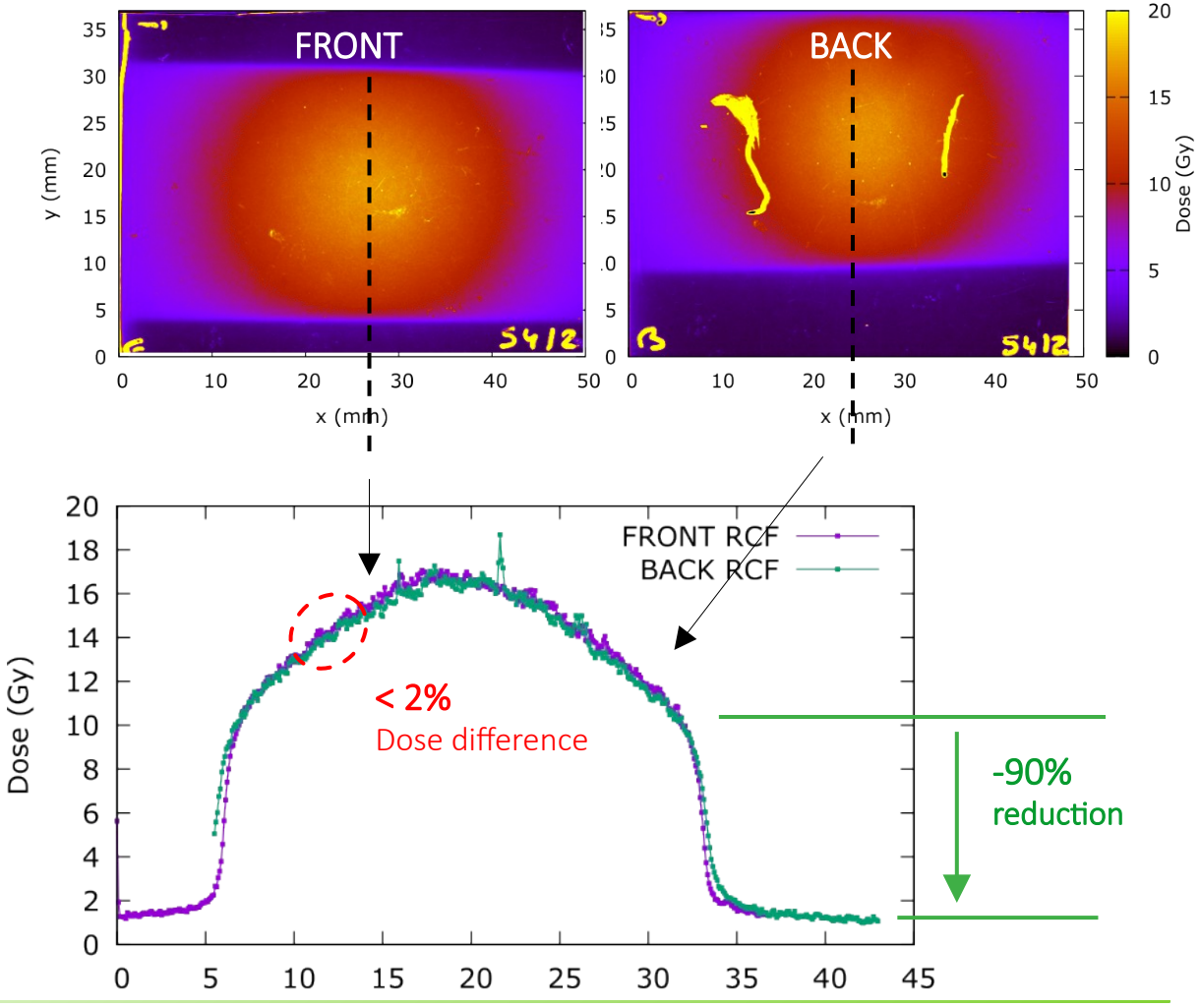


In vivo mice experiment (May 2024)

