Radiation Baseline in WuXi Syngeneic Models

WuXi Oncology

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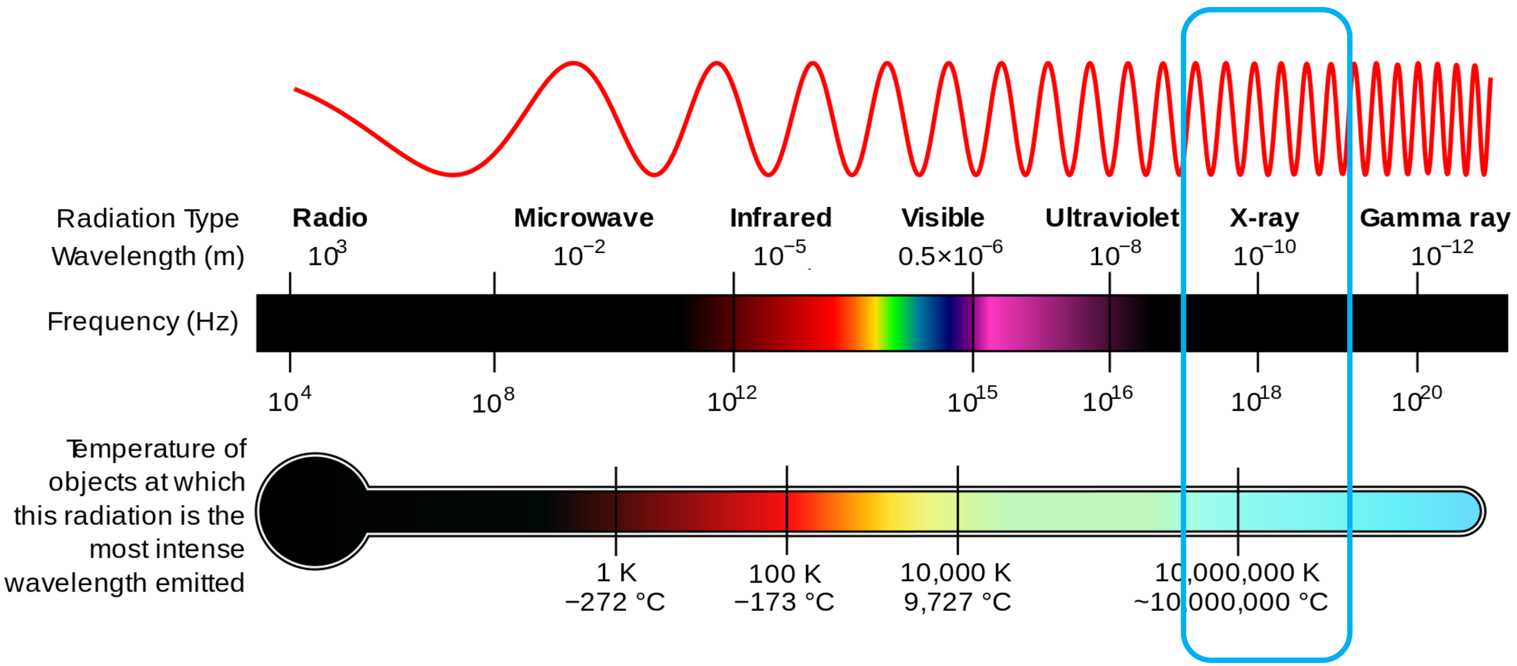
Radiation therapy introduction

