
It really does matter where you go.
Riverside Cancer Services
2008 ANNUAL REVIEW

2008
Oncology Committee Members

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Michael Peyser, MD, Cancer Liaison Physician ..... *Surgical Oncology*
Steven Scott, MD ..... *Cardiothoracic Surgery*
Christine Marcuson, MD ..... *Dermatology*
Carl Lindemann, MD ..... *Family Practice*
Marshall Cross, MD ..... *General Surgery*
William Irvin, MD ..... *GYN Oncology*
Mark Ellis, MD ..... *Medical Oncology*
John Mattern, II, DO ..... *Medical Oncology*
Guy Tillinghast, MD ..... *Medical Oncology*
Mashour Yousef, MD ..... *Medical Oncology*
John C. Maddox, MD ..... *Pathology*
Michael Schwartz, MD ..... *Pathology*
Larry Davis, Pharm.D ..... *Pharmacy*
Lori Gillespie, MD ..... *Radiation Oncology*
Curtis Stoldt, DO ..... *Radiology*
Scott Burgess, MD ..... *Urology*
Richard Rento, MD ..... *Urology*
Faye Petro Gargiulo ..... *Vice President, Physician/Service Line Development*
Gwen Hartzog ..... *Vice President, Patient Care Services/CNO*
Carrie Schmidt ..... *Service Line Director, Oncology*
Paula Burcher ..... *Administrative Director, Radiology*
Beverly Voglewede ..... *Director, Radiation Oncology Services*
Michelle Wooten ..... *Dir. Med/Surg. Svcs/Oncology Services*
Ed Heckler ..... *Director, Rehab*
Celia Grinstead ..... *Nurse Manager, 5-West, Hem/Onc*
Kim Monroe ..... *Clinical Coordinator, Hem/Onc*
Arlene Messina ..... *Director, Performance Improvement*
Reverend Doug Watson ..... *Director, Pastoral Care*
Ora Mae Jackson ..... *Protocol Manager*
Yvonne Pike ..... *Breast Cancer Patient Navigator*
Angie Claud ..... *Prostate Cancer Patient Navigator*
Pat Emerson ..... *Lung Cancer Patient Navigator*
Charlene Thompson ..... *Social Worker, Care Management*
Jackie Ward ..... *Educator, Staff Development*
Sharron Nichols ..... *Nurse Manager, Riverside Hospice*
Ann Tatterson ..... *Director, Riverside Hospice Agencies*
Paige Williams ..... *Registered Dietician, Dietary*
Fran Holcomb ..... *Cancer Education/Outreach Nurse*
Jennifer Brown ..... *Cancer Registry Supervisor*
Pauline Shofner ..... *Cancer Registrar*
Carol Richards ..... *Cancer Registrar*
Pennie Faircloth ..... *Representative, American Cancer Society*

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For additional information regarding Riverside Cancer Services, please call (800) 520-7006.
For comments or questions regarding this Annual Report or the Cancer Registry, please call (757) 594-3054.

Cancer Services Annual Report 2008

The Riverside Health System continues to actively grow its cancer program. The following report from Cancer Services will surely attest to the depth and quality of our program. Support of administrative leaders makes this program possible, and I would like to thank Mark Ellis, Golden Bethune, Faye Garguilo and Carrie Schmidt for providing that leadership.

Riverside continues to work to receive the highest levels of accreditation for excellence as attested by our Breast Center of Excellence accreditation by the American College of Radiology (ACR) for excellence in mammography, ultrasound and stereotactic biopsy at our Riverside Diagnostic and Breast Imaging Center, located in Oyster Point. Also the Cancer Treatment Center in Gloucester received accreditation from the ACR, bringing all three Riverside radiation therapy centers up to accreditation by ACR. The American College of Surgeons Commission on Cancer has given multiple commendations to our cancer program, which was surveyed in December 2006 and passed with commendations. Surgical Oncologist Michael Peyser has received the Outstanding Performance Award for his work as Community Cancer Liaison Physician for the second year in a row by the ACoS CoC.

A number of new surgeons have been added to the Riverside staff who have specific interest in the cancer program. Dr. Steven Scott has been active in the lung cancer program, Dr. Pierre Martin has training in oncology from the ENT perspective, and Dr. Brian Billings has advanced training in colorectal surgery. In addition the radiation oncology program expanded with the addition of Dr. Mark Chisam. I would like to thank Dr. Richard Robins for the many years of service in ENT. Although he recently retired, he remains active in Tumor Board sessions.

The Neurosciences Center has expanded rapidly with whole body Stereotactic Radiosurgery. We remain the only program in Virginia providing the precision of Gamma Knife and Stereotactic Radiosurgery.

In Urology, the use of the daVinci robotic surgery continues to grow, and we continue to provide highly precise external beam treatments for prostate cancer with IMRT and IGRT.

In ENT, Riverside has purchased four VEL scopes for oral cancer screening. They were donated to the following community organizations to promote screening and early diagnosis: the Lackey Free Clinic (Williamsburg), the Old Town Medical Center (Williamsburg), Peninsula Regional Dental Clinic (Newport News), the Gloucester-Mathews Free Clinic (Gloucester) and the Virginia Dental Association for their Missions of Mercy Dental Clinic. The navigation program had an active year with Yvonne Pike leading the program and focusing on breast cancer. Angie Claud expanded the prostate cancer navigation program and Pat Emerson was active in expanding the lung cancer program, which includes an excellent tumor board held several times monthly. The research program continues to expand under the direction of Ora Mae Jackson and cancer education and outreach continues to provide valuable services to patients with limited resources and remains under the direction of Fran Holcomb.

We would like to thank Brad Kirby for all the years of dedication to the Cancer Registry and Cancer Program at Riverside. We now have Jennifer Brown who is doing a very nice job handling these responsibilities. My thanks also go to the many Riverside employees who may have been unmentioned in this introduction but provide important services to our cancer patients.

Joseph Layser, MD
Chair, RRMC Oncology Committee
Medical Director, Riverside Cancer Care Center Radiation Oncology

The Riverside Cancer Program has had another exciting year. With the growth of Riverside Medical Group to more than 325 physicians, the Riverside Cancer Program continues to provide services to an increasing number of cancer patients and their families over an increasing geographic area.

In addition to our outpatient program, the renovation of our inpatient facilities at Riverside Regional Medical Center, will serve as the cornerstone to an improved in-patient experience for our hospitalized cancer patients. The current project includes construction of a state-of-the-art inpatient cancer treatment facility on 5 West, as well as an upgraded Oncology Intensive Care Unit adjacent to 5 West. The effort has truly been collaborative, with input from Riverside's clinical and administrative teams, to optimize the care of our cancer patients and their families.

In October of 2008, we announced the Riverside's Cancer Heritage Program. This effort will facilitate the testing and counseling for those cancers for which a genetic link has been established, including cancers of the breast and colon. The program is designed for the counseling of patients with these diseases, who have risk factors suggesting a potential genetic link, as well as family members of affected patients.

In addition, our Patient Navigator Program continues to grow, now with designated Navigators for cancers of the breast, prostate, and lung. This program has continued to be very popular with our patients and their families, and we plan to expand the program to help us continue to provide seamless continuity of care within the Riverside Health System.

Finally, in association with our colleagues at the University of Virginia (UVA), we are exploring opportunities to cooperate in research and clinical care, to allow Riverside patients to benefit, when needed, from the expertise of this world-class academic medical system. The Riverside-University of Virginia Stereotactic Radiosurgery Center (on the campus of Riverside Regional Medical Center) is a tangible example of the cooperation between Riverside and the University. We look forward to expanding our relationship with UVA in the development and provision of cancer services to the patients in our area.

The future of the Riverside Cancer Program continues to be very bright, and I am optimistic that our program will continue to be the leader in cancer care in our region.

Mark Ellis, MD
Medical Director, Riverside Cancer Care

Riverside Cancer Services

American College of Surgeons Accreditation: Riverside Regional Medical Center has been accredited as a Community Hospital Comprehensive Cancer Program by the American College of Surgeons' Commission on Cancer since 1982. Riverside Regional Medical Center was recently re-accredited in December 2006 and received approval with no contingencies and 7 of 9 possible commendations from the College. Accreditation by the ACOS indicates that the five key elements of a cancer program are in place:

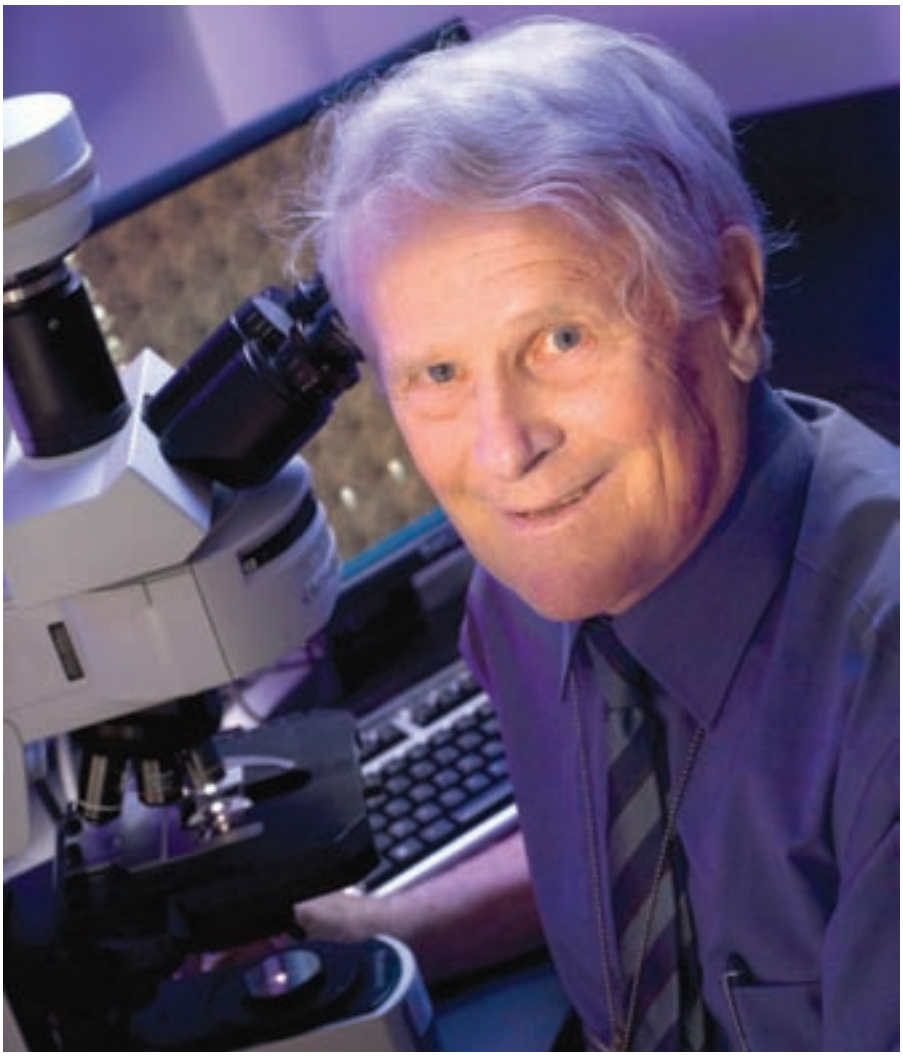
1) state of the art clinical services;
2) a multidisciplinary cancer committee;
3) a cancer registry to monitor the quality of care;
4) patient oriented case-conferences; and
5) a quality improvement program for improving patient outcomes.

Oncology Committee: Riverside Regional Medical Center's Oncology Committee is a multi-disciplinary team that convenes every other month to provide leadership and professional guidance to the cancer care program.

Cancer Registry: To adhere to state, federal and ACOS guidelines, RRMC's Cancer Registry has been maintaining its database of cancer cases since 1979. Data from the registry is submitted to the Virginia Cancer Registry and the National Cancer Data Base (NCDB), which serves as a comprehensive clinical surveillance center for the entire country. Information on each case is submitted annually to keep the information current. The NCDB combines the data from 1,438 hospitals in all 50 states to provide insight into the long-term outcomes of treatments. This helps researchers and physicians better investigate and evaluate advances in diagnostics and treatment. This Annual Report contains a review of all 2007 accessions (new cases), as well as site-specific studies on melanoma and bladder cancer.

Cancer Case Conferences (Tumor Boards): Tumor Boards provide an opportunity for physicians to prospectively review cases with the multidisciplinary team. There are weekly general tumor boards, breast cancer case conferences, neurosciences case conferences and regular lung cancer case conferences. In addition to helping determine treatment plans, case conferences serve as important education offerings for the physicians and other members of the healthcare team.

Research and Clinical Trials: Offering access to clinical trials is an important aspect of any cancer care program. While not appropriate for every patient, clinical trials can sometimes offer access to treatments that would be otherwise unavailable. The ACOS requires that 2% of the patients each year be enrolled in clinical trials, and Riverside is proud to once again exceed that benchmark.

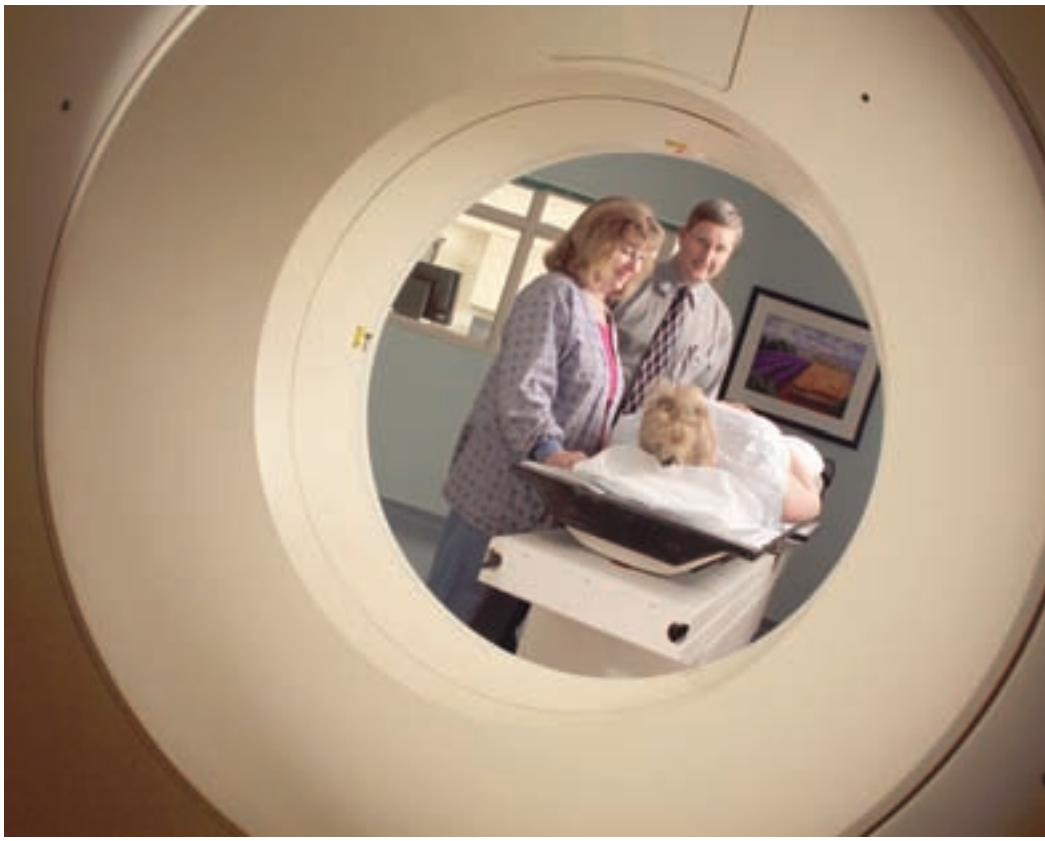


Diagnostic Services

Imaging: Riverside offers a wide range of diagnostic imaging services across five locations (Riverside Regional Medical Center, Riverside Diagnostic and Breast Imaging Center - Oyster Point, Riverside Diagnostic Center - Williamsburg, Riverside Walter Reed Medical Center and Riverside Tappahannock Hospital). Riverside is proud to work with the physicians of Peninsula Radiologic Associates to bring you the following services:

- Mammography and Breast Imaging Services (screening, diagnostic, stereotactic, ultrasound, MRI, breast specific gamma imaging)
- X Ray
- Ultrasound
- CT
- MRI
- Nuclear Medicine
- PET/CT

Laboratory and Pathology: Riverside provides a complete range of laboratory and pathology services. The physicians of Peninsula Pathology Associates work closely with the referring physicians and surgeons to provide the most accurate diagnosis to allow for the most precise treatment plan. In addition to the expertise of the physicians on staff, Riverside has partnered with The Mayo Clinic in Minnesota as a reference lab for the more unique tests that may be required or for second opinions on some specimens.