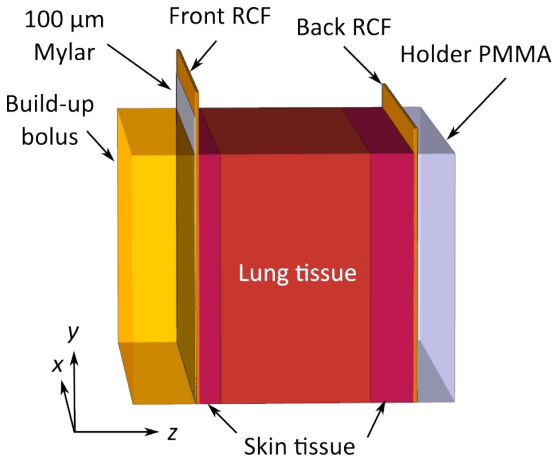
Scintillating screen
(beam monitor)
+ bolus & **RCFs**

Alignment laser &
e- Beam shaping





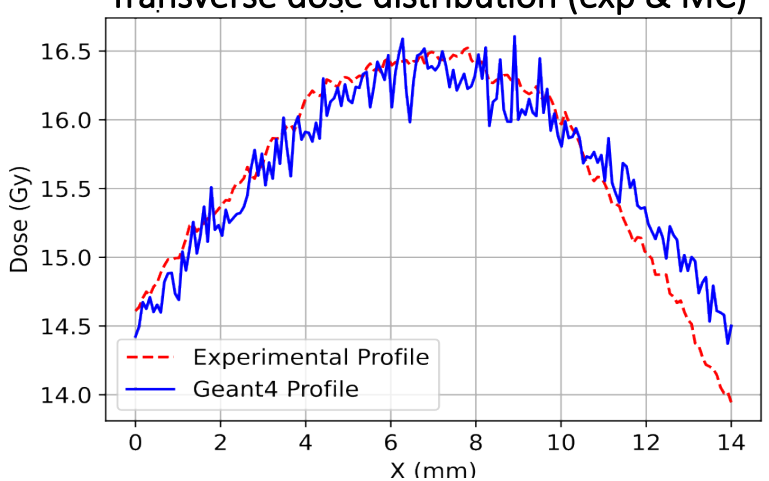
Monte Carlo source modeling



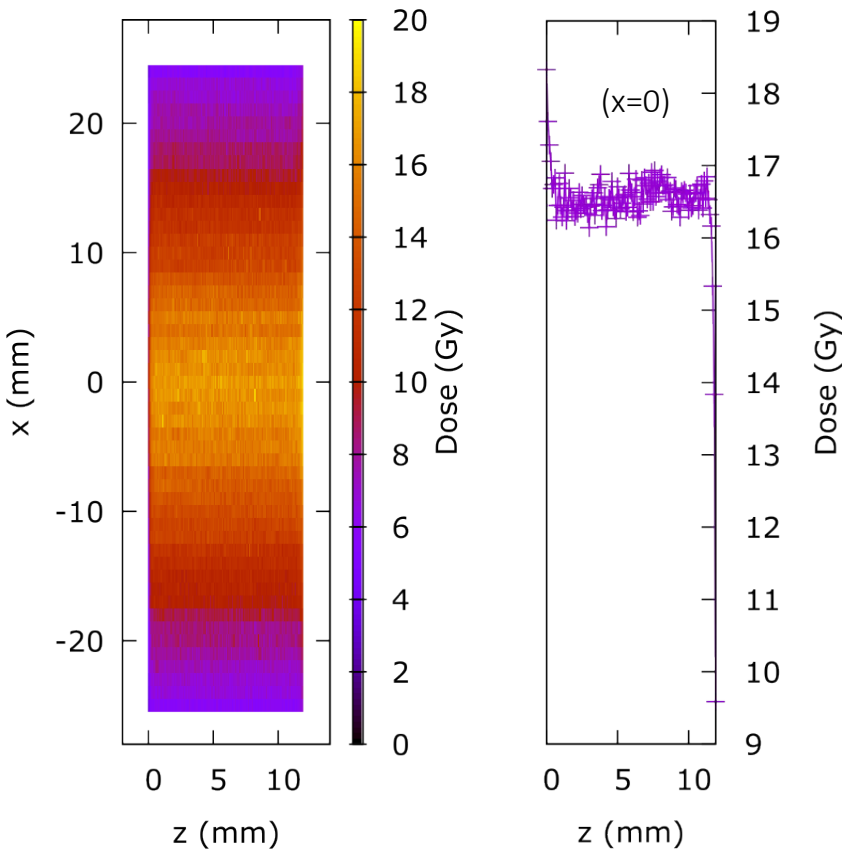
Average exposure dose: **15.67 Gy**
Num shots: 542