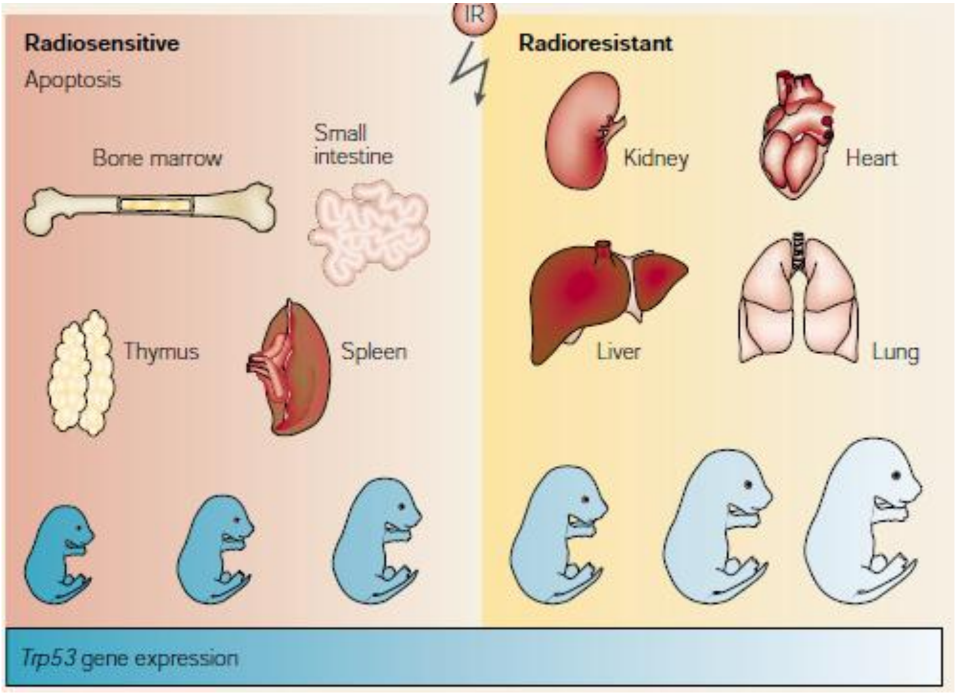
- Radiation therapy uses high-energy radiation to shrink tumors and kill cancer cells. X-rays, gamma rays, and charged particles are types of radiation used for cancer treatment.
- Radiation therapy kills cancer cells by damaging their DNA. Radiation therapy can either damage DNA directly or create charged particles (free radicals) within the cells that can in turn damage the DNA.
- About half of all cancer patients receive some type of radiation therapy sometime during the course of their treatment.



Radiation therapy introduction

Whether a cancer patient is sensitive to radiotherapy depends on many factors, including:

- The cancer **type, size, stage and location**.
- The patient's **general health**, age and other medical conditions.
- Generally, certain cancer types are radio-sensitive, while others are less sensitive.
- Some research also intends to find genetic variants and biomarkers to predict radiation sensitivity which are not well accepted in clinic.



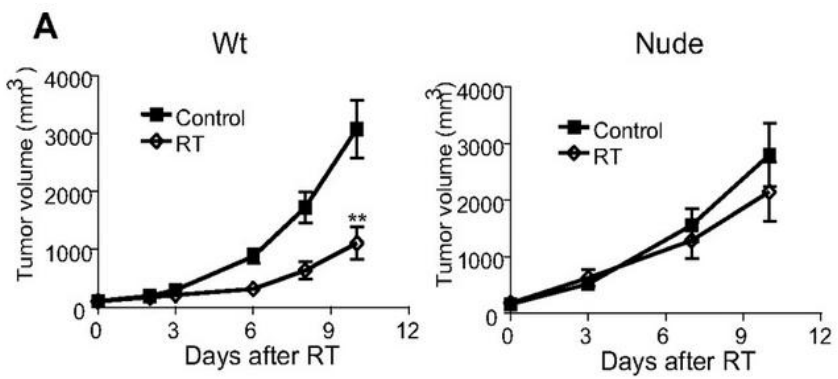
Nat Rev Cancer. 2003 Feb;3(2):117-29.
Nature **459**, 587-591 (28 May 2009) | **doi:10.1038**

