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Aurora Health Care Metro Region Cancer Program Annual Report 2004

Aurora Health Care

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Aurora Health Care Metro Region Cancer Program

Annual Report 2004

Rectal Cancer

Aurora St. Luke’s Medical Center
St. Luke’s South Shore
West Allis Memorial Hospital
Aurora Sinai Medical Center
Aurora Medical Center in Washington County

Aurora Health Care®
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Director's Report

Many exciting events have occurred over the past year within our oncology program. The most visible, and perhaps the most far-reaching, was the recognition by the American College of Surgeons' Commission on Cancer that the Metro Region Cancer Program is truly an integrated cancer care provider. Having received ACoS approval as a Network Cancer Program, Aurora Health Care's Metro Region is one of only eight in the country to achieve this distinction. This approval is granted only to system facilities, which voluntarily commit to provide the best in diagnosis and treatment of cancer and also choose to undergo a rigorous evaluation process and performance review. We are most proud that the dedicated efforts of our physicians and staff allowed us to join this elite group of Network Cancer Programs.

The coming year's challenge will be to further integrate our operational focus and committee structure into an organization which maximizes our ability to detect, prevent and treat cancer while still allowing for a community-based, local approach to cancer care. Whether regionally or locally, we are confident that a combination of education, screening, prevention, detection and treatment is the correct approach for a comprehensive oncology program.

William Laffey
Director, Cancer Services,
Aurora Health Care
As Co-chairs of the Network Cancer Committee, we are pleased to describe our progress in consolidating three hospital cancer committees into a single, regional body. We have organized as a Regional Committee with five subcommittees: Community Outreach, Cancer Conference, Registry Data, Quality Improvement and Clinical Management. The latter subcommittee is not required by the American College of Surgeons, as are the other four, but it was determined that the complexity of our organization warranted such an addition.

Much of our first year was spent on organizational issues: we reviewed committee functions, refined membership, and focused committee meetings on subcommittee reports and educational offerings to our members. We held numerous sessions at the hospital sites to determine how best to transition from three committees into one.

Most of our committee goals for the year were directed toward determining baselines and standards for capturing the information currently compiled throughout the region. Our Cancer Conference Subcommittee determined demand for increasing our videoconferencing capabilities, and we then expanded our current videoconference efforts. This has been especially helpful at Aurora Medical Center in Hartford. The Quality Improvement Subcommittee developed successful systems for tracking and reporting on the areas of clinical trial participation, quality outcome studies and patient care improvements. This was a massive task across the region but the results have been worth the effort. We have a tremendous baseline platform from which to grow. A similar process was completed by the Community Outreach Subcommittee regarding regional consolidation of outreach activities, speaking engagements and health fairs. Quality issues were by no means neglected as the Clinical Management Subcommittee commissioned a study at St. Luke’s Medical Center to improve the process of chemotherapy delivery to inpatients in order to decrease errors and increase timeliness.

It has been an active year and one for which we take pride. As one of few approved networks in the country, we found that we had very few road maps to follow from other organizations. We have covered new ground in very creative ways, all with the goal of quality patient care for those who entrust their care to our health care providers.
Multidisciplinary Cancer Conferences take place weekly in the Metro Region of Aurora Health Care.

Tumor Board Conferences meet regularly at noon each Friday and provide an opportunity for current case discussion and continuing education. The conferences facilitate the exchange of ideas between the departments of Medical Oncology, Pathology, Radiology, Radiation Oncology and Surgery, as well as all other ancillary services involved in the care and treatment of cancer patients. Case presentations cover all major cancer sites seen within the Network and include pertinent case details, presentation of pathological, radiological and surgical findings, pre-treatment evaluation, treatment modalities and follow-up care. Patient names are always withheld to protect confidentiality and privacy.

Representatives from all disciplines are encouraged to present cases at the conferences and to express their opinions concerning diagnosis and treatment. Participation in multidisciplinary case review and management discussions aids in the exchange of new information and knowledge. This helps in achieving the goal of providing consultative services to patients, educating the medical staff, and improving care for all cancer patients.
The Cancer Registry of the Metro Region is managed and staffed by Certified Tumor Registrars and is in compliance with state statutes and American College of Surgeon (ACoS) requirements. The registrars coordinate and attend cancer conferences, participate in cancer committee meetings and complete physician-assisted quality control studies on 10% of the yearly analytic caseload.

