

MAINE MEDICAL CENTER CANCER PROGRAM

# 2000

*ANNUAL REPORT*



***THE MAINE RESOURCE FOR  
CANCER CARE AND PREVENTION***





The Maine Center for Cancer Care and the Maine Medical Center strive to provide a fully integrated, multimodality approach to the care of the cancer patient. The cancer program is fully accredited as a Teaching Hospital Cancer Program by ACOS Commission on Cancer. This designation recognizes the full service capability of the program, including an active clinical research effort aimed at bringing the newest therapies to Maine. Over the last year, program professionals and staff have worked hard to live up to this designation and to fulfill our mission to be the best possible cancer program. Highlights of this year's accomplishments in patient care, education, and research include:

- The number of patients seeking cancer care services at the Maine Center for Cancer Care, including the adult and pediatric units, the Breast Care Center, the IV Therapy Service, and the Women's Health Program has continued to grow. To handle the increased volume of outpatients, the Maine Center for Cancer Medicine and Blood Disorders is planning an expansion of their space and the hours of the IV Therapy Room have been extended, including scheduling treatments on Saturdays. In addition, the radioactive seed implant program, sponsored by Urology and Radiation Oncology, has been fully relocated to its own space at the Brighton Campus.
- The Children's Cancer Center has initiated an autologous/stem cell transplant program as a part of its clinical trials program. This provides a service that previously required children to leave the state for care.
- The pilot studies of the data management system known as *iKnowmed* were successfully completed and the usefulness of the program in facilitating patient care validated. As a result, the Maine Center for Cancer Medicine and Blood Disorders has adopted *iKnowmed* as its electronic medical record system. In the future, the *iKnowmed* system will also be the common database program for the NCCN Breast Cancer Project, allowing automatic data collection among participating institutions, including the oncology joint venture. *iKnowmed* has also been adopted for the Lung Cancer Database effort, both locally and, in the

future, for the Maine Medical Assessment Foundation statewide lung cancer database project.

- A Maine Center for Cancer Care website has been developed and implemented as a part of the Maine Medical Center website. The cancer website can also be accessed under [www.mmc.org/oncology](http://www.mmc.org/oncology).

Users will be able to search for program descriptions, locations, and phone numbers; support services; individual physician credentials; research protocols/clinical trials offered by the cancer center; and national cancer databases.

- The Maine Cancer Physicians Organization (MCPO), an organization of 65 area physicians involved in cancer care, was formalized this year. Discussions are now underway with Maine Medical Center, Mid-Coast Hospital, Southern Maine Medical Center, and Mercy Hospital to develop a joint venture for the purpose of better coordinating and improving cancer care services. The joint venture will begin by developing a common database system to better document services provided according to practice guidelines and the costs involved. The joint venture will also conclude a formal agreement with the Dana Farber Cancer Institute to become the first affiliate member of the NCCN.

- The Genetics Program, initiated in 1999, has flourished, coordinating education efforts for health professionals and the public, and providing clinical assessment and consultation services to MCCM and the Breast Care Center. A genetics database has been developed to help track patients and their families and to support the tissue bank. Dr. Karen Rasmussen was also awarded an NIH visiting fellowship at the Jackson Laboratories. During the coming year, she will be working with scientists at the laboratories to foster her expertise in molecular genetics and to help bridge the gap between mouse genetics and human disease.

- A tissue bank is under development as a cooperative effort of the Department of Pathology, Maine Medical Center Research Institute, and the Genetics Program. It has continued to receive grant support from the Maine Cancer Research and Education

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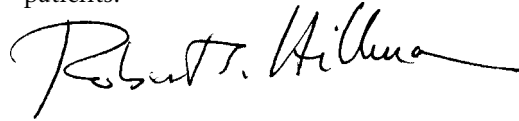
*Oncology Steering Committee Chairman's Report, Continued*

Foundation to purchase the necessary equipment and to develop the staff for the collection, preparation, and storage of frozen cancer tissues. Dr. Rasmussen has worked to organize the genetics database to support the archiving process.