Radiation in combination with immunotherapy

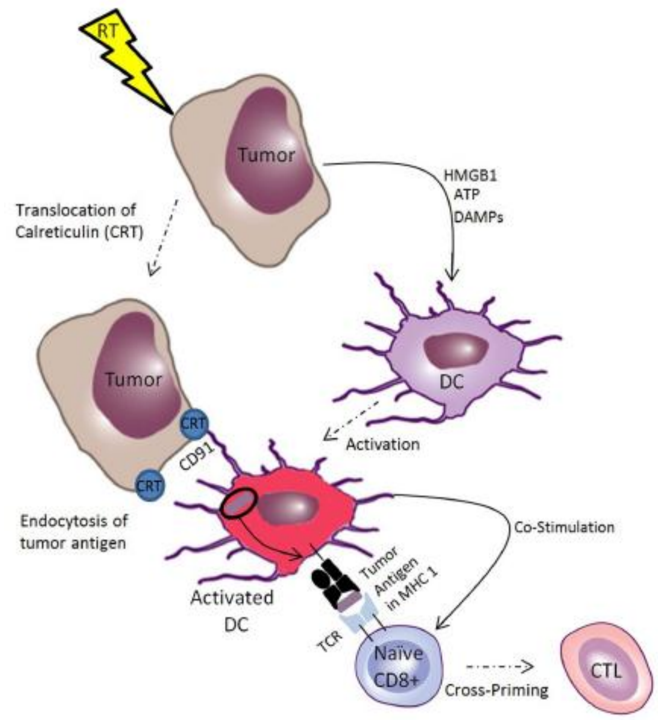
Radiation, initially thought immunosuppresive, was recently considered to be promising in combination with immunotherapy, based on its capacity of mobilizing immune responses.

- Radiation induces immunogenic cell death, facilitates DC maturation, tumor antigen up-taking, and the priming of anti-tumor CTLs.
- Up-regulation of PD-L1 on tumor is discovered following the radiation, rationalizing its combination with checkpoint blockage.
- In syngeneic tumor models, the therapeutic activity of radiation is linked with the host adaptive immunity.

Radiation efficacy on B16 melanoma syngeneic model in C57 mice vs. nude mice



Lee et al., *Hum Gene Ther.*, 2014 Nov 1; 25(11): 955–965



Vatner et al., *Front Oncol.*, 2014 Nov 28;4:325

Radiation procedures using a RS2000 X-Ray irradiator

- RadSource 2000 X-ray irradiator preparation
  - Turn on the X-ray irradiator.
  - Warm up the irradiator for ~ 30 mins.
- Dose rate measurement and radiation time calculation
  - The X-ray irradiator possesses the linear actuation system (spot beam collimator) for targeted radiation. The irradiated area is guided by a lighted square (Fig. 1).
  - The radiation dose rate (mGray/min) is measured by an Accu-Dose radiation measurement system (Fig. 2), and the radiation time can be calculated based on the measurement.
- Radiation treatment
  - Anesthetize the animal by isoflurane inhalation.
  - Place the animal in the radiation chamber. Ensure the center of irradiated area overlap with the center of the tumor and the whole tumor is covered by the irradiated area guided by the lighted square (Fig. 3).
  - Turn on X-ray radiation.