The registrars enter data into a combined multi-hospital Internet-based software program that serves the Metro and South Region hospitals. All facilities are able to enter data, which can then be combined and pulled up from any location as needed for purposes of assessing patient outcome, facilitating research, assisting with marketing, administrative planning and quality benchmark purposes. All information is kept strictly confidential and only aggregate data is released. Both inpatients and outpatients are included in the registry database. In addition, at the request of the Cancer Committee, certain benign and borderline tumors are also included. Data is submitted yearly to the National Cancer data base (NCDB) and is reviewed for completeness, accuracy and timeliness.

We hope you enjoy this year’s annual report that takes an in-depth look into the treatment and outcome of those with rectal cancer.
Colorectal Cancer Screening

This year approximately 58,000 Americans will die from colorectal cancer. It is the second leading cause of cancer death in both men and women, and accounts for 10% of cancer deaths overall.

Despite current evidence that colorectal cancer screening can decrease mortality from colorectal cancer by 50%, screening rates in the population remain very low. Because screening tests make it possible to detect early tumors at a treatable stage, we need to focus our attention on persons without symptoms of colorectal cancer if we are to make an impact in survival. According to a 1998 National Health Survey, only 20 to 30 percent of eligible respondents reported having had fecal occult blood testing during the preceding two years, and only 5 to 21 percent had a screening endoscopy during the preceding three years.

Experts agree that men and women over the age of 50, i.e., people at average risk, need to undergo colorectal cancer screening with any one (or a combination) of the modalities listed in Table 1. Because there is no single test of unequivocal superiority, the decision on which screening tool to choose depends on patient and physician preference, as well as available equipment and expertise (Table 1). Incorporating these factors in the decision-making process may increase the likelihood of screening. In addition, increasing public awareness may lead to better adherence to evidence-based screening guidelines.

People at increased risk for colorectal cancer should be approached differently. For example, those with a first-degree relative (parent, sibling or child) with colon cancer or adenomatous polyps diagnosed at age <60 years or two first-degree relatives diagnosed with colorectal cancer at any age should be advised to have screening colonoscopy starting at age 40 years or 10 years younger than the earliest diagnosis in their family, whichever comes first, and repeated every five years.

In recent years, we have seen dramatic advances in the technical aspects of colon cancer screening. However, we still have quite a ways to go in terms of making our tests more convenient (e.g., more tolerable bowel preparation) and acceptable (e.g., more respectful of our patient's privacy). Future advances will likely include more accurate noninvasive screening tests, and the development of familial genetic testing that can be used in the general population.
### Table 1. Colorectal Cancer Screening Modalities

<table>
<thead>
<tr>
<th>Test</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fecal occult</td>
<td>• Convenient</td>
<td>Significant false positive and</td>
</tr>
<tr>
<td>blood test</td>
<td>• Inexpensive</td>
<td>false negative rate</td>
</tr>
<tr>
<td>Sigmoidoscopy</td>
<td>• Can be performed without sedation</td>
<td>Can miss proximal</td>
</tr>
<tr>
<td></td>
<td>• Shown to reduce</td>
<td>colon lesions</td>
</tr>
<tr>
<td></td>
<td>mortality (case-control studies)</td>
<td></td>
</tr>
<tr>
<td>Barium enema</td>
<td>No sedation required</td>
<td>If positive, often leads to</td>
</tr>
<tr>
<td></td>
<td></td>
<td>colonoscopy</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>Permits removal of polyps throughout</td>
<td>Invasive</td>
</tr>
<tr>
<td></td>
<td>the colon</td>
<td></td>
</tr>
<tr>
<td>Virtual colonoscopy</td>
<td>• Non-Invasive</td>
<td>• Not sensitive for small polyps</td>
</tr>
<tr>
<td></td>
<td>• Technology improving but clinical</td>
<td>• Not covered by most insurers</td>
</tr>
<tr>
<td></td>
<td>utility still being determined</td>
<td></td>
</tr>
</tbody>
</table>

### Gender of Patients with Rectal Cancer

- According to the National Cancer data base (NCDB), males account for 57% of the incidence of colorectal cancer, whereas females account for 43%.

- In AHC-Metro Region 58% were male and 42% were female.
In patients with rectal cancer, prognosis and treatments are dependent on accurate staging of disease. Evaluation of rectal cancer should address the depth of tumor invasion into or through the wall of the rectum, local disease in the pelvis, including lymph node involvement, and distant metastatic disease. Imaging is important for pretreatment assessment, as well as follow-up studies. The imaging modalities available for rectal cancer include computerized tomography (CT scan), endorectal ultrasound (EUS), magnetic resonance imaging (MRI), and positron emission tomography (PET). Initial workup should also include evaluation of the entire colon for concomitant colorectal tumors, either with colonoscopy or barium enema.

