



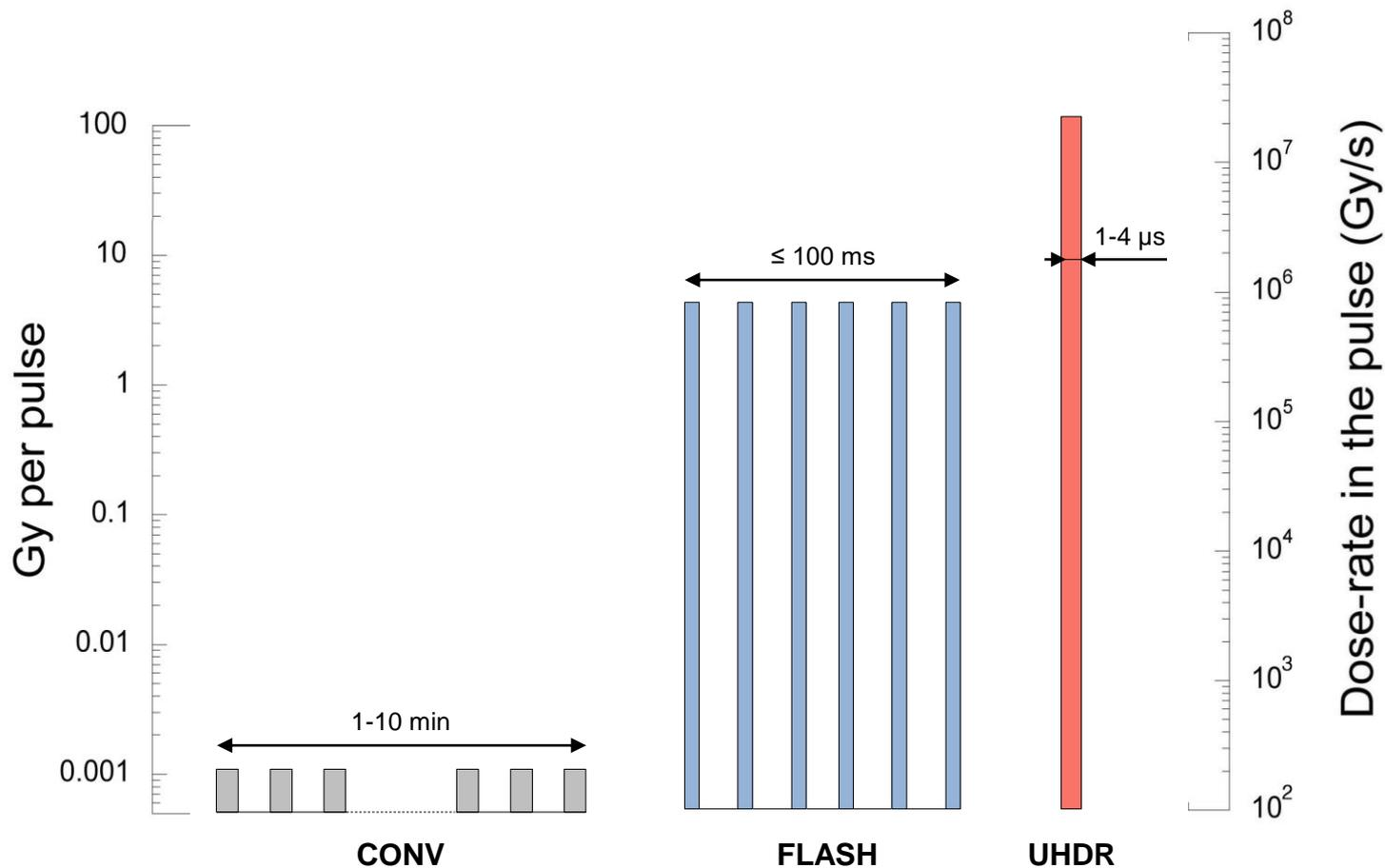
institut**Curie**

Cherenkov light for time-resolved dosimetry of electron beams in ultrahigh dose-rate, FLASH radiotherapy

