It is rewarding to see how our excellent, state-of-the-art cancer programs are evolving and growing, as we look to a future Avera Cancer Institute that is becoming world-class in its offerings.

As breast cancer is the number one diagnosis in our cancer program, we have done tremendous work to bring breast health care to a new level. I am proud of the physicians and staff who have been on the ground floor in the development of a comprehensive breast health program. Physician leadership has been outstanding through a multidisciplinary work group that includes primary care, gynecology, radiology, pathology, surgery, plastic surgery, medical oncology and radiation oncology. Carole Chell, CNP, has accepted the position of breast health navigator. She will assist patients who have been diagnosed with breast cancer through the journey ensuring that they get the needed support, education and services. Dr. Amy Krie and Carole Chell have also begun the important work of offering a high-risk breast clinic. Genetic testing and advanced detection methods are among options offered to these patients.

Survivorship is another key area of focus. There are over 10 million cancer survivors today in the United States. We plan to be proactive in our service to them in various ways, including the establishment of survivorship plans of care for our patients. These plans will outline the critical information related to the patient’s diagnosis and treatment, as well as ongoing care. Patients will receive a copy of this important document, and can take it wherever they might go in the future.

We continue to have a strong presence in our community related to the prevention and early detection of cancer.

- **Our October Think Pink campaign** to raise breast cancer awareness was successful in helping women to understand the importance of early detection. In 2006, during October alone, mammography appointments increased by 67 percent over average. Mammography also increased during the months of November, December and January.
- **During our SunSmart campaign**, we launched education efforts about the importance of skin protection for the prevention of skin cancer. We coordinated and participated in a city-wide Melanoma Monday event through a partnership with Lewis Drug and Sioux Falls dermatologists.
- **Our ColonCare education program** stressed the importance of colon cancer screening.
- **Our Prostate screening event** in partnership with urology specialists allowed men to be screened free of charge.

All of these programs have been initiated through all 52 of our clinics in the region as well as locally through marketing and health fairs.

Thank you to the physicians, clinical staff and support staff of the Avera Cancer Institute, and thanks also to our local and regional referring physicians. Together, we are providing state-of-the-art, comprehensive cancer care in a caring environment that’s close to home.

Ellison Kalda, MD
Cancer Committee Chair
In years to come, as we walk in and around the new, world-class Avera Cancer Institute building on the Avera McKennan campus, we’ll look back on the year 2007 as the time when significant planning took place to lay the groundwork on this exciting project.

The goal of our planning has been to create an environment that is an extension of the Avera ministry of healing. We’ll have additional space and state-of-the-art technology for the physical treatment of patients, but also for programs that will allow restoration of health and wholeness in emotional, spiritual and social realms.

We’re thankful for the dedication of the physicians, staff, community members and most of all our patients who have joined in on this investment in the future.

In the meantime, we continue to provide our patients with the highest quality of clinical excellence as we strive toward a complete scope of cancer care, including elements of integrative medicine, survivor care, and continued efforts toward education, prevention and early detection.

We’re proud that in 2006, Avera McKennan along with the Avera Cancer Institute received approval from the American College of Surgeons Commission on Cancer as a Community Hospital Comprehensive Cancer Program with Commendation. This represents the high level of dedication of our physicians and staff as well as the outstanding quality of our cancer program. This year marks the 21st year our cancer program has been approved.

I’d like to include a word of thanks to the community for their outpouring of support to make our 19th annual Avera Race Against Breast Cancer a success. More than 3,700 participants came out for the event in support of cancer survivors. We especially appreciate the “Think Pink” ladies – a special group of breast cancer survivors who are willing to share their experiences, and the important message of early detection.

We have a phenomenal future ahead of us as our world-class cancer care program takes shape. For all the reasons you’ll read about within this report, patients within our region need “look no further” than the Avera Cancer Institute for the best in cancer care.

Fred Slunecka
Regional President, Avera McKennan

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For more than 17 years, the Avera Cancer Institute and Avera McKennan Hospital & University Health Center have been improving the health of people with cancer through comprehensive adult and pediatric oncology services. The residents of our region need look no further than Avera for state-of-the-art prevention, diagnosis, treatment, technology, support and consultation in a caring environment.