CT imaging is a high-resolution imaging modality with very reliable technique, and is the mainstay of rectal cancer imaging. It is an excellent means of evaluating for distant metastases, including lung and liver metastatic disease, at the same time assessing for regional disease in the pelvis. Unfortunately, conventional CT scan is relatively inaccurate in assessing mural depth of tumor in the rectum (only up to 79% accurate), and also is relatively inaccurate in determining involvement of regional lymph nodes (60% to 80% accuracy). CT, US and MRI evaluation of lymphadenopathy relies on change in size of nodes, which is not sensitive for detection of metastatic involvement. Unfortunately, lymph nodes can become positive with malignancy before they become enlarged. Other imaging modalities must be used to assess tumor margin and regional lymph nodes (multidetector CT, US and MRI).

Recently, improved CT imaging with multidetector CT scanners has shown an improvement in accuracy of staging. The use of multidetector scanners with rectal distention by an air balloon device, and both sagittal and coronal reconstruction images, improve tumor detection (90% to 100% accurate) and detection of depth of tumor invasion over conventional CT.

Endorectal ultrasound (EUS) can accurately (80% to 95%) stage mural depth of tumor, and can also offer EUS-guided fine needle biopsy of masses or even abnormal sized lymph nodes. Please see in-depth article on this modality.

US is user-dependent in its accuracy and is not available in all areas.
MRI with either external detector coil or endorectal coil is a useful means of detecting local invasion of tumor, but faces similar limitations of nodal detection as other modalities.

PET scan imaging utilizes chemical and metabolic changes in tumor tissues. Tumor tissue or lymph nodes are shown as positive uptake. Unfortunately, false positive uptake is also possible. PET lacks spatial resolution, but images can be fused with CT scan images to yield a higher specificity of positive uptake. PET scanning is not readily available in all areas.

To summarize, diagnostic imaging of rectal cancer requires reliable, reproducible examinations which can detect initial stage of disease, as well as serial reassessment for follow up. Many imaging modalities are available, each with individual strength and limitations. By combining multiple studies in an individualized fashion, accurate assessment of rectal cancer can be achieved.

Data from the NCDB Annual Review of Rectal Cancer indicates that Stage I disease is diagnosed most frequently (27%). As illustrated in the accompanying graph, 7% more Stage I cases were diagnosed within AHC Metro Region 34% compared to (27%). More Stage II, Stage III and Stage IV cancers were also diagnosed, whereas the NCDB had 9% more unknown cases.

Rectal Cancer Stage at Diagnosis
Endoscopic Ultrasound in Staging Rectal Cancers: Gimmick or Godsend?

Rectal endoscopic ultrasound (EUS), which is an endoscope equipped with a high-frequency ultrasound probe, has emerged as an accurate imaging test for staging rectal cancer. By providing high-resolution images of tumor depth and lymph node involvement, the information gathered from EUS can assist the clinician in directing therapy for patients with rectal cancer.

Accuracy
Preoperative staging procedures for rectal cancer include computed tomographic (CT) scan, magnetic resonance imaging (MRI) scan, and EUS. The TNM classification is commonly used to stage rectal cancer. T stage involves depth of tumor invasion into the rectal wall, while N and M stages refer to the presence or absence of lymph node and distant metastasis, respectively. For T and N staging, EUS is superior to CT and MRI (Table 1). Although widely accepted as the procedure of choice for loco-regional staging, EUS is by no means a replacement for other imaging tests such as CT scan. Because CT can detect distant metastasis whereas EUS cannot, these 2 modalities are in fact complementary to each other.

Why EUS?
Rectal cancer is highly treatable and often curable by surgery when localized. The prognosis of rectal cancer is primarily related to the degree of tumor depth and the presence or absence of nodal involvement. Accurate staging using EUS can influence therapy by helping to determine which patients may be candidates for preoperative chemotherapy and radiation therapy to maximize the likelihood of resection with clear margins, and which patients may be candidates for local excision or sphincter-preserving operation rather than a permanent colostomy.