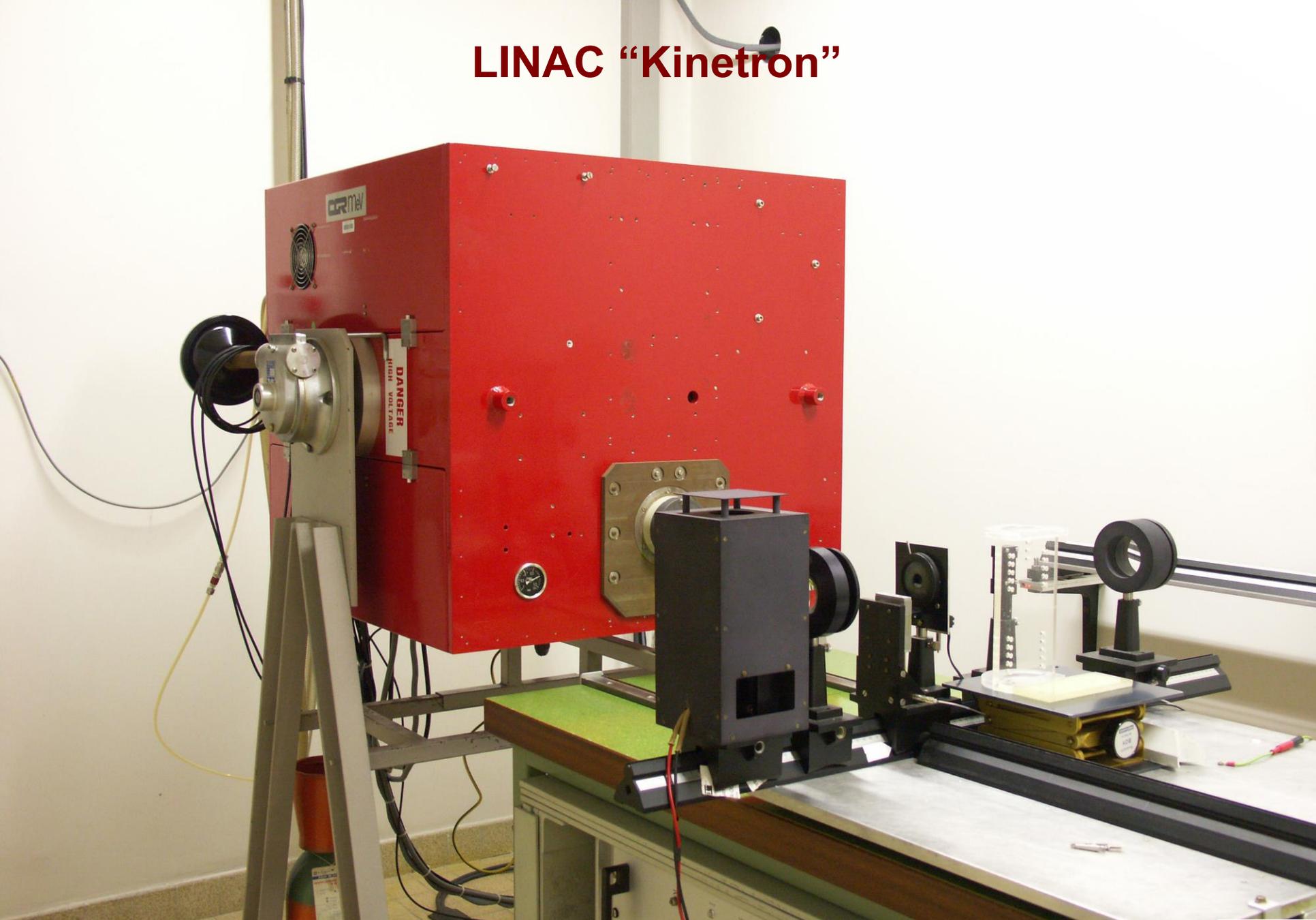
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No conflict of interest to disclose

Temporal structure of energy deposition



LINAC "Kinetron"



Specifications

Pulse 1

Pulse 2

Variable delay

LINAC “Kinétron” (1987)

3.9-5.1 MeV electrons

TEL = 0.19 keV/ μm

RBE = 1.00 relative to ^{60}Co (Compton only)

Pulse width 0.05 - 2.2 μs

Repeat frequency 0.1 - 200 Hz

Peak current 0.01 - 200 mA

Dose per pulse 0.002 - 50 Gy

Mean dose-rate 0.01 - 7500 $\text{Gy}\cdot\text{s}^{-1}$

Maximum dose-rate during the pulse $\approx 3 \cdot 10^7 \text{ Gy}\cdot\text{s}^{-1}$

FLASH spares normal tissues from radio-induced complications whilst preserving the antitumor efficiency

➤ Lung fibrosis (mice)

Favaudon et al. (2014) *Sci Transl Med* 6: 245ra93.

➤ Neural stem cells & cognition (mice)

Montay-Gruel et al. (2017) *Radiother Oncol* 124: 365-9.

➤ Intestinal crypt stem cells

Loo et al. (2017) *Int J Radiat Oncol Biol Phys* 98-e16.

