

Table SI. *In vitro* experiments.

First author, year	<i>In vitro</i> conditions				Physical irradiation parameters						(Ref.)
	Irradiation object	Assay	O ₂ conditions	FLASH effect	Radiation source	Dose, Gy	Mean dose rate, Gy/sexc	Instantaneous dose rate, Gy/sec	Pulse rate, Hz	Pulse duration, sec	
Dewey and Boag, 1959	<i>Serratia marcescens</i>	Colony	100% N ₂ ; 1% O ₂ in N ₂ ; 5% O ₂ in N ₂ ; 100% O ₂	N; Y; NA; NA	FLASH: Electron. CONV: 1.5 Mv X-ray	FLASH: 90-200 CONV: 30/70/100	FLASH: 5-10x10 ⁵ CONV: 0.167	FLASH: 5-10x10 ⁵ CONV: 0.167	Single pulse	FLASH: 2x10 ⁻⁶	(7)
Kiefer and Ebert, 1970	Diploid yeast 211	Colony	100% N ₂ ; 100% O ₂	N N	FLASH: 12 Mev electron. CONV: 12 Mev electron	410-4000	FLASH: 3x10 ⁸ CONV: 10	FLASH: 3x10 ⁹ CONV: 10	Single pulse	FLASH: 1x10 ⁻⁷ -5x10 ⁻³	(41)
Berry <i>et al</i> , 1969	HeLa S3 CHL-F	Colony	Air	Y	FLASH: 2 MVp/4.5 MV X-ray. CONV: ⁶⁰ Co γ-ray	2 -150	FLASH: 0.3-2.0x10 ⁹ CONV: 0.0167	FLASH: 0.3-2.0x10 ⁹ CONV: 0.0167	Single pulse	FLASH: 1. Generators code-named PLATO: 1.1x10 ⁻⁸ 2. Generators code-named MOGUL: 1.5/1.9/3.5/5x10 ⁻⁸	(20)
Purrott and Reeder, 1977	Human lymphocytes	Chromosome, aberration	Air	N	FLASH: 15 Mev electron. CONV: 15 Mev electron	FLASH: 0.44-7.42 CONV: 0.53-7.64	FLASH: 5.3x10 ⁵ -7.6x10 ⁶ CONV: 0.0167	FLASH: 5.3x10 ⁵ -7.6x10 ⁶ CONV: 1.67x10 ⁴	FLASH: Single pulse CONV: 100	1x10 ⁻⁶	(49)
Tillman <i>et al</i> , 1999	Chinese hamster lung fibroblast cells V79 CH	Colony	Normoxia	N	FLASH: X-ray. CONV: X-ray	1-15	FLASH: ~1.67x10 ⁹ CONV: 0.001-0.0105	FLASH: ~1.67x10 ⁹	10	1.35x10 ⁻¹³	(33)
Shinohara <i>et al</i> , 2004	L5178Y cells and M10 cells	Colony	Normoxia	N	FLASH: X-ray. CONV: 662 keV ¹³⁷ Cs γ-ray	0-8	FLASH: 10 ¹² -10 ¹³ CONV: 0.00167-0.0117	FLASH: 10 ¹² -10 ¹³	NA	5x10 ⁻¹³ -10 ⁻¹²	(34)
Auer <i>et al</i> , 2011	HeLa cells	Colony, Apoptosis, Cell cycle	Normoxia	N N Y	FLASH: Proton. CONV: Proton; 250 kV X-ray	0-5	FLASH: >10 ⁹ CONV: ~30; 9.3x10 ⁻³	FLASH: >10 ⁹	100	FLASH: <10 ⁻¹² CONV: 0.1	(35)
Doria <i>et al</i> , 2012	Chinese Hamster cell V79	Colony	Normoxia	N	FLASH: Proton. CONV: 225 kVp X-ray	0.8-5	FLASH: >10 ⁹ CONV: NA	FLASH: >10 ⁹	NA	7x10 ⁻¹³	(36)
Zlobinskaya <i>et al</i> , 2012	HeLa cells	DSB (DNA double-strand breaks)	Normoxia	N	FLASH: Proton. CONV: 20 MeV proton; 70/200 Kv X-ray	1-5	FLASH: >10 ⁹ CONV: ~30; 0.0167	FLASH: >10 ⁹	100	FLASH: <10 ⁻¹² CONV: 0.1	(42)
Laschinsky <i>et al</i> , 2012	Human squamous cell carcinoma FaDu and normal mammary gland epithelium	Colony, DSB	Normoxia	N Y	FLASH: 6.5 MeV electron. CONV: 6 MeV electron	0.4-10.2	FLASH: 0.0062-0.0058 CONV: 0.0058-0.023	FLASH: 2.4x10 ⁹	2.5	10 ⁻¹²	(37)