Inpatient Services

Riverside Regional Medical Center, the Peninsula's only Level II Trauma Center, offers a wide range of inpatient services. For oncology patients, the most commonly utilized departments and services include:

Care Management: The Inpatient Oncology Care Management team is there to help patients and their supporters navigate the often confusing array of tests, treatments and feelings. The care coordinator works with the entire inter-disciplinary healthcare team to focus on minimizing the length of necessary hospital stays, while maximizing access to the best care available and preparing the patient and family for discharge to home or another facility.

5-East Post Surgical Unit: 5-East is a general surgical unit, which specializes in the care of the post-operative patient. 5-East also offers a four bed step-down unit for patients requiring an increased level of nursing care following surgery. The nursing staff on 5-East are experts in helping a patient recover as rapidly as possible from a surgical intervention, including wound care issues, anesthesia recovery, pain management and getting the patient back to the activities of daily living.

Outpatient Services

5-West Oncology Unit: 5-West is a medical unit which specializes in the care of the oncology patient. Specialized offerings include lead-lined rooms for patients who have received cesium implants and radioactive iodine therapy. Additionally, all of the RNs are certified in chemotherapy, and there are Oncology Certified Nurses on the unit.

Hematology/Oncology Unit: The Hematology/Oncology Intensive Care Unit ("Hem/Onc") is a six-bed specialty care unit designed for the critically ill oncology patient. As on 5-West, the nursing staff is chemotherapy certified, and the unit boasts Oncology Certified Nurses. The Hem/Onc staff members are also trained in critical care nursing, and are able to accommodate the most complex oncology patients, including intra-peritoneal chemotherapy.

Surgeons: Riverside's surgeons are talented physicians who have spent years studying how to best operate on specific areas of the body. Depending on the type of cancer a patient has, they could see one of the following: Ear Nose & Throat (ENT) Surgeon, General Surgeon, Colorectal Surgeon, Gynecologic Oncologist, Neurosurgeon, Plastic Surgeon, Surgical Oncologist, Thoracic Surgeon or Urologist.

Surgical Services: For many cancer patients, their only inpatient stay is immediately following surgery. Riverside's Surgical Services – from pre-operative testing, to the Operating Room to the Post-Anesthesia Care Unit (PACU) - is there to ensure that the right patient has the right procedure in the most safe and effective manner, and recovers as quickly as possible.

Home Care: Riverside Home Care offers a variety of services to patients in the Peninsula, Middle Peninsula and Northern Neck regions including home health, infusion, pharmacy and hospice services. Admission begins with a referral from the physician and a visit from an RN, physical or speech therapist to identify needs, establish goals for treatment and begin planning for continued care when home care services are no longer required.

Hospice: The Hospice program affirms life and regards dying as a natural process. The hospice program exists to provide support and care for patients, their families and caregivers in the last phases of incurable disease so the patient might live as fully and comfortably as possible. Hospice services neither hasten nor postpone death.

Medical Oncology / Peninsula Cancer Institute: Medical Oncology is a critical component of any cancer program. Riverside partners with the physicians of Peninsula Cancer Institute to offer medical oncology services, including outpatient chemotherapy at three sites (Newport News, Gloucester and Williamsburg).

Radiation Oncology: Riverside Cancer Care Center, Riverside Middle Peninsula Cancer Center and Williamsburg Radiation Therapy Center provide radiation oncology services to patients across the service area. A full range of external beam radiation and brachytherapy services, with the latest treatment options such as Intensity Modulated Radiation Therapy (IMRT), Prostate Seed Implants and Mammosite, are available for the Newport News, Williamsburg and Middle Peninsula communities.

Riverside and University of Virginia Radiosurgery Center: Offering both Gamma Knife® and Synergy–S® technology, the Riverside and University of Virginia Radiosurgery Center opens up the world of knifeless surgery to patients with tumors in the brain, spine and other areas of the body. Using precise beams of intense radiation, the center allows outpatient surgery to previously inoperable tumors. Riverside is proud to offer the only Gamma Knife® in the Tidewater region, and is proud to be the only health system to offer both Gamma Knife® and Synergy-S® technology in the Commonwealth of Virginia.

Support Services

Bereavement Support: Riverside Hospice's Bereavement Aftercare Program provides support to adults as they adjust to life following the death of a loved one. Support and education are offered to help individuals learn about the grief process, and a support group meets twice a month.

Cancer Resource Library: Now located on the first floor of the Riverside Cancer Care Center, the new and expanded library is for patients, family members, community members and staff who want to learn more about cancer issues. The library offers resources on specific types of cancer – including prevention, diagnosis and treatment issues. There is also a wide array of books on the important psychosocial concerns of facing a cancer diagnosis. Additionally, there are two computers where individuals can research issues online, as well as a children's section.

Cancer Services – Outreach and Community Education: Riverside's Cancer Services offers a wide range of support, outreach, education and early detection programs to the community. Working with medical staff, oncology nurses, allied health care professionals and community partners, such as The American Cancer Society and the Leukemia and Lymphoma Society, Cancer Services sponsors numerous educational and screening events throughout the year. Programs include: community health fairs, prostate, cervical, breast and skin cancer screenings, Look Good Feel Better classes, Tell A Friend programs, nutritional programs and continued work with the Healing Eagle Free Clinic.

Connections with Community Organizations: Riverside Cancer Services recognizes its role in the broader cancer community, and works actively with numerous local and national cancer organizations. In addition to its work with local health departments, Riverside works with American Cancer Society, Leukemia and Lymphoma Society, Susan G Komen Foundation, Colon Cancer Prevention Coalition, many local church groups, and the Lackey, Healing Eagle and Gloucester-Matthews Free Clinics.

Grant Programs: Riverside is proud to be the recipient of two major grants that allow access to breast and cervical cancer screenings for women who might not otherwise be able to get screened. The Every Woman's Life Grant is a part of the Centers for Disease Control and Prevention's Breast and Cervical Cancer Early Detection Program as managed through the Virginia Department of Health. Additionally, Riverside also receives funds from the Susan G. Komen Foundation for the Breast Health Alliance Program. Between the two programs, Riverside is able to provide these critical screenings to uninsured or underinsured women who meet the necessary age and income guidelines. Additionally, those women who detect a breast cancer through the Breast and Cervical Cancer Early Detection Program (BCCEDP) can be enrolled in Medicaid to receive treatment.

Pastoral Care: The Riverside Chaplains are there to support cancer patients, families and friends in making use of faith or spiritual values to work with the challenges of cancer. Pastoral Care may include conversation, prayer, liturgy, worship, sacraments, scripture reading, reflection and referral. The pastoral care service is interfaith, personal, and specific for the individual and family in need. In addition to the community clergy and volunteers who support the program, Riverside's Pastoral Care consists of five full-time chaplains, including one chaplain dedicated to cancer care.

Patient Navigation: Patient Navigators are there for patients and their loved ones from diagnosis through the entire treatment process. As most cancer patients discover, the diagnosis and treatment process is often confusing, and involves many physicians, nurses, therapists and locations, not to mention the overwhelming emotional

component in addition to being sick. Patient Navigators are there to simplify the journey, and to be the one person you can always call with a question. They also help patients and caregivers know what to expect from various procedures and treatments. Currently, Riverside offers Patient Navigation to any patient in the breast, prostate or lung cancer programs. The hope is to expand that to additional diagnoses in coming years.

Support Groups: There are numerous support groups to support the cancer patient and their loved ones. Call Cancer Services for an up to date schedule of times and locations of the various groups.

Review of 2007 Accessions

With increasing technologies and methods for early detection, Riverside's Cancer Programs continue to grow. From 2005 to 2007, Riverside has seen a steady increase in its annual analytic caseload each year. As expansion occurs, the Riverside Cancer Registry continues to maintain accurate documentation of this increasing population. The registry diligently performs the tasks of tracking, collaboratively staging, and performing follow-up on cases within its database. Through database analysis, Riverside Cancer Registry provides valuable information to physicians regarding developing trends in staging, overall case accruals, referral information and outcomes in the population. Information provided by the hospital registry database assists Riverside in identifying where timelines can be shortened and quality of care can be improved. In an effort to improve how cancer is approached today, the hospital registry compiles data for the incidence of cancer occurrence for the hospital and forwards the information to the Virginia Cancer Registry and the National Cancer Database (NCDB) for state and national studies.

In 2007 the Riverside Cancer Registry identified a total of 1,479 new cases of cancer. Of those, 1,090 (74%) were analytic - either diagnosed and/or treated at Riverside Regional Medical Center. The remaining 26% of cases were classified as non-analytic, meaning that those cases did not receive treatment at Riverside.

Breast cancer continues to account for most analytic cases for the hospital. In 2007 a total of 229 breast cancer cases were identified, 21% of the analytic caseload. From 2006 to 2007 Riverside observed a 14.5% increase (200 to 229) in breast cases. Approximately 86% of breast cancer cases were diagnosed Stage 0, I or II. The Riverside Cancer Registry participates in three national breast studies conducted by the NCDB to promote quality improvement activities for compliance with standard of care. Riverside continues to maintain a 93%+ performance rate average for these selected indicators.

In addition to breast cancer, prostate and lung again round out the top three cancer sites. In 2007 there were 208 lung cases and 178 prostate cases identified at Riverside. These sites accounted for 19% and 16% of the annual analytic caseload, respectively. An overwhelming majority (90%) of prostate cases were diagnosed as a Stage II. This may be because as a Stage II cancer, the mass can be felt upon digital rectal exam (DRE) or consistent monitoring of prostate specific antigen (PSA) levels. A continued rise in prostate cases (12.4% from 2006) may be attributed to the da Vinci Robot Assisted Surgery available at RRMC. Often lung cancer presents at a later stage. Controversies over earlier detection versus exposing patients to invasive, and sometimes unnecessary risk continue to circulate. For 2007 only 25% of lung cases were localized cancers (Stage I), while approximately 75% had spread to lymph nodes or other distant parts of the body (Stage II, III or IV). From 2006 to 2007 Riverside observed a 5.3% (9 case) increase.

The most significant increase in cases occurred in pancreatic cancer. Over the past year, Riverside has seen a 53.8% increase (from 13 to 20 cases). Unfortunately, 60% of analytic pancreatic cases were Stage IV at diagnosis, meaning that the cancer had spread to a distant site beyond the pancreas (such as the liver or lungs). Currently no standard screening exists for pancreatic cancer, and symptoms often do not present until the disease has become advanced.

A decrease in the percentage of ovarian cases was noted, however, it only reflected a decrease of 4 cases, while the Riverside Gynecological Oncology program noted an overall increase of 11.8% in female genital system cancers.

Overall, Riverside Regional Medical Center experienced an increase in analytic cases for ten of its key cancer sites and a decrease in only four. As early detection methods improve, Riverside Cancer Registry expects to observe an increase in its annual caseload each year. These statistics are only representative of Riverside Regional Medical Center.

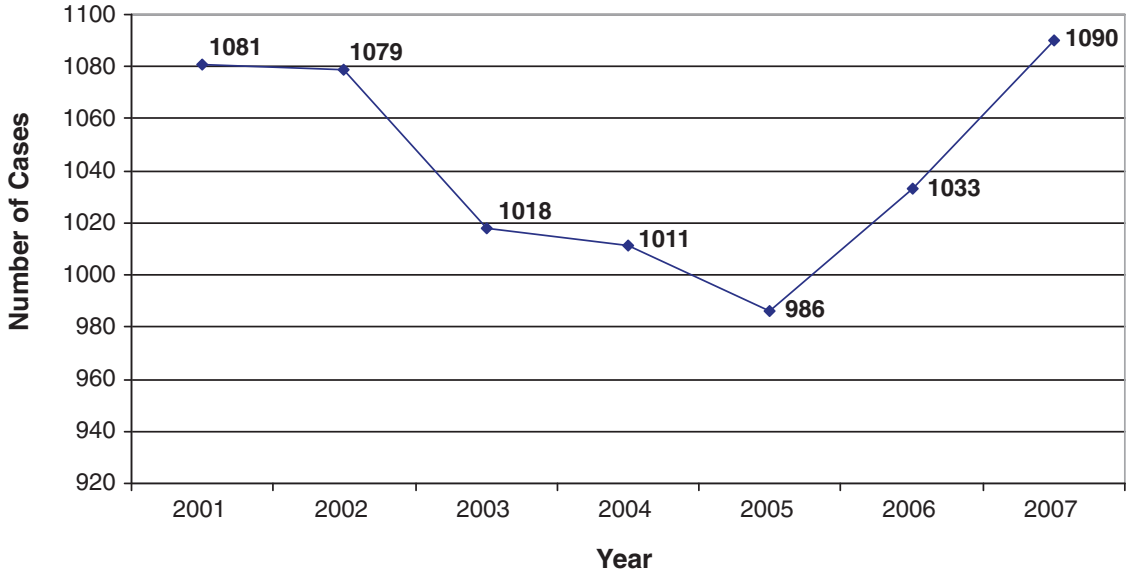
Jennifer L. Brown, BS
Cancer Registry Supervisor

Review of 2007 Accessions

Primary Site	Cases	%	Sex		Class of Case		Stage Distribution - Analytic Cases Only							
			M	F	Analytic	Non-Analytic	0	I	II	III	IV	NA	Unk	Blank/Inv
ORAL CAVITY & PHARYNX	**19**	**1.3%**	**16**	**3**	**11**	**8**	**0**	**2**	**2**	**1**	**6**	**0**	**0**	**0**
Tongue	4	0.3%	3	1	1	3	0	0	0	0	1	0	0	0
Salivary Glands	3	0.2%	3	0	2	1	0	0	1	1	0	0	0	0
Floor of Mouth	1	0.1%	1	0	0	1	0	0	0	0	0	0	0	0
Gum & Other Mouth	5	0.3%	3	2	4	1	0	2	0	0	2	0	0	0
Tonsil	4	0.3%	4	0	2	2	0	0	1	0	1	0	0	0
Oropharynx	2	0.1%	2	0	2	0	0	0	0	0	2	0	0	0
DIGESTIVE SYSTEM	**139**	**9.4%**	**83**	**56**	**108**	**31**	**0**	**22**	**24**	**22**	**26**	**7**	**7**	**0**
Esophagus	13	0.9%	12	1	9	4	0	0	1	1	5	0	2	0
Stomach	7	0.5%	5	2	4	3	0	0	0	2	1	0	1	0
Small Intestine	4	0.3%	2	2	4	0	0	0	0	2	0	2	0	0
Colon Excluding Rectum	45	3.0%	23	22	35	10	0	10	9	8	6	0	2	0
Rectum & Rectosigmoid	32	2.2%	21	11	25	7	0	7	10	6	1	1	0	0
Anus, Anal Canal & Anorectum	3	0.2%	3	0	3	0	0	0	2	1	0	0	0	0
Liver & Intrahepatic Bile Duct	5	0.3%	3	2	4	1	0	3	0	0	1	0	0	0
Pancreas	26	1.8%	14	12	20	6	0	2	2	2	12	0	2	0
Peritoneum, Omentum & Mesentery	4	0.3%	0	4	4	0	0	0	0	0	0	4	0	0
RESPIRATORY SYSTEM	**219**	**14.8%**	**128**	**91**	**193**	**26**	**0**	**50**	**16**	**41**	**83**	**2**	**1**	**0**
Nasal Cavity, Middle Ear & Accessory Sinuses	1	0.1%	1	0	1	0	0	1	0	0	0	0	0	0
Larynx	14	0.9%	13	1	13	1	0	5	2	4	2	0	0	0
Lung & Bronchus	203	13.7%	114	89	178	25	0	44	14	37	80	2	1	0
Trachea, Mediastinum & Other Respiratory Organs	1	0.1%	0	1	1	0	0	0	0	0	1	0	0	0
BONES & JOINTS	**1**	**0.1%**	**0**	**1**	**1**	**0**	**0**	**0**	**0**	**0**	**1**	**0**	**0**	**0**
Bones & Joints	1	0.1%	0	1	1	0	0	0	0	0	1	0	0	0
SOFT TISSUE	**7**	**0.5%**	**3**	**4**	**5**	**2**	**0**	**1**	**2**	**0**	**1**	**0**	**1**	**0**
Soft Tissue (including Heart)	7	0.5%	3	4	5	2	0	1	2	0	1	0	1	0
SKIN EXCLUDING BASAL & SQUAMOUS	**61**	**4.1%**	**40**	**21**	**31**	**30**	**5**	**13**	**8**	**3**	**1**	**0**	**1**	**0**
Melanoma — Skin	59	4.0%	39	20	31	28	5	13	8	3	1	0	1	0
Other Nonepithelial Skin	2	0.1%	1	1	0	2	0	0	0	0	0	0	0	0
BREAST	**255**	**17.2%**	**1**	**254**	**229**	**26**	**50**	**86**	**61**	**21**	**6**	**0**	**5**	**0**
Breast	255	17.2%	1	254	229	26	50	86	61	21	6	0	5	0
FEMALE GENITAL SYSTEM	**69**	**4.7%**	**0**	**69**	**57**	**12**	**4**	**29**	**1**	**10**	**10**	**2**	**1**	**0**
Cervix Uteri	9	0.6%	0	9	7	2	0	5	0	1	1	0	0	0
Corpus & Uterus, NOS	44	3.0%	0	44	39	5	1	23	1	4	7	2	1	0
Ovary	8	0.5%	0	8	6	2	0	0	0	4	2	0	0	0
Vulva	8	0.5%	0	8	5	3	3	1	0	1	0	0	0	0
MALE GENITAL SYSTEM	**334**	**22.6%**	**334**	**0**	**213**	**121**	**1**	**2**	**187**	**19**	**4**	**0**	**0**	**0**
Prostate	328	22.2%	328	0	208	120	0	0	187	18	3	0	0	0
Testis	4	0.3%	4	0	3	1	0	2	0	1	0	0	0	0
Penis	2	0.1%	2	0	2	0	1	0	0	0	1	0	0	0