The Avera Cancer Institute’s cancer specialists are committed to the fight against cancer. Our expert team focuses exclusively on cancer and works with patients every step of the way to ensure the most effective, personalized treatment. Working alongside our experienced medical team are more than 20 nurses who hold the Oncology Certified Nurse designation, an indication of additional education and tested knowledge of oncology nursing.

The proof can be found in our results. We are the region’s first recipient of the American Cancer Society’s Corporate Crown Award, which recognizes leadership, initiative, program creativity and an overall positive impact on the effects of cancer for citizens of the South Dakota region.

The Avera McKennan Cancer Program also has earned national approval from the Commission on Cancer of the American College of Surgeons for more than 20 years. The designation is only awarded to facilities that have shown a commitment to providing the best in cancer diagnosis and treatment. To meet the standards necessary to gain approval from the Commission on Cancer, each cancer program must undergo a rigorous on-site review every three years.

COMPREHENSIVE CANCER CARE

Our Mission

Avera Cancer Institute is dedicated to providing the highest quality of care through prevention and early detection, evidence-based therapies and a multidisciplinary approach guided by the philosophy of healing the whole person.
According to the Commission on Cancer, receiving care through the Avera McKennan Cancer Program means that patients have access to:

- Quality care close to home.
- Comprehensive care offering a range of technologically advanced, state-of-the-art services and equipment.
- A multi-specialty team approach to determine the best-possible treatment options.
- Cancer-related information, education and support.
- A cancer registry that collects data on cancer type, stage and treatment results offering lifelong patient follow-up.
- Continuous monitoring and enhanced care.
- Information about ongoing cancer clinical trials and new treatment options.

As the area’s leader in cancer care, we are at the forefront of all aspects of fighting the disease. We offer:

- The region’s first comprehensive cancer program located in one facility, providing more convenience for patients and their families.
- The only bone marrow transplant program and National Marrow Donor Collection Center in South Dakota.
- Advanced radiation therapy and brachytherapy for breast and prostate cancer.
- Treatment of brain tumors using stereotactic radiation therapy.
- Cancer support groups, including the only bone marrow transplant support group in South Dakota.
- The Care Store and Care Store Salon for cancer patients and families.
- Our community Cancer Resource Library, providing educational materials and a video viewing area in a relaxing environment.
- The region’s only Cancer Fitness Program providing rehabilitation to people during or after cancer treatment by certified cancer rehabilitation specialists.

CARE CONNECTION

With one phone call, physicians can connect their patients to a comprehensive team of physicians, nurses, social workers and patient advocates who will care for them during cancer treatment. Patients are seen as quickly as possible to address their physical and emotional needs. The Avera Cancer Institute not only ensures timely physician consultation, but is committed to meeting the physical, emotional and spiritual needs of patients and their families undergoing cancer treatment.

First the patient will meet with a hematologist or oncologist and their nurse, who will:

- Review the diagnosis with the patient
- Outline the next steps in cancer treatment such as diagnostic testing and treatment options

Social workers and patient advocates meet with the patient to:

- Provide a tour through the Avera Cancer Institute

Oncology social workers provide education, facilitate support groups and are available for individual counseling with oncology patients as well as their family members. Support groups help people affected by cancer feel less alone while improving their ability to deal with cancer and the lifestyle changes that accompany the disease.

Cancer cannot be fought alone. Support helps patients cope with stress and resolve difficult changes, in order to focus their energy on becoming well.
Battling cancer requires experienced specialists, the latest technology and a variety of treatment options. Just as important is a team that understands each patient’s needs and offers compassionate care.

Our highly-skilled team of physicians, nurses, social workers, pharmacists and patient advocates develops individual treatment plans for patients with conditions including:

- Solid tumors
- Lymphoma
- Multiple myeloma
- Hypercoagulable states
- Coagulation disorders

We also provide palliative care and pain control for patients with such conditions.
The 19th Avera Race Against Breast Cancer, held May 12, 2007, exceeded expectations to become the largest and most successful event ever. Approximately 3,700 people registered for the Race, an increase of 1,400 over the 2006 event. Donations exceeded $232,000 compared to a total of $160,000 raised the previous year. All proceeds go toward the enhancement of cancer detection, treatment and survivor care for people in Sioux Falls and neighboring communities. Funds from the 2007 Race will help establish integrative therapies and additional navigation services which assist women newly diagnosed with breast cancer. Donations will also go toward sustaining many of the programs already in place.

