

# 2402. Fractionated dosing: A more clinically relevant approach to radiotherapy in preclinical tumor models

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## Introduction

- Upwards of 50% of cancer patients will receive radiation during the course of their treatment, mostly through a fractionated dosing schedule.
- Labcorp Drug Development has a wealth of data across syngeneic models employing a single dose of focal radiation. To bolster this data set, fractionated dosing regimens were employed in the CT26, MC38, E.G7-OVA and EMT-6 models to compare response to bolus focal radiation therapy.
- These more translationally relevant dosing regimens produce moderate responses that more accurately reflect the clinical landscape and provide a more viable framework for interrogating rational combination strategies in preclinical development.

## Methods

- CT26 and EMT-6 cells were implanted subcutaneously or in the mammary fat pad, respectively, of female BALB/cAnNHsd. MC38, E.G7-OVA and B16F10 cells were implanted subcutaneously in C57BL/6J or C57BL/6NHsd mice. Mice were staged into treatment groups when the mean tumor volume was  $\sim 100\text{mm}^3$ . Tumor growth changes were tracked by caliper measurements.
- All animal work was performed in an AAALAC-accredited facility, in alignment with applicable animal welfare regulations and with predetermined humane euthanasia criteria on all studies.
- Image-guided irradiation was performed under 1-2% isoflurane anesthesia on the Small Animal Radiation Research Platform (SARRP; Xstrahl Inc., Suwanee, GA). Treatment was delivered at 220 kV and 13.0 mA using an appropriately sized collimator to the total indicated dose (in Gray; Gy) in two equally weighted beams.

