Regional immunological effects of proton therapy on the brain

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Abstract

Proton therapy is increasingly being used to reduce normal tissue radiation dose in the treatment of brain tumors. Previous studies have suggested that brain irradiation with standard photons leads to a neuroimmune response. It is currently unknown whether proton irradiation gives the same response as photon irradiation and what the in- and outfield effects of proton irradiation on the neuroimmune response are. This study aims to investigate the neuroimmunological effect of proton irradiation.

To this end, rats were irradiated to the whole brain, 50% anterior and 50% posterior sub-volumes with either 14 Gy photons or 14 Gy protons. Bulk transcriptomic analysis and microglia morphometric analyses were performed for different brain regions at 12 weeks post irradiation.

Photon and proton irradiation showed a similar upregulation of neuroinflammatory genes, specifically genes related to reactive microglia and microglial priming. This was validated by a morphometric analysis of microglia, which showed a similar increase in microglia reactive morphotypes in both photon and proton irradiated rats compared to control. Additionally, partial brain proton irradiation caused a local neuroinflammatory response in the irradiated region only and no clear volume effect as measured by transcriptomic and microglia morphometric analyses.

Overall, we show a similar neuroimmune response after photon and proton irradiation. Importantly, partial brain proton irradiation causes a local and not systemic neuroinflammatory response. Therefore, sparing sensitive brain structures with proton therapy might avoid an inflammatory response in these regions and possibly reduce the risk of radiation-induced neurocognitive decline.