RadSource RS2000/XE X-ray irradiator

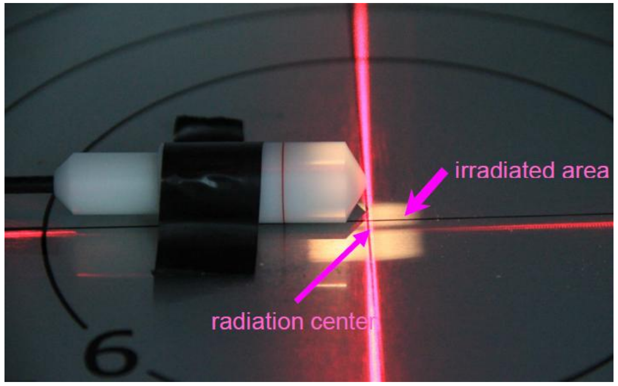


Figure 1

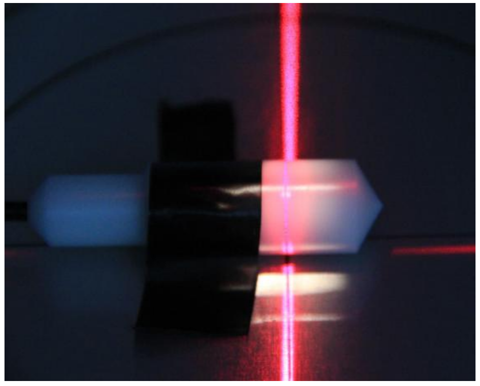


Figure 2

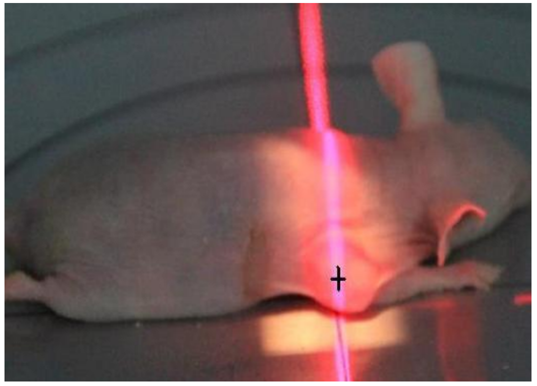
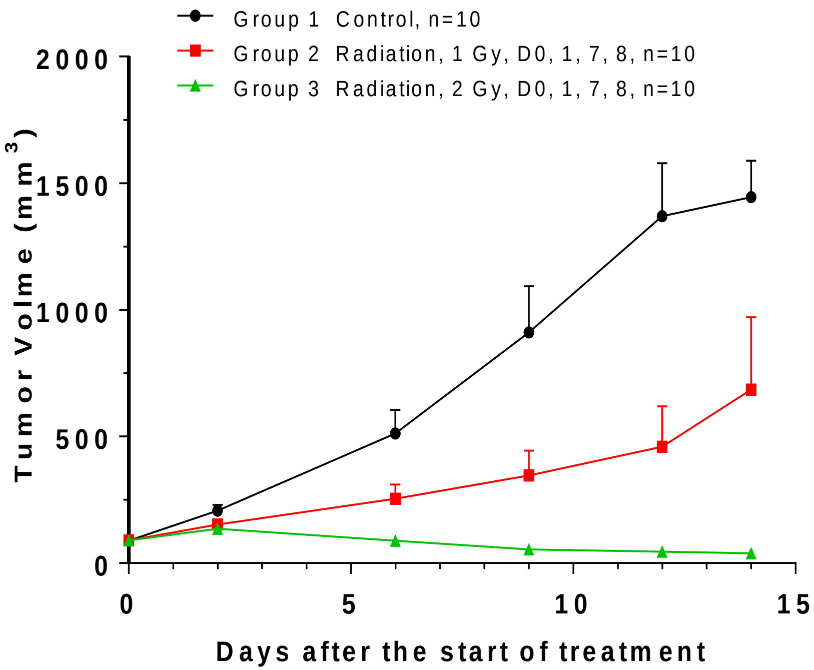


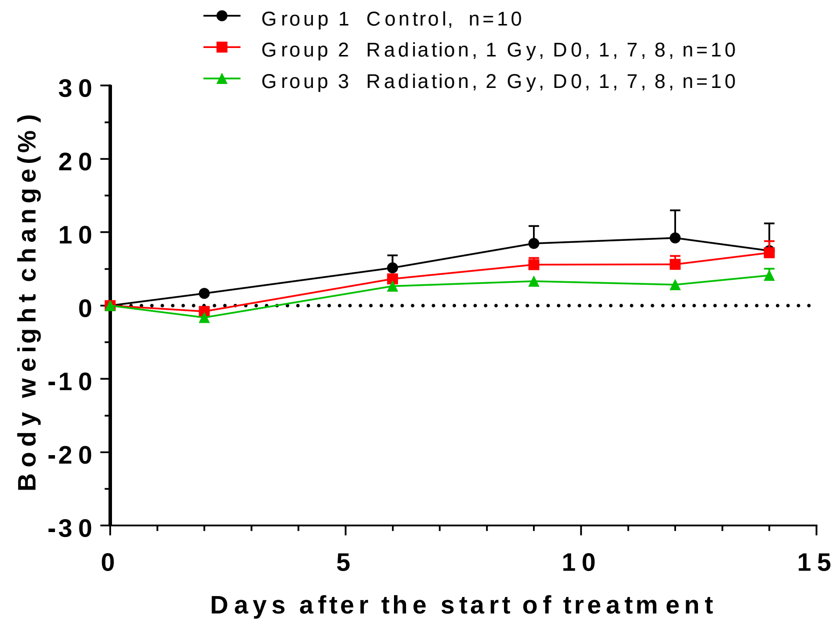
Figure 3

Summary of radiation baseline in WuXi syngeneic models

Model ID	Cancer Type	Treatment	Dosage (Gy)	Schedule	TGI (%)
3LL	Lung cancer	Radiation	1	Day 0, 1, 7, 8	56
		Radiation	2	Day 0, 1, 7, 8	104
3LL repeat		Radiation	1	Day 0, 1, 7, 8	51
		Radiation	2	Day 0, 1, 7, 8	82
B16F10	Melanoma	Radiation	1	Day 0, 1, 7, 8	45
		Radiation	2	Day 0, 1, 7, 8	64
B16F10 repeat		Radiation	1	Day 0, 1, 7, 8	33
		Radiation	2	Day 0, 1, 7, 8	50