➤ Pig skin – Cat patients

Vozenin et al. (2019) *Clin Cancer Res* 25: 35-42.

➤ Human fibroblasts (protons) *in vitro*

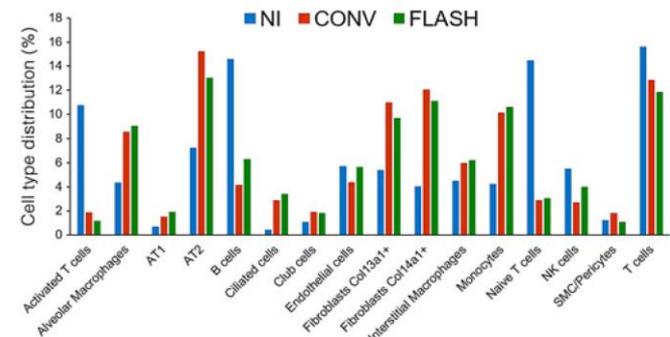
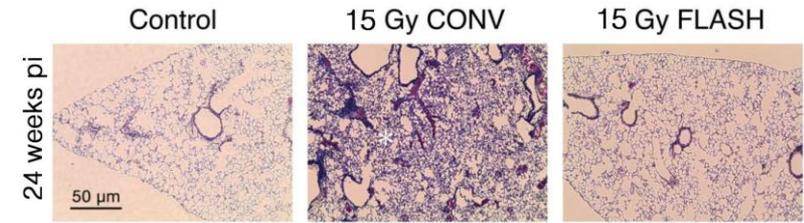
Buonanno et al. (2019) *Radiother Oncol* 139: 51-5.

➤ The FLASH effect depends on oxygen

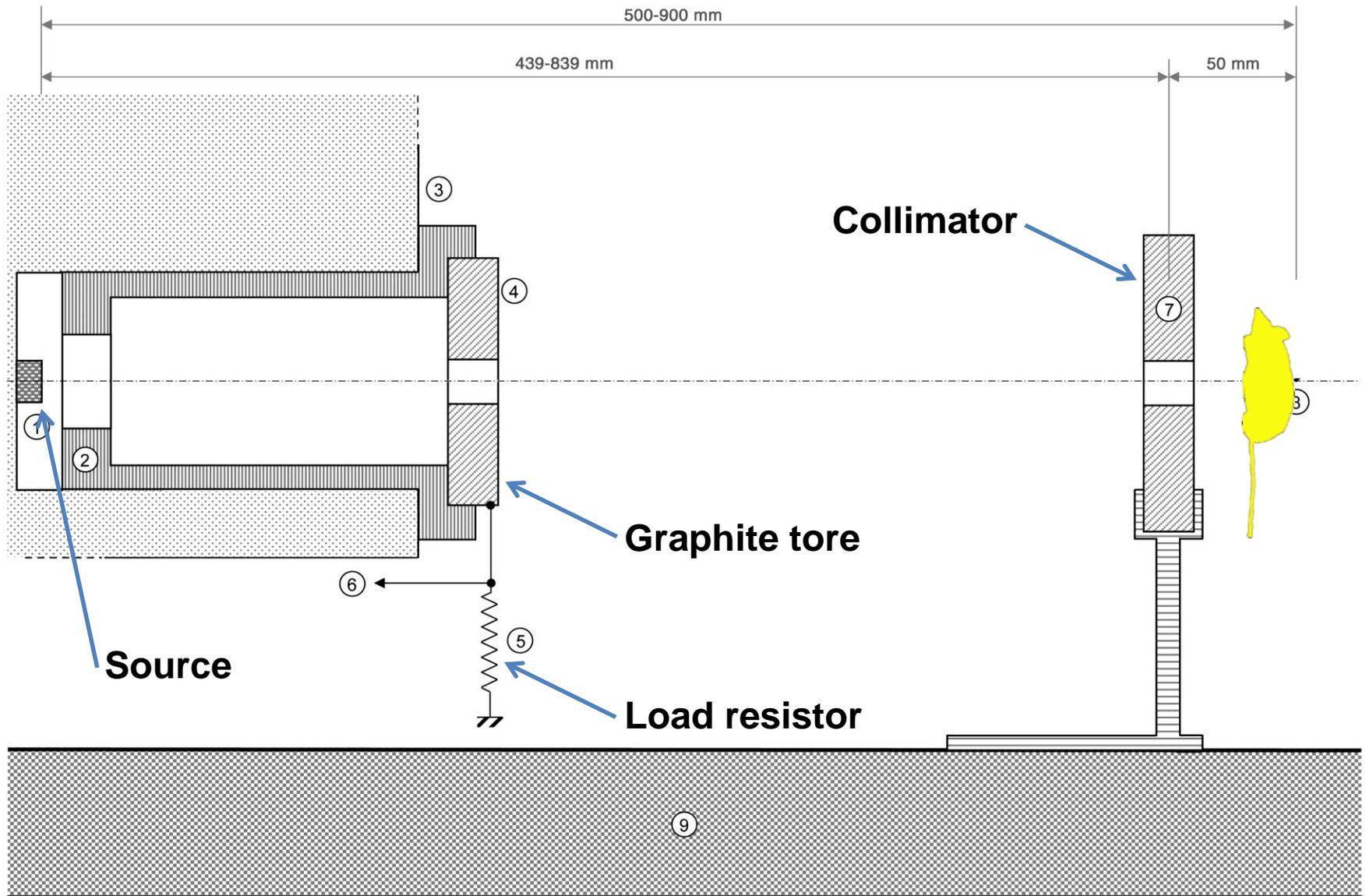
Montay-Gruel et al. (2019) *PNAS* 116: 10943-51.