Full-field digital mammography at the Avera McKennan Breast Care Center offers patients the most advanced cancer screening technology available. Digital mammography provides a clearer, state-of-the-art image of the breast, which means better diagnosis and better treatment.

“Currently, mammograms are the best test we have for screening the population for breast cancer,” said Dr. Josie Alpers, director of mammography at Avera McKennan. “However, at least 10 percent of breast cancers are not found by traditional mammography. That’s why improvements to mammography are so vital.”

Turnaround time has been significantly reduced by up to 50 percent as compared to conventional mammography. From a patient’s perspective, digital mammography at Avera McKennan is now a more comfortable experience, with the use of the Soft-Touch MammoPad, a single-use foam cushion.

Based on research from the American College of Radiology incorporating 50,000 participants, digital mammography detects 15 percent to 28 percent more breast cancer in women with dense breast tissue. Additionally, it is an excellent screening measure for women younger than 50 and those who are premenopausal.
In association with Avera McKennan’s Transplant Institute, Avera Hematology and Transplant provides the region’s only bone marrow transplant program, through which people from a five-state area receive world-class care.

Bone marrow transplant is a standardized form of therapy for malignant and non-malignant conditions including:

- Acute and chronic leukemia
- Aplastic anemia
- Multiple myeloma
- Germ cell cancers
- Myelodysplastic syndromes
- Hodgkin’s and non-Hodgkin’s lymphoma

With 10 years of patient care, outcomes of the Avera McKennan Bone Marrow Transplant Program meet or exceed national and international standards for quality. The program is fully accredited.
In 1998, Avera McKennan made a commitment to expand our involvement in clinical drug and medical device research by establishing a separate department for research. Now called the Avera Research Institute, it provides complete coordination of Phase I-IV clinical research studies. The Avera Research Institute allows professionals with experience in working with clinical trials to ensure timely enrollment of patients, strict compliance with protocols and exacting documentations. Carefully conducted clinical studies are the fastest and safest way to find treatments that work.

Clinical research in the area of oncology has been a major area of growth in the Avera Research Institute. The Institute placed the first patient in the world on a graft versus host disease study for post bone marrow transplant patients, and in 2007 was the first center in the world to enroll patients in a new lung cancer study. Physicians in 2007 had access to a number of studies sponsored by the National Cancer Institute as well as industry-sponsored studies in areas such as multiple myeloma, leukemia, colorectal cancer, and cancers of the breast, lung and prostate.

To learn more, go to www.avery-research.org.

**MEDICAL X-RAY CENTER**

Radiation therapy is a common treatment for people with cancer. This approach can be used with other treatments, including surgery or chemotherapy.

Our highly experienced physicians and team of professionals understand each patient has individual needs and focus on the best treatment plan to meet those needs. We follow the treatment process closely and monitor and treat side effects to ensure patients maintain the highest possible quality of life.

Treatment options include:
- External beam radiation therapy
- Intensity modulated radiation therapy
- High-dose rate brachytherapy
- Prostate seed implantation
- X-Knife stereotactic radiosurgery
- Total body irradiation
- Mammosite breast brachytherapy

**AVERA RESEARCH INSTITUTE**

The Avera Cancer Institute along with Avera McKennan Hospital & University Health Center, has an impressive history of participating in national research efforts.

In 1998, Avera McKennan made a commitment to expand our involvement in clinical drug and medical device research by establishing a separate department for research. Now called the Avera Research Institute, it provides complete coordination of Phase I-IV clinical research studies. The Avera Research Institute allows professionals with experience in working with clinical trials to ensure timely enrollment of patients, strict compliance with protocols and exacting documentations. Carefully conducted clinical studies are the fastest and safest way to find treatments that work.