All of this sounds great, but in the real world it may not always be as simple. Managing rectal cancer is often challenging, and this is why neoadjuvant therapy is increasingly used in the context of EUS to improve the chance of cure and enhance the quality of life of these patients.

High rate of local recurrence after surgery
The presence of the bony pelvis makes it difficult to obtain wide surgical margins. In those patients with advanced disease, the local recurrence rate following surgery is up to 50% (higher compared to colon
cancer) and often ultimately results in death. Thus, adjuvant or neoadjuvant therapy is utilized to address this issue. Interestingly, preoperative tagging using both CT and EUS results in more frequent use of neoadjuvant therapy than if staging was performed with CT alone. It appears that by upstaging tumors, the information gathered from EUS can change management by directing neoadjuvant therapy to patients who would have been denied of this treatment had they undergone CT alone. This is because CT can inaccurately understage rectal cancer in up to one-third of patients. It is important to understand the phenomenon of upstaging by EUS, because neoadjuvant therapy can diminish local recurrence rates of transmurally infiltrating (T3 or T4) rectal tumors.

In conclusion, EUS is the preoperative staging procedure of choice for rectal cancer because its ability to evaluate tumor depth and lymph node involvement is superior to CT scan or MRI. More importantly, adding EUS to the standard work-up of these patients leads to a change in management (neoadjuvant therapy) in one-third of patients.

### Table 1. Accuracy of EUS, CT scan and MRI in rectal cancer staging

<table>
<thead>
<tr>
<th></th>
<th>T Stage (%)</th>
<th>N Stage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EUS</td>
<td>80 – 95</td>
<td>70 – 75</td>
</tr>
<tr>
<td>CT Scan</td>
<td>65 – 75</td>
<td>55 – 65</td>
</tr>
<tr>
<td>MRI</td>
<td>75 – 85</td>
<td>60 – 65</td>
</tr>
</tbody>
</table>

### Histologies of Rectal Cancer

<table>
<thead>
<tr>
<th>Histology</th>
<th>AHC Metro Region</th>
<th>NCDB:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>66%</td>
<td>67.20%</td>
</tr>
<tr>
<td>Adenocarcinoma in adenomatous polyp</td>
<td>2%</td>
<td>4.6%</td>
</tr>
<tr>
<td>Adenocarcinoma in villous adenoma</td>
<td>2%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Adenocarcinoma in tubulovillous adenoma</td>
<td>16%</td>
<td>7%</td>
</tr>
<tr>
<td>Mucinous adenocarcinoma</td>
<td>2%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Other</td>
<td>12%</td>
<td>15%</td>
</tr>
<tr>
<td>Total</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>
Colorectal carcinoma is the fourth most common cancer in the United States, with approximately 150,000 new cases diagnosed each year. Colorectal carcinoma accounts for approximately 58,000 deaths per year, comprising nearly 15% of all cancer related deaths in the United States. Peak incidence for colorectal carcinoma is age 60 to 70. Less than 20% of cases occur in patients under 50 years of age. Rectal carcinomas are a subset of the colorectal carcinoma group.

The rectum normally measures approximately 12 cm in length. The rectum is covered by peritoneum in front and on both sides in its upper third and only the anterior wall in its middle third. There is no peritoneal covering in the lower third.

The majority of rectal carcinomas are adenocarcinomas. Many patients have dysplastic or "pre-malignant" rectal polyps, which may evolve into adenocarcinoma if left untreated. Dysplastic or adenomatous polyps may have a tubular architectural configuration, a villous architectural configuration or a combination of the two ("tubulovillous adenomas"). Adenomas with high grade dysplasia demonstrate increasing cytologic and architectural atypia. A lesion becomes an invasive adenocarcinoma if glandular invasion into or through the muscularis mucosa is present. Once this occurs, the patient has an invasive adenocarcinoma which must be resected.

Pathologists evaluate many items after receiving a rectal resection specimen. The tissue is "grossed" and tissue sections are placed in cassettes for histologic processing. The end result of this process is the formation of hematoxylin and eosin stained glass slides which are evaluated under a microscope. The following factors are assessed when evaluating rectal adenocarcinomas:

- Histologic grade
- Extent of invasion
- Blood/lymphatic vessel invasion
- Extramural venous invasion
- Perineural invasion
- Peritumoral lymphocytic response
- Specimen margins
- Regional lymph nodes

The histologic grade is defined as follows:

- Well differentiated = > 95% gland forming
- Moderately differentiated = 50% – 94% gland forming
- Poorly differentiated = 5% – 49% gland forming
- Undifferentiated = < 5% gland forming