➤ FLASH spares normal stem cells from radio-induced senescence

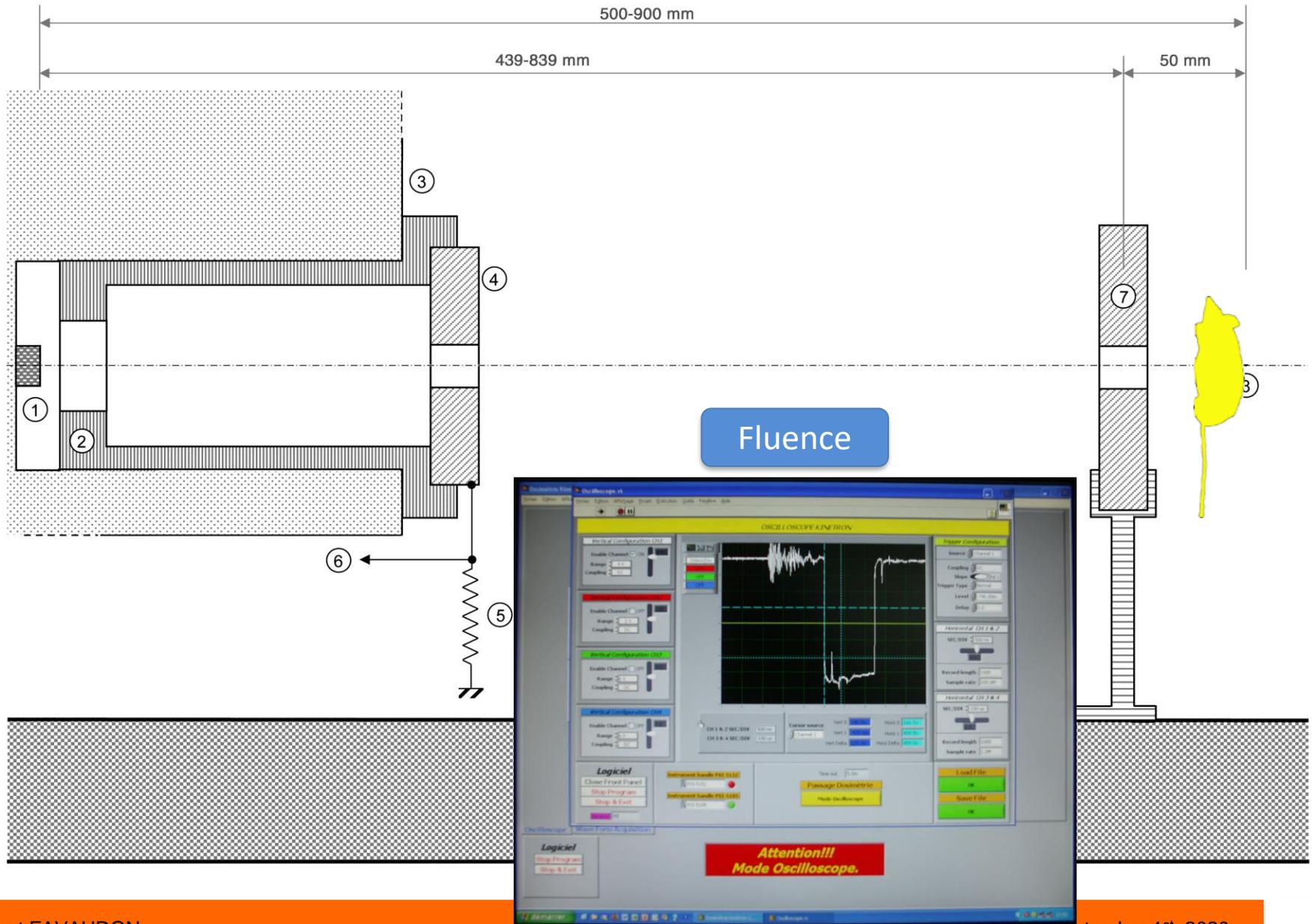
Fouillade et al. (2020) *Clin Cancer Res* 26: 1497-1506.