	cell line 184A1										
Beddo <i>et al</i> , 2017	Human lung fibroblasts MRC5 /IMR 90 and human lung cancer cell line A549	Colony	Normoxia	N	FLASH: 4.5 MeV electron. CONV: 4.5 MeV electron	0-10	FLASH: >40 CONV: 0.03	FLASH: >40	NA	NA	(38)
Buonno <i>et al</i> , 2019	Human lung fibroblasts IMR90	Colony, DSB, TGF- β 1, Senescence	Normoxia	N Y Y Y	FLASH: 5.5 MV proton. CONV: 5.5 MV proton	0-20	FLASH: 100/1,000 CONV: 0.05	FLASH: 100/1,000	NA	NA	(39)
Hanton <i>et al</i> , 2019	Human skin fibroblasts- AG01522B cells	DSB	Normoxia	N	FLASH: 10 MeV proton. CONV: 225 kVp X-ray	1-2	FLASH: 110 ⁹ CONV: NA	10 ⁹	Single pulse	10 ⁻⁹	(43)
Venkat esulu <i>et al</i> , 2019	Murine pancreatic cancer cell line KPC/Panc02 and human peripheral blood mononuclear cells	Colony	Normoxia	N	FLASH: 20 MeV electron. CONV: Electron	0-8	FLASH: 35 CONV: 0.1	NA	NA	NA	(40)
Fouilla de <i>et al</i> , 2020	Human lung fibroblasts MRC5/IMR 90 and human lung cancer cell line A549	Colony, DSB	Normoxia	Y Y	FLASH: 4.5 MeV electron. CONV: 4.5 MeV electron	0-10	FLASH: >40 CONV: 0.03	NA	100-150	NA	(28)
Adrian <i>et al</i> , 2020	Prostate cancer cells	Colony	1.6% O ₂ 2.7% O ₂ 4.4% O ₂ 8.3% O ₂ 20% O ₂	Y Y Y N N	FLASH: 10 MeV electron. CONV: 10 MeV electron	0-25	FLASH: 600. CONV: 0.23	NA	200	NA	(18)

Y, occurrence of the FLASH effect; N, no occurrence of the FLASH effect; NA, unknown Normoxia, P_{O2} in a standard cell culture incubator (~18.5 kPa); CONV, conventional radiotherapy.

Table SII. *In vivo* experiments.

Authors, year	<i>In vivo</i> conditions			Physical irradiation parameters							(Ref.)
	Irradiation object	Assays	FLASH effect	Radiation source	Dose, Gy	Mean dose rate, Gy/sec	Instantaneous dose rate, Gy/sec	Pulse rate, Hz	Pulse duration, sec	Treatment time, sec	
Favaudon <i>et al</i> , 2014	C57BL/6J mice (bilateral thorax); nude mice (tumor model)	Pulmonary fibrosis, apoptosis, Tumor growth	Y	FLASH: 4.5 MeV electron. CONV: 4.5 MeV electron. ¹³⁷ Cs γ -ray, 200 kV X-ray	7.5-30	FLASH: >40. CONV: 0.03	NA	100-150	NA	NA	(3)
Fouillade <i>et al</i> , 2020	C57BL/6J mice and Terc ^{-/-} mice (bilateral thorax)	Proliferation of cells in lung Sc-RNA seq, Chromosomal damage, Senescence Lung fibrosis,	Y	FLASH: 4.5 MeV electron. CONV: 4.5 MeV electron	0-10	FLASH: >40. CONV: 0.03	NA	100-150	NA	NA	(28)
Gao <i>et al</i> , 2022	BALb/c mice (tumor); C57BL/6J mice (thorax and abdomen)	Tumor growth, Fibrosis, Survival,	Y	FLASH: 8/6 MeV electron. CONV: 6 MeV electron	12-30	FLASH: 100/937/1200. CONV: 0.1	FLASH: 100/937/1200	Single Pulse	NA	NA	(54)
Montay-Gruel <i>et al</i> , 2017	C57BL/6J mice (brain)	Cognitive tests, De novo neurogenesis	Y	FLASH: 4.5/6 MeV electron. CONV: 4.5/6 MeV electron	10	FLASH: 5.6x10 ⁶ . CONV: 0.1-30	FLASH: 5.6x10 ⁶	FLASH: 100. CONV	1.8/1.0x10 ⁻⁶	NA	(55)