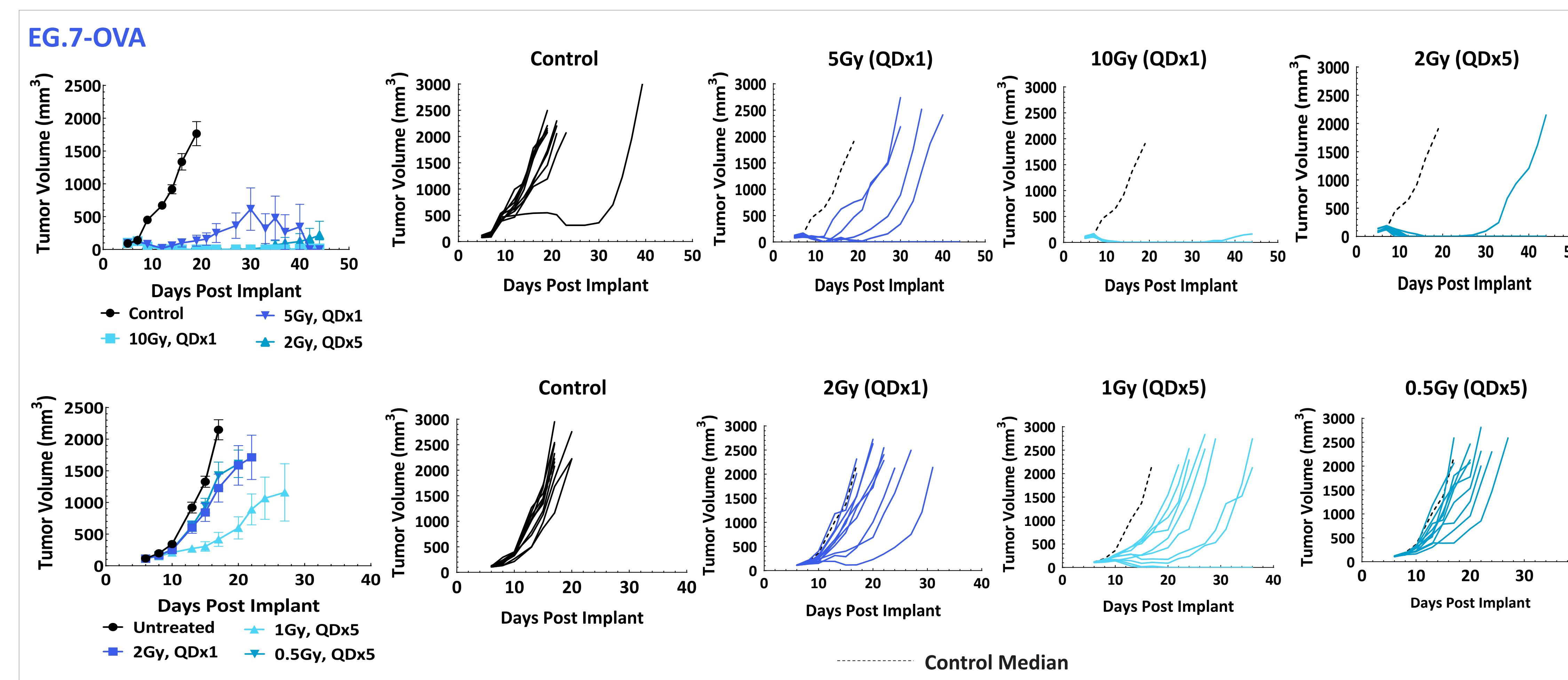


Figure 2. Response of the E.G7-OVA murine lymphoma model to bolus and fractionated focal radiation