Sim: 4.9 10^{-5} Gy/pC
Average Dose: **28.9 mGy/shot**
Average Charge: **589 pC/shot**

Transverse dose distribution (exp & MC)

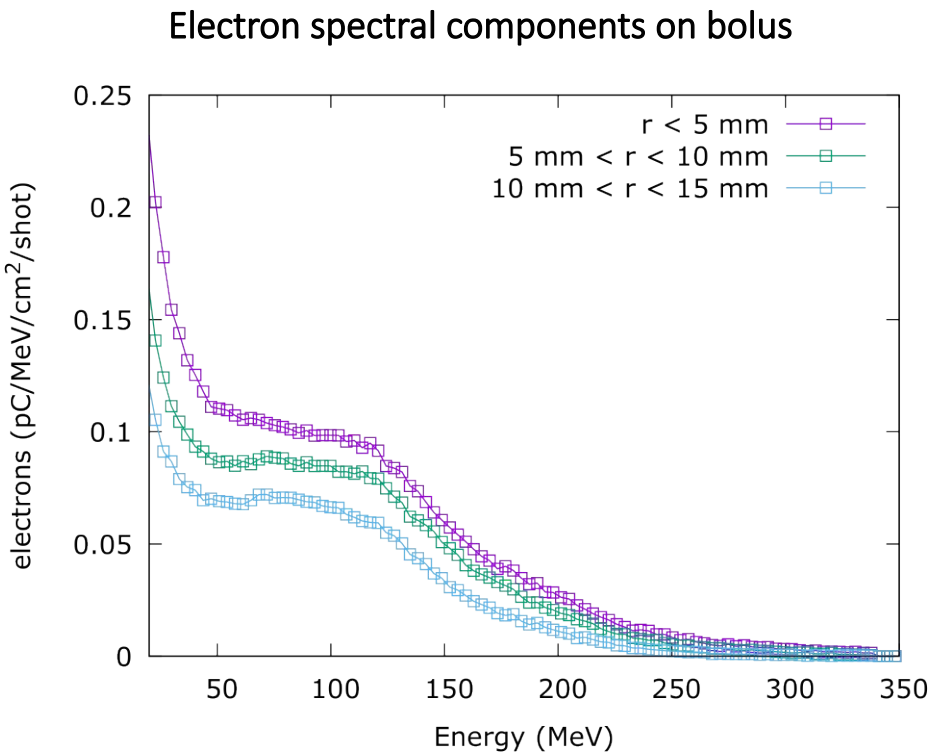


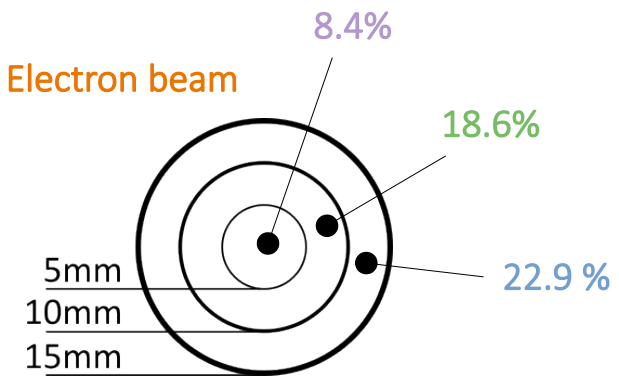
Longitudinal dose distribution (MC)