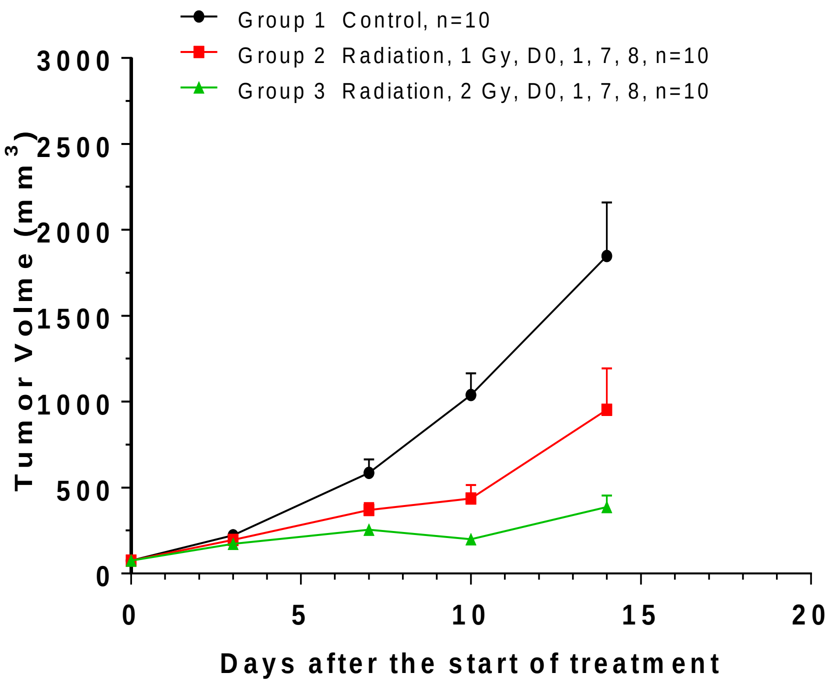
Radiation in syngeneic model_3LL

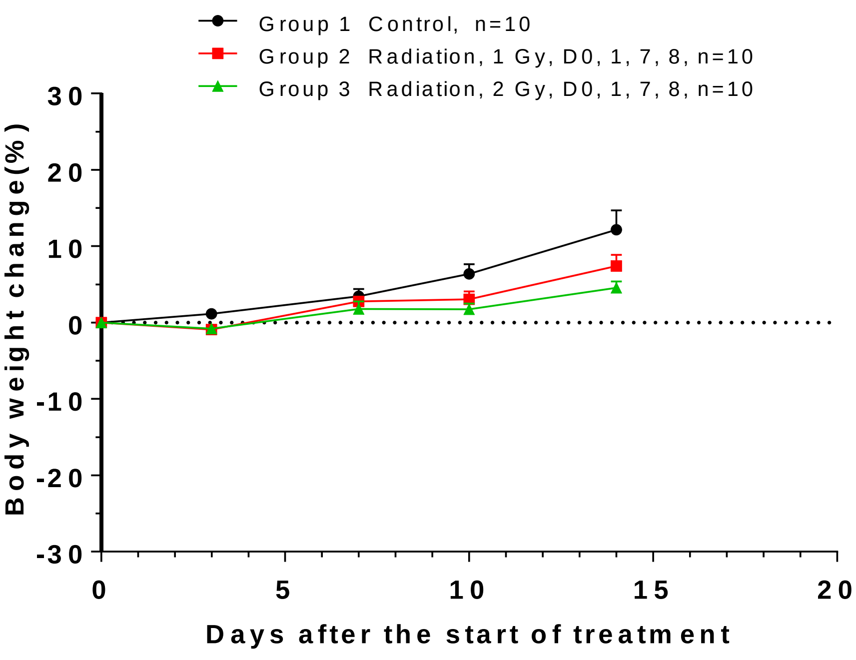




Animal	Tumor inoculation (cells/mouse)	Date of Inoculation	Latent Period (Days)	Study Operator
C57BL/6J, Female (VTLH, Beijing)	2×10^6/0.1ml	2016-04-29	5	Li Wentao