- The radiosurgery program, sponsored by Radiation Therapy, has continued to grow. Efforts are now underway to shorten the length of stay and to permit same day outpatient treatments. The Radiation Therapy Department also acquired a second Varian simulator, to support a growing patient volume.
- Professional and community education and screening efforts during the year have included: the annual symposium which covered new developments in breast cancer; patient information sessions on issues surrounding chemotherapy, cancer biology and genetics; and screening clinics for both skin cancer prevention and prostate cancer

detection. Each year, the Breast Care Center participates in a statewide effort to increase the accessibility to mammography services. The MaineHealth Learning Resource Centers continue to provide a library resource for the public, offering a selection of printed materials and online internet searches.

None of these accomplishments would have been possible without the the hard work and dedication of the professionals and staff who work every day in the cancer program. These individuals need to be recognized for their devotion to the better care of cancer patients.



Robert Hillman, M.D.  
Chairman

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*Radiation Oncology*

**Breast cancer continued to be the most frequently diagnosed cancer at Maine Medical Center in 1999, increasing 7% since 1997.**

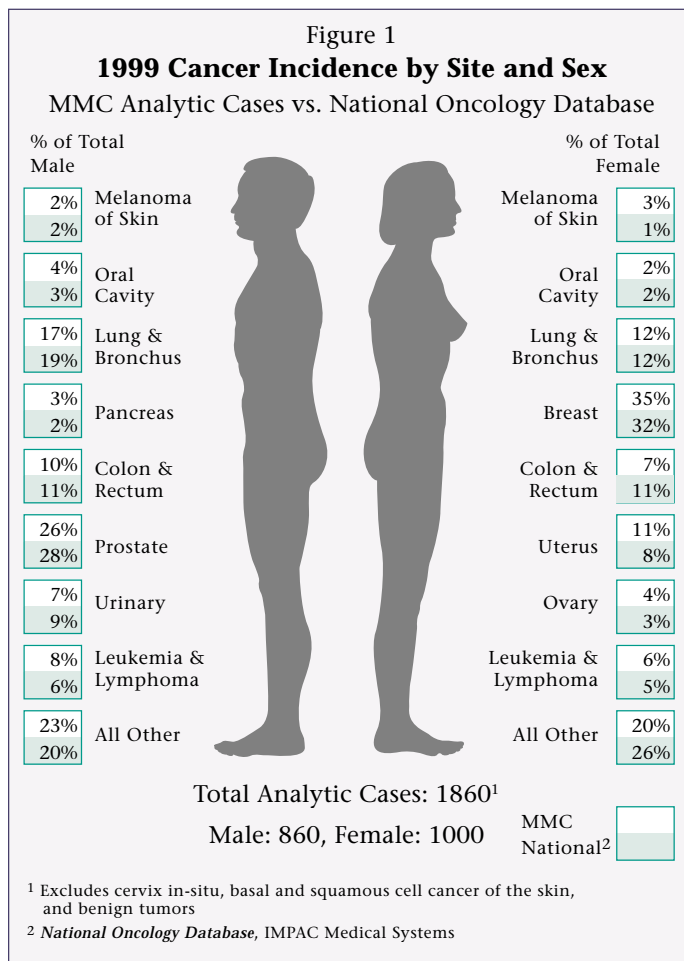
There were 2108 cases seen during 1999 (Table 1). Of this total, 1860 were either diagnosed and/or treated at Maine Medical Center (analytic cases). The remaining 248 cases received their initial treatment elsewhere and sought services at Maine Medical Center for progression or recurrence of their disease.

Breast cancer continued to be the most frequently diagnosed cancer at Maine Medical Center in 1999, increasing 7% since 1997. Lung cancer, the second most frequently diagnosed cancer, continued to have a higher incidence in men both locally and nationally. Prostate cancer was the third most frequently diagnosed cancer, with an overall increase in incidence of 4% since 1997.

