The Challenge of Integrating Radiotherapy in the Multimodal Treatment of Breast Cancer

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Radiotherapy is a local therapy modality and is integrated in a multimodal treatment concept. It is mandatory and standard in all patients with breast-preserving therapy and is also indicated in the majority of patients who undergo mastectomy. Adjuvant radiotherapy generally improves local tumor control and reduces the risk of a locoregional recurrence by a factor of 3–4 [1–3]. In patients with a high risk of local recurrence, improved local control is associated with improved survival [1, 3–8]. Antineoplastic adjuvant systemic therapy may contribute to local control and enhances the efficacy of radiotherapy but its effect alone is not sufficient to replace radiotherapy [1, 3, 9].

In the past years, a variety of major changes in radiotherapy have been implemented in the treatment of breast cancer. This includes radiobiology (e.g., alternative fractionation regimens such as hypofractionation), target volume concepts (e.g., partial breast irradiation) and new techniques (e.g., intraoperative radiotherapy). All these developments have to be integrated in the complex multimodal treatment concepts in breast cancer and treatment should meet well-defined quality criteria [10]. The objective of the focus in this issue of *BREAST CARE* is to discuss some of the burning questions currently discussed in radiotherapy in the light of the actual data.

Dunst and Dellas [11] discuss the impact of margin status in breast-preserving therapy. There is no evidence that a specific margin width is required in patients undergoing radiotherapy. In particular, a benefit of re-resections after R0-resection is questionable. On the other hand, efforts should be made to ensure optimal delivery of whole-breast and boost radiotherapy because of its significant impact on tumor control.

Offersen and coworkers [12], on behalf of the Radiotherapy Committee of the Danish Breast Cancer Group (DBCG), comment on long-term data of postmastectomy radiotherapy (PMRT) from the Danish DBCG trials 82b and 82c. These large trials included patients after mastectomy and axillary dissection with at least 8 nodes removed. Both trials provide evidence for a survival benefit by PMRT in patients with 1–3

positive nodes and have led to changes in international guidelines from avoidance of PMRT in this subgroup to now ‘strongly consider’ [13–17]. Moreover, new data from the Danish studies show no excess cardiac mortality despite the fact that the radiotherapy techniques in this period were not yet able to meet contemporary quality criteria. Therefore, cardiac risk due to radiation can be considered low if modern techniques are used.

Dellas [18] focuses on a new and highly interesting topic, namely the impact of local therapy on metastatic lesions in patients with a limited number of metastases; this state of disease with only few (not more than 3–4) detectable metastatic sites has been described as ‘oligometastatic’ disease. There is some evidence that these patients may have a better prognosis than other metastatic patients and that the progression of disease often arises from the initially visible metastases. Improving local control at metastatic sites may therefore impact on the further course of disease. Currently, local therapy to metastatic sites is administered only with the objective of palliation but the hypothesis for future studies is to test whether radiotherapy may have a curative potential in subgroups with (oligo-)metastatic disease.

Hermann and Nitsche [19] discuss the impact of axillary irradiation. They emphasize that interpretation of data requires differentiation of studies with regard to prognosis (node-negative vs. node-positive patients), surgical procedures (axillary clearance, sampling, sentinel-node biopsy, or nothing) and radiotherapy techniques (unavoidable partial irradiation of lymph nodes by breast radiotherapy vs. full axillary irradiation). Radiotherapy is clearly effective in reducing the risk for axillary recurrence and can be used as alternative or in addition to surgical procedures. Recent and yet early data suggest that lymph node irradiation may contribute to improved disease-free survival in certain subgroups of patients. The impact of radiotherapy is currently further investigated in a variety of ongoing studies.

Petersen and Würschmidt [20] outline how changes in techniques and understanding of the biology of normal tissue reactions to radiation have improved treatment safety. This holds true for local complications such as breast fibrosis, lymphedema or brachial plexopathy, but also for late risks, such as cardiac morbidity and mortality.

Breast cancer treatment is a challenge for a multidisciplinary team. This issue of *BREAST CARE* hopefully helps to

better understand the complex interactions between radiotherapy and other modalities in multimodal treatment concepts and opens minds for further improvement in the future.

Disclosure Statement

The authors declare that there are no conflicts of interest.

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