

in the mouse carcinoma after treatment with RT + CTLA-4 blockade. Significant changes in TCR repertoire were also seen in peripheral blood of responding patients, supporting the hypothesis that RT can convert the irradiated tumor into an *in situ* vaccine.

Immunogenic cell death is induced by radiation in a dose-dependent way, with higher ablative single doses being more effective *in vitro* (Golden et al., *Oncolmunology* 2014). However, *in vivo* the interaction between the dying cancer cells and the pre-existing immune microenvironment determines the ability of RT to prime effective anti-tumor T cell responses. For instance, we have shown that the number of DCs available in the tumor and draining lymph nodes to uptake and present the antigens released by RT is a critical determinant of the magnitude of the immune response elicited (Pilonis et al., *J Immunother Cancer* 2014). We have recently found that canonical pathways mediating the induction of type I interferon responses in epithelial cells during viral infection are induced by fractionated but not single dose RT. RT-induced cancer cell intrinsic interferon- λ production enhanced DCs infiltration and was required for development of tumor-specific T cells capable of rejecting not only the irradiated tumor but also non-irradiated metastases (abscopal effect). This explains, at least in part, the synergy of fractionated RT regimens (8GyX3 or 6GyX5), but not a single ablative RT dose of 20 Gy, with anti-CTLA-4 in achieving abscopal responses against poorly immunogenic carcinomas (Dewan et al., *Clin Cancer Res* 2009). In addition, we have shown that immunosuppressive mediators such as TGF- β , which is released in its active form by RT-generated ROS, need to be neutralized to improve DC maturation and activation of T cells capable of rejecting the tumor (Vanpouille-Box et al., *Cancer Res* 2015).

Overall, optimal RT regimens combined with targeting of dominant immune suppressive pathways enable RT use as a simple, widely available tool for patient and tumor-specific *in situ* vaccination.

Supported by DOD BC100481P2, NIH R01CA201246, Breast Cancer Research Foundation, and The Chemotherapy Foundation.

SP-0592

Combining immunotherapy and anticancer agents: the right path to achieve cancer cure?

L. Apetoh¹

¹INSERM UMR866, Department of Immunology, Dijon, France

Recent clinical trials revealed the impressive efficacy of immunological checkpoint blockade in different types of metastatic cancers. Such data underscore that immunotherapy is one of the most promising strategies for cancer treatment. In addition, preclinical studies provide evidence that chemotherapy and radiotherapy have the ability to stimulate the immune system, resulting in anti-tumor immune responses that contribute to clinical efficacy of these agents. These observations raise the hypothesis that the next step for cancer treatment is the combination of cytotoxic agents and immunotherapies. This presentation will discuss the immune-mediated effects of anticancer agents and their clinical relevance, the biological features of immune checkpoint blockers and finally, the rationale for novel therapeutic strategies combining anticancer agents and immune checkpoint blockers.

Joint Symposium: ESTRO-AAPM-EFOMP: Functional / biological imaging and radiotherapy physicists: new requests/challenges and the need for better and more specific training

SP-0593

The role of the medical physicist in integrating quantitative imaging in RT: practical and organisational issues

G.M. Cattaneo¹, V. Bettinardi²

¹Ospedale San Raffaele IRCCS, Department of Medical Physics, Milan, Italy

²Ospedale San Raffaele, Nuclear Medicine, Milan, Italy

The evolution of radiation oncology is based on the increasing integration of imaging data into the design of highly personalized cancer treatments.

Technologically advanced image-guided delivery techniques have made modern radiotherapy treatment extremely flexible in term of optimal sparing of the organs at risk and shaping different prescribed target doses to tumor volumes delineated on the basis of functional imaging information.

In the last 10 years a remarkable development of more sensitive and specific signals (quantitative dynamic contrast-enhanced CT and MRI; diffusion MRI, specific PET tracers, multi-parametric MRI/PET, etc) have contributed to the prescription and design of radiation treatment plan.

The main contribution of new imaging modalities can be summarized:

- Improved delineation of target and normal structures (new hybrid imaging devices offer co-registration of anatomical, functional and molecular information); a further refinement of this approach is the possibility to shape the dose gradually according to the functional parameters (dose painting);

- Adaptation, the radiation technique defined at planning simulation can often require modification not only due to the changes in patient anatomy but because of early variations of certain imaging related parameters surrogates of treatment outcome.

- Predictive biomarkers, the use of more advanced image analysis methods (texture feature parameters) could be a surrogate of important tumor characteristics and have a higher predictive and prognostic power than simpler numeric approaches;

- Radiomics, the extraction of large amount from diagnostic medical images may be used to underlying molecular and genetic characteristics and this genetic profile may change over time because of therapy.

Despite the multiple benefits that the quantitative imaging can offer for radiation therapy improvement, there are a number of technical challenges and organisational issues that need to be solved before its fruitful integration into RT treatment planning process.

The main aspects covered by this lecture will be:

- Standardized procedures for acquisition, reconstruction and elaboration of PET data set;

- Methods for delineation of the PET-related biological target volume (BTV).

- Data acquisition and processing techniques used to manage respiratory motion in PET/CT studies; the use of personalized motion information for target volume definition.

- A procedure to improve target volume definition when using contrast enhanced 4D-CT imaging in pancreatic carcinoma.

SP-0594

Individualised image-guided adaptive therapy in Michigan: lessons learned from clinical trial implementation

J. Balter¹

¹University of Michigan, Ann Arbor, USA

SP-0595

Training in biological/functional imaging: lacks and opportunities

A. Torresin¹, M. Buchgeister²

¹Azienda Ospedaliera Ospedale Niguarda Ca'Granda, Department of Medical Physics, Milan, Italy

²Institution: Beuth University of Applied Sciences Berlin, Department of Mathematics- Physics & Chemistry, Berlin, Germany

Pubmed references, presentations and posters during a lot of Conferences (ESTRO, EFOMP, ESMRMB, EANM,...) are introducing a lot of biological and functional imaging for radiotherapy applications: MRI, PET, SPECT, functional CT are able to support radiation therapy for target and Organ at Risk definition. Looking at the EUROPEAN GUIDELINES ON MEDICAL PHYSICS EXPERT (RP 174) the competence on biological and functional imaging is not specific item into RT skill and competences. We can find the key activities of MPEs inside the following: Diag.& Therap. NM Internal Dosimetry Measurements(K23: Explain methods for determining