(Credit J. B. Amakkattu)

Spectral condition on target

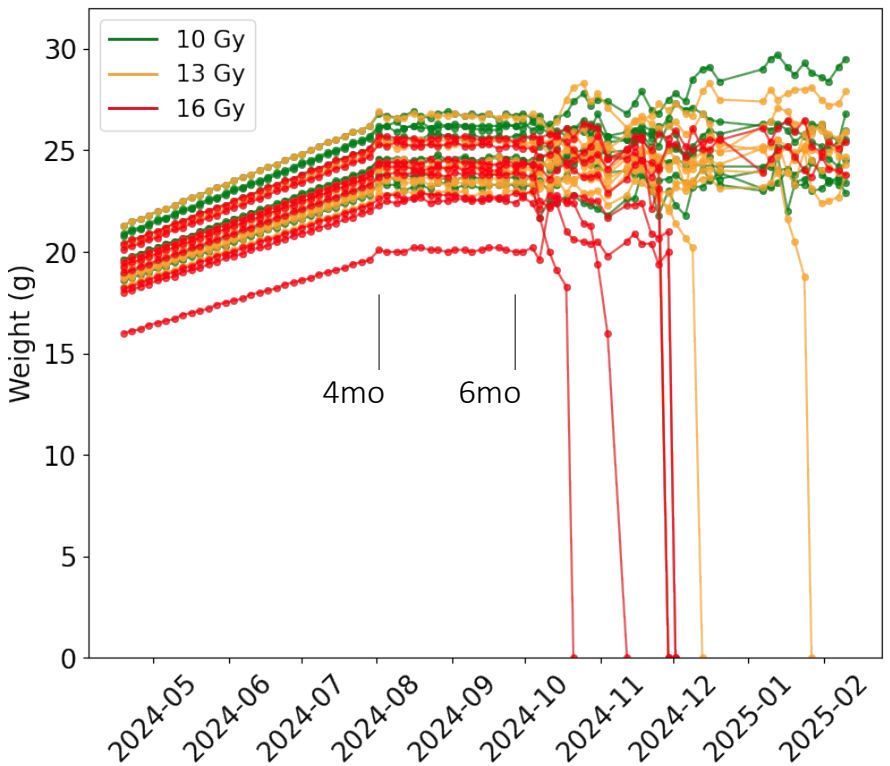


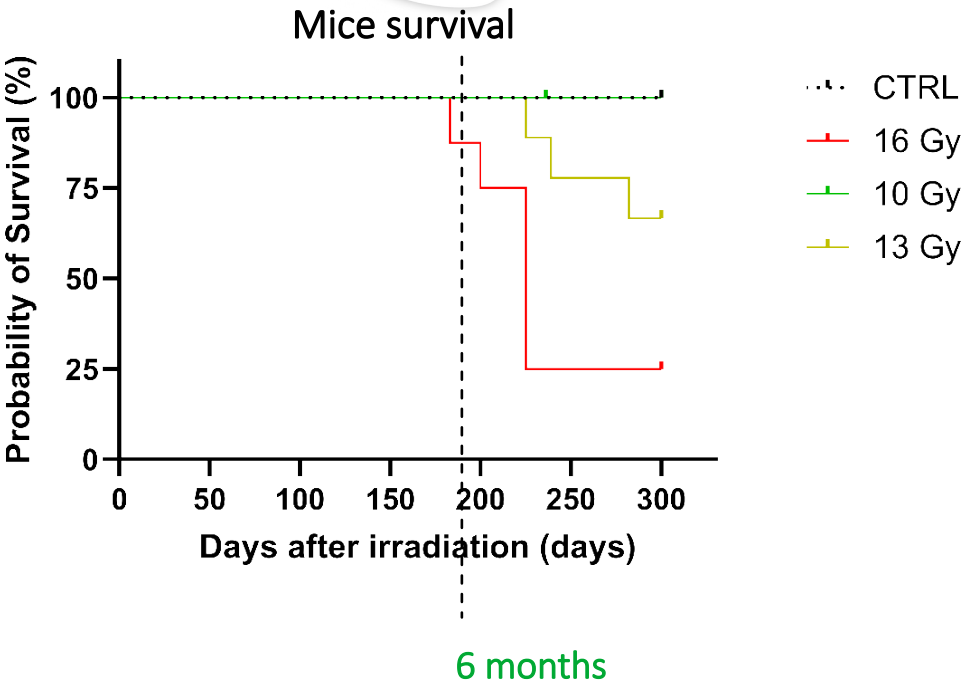


Total energy fraction (source to target): 49.9%

(Credit J. B. Amakkattu)