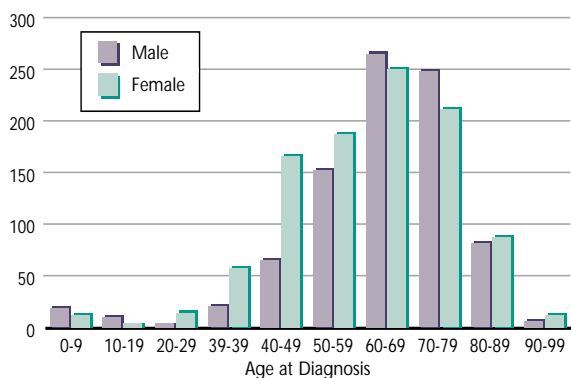
Data from a 5-year cancer incidence trend analysis suggests a three-fold increase in melanoma cancer diagnosed at Maine Medical Center since 1994. While better detection could be a factor, there is a nationwide increase in the incidence of melanoma.

*Diane E. Skog*

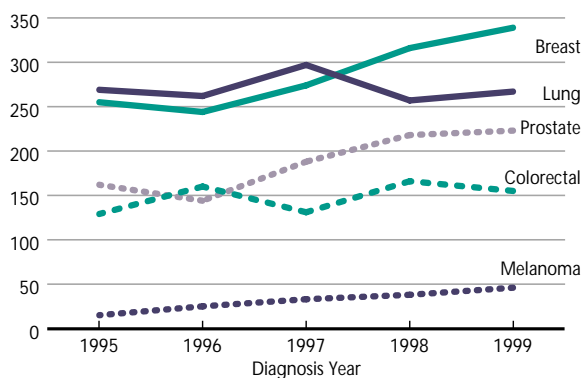
Diane E. Skog, MSB  
Clinical Data Coordinator  
Oncology Administration



**Figure 2**  
**1999 Cancer Incidence: Age at Diagnosis**  
MMC Analytic Cases



**Figure 3**  
**1995-1999 Cancer Incidence: Five Year Trends**  
MMC Analytic Cases



**Analytic:**  
diagnosis and/or first course of therapy at MMC.

**Nonanalytic:**  
diagnosis and all of first course of therapy elsewhere (seen here for recurrence).



Table 1  
**1999 Maine Medical Center Cancer Incidence**

	# Analytic	# Male	# Female	Male %	Female %	Median Age	# Nonanalytic	Total
Lip, Oral Cavity & Pharynx	48	30	18	62	38	68	7	55
Esophagus	16	14	2	88	12	77	1	17
Stomach	48	36	12	75	25	65	5	53
Small intestine	5	1	4	20	80	48	1	6
Colon	87	44	43	51	49	72	21	108
Rectum, Rectosigmoid & Anus	68	40	28	59	41	65	9	77
Liver & Intrahepatic Bile Ducts	16	14	2	87	13	63	0	16
Gallbladder & Extrahepatic Bile Ducts	16	8	8	50	50	73	1	17
Pancreas	43	23	20	53	47	69	1	44
Nasal Cavities and Sinuses	1	1	0	100	0	64	0	1
Larynx	29	24	5	83	17	62	1	30
Lung, Trachea & Bronchus	267	147	120	55	45	67	27	294
Pleura, Mediastinum, Thymus & Other Respiratory	6	4	2	67	33	65	1	7
Melanoma	46	20	26	43	57	60	11	57
Skin, Other Than Melanoma	5	4	1	80	20	76	6	11
Retroperitoneum & Peritoneum	2	0	2	0	100	73	0	2
Connective & Other Soft Tissue	10	3	7	30	70	62	3	13
Breast, Female	339	-	339	-	100	57	27	366
Breast, Male	1	1	-	100	-	74	0	1
Cervix uteri	34	-	34	-	100	48	1	35
Corpus uteri	74	-	74	-	100	64	5	79
Ovary	41	-	41	-	100	63	7	48
Other Female Genital	30	-	30	-	100	73	3	33
Prostate gland	223	223	-	100	-	68	38	261
Testis	7	7	-	100	-	41	0	7
Urinary bladder	53	43	10	81	19	70	17	70
Kidney & Other Urinary Organs	31	18	13	58	42	63	9	40
Brain & Other Nervous System	46	28	18	61	39	52	4	50
Thyroid gland	23	8	15	35	65	45	2	25
Adrenal & Other Endocrine	1	1	0	100	0	1	1	2
Non-Hodgkin's Lymphoma	67	35	32	52	48	66	16	83
Hodgkin's Lymphoma	20	11	9	55	45	31	1	21
Acute Lymphocytic Leukemia	12	9	3	75	25	5	1	13
Chronic Lymphocytic Leukemia	0	0	0	0	0	0	3	3
Acute Myelogenous Leukemia	23	9	14	39	61	68	1	24
Chronic Myelogenous Leukemia	3	3	0	100	0	53	0	3
Leukemia, Not Otherwise Specified	1	1	0	100	0	0	0	1
Other Hematopoietic & Reticuloendothelial	1	0	1	0	100	86	2	3
Multiple myeloma	21	14	7	67	33	68	7	28
Unknown primary site	40	20	20	50	50	73	2	42
Benign	36	11	25	31	69	51	6	42
Uncertain Malignancy	20	5	15	25	75	45	0	20
<b>Total</b>	<b>1860</b>	<b>860</b>	<b>1000</b>	<b>46</b>	<b>54</b>	<b>65</b>	<b>248</b>	<b>2108</b>

