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# 29 Conclusions and Future Possibilities—IORT

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Experience thus far has demonstrated that variable combinations of external beam irradiation (EBRT), intraoperative irradiation (IORT) with electrons (IOERT) or high dose rate brachytherapy (HDR-IORT) and surgical resection are feasible and practical in settings where close interdisciplinary cooperation exists, and that these aggressive approaches appear to impact local control with and without survival. With primary colorectal cancers that are unresectable for cure or for locally recurrent colorectal cancers, both local control and long-term survival appear to be improved with the aggressive combinations including IORT when compared with results achieved with conventional treatments. These findings are consistent from various institutions and countries (MGH, Mayo, Pamplona, Japan; *see* Chapters 14–16). When residual disease exists after resection of gastric cancers, IOERT with or without external radiation has achieved encouraging survival results (Chapter 11). Excellent local control and long-term survival have been achieved with abdominal and pelvic soft tissue sarcomas with IORT-containing treatment approaches for both primary and recurrent lesions (Chapters 18 and 19). In the randomized National Cancer Institute trial, improved local control was achieved with lower small-bowel morbidity with IOERT plus EBRT versus EBRT alone in patients with marginally resected primary retroperitoneal sarcomas. Mayo Clinic investigators have reported excellent results for locally recurrent as well as locally advanced primary abdominal and pelvic sarcomas. Long-term salvage of approximately 30% has also been achieved with IORT-containing treatment approaches for locally recurrent gynecologic and renal malignancies (Chapters 22 and 23, respectively). With locally unresectable pancreatic cancer, an apparent improvement in local control has been noted with IOERT

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plus EBRT, but survival has not been altered because of a high incidence of abdominal failure, both liver and peritoneal (Chapter 12). In the treatment of pediatric malignancies with IOERT or HDR-IORT, single-institution reports reveal excellent local control and survival (Chapter 26). In lung cancer management, IOERT has reported promising local control rates when integrated in the multidisciplinary treatment of Pancoast tumors (boosting a tumor bed chest wall region after preoperative chemoradiation plus resection), or in parenchymal lesions with or without mediastinal involvement (Chapter 24). Extremity soft tissue sarcomas are technically simple to treat with IORT (either IOERT or HDR-IORT) with attractive results in terms of cosmesis, function, and limb preservation rates (Chapter 20). IORT in the context of multimodal treatment for bladder cancer has proven to be able to sterilize transitional cell carcinoma and should be evaluated more extensively as an addition to chemo-EBRT for bladder preservation (Chapter 23). IORT is also being evaluated in other sites, including bone sarcomas, marginally resected or locally recurrent head and neck cancers, and selected CNS and breast cancers (Chapters 21, 25, 27, and 28, respectively).

## 1. PATIENT SELECTION, MULTISPECIALTY TREATMENT APPROACHES

Optimization of results with IORT treatment approaches will continue to be dependent on proper patients selection as well as appropriate multispecialty treatment (facilities and equipment; aggressive skilled team of multispecialty physicians—surgeon(s), radiation oncologist, and medical oncologist). Previously untreated patients remain the best overall candidates for the aggressive IORT-containing treatment approaches discussed in this book, as optimal combinations of EBRT (with and without sensitizers), resection, IORT (with and without dose modifiers), and systemic therapy can be used as planned sequential treatment to optimize both local and distant control of disease.

The best long-term results will be achieved in patients without evidence of distant metastases at time of treatment and in whom good systemic treatment options can be given to high-risk patients in planned sequential fashion. Use of adequate pretreatment staging evaluations is necessary before subjecting patients to the potential risks of the locally aggressive techniques discussed in this book. More frequent use of laparoscopy, chest and abdominal computed tomographies (CTs), and newer imaging techniques including positron emission tomography (PET)-scanning and tumor-specific antibody studies would be desirable after preoperative EBRT (with and without chemo) and prior to exploration, resection, and IORT.

In the future, an area of conceptual interest is the systematic evaluation of IORT for the management of tumor sites and stages in which adjuvant or neoadjuvant EBRT has proven to be a mandatory treatment component. This means the evaluation of “adjuvant IORT,” in the strict understanding of the concept (treatment of an anatomical region at high risk for local recurrence following resection with negative but narrow margins). In some of these settings, the use of IORT may allow a decrease in the dose of EBRT with an improvement in the overall therapeutic ratio. This may optimize further the benefits in terms of improvements in the therapeutic index seen when using IORT plus EBRT with and without chemo for known residual disease after maximal resection. Several European groups have already activated clinical trials, including IORT as a component of the adjuvant loco-regional irradiation segment of treatment (1–3). Preliminary results are

2.9 Conclusions and outlook. Rh(III) diaryl porphyrin was shown to bind to a range of mono- and bidentate nitrogen ligands. The aromatic heterocycles pyridine, 4,4'-bipyridine, 4,4'-bipyrimidine and diazapyrene bound to the Rh porphyrin with similar geometries in the solid state, and solution. However tilting of the ligand with respect to the normal to the porphyrin was observed in several cases in the solid state and this is attributed to a crystal packing effect. Pyridine ligands bound with an affinity constant  $> 10^7$  and were always observed to be in slow exchange with free liga