ESRF	**Experiment title:** Studying the effects of different combinations of peak and valley doses, as well as, microbeam spacing.	**Experiment number**: LS2748
Beamline: ID17	**Date of experiment**: from: 28 June 2018 to: 30 June 2018	**Date of report**:
Shifts: 6	**Local contact(s)**: Elke Brauer-Krisch	*Received at ESRF:*

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Report

Background: In collaborative work with the Australian Synchrotron, we combined AuNPs with MRT at this facility in order to reproduce the results obtained at its European counterpart. The data from the longitudinal tumor growth showed that the MRT collimator used in the Australian Synchrotron did not reproduce the same results. The reason? Although the peak dose was the same (400 Gy MRT) the spacing between the microbeams was different; in the European Synchrotron, the spacing is 200 microns while at the Australian Synchrotron is 400 microns. We hypothesize that some factor (or parameter) related to the increase in the spacing is abolishing the characteristic tumor control after MRT, which is normally represented as a tumor shrinkage 5 days after the treatment (Figure 1).

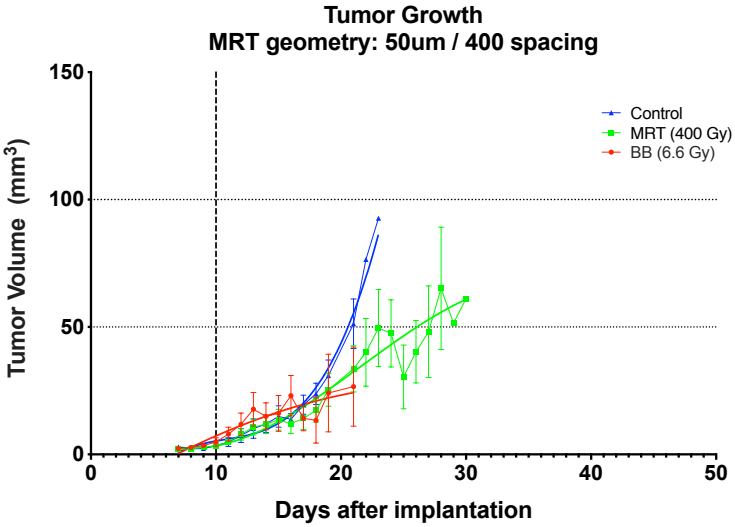

Figure 1. Tumor growth after MRT with a spacing of 400 microns performed at the Australian Synchrotron. All the melanomas were implanted on day 0. Tumor measurements started on day 8. The irradiation took place on day 10, which is represented by the vertical line. The BB dose was 6.6Gy, while the MRT dose was composed of peaks doses of 400 Gy and valley doses of 1.1Gy. Each group had 9 mice. Error bars indicate SEM. The solid curved-line corresponds to the best fit of a Third Order Polynomial equation.

Experiment at the ESRF: The discovery that the geometry of the beam is a crucial factor that influences the outcome of MRT-treated tumors, prompted the creation of a follow-up study at the European Synchrotron. This study aimed at identifying how the interaction between high-peak doses and low-valley doses, which are the results of the MRT geometry, determine the tumor control. Table 1 shows the experimental plan and the logic behind the design of each group.

Table 1. Experimental design and rationale of the experiment.