Excludes CIN III / CIS of cervix and basal and squamous cell carcinomas of the skin.



Historically, most cancers of the esophagus presented with advanced metastatic disease and squamous histology. The most frequent environmental association was with a long history of heavy smoking and heavy drinking. Treatment was limited to surgical resection or radiation and five-year survivors were infrequent. In the early 1990's this pattern changed.

A dramatic increase in the incidence of adenocarcinoma of the esophagus and esophagogastric junction was noted in both North America and Europe. While the reasons behind this change are not certain, it has been linked to glandular metaplasia of the normal squamous mucosa (Barrett's esophagus). Characteristics of patients with adenocarcinoma differ from those with squamous tumors. With adenocarcinoma, three quarters of the patients are male. There is no association with drinking or smoking, and long-standing symptoms of gastroesophageal reflux are common. Patients' may be surprisingly young, with many in their forties and fifties.

In 1992-93, a multidisciplinary group of physicians at Maine Medical Center led by Dr. Ronald Carroll, Director of the Division of Medical Oncology, met regularly over nearly a year to review the literature dealing with the management of adenocarcinoma of the esophagus and to design a protocol that would standardize the institutional treatment of this disease. The group included medical oncologists, radiation therapists, surgeons, and gastroenterologists. The data at that point indicated poor results with single modality treatment, whether surgical resection or radiation therapy. Moreover, combinations of surgical resection and radiation therapy either before or after surgery did not improve the generally poor outcomes. Given this dismal history for single or bi-modality treatment, the group at Maine Medical Center developed a protocol for tri-modality treatment, which included chemotherapy, radiation therapy, and surgical resection. Cancer centers throughout the United States have taken a similar approach. Although the exact combination of drugs and sequence of therapy varies, a unifying principle is the administration of chemotherapy and radiation prior to surgical resection.

The protocol developed at Maine Medical Center and implemented in mid 1993 consisted of four courses of neoadjuvant treat-

ment (neo meaning prior to surgery) followed by surgical resection. The two drugs were Cisplatin and 5FU, which had already been shown effective in treatment of squamous carcinoma of the esophagus. Two cycles of chemotherapy were given first, separated by two weeks, followed by two further cycles of chemotherapy given sequentially with radiation therapy. Simultaneous administration of 5FU with radiation therapy has a synergistic effect, making the malignant cell more vulnerable to the effects of radiation. A total of 32cGy were given. Four to six weeks following completion of this neoadjuvant treatment surgical resection was performed. Two years into this protocol, Leucovorin was added to the chemotherapy regime to further enhance the effects of 5FU.

