Dose, dose-rate, beam-on time... what requisites for the “FLASH effect”? 
Radio-induced lung fibrosis in C57BL/6J mice
15 Gy in single dose (bilateral thorax irradiation)

Conventional dose-rate (CONV)
\( \gamma \)-rays or 4.5 MeV electrons
30 mGy.s\(^{-1}\)
➤ Beam-on time 8 min

FLASH irradiation
4.5 MeV electrons
40-200 Gy.s\(^{-1}\)
➤ Beam-on time < 500 ms

1 h - 2 h - 24 h

Pneumonitis
Inflammation
TGF-\( \beta \) activation
Lung fibrosis

8 - 16 - 24 - 32 - 36 weeks

Hair depigmentation
Skin necrosis

Apoptosis
FLASH spared normal lung tissue at doses known to induce fibrosis in mice exposed to conventional dose-rate irradiation (CONV).

FLASH spared smooth muscle cells in arterioles from radio-induced apoptosis.

No difference between FLASH and CONV with regard to tumor growth inhibition.

However, normal tissue sparing by FLASH allowed dose escalation without complications, resulting in complete tumor cure in some xenograft models.
Kinétron
Specifications

LINAC “Kinétron” (1987)

3.9-5.1 MeV electrons
Triode electron gun
Thermoionic cathode

Pulse width 0.05 - 2.2 µs
Repeat frequency 0.1 - 200 Hz
Peak current 0.01 - 200 mA (whole emission lobe)
Dose per pulse 0.001 - 50 Gy

Maximum dose-rate during the pulse ≈ 3 \times 10^7 \text{ Gy.s}^{-1}
Other available dosimetric methods:

- Methyl viologen radical: submicrosecond, real-time optical detection
- Mallet-Cerenkov light: nanosecond, time-resolved dosimetry
- Gafchromic EBT3 films (leucomalachite green)
- LiF pellets (thermoluminescence)
- Low dose-rate: Markus ionisation chamber
Mounting - Dose distribution with 4.5MeV electrons

35 mm
Temporal structure of energy deposition in the FLASH effect

Conventional dose-rate (LINAC)

1/ν 3 µs
0.001

1-2 µs

Conventional dose-rate (Cyclotron)

100 MHz

FLASH (LINAC)

Single pulse

2 µs
Radio-induced peroxyradicals evolving to peroxides are found in pyrimidines, deoxyribose and membrane lipids and are amplified through a chain reaction.

The FLASH effect depends on the presence of oxygen.
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