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To learn more, go to www.avery-research.org.
The Avera Cancer Institute, in partnership with the Avera McKennan Fitness Center, offers a unique Cancer Fitness Program to help patients manage their symptoms and cope with the effects of treatments. Exercise has been proven to have a profound impact on the recovery process in patients with cancer, both physically and emotionally. It improves the body’s ability to be efficient in performing daily functions and allows the body to respond better to cancer treatments, with fewer side effects and better sleep and rest patterns. Most importantly, physical exercise can have a positive impact on cancer patients’ quality of life.

Our team of physicians, nurses and social workers link patients and their families to many additional services, including:

- Dietary consultation
- Physical, speech and occupational therapies
- Financial assistance

OBSTETRICS & GYNECOLOGY AND GYNECOLOGICAL ONCOLOGY

Dr. Samir, Dr. Rojas and their staff provide patients with the most advanced women’s health care available, offering evaluation, diagnosis and treatment for women with gynecological cancers. The expert team uses combined therapies to treat cancer, including surgery, chemotherapy and radiation therapy.

CANCER CARE SPECIALISTS

Samir Abu-Ghazaleh, MD, FACOG, FACS
Luis Rojas, MD
Christina Gant, CNP

CANCER FITNESS PROGRAM

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- Financial assistance

AVERA CHILDREN’S HOSPITAL & CLINICS

The specialists at Avera Children’s provide oncology and hematology care for children who have been diagnosed with childhood cancers, especially acute leukemia, hemophilia or other blood diseases.

Our physicians, nurses, social worker and pharmacists work together to establish the best individual treatment plan for each child. Our team was the first to provide this care in South Dakota and we continue to be the leader in pediatric oncology.

CANCER CARE SPECIALISTS

Marwan D. Hanna, MD
PALLIATIVE CARE

The Palliative Care Team at Avera McKennan addresses pain or other symptoms to people of any age, with the goal of providing the best comfort and quality of life possible for those living with a life-threatening illness.

The team assists families in making decisions about their care and treatment, and then ensuring that care is received. This team also provides answers, assistance and emotional support to patients and families who are facing difficult medical decisions.

DOUGHERTY HOSPICE HOUSE

Just completed in November 2007, the new Dougherty Hospice House is the largest Hospice residence in the state of South Dakota, and the only service of its kind in the Sioux Falls area. All levels of Hospice care, from residential to acute, are provided in an environment where patients and their families can enjoy the comforts of home with the needed level of end-of-life care.

The Dougherty Hospice House is over 25,000 square feet in size, with beautifully landscaped surroundings. Sixteen private patient rooms are complete with a full bath and adjoining family room. Each family suite is furnished with a fireplace, flat screen television, a table for games or dining, and comfortable furniture which converts for sleeping. In addition, there is a meditation room, sunroom, resource library for families, dining area, living room, and children’s play area. Not only are medical needs addressed in the design, such as oxygen connections in the walls near patient beds, but also psychosocial needs, such as having family nearby, seeing the outdoors through ample windows and the setting of a calming, beautiful décor.
Multiple myeloma is a form of cancer which is comprised of plasma cells. The plasma cell is a type of cell that produces antibodies after exposure to an antigen and is derived from a B-lymphocyte. These cells regulate natural breakdown and synthesis of new bone as well as synthesizing compounds known as cytokines that can mediate inflammation. Plasma cells are also important in maintaining a part of our immune system known as humoral immunity. Plasma cells typically produce one of three types of immunoglobulin or types of antibodies, known as either IgM, IgG or IgA. When functioning normally, antibodies recognize a wide variety of different antigens or targets and work with other cells in the body to destroy what the body recognizes as foreign. Each immunoglobulin protein has a slightly unique shape due to a diversity in the cell’s genetic sequence.

When this cell proliferates abnormally, a population of plasma cells that all synthesize the exact same immunoglobulin protein is formed. This abnormal appearing protein can be detected in the blood and is known as a monoclonal spike. The monoclonal spike then is simply an elevated level of identical immunoglobulin protein. A monoclonal spike is the hallmark of a group of disorders broadly termed plasma cell dyscrasias, of which multiple myeloma is a part.