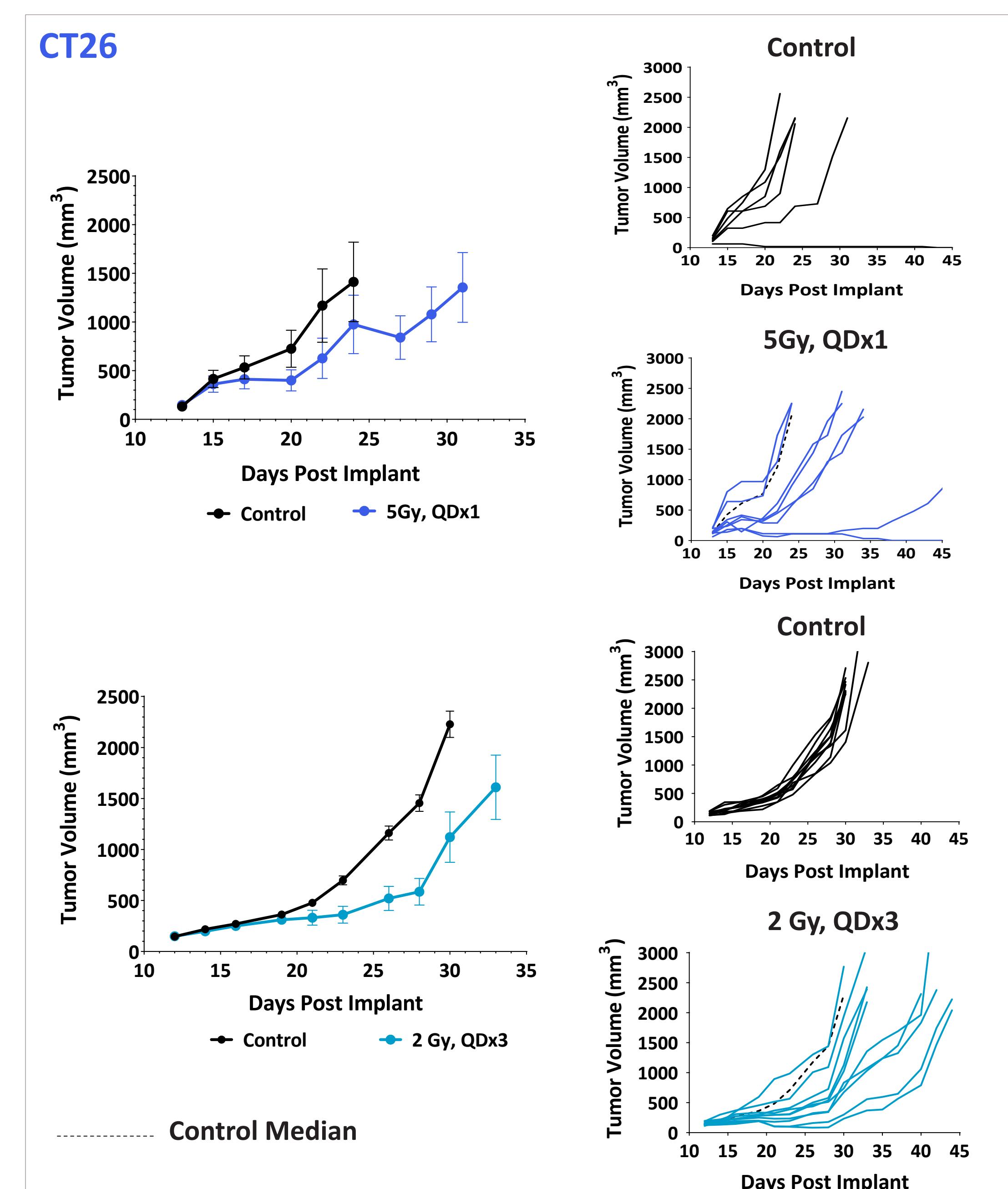


Figure 3. Response of the CT26 murine colorectal tumor model to bolus and fractionated focal radiation

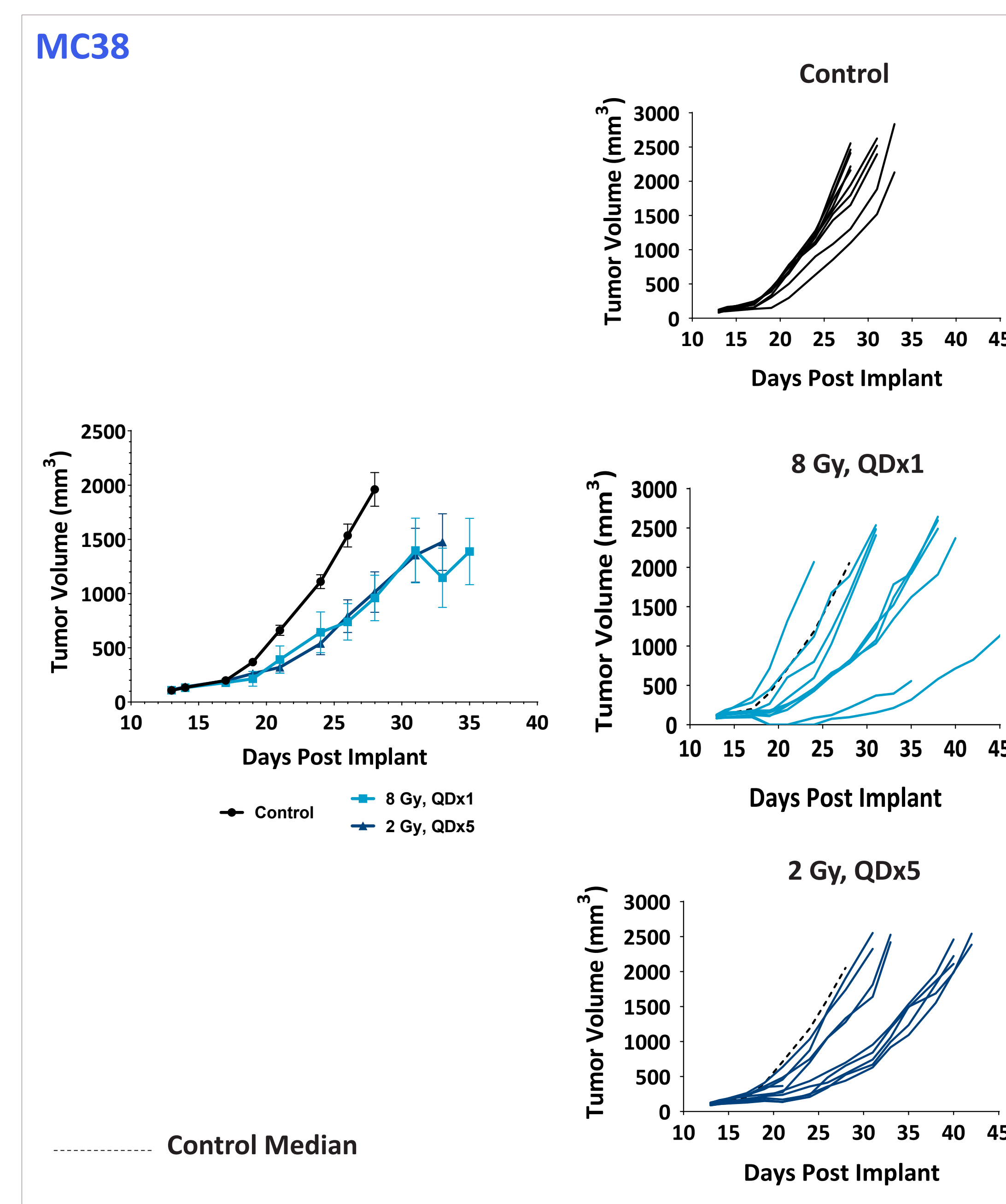


Figure 4. Response of the MC38 murine colorectal tumor model to bolus and fractionated focal radiation