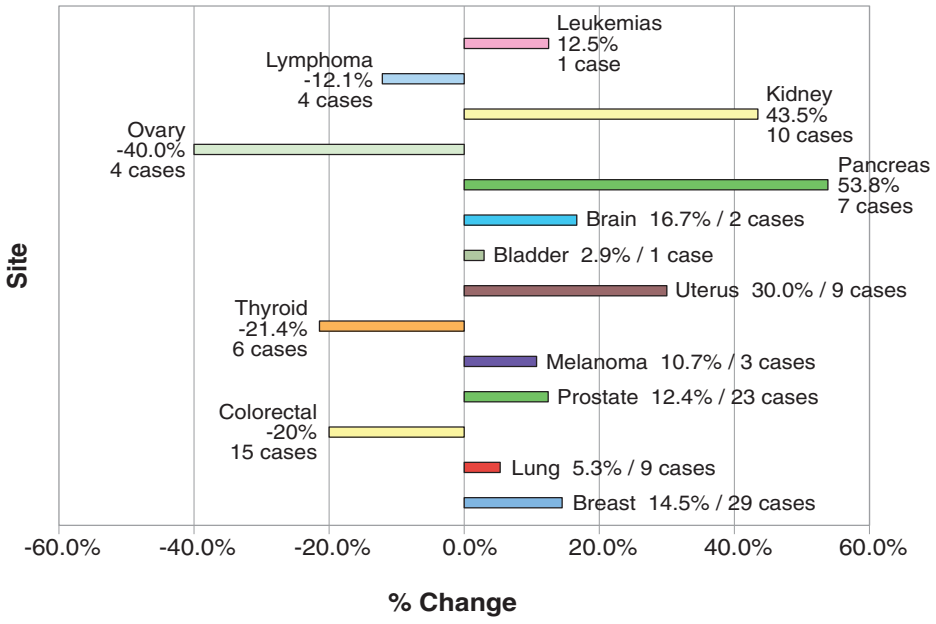
Primary Site	Cases	%	Sex		Class of Case		Stage Distribution - Analytic Cases Only							
			M	F	Analytic	Non-Analytic	0	I	II	III	IV	NA	Unk	Blank/Inv
URINARY SYSTEM	**105**	**7.1%**	**73**	**32**	**69**	**36**	**16**	**24**	**5**	**11**	**11**	**0**	**2**	**0**
Urinary Bladder	63	4.3%	48	15	35	28	14	9	3	3	5	0	1	0
Kidney & Renal Pelvis	40	2.7%	24	16	33	7	1	15	2	8	6	0	1	0
Ureter	1	0.1%	0	1	1	0	1	0	0	0	0	0	0	0
Other Urinary Organs	1	0.1%	1	0	0	1	0	0	0	0	0	0	0	0
BRAIN & OTHER NERVOUS SYSTEM	**46**	**3.1%**	**22**	**24**	**36**	**10**	**0**	**0**	**0**	**0**	**0**	**36**	**0**	**0**
Brain	17	1.1%	11	6	14	3	0	0	0	0	0	14	0	0
Other Nervous System	29	2.0%	11	18	22	7	0	0	0	0	0	22	0	0
ENDOCRINE SYSTEM	**29**	**2.0%**	**11**	**18**	**28**	**1**	**0**	**14**	**1**	**5**	**2**	**6**	**0**	**0**
Thyroid	22	1.5%	6	16	22	0	0	14	1	5	2	0	0	0
Other Endocrine (including Thymus)	7	0.5%	5	2	6	1	0	0	0	0	0	6	0	0
LYMPHOMAS	**56**	**3.8%**	**34**	**22**	**29**	**27**	**0**	**7**	**6**	**4**	**11**	**0**	**1**	**0**
Hodgkin Lymphoma	2	0.1%	1	1	1	1	0	1	0	0	0	0	0	0
Non-Hodgkin Lymphoma	54	3.6%	33	21	28	26	0	6	6	4	11	0	1	0
MULTIPLE MYELOMA	**25**	**1.7%**	**13**	**12**	**17**	**8**	**0**	**0**	**0**	**0**	**0**	**17**	**0**	**0**
Multiple Myeloma	25	1.7%	13	12	17	8	0	0	0	0	0	17	0	0
LEUKEMIAS	**34**	**2.3%**	**18**	**16**	**9**	**25**	**0**	**0**	**0**	**0**	**0**	**9**	**0**	**0**
Lymphocytic Leukemia	20	1.4%	11	9	2	18	0	0	0	0	0	2	0	0
Myeloid & Monocytic Leukemia	13	0.9%	7	6	7	6	0	0	0	0	0	7	0	0
Other Leukemia	1	0.1%	0	1	0	1	0	0	0	0	0	0	0	0
MESOTHELIOMA	**17**	**1.1%**	**15**	**2**	**8**	**9**	**0**	**0**	**3**	**0**	**5**	**0**	**0**	**0**
Mesothelioma	17	1.1%	15	2	8	9	0	0	3	0	5	0	0	0
MISCELLANEOUS	**64**	**4.3%**	**33**	**31**	**46**	**18**	**0**	**0**	**0**	**0**	**0**	**46**	**0**	**0**
Miscellaneous Sites	64	4.3%	33	31	46	18	0	0	0	0	0	46	0	0
Total	**1,480**		**824**	**656**	**1,090**	**390**	**76**	**250**	**316**	**137**	**167**	**125**	**19**	**0**

RRMC Cancer Registry Data Base
Analytic Cases 2001-2007

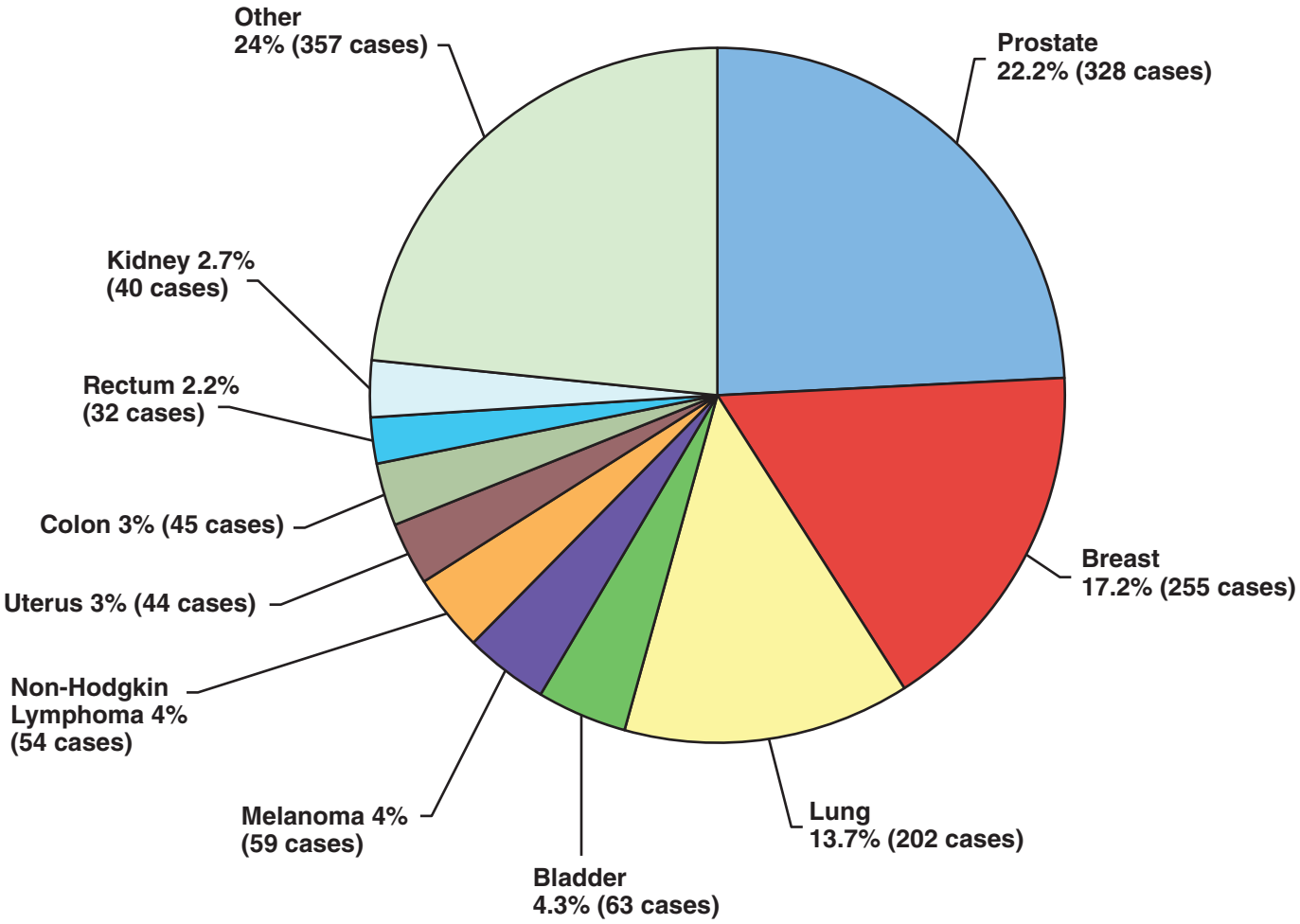


*NOTE: These are analytic cases ONLY (diagnosed and/or treated here during the first course of treatment). Since 2005, RRMC has experienced a steady increase in the analytic caseload.

Analytic Cases: % Change 2006-2007
(Diagnosed and /or Treated at RRMC)



RRMC 2007 Top 10 Cancer Sites
(Accounting for both Analytic and Non-Analytic Cases)



Melanoma at Riverside Regional Medical Center

Dermatologist

Christine Marcuson, MD
Dermatology Specialists

The incidence of melanoma is increasing. We are all aware of the statistics: 1 in 50 risk for the development if invasive melanoma over a lifetime by 2010. One person dies from melanoma every 62 minutes in the United States. Melanoma is the number one cancer in young adults 25-29 years old. How do we deal with the increasing risk? Here we will explore new insights into early detection, recommendations for diagnosis, treatment options, controversies in prevention (including Vitamin D) and navigate the newer sunscreen agents

Early detection is the mainstay of success in treating melanoma, as the number one indicator of survival is Breslow's depth, or the thickness of the melanoma, at diagnosis. Early detection starts with education and awareness of the public and ends with the diagnostic biopsy.

Public awareness has improved dramatically over the past 10 years with many patients already familiar with the ABCD & E of suspicious moles before they present to the physician for evaluation. "E" is the latest addition to the mnemonic, which emphasizes "Evolution", or change over time, and is a potent predictor of melanoma. Patients most at risk remain the well known: 1) Caucasian with fair complexion, 2) Blue or green eyes, 3) Patients with greater than 100 nevi and or dysplastic nevi, 4) Family history of melanoma 5) Personal history of non-melanoma skin cancer such as basal cell or squamous cell cancer 6) Blistering sunburn before age 18, and 7)Long-term exposure to artificial light (tanning beds). However, as melanoma can arise anywhere on anyone, we need to maintain an index of suspicion even in patients of color and when examining non-sun exposed sites.

On whom and when to biopsy is a tremendous challenge especially in the era of managed care. One powerful tool to improve diagnostic accuracy is patient self-exam. "Check your birthday suit on your birthday", is one of the new slogans of the American Academy of Dermatology (AAD) encouraging patients to be aware of lesions growing or changing on their bodies. Downloadable skin self exam instructions and diagrams of what to look for are available at the AAD web site. Studies of patients at risk for melanoma have demonstrated improved accuracy when not just the patient but the patient's spouse or family is recruited to participate in monitoring for change. Another tool is mole mapping through total body photography in which a medical photographer creates a portfolio of the patients existing nevi allowing direct comparison for change in the future. This is currently an out of pocket expense for the patient but can aid in preventing unnecessary biopsies and aid in detection on small non-descript melanomas that would fail the ABCD criteria. An exciting extrapolation of this technology is computer assisted mole mapping in which sets of photos are compared with the aid of the computer to detect early changes or new lesions. Although a great concept, the systems are currently expensive and thus not practical for general use.

Bypass the biopsy? Future fact or science fiction? Currently there are technologies in development that are able to assess the histology of a lesion in-vivo i.e. on the patient without the need for biopsy. One that shows promise is confocal microscopy. Resolution is improving to the point of being able to visualize hair structures and some tumor nests but is not adequate for cellular detail. The major limitation of this technology is that the plane examined is horizontal instead of the conventional vertical cross-section conventionally used in histology, and structures usually accentuated by stains and counter stains are more difficult to discern.

Genetic tools in melanoma detection:
We know that approximately 10% of melanomas are hereditary. Of these "melanoma families" 40% share an autosomal dominant mutation of the p16 tumor suppressor gene. The risk of primary melanoma in these families is 50% by age 50 as compared to <1% of the general population, also with increased risk of a second primary melanoma and 17% risk of pancreatic cancer as well. Genetic testing is available for the geneline mutation in p16 and identifies patients at increased risk of melanoma and pancreatic cancer. Genetic testing can be considered in patients with two or more melanomas in the individual or the family, melanoma and pancreatic cancer in an individual or family, and in relatives of a p16 mutation carrier. The test, although available, is of uncertain clinical utility. Patients and family members of those with melanoma are recommended to have semi-annual or annual skin exams with a dermatologist regardless of their p16 gene status. Testing positive could, however, have

a tremendous impact on pancreatic cancer and aid in developing criteria and insurance coverage for screening this high risk population.

The biopsy:
An appropriate biopsy is crucial to the diagnosis and management of melanoma as the plan of management and prognosis are contingent on the accurate Breslow's depth. The Breslow's depth is the lesion thickness measured in millimeters by the pathologist. A full thickness sample to fat is recommended to avoid transecting the base of a melanoma. In addition to depth, an adequately wide sample allows the pathologist to view the architecture or arrangement of cells which, in skin pathology, can be as, or more important than cytology in deciding if a nevus is benign or malignant. Excisional biopsy is preferred, followed by an incisional full thickness sample as large as can be removed easily. Occasionally deep saucerizations to fat also give excellent samples. That having been said, the recommendations surrounding biopsy of pigmented lesions should not be so strict as to discourage or delay sampling of a suspicious lesion.

Also, a benign pathology report in the face of a clinically suspicious lesion warrants clinical pathologic correlation such as a phone call to alert the pathologist of the clinical concern.