Group	Description	Configuration			Doses		Aim of this group	Doses for GUI (MSC or Film)
		Modality	microbeam	spacing	Peak dose	Valley dose		
Group C	Best Tumor Control achieved at the ESRF	MRT (PVDR: 67.81)	50 um	200 ctc	404 Gy	6.0 (5.96) Gy	Best Tumor Control achieved at the ESRF	400 Gy (GUI MSC)
Group D	Experiment done in Melbourne	MRT (PVDR: 366.3)	50 um	400 ctc	404 Gy	1.1 Gy	Mattia's Calculations with newest Mouse Ear Model (This replaces calculations by Liam).	400 Gy (GUI MSC)
Group E	Decreasing the Peak Dose	MRT (PVDR: 67.81)	50 um	200 ctc	74.58 Gy	1.1 Gy	**Decreasing the Peak Dose** to **match** the **Valley Dose** to "Group D" (Valley dose calculated by Mattia on 28.05.2018)	73.76 Gy (GUI MSC)
Group F	Increasing the Peak Dose	MRT (PVDR: 366.3)	50 um	400 ctc	2196 Gy	6.0 (5.96) Gy	**Increasing the Peak Dose** to **match** the **Valley Dose** to "Group C" (Best Tumor Control at the ESRF) while having larger spacing	2171 Gy (GUI MSC)
Group G	Reinfocing the Valley dose with Broad Beam	MRT (PVDR: 366.3)	50 um	400 ctc	404 Gy	1.1 Gy	**Reinfocing the Valley Dose** of "Group D" with **Broad Beam** to increase the valley dose up to 5.6Gy and thus, match it to "Group C"	400 Gy (GUI MSC)
		BB	-	-	4.9 Gy			4.57 Gy (GUI Film) Gap 40
Group I	Reinfocing the Valley dose with Broad Beam	MRT (PVDR: 67.81)	50 um	200 ctc	74.58 Gy	1.1 Gy	**Reinfocing the Valley Dose** of "Group E" with **Broad Beam** to increase the valley dose up to 5.6Gy and thus, match it to "Group C"	73.76 Gy (GUI MSC)
		BB	-	-	4.9 Gy			4.57 Gy (GUI Film) Gap 40
Group J	Unirradiated Tumor Control	-	-	-	-	-	-	-

The preliminary results show that a collimator with a 400-micrometer spacing can be used as long as the peak-dose is increased by 80%, which in turn directly increases the valley dose in 80%. This suggests the presence of a valley-dose threshold above which MRT is effective (Figure 2).

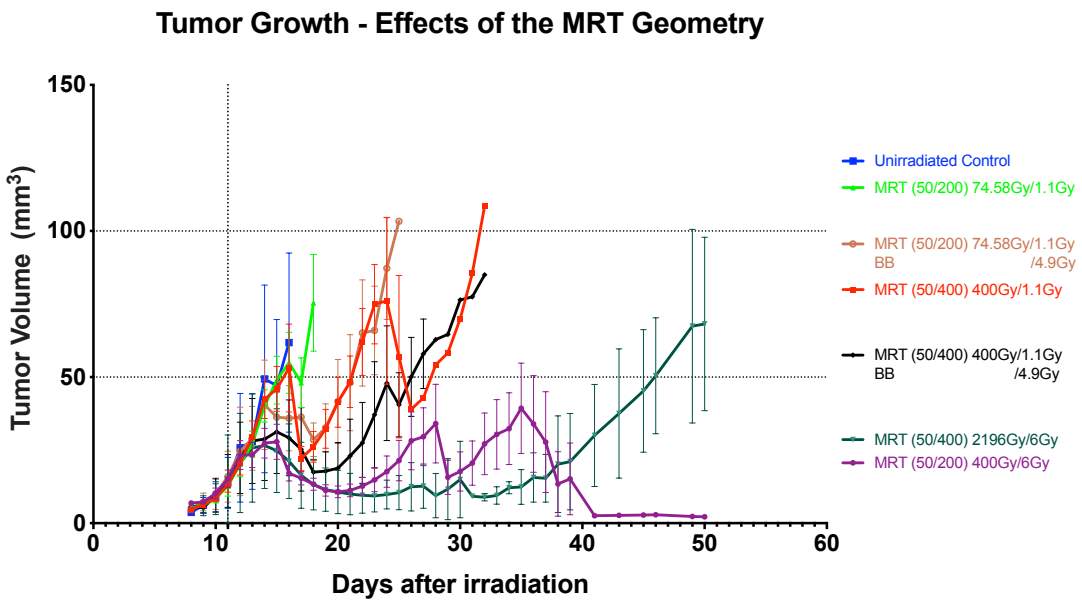

Figure 2. Effects of the MRT Geometry at the European Synchrotron. The melanomas were implanted on day 0 and 1 given the high number of animals for this experiment. Tumor measurements started on day 8. The irradiation took place on day 11, which is represented by the vertical line. The geometries studied were two 200 um and 400 um of spacing. The peak and valley doses were also studied according to Table 1. The dose and geometry of each group are indicated in the legend of the figure. Error bars indicate SEM.