Mice followup: 10 months





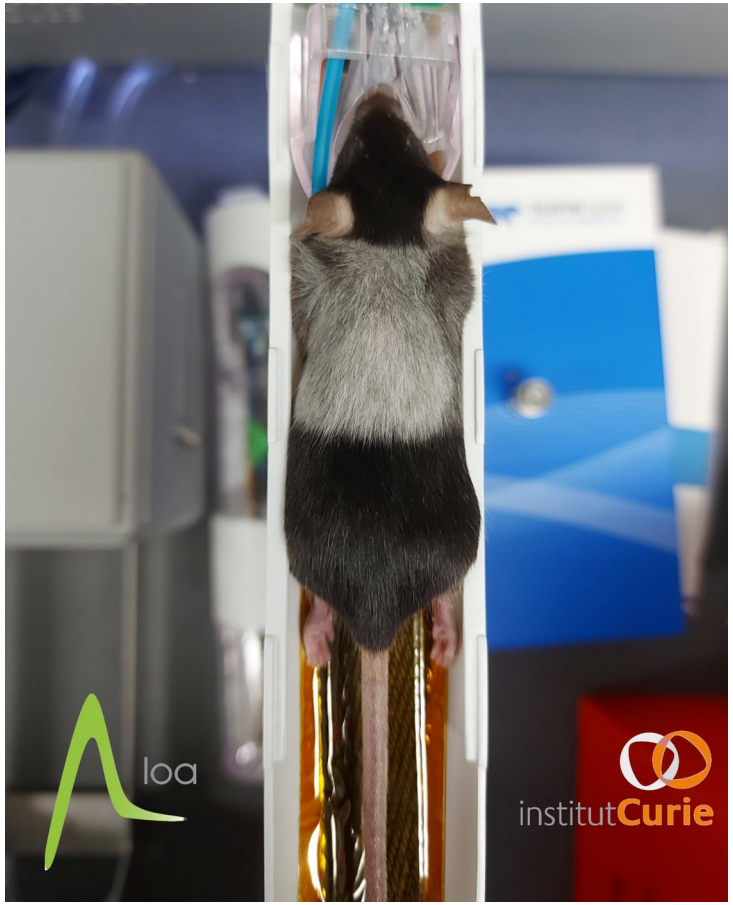
6 months

- No sudden death for dose at intestine
- No head/larynx/esophagus complications
- No cardiac problems for excess dose
- No volume effect