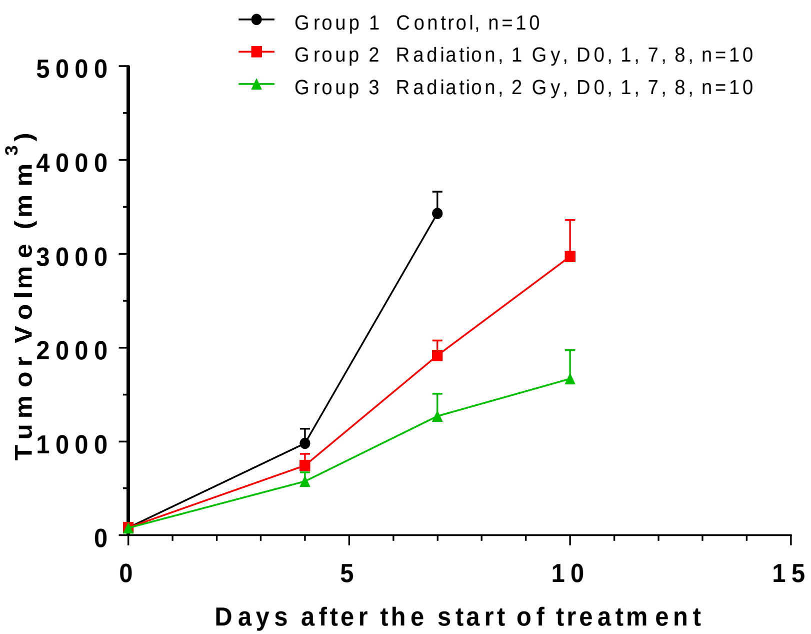
Radiation in syngeneic model_3LL-repeat

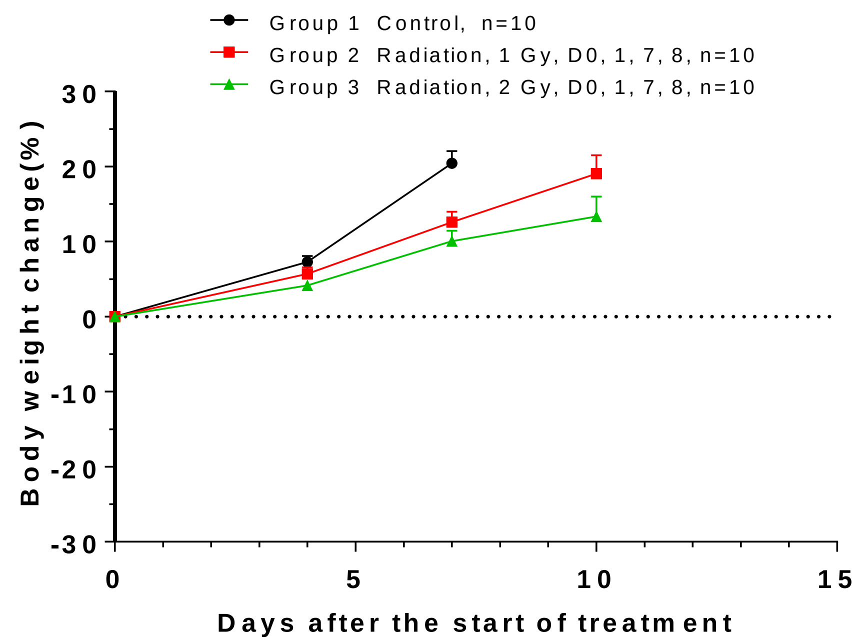




Animal	Tumor inoculation (cells/mouse)	Date of Inoculation	Latent Period (Days)	Study Operator
C57BL/6J, Female (VTLH, Beijing)	2×10^{6}/0.1ml	2016-06-27	4	Wang Qixin