There are approximately 20,000 new cases of multiple myeloma yearly (www.nci.gov) and 10,790 deaths yearly. This would make it a relatively rare type of cancer but one of the more common hematological cancers with an incidence of approximately three cases per 100,000 patients per year. The median age at diagnosis is 66 years old, with 38 percent of patients diagnosed with this disease older than 70 years of age. Approximately 70 percent of patients are older than age 60. There is a slight predilection for males more than females with 59 percent of patients diagnosed being male (Mayo Clin Proc 2003; 78: 21). Risk factors are not well understood. Age is the most important, 98 percent of patients are older than 40. Radiation may also have a role. Chernobyl cleanup crews reported an increase of two-fold in their incidence of myeloma. Other risk factors include race, as African Americans have a two-fold higher risk for unclear reasons. The disorder known as monoclonal gammopathy of unknown significance (MGUS) is also a risk for myeloma as 1 percent of these patients per year develop a plasma cell malignancy.

Family history of multiple myeloma is not believed to be important in this disease as a risk factor. Only 2 percent of patients with myeloma have a first-degree relative with myeloma. A family history of malignancy may still be of significance, as 42 percent of myeloma patients did have cancer in a first-degree relative (Mayo Clin Proc 2003; 78: 21).
As described above, myeloma typically arises from a mature B-lymphocyte cell that has been activated. Plasma cells typically live in the bone marrow. People who develop multiple myeloma frequently seek medical attention for bony pain, which has developed from pockets or collections of these plasma cells destroying the bone. A large collection or pocket of plasma cells is known as a plasmacytoma. Approximately 66 percent of patients diagnosed with multiple myeloma have lytic lesions of the bone at diagnosis. About 26 percent have a bony fracture as a result of myeloma. Other patients have less focal bony lesions and have a more diffuse process, resulting in diffuse osteoporosis with no lytic lesions, seen in about 23 percent of patients. The most common initial complaint of a person diagnosed with myeloma was bone pain (58 percent), followed by fatigue (32 percent) and weight loss (24 percent) (Mayo Clin Proc 2003; 78: 21).

Renal dysfunction is quite common in patients with multiple myeloma, up to 48 percent. The large excess of immunoglobulins produced can be difficult for the kidney to process effectively, leading to a decrease in the kidneys' ability to filter the blood. The most common problem that people with myeloma have in their kidneys is related to formation of a “cast” or conglomerate of antibody that blocks the renal tubules in about 40 percent to 60 percent of patients. Patients can also have precipitation of the immunoglobulin into “sheets” of protein that can be difficult to break down. These “sheets” of protein are called amyloid and can result in diffuse renal damage. Other causes for renal failure are related to the decreased reserve of function that the kidneys retain as a result of damage from the immunoglobulin. Patients with myeloma are especially sensitive to dehydration which can cause acute tubular necrosis. Also, contrast dye given intravenously can precipitate light chains in the renal tubules and causes renal failure in about 1.5 percent of people with myeloma. Other causes of renal failure include uric acid nephropathy, plasma cell infiltration and damage from non-steroidal anti-inflammatory drugs, such as ibuprofen.

Anemia is also common in multiple myeloma, with 72 percent of patients having a hemoglobin less than 12 and 35 percent with a hemoglobin less than 10. The other blood counts such as the white cell line and the platelets are most often normal but can be abnormal about 20 percent and 5 percent of the time, respectively.

Diagnostic criteria for multiple myeloma are listed in Tables 1 and 2. The World Health Organization (WHO) criteria specify that at least one major and one minor criteria, or three minor criteria, be present.
Treatment of multiple myeloma is generally initiated to control symptoms. Symptoms are typically from one of four different areas: calcium elevation, renal insufficiency, anemia and bone lesions. If the pathologic criteria for multiple myeloma are met, treatment is initiated for symptomatic disease or for disease that is expected to cause symptoms imminently.

