

Special issue on intraoperative radiotherapy—guest editor's preface

The considerable technical advancements of irradiation techniques over the past decade lead to an increased use of high(er) single doses with less side effects. In some cancers, stereotactic radiosurgery (SRS) or stereotactic body radiotherapy (SBRT) with high single doses to one or more lesions have proved to be equally (or even more) effective as surgery. However, the delivery of ablative doses in a single fraction bears more advantages than instantaneous sterilization of the treated volume: a variety of effects on non-irradiated cells that are located *adjacent* (bystander effect and cohort effect) and *distant* (abscopal effects) to the initial tumor site have been observed (1-3). Corresponding to this, there is also increasing evidence for systemic effects after high-dose radiotherapy in metastasized malignancies (4,5), whereas this effect may be further augmented by checkpoint inhibitors such as ipilimumab (6,7).

The application of intraoperative radiotherapy (IORT) resembles the most effective approach to spare healthy tissue and at the same time to deliver extraordinarily high single doses of radiotherapy to (microscopically or macroscopically) remaining tumor cells. Modern devices resemble portable miniature linear accelerators, that are either using low-energy photons or electrons and thus require similar shielding requirements as c-arm fluoroscopy (8). The facilitated room-to-room portability can also be seen as a powerful metaphor for an interdisciplinary use of these devices. Beside the most widely known application in early-stage breast cancer, where IORT turned out to be non-inferior to postoperative external beam radiation therapy in two large phase III trials (9,10), IORT is to date increasingly used by multiple disciplines to treat a broad variety of tumors, including sarcoma, high-grade gliomas, brain and spinal metastases, head-and neck carcinomas or cervical cancer (11-20).

Although for most of these indications, IORT does not bear the requirements of expensive study drugs or complicated resection techniques, randomized clinical trials that generate level I evidence are still lacking for most indications (except breast cancer). In the light of ever-increasing costs for targeted molecular therapies and tighter budgets for healthcare, targeted radiotherapy in the form of IORT carries the excitement of a low-cost-high-efficiency approach. The IORT community is therefore encouraged to follow the example of IORT in early-stage breast cancer in creating high level evidence in order to modify clinical guidelines for cancer treatment in the era of evidence-based medicine.

With the objective of forming such an interdisciplinary community that may collaboratively set up prospective trials and, as a consequence of the positive response to the first special issue on IORT in 2014, *Translational Cancer Research* has decided to once more provide a forum, in which IORT experts give insights on their views and where researchers publish novel developments in this moving field.

In this issue, Emami *et al.* address normal tissue complications after (high-dose) IORT and question the use of the linear-quadratic formalism for predicting such. Tallet and her colleagues staged patients planned for IORT using pre-operative MRI and report ipsilateral second breast cancer in 4%. Reis *et al.* present their approach of combined intraoperative radiotherapy and kyphoplasty (Kypo-IORT) and also provide an outlook on an upcoming phase III trial. Massarut and colleagues give an overview on the current knowledge about wound response(s) after surgery and Veldwijk *et al.* contributed a brief report on their findings when analyzing growth promoting effects of wound fluids collected from breast cancer patients with and without IORT.

Münter *et al.* provide a comprehensive review on various techniques including HDR-brachytherapy, intraoperative electron radiation therapy (IOERT) or IORT with low-energy photons in head and neck carcinomas. Sethi *et al.* investigated the impact of commonly encountered tissue heterogeneities on measured dose in heterogeneous media. Potemin *et al.* report on outcome after IORT in patients with locally advanced or recurrent rectal cancer.

As adequate documentation of IORT is still a major challenge the introduction of a treatment planning software for IORT displays a major advantage for the community. Valdivieso-Casique *et al.* introduce the software and review the process of establishing it.

We wish to thank all contributors and the editorial office for supporting this special issue and hope that it resembles an inspiring source not only to physicians and physicists practicing in IORT, but also for those interested IORT.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Translational Cancer Research* for the series “Intraoperative Radiotherapy II”. The article did not undergo external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.3978/j.issn.2218-676X.2015.04.09>). The series “Intraoperative Radiotherapy II” was commissioned by the editorial office without any funding or sponsorship. FAG and PCL served as the unpaid Guest Editors of the series. FW served as the unpaid Guest Editor of the series and serves as an unpaid editorial board member of *Translational Cancer Research*. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Submitted: 15 April 2015; Accepted for publication: 16 April 2015

doi: 10.3978/j.issn.2218-676X.2015.04.09

View this article at: <http://dx.doi.org/10.3978/j.issn.2218-676X.2015.04.09>

Cite this article as: Giordano FA, Lara PC, Wenz F. Special issue on intraoperative radiotherapy—guest editor's preface. *Transl Cancer Res* 2015;4(2):137-139. doi: 10.3978/j.issn.2218-676X.2015.04.09