Setup



Setup



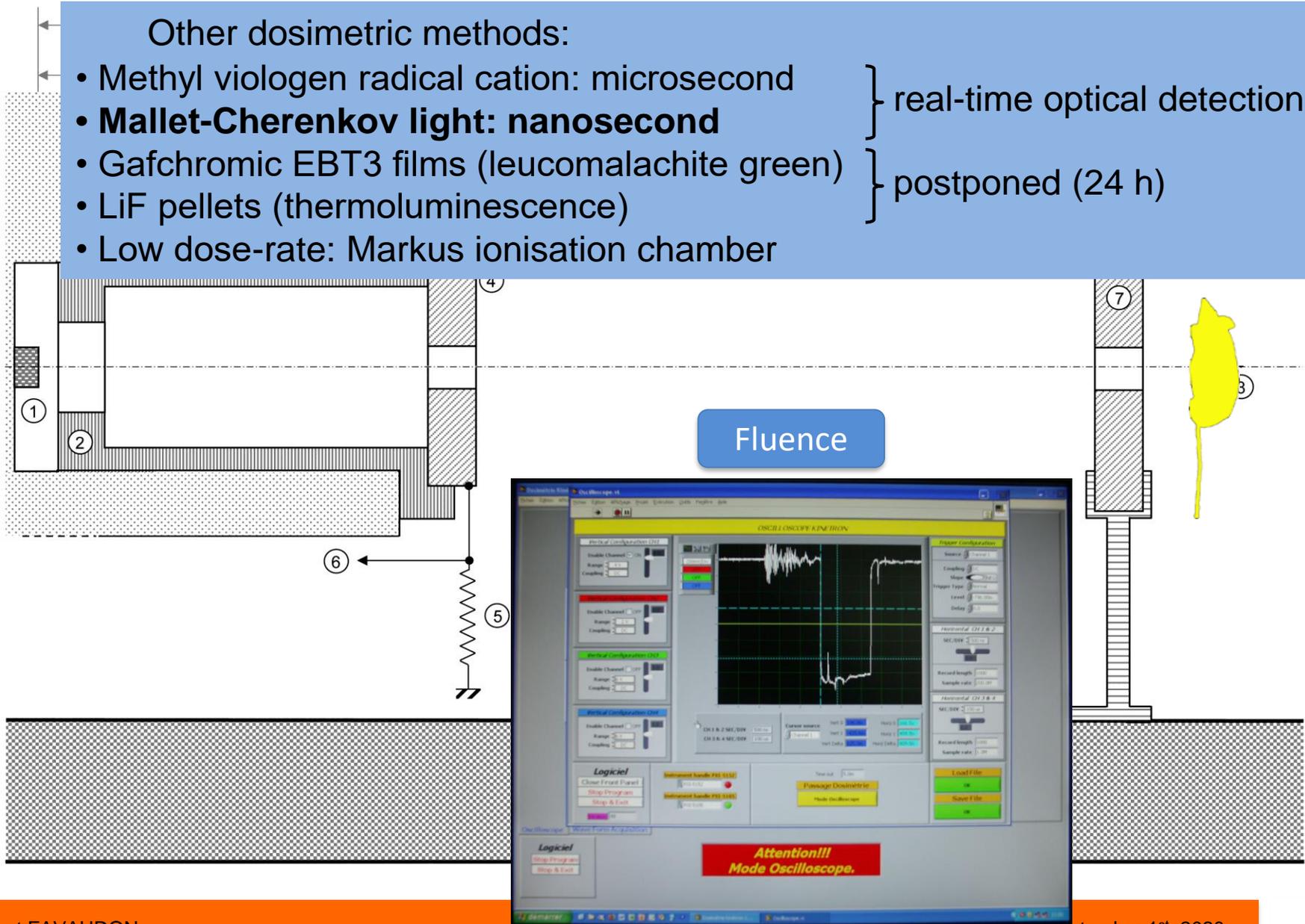
Setup

Other dosimetric methods:

