Foreword

A variety of techniques are now available to radiation oncologists to optimize treatment of cancers, including altered fractionation schedules, enhanced image guidance, intensity modulation allowing radiation dose escalation and improved brachytherapy techniques. In recent years, there has been increasing interest in the concurrent or sequential use of chemotherapeutic agents with radiosensitizing ability to enhance the effectiveness of radiotherapy. These agents include cisplatin, 5-fluorouracil, taxanes, topotecan, gemcitabine, vinorelbine, and tirapazamine. In certain malignancies (e.g., non-small-cell lung cancer, head and neck cancers, esophageal cancer and cervical cancer), concurrent chemotherapy and radiotherapy protocols have resulted in better tumor control and/or patient survival than with radiotherapy alone. The review by Dr. *Curran* in this supplement provides an update of recent clinical trials in this area, and emphasizes that while much has been achieved in the quest for new combined modality regimens capable of improving the outcomes for patients with cancer, important questions concerning the selection of patients, and the optimal dosages and timing of sequential therapies remain to be answered in future studies.

Other evolving approaches to optimizing radiotherapy include the use of radioprotectants to reduce radiotherapy-induced toxicity without affecting its antitumor efficacy, cytotoxic agents such as mitomycin C to specifically target hypoxic tumor cells, and strategies to counter anemia such as treatment with epoetin alfa (recombinant human erythropoietin). It is postulated that anemia in cancer patients may result in a poor treatment outcome because of an increased resistance to radiation or chemotherapy. Radioprotectants currently under investigation include amifostine (WR-1065), which has been shown in experimental studies to prevent both radiation-induced cell death and radiation-induced mutagenesis. Moreover, this agent reduced the incidence of early and late radiotherapy-induced xerostomia in a multicenter clinical

study of patients with head and neck cancers. Other potential applications of amifostine are reviewed in the article by Dr. *Grdina* and colleagues, along with recent advances in the development of newer cytoprotectants to reduce the acute and chronic toxicities associated with high-dose treatment strategies and aggressive combined modality protocols.

The occurrence of anemia in cancer patients is an often overlooked complicating factor that is associated with poorer outcome possibly by decreasing the response to radiotherapy, presumably via lowering the oxygen-carrying capacity of the blood and thus exacerbating intratumoral hypoxia. In addition, anemia has an adverse effect on the quality of life of cancer patients, as evidenced by the increased fatigue that has been associated with low hemoglobin levels. Studies in various types of cancers have indicated that a high proportion of patients are anemic prior to or during radiotherapy, and that low hemoglobin levels are associated with poor clinical outcomes with radiotherapy. As emphasized in other articles in this supplement, these findings underline the importance of early detection and treatment of anemia in cancer patients. Administration of epoetin alfa to correct anemia has been reported to enhance locoregional response rates to chemoradiation therapy in patients with certain types of cancers (e.g., oropharyngeal squamous cell carcinomas) and to improve quality of life. Whether epoetin alfa therapy will also increase long-term survival is currently being investigated. Other ongoing studies are investigating whether epoetin alfa may also be effective in protecting against radiotherapy-induced neurotoxicity.

The challenge for the future is to utilize our present knowledge to optimize the management of cancer patients undergoing radiotherapy or combined modality protocols with the objective of improving both the outcome of treatment and quality of life.

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