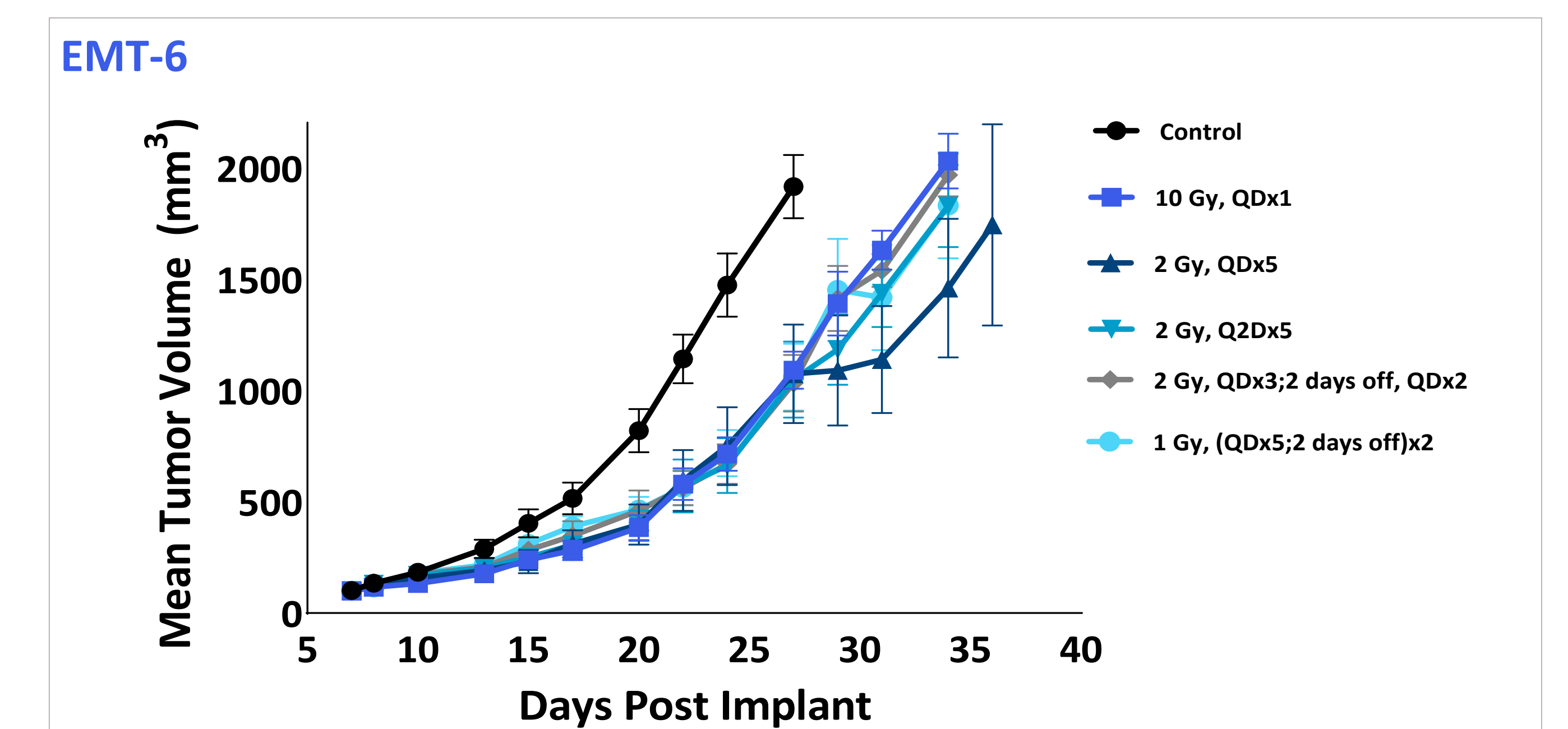


Figure 5. Response of the orthotopic EMT-6 murine breast tumor model to bolus and fractionated focal radiation.

