

Radiotherapy in Immunotherapy Era - New Concept of Target Volumes/Organs at Risks [†]

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Abstract: Radiotherapy and immunotherapy are already a “successful partnership” in locally advanced diseases since the PACIFIC trial demonstrated the benefit of immunotherapy as a consolidation treatment after the consistent response to curative radio-chemotherapy. These results, as well as the data related to the ab-scopal effect correlated especially with the double inhibition of CTLA-4 and PD-1/PD-L1 in malignant melanoma, encouraged the expansion of the indication of radiotherapy beyond the direct tumoricidal potential, being explored the capacity of treatment with radiation to potentiate the antitumor immune response. In expanding the indication of radiotherapy from the loco-regional concept to that of systemic treatment applied including in pluri-metastatic disease, it is necessary to lean in favor of the benefit of two balances (immune-potential/immunosuppression and tumoricidal effect/toxicities). For this purpose, we propose a new concept of target volumes in radiotherapy, including suboptimal irradiation (partial volumes) and limiting doses to the tumor microenvironment and lymph nodes, but also defining the structures involved in lymphopenia as organs at risk and limiting irradiation doses to reduce immunosuppression by lymphopenia. Based on this concept, all patients with metastatic/recurrent disease could benefit from radiotherapy or re-irradiation, either delivered with an ablative-tumoricidal purpose or only for the conversion of an immunologically “cold” tumor into a “hot” tumor and the re-setting of the antitumor mechanisms of the immune system.

Keywords: immunotherapy; radiotherapy; synergy.

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Conflicts of Interest

The authors declare no conflict of interest.