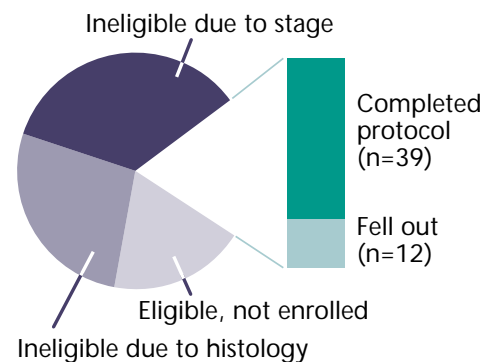
Only patients with an intermediate level of disease (stages IIb and III) were considered eligible for this rigorous therapeutic regime. Patients with advanced metastatic disease (stage IV) were excluded and offered palliative, generally nonsurgical treatment. At the other end of the spectrum, tumors were picked up "incidentally" at time of endoscopy, usually for unrelated symptoms. These were confined within the wall of the esophagus without evidence of nodal metastasis (stages I and IIa), and were treated by conventional means, usually surgery. Later on, however, because of the general prevalence of positive lymph nodes despite a negative pretreatment evaluation, sizeable stage IIa tumors were included, even if the tumor only extended into the muscularis. The primary preoperative staging tools were CAT scans of the abdomen and chest, and upper endoscopy and endoscopic ultrasound.

From 1993 through the end of 1999, a total

*Continued*

Figure 1

1993-1999 Esophagus and Esophagogastric Cases  
MMC Analytic Cases (n=259)



### Tri-Modality Treatment of Adenocarcinoma, Continued

of 259 patients at Maine Medical Center were diagnosed with carcinoma of the esophagus or the gastroesophageal junction. One hundred and eighty five (71%) were adenocarcinomas and about half of these were stage II or III and, therefore, eligible for the protocol. A quarter of these had co-morbid disease, which precluded the rigors of tri-modality treatment, and another quarter was not entered because of physician or patient preference. As a result, a total of 51 patients were enrolled to the protocol. Of the 51 patients entered, 39 patients completed the protocol, the remainder showed progression of their disease on protocol and were switched to alternative therapy. A major down side of the tri-modality treatment is its rigor and length. The four courses of neoadjuvant treatment are very demanding on the patient. Many of our patients required additional weeks of rest to recover from surgery, extending the entire treatment course beyond four months.

One post-operative death was the only treatment mortality. The overall median survival for patients who entered the protocol was 25 months with a 3-year predicted survival by Kaplan-Meier analysis of 32% (Fig 2). For those who completed the protocol, median survival was 34 months with a 3 year predicted survival of 44%. Evaluating these results is difficult, however, since an improvement in survival with surgical treatment alone has also occurred over the last 10 years. Single institution series of patients treated by surgery alone reported from 1987 through 1996 note 3-year survival rates varying from 23 to 32%. Six other single institution experiences with tri-modality treatment were reported in the 1990's (non-randomized) with 3-year survival figures

varying from 33 to 53%, comparable to the Maine Medical Center experience. Four randomized studies comparing tri-modality treatment with surgery alone have also been reported. Walsh et al: *N Engl J Med*, 1996, 335: 462-7 reported a clear cut improvement in 3-year survival with combined modality treatment, 32% vs. 6% for surgery alone. This study is flawed, however, by the unusually poor outcome from surgery alone. Two randomized studies from France failed to show any benefit of tri-modality treatment over surgery. A fourth study from the University of Michigan has been reported in abstract form. At 2 years there was no difference between the groups but at 3 years tri-modality treatment showed a 32% 3-year survival where surgery alone had only 15%. The definitive report of this randomized clinical trial has not been published to date.

Future efforts are proceeding along three lines. First of all, the apparent improvement in outcome must be confirmed by randomized studies. Secondly, newer drugs, such as Taxol, need to be included in the chemotherapy arm. The third line of investigation is to better identify those patients who will respond to neoadjuvant therapy. In our series, approximately three-quarters of the patients had at least a partial clinical response to neoadjuvant treatment. Attempts are now being made to look at molecular markers, particularly cell surface antigen and DNA markers, that might correlate with either very good or very poor responses to treatment. A better understanding of the molecular basis of tumor behavior will not only lead to the design of better therapies, but also will help spare non-responders the toxicities associated with treatment.

Figure 2

#### Kaplan-Meier survival curves of MMC patients with adenocarcinoma of the esophagus and esophago-gastric junction treated with tri-modality therapy, 1993-1999 inclusive.

