Advances in Breast Radiotherapy: Brachytherapy, Intraoperative Electron Therapy, Protons, and Nodal Irradiation

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The prognosis of breast cancer has improved and continues to do so due to a wide range of approaches, which has markedly increased the proportion of patients who can be treated for cure. Improvements extend to every stage of the disease and even the pre-clinical phase of increased risk, and include the treatment of screen- and clinically detected tumors, recurrent disease, and incurable stages where symptoms become increasingly preventable and controllable for ever longer periods of time. These improvements rest on two fundamental principles that have been clearly confirmed in virtually all breast cancer-related clinical investigations.

The first principle is to tailor treatment modalities to the given biology of an individual's disease. Tumor biology becomes apparent as clinical and molecular pathological features of the tumor, and in turn is embedded in patient-related factors such as age, comorbidities, and personal preferences including attitudes towards risk and body image. The second principle is close coordination among the involved treatment modalities, i.e. surgical, radiation and systemic therapies, as each single one can only exert its full potential by fitting their respective techniques into an overall therapy for a given patient, because techniques mutually relate to each other. Classically, the extent of resection depends on which perioperative systemic as well as radiation therapies are given, or the extent – volume and dose – of radiotherapy will depend both on the extent of surgery and the administration of systemic treatments. The multidisciplinary tumor board translates this second principle into daily practice, while clinical trials form the basis of refining treatment techniques (or drugs) according to tumor biology and patient-related factors.

Progress in breast cancer radiotherapy is made within the framework of these two general principles of breast cancer treatment. As the present state of the art has achieved a very high level of locoregional disease clearance together with a high probability of preventing metastatic spread, developments in radiation oncology in breast cancer focus on maintaining this high level of locoregional control of disease. In parallel, they aim to further reduce

acute radiation and combined 'surgery plus radiation'-related toxicities, radiotherapy-related patient inconvenience such as duration of treatment and short-term morbidity, as well as long-term adverse effects such as tissue fibrosis, cosmesis, lymphedema, and cardiac toxicity, although the frequency and severity of these adverse effects are already limited with state-of-the-art radiotherapy approaches. Therefore, clinical trials investigating further improvement of breast radiation therapy usually come as non-inferiority or equivalence trials that aim at maintaining the high level of disease clearance while further reducing any radiation-related adverse effects.

For this issue of BREAST CARE with a focus on 'Radiotherapy', we have selected a few areas of recent active research in the primary curative setting of breast cancer radiation oncology. All four papers exemplify the common aim of further reducing adverse effects by further confining the radiation dose to the area that has to be treated [1–3] or by discussing the use of radiotherapy instead of surgery in the treatment of regional lymph nodes [4].

The two main options for reducing both the irradiated volume and the treatment duration when the bed of the surgically removed tumor needs to be irradiated, either alone – as partial breast irradiation – or as a boost dose, are discussed in the articles on interstitial brachytherapy [1] and on intraoperative radiotherapy [2], respectively. Brachytherapy arguably is the most conformal method to administer radiation, meaning that the radiation dose targeting the volume to be treated is maximally confined, therewith optimally sparing surrounding non-affected breast and connective tissues and organs (heart, lung, ribs). Brachytherapy can be delivered via interstitially applied tubes that are inserted into the tumor bed, get loaded consecutively with the radiation source for a few fractions, and are removed after a few days [1]. Interstitial brachytherapy can be used for delivering a boost dose to the tumor bed in addition to whole breast external radiotherapy, or as partial breast irradiation alone if appropriate, the latter reducing the overall treatment duration to only a few days. This modality presently is the

best evidence-based option for partial breast irradiation in terms of tumor control and has a favorable adverse effects profile. Alternatively, the dose can be administered by electrons using a dedicated linear accelerator intraoperatively. This treatment technique only slightly prolongs the duration of surgery and as such does not require an extra course of radiotherapy. Kaiser et al. [2] discuss ongoing trials of intraoperative radiotherapy both as partial breast treatment and as a method to deliver a booster dose.

Niehoff and Hey-Koch [4] address the management of regional lymph nodes, discussing regional node irradiation along with sentinel node biopsy, lymph node dissection, as well as sonography-guided biopsy. To avoid the toxicity of axillary dissection, which further increases when combined with nodal irradiation, a number of trials have investigated limiting the extent of nodal treatment. Here, radiotherapy plays a distinct part, which is discussed in this contribution along with a perspective of eventual future management of the axilla [4]. Taking nodal irradiation a step further and in line with aiming at maximal sparing of the lung and especially the heart in even moderately regionally advanced breast cancer, where axillary, periclavicular and internal mammary nodes would

require radiotherapy, proton radiation therapy may offer advantages over classically employed photons. In addition, in highly individual cases of anatomic variants (e.g. funnel chest), which may constitute a challenge for radiotherapy delivery, protons may offer favorable dose distributions compared with photons. Hug [3] presents the basic rationale of this worldwide still scarcely available option together with recent data as well as ongoing studies in breast cancer proton therapy.

The articles of this focus on recent advances in breast cancer radiotherapy that aspire to sketch essentials of proton therapy, interstitial brachytherapy, intraoperative radiotherapy, and regional nodal irradiation (also for the non-radiation oncologist) thus clearly illustrate the close integration of progress in radiation technology with developments both in surgery and systemic treatments in breast cancer care.

Disclosure Statement

No conflict of interest.

References

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