HAL
open science

PD-0763 Role of the immune system in anti-tumoral resopnse to proton minibeam radiation therapy

A. Bertho, E. Brisebard, M. Juchaux, C. Gilbert, C. Lamirault, A. Patriarca, L. de Marzi, F. Pouzoulet, Y. Prezado

To cite this version:

A. Bertho, E. Brisebard, M. Juchaux, C. Gilbert, C. Lamirault, et al.. PD-0763 Role of the immune system in anti-tumoral resopnse to proton minibeam radiation therapy. Radiotherapy & Oncology, 2021, 161, pp.S593. 10.1016/S0167-8140(21)07042-0 . hal-03366806

HAL Id: hal-03366806

https://hal.science/hal-03366806v1

Submitted on 4 Oct 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

contrast, the irradiated tumor regressed completely and lung metastases were strongly reduced in both RT-treated ($p < 0.001$) and RT + aPD-1-treated mice ($p < 0.001$), compared to untreated and only aPD-1-treated mice. Control of the lung metastases strongly depended on CD8+ T cells, and control of the irradiated tumor depended partly on CD8+ T cells. RT and RT + aPD-1 strongly reduced immunosuppressive granulocytic MDSCs in the irradiated tumor, the spleen, and – to a lesser extent – in the lung. Moreover, RT and RT + aPD-1 increased bulk CD8+ T cells and tumor-specific CD8+ T cells in the irradiated tumor and in the lung, but not in the non-irradiated subcutaneous tumor. The frequencies of tumor-specific CD8+ T cells as measured with MHC tetramers were increased in the circulation both in mice treated with RT or with RT + aPD-1, with a trend towards higher frequencies upon combined RT and aPD-1 (RT vs. RT + aPD-1: $p < 0.001$), and tumor-specific T cells found in the spleen of mice treated with RT + aPD-1 lysed 4T1 tumor cells *ex vivo*.

Conclusion

Our study supports the notion that high-dose ablative RT can induce abscopal effects on micrometatases even in poorly immunogenic tumor models. We show that these effects depend on CD8+ T cells and that ablative RT alone can induce systemic T cell-mediated effects against micrometastases almost as effectively as RT + aPD-1. In addition, our study reveals that RT can induce T cell-mediated abscopal effects on micrometastases even if macroscopic metastases do not respond or progress. These findings have implications for clinical radiation oncology.

PD-0763 Role of the immune system in anti-tumoral resopnse to proton minibeam radiation therapy

A. Bertho[1], E. Brisebard[2], M. Juchaux[1], C. Gilbert[1], C. Lamirault[3], A. Patriarca[4], L. De Marzi[5], F. Pouzoulet[3], Y. Prezado[1]

[1]Institut Curie, U1021-UMR3347, Orsay, France; [2]Oniris, UMR703 – PAnTher – APEX , Nantes, France; [3]Institut Curie, Experimental Radiobiology Plateform, Orsay, France; [4]Institut Curie, Hospital - Protontherapy Center, Orsay, France; [5]Institut Curie, Hospital - Protontherapy center , Orsay, France

Purpose or Objective

Proton minibeam radiation therapy (pMBRT) is a novel therapeutic approach which uses spatially modulated narrow (< 1 mm) proton beams [1]. In this approach, the dose distribution consists in high doses (peaks) in the path of the beams and low doses (valleys) between the beams. Experiments on small laboratory animals have shown that pMBRT displays a remarkable reduction of neurotoxicity [2] and an equivalent or superior tumor control than conventional proton radiations [3], even when with highly heterogeneous dose distribution. Even though the toxicity and efficiency of pMBRT have been established, the underlying biological mechanisms under pMBRT efficiency remain to be unravelled. In this study, we hypothesised that immune system was involved in the anti-tumor response to pMBRT.

Materials and Methods

For that purpose, we performed two experimentations, collecting original *in vivo* radiopathological data in rats, thanks to the implementation of pMBRT at the Institut Curie Protontherapy Center. Firstly, we compared the response of RG2 glioma bearing-Nude (athymic) rats versus immunocompetent (Fischer) rats (n= 12 Fischer rats per group, n= 6 irradiated Nude rats, and n=3 non-irradiated Nude rats). Animals of the irradiated groups received a dose prescription of 30 Gy (average) in one fraction, with approximately one third of the tumor volume receiving (valley) doses of less than 10 Gy. A survival survey was performed as well as histopathological analysis.

Results

While a significant increase of lifespan was observed in the irradiated immunocompetent rats compared to non-irradiated controls, the irradiated Nude rats showed no response to the treatment (See figure 1). So, we aimed to investigate the immune microenvironment of the RG2 glioma. Seven days after radiation, and a histopathological and immunohistochemical analysis was performed on tumor samples (n= 7 for controls and conventionally irradiated (BB) rats, n= 6 for pMBRT). pMBRT irradiated-tumor displayed a composite morphological pattern, characterized by areas of small spindle-shaped cohesive cells (non-irradiated RG2 glioma histological aspect) interspaced with areas of large round non-cohesive cells presenting numerous nuclear and mitotic atypies (conventionally irradiated RG2 glioma histological aspect). The mitotic index was similarly reduced in pMBRT and BB groups, compared to control group. While quantification of immunolabelling for CD3, CD4, CD8 (T cells) and for CD68 (macrophages) is still ongoing, preliminary results showed an increased proportion of infiltrating CD4 positive T cells in pMBRT irradiated tumors as compared to conventional proton irradiated and non-irradiated tumors.

Conclusion

Together, these results demonstrate an important role of T cells in pMBRT anti-tumor response and that pMBRT induce changes in the immune microenvironment of tumor that may lead to efficient tumor elimination.

[1] Prezado Med. Phys 2013
[2] Lamirault et al. Scie Reports 2020
[3] Prezado Scie Reports 2018

Poster discussions: Poster discussion 7: Prostate

PD-0764 Quality of life, toxicity, and PSA control after 50 Gy SBRT to the dominant intraprostatic nodule

M. Cloitre[1], M. Valerio[2], B. Roth[2], D. Berthold [3], T. Tawadros[2], J. Meuwly[4], L. Heym[1], F. Duclos [5], S. Viguet-Carrin [6], V. Vallet [1], J. Bourhis[5], F. Herrera[1]

[1]Lausanne University Hospital , Radiation Oncology, Lausanne, Switzerland; [2]Lausanne University Hospital , Urology, Lausanne, Switzerland; [3]Lausanne University Hospital , Oncology, Lausanne, Switzerland; [4]Lausanne University Hospital , Radiology and Interventional Radiology, Lausanne , Switzerland; [5]Lausanne University Hospital , Radiation Oncology, Lausanne , Switzerland; [6]Lausanne University Hospital , Center for Experimental Therapeutics, Lausanne , Switzerland