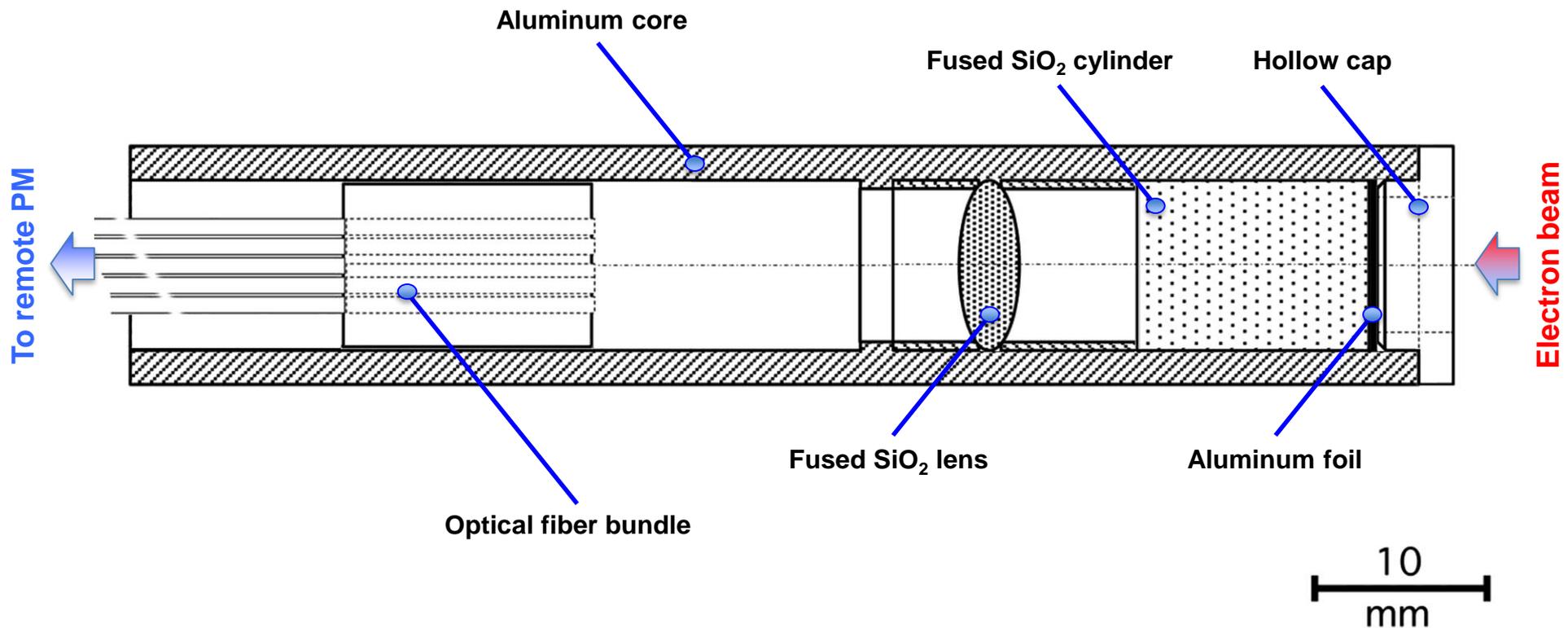
- Methyl viologen radical cation: microsecond
- **Mallet-Cherenkov light: nanosecond**
- Gafchromic EBT3 films (leucomalachite green)
- LiF pellets (thermoluminescence)
- Low dose-rate: Markus ionisation chamber

} real-time optical detection

} postponed (24 h)

