research to develop novel techniques for using radiological images (MRI/CT) to precisely guide neurosurgical procedures in real-time.

f) Sustained-Release Chemotherapy. We have been involved in sustained release chemotherapy for the past 10 years. Sustained-release chemotherapy is known to be more effective than single-dose techniques and has been shown to be an effective radiosensitizer. Our most recent study involves the use of calcium phosphate material (non-polymeric), which can bind chemotherapeutic agents, and be injected directly into the tumor. The release kinetics of this new compound are very attractive in terms of high drug-dose delivery to the tumor, and low drug-dose delivery to the normal tissues.

g) Radiofrequency Nerve Ablation for Treatment of Chronic Back Pain. This ongoing study funded by DePuy Corp (Johnson & Johnson) is aimed at using interstitial radiofrequency energy to ablate specific nerves for alleviation of chronic back pain.

h) Assessment of the Effects of Erythropoietin and Specific Cytokines in Lung Cancer Patient Fatigue and Survival. In this study we have worked with Dr. Jan Rigan to assess the effects of exogenous erythropoietin on radiation chemotherapy induced fatigue levels and survival in lung cancer patients. The study has now been expanded to involve Glycofci Corp (Lebanon, NH) in pursuit of researched based erythropoietin for development of an effective large animal model.

i) Medical corporations initiating investigations in the Surgical Research Laboratories during 2000-2003

ETEX Corp - in vivo assays
Cohion Corp - in vivo assays
Aurora Optic Corp. – PDT/SBR
Bard Corp. – in vivo assays
DePuy Corp. – in vivo assays
TissueLink Corp – in vivo assessment
Amika Collagenasis Corp – in vivo assessment
EndoVia Corp. – in vivo assessment
NDO Corp. – in vivo assessment
Radiomed Corp. – in vivo assessment/SBR
Synthon Corp. – in vivo assessment
Wilson Cook Corp. – in vivo assessment
ThermalVision Corp. – in vivo assessment/SBR
Onyx Medical Corp. – in vivo assessment
Varian Corp. – in vivo assessment
Glycofci Corp. – in vivo assessment
Ortho-Biotech Corp (Johnson and Johnson) – in vitro assessment

j) Department of Surgery physician users of SRL:

Anthony DiScipio, MD – CT Surgery
Ann-Christiane Dulhamie, MD – Pediatric Neurosurgery
Joseph Rosen, MD – Plastic Surgery
Michael Zegans, MD – Ophthalmology
William Laycock, MD – Gen Surgery
Thadeus Trus, MD – Gen Surgery
Walter Chang, MD – Plastic Surgery
Mark Edsey, MD – Urology
Richard Don, MD – Gen Surgery
Daniel Wallach, MD – Vascular Surgery

Patient Care

During the past year, our clinical initiatives emphasized less invasive vascular procedures, including endovascular aneurysm repair, stent grafting for diffuse iliac disease, and renal/mesenteric stenting. Importantly, we developed a new program in carotid artery stenting which has achieved excellent results in high-risk patients. Overall clinical volume continued to expand, and has broadened to include the full spectrums of both open and endovascular operations. The Vascular Laboratory remained very active, and a new Chief, Technology, Kari Olsteinstad, RVT, was recruited to replace Anne Musson, RVT, who stepped down as Technical Director after serving for 19 years in this capacity.

Research

In research, Mark Filling, MD continued his pioneering efforts to predict abdominal aortic aneurysm rupture risk by measuring wall stress using CT scans and finite element analysis. Work published this year identified wall stress as an important clinical parameter, and has led to collaboration with Medical Media Systems, a local engineering-based company to develop a commercially-based application. In basic research, Mary Jo Mulligan-Kellow, PhD received a $1.2 million 4 year award from the NIH ROI award to continue her studies concerning the role of plasminogen activator inhibitor in anti-angiogenesis. Kathleen Martin, PhD continues innovative work to investigate the intracellular signaling mechanisms that regulate the effect of rapsynam on smooth muscle cell phenotype. This research program, under the direction of Dr. Richard Poole, has now attracted several graduate students and ongoing extramural funding. The Vascular Study Group of Northern New England continues in its second year with funding from CMS. This cooperative group of surgeons from 12 different hospitals in ME, NH, and VT, has now collected data on more than 1,000 vascular operations with the goal of improving outcomes. VSNINE is patterned after the NNE Cardiovascular Study Group, and based at DHMC with Jack Kronewett, MD as Principle Investigator. Other important research contributions during the past year included ongoing publications by Daniel Wallach, MD concerning the value of duplex arterial mapping before infra-inguinal bypass; by Dr. Powell concerning the value of femoral endarterectomy in addition to external iliac artery stenting, by Dr. Eva Runcillo concerning the utility of stent grafting for diffuse iliac artery disease; and by Dr. Marc Schermerhorn concerning decision analysis for endovascular aneurysm repair. This activity resulted in 19 peer-reviewed journal articles and 4 book chapters published by the faculty this year. In addition, there were 14 presentations made at surgical society meetings. Section faculty participated in 13 external research grants and contracts this year for a total direct funding of $620,000.

Education

Vascular fellowship training has evolved from one to two years, in order to incorporate sufficient endovascular/interventional training. Our current vascular fellow, Mark Wyers, MD, recently completed the two-year fellowship program as of June 2003. During his two year training, Dr. Wyers performed or directed 493 total vascular operations, including 318 major arterial procedures. He performed 118 endovascular/interventional procedures, sufficient to meet SVS endovascular credentialing requirements. Dr. Wyers made the following scientific presentations “Endovascular repair of abdominal aortic aneurysms without preoperative arteriography;” at the New England Society for Vascular Surgery, and “Internal iliac occlusion without coil embolization during endovascular AAA repair;” at the Eastern Vascular Society. The Section continues to train general surgery residents as part of the core program in General Surgery. At MMH, three surgical residents (PGY 1, 3 and 5) constitute a separate Vascular Surgery service with the Vascular Surgery fellow. Finishing senior residents each performed or directed an average of 362 total vascular operations during their training, including 172 major arterial procedures.