With the exception of allogeneic stem cell transplantation, multiple myeloma has generally not been regarded as curable. There have been a wide variety of treatments and approaches to this disease over the years that have led to a significant improvement in survival rates. The median survival without treatment is approximately seven months. In the 1960s, treatment with melphalan and prednisone improved this median survival to 24-36 months. Newer approaches tried in the 1990s with high-dose chemotherapy in combination with stem cell support significantly improved median survival over standard therapy in individuals younger than age 65. In the last five years, more experience with autologous transplants has shown that even patients as old as 70 can still safely undergo transplant. At the same time, new drugs such as lenalidomide and bortezemib have been more effective in treating patients, including patients with high-risk disease as defined by specific cytogenetic abnormalities.

As our knowledge of the disease expands and more effective drugs are developed, the treatment of multiple myeloma is getting more complicated. Greater understanding of the importance of the genetic mutations is allowing us to target patients with high risk disease earlier for more aggressive therapy. Aggressive therapy typically includes stem cell transplantation. Autologous transplantation involves reinfusion of a patient’s own hematopoietic stem cells collected prior to high-dose chemotherapy. Allogeneic transplantation involves collecting hematopoietic stem cells from another person and re-infusing these after high-dose chemotherapy. The role of autologous transplantation has been prominent over the last decade. However, with new drugs available, timing of the transplant is becoming controversial. Autologous transplantation has been shown to extend progression-free survival, translating into increased quality of life as patients often do not require maintenance chemotherapy after transplant. For patients who do not obtain a complete remission from single transplant, tandem autologous transplants have been shown to have a role (N Engl J Med 2003; 349: 2495-2502). Tandem autologous stem cell transplant delivers two transplants using high-dose chemotherapy within six months of each other. Additionally, allogeneic transplantation has been shown to be effective at prolonging survival in selected populations of patients with myeloma (N Engl J Med 2007; 356: 1110-20).

---

**Diagnostic Criteria for Symptomatic Multiple Myeloma**

1. Monoclonal plasma cells in the bone marrow ≥ 1%, and/or presence of a bone marrow plasmacytosis
2. Monoclonal plasma protein in the serum and/or urine
3. Myeloma-related organ dysfunction (1 or more)

<table>
<thead>
<tr>
<th>Organ dysfunction</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium elevation</td>
<td>Serum calcium &gt;10.5 mg/dL or LLN</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>Serum creatinine &gt;2 mg/dL</td>
</tr>
<tr>
<td>Anemia</td>
<td>Hb &lt; normal</td>
</tr>
<tr>
<td>Bone</td>
<td>Lytic bone lesions or osteoporosis</td>
</tr>
</tbody>
</table>

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**TABLE 2**

Strategies utilizing tandem transplant with autologous stem cell transplant followed by allogeneic transplant are being done more frequently in selected patients as survival advantages have been demonstrated.

**CONCLUSION**

Multiple myeloma is a cancer that typically requires careful evaluation. Management is complex and entails using old “standards” of therapy as well as newer medications. Utilization of transplantation to treat this disease in eligible patients is the standard of care as it has been shown to improve the quality of life for people with this disease. However, timing of this procedure can be controversial. Newer drugs such as lenalidomide and bortezomib give us additional treatment options. These, and other drugs utilized as single agent or in combination regimens, offer hope for even better treatment options and quality of life for people with this disease in the future.

Statistics and survival curves for patients treated at Avera McKennan are listed below.

**FIVE YEAR RELATIVE SURVIVAL RATE BY YEAR OF DIAGNOSIS FOR MULTIPLE MYELOMA**

<table>
<thead>
<tr>
<th>Source</th>
<th>All Ages</th>
<th>Age &lt; 65</th>
<th>Age &gt; 65</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Cancer Institute</td>
<td>1996-2003</td>
<td>33.5%</td>
<td>45%</td>
</tr>
<tr>
<td>American Cancer Society</td>
<td></td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>Avera McKennan</td>
<td>2000-2003</td>
<td>33%</td>
<td>44%</td>
</tr>
</tbody>
</table>
Breast cancer remains the most common malignancy in women. A significant proportion of these women will be offered adjuvant therapy following their surgery in an attempt to decrease rates of recurrence and improve survival. One of the mysteries of breast cancer is that doctors cannot always accurately predict which women will have a higher risk that their cancer will come back. Currently oncologists use several prognostic features including tumor size, the number of lymph nodes involved, and the grade of the tumor to determine how “at risk” a woman is for recurrence of her disease over the next 10 years. From that information, decisions are made regarding the need for adjuvant systemic therapy. Inherent in the adjuvant treatment of breast cancer is the fact that we are treating a large number of women with chemotherapy to benefit a few. Otherwise stated, we are exposing many women to unnecessary toxicities, both acute and chronic.

