

## Preface



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*Guest Editor*

Surgeons have had a major role in the long history of regional therapy for cancer and continue to explore and develop the field. The development of chemotherapeutic agents in the early 1940s fostered interest in the ability to adequately deliver a drug to the tumor. The early development of nitrogen mustard provided an active agent and the technique of intra-arterial infusion provided access to the tumor. As the field evolved investigators continued to explore regional therapy as a technique to ensure access to the cancer using rather primitive drugs. The initial agent nitrogen mustard was useable but toxic. Subsequent refinement (phenylalanine mustard) provided a more user-friendly agent for clinical use. Following pioneering efforts at intra-arterial therapy by Klopp and colleagues and Brennan in 1950, the field was rapidly advanced by Ryan, Krementz, and Creech (1957) who adapted the extracorporeal circuit for drug delivery capitalizing on the newly developed device for cardiac surgery. This set the stage for a technique that not only provided intra-arterial access to the tumor but also provided oxygenation and heat to potentiate the anticancer effect of the drug.

This issue of the *Surgical Oncology Clinics of North America* provides a forum for presentation of the various regional therapy modalities as they have evolved over the decades with the added refinement of use of the clinical trial to examine the long-term outcome with regional therapy. Perusal of the index highlights the major thrust of this volume beginning with an overview of regional chemotherapy by Drs. Muchmore and Wanebo discussing the historic overview and rationale for the development of various techniques to improve drug delivery (with or without use of the extracorporeal

circuit) and to take advantage of evolving drug pharmacology to enhance drug therapy. The pharmacokinetics of drug delivery to the extremities are explored by Dr. Tyler and colleagues with an emphasis on regional perfusion/infusion for melanoma. The article on pelvic perfusion (Dr. Belliveau and Dr. Wanebo) explores the basic pharmacokinetics of regional therapy in a major body cavity.

Regional therapy of the liver by chronic hepatic artery infusion for metastatic colorectal cancer is reviewed by Dr. Don Dizon and his mentor Dr. Nancy Kemeny who has made numerous seminal contributions to the field. Clinical trial outcome for extremity perfusion for melanoma is reviewed by Dr. Ben Kroon. The modification of isolated perfusion by use of the low-flow infusion technique in the management of extremity melanoma is outlined by the Australian group under Dr. John Thompson. Extremity perfusion for sarcoma is reviewed from the Dutch perspective by Dr. Harold Hoekstra, who summarizes not only the extensive Dutch experience but also other world studies for these relatively rare but challenging tumors. The challenge of providing adequate drug therapy (with control of toxicity) for advanced or recurrent rectal cancer in the pelvis with its vascular complexity is addressed by Dr. Begossi and colleagues. Isolated perfusion for gynecologic malignancy is addressed by the Kobe group of Dr. Maruo and colleagues. Each of the tumor systems involved in the pelvic site has a unique interaction with the perfused drug regarding toxicity and has variable responsiveness and potential for an antitumor response. The inability to provide complete vascular isolation in the pelvis provides the challenge of adequate drug delivery to maximize the antitumor response and minimize toxicity as much as possible. Regional perfusion for liver malignancy is reviewed by Dr. Richard Alexander and colleagues. The challenge of hepatic perfusion with the use of modified extrahepatic and hepatic techniques is addressed by the Eggermont group, which highlights the potential for isolation with oxygenated and hyperthermic perfusion using an extracorporeal technique. This view is counterbalanced by the clinical trial results with continuous infusion using delivery systems, such as implantable pumps, that facilitate chronic infusion-defined effects on tumors of colorectal cancer origin as previously discussed by Drs. Dizon and Kemeny. The area of pulmonary perfusion and infusion for primary and metastatic lung disease is addressed by Dr. Muller, whose group has had extensive experience with this technique for many years. Head and neck cancer has long been a therapeutic site for intra-arterial regional therapy making use of well-known and accessible vascular pathways to these tumors. Recent clinical trial results are summarized by Dr. K. Thomas Robins, a major contributor to the field. Last there is a section on regional therapy with biologics and radiotherapeutics. Dr. Sato reviews regional therapy with biologic agents, and Drs. Dubel and Soares review the potential for therapy with radiolabeled microspheres, which couples radiotherapeutics with a microsphere drug delivery system, a unique combination.

The current issue highlights the experience and the potential value of regional therapy and addresses many of the challenges to cancer therapy. The field continues to evolve and there is definite room for continued innovation not only for tumor access for the anticancer drugs but also for techniques to modify the drug delivery to improve access to the tumor cells themselves, which are often protected by various mechanisms, such as peri-tumor edema, in addition to the unique drug-resistant mechanisms in the tumor cell. The role for coupling biologic agents with chemotherapy to facilitate cancer therapy is under active exploration as is therapy with other agents that are gene derived or genetically engineered to facilitate therapy. These efforts will provide grounding for future development. The current articles highlight many future possibilities and past successes and limitations and we look forward to the continued future development of regional therapy.

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