Extent of invasion is classified as into the submucosa, muscularis propria or beyond the muscularis propria into the subserosa, adjacent adipose tissue or adjacent organs. Simply put, the deeper the tumor invades, the worse the prognosis. Additional adverse prognostic factors include blood/lymphatic vessel invasion, extramural venous invasion and perineural invasion. Metastatic adenocarcinoma in regional lymph nodes is an additional adverse prognostic factor. The tumor is classified as N1 if metastasis is seen in 1 to 3 regional lymph nodes. The tumor is categorized as N2 if there is metastasis in 4 or more regional lymph nodes. Margins are also assessed to ensure that the tumor has been completely resected. Proximal, distal, serosal and radial/mesenteric margins are evaluated.

The information provided by the pathologist concerning the rectal carcinoma patient is incorporated into the formulation of a treatment plan for the patient.
Surgical Treatment of Rectal Cancer

Approximately 40,000 new cases of rectal cancer are diagnosed each year. Although many of these tumors require radical resection, with earlier detection more local procedures are now possible. Advantages of local therapy are preservation of the anal sphincter, avoidance of a colostomy, and avoidance of radical pelvic surgery with improved quality of life.

Initial assessment of intent of surgery (palliative versus curative) must be made, and if curative resection is possible, location and staging of the tumor must be considered. Location of the tumor, proximal two-thirds of the rectum versus distal one-third, is key. For resectable tumors in the proximal to mid rectum, a low anterior resection (LAR) is the procedure of choice. Most cases do not require a proximal colostomy as circular stapling devices (EEA) allow for a very low anastomosis with little technical difficulty. Also, pathologic studies have shown that distal spread beyond two centimeters is extremely rare and, in tumors that do, survival is poor regardless of clear distal margins. This allows for smaller distal margins and resectability of lower rectal tumors. In addition, preoperative chemo and radiation therapies have been shown to reduce the degree of rectal wall invasion and lymph node involvement in up to 70% of patients. Preoperative treatment to “downstage” the tumor is preferred as post operative tissues are relatively ischemic and chemotherapy is not as effective then. With new techniques, smaller distal resection margins and pre-op chemo-radiation, most rectal tumors may be resected with LAR.

Distal rectal tumors have traditionally been treated with the Miles Procedure or APR (abdomino-perineal resection). This involves resection of the rectum, anus and permanent perineal closure with creation of a permanent colostomy. However, patients with limited disease, stages T1-T2 (Table 1), have been successfully treated with sphincter-sparing procedures. Today, staging of early rectal tumors is most accurate with endoscopic ultrasonography.

continued on next page
Table 1.

<table>
<thead>
<tr>
<th>Primary Carcinoma (T)</th>
<th>Metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis In situ</td>
<td>M0 No metastases</td>
</tr>
<tr>
<td>T1 Submucosal invasion</td>
<td>M1 Metastases</td>
</tr>
<tr>
<td>T2 Muscularis propria invasion</td>
<td></td>
</tr>
<tr>
<td>T3 Perirectal fat invasion</td>
<td></td>
</tr>
<tr>
<td>T4 Invasion of adjacent organ</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regional Lymph Nodes (N)</th>
<th>Metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0 No Nodes</td>
<td>M0 No metastases</td>
</tr>
<tr>
<td>N1 1-3 perirectal nodes</td>
<td>M1 Metastases</td>
</tr>
<tr>
<td>N2 &gt;3 regional nodes</td>
<td></td>
</tr>
<tr>
<td>N3 Metastases to node along named vascular trunk</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage</th>
<th>5-yr Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 T1-2, N0, M0</td>
<td>75% – 85%</td>
</tr>
<tr>
<td>2 T3-4, N0, M0</td>
<td>55% – 77%</td>
</tr>
<tr>
<td>3 T1-4, N1-3, M0</td>
<td>30% – 44%</td>
</tr>
<tr>
<td>4 T any, N any, M1</td>
<td>&lt;25%</td>
</tr>
</tbody>
</table>

2McArdle CS, Hole D. Impact of variability among surgeons on post-operative mortality and ultimate survival. BJM 1991;302:1501-1505

Colo-anal anastomosis is performed in younger patients with favorable body habitus and involves rectal resection with careful preservation of the sphincter muscles to anastomose the sigmoid colon to the anal verge. Local/transanal excision is possible if the tumor is small, mobile and superficial. Fulguration uses electrocautery to destroy the tumor through the entire rectal wall. The above mentioned sphincter-sparing procedures, however, must be used in a select group of patients who have been accurately staged at an early stage preoperatively. Understaging can be disastrous as later stage tumors, >T2, have much greater recurrence rates, and in rectal cancer recurrence is usually incurable.

