

Report on the experiment MD 444, Study of the healthy tissue dose tolerances to minibeam radiation therapy

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This was a dose escalation study to assess the dose response curves of healthy tissues to MBRT in order to establish the dose tolerance of the rat brain to MBRT. The doses delivered were the same as in the in vitro study MD 398.

60 animals were irradiated in 7 groups of doses

In each group:

- n=3 rats kept alive to assess the survival curve and to study possible adverse symptoms. This work is being performed by S. Sarun and Y. Prezado
- n=6 rats were sacrificed 24 hours (3 rats) and 48 hours (3 rats) for histopathological H2AX immunofluorescence studies to assess the quantity of double strand breaks in the DNA. This work is being performed by S. Sarun.

Figure 4 shows the survival curves analyzed by G Le Duc at the beginning of April. Basically, the higher doses (from 200 Gy on) were not well tolerated and the rats died some days after irradiation. Animals irradiated with peak doses of 50, 100 and 150 Gy present a good general state. It is not clear why we still have rats at 300 while 200, 250, 350 and 400 are perfectly coherent.

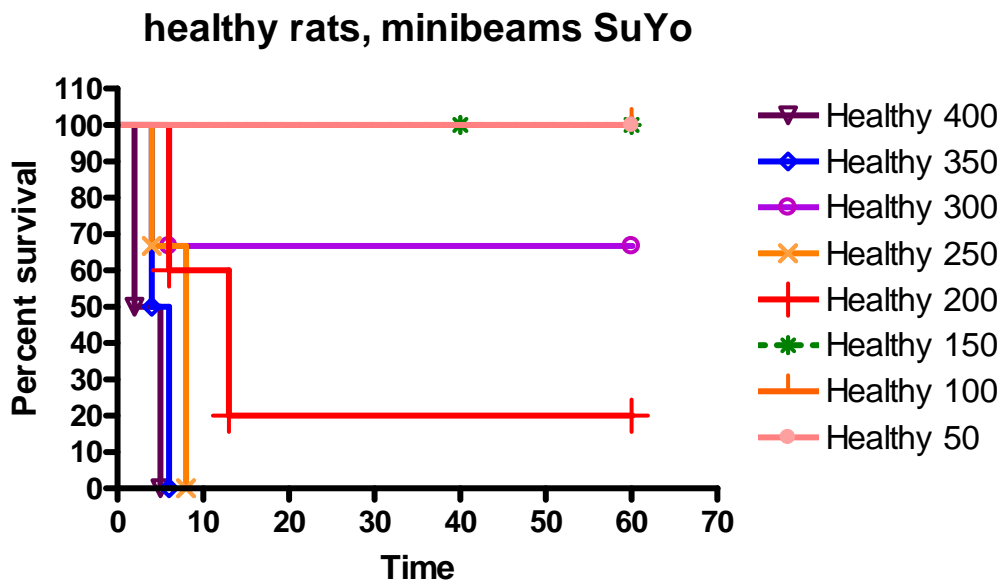


Figure 4. Survival curves for the irradiated healthy rats. By G. Le Duc.

On the 2nd of August, the survival rats present a normal behaviour and they are gaining weight.

MRI images were taken on the 7th of February (24 hours after irradiation), on the 14th of March (around 1 month after irradiation) and on the 4th of July. Anatomical T2 and diffusion sequence (edema) as well as T1 + Gadolinium (blood brain barrier rupture) sequences were used. 24 hours after irradiation the brain presented a normal appearance. However one month after, minibeam tracks are visible in the MRI images for the rats irradiated at 150 Gy indicating a disruption of the blood brain barrier. However the last images taken on the 4th of July show that this damage has almost been repaired.



Figure 1: MRI images of one of the rats irradiated at 150 Gy taken one month after (left) and 5 months (right) after the irradiation. The blood brain barrier disruption has almost been repaired.

The preliminary conclusions of this experiment is that doses as high as 150 Gy (peak dose) in one fraction are well tolerated by the rat brain. This might allow the use of higher and potentially curative doses in clinical cases where the tissues tolerance is limit for conventional therapy.