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Montay-Gruel <i>et al</i> , 2018	C57BL/6J mice (brain)	Cognitive tests, De novo neurogenesis, Reactive astrogliosis	Y	FLASH: 102 keV X-ray. CONV: 225 keV X-ray	10	FLASH: 37. CONV: 0.05	FLAS H: 1.2x10 ⁴	NA	NA	0.27	(24)
Montay-Gruel <i>et al</i> , 2019	C57BL/6J mice (brain)	Cognitive tests, Oxidative stress, Neuroinflammation, Neuronal structure and synaptic protein levels	Y	FLASH: 6 MeV electron. CONV: 6 MeV electron	10-14	FLASH: >100. CONV: 0.07-0.1	FLAS H: 1.8x10 ⁶	FLAS H: 100. CONV: 10	FLASH: 1.8x10 ⁻⁶ . CONV: 1.0x10 ⁻⁶	FLASH: 1.8x10 ⁻⁶ . CONV: 63.8-117.9	(23)
Montay-Gruel <i>et al</i> , 2020	C57BL/6J mice (brain)	Astrogliosis, Expression of complement cascade proteins	Y	FLASH: 6 MeV electron. CONV: 6 MeV electron	10	FLASH: 5.6x10 ⁶ . CONV: ~0.0085	FLAS H: 5.6x10 ⁶	FLAS H: 100. CONV: 10	FLASH: 1.8x10 ⁻⁶ . CONV: 1.0x10 ⁻⁶	FLASH: 1.8x10 ⁻⁶ . CONV: 116.9-117.9	(25)
Montay-Gruel <i>et al</i> , 2021	Nude (NU _(Ico) -Foxn1 ^{nu}) mice (glioblastoma model)	Cognitive tests, Tumor growth	Y	FLASH: 6 MeV electron. CONV: 6 MeV electron	10, 14, 4x3.5, 2x7, 3x10, 25	FLASH: 2.5x10 ³ -5.6x10 ⁶ . CONV: 0.1	FLAS H: 2.5x10 ³ -5.6x10 ⁶ . CONV: 8.5-9.5x10 ³	FLAS H: 100. CONV: 10	FLASH: 1.8x10 ⁻⁶ . CONV: 1.0x10 ⁻⁶	FLASH: 0.01/1.8x10 ⁻⁶ . CONV: 40.9-261.9	(56)
Simmons <i>et al</i> , 2019	C57BL/6J mice (brain)	Cognitive tests,	Y	FLASH: 16 M/20 eV electron.	30	FLASH: 200/300.	8.75 x10 ⁵	108/180	FLASH and	FLASH: 0.1-0.16.	(57)

		Neuroinflammation, Spine density of dendrites		CONV: 16/20 MeV electron		CONV: 0.13			CONV: 2×10^{-6}	CONV: 240	
Allen <i>et al</i> , 2020	C57BL/6J mice (brain)	Vasogenic Edema or expression of eNOS in microvasculature, Degeneration of tight junction protein, Apoptosis	Y	FLASH: 6 MeV electron. CONV: 6 MeV electron	10/25	FLASH: 2,500 and 5.6×10^6 . CONV: 0.09/0.1	FLASH: 5.6×10^6 and 6.9×10^6 . CONV: 8.5×10^3 and 9.5×10^3	FLASH: 100. CONV: 10	FLASH: 1.8×10^{-6} . CONV: 1.0×10^{-6}	FLASH: 0.01 CONV: 1.8×10^{-6} . CONV: 116.9-117.9/261.9	(59)
Alaghband <i>et al</i> , 2020	C57BL/6J mice (brain)	Cognitive tests, De novo neurogenesis, Activation of microglia, Growth hormone level,	Y	FLASH: 6 MeV electron. CONV: 6 MeV electron	8	FLASH: 4.4×10^6 . CONV: 0.077	FLASH: 4.4×10^6 . CONV: 7.7×10^3 .	FLASH: 100. CONV: 10	FLASH: 1.8×10^{-6} . CONV: 1.0×10^{-6}	FLASH: 1.8×10^{-6} . CONV: 103.2	(58)
Loo <i>et al</i> , 2017	C57BL/6J mice (abdomen)	Survival	Y	FLASH: 20 MeV electron. CONV: 20 MeV electron	13-19	FLASH: 70/210. CONV: 0.05	NA	NA	NA	NA	(60)
Levy <i>et al</i> , 2020	C57BL/6J mice (abdomen) (tumor model)	Lethality of gastrointestinal syndrome, Intestinal function and	Y	FLASH: 16 MeV electron. CONV: 16 MeV electron	14/16	FLASH: 216. CONV: 0.079	FLASH: 216 CONV: 72	FLASH: 108. CONV: 10	FLASH: 0.093. CONV: 0.014	FLASH: 0.065-0.074. CONV: 2.95-3.37	(61)