Laparoscopic resections have also recently become an option, however many authors question the possibility of a surgical cure. Of course laparoscopy has an advantage of decreased post-operative pain and shorter hospital stays, however adequacy of lymphadenectomy remains controversial.

In summary, rectal cancers, if resectable, are treated based on their location. Tumors in the proximal two-thirds require LAR. Distal tumors at a late stage and those involving the sphincter muscles require APR, while early stage tumors can be treated with a variety of sphincter-sparing procedures.
A multidisciplinary approach to treating rectal cancer is evident in the Metro Region of Aurora Health Care, as 48% of cases were treated with a combined modality approach.

- 34% were treated with surgery, radiation and chemotherapy vs. 30% nationally.
- 14% were treated with surgery and chemotherapy vs. 4% nationally.
- Surgical resection alone of the primary tumor was done in the majority of the cases reported through the NCDB at 40%. Definitive surgery alone in the Metro Region of Aurora Health Care was 24%. The difference can be accounted for, due to the number of patients with advanced stage at diagnosis.

Graph Key:
- S = Surgery
- C = Chemotherapy
- R = Radiation
- N = No Treatment

Treatment Modalities for Rectal Cancer

Surgical Approach to Rectal Cancers
Chemotherapy for Rectal Cancer

Rectal cancer is a relatively common disease in the United States. Approximately 40,000 patients are diagnosed with this malignancy every year and 8,500 patients die from it. While surgery remains the primary treatment for rectal cancer, this malignancy is rapidly becoming the model for multidisciplinary management of solid tumors. Chemotherapy is an important part of neoadjuvant or pre-operative treatment, as well as adjuvant therapy aimed at eradicating micrometastatic disease. It is the mainstay of palliative treatment of patients with metastatic rectal cancer.

**Adjuvant Therapy**

In contrast to colon cancer, where the failure pattern is predominantly distant metastases, an analysis of site of first failure in patients with rectal cancer indicates an equal distribution locally in the pelvis and distally (liver and lung). Local recurrence is mainly related to difficulties in obtaining optimal surgical clearance of the radial margin. Local failure is a component of first failure in less than 10% of patients with T1-2 disease. This goes up to 30% for T3N0 disease and can be as high as 65% in stage T3-4, N1-2 disease.

A meta-analysis has amply demonstrated that radiation therapy can reduce the rate of local recurrence without necessarily prolonging survival. However, chemotherapy, when added to radiation, can positively influence survival. Clinical trials have established the following facts regarding adjuvant therapy in rectal cancer:

- The risk of local recurrence with chemotherapy plus radiation (CMT) in Stage II/III rectal cancer is 33% versus 55% with surgery alone (GITSG 7175)
- Compared to radiation (RT) alone, CMT reduces the likelihood of distant relapse by 37% and overall death rate by 29% (NCCTG)
- SFU, when given as continuous infusion rather than in bolus fashion during RT, improves the overall survival from 60% to 70% (INT 864751)
- Addition of leucovorin and levamisole, or giving SFU as continuous infusion rather than in bolus fashion before and after RT, does not improve survival (INT 0144)

Therefore, the standard of care is to administer SFU as bolus injection five days in a row, every 28 days for two cycles before radiotherapy, followed by RT plus SFU as continuous infusion, followed by two more cycles of SFU as administered pre-radiotherapy.

**Neoadjuvant Therapy**

Neoadjuvant or pre-operative therapy is utilized to promote tumor regression in patients with distal rectal tumors. The goal of preoperative treatment is to convert the surgical procedure from an APR to sphincter-sparing operation, such as LAR with coloanal anastomosis.
Because of the success of CMT in the post-operative setting, there is intense interest in using this approach neoadjuvantly. Following moderate to high dose RT (45 to 50 Gy), pathological complete response (pCR) occurs in only 6% – 12%, while addition of 5FU based chemotherapy to RT increases the pCR to 16% – 31%. Preliminary data support a beneficial effect of tumor downstaging on both local control and survival. Roswell Park Cancer Institute’s experience presented in May 2003 at the American Society of Clinical Oncology meeting indicates improvement in overall survival in patients who experienced tumor downstaging (Median 45.3 months for the whole group versus 73.2 months for the downstaged group). Downstaging of T status occurred in 33% of patients.