Why send all suspicious lesions for biopsy?
Amelanotic melanomas. These are malignant melanomas without pigment that mimic nodular and superficial basal cell carcinomas, or other non-descript skin lesions. In the age of managed care there is often a temptation to go ahead and treat "obvious" skin lesions without sending a biopsy, however this can have devastating effects for the patient if an amelanotic melanoma is missed only to become evident when the lesion metastasizes. Clinical experience of the provider has little impact on the ability to foresee this. In fact, after 10 years practicing Mohs surgery and well over 10,000 tumors tracked both clinically and histologically, I continue to be impressed at the discordance in the clinical vs histological appearance of tumors.

Treatment:
Melanoma-in-situ (mm-in-situ) (stage 0) is intra-epidermal disease only. As there is no invasion to the dermis, it has no risk of metastasis. Treatment is surgical and recommended margins are 5mm around the periphery of the biopsy site scar or scar plus any residual lesion. A woods light can be used to accentuate epidermal vs dermal pigment around the site. A subset of mm-in-situ is lentigo maligna which can have extensive sub-clinical spread well beyond the 5 mm margin and, thus, is at high risk for recurrence. On high risk locations such as the face or with recurrent lesions of lentigo maligna a variation on routine surgical excision can be offered to the patient. The mapping tequniques of Mohs surgery can be applied for these but with rush permanent section processing ("Slow Mohs"). Routine Mohs surgery is typically performed on frozen section tissue for basal cell and squamous cell skin cancers. However, the safety and reliability of frozen sections for melanomas is debatable, thus permanent section paraffin processing is preferred despite the inconvenience to the patient.

How is a staged resection performed?
For staged excision or "Slow Mohs" a debulking layer is removed in the center and processed by vertical sectioning to confirm the lack of invasive disease in the remaining pigmented lesion. A 5 mm rim is then resected, inked and mapped according the usual principles of Mohs surgery, flattened, maintained in its orientation, placed in formalin, and submitted for rush permanent processing at a lab prepared to address the special needs of the en-face sectioning. The patient is then bandaged and released until the following day when the results are available. The patient either returns for resection of additional tissue only where indicated by the mapped tumor or is released for repair of the defect.

Lentigo Maligna commonly occurs in broad pigmented patched on the face of elderly patients. These can remain with minimal change over a number of years or progress to invasive melanoma with its intrinsic risk of metastasis. Although surgery is usually recommended, correlation to the patient's health, size of the lesion, proximity to vital structures, and morbidity associated with management should be taken into account prior to management. In patients who are a poor surgical candidate due to significantly advanced age and any of the above factors but do not wish observation only, a palliative treatment can be offered in the form of topical imiquimod, an immune response modifier, FDA approved for actinic keratosis and superficial basal cell skin cancers. Management for this purpose is off label, should be performed only by those familiar with its use, and is not recommended for the general population.

Treatment of invasive malignant melanoma:
Stage1A: Tumor depth 1.0 mm or less, no ulceration. Treatment is surgical with a full 1 cm margin, in addition to the original biopsy site size, to the level of the deep fat. Base line CXR and LDH are no longer recommended for stage 1A disease.

Stage 1B: Tumor depth 1.0 mm or less with ulceration, and Stages 2,3,4 requires referral to a surgeon able to perform sentinel lymph node mapping for evaluation, management and discussion of appropriate adjunctive therapy.

Prevention:
Death from melanoma is preventable through early detection, but can we prevent new melanomas?

It is well known that Australians have the highest rates of melanoma worldwide. There, widespread public awareness and interventions have been successful in not only halting the increase in incidence but also decreasing the incidence in certain age groups at the same time that rates here in the U.S. have tripled! We know through their experience that programs and education to promote sun avoidance and sun protection can affect the incidence of new disease.

Multiple programs exist for increasing public awareness starting with the "Slip, Slop, Slap" campaign and now the "Be Sun Smart" recommendations available through the Skin Cancer Foundation and AAD web sites.

Sunscreens:
New sunscreen agents are making it easier then ever to enhance patient compliance, from the non-greasy lotions designed for daily use to the water proof , sweat proof "dry" lotions, creams, gels, sprays, and wax sticks designed for outdoor activities. We all know they should be applied 20 minutes prior to sun exposure, as they are chemicals that require time to bind prior to becoming effective and should be re-applied every two hours. Titanium dioxide and zinc oxide are inert, sun blocking agents that sit on the skin surface reflecting the light. They are less sweat proof and rub proof than their chemical counterparts but are useful in those with sensitivity to the chemical agents. There are innumerable chemical sunscreens usually used in combination to achieve full spectrum coverage. Usually these are formulated as a mix of agents that block the UVB spectrum and UVA achieving varying degrees of protection depending on the agents used, their concentration and vehicle or base. Avobenzone was the first very effective blocker for the UVA spectrum but early formulations were not photo stable, meaning they lost their efficacy after two hours of sun exposure. Newer "stabilized" avobenzone products with varying proprietary names are available and should be indicated on the product label. The biggest breakthrough has been ecamsule (Mexoryl) which is important in providing a photostable UVA blocking agent that also bridges a gap in the spectrum between UVB and UVA left by prior combinations of sunscreens. It is available in the US in an SPF 15 and 20 products but is available from France in multiple products over SPF 50 with superior aesthetic qualities. They are available through US web sites under the name "Anthelios with Mexoryl." As always, sunscreens should be used along with other sun protection and sun avoidance behaviors.

Most of the notoriety recently regarding sun protection and "prevention" of melanoma centers around the "Vitamin D debate". The controversy centers around new findings that suggest the Recommended Dietary Allowance (RDA) for vitamin D was set too low, and we would derive anti-cancer and other benefits from maintaining higher levels of vitamin D in our bodies. There are many sources for vitamin D in the diet but insufficient to meet the new RDAs. Other sources include dietary supplements (vitamin D pills), fortified foods and exposure to sunlight… hence the "controversy" of intentional sun exposure as a source of vitamin D vs sun protection.

Regardless of the merit of the new RDAs and the perceived health benefits of vitamin D, the real question is that if higher levels of vitamin D are desirable, how do we achieve these in a safe manner. Unfortunately the tanning bed industry employs powerful lobbyists and publicists', declaring that sun protection is leading to an "epidemic" of vitamin D deficiency, and the deficiency, of course, should be cured not by dietary supplements but by a "healthy tan". The sensationalism unfortunately leaves the public vulnerable and creates an avenue for rationalization for continued sun exposure in individuals at high risk for malignancy.

We know exposure to sunlight and artificial light (tanning beds) by light skinned individuals, especially in children and young adults, is a known carcinogen. This is the population targeted by the tanning industry with the message, be healthy, get your vitamin D "naturally". Interestingly, studies have shown that even in the setting of intense regular sun exposure, individuals were found to be vitamin D deficient indicating that even intense sun exposure is insufficient as a sole source of vitamin D. (referenced in lectures as "Surfer dudes and vitamin D"; journal reference below)

The future trends in melanoma management and early detection are exciting, as is the hope that we can impact behaviors through increased awareness and education.

Reference

Brinkley N, Novotny R, Krueger D, et al. Low vitamin D status despite abundant sun exposure. J Clin Endocrinol Metab 92(6):2130-5 (2007 Jun)

Surgeon

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Surgical Specialists

According to recent cancer statistics, in 2008, there will be over 62,000 newly diagnosed cases of malignant melanoma and over 8000 deaths.[1] The incidence of melanoma is also dramatically rising, and will surpass all other malignancies in both men and women, with the only exception of lung cancer in women. Most melanomas present as early stage disease, with a good overall prognosis, and these patients typically do not require any form of adjuvant (i.e., post-operative) treatment (such as radiation therapy or medical oncology). The key is early diagnosis and treatment.

As with other malignancies, melanomas are classified according to the American Joint Committee on Cancer (AJCC). A revised version is pending in 2010 as tens of thousands of additional patients have been assessed and entered into a database to update staging data and prognosis. Melanoma is staged according to the **TNM** system. The **T** represents the depth of the primary tumor: **Tis** is melanoma in situ or non-invasive melanoma; **T1** is melanoma less than or equal to 1 mm thickness; **T2** is 1.01 to 2.0 mm; **T3** is 2.01 to 4.0 mm; and **T4** is greater than 4.0 mm. The subscripts, **a** and **b** have recently been added, and refer to the presence or absence of ulceration as this has a negative impact on survival. The **N** represents the status of the regional lymph nodes: **N0** indicates no regional lymph node involvement; **N1** is metastasis in one lymph node; **N2** generally means metastasis in two or three lymph nodes; and **N3** generally represents metastasis in four or more lymph nodes. The **M** indicates the presence of distant metastatic disease such as to the subcutaneous tissues, lungs, or other organs. The Stage Groupings includes these three letters and is divided into **Stage I, II, III,** and **IV.**

Cancer staging is very important because it helps determine what kind of operation a patient needs, adjuvant therapy, inclusion in a cancer trial, and prognosis. Typically, a patient presents to the Surgical Oncologist with a suspicious skin tumor, which was biopsied by a dermatologist. The information obtained from the pathology report includes the depth of invasion of the melanoma which is measured by the **Breslow** depth and **Clark's** stage. These are two independent staging systems with some overlap noted. In addition, other poor prognostic microscopic features are assessed such as ulceration, regression, and radial growth phase. Examination of the biopsy site can show other associated metastatic melanoma deposits along the lymphatic channels under the skin. Of course, a thorough physical examination is performed on all regional lymph node basins. Preoperative studies include both laboratory and imaging tests. The practice of obtaining these labs and diagnostic imaging studies is a point of some controversy; but suffice it to say that in most instances with earlier stage disease, the extent of these studies is left to the discretion of the treating physician.

Most patients present with malignant melanomas which can initially be treated with surgery. Surgery involves wide local resection of the tumor and occasionally surgical evaluation of the associated regional lymph node basin for metastatic disease. Optimal surgical margins are important as this affects the recurrence rate and disease specific survival. The surgical margins are clearly defined in the literature and are based on national and international prospective studies and meta-analysis. Essentially, in-situ melanomas should be excised with a 0.5 cm margin. For melanomas 1 mm and less, wide excision with a 1.0 cm margin is recommended. Melanomas measuring 1.01 to 2.0 mm may be excised with 1 – 2 cm margins. A 2.0 cm margin is recommended for melanomas more than 2.0 mm in thickness. Intermediate and thick melanomas of the face and scalp sometimes require less than the recommended margins because these are difficult locations and it is left to the surgeon's discretion. Often, it is necessary to cover larger tissue defects with split or full thickness skin grafts. This can often be preoperatively determined and may be done in conjunction with a Plastic Surgeon.

The regional lymph node status is the most important prognostic factor in patients with localized malignant melanoma. Ten percent of melanoma patients present with lymph node disease. The regional lymph node basin can be evaluated with the Sentinel Lymph Node technique. This is a minimally invasive procedure that allows identification of the major draining lymph nodes typically using a combination of blue and radioactive dye. The sentinel lymph node can be identified by its distinctive blue color and/or radioactive activity. Evaluation of the regional nodal basin is undertaken when the melanoma is thicker than 1 mm as the incidence of positive sentinel lymph nodes is approximately 10%, which is greater than the morbidity associated with this procedure. Although melanomas less than 1 mm do not typically

qualify for this technique, there are instances when it may be useful depending on certain poor microscopic features of the primary tumor. A sentinel lymph node positive for metastatic disease mandates a complete lymphadenectomy of that particular lymph node basin.

Five percent of those patients at initial presentation have metastatic disease or Stage IV. Surgical treatment depends on whether the disease is resectable or not. Tumors located in the lung can sometimes be surgically removed with a lung resection. The same is true for disease confined to the liver and other solitary visceral sites. Long term survival for these patients is poor and is around 14%. [2]

The adjuvant use of radiation is controversial but may have a role in those patients who present with advanced stage disease with multiple positive lymph nodes, extranodal soft-tissue extension, and for those patients rendered free of disease from recurrent or metastatic melanoma (Stage III or Stage IV).[3] In addition, radiation therapy may be used for palliation of symptoms such as gastrointestinal bleeding, bulky adenopathy, or ulcerating skin lesions.[4]

Reference

1. NCCN Practice Guidelines in Oncology, Melanoma, Version 1.2009, 09/15/08; pp. MS-1.
2. Current Management of Melanoma: From Ambiguous Lesions to Metastatic Disease. Published by the Society of Surgical Oncology in conjunction with Medical Association Communications, SSO Annual Meeting in Chicago, Illinois, March 13 – 16, 2008.
3. NCCN Practice Guidelines in Oncology, Melanoma, Version 1.2009, 09/15/08; pp. MS-9.
4. NCCN Practice Guidelines in Oncology, Melanoma, Version 1.2009, 09/15/08; pp. MS-11.

Radiologist

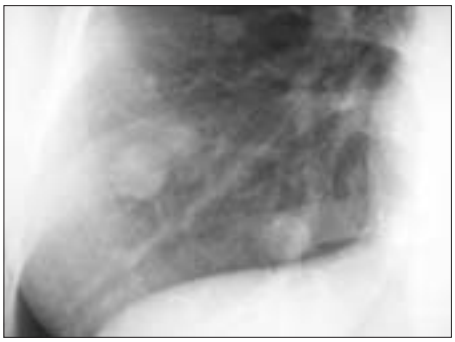
Timothy Farrell, MD
Peninsula Radiological Associates, Ltd.

Most melanomas are skin lesions, although primary melanoma can also be found in the bowel and in other areas which will be reviewed later. Because melanoma has "easy access" to the blood stream and lymph channels, it is prone to spread - even to remote areas of the body. Of all malignant tumors, melanoma probably has the greatest likelihood of relatively rapid remote spread (metastasis) - and it can literally metastasize to any organ in the body.

It is important to "stage" melanoma - determining local invasion or sites of remote spread. After diagnosis is made with a skin biopsy, one of the first procedures performed for this is called "sentinel node biopsy". The lymph nodes are glands that are part of the body's immune system—the system that helps protect against disease. The human body has many lymph nodes, especially in the armpit, neck, and groin. The lymph nodes are connected by lymph channels through which bacteria and other harmful substances from the body are drained. These substances are eventually trapped in the lymph nodes. Sometimes, cancer cells can break off from a tumor and enter a lymph channel. These cancer cells can get trapped in the draining lymph node and begin to grow there. The first lymph node draining the area of the melanoma is called the "sentinel lymph node." If the sentinel lymph node has cancer cells in it, there is a chance that the cancer has spread. If the sentinel node does not have cancer cells, the other lymph nodes in that area are probably also cancer-free, and the cancer probably has not spread. In order to evaluate this lymph node, a radioactive compound is injected at the site of the melanoma. This compound travels through the lymph channels and is trapped by the sentinel node. A special camera, called a gamma camera is then used to identify the node. The skin overlying it is marked and the lymph node is removed surgically.

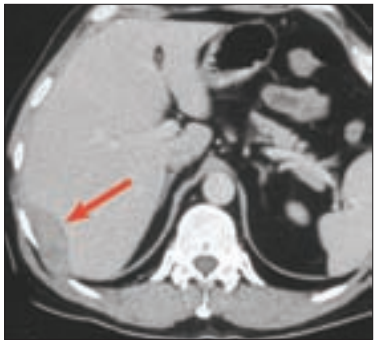
In addition to sentinel node biopsy, a variety of imaging tests are used in melanoma staging: plain radiography (x-rays), Computed Tomography (CT or "CAT" scans), Magnetic Resonance Imaging (MRI), Ultrasound, Nuclear Medicine and Positron Emission Tomography (PET).

Plain Radiography: Because of the emergence of more sensitive (accurate in detecting abnormalities) imaging procedures, regular x-rays are currently not used very often in the staging of melanoma. However, they can be very helpful in increasing the specificity (determining what the abnormalities actually are) of other tests such as PET scans or Nuclear Medicine bone scans.

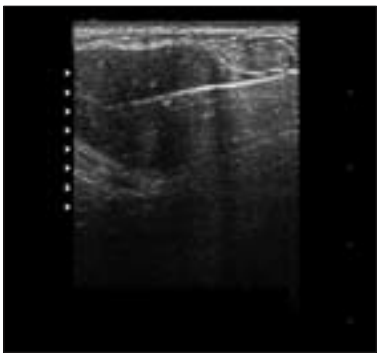


Chest x-ray showing multiple metastatic lung masses.