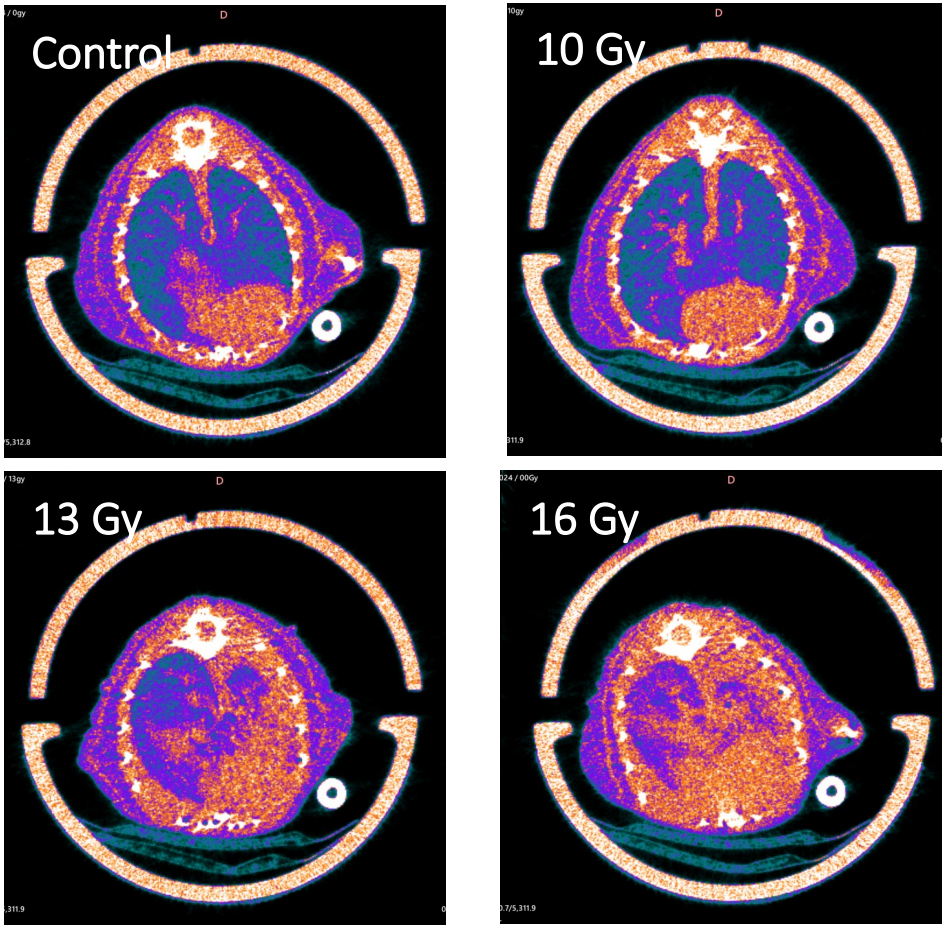
(Credit C. Giaccaglia)

Irradiation follow-up

Irradiated mouse, 16Gy full thorax, 4mo. post
Dose per pulse: 50 mGy/shot @0.5Hz (1.5 Gy/min)



Coronal cut, 7mo post-exposure



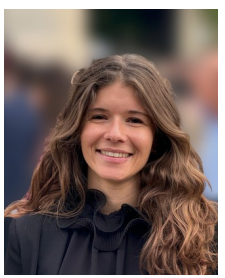
(Credit C. Giaccaglia)

Conclusions

- Laser-driven electron beam for radio-biology in novel temporal modalities
- Beam and protocols for in vivo manipulation and irradiation
- Controlled exposure of 24x C57BL/6 mice, 1.5Gy/min, fast-fractionation
- Uniform dose deposition in depth over >15 mm, 40 mm^2
- Toxicity study is ongoing.

Acknowledgments

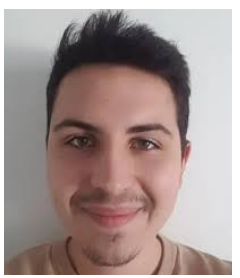

J. B. Amakkattu


C. Giaccaglia


E. Bayart


Ch. Fouillade


S. Heinrich


M. Dubail


C. Varma