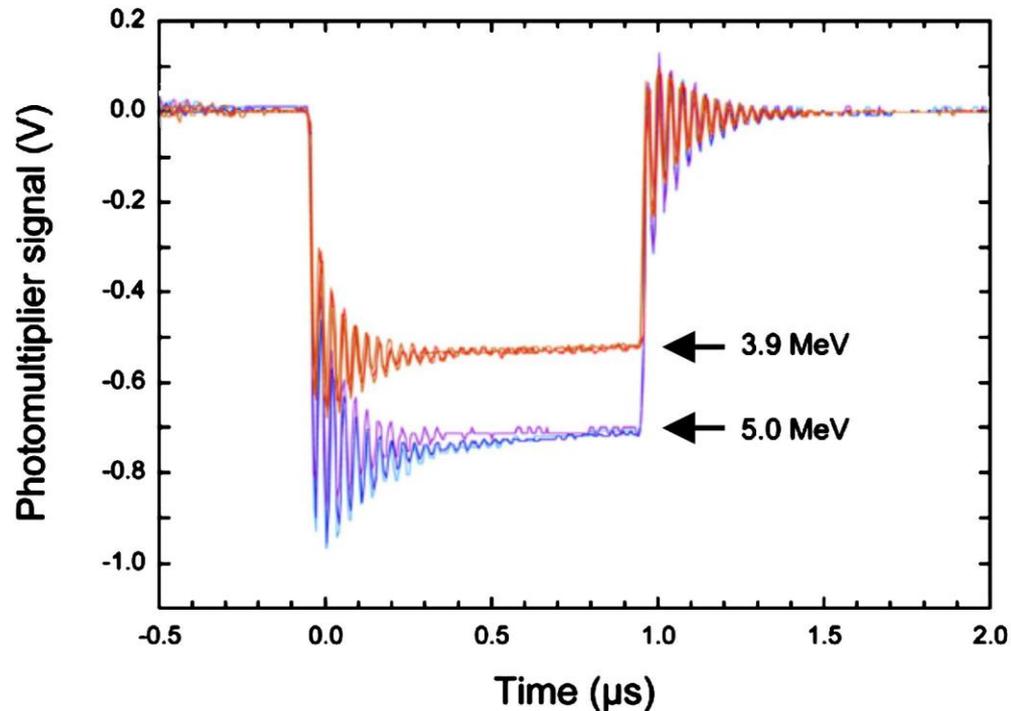


Cherenkov probe



Analysis of Cherenkov light

1 – Fast response and dependence on energy



Pulse width: 1.0 μs

Dose per pulse: 0.47 Gy.

Load resistor at the photomultiplier: 50 Ω .

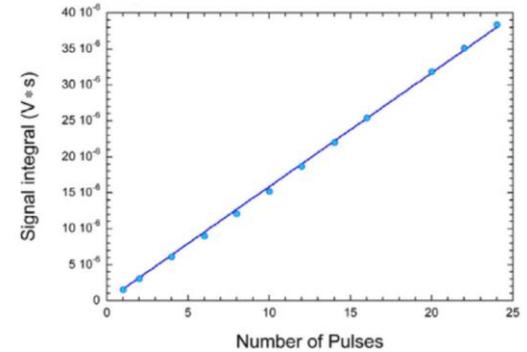
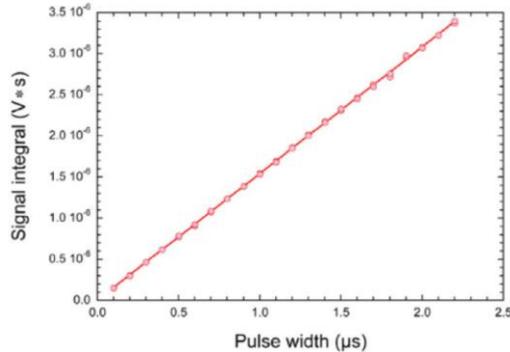
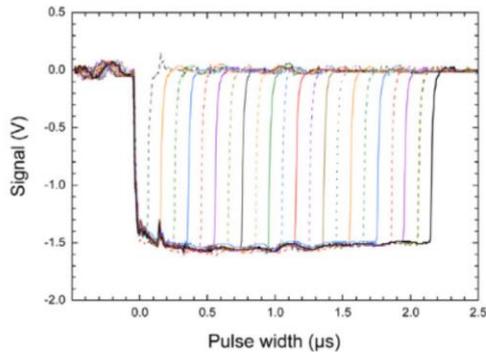
Analysis of Cherenkov light

2 – Linearity at high beam current

Graphite tore (Faraday cup)

Beam current: 30.9 mA

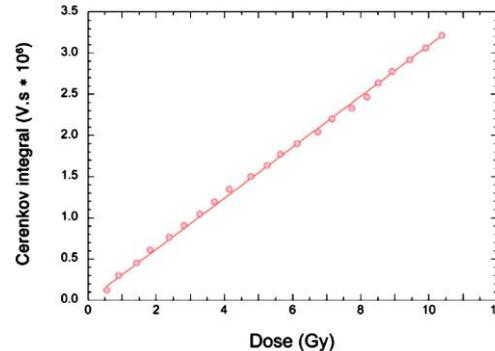
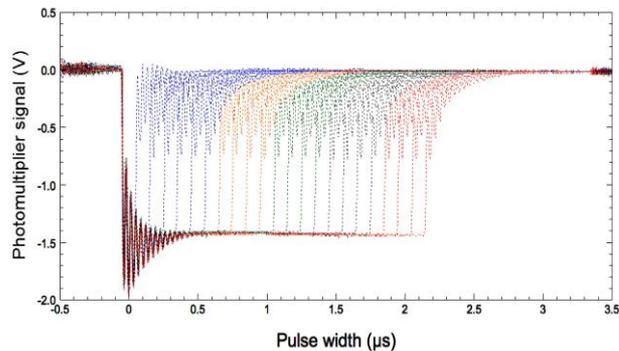
Load resistor : 50 Ω