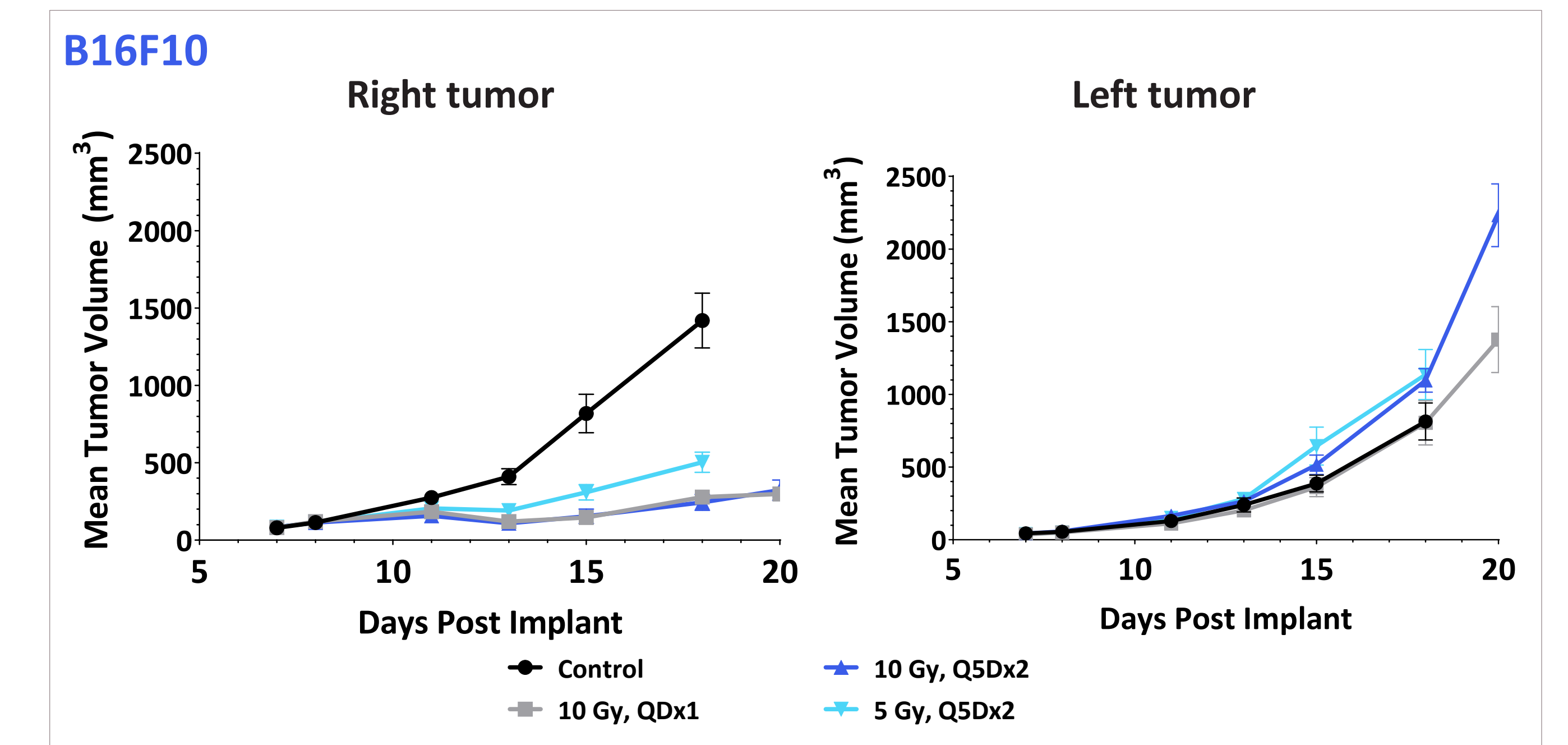


Figure 6. Response of the B16F10 murine melanoma model to bolus and fractionated focal radiation. Radiation was delivered to the right side tumor only and did not have an abscopal effect.