Computed Tomography: CT scans are excellent in evaluating the brain, lungs, abdominal organs (liver, spleen, kidneys, etc.) and for detecting enlarged lymph nodes in the armpit, chest, abdomen and groin. If an abnormality is detected, CT is also a great tool used in the performance of image-guided biopsy.

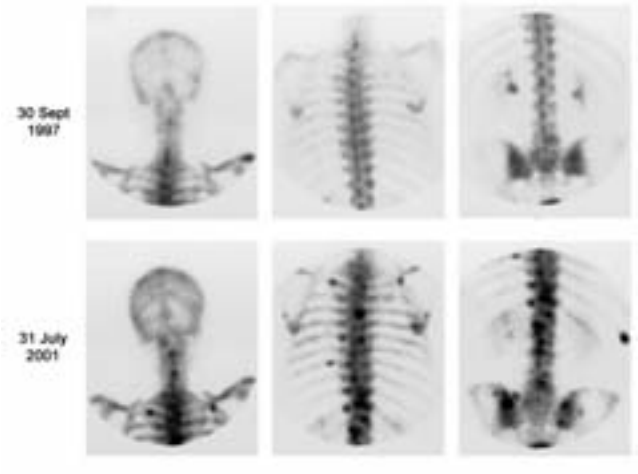


Magnetic Resonance Imaging: MRI is an excellent tool for evaluating the brain and spinal cord. It is very useful for determining local extent of bulky primary tumors or metastatic masses. As a rule, CT is better in the chest and abdomen than MRI.

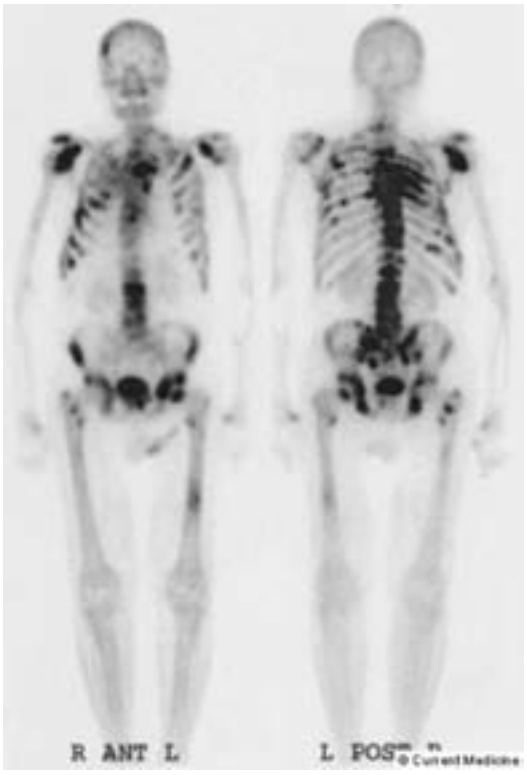


Ultrasound: The best use of ultrasound is typically in the evaluation, and possible biopsy, of local lymph nodes.

Nuclear Medicine: Bone scans are very sensitive in the detection of abnormalities. Metastatic deposits in bone are "hot" on these exams, meaning they absorb the radioactive material. Unfortunately, other, less ominous, conditions such as arthritis can also be "hot" on bone scan. The pattern of abnormality, comparison with previous sequential bone scans and correlation with other imaging studies such as plain x-rays, is necessary when evaluating for melanoma metastases.

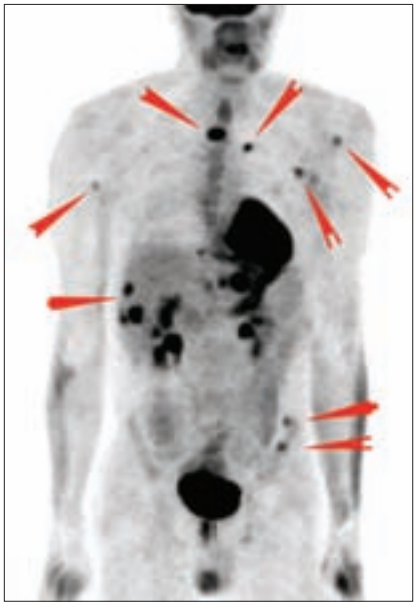


Bone scan, initially normal (1997), showing melanoma metastases – "dark spots" – in 2001.

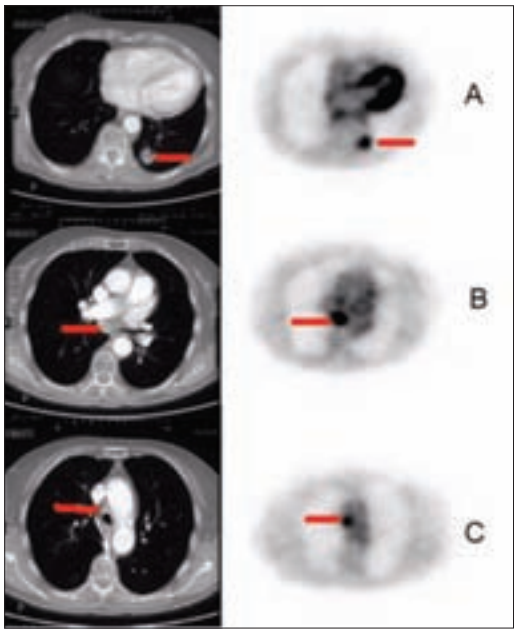


Bone scan – melanoma metastases (dark spots)

Positron Emission Tomography: Probably the single best imaging test in evaluating melanoma is PET combined with CT. In PET imaging, a sugar-based radioactive compound is injected intravenously. "Active" cancer cells extract this compound from the blood and use it in their metabolism. Melanoma cells, primary and metastatic, are very "active". PET imaging is 3-dimensional and is very sensitive, but its anatomical resolution is not very good. To increase accuracy and to add important anatomical detail, PET is combined with CT scanning, with both components being performed at the same time.



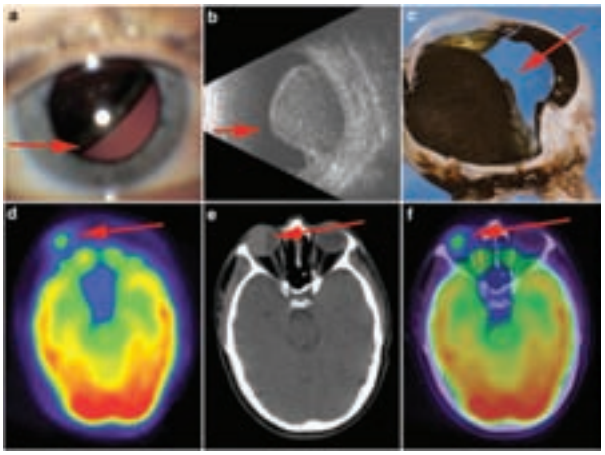
PET Scan – melanoma metastases (red arrows)



CT PET – masses seen on CT scan (red lines) are "hot" on PET.

In addition to cutaneous melanoma, other rarer forms exist.

Ocular: Ocular melanoma is the most common intraocular tumor in adults. It is a rare but frequently fatal disease, most common in patients of Northern European origin. Most of these tumors are asymptomatic, but non-specific symptoms such as blurred vision, decreased visual field and/or the presence of "floaters" can occur. Ocular melanoma is best initially diagnosed with an ophthalmic exam. Both ultrasound and MRI are helpful in evaluating for local extent of disease.



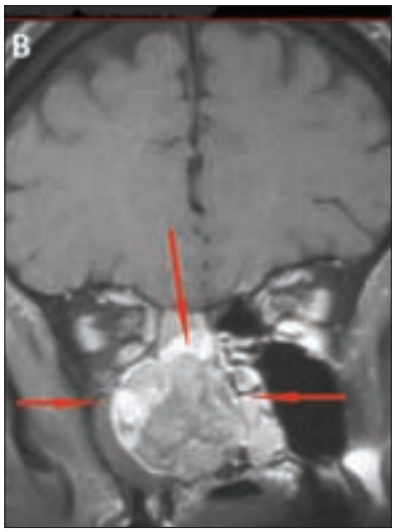
Ocular Melanoma (red arrow):

a. Direct Visualization
b. Ultrasound
c. Pathologic specimen
d. PET
e. CT
f. CT PET

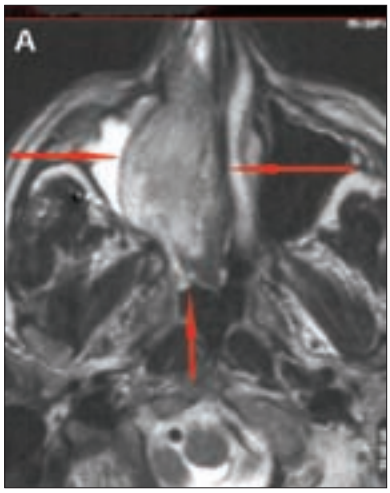
Cervix: Melanoma of the cervix is a rare tumor, typically found in middle-aged females. It is much less common than the "typical" cervical carcinoma. It can present with vaginal bleeding or discharge. Its size is variable. It is usually detected on physical examination and diagnosis is made by biopsy. MRI is the best imaging exam for locally staging this often-fatal tumor. CT can be helpful in the evaluation of pelvic and abdominal lymph nodes. Treatment is radical hysterectomy.

Vulva: Melanoma of the female external genital organs is a rare but important subtype of cutaneous melanoma. It behaves like cutaneous melanoma, in terms of metastasis, prognosis, etc. MRI is useful in evaluating local extent. As in cutaneous melanoma, the primary tumor and areas of metastatic involvement tend to be very "hot" on PET scanning.

Sinonasal: Melanoma of the nasal cavity or sinuses is an uncommon but deadly tumor of middle-aged/elderly patients. Patients can present with nasal congestion, often associated with nose-bleed. If small, these lesions can look like a "routine" nasal polyp on CT. When larger, they can appear lobulated and cause modeling of adjacent bone, but no bone destruction. Diagnosis is typically made through direct visualization (dark mass). The best single test for evaluation of local extent is MRI.



Sinonasal Melanoma (red arrows) – MRI



Sinonasal Melanoma (red arrows) – MRI

As you can see, even though most people consider melanoma a skin disease, it is not a disease of the skin alone. Its propensity for local and distant spread – with devastating consequences – make it paramount that melanoma is completely evaluated using a variety of imaging techniques, so that the proper therapy can be undertaken.

Pathologist

Michael Schwartz, MD
Peninsula Pathology Associates

Cutaneous melanoma is a tumor derived from activated or genetically altered epidermal melanocytes, the result of complex interactions between genetic, constitutional and environmental factors. Melanoma may develop within a preexistent benign (congenital or acquired) melanocytic nevus, complicate a dysplastic nevus or arise de novo (majority). Five major subtypes of melanoma are recognized: lentigo maligna melanoma, superficial spreading melanoma, acral lentiginous melanoma, nodular melanoma and desmoplastic melanoma. While melanoma tumor types differ in their respective clinical presentations and their biological behavior, in general, there is no significant difference between the different histologic tumor types in terms of prognosis once the tumor thickness and other risk factors have been taken into account. Superficial spreading and nodular melanoma are the prototypical melanoma types in terms of prognostic assessment and treatment approach as they account for 85% of tumors. Lentigo malignant melanoma is most commonly located on the face and neck. This tumor type often poses several surgical challenges due to its location near vital functional and cosmetically important areas, as it can become very large (up to several centimeters in diameter) and often has microscopically involved margins. The most common location for acral lentiginous melanoma is the sole but it may also develop on the palms and nailbed. Acral lentiginous melanoma is generally associated with a poor prognosis since tumors are often thick at the time of diagnosis. The diagnosis of desmoplastic melanoma is often delayed since it can resemble a flesh colored (40% are amelanotic) hypertrophic scar. The most common location for desmoplastic melanoma is the head and neck area and it often demonstrates significant infiltration of nerves (neurotropism). These tumors typically spare regional lymph nodes and most often metastasize to the lung.

A host of clinical prognostic factors impacting treatment decisions have been determined for cutaneous melanoma. Older age is considered to be an adverse prognostic factor for melanoma. A study of 488 patients by the Pigmented Lesion Group demonstrated an 84% ten-year survival for patients <65 years, compared with 57% in patients $\geq$ 65 years of age. Other studies show that the median tumor thickness in patients diagnosed in their 30's was 1.1 mm compared with 1.5 mm in patients diagnosed in their 50's

and 2.8 mm in patients in their 70's. Melanoma shows a male preponderance (3:2) and males have a higher mortality. While this may be due to females generally having thinner tumors at presentation compared to males, even after matching for thickness, age and location, women still demonstrate longer survival times. Women more commonly tend to have non-ulcerated tumors and tumors located on the extremities (particularly the calf), both carrying a more favorable prognosis, while the back and the head and neck are the most commonly involved sites in males. Many studies have established a correlation between prognosis and anatomic location, showing that tumors arising on the BANS sites (upper back, posterior arm, posterior neck and posterior scalp) behave less favorably than those on the extremities. In one recent study, a multi-variate analysis showed that patients with melanoma of the scalp/neck died of melanoma at 1.8 times the rate of those with melanoma on the extremities, controlling for age, Breslow thickness, sex and ulceration. For this reason, the scalp/neck should be checked carefully during routine skin examinations. As mentioned previously, acral sites are also thought to be associated with a poor prognosis.

Various histologic prognostic factors in cutaneous melanoma are also well recognized, and are in fact a key component of the American Joint Committee on Cancer (AJCC) 2002 revised staging system for cutaneous melanoma. When reporting melanoma, it is essential for the pathologist to record the tumor thickness, growth phase, level of invasion, presence or absence of ulceration, mitotic rate, presence of tumor infiltrating lymphocytes, regression, microsatellitosis and the status of the margins of resection.

The Breslow tumor thickness is measured from the most superficial aspect of the granular cell layer (stratum granulosum) to the deepest point of invasion of the tumor by ocular micrometer. Optimal cutoff points have specifically been shown to be $\leq$ 1.0 mm, 1.01 mm – 2.0 mm, 2.01 – 4.0 mm and > 4.0 mm and have been incorporated into the 2002 AJCC staging system. The tumor thickness is well established as the most reliable independent prognostic factor for primary melanoma. Thin tumors ($\leq$ 1.0 mm) without other adverse histologic features have a 5 year overall survival of 95-97%, and fewer than 5% of these patients have micrometastases in their regional lymph nodes. In thin melanomas, it is important to recognize the features of regression including the absence or reduced numbers of malignant melanocytes, apoptotic forms, a chronic inflammatory cell infiltrate, melanophages, horizontal scarring, isolated tumor islands and telangiectatic vessels as numerous experts believe that, in thin tumors, it correlates with an impaired prognosis. The implication for regression in the setting of the thin melanoma is that the tumor thickness, and hence its propensity for metastasis may be underestimated. Thus, some authors recommend sentinel node biopsy for thin melanomas if there is evidence of $\geq$ 50% regression.

An important concept in melanomas is the identification of the "growth phase" of the tumor. The microinvasive radial growth phase is recognized by single cells or small aggregates of melanoma cells in the dermis histologically similar to the intraepidermal component and forming tumor nests smaller than those present within the overlying epidermis. A lymphohistiocytic infiltrate is typically present, and mitotic figures should be absent. The vertical growth phase of melanoma is characterized by cohesive nests, nodules or plaques of cells in the dermis larger than those present within the epidermis and comprised of tumor cells that are also cytologically different than those in the epidermis. Mitotic figures are common, the cells are pleomorphic and apoptosis is often seen. The vertical growth phase implies an alteration in biological potential with a capacity for lymphvascular invasion and metastatic spread. Indeed, a follow-up study showed that the prognosis of thin melanomas in the radial growth phase approaches 100% survival at 8 years, suggesting an almost zero risk of metastases in patients with tumors only in the radial growth phase, in contrast with 71% survival in those with vertical growth phase tumors.

In one recent study of 229 patients with thick tumors (> 4.0 mm), the five-year overall survival (OS) was 49% in patients with tumors between 4.01 – 8.0 mm compared with 33% in patients with tumors > 8.0 mm, and median OS of 5.0 years vs. 2.6 years, respectively. When additional histological risk factors were evaluated by multivariate analysis, lymph node status, ulceration, and vascular involvement were found to have the greatest impact on the outcome of thick melanomas. Patients with thick tumors lacking ulceration and lymph node involvement had a 5 year OS of 62% and a medial OS of 6.0 years. If both ulceration and nodal involvement were present, the five year OS decreased to 18% with a median OS of 1.6 years.