The focus more recently in breast cancer has been to move away from a “one-size-fits-all” approach to care. This new type of prediction focuses on the molecular/genetic aspects of breast cancers rather than the previous microscopic features. Gene expression studies have led to new classifications of cancers. Four main types of breast cancers have emerged from this. The first two types, Luminal A and Luminal B types, tend to be estrogen receptor positive. They are very often low grade. Such luminal tumors tend to have a better overall prognosis and are often much slower growing. The third type is the HER2 type. These cancers overexpress Her2/neu. They tend to be high grade and grow very rapidly. Overall they tend to have a poor prognosis. Recent advances with targeted agents such as traztuzumab and lapatanib have drastically improved survival with these tumors. The fourth type is the basal type. These tumors tend to be estrogen and progesterone receptor negative with no overexpression of Her2/neu. These are the so-called “triple negative” tumors. This type is common among women with BRCA gene mutations and young African-American women and also tends to be a very aggressive type of cancer with a poor prognosis.

One such molecular-based approach to risk stratifying breast cancer patients is now commercially available. The OncotypeDX assay has been validated as quantifying the likelihood of distant recurrence in Tamoxifen-treated patients with node-negative, estrogen receptor-positive breast cancer. The assay is an RT-PCR based method, which looks at the molecular expression of 16 cancer-related genes to predict a woman’s risk for distant recurrence. The gene panel includes several genes related to proliferation, invasion, Her2/neu and
estrogen receptor overexpression. From this analysis a patient is provided with a recurrence score, which correlates with the patient's rate of distant recurrence at 10 years.

The study has been clinically validated using archival tissue from the NSABP B14 trial. Results demonstrate that OncotypeDX is an accurate and reliable predictor of breast cancer recurrence. In fact, the recurrence score was found to be superior to age, tumor size or tumor grade in predicting the risk of relapse. The recurrence score has also been found to correlate with the magnitude of chemotherapy benefit with low risk patients deriving no benefit from adjuvant chemotherapy and high risk patients deriving a 28 percent absolute benefit from chemotherapy. Thus the score not only quantifies the risk of recurrence, but is also useful for predicting the magnitude of chemotherapy benefit.

A similar study using MammaPrint has also been FDA approved for women under the age of 61 with lymph node-negative tumors. Unfortunately this test is not available in the United States off clinical trial and requires fresh frozen tissue for analysis as opposed to the OncotypeDX assay, which can be used on formalin-fixed tissue.

Both the OncotypeDX and MammaPrint gene expression tools are currently undergoing prospective validation trials in the United States. The test remains available commercially and is now covered by the majority of insurance providers including Medicaid. In addition, the updated recommendations from the American Society of Clinical Oncology in 2007 state that in newly-diagnosed patients with node-negative, estrogen receptor positive breast cancer, the OncotypeDX assay can be used to predict the risk of recurrence in patients to identify which groups may not benefit from chemotherapy.

The TAILORx Trial is currently accruing patients at the Avera Cancer Institute through the Sioux Community Cancer Consortium and is being conducted throughout the United States. Such gene expression assays will likely continue to be used in breast cancer, and new developments are under way in several other cancers as well, in an attempt to better apply adjuvant therapies to the patients who will truly benefit.


