Synchrotron Microbeam Radiation Therapy and Gold nanoparticles: a combined preclinical treatment in a mouse melanoma model.

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Introduction:
This research shows the treatment of orthotopic melanoma in mice by employing a combined approach of Synchrotron Microbeam Radiation Treatment (MRT) and gold nanoparticles (AuNPs). An MRT array is composed of spatially fractionated microbeams (each 50 µm wide) ~~using~~ of synchrotron x-rays, spaced at 200 µm from their center. This configuration is relevant for anti-cancer treatment because the basal dose of 5.6 Gy that extends over the whole field size is reinforced (every 200 µm) by the narrow (50 µm) microbeam peak-dose of 400 Gy. The work presented here demonstrates that this has better tumor control than a single fraction of a homogenous broad beam dose. We also tested whether a lower "sensitizing" peak-dose of 150Gy was able to promote vascular permeability to facilitate the extravasation of AuNPs into the tumor before to the delivery of MRT with peak-doses of 400Gy.

Methods:
B16-F10 melanoma cells were implanted in the ears of C57BL/6J mice. Animals were subjected to a combination of therapies from 8 to 11 days after implantation. The therapies involved MRT with and without gold nanoparticles, with and without the sensitizing dose, as well as~~,~~ a homogenous beam to mimic conventional radiotherapy. The tumor size was recorded daily for longitudinal tumor growth analysis.

Results:
Combining AuNPs with MRT delayed the tumor growth beyond of what was achieved by MRT alone. The use of the sensitizing dose - prior to the administration of AuNPs – significantly influenced the delay of the tumor re-growth and thus prolonged the median survival times (MST) of the mice. The MST were 6, 19.5, 20, 29, and 39.5 days for the following groups: tumor control, MRT alone, AuNPs + MRT, sensitizing dose + MRT, and sensitizing dose + AuNPs + MRT respectively. Importantly, in all the groups treated with MRT, there was at least 1 animal with no tumor recurrence per group (13 mice in each group). All these animals show currently no sign of tumor recurrence (11 months after treatment).

Conclusion:
This work demonstrates that combining MRT with AuNPs is an effective treatment for melanoma in mice. It also shows that delivering a lower "sensitizing" dose of microbeams prior to the administration of AuNPs increases survival even further. This paves the way to use such approaches with other tumor models to get closer to the human applications.

Kommentar [CF1]: Verdiana's name is in bold because she will be presenting this research. I won't be able to assist to the conference.

Kommentar [BE2]: Replace dose-peaks by peak doses?

Kommentar [CF3]: Done!

Formatiert: Hervorheben

Kommentar [CF4]: In which group di all mice have recurrent tumors?

Kommentar [CF5]: It was the MRT group that was exposed to the sensiting dose 150Gy. But since it was 150Gy MRT and no 400Gy MRT, I decided to eliminate it from the abstract. I reduced the number of groups to 4.

Kommentar [BE6]: This proves, that such low peak dose values achievable in depth for possible future human applications may still increase the permeability to improve drug delivery.

Kommentar [CF7]: Technically yes, but we haven't yet quantified the amount of gold or other drugs after the low peak dose. That is why we cannot be 100% sure that this will be the case.