The anatomic depth of invasion, or Clark Level, classifies the anatomic involvement of the tumor and consists of level I – intraepidermal growth with intact basement membrane (in situ); level II – invasion of the papillary dermis by single cells or small nests; level III – tumor usually as an expanded cell nodule filling the papillary dermis and abutting on the

reticular dermal interface; level IV – invasion of the reticular dermis; and level V – invasion of tumor cells into the subcutaneous fat. Although the Breslow tumor thickness is the single most important prognostic indicator, Clark level has been shown to be of significant prognostic value in thin melanomas. For tumors thicker than 1 mm, Clark level becomes less predictive than ulceration, patient age or anatomic location; thus, in the current 2002 AJCC staging system, thin tumors are further classified by Clark level, in addition to the presence or absence of ulceration.

Ulceration, defined as "the microscopic observation of the loss of epidermis overlying the tumor" is an important independent prognostic indicator and should also be reported. As many studies have shown that ulceration is an adverse prognostic feature, it has been included as the second determinant for the T classification. A recent article suggests that tumors ulcerate as a result of increased angiogenesis.

In one study of 526 patients by Kashani-Sabet, vascular involvement proved to be the second most important prognostic factor after tumor thickness. They found that distant metastases were observed in up to 74% of patients with vascular involvement, compared with only 22% of patients without vascular involvement. In a study by Zettersten of 329 thick melanomas, they showed that the presence of vascular involvement decreased the five year survival to 25%, compared with a five year overall survival of 50% absent vascular involvement. This study demonstrated that vascular involvement had the greatest impact on survival of thick melanomas after lymph node status.

Mitotic rate is determined by the number of mitotic figures per high power field or per mm square of invasive tumor. While some authors believe that tumors displaying a high mitotic rate are associated with a poor prognosis, others have linked the influence of mitotic rate with tumor thickness.

As previously mentioned, regression in melanoma is a histologic reflection of host immune interaction with malignant cells. This immune reaction often consists of an inflammatory cell response to the tumor mass. This interaction is termed the Tumor Infiltrating Lymphocyte (TIL) response and is typically categorized as brisk, non-brisk or absent. The brisk category implies lymphocytes invading throughout the whole vertical growth phase or extending across its entire base. Non-brisk implies focal infiltration only. Absent includes two categories: either no lymphocytes at all or lymphocytes are present, but do not infiltrate the melanoma. Brisk lymphocytic responses tend to be a feature of thin melanomas, whereas an absence of lymphocytic response is generally seen in thick melanomas. In a study of 285 vertical growth phase tumors, the ten year survival rates for brisk, non-brisk and absent TIL were 55%, 45% and 27%, respectively.

The presence of a microscopic satellite is defined by a distinct tumor nodule measuring 0.05 mm or more in diameter, separate from the main tumor mass. It is typically found in thicker tumors and is associated with an increased risk of local recurrence, region lymph node metastases and diminished survival. One study found an incidence of microsatellitosis of 4.6% for tumors between 0.76 mm and 1.5 mm thick, while another found no microsatellites in tumors < 1 mm thick. The incidence of microsatellitosis increases to 22% in tumors >2.25 mm thick, to 37% in tumors greater than 3.0 mm thick and to 65% in tumor depths greater than 4 mm. As the impact of microsatellites on local relapse is clear, and thereby effecting re-excision margins, the presence of microsatellitosis has been classified as N2c in the 2002 AJCC staging system.

In summary, the pathologist plays a central, critical role in the evaluation and treatment of patients with melanoma by diagnosing the melanoma and contributing to its risk assessment by providing a detailed list of histologic prognostic indicators.

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Medical Oncologist

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What is melanoma?

Melanoma is a type of skin cancer, the most serious type of skin cancer. Normally within the skin, at the bottom-most layer are cells called melanocytes. These cells are what give the skin its color. Darker skinned people have more melanocytes; lighter skinned people have fewer melanocytes. These are the cells that react to sunlight to protect us from too much sun exposure. Melanoma is the process by which the normal system of controls is lost and melanocytes grow and reproduce in an unchecked manner.

Melanoma cases are becoming more frequent. In 1985, the risk for developing melanoma was 1 in 150 for men and 1 in 600 for women. Today, the ratios are different, with 1 in 55 for men and 1 in 82 for women being at risk. It ranks as the sixth most common cancer in the United States, and approximately 80% of deaths from skin cancers are attributable to melanomas. People of any age can get melanoma, though the highest percentage of people are between the ages of 20 and 50. While melanomas only account for 3% of skin cancers, they account for 75% of the skin cancer deaths.

Not every overgrowth of melanocytes is cancerous. Moles (or nevi in medical terms) are benign overgrowths of tissue with no risk of transforming into a malignancy. However, some nevi may be different from the classic mole, and those types of lesions do have an increased risk of becoming a malignancy.

How to know the difference? When showering or bathing, one should always do some surveillance of the skin. Have a friend or a loved one keep an eye on those parts of the skin that are difficult to see (like one's back.) What to look for? The ABCDE's of melanoma: A=Asymmetry: is the mole basically round or is the shape of the mole haphazard appearing? B=Borders: are the borders of the mole sharp or are they ill defined? C=Color: does the mole have a uniform color to it, or is the color different or variegated within the mole? D=Diameter: the larger the mole, the higher the risk it could be or become cancerous. Six millimeters or greater is the diameter used to help us discriminate. E: Evolution: Watching moles over time for changes in A, B, C, and/or D.

What if changes are found? Whenever a mole looks suspicious in any way, bring it to your doctor. A simple skin biopsy done in the office will make the diagnosis.

Where can melanoma grow?

ANYWHERE! The skin is the most common place, and it can involve the palm of a hand, the sole of a foot, a mucous membrane, under a fingernail (the subungual space), the vulva, the vagina, the anorectal area, and the eye.

What are the risk factors?

1. Ultraviolet (UV) exposure: UV light is part of sunlight. UV light is also used in tanning salons. UV light is further broken down categorically as either UV-A or UV-B. Traditionally, UV-B is considered to be the causal agent, but the use of UV-A light in tanning beds and in a certain type of medical treatment called PUVA, have also been associated with melanoma.

2. Endometriosis: The risk for melanoma is slightly higher in women with a history of endometriosis than for women who have not had that condition.

3. Parkinson's disease: Melanoma is more common in people with this disease as well.

4. Genetic issues: There have been genes that are associated with an increased risk of developing melanoma. If you have blood-related family members with a history of melanoma, you may need to be tested for the presence of those genes.

5. Prior history of melanoma: People who have had melanoma previously are at a higher risk of getting a second melanoma. The risk is highest within the first year after diagnosis of the first melanoma, and decreases from that point, but even 5 years later, the risk is still higher than the general population. People who have had 2 melanomas are at even higher risk for a third.

6. Other issues: Multiple other behaviors and exposures have been explored as possible risk factors for development of melanoma. Among these factors: Smoking, chemical exposures, radiation exposure, vitamin deficiencies, vitamin overdoses, oral contraceptives. While each of these factors could have a bad effect on any other number of systems in your body, none of them have been shown to be causally related to melanoma.

How do I prevent melanoma?

First and foremost, protect yourself from the sun. Any part of your body exposed to the sun is at risk. People who work outside are at increased risk if they don't protect themselves.

It is also important to protect your skin from other UV sources, especially tanning beds. The myth that tanning salons are safe is a dangerous one. Tanning beds emit doses of ultraviolet radiation that can be as much as 12 times the amount of the sun's radiation. In fact, exposure to tanning salons prior to age 35 increases one's melanoma risk by 75%. People with genetic risks, endometriosis, or Parkinson's disease cannot avoid having those conditions; but they too need to be very cautious to protect their skin from sunlight and UV exposure.

What does SPF mean?

It stands for **S**un **P**rotection **F**actor. The higher the number, the more protection you have. The number tells you how much additional protection you have compared to bare skin. For example, if you burn after 20 minutes in the sun without anything on your skin, SPF 15 will give you 15 times that protection (15x 20 minutes = 5 hours). Generally speaking, an SPF of 15 should be enough for most people; however, some fair-skinned people or people with risk factors listed above might need more protection than that. Of note, not all clothing is impervious to sunlight and UV light (e.g. The SPF of a plain white T-shirt is only 4!!). It is also important to look for a sunscreen that offers protection against both UVA and UVB rays.

What if I am diagnosed with melanoma?

First, it must be staged. The stage is dependent on the depth the melanoma has invaded into the skin, whether or not it has spread to lymph nodes, and whether or not is has spread to other sites within the body. The deeper the invasion, the presence and location of the nodes involved and the presence of spread to other parts of the body (known as metastatic disease) are all used in determining stage.

What are the stages?

Stage I: A small tumor (up to 2mm) without any involvement of lymph nodes or any other sites of spread.

Stage II: A larger tumor (> 2mm) without any lymph nodes or other sites involved.

Stage III: Any tumor with lymph node involvement, but no other sites of disease.

Stage IV: Any tumor, with or without lymph node involvement, but with spread of disease to a different site.

How do we treat it?

That is dependent on the stage of the disease:

The first step is resection, or the removal of the primary tumor and of any local lymph nodes, if they are involved. Depending on the size and physician's clinical assessment, this may be completed in the office setting or in the OR. Sometimes an initial removal in the dermatologists' office is enough for a small tumor. But, if there are non clear margins, or a large tumor, then a surgeon is needed and the procedure is often completed in outpatient surgery. If the melanoma has spread to other sites, surgery cannot be used to remove those lesions. If the disease is local (only involves the skin) and low risk (based on what it looks like under the microscope), then surgery is all that is required. If the tumor is high risk and lymph nodes near the primary tumor are involved, the nodes can be removed as well, but further treatment will be needed. If there are distant sites, the primary tumor and any local nodes should be removed and further treatment will be needed.

Following resection, some patients require additional treatment, which may include radiation therapy (XRT) or systemic therapy with medical oncology.

Systemic treatment is designed to treat your whole body. The nature of any cancer, including melanoma, is that one cell goes bad. Going bad could mean that old cells that should be removed from the system are resisting being removed from the system. Or, it could mean that cells are reproducing when they are not supposed to be reproducing. Possibly both of these processes are happening.

Primary treatment with surgery (and XRT if it is needed) is designed to remove those cells. But what if, after primary treatment, one of those bad cells remained? Maybe it was out of the field of surgery (or radiation); maybe a cell had already broken away from the primary tumor before it was removed; or maybe a new tumor cell 'went bad' elsewhere. This is where systemic treatment is used.

By treating the whole body, we treat that cell, wherever it is. People with early stage disease almost never have that cell, so they usually don't need systemic therapy. But everyone else, from those with high risk tumors to those with spread elsewhere, should receive systemic therapy.

The standards of care, as they exist now, include the use of an immune-modulating agent called *interferon-alfa* (IFN-a). This is a medicine that is given intravenously for 5 days per week for 4 weeks, followed by injections of a lower dose into the subcutaneous tissue 3 times per week for 11 months. There have been several trials looking at this method of therapy, and to date, it is the only therapy shown to improve the risk of melanoma recurrence. An analysis of pooling all the studies together did not show a change in the percentage of people who survive after being diagnosed; but this finding is debated, as 2 of the 3 studies did show an improvement in overall survival.

Other drugs and immune agents have been used in various combinations. Some of those studies are still on-going and we are awaiting the results.

Vaccines are being analyzed at present as well. There are several animal models looking at various targets to produce vaccines against. Results of human studies have not yet begun, but are eagerly anticipated.

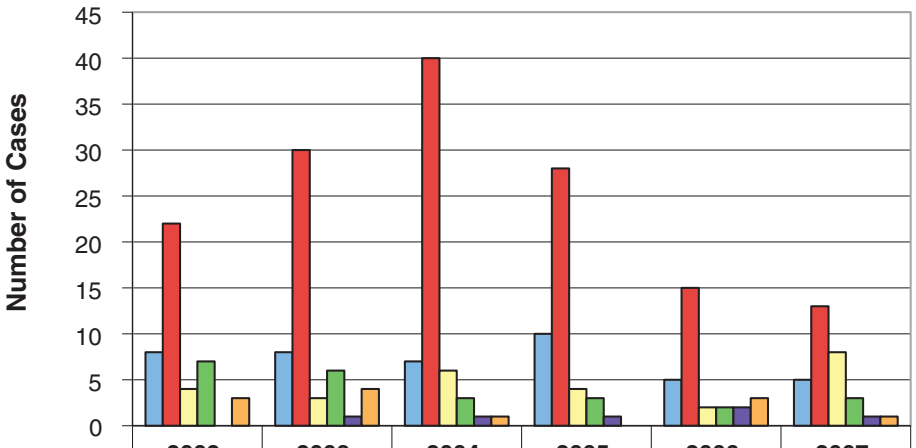
Gene therapies, designed to make melanoma tumor cells more attractive to your own immune system, are also being studied and may provide a separate mechanism to attack these cells as well.

Summary

Melanoma is a skin cancer of the melanocytes, seen most commonly in people aged 20-50, that has the potential to spread to the lymph nodes and to other tissues in the body. Of the risk factors we know of for the disease, exposure to UV light tops the list. There are also genetic factors in some people that can increase the risk of having melanoma. The disease is staged by the depth of invasion, the involvement of lymph nodes and the spread of the disease. Melanoma is treated primarily by surgery and XRT can be used for locally advanced disease. Systemic treatment is necessary for more advanced disease, and there are multiple studies on-going in an effort to improve both the disease-free survival and the overall survival for malignant melanoma.

Riverside Cancer Registry Data

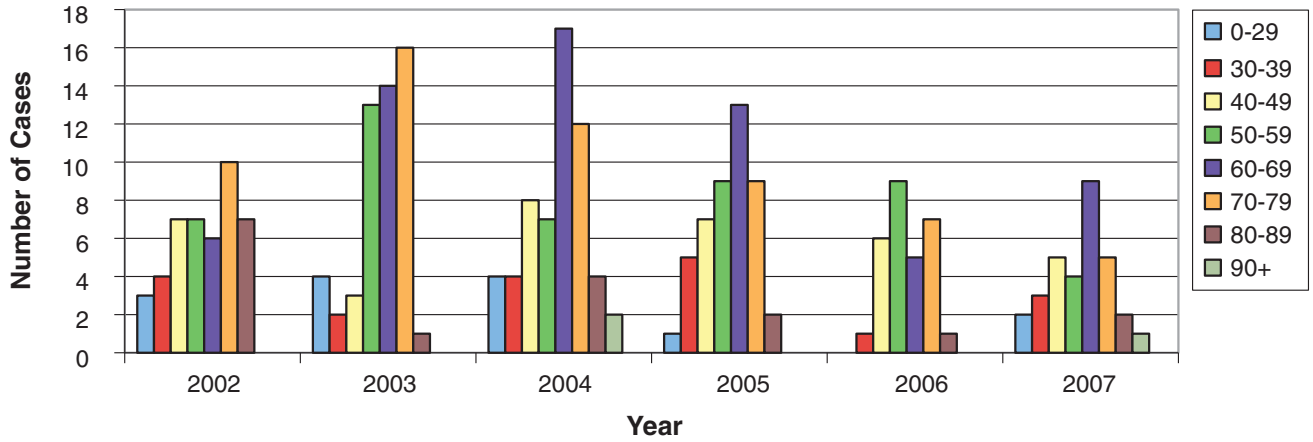
2002-2007 Number of Analytic Cases by Stage at Diagnosis



	2002	2003	2004	2005	2006	2007
Stage 0	8	8	7	10	5	5
Stage I	22	30	40	28	15	13
Stage II	4	3	6	4	2	8
Stage III	7	6	3	3	2	3
Stage IV	0	1	1	1	2	1
Stage Unknown	3	4	1	0	3	1

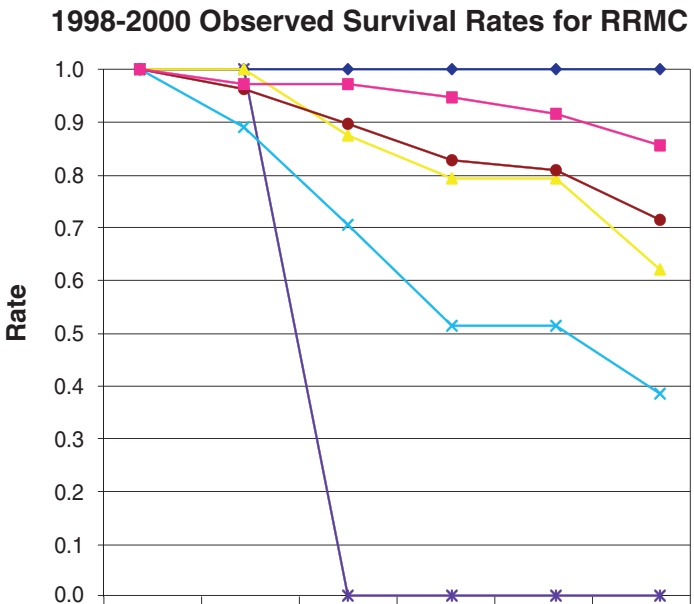
Year

2002-2007 Age at Diagnosis of Melanoma RRMC Analytic Cases Only



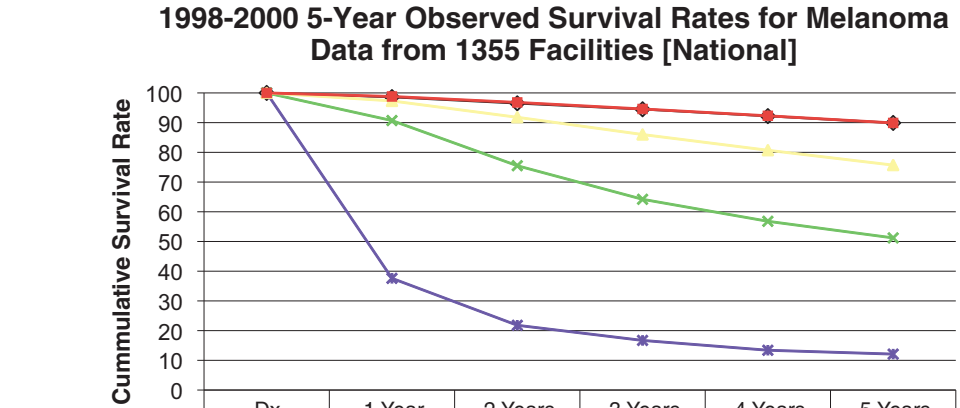
The above graphs illustrate the predominance of Stage I diagnosis among RRMC analytic cases. This early detection in turn supports the 5-year survival outcomes with positive response (85% for Stage I). However, the age at diagnosis typically seen at RRMC falls within the ages 50-79 bracket.