2006 STATISTICAL REVIEW

TOTAL CASES

0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200

192  BREAST
188  LUNG
110  HEMATOPOIETIC
109  PROSTATE
 73  COLON
 50  ENDOMETRIUM
 50  SKIN
 48  LYMPH NODES
 43  KIDNEY
 40  BLADDER
 35  PANCREAS
 29  BRAIN/CNS
 23  OVARY
 22  THYROID
 21  RECTOSIGMOID/RECTUM
 20  UNKNOWN PRIMARY
 15  HEAD AND NECK
 15  STOMACH
 13  CERVIX
 12  ESOPHAGUS
 10  CONNECTIVE/SOFT TISSUE
 10  VULVA
  9  BILIARY TRACT
  8  HEPATOBLIARY
  7  SMALL INTESTINE
  6  TESTIS
  5  BONES/JOINTS
  5  PERITONEUM
  4  PAROTID GLAND
  3  VAGINA
  3  OTHER GU
  2  OTHER GI
  2  PENIS
  2  URETER
  2  OTHER SITE NOS

AVERA MCKENNA/AVERA CANCER INSTITUTE

DIAGNOSIS BY SITE* AND SEX

1,186 ANALYTIC** CASES

637 FEMALE (53.7%)
549 MALE (46.3%)

* EXCLUDES CARCINOMA IN SITU OF CERVIX AND BENIGN/BORDERLINE CASES.
** ANALYTIC CASES ARE DIAGNOSED OR INITIALLY TREATED AT AVERA MCKENNA/AVERA CANCER INSTITUTE/SIOUX FALLS AVERA SPECIALTY CLINICS.
### TOP 10 SITES, AVERA MCKENNAN CANCER REGISTRY

<table>
<thead>
<tr>
<th>Primary Site</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder</td>
<td>29</td>
<td>24</td>
<td>35</td>
<td>40</td>
<td>128</td>
</tr>
<tr>
<td>Breast</td>
<td>192</td>
<td>164</td>
<td>188</td>
<td>192</td>
<td>736</td>
</tr>
<tr>
<td>Bronchus &amp; Lung</td>
<td>157</td>
<td>166</td>
<td>185</td>
<td>188</td>
<td>696</td>
</tr>
<tr>
<td>Colon</td>
<td>85</td>
<td>94</td>
<td>80</td>
<td>73</td>
<td>332</td>
</tr>
<tr>
<td>Corpus Uteri</td>
<td>61</td>
<td>47</td>
<td>56</td>
<td>50</td>
<td>214</td>
</tr>
<tr>
<td>Hematopoietic &amp; Reticuloendo System</td>
<td>96</td>
<td>127</td>
<td>115</td>
<td>110</td>
<td>448</td>
</tr>
<tr>
<td>Kidney</td>
<td>32</td>
<td>25</td>
<td>32</td>
<td>39</td>
<td>128</td>
</tr>
<tr>
<td>Lymph Nodes</td>
<td>46</td>
<td>37</td>
<td>50</td>
<td>48</td>
<td>181</td>
</tr>
<tr>
<td>Prostate Gland</td>
<td>108</td>
<td>90</td>
<td>93</td>
<td>109</td>
<td>400</td>
</tr>
<tr>
<td>Skin</td>
<td>22</td>
<td>32</td>
<td>43</td>
<td>50</td>
<td>147</td>
</tr>
<tr>
<td>Total</td>
<td>828</td>
<td>806</td>
<td>877</td>
<td>899</td>
<td>3,410</td>
</tr>
<tr>
<td>Total Cases by Year</td>
<td>1,130</td>
<td>1,142</td>
<td>1,221</td>
<td>1,208</td>
<td>4,701</td>
</tr>
</tbody>
</table>

![Bar chart showing counts per site and year](image)
The Avera Cancer Institute – bringing care, hope and healing to your community with caring physicians seeing cancer patients in the communities of:

- Aberdeen, S.D.
- Estherville, Iowa
- Luverne, Minn.
- Milbank, S.D.
- Pipestone, Minn.
- Rock Valley, Iowa
- Spirit Lake, Iowa
- Winner, S.D.
- Brookings, S.D.
- Hendricks, Minn.
- Marshall, Minn.
- Pierre, S.D.
- Platte, S.D.
- Sioux Center, Iowa
- Tyler, Minn.
- Worthington, Minn.

The Avera Regional Cancer Centers also include:

- Avera Queen of Peace Hospital, Mitchell, S.D.
- Avera Sacred Heart Hospital, Yankton, S.D.
- Avera St. Luke’s Hospital, Aberdeen, S.D.

Learn more about the Avera Cancer Institute – healing through compassion and technology in your community. Please call (605) 322-3000 or (800) 657-4377, or visit www.averacancer.org.