Therefore, all patients with distal rectal cancers, i.e., within 6 cm of the anal verge, who have been determined by endorectal ultrasound to have at least a T3 lesion, are candidates for neoadjuvant chemo-radiotherapy. These patients are treated with RT plus continuous infusion of 5FU.

**Metastatic Disease**

In metastatic colorectal cancer, chemotherapy has been shown to improve quality of life and survival. For many years, 5FU plus leucovorin had been the standard of care. This has a response rate of 15% with median survival of 11 months. Recently reported clinical trials have established the following facts regarding chemotherapy for metastatic colorectal cancer:

- Intravenous 5FU plus leucovorin and oral 5FU (Xeloda) are equivalent in survival and response rate
- Addition of CPT-11 (Camptosar) to 5FU plus leucovorin improves the rate to 30% and survival to 15-16 months.
- Oxaliplatin plus 5FU plus leucovorin is superior in response rate (40% vs. 30%) and survival (19 vs. 15 months) to CPT-11 plus 5FU plus leucovorin

Therefore, 5FU plus leucovorin plus Oxaliplatin/CPT-11 should be the new standard for chemotherapy in this disease, at least for patients with good performance status. Older patients can be treated with oral Xeloda.

**Future Direction**

The incorporation of newer agents such as CPT-11 and Oxaliplatin in adjuvant programs is likely to improve the surgical cure rate seen in Stage II/III rectal cancer. Clinical trials are underway, but it is logical to offer a triple drug combination to younger individuals with good performance status off study.

A phase I/II trial of neoadjuvant FU plus CPT-11 with RT was recently reported with encouraging results. This needs to be explored further, and is still investigational.

In metastatic disease, the addition of Bevacizumab, an angiogenesis inhibitor, to 5FU plus leucovorin plus CPT-11 has been shown to improve survival (20 months) in a recently reported trial. There is also considerable interest in C225, another monoclonal antibody.

Therefore, the treatment of colorectal cancer is entering the molecular age of targeted therapy. This is likely to improve cure rates and survival, and decrease toxicity as treatments in future are more likely to be target specific.
Radiation Therapy for Rectal Cancer

Rectal cancer affects approximately 40,000 people annually. It is estimated that 8,500 people will die this year from rectal cancer. Mortality from rectal cancer has decreased over the past 30 years, possibly because of the earlier diagnosis through screening and/or better treatment modalities.

Surgery remains the primary treatment, with radiation therapy and chemotherapy functioning primarily as adjuvant modalities. Low anterior resection or coloanal anastomosis preserve sphincter function. In cases where an adequate resection would be compromised by the location of the tumor, it is necessary to do an abdominoperineal resection.

In the adjuvant setting, randomized studies have supported combined chemotherapy and radiation therapy. This treatment is indicated for Stage T3-4 or N1-2 disease. Local control with adjuvant treatment is 60% – 90%, with surgery alone at 50% – 75%. Survival at 5 years with adjuvant treatment is 50% – 70%, with surgery alone 25% – 50%. Generally this involves six cycles of postoperative chemotherapy plus concurrent radiation during cycles 3 and 4. The radiation consists of 5-6 weeks of daily treatment utilizing modern radiation therapy techniques.

The standard management for low-lying rectal tumors is abdominoperineal resection. There has been increased interest in the use of radiation therapy in an attempt to preserve anal sphincter function. Strategies include radiation therapy alone, radiation therapy followed by coloanal anastomosis or local excision, local excision followed by radiation therapy and preoperative chemoradiation. These approaches require careful selection of patients for appropriateness.

**Radiation alone:** 5 year survival is 40% – 50% for mobile lesions, 2% – 4% for fixed lesions. Allow 2-4 months after completion of treatment before making a decision regarding salvage resection because these tumors tend to regress slowly. It is estimated that about 25% of potentially resectable tumors undergoing primary radiation therapy achieve durable local control and are able to avoid colostomy. However, the control rates in patients with fixed tumors is poor with radiation alone.