Riverside Cancer Registry Data



	Dx	1 Year	2 Years	3 Years	4 Years	5 Years
Stage 0 (n=10)	1.000	1.000	1.000	1.000	1.000	1.000
Stage I (n=37)	1.000	0.973	0.973	0.946	0.916	0.855
Stage II (n=24)	1.000	1.000	0.875	0.792	0.792	0.620
Stage III (n=19)	1.000	0.889	0.705	0.513	0.513	0.385
Stage IV (n=1)	1.000	1.000	0.000	0.000	0.000	0.000
OVERALL (n=107)	1.000	0.962	0.895	0.827	0.807	0.713

Years



	Dx	1 Year	2 Years	3 Years	4 Years	5 Years
0 n=15498	100	98.6	96.5	94.5	92.2	89.9
I n=27535	100	98.8	96.8	94.6	92.3	89.9
II n=11504	100	97.3	91.8	86	80.7	75.7
III n=8208	100	90.7	75.5	64.2	56.8	51.2
IV n=2924	100	37.6	21.8	16.7	13.4	12.1

Years Since Diagnosis

When comparing the 5-year survival rates of Riverside Regional Medical Center's (RRMC) melanoma patients (n= 107) to the Commission on Cancer's National Cancer Data Base (NCDB) patients (n=65,669), RRMC is in accordance with the national survival rates of Stage 0 and Stage I melanomas. Stages II, III, and IV all tend to have approximately 12 % higher survival rates nationally, however this difference could be accredited to the smaller volume of cases. From 1998-2000 RRMC's Melanoma caseload was concentrated in the Stage I category, as were cases nationally.

Bladder Cancer at Riverside Regional Medical Center

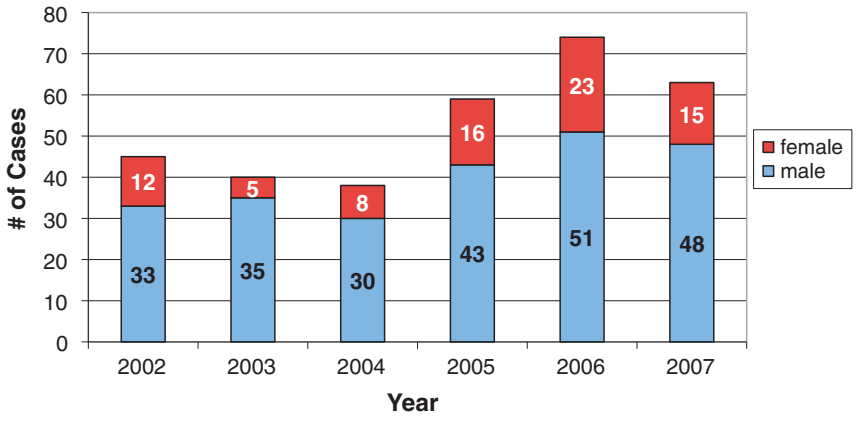
Surgeon

Richard Rento II, MD
Hampton Roads Urology

BLADDER CANCER

Bladder cancer is the fourth most common cancer in men and is three times more common in men than in women in the United States. An estimated 68,810 new cases of bladder cancer will be diagnosed in the United States (51,230 men and 17,580 women) in 2008. During that same period, approximately 14,100 deaths from bladder cancer are anticipated. The same national male-to-female ratio of 3:1 has been seen at Riverside Regional Medical Center over the past 6 years (Fig. 1).

Figure 1: 2002-2007 Cumulative Bladder Cancers by Gender- RRMC Only



The most common type of bladder cancer in this country is urothelial carcinoma, formerly known as transitional cell carcinoma (TCC). The urothelium in the entire urinary tract may be involved. More than 90% originate in the urinary bladder, 8% in the renal pelvis, and the remaining 2% in the ureter and urethra. Less common histologic subtypes in the urinary system include squamous cell carcinoma associated with chronic trauma from indwelling foley catheters or bladder stones (3%), adenocarcinoma typically seen at the dome of the bladder in the embryonal remnant of the urachus (2%), and small-cell tumors (1%).

The most common risk factor for developing bladder cancer is smoking, accounting for an estimated 50% of all cases. Other risk factors include being exposed to certain substances at work, such as rubber, inks, certain dyes and textiles, paint, and hairdressing supplies. A diet high in fried meats and fat as well as being male, white or older (median age at diagnosis is 68 years), and prior exposure to radiation treatment to the pelvis increases the risk of bladder cancer.

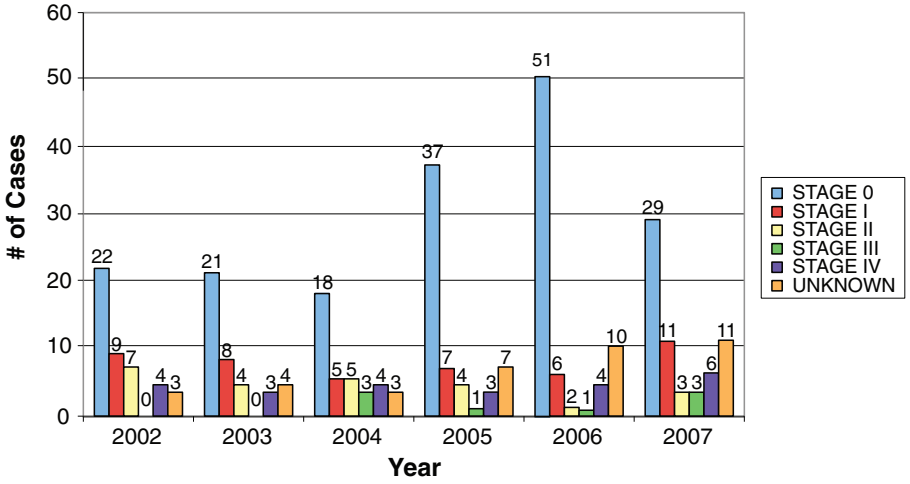
The most common presenting symptom in patients with bladder cancer is microscopic hematuria, or blood in the urine. All patients with painless gross hematuria should be considered to have bladder cancer until proven otherwise. Urinary frequency, dysuria or urgency from irritation or a reduced bladder capacity can also develop. Patients presenting with these symptoms should be evaluated with office cystoscopy to determine if a lesion is present.

Bladder cancer is diagnosed through pathologic examination of tissue obtained by TURBT (transurethral resection of bladder tumor). Radiographic imaging with CT urography, MRI, intravenous pyelography (IVP) or renal/bladder US may reveal a bladder mass or wall thickening suggestive of an underlying bladder cancer. Urinary cytology may also detect suspicious cells but its routine use for screening is controversial. The use of additional urine markers such as UroVysion (FISH), BTA, and NMP-22 in the initial diagnosis of bladder cancer is also controversial. Cystoscopy remains the primary diagnostic tool allowing visualization of the mucosal lining of the bladder for detection of a mass.

TURBT with a bimanual examination under anesthesia (EUA) is performed to resect visible tumor and to sample muscle within the area of the tumor to assess whether invasion has occurred. Treatment decisions are then based on disease extent within the 3 general categories: noninvasive, invasive, or metastatic. More than 70% of all newly diagnosed urothelial bladder cancers are exophytic papillary tumors. Approximately 50-70% are stage Ta (confined to epithelium), 20-30% are T1 (invades lamina propria), and 10% are CIS

(carcinoma in situ). Approximately 25% of patients present with muscle-invasive disease at the time of diagnosis. Metastatic disease is seen in 5% of patients commonly involving the regional lymph nodes, lung, liver, and bone. At RRMC over the last 6 years, 75% of cases have been Ta/T1 while 25% have presented with T2-T4 disease (Fig. 2).

Figure 2: 2002-2007 Total Bladder Cancer Cases by AJCC Stage at Diagnosis



Treatment in noninvasive bladder cancer is directed at reducing recurrences and preventing progression to a more advanced stage. Papillary noninvasive tumors are generally managed endoscopically with complete resection. Though noninvasive, recurrence rates are high with as many as 80% of patients having at least one recurrence. Depending on the depth of invasion and grade, intravesical therapy may be recommended based on the estimated probability of recurrence or progression to a more advanced stage.

BCG immunotherapy is the most effective intravesical therapy and involves a live attenuated strain of *Mycobacterium bovis*. BCG is administered weekly for 6 weeks in an office setting by instilling 2 ounces into the bladder through a simple catheterization. Maintenance therapy for 3 weeks every 6 months for 1-3 years may provide more lasting results. Alpha Interferon is an alternative immunotherapy agent. More recently, intravesical chemotherapy with mitomycin-C in the immediate post-operative period has been shown to be effective in decreasing recurrence rates.

When faced with a localized invasive bladder cancer, the primary goal of therapy is to determine if the bladder should be removed or preserved without compromising survival. The second goal is to determine if the primary lesion can be managed independently or if patients who are at high risk for distant spread will require systemic approaches to improve the likelihood of cure. A partial cystectomy can be considered in fewer than 5% of cases when an initial invasive tumor develops in an area of the bladder where an adequate margin of soft tissue and a minimum of 2 cm of uninvolved urothelium can be removed along with the tumor without compromising continence or significantly reducing bladder capacity. Surgical treatment with radical cystectomy with the consideration of neoadjuvant chemotherapy is still the most effective local therapy in muscle-invasive bladder cancer.

The appropriate surgical procedure involves a cystoprostatectomy in men and, in women, a cystectomy and commonly a hysterectomy (anterior pelvic exenteration), followed by the formation of a urinary diversion. A pelvic lymph node dissection adds prognostic information through staging and may confer a therapeutic benefit with 25% of patients having positive nodes at the time of radical cystectomy. Various forms of urinary diversions are created from an intestinal segment and are separated into incontinent and continent diversions.

An ileal conduit is the most common incontinent diversion performed and has been used for more than 50 years with excellent reliability and minimal morbidity. A small segment of ileum allows urine to continuously flow into an external collection device worn over a rosebud stoma. Continent diversions are either ectopic (Kock or Indiana pouch) or, more commonly, orthotopic (ileal neobladder). The former creates a urinary reservoir requiring clean intermittent catheterization 4-6 times per day through a small stoma on the abdominal wall. The orthotopic neobladder most closely restores the natural storage and voiding function of the native bladder allowing for "normal" urination. With the recent advances in surgical technique, this procedure is becoming the diversion of choice for men. It provides good daytime urinary control, with about a 20% chance of nighttime incontinence. Some women may have trouble completely emptying the neobladder and may sometimes need to use a catheter.

The overall early and late complication rate for a radical cystectomy is approximately 25%. The two most common early complications are wound infection and bowel obstruction. Many patients have multiple comorbid health risk factors (eg; advanced age, cardiovascular or pulmonary disease) with a perioperative mortality rate of 1-2%. However, the morbidity of untreated bladder cancer is significant and includes hematuria, dysuria, irritative voiding symptoms,

urinary retention, incontinence, ureteral obstruction, and pelvic pain. All men are impotent following a radical cystectomy unless a nerve-sparing approach is attempted reducing the impotency rate to approximately 40-50%.

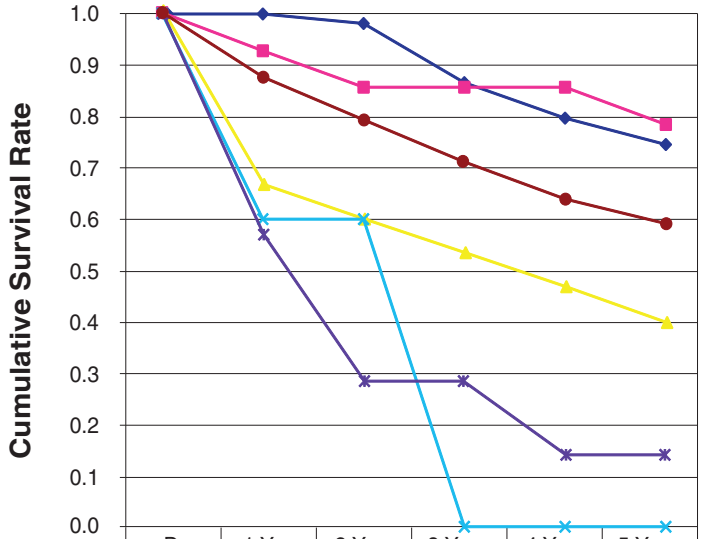
Patients who have undergone radical cystectomy require routine surveillance to monitor for local recurrence or the development of metastatic disease. CT scanning of the abdomen and pelvis and a chest radiography should be performed semi-annually for 2 years then annually through 5 years.

Noninvasive bladder cancer has a good prognosis, with 5-year survival rates of 82-100%. The risk of stage progression increases with tumor grade. CIS carries a poorer prognosis and a recurrence rate of 63-92%. 5-year survival rates for localized muscle invasive disease (Stage T2) drop to 63-83% while disease into the perivesical fat (Stage T3) results in a much worse 5-year survival rate of 17-71%. Patients with tumor involving adjacent organs such as prostate, rectum or pelvic sidewall (Stage T4) have poor 5-year survival rates of 0-22%. Riverside Regional Medical Center 5-year observed survival rates (Fig. 3) are very comparable to national rates (Fig. 4).

Patients who present with unresectable or metastatic disease or who subsequently develop metastatic disease are generally treated with systemic chemotherapy and/or radiotherapy. The specific chemotherapy regimen recommended partially depends on the presence or absence of medical comorbidities along with the risk classification of the patient based on disease extent. Prognosis for metastatic urothelial carcinoma is poor, with only 5% of patients living two years after diagnosis.

In summary, urothelial tumors represent a spectrum of diseases with a range of prognoses. After a tumor is diagnosed anywhere within the urothelial tract, the patient remains at risk for developing a new lesion at a different, or at the same location, and with a similar or more advanced stage. Continued monitoring for recurrence is an essential part of management because most recurrences are superficial and can be treated endoscopically. For patients with more extensive disease, newer treatments typically involve combined modality approaches using recently developed surgical procedures or 3-dimensional treatment planning for more precise delivery of radiation therapy. Finally, for the patient with metastatic disease, several new agents have been identified that seem superior to those considered standard therapies offering hope for improved survival rates in the near future.