Vascular Surgery conferences are held each Monday from 7-11 am, and include a bi-weekly Clinical Conferences at which interesting patients are discussed, a bi-weekly clinical didactic conference, a bi-weekly Morbidity & Mortality conference, a bi-weekly research conference, and a weekly pre-operative conference to discuss procedures to be performed that week. Vascular Journal Club
Section faculty continue to be extensively involved in national and regional vascular societies, where they hold 20 officer or committee roles, in addition to 6 positions on the editorial boards of peer-reviewed journals. Section faculty members were also active in continuing medical education, delivering 24 CME presentations this year outside DHMC. As President of the Society for Vascular Surgery this year, Dr. Cronenwett led a successful effort to merge the two major national vascular societies, to develop independent executive management for the Society, and to develop a national vascular headquarters for the Society in Chicago. Dr. Cronenwett also assumed responsibility as Editor of the Journal of Vascular Surgery, including the transfer of the editorial offices to DHMC, and the establishment of a Web-based manuscript submission and review process. Dr. Zvolak continued his extensive national efforts to improve reimbursement for vascular procedures through his membership on the AMA Relative Value Committee, and by congressional interactions. This resulted in creation of new vascular CPT codes, updating undervalued existing codes, and reducing the severe underpayment for noninvasive vascular diagnostic studies by major changes at CMS concerning practice expense calculations. Dr. Powell was appointed to the Program Committee for New England Society for Vascular Surgery, the Program Committee Society for Vascular Surgery, the Society for Vascular Surgery Endovascular Issues Committee, as a NIH Clinical Cardiovascular Sciences Study Section Member, and also to the Society of Vascular Surgery Research Council. Dr. Fillinger was appointed Chair of the Issues Committee, New England Society of Vascular Surgery. Dr. Rizcicillo received the Deterling Award at the New England Society of Vascular Surgery Meeting.

Lab Activity

During the past year our lab has concentrated in research efforts in the areas: a) photodynamic therapy (PDT); b) radiation effects in tumors and normal tissues; c) ophthalmology/cornea reshaping; d) electrical impedance spectroscopy; e) image guided neurosurgery; f) sustained release chemotherapy; g) radio-frequency nerve ablation for the treatment of back pain; h) the assessment and role of cytokines and erythropoietin in lung cancer treatment. Additionally, we have participated in and/or facilitated a number of training/training/technology development endeavors for pharmaceutical corporations and Dartmouth College faculty and staff who are employed within and outside of the Department of Surgery.

a) Photodynamic Therapy: We continue to be heavily involved in photodynamic therapy research. Currently, three NIH grants support our work. One of these grants is an NIH program project grant based at Harvard University. Three PDT focused NIH grants are currently pending. Our studies are focused on improving PDT through the development of new biology and delivery techniques and mechanisms. We also plan to develop a noninvasive detector (probe) for real-time in vivo quantification of photosensitizer levels in normal and tumor tissues. Currently our PDT treatment efforts are directed at prostate cancer and Barrett's Esophagus. We have also studied the use of photodynamic therapy in the treatment of coronary artery disease, and long-term patency in tran-surgical infrahepatic portosystemic shunt (TIPS).

b) Radiation Effects in Tumors and Normal Tissues: We continue to work on identification of inflammatory and molecular pathways that are involved in radiation tissue injury, especially in the CNS, prostate, and heart. The goal of these studies is to better understand the radiation-effect cascade in tumors and normal tissues for therapeutic improvement gains. Our CNS radiation studies are centered at understanding if, to what extent, and how post irradiation hyperbaric oxygen (HBO) spares potentially devastating late radiation effects in the brain and spinal cord (NIH R01 grant resubmission June 2004). We are also performing preclinical studies (funded NIH-SBIR) to determine the feasibility and potential toxicity of interstitial radioactive Palladium wires for the treatment of prostate cancer. Finally, for the past 6 years we have studied the feasibility of using cardiac cycle gated radiation to spare heart damage in cancer treatment fields which include the heart. This study is currently funded by the Varian Corp. (NIH R21 grant is pending). Finally Sujatha Sundaram, PhD is exploring the use of vitamin D and radiation as a primary tumor treatment that would reduce the incidence of tumor metastasis (pending K01 and K22 grants).

c) Ophthalmology/Cornea Reshaping: The surgical research laboratory has long-standing interest and expertise in cornea reshaping for vision correction. Both NIH and corporate funded projects are currently active. DOS ophthalmologist, Mike Zegans, MD is the current holder of an NIH K08 award for studying the association of bacterial biofilms and corneal healing.

d) Electrical Impedance Spectroscopy for Diagnostic Imaging: The involvement of Dartmouth bioengineers has been an integral component of surgical research for more than 15 years. This involvement has increased in recent years and there is now a formal research collaboration agreement between the Thayer School of Engineering and the Department of Surgery (DMS). Current collaborative projects include: modeling and predicting brain movement during surgery; the use of electrical impedance spectroscopy for tumor diagnosis and assessing tissue change following radiation; photodynamic therapy; the use of microwave energy in cornea reshaping; prostate cancer and benign prostatic hyperplasia (BPH) treatment; and brain cooling for stroke therapy.

e) Image Guided Neurosurgery: For the past 12 years the SRL has been involved in NIH supported image guided neurosurgery research. These studies use computational, mechanical engineering, and large animal model biology