**Local excision** is appropriate in patients with tumors confined to the rectal wall in which there is a low probability of lymph node metastases. The selection criteria is:
- Well or moderately well differentiated histology
• Tumor size less than 4 cm  
• Location 8 cm or less from the anal verge  
• Mobile lesions  
• Not ulcerated  
• No suspicion of perirectal or pre-sacral nodes

Postoperative radiation is not indicated for locally excised T1 tumors unless the margins are compromised or the histology shows poor differentiation or angiolymphatic invasion. Postoperative chemoradiation is advised for T2 lesions. Patients with T3 lesions are generally considered for radical resection.

Preoperative radiation alone: Eleven (11) modern radiation alone trials for resectable lesions have been reported. Only one trial showed survival advantage. The Swedish trial randomized 1,168 patients to either preoperative radiation in which 25 Gy in one week (resected lesions) versus surgery alone. The results showed improvement in survival and local control versus surgery alone. However, these results must be interpreted with caution given that 10 other randomized trials did not show survival advantage.

Preoperative vs. Postoperative radiation: Swedish trial randomized 474 patients, half to preoperatively Z 25.5 Gy in one week vs. 60 Gy split course postoperatively (T3, N1-2). Preoperative radiation arm lead to improved local control but no survival advantage. Also the preoperative arm resulted in decrease in small bowel obstruction, and decreased total grade 3+ non-hematologic toxicity (proctitis, cystitis, skin fibrosis, and nerve symptoms).

Preoperative chemoradiation can be considered in patients who refuse abdominoperineal resection and who are not technically able to undergo local excision because of tumor size (T3-4, N1-2) or anatomic constraints. Transrectal ultrasound is commonly used to stage rectal lesions preoperatively for muscle invasion and nodal involvement. The percentage of patients treated with preoperative radiation or preoperative chemoradiation who are able to ultimately undergo low anterior resection or coloanal anastomosis is quite variable at 30% – 70%. Excellent sphincter functions is reported in 60% – 70% of patients. Recent trials indicate downstaging of both the T stage and the N stage was significantly associated with improved local control of the tumor and disease free survival and overall. All patients with pN0 demonstrated superior survival when compared to pN+ patients. Finally, shrinkage of the tumor was directly associated with superior survival.

Preoperative vs. Postoperative Chemoradiation: Currently the NSABP R-03 in USA is randomizing neoadjuvant 5FU/Leucovorin/pelvic XRT vs. 5FU/Leucovorin/pelvic XRT. The primary purpose of this study is to determine whether the administration of preoperative chemotherapy (SFU + Leucovorin) and radiotherapy, followed by postoperative chemotherapy is more effective than the administration of postoperative chemotherapy and radiotherapy in improving the disease-free survival and survival of patients with operable carcinoma of the rectum. The preliminary data (116 patients) suggests that the preoperative chemotherapy and radiation therapy regimen used are at least as safe and tolerable as standard postoperative treatment. There was a trend to tumor downstaging and sphincter preservation in the preoperative arm. Whether this arm will have greater or lesser survival and long-term toxicity awaits the completion of the study.
Five-Year Survival Rates for Rectal Cancer Cases

In the Metro Region of Aurora Health Care, the five-year overall survival rate for those with rectal cancer is slightly higher than that published by the National Cancer Database (NCDB), but not statistically significant. See graph and table below.

![Graph and Table]

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<tr>
<td>NCDB</td>
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2002 and 2003 Metro Region Cancer Data

New Cases Breakdown – Analytical vs. Non-Analytical
(First Course vs. Subsequent Rx)

2002 and 2003 Analytical vs. Non-Analytical Breakdown of New Cancer Cases by Year of Diagnosis

Benchmark Comparisons – Top 5 Sites

When comparing the top five sites in order of decreasing frequency in the Metro Region to the incidence of cancer cases reported by the state and the National Cancer Data Base (NCDB), it is noted that the Metro Region sees a higher percentage of lung and leukemia cases, fewer prostate cases than both the state and the nation, and a relatively equal number of breast and colorectal cases.
Race in 2002 and 2003

Hospital Review of new cases in 2002 and 2003 shows the population by race served at St. Luke’s Medical Center, West Allis Memorial Hospital and Aurora Medical Center in Hartford is predominantly white. By contrast, the central city location of Aurora Sinai Medical Center serves a more diverse population with the majority being of African American descent.

Male vs. Female – Sex by Facility

In reviewing the percentages of males vs. females over a two-year time frame at each facility, you can see that many more females are being seen at three of the four facilities and is quite a significant difference compared to the NCDB percentages. This is reflective of the fine women’s services provided; however, may indicate a need for men to be educated about the importance of regular check-ups and screening.