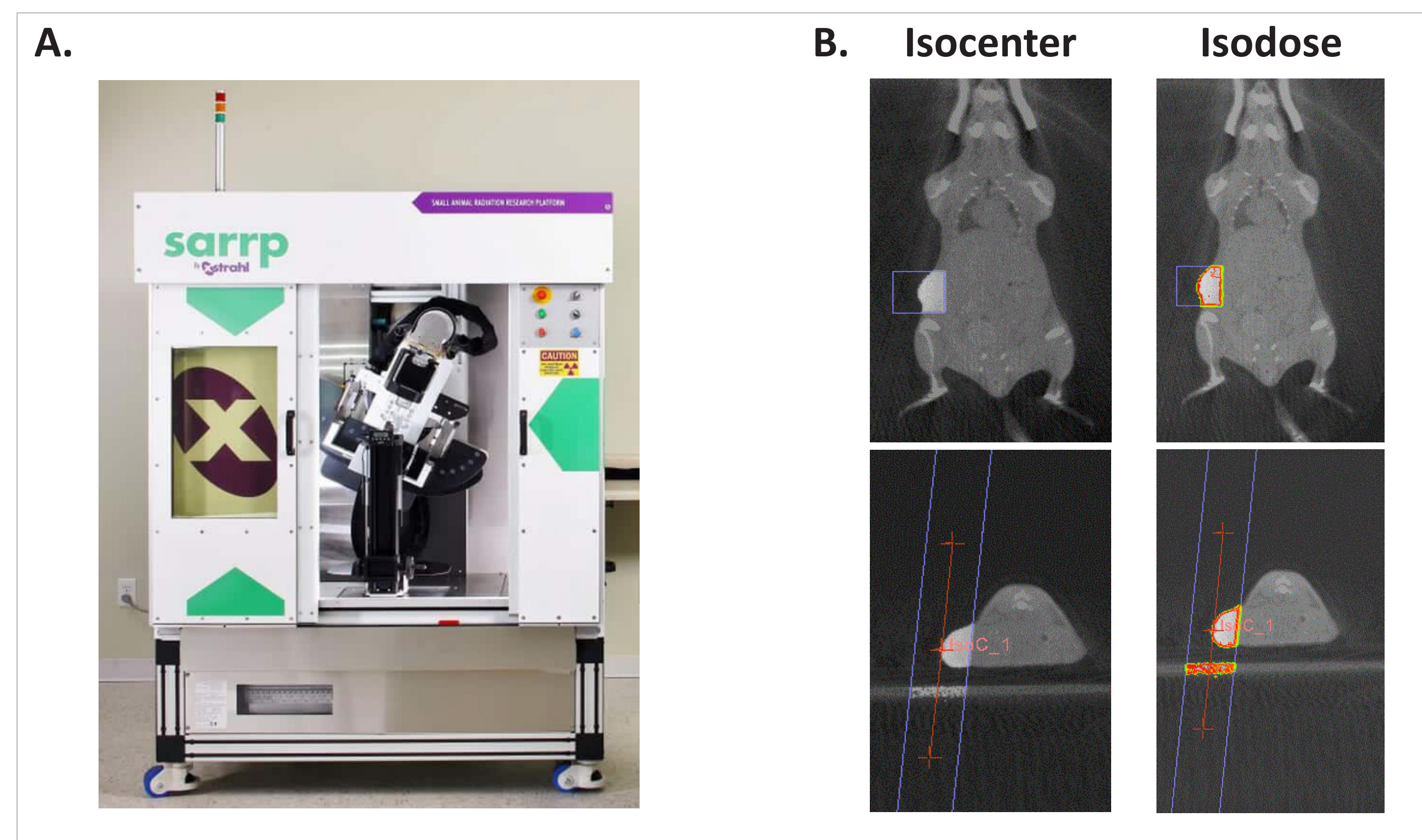


Figure 1. Small Animal Radiation Research Platform (SARRP). A. Equipment for focal radiation dosing. B. Representative CT image showing dose delivery with limited to no scatter.

## Conclusions and Next Steps

- Moderately responsive treatment regimens of bolus and fractionated focal radiation were identified for the five models tested.
- No difference in overall tumor growth was seen between bolus and fractionated dose regimens in any model tested.
- These dose regimens are well suited for combination strategies.
- Next steps include assessing differences in combination activity between bolus and fractionated radiation as well as differences in the tumor microenvironment under these conditions.