Cerenkov probe

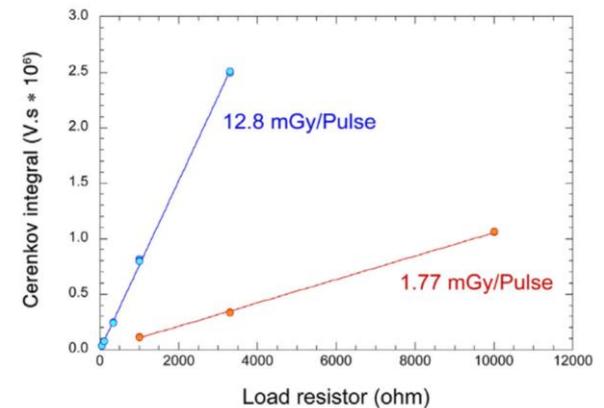
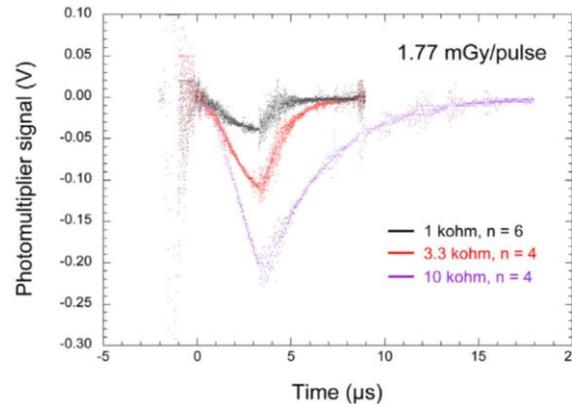
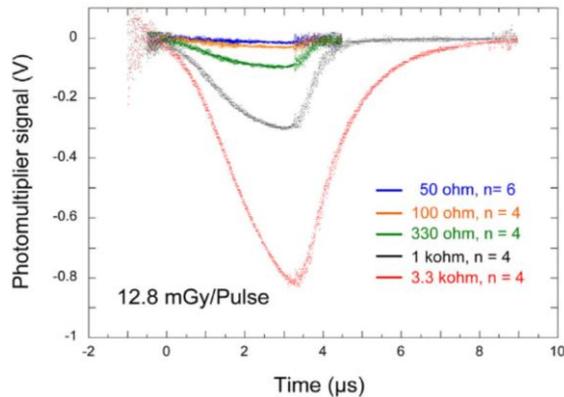
Fast-responding photomultiplier (7 dynodes)

Load resistor : 50 Ω



Analysis of Cherenkov light

3 – Wide dynamic range



Time profiles of the Cherenkov signal generated by 12.8 mGy (upper left) vs. 1.77 mGy pulses (middle) for different values of the load resistor set at the photomultiplier output.

Summary and prospects

- **Time-resolved dosimetry, nanosecond time response.**
- **Proportional dose response, no saturation.**
- **Wide dynamic range (> 5 decades).**
- **Superior to ionisation chambers at low dose per pulse.**
- **Cheap, robust, no fading.**
- **High spatial resolution: well suited to small fields, mini- to microbeams.**
- **Growing interest for use in radiotherapy.**

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- (2) Glaser *et al.* (2013) Projection imaging of photon beams using Cerenkov-excited fluorescence. *Phys Med Biol* 58, 601–619.
- (3) Glaser *et al.* (2014). Optical dosimetry of radiotherapy beams using Cerenkov radiation: the relationship between light emission and dose. *Phys Med Biol* 59, 3789-3811.
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- (15) Bruza *et al.* (2019). Imaging Cerenkov photon emissions in radiotherapy with a Geiger-mode gated quanta image sensor. *Opt Lett* 44, 4546-4549.
- (16) Soter *et al.* (2020). Tracking tumor radiotherapy response *in vivo* with Cerenkov-excited luminescence ink imaging. *Phys Med Biol* 65, 095004.
- (17) Hachadorian *et al.* (2020). Imaging radiation dose in breast radiotherapy by X-ray CT calibration of Cerenkov light. *Nat Commun* 11, 2298.
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Collimated field

35 mm