		epithelial integrity, Proliferation of crypt cell, Apoptosis and DSB, Tumor growth									
Diffenderfer <i>et al</i> , 2020	C57BL/6J mice (abdomen) (tumor model)	Proliferation of crypt cell, Fibrosis, Tumor growth	Y	FLASH: 230 MeV proton. CONV: 230 MeV proton	15 12/18	FLASH: 94/63. CONV: 0.71/0.73/1	NA	1.06x10 ⁸	2x10 ⁻⁹	NA	(62)
Vozenin <i>et al</i> , 2019	Mini-pig (skin); cat-cancer patients (tumor model)	Skin toxicity, Tumor growth	Y	FLASH: 4.5/6 MeV electron. CONV: 4.5/6 MeV electron	22-41	FLASH: 300. CONV: 0.083	NA	FLASH: 100. CONV: 10	1.8/1.0x10 ⁻⁶	NA	(70)
Soto <i>et al</i> , 2020	C57BL/6J mice (skin)	Skin toxicity, Survival	Y	FLASH: 16 MeV electron. CONV: 16 MeV electron	10-40	FLASH: 180. CONV: 0.0747	FLASH: 4.5x10 ⁵ . CONV: 207	FLASH: 90. CONV: 72	5x10 ⁻⁶	NA	(63)
Konradsson <i>et al</i> , 2021	Canine patients (tumor model)	Side effects, Tumor growth	Y	FLASH: 10 MeV Electron	15-35	FLASH: 400-500	FLASH: ~7x10 ⁵	200	3.5x10 ⁻⁶	0.030-0.075	(66)
Cunningham <i>et al</i> , 2021	C57BL/6J mice (leg) (tumor model)	Skin toxicity, Leg contracture, Tumor growth	Y	FLASH: 250 MeV proton. CONV: 250 MeV proton	15/35	FLASH: 57/115. CONV: 1	FLASH: 191.6-207.6 CONV	7.2x10 ⁶	NA	NA	(64)

							: 3.3/3.7					
Venkatesulu <i>et al</i> , 2019	C57BL/6J mice (spleen); BALB/c mice (heart abdomen)	Level of circulating lymphocyte, Gastrointestinal mucosal injury	N	FLASH: 20 MeV electron. CONV: Electron	5-16	FLASH: 35. CONV: 0.1	NA	NA	NA	NA	NA	(40)
Beyreuther <i>et al</i> , 2019	Zebrafish embryo	Survival, Rate of pericardial edema and spinal curvature	N	FLASH: 224 MeV proton. CONV: 224 MeV proton	10-42	FLASH: 100. CONV: 0.083	FLASH: 500 CONV: 0.4	1.06x 10 ⁸	2x10 ⁻⁹	NA	NA	(53)
Chabi <i>et al</i> , 2021	Immunocompromised mice (total body irradiation)	Hematopoiesis, expansion of leukemic cell	N	FLASH: 6 MeV electron. CONV: 6 MeV electron	4	FLASH: 200. CONV: 0.072	FLASH: 7.4x10 ⁵ . CONV: <7.2x 10 ³	FLASH: 100. CONV: 10	FLASH: 1.8x10 ⁻⁶ . CONV: 1.0x10 ⁻⁶	FLASH: 0.02. CONV: >55.6	FLASH: 0.02. CONV: >55.6	(65)

Y, occurrence of the FLASH effect; N, no occurrence of the FLASH effect; NA, unknown; CONV, conventional radiotherapy; Sc-RNA seq, Single cell RNA sequencing.