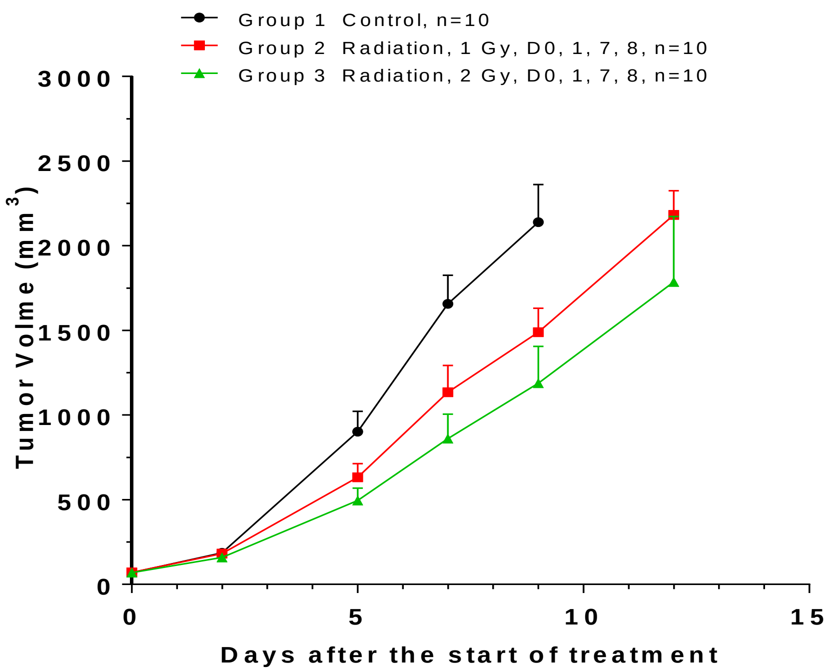
Radiation in syngeneic model_B16F10

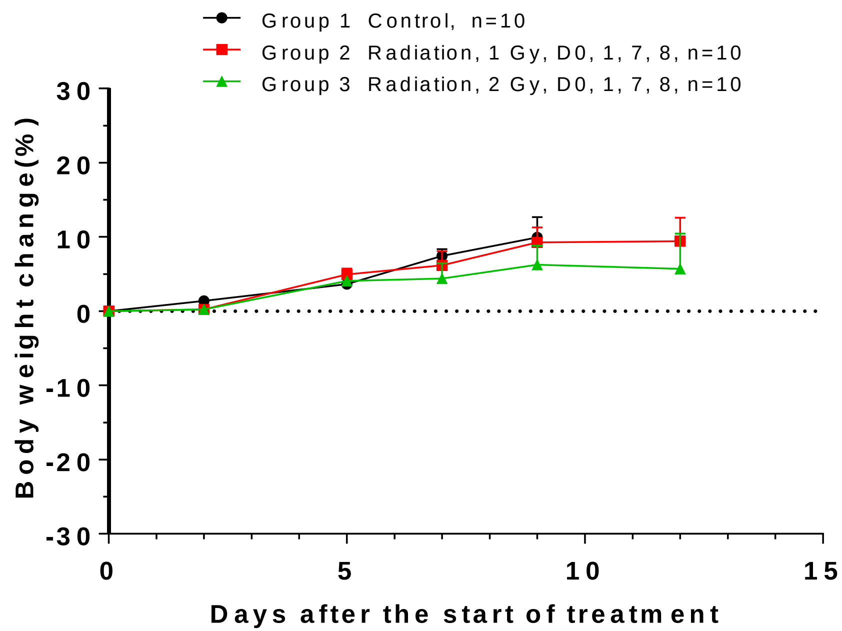




Animal	Tumor inoculation (cells/mouse)	Date of Inoculation	Latent Period (Days)	Study Operator
C57BL/6J, Female (VTLH, Beijing)	5×10^4/0.1ml	2016-04-29	7	Li Wentao

Radiation in syngeneic model_B16F10-repeat





Animal	Tumor inoculation (cells/mouse)	Date of Inoculation	Latent Period (Days)	Study Operator
C57BL/6J, Female (VTLH, Beijing)	5×10^4/0.1ml	2016-06-23	6	Wang Qixin

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