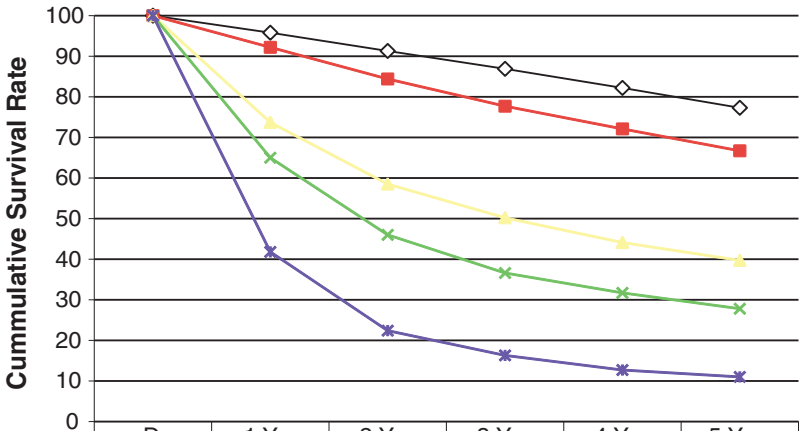
Figure 3: 1998-2000 5-Year Observed Survival Rates for RRMC



	Dx	1 Year	2 Years	3 Years	4 Years	5 Years
Stage 0	1.000	1.000	0.978	0.864	0.794	0.747
Stage I	1.000	0.929	0.857	0.857	0.857	0.786
Stage II	1.000	0.667	0.600	0.533	0.467	0.400
Stage III	1.000	0.600	0.600	0.000	0.000	0.000
Stage IV	1.000	0.571	0.286	0.286	0.143	0.143
OVERALL	1.000	0.875	0.794	0.713	0.641	0.593

Years Since Diagnosis

Figure 4:
Observed Survival For Bladder Cases Diagnosed in 1998 - 2000 Data from 1346 Facilities [National]



	Dx	1 Year	2 Years	3 Years	4 Years	5 Years
0 n=40239	100	95.8	91.3	86.9	82.2	77.3
I n=21093	100	92.2	84.4	77.7	72.1	66.7
II n=10352	100	73.7	58.5	50.2	44.1	39.7
III n=5022	100	65	46	36.6	31.7	27.8
IV n=5795	100	41.8	22.4	16.3	12.7	11

Years From Diagnosis

Pathologist

David Smith, MD
Peninsula Pathology Associates

Urine flows from the kidneys, where it is made, and into the bladder to be stored until urination. The bladder is a hollow organ that has a wall made up of several layers. Cancer begins in the lining layer and grows into the bladder wall. As the cancer grows deeper into the layers of the wall of the bladder, it is at increasingly higher stages and becomes harder to treat.

The inside of the bladder is lined with a layer of cells, called urothelial cells. The same type of cells also lines the kidneys, the tubes connecting the kidneys to the bladder (ureters), and the urethra. Cancer can begin in the lining cells in any of these structures, which are part of the urinary system.

There are four main types of bladder cancer, grouped by the way the cancer cells look under a microscope. Urothelial carcinoma: This is by far the most common type of bladder cancer. It starts in the lining urothelial cells. Historically, this type of cancer was called transitional cell carcinoma. Within this group are also several subtypes, which are designated based upon their growth structure and pattern.

Squamous cell carcinoma, adenocarcinoma, and small cell carcinoma represent the other three main types of bladder cancer. Each of these is much less common than urothelial carcinoma, but is often more likely to be invasive at the time of diagnosis and therefore harder to treat.

Screening tests for bladder cancer are available, but are not used unless a patient has strong risk factors or symptoms. These include things such as: blood in the urine, changes in bladder habits, having had bladder cancer in the past, defects or malformations of the bladder, and a history of exposure to certain chemicals. One common screening test is urine cytology. Either urine that is voided by the patient, or "washings" of the bladder taken by the physician during cystoscopy can be prepared for cytologic examination. Cells from the urinary sample are then examined under the microscope by the pathologist. Abnormal or cancerous cells can be detected by this method.

If the urologist identifies a lesion or mass during cystoscopy, a portion of the suspicious tissue may be removed by biopsy. Biopsy samples are then prepared in the laboratory, and the pathologist examines the specimen under a microscope. Through microscopic investigation the pathologist can tell if cancer is present, what type of bladder cancer it is, and if the tumor has invaded into the bladder wall.

Bladder cancers are graded according to their degree of differentiation. The grade of the tumor is an important predictor of how aggressively the tumor will behave in growth and response to treatment. Low-grade urothelial carcinomas tend to respond much better to various forms of treatment. On the other hand, high-grade carcinomas are much more aggressive, and likely to invade the bladder wall, spreading to other areas.

Radiologist

Valentine Curran, MD
Peninsula Radiological
Associates, Ltd.

Imaging plays an important role in the initial diagnosis, staging, and surveillance of bladder cancer.

Bladder cancer will present as blood in the urine approximately 80% of the time. An initial CT evaluation of the abdomen and pelvis dedicated to evaluation of the urinary system (CT urography) may be utilized to identify a cause of hematuria. This may detect the presence of a mass within the bladder.

Initial contrast enhanced CT images may demonstrate an enhancing bladder mass against the background of unopacitied urine (Fig.1). A five minute delayed scan through the renal collecting system allows for opacification of the urine improving detection of masses arising from the bladder wall (Fig.2). Bladder cancer may present as a focal lobulated mass arising from the bladder wall (Fig.2) or as diffuse, irregular bladder wall thickening (Fig.3). When a CT scan determines the presence of a bladder mass, the patient will then undergo cystoscopy to obtain a tissue diagnosis and determine the depth of the lesion within the bladder wall.

The treatment of bladder cancer will be determined by the stage at initial diagnosis. Initial staging will be based upon results of cystoscopy and clinical examination, which are limited in their ability to detect the presence of tumor extension beyond the bladder wall. CT and MRI of the pelvis can both be utilized to determine whether the tumor has extended through the thickness of the bladder wall into surrounding fat, local lymph nodes, or the pelvic sidewall. A chest radiograph will also be obtained to exclude metastatic nodules to the lungs, which is the most common site of hematogenous spread of bladder cancer. The presence of tumor extension beyond the bladder wall and distant metastatic disease will alter the treatment regimen.

Unfortunately, bladder cancer has a high recurrence rate. Routine CT urography will aid in the early diagnosis of new masses within the urinary collecting system and exclude the development of metastatic disease to lymph nodes and other organs.

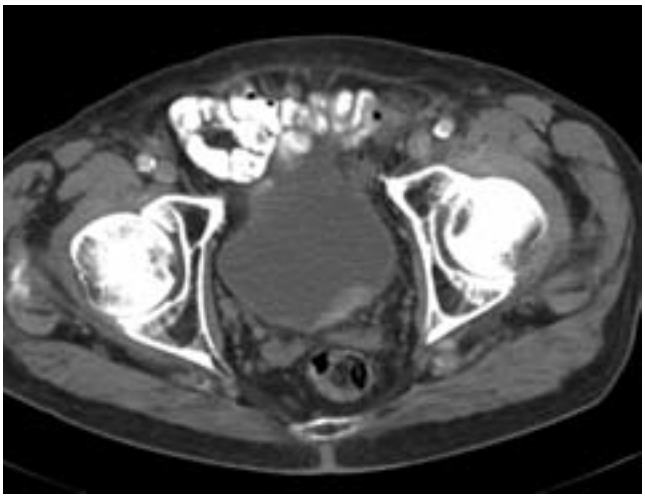


Figure 1. CT demonstrates an enhancing area of focal bladder wall thickening in the bladder base. Biopsy demonstrated transitional cell carcinoma.

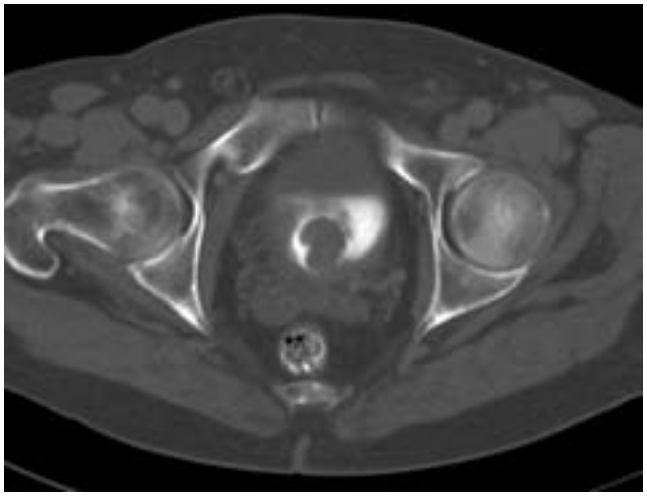


Figure 2. CT demonstrates a round, lobulated mass against backdrop of bright contrast material in the bladder. Biopsy demonstrated transitional cell carcinoma.

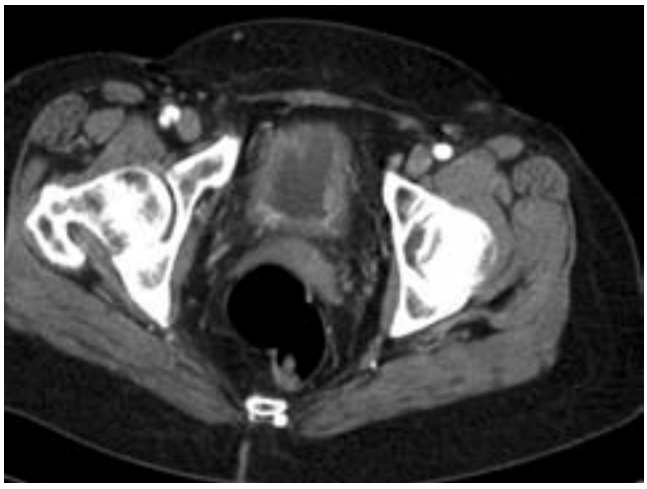


Figure 3. CT demonstrates diffuse irregular bladder wall thickening found to represent transitional cell carcinoma.

Medical Oncologist

Guy Tillinghast, MD
Peninsula Cancer Institute

The bladder is a bag-like organ that stores urine made by the kidneys. Two "pipes," known as the ureters, drain the urine from the kidneys to the bladder. During urination, muscles in the wall of the bladder squeeze, shrinking the size of the bladder's internal volume.

Bladder cancer affects 69,000 patients each year in the United States, 70 percent of whom are men. Ninety percent of bladder cancer patients are diagnosed over age 55. Caucasians are diagnosed twice as often as African Americans, and African Americans are diagnosed more than Hispanics. Additionally, African Americans tend to have more advanced disease at the time of diagnosis, as compared to Caucasians and Hispanics.

Assessing the spread of bladder cancer can be divided into four stages. "Stage One" means that the disease has been detected early by means of a biopsy and is confined to the inside of the bladder wall. Seventy-four percent of bladder cancer patients are diagnosed Stage One, in which case the treatment can be managed by a urologist. Stage One bladder cancer prognosis is very good, with approximately a half-million bladder cancer survivors in the United States.

However, if the initial biopsy indicates that the bladder cancer has become more extensive, i.e. if it has progressed beyond the inside of the bladder wall, a team of doctors assembles to assist with management. This team includes a medical oncologist because the bladder is a chemotherapy-responsive organ. The first task of the medical team is to properly "stage" the patient, which means determining how far the cancer has spread. This staging consists of blood work, a chest x-ray, and a CT scan or MRI of the abdomen and pelvis. A bone scan is performed if an elevated level of phosphatase is detected with a blood test. A bone scan is also done if the patient has experienced any bone pain. Additionally, it is recommended that the ureters (the tubes leading from the kidneys to the bladder) be examined with ultrasound imaging or a CT urograph.

"Stage Two" bladder cancer means that the disease has spread into the muscle layer in the outer bladder wall and, therefore, much more aggressive therapy is needed. "Stage Three" indicates that the cancer has spread outside the bladder to the prostate, uterus or vagina, etc. If the disease has spread to the distant pelvis wall, for example, or even to a single lymph node, this constitutes a "Stage Four" diagnosis. On average, 19 percent of bladder cancer patients have cancer that has spread to tissues near the bladder (Stages Two and Three) and three percent of patients have cancer that has spread to distant sites (Stage Four).

If there is no radiographic evidence of distant disease, the patient may still be a surgical candidate. To determine whether surgery is still possible, the urologist performs a manual examination under general anesthesia. It is necessary to relax the muscles under general anesthesia to properly feel the presence of tumor masses. A "moveable mass" suggests "T3b disease," whereas a "fixed" tumor mass suggests "T4b disease." Unfortunately, "T4b disease" is inoperable.

After staging, the medical team meets to discuss the condition of the patient and make a recommendation for treatment. There are three treatment options to consider: surgery, radiation, and chemotherapy. These can be given individually or in combination. For patients with "node-negative early muscle-invading cancer" (the cancer has spread beyond the bladder wall but has not been detected in any lymph nodes), all three treatments may be given in an otherwise "healthy" patient. However, in a patient with kidney failure or other ailment, only one of the treatments may be offered.

Chemotherapy is a vigorous therapy, meant for highly motivated patients who are medically strong enough for treatment. Patients receiving chemotherapy depend on reliable support from family, friends and/or community resources. The evidence suggests that chemotherapy works best when given before surgery. Although chemotherapy can be given after surgery, the evidence does not strongly indicate that chemotherapy after surgery is effective. When bladder cancer is Stage Four, then chemotherapy is the only realistic option.

Radiation Oncologist

James Wassum, MD
Radiation Oncology Specialist

RADIATION THERAPY FOR BLADDER CANCER

While muscle invasive bladder cancer is usually treated with surgery, radiation therapy may be used with curative intent in selected patients who either refuse surgery or have preexisting medical conditions that preclude surgery. Best results with radiation therapy are generally seen in patients with solitary low-grade T2 transitional cell cancers. The latest reports in the literature indicate the best results are obtained in patients who are able to undergo transurethral resection of all visible tumor prior to beginning radiation therapy. Combined chemotherapy and radiation therapy gives better results than radiation therapy alone. Most reports favor initial radiation therapy and chemotherapy for approximately five weeks followed by repeat cystoscopy. Those patients who have no evidence of residual cancer, continue with radiation therapy and chemotherapy for an additional two weeks. Those patients who have residual cancer undergo radical cystectomy if possible. Both groups may receive further adjuvant chemotherapy after their primary therapy. Early results in small single institution studies compare favorably with surgery for similar stages of cancer, but long term follow-up is not yet available and surgery remains the standard of care for most patients. Acute side effects of combined therapy for bladder cancer include neutropenia, thrombocytopenia, cystitis, proctitis, nausea and vomiting and fatigue. While older reports in the literature indicate a considerable incidence of long term side effects and complications including contracted bladder and proctitis, newer techniques such as IMRT and IGRT are able to reduce doses to normal tissues resulting in a significant decrease in long term effects.

Enterostomal Nurse

Phyllis Kohlman, RN, BSN
CWOCN - Enterostomal Therapy Services

When someone gets a diagnosis that requires an ostomy (surgically created opening using the bowel to bring stool or urine to the skin surface), they have a double impact psychologically, their illness and "now having to wear a bag". They have questions concerning their illness and then they start worrying, "How is this ostomy going to change my life?"; "Will I smell all the time?"; "Will everyone look at me and know I have an ostomy?", etc. If they have known someone who has had an ostomy that lived a normal life style, then they have a basic understanding. Usually the patient does not know what to expect. Patients want the bag to be placed as low on their abdomen as possible, however this is usually out of their field of vision and not a good site for the appliance to stay intact. There are a lot of misconceptions that need to be worked through to have a successful outcome for the ostomy patient.

Efforts are made to see patients that are scheduled to have an ostomy surgery about 3-5 days before surgery. This allows time to explain the anatomy of the gastrointestinal (GI) or genitourinary (GU) tract, depending on the planned surgical procedure. The expected surgical procedure is explained in detail; as well as ensuring the patient understands why these steps are important for a good surgical outcome. This visit is typically when the patient or significant other begins asking about the "pouch". There are different pouches for fecal and urinary stomas. The appropriate pouch and wafer, or mounting plate, for the particular patient is shown to them and discussed how the pouch attaches to and releases from the wafer, how to clean the pouch, how often the entire system of wafer/pouch is changed, and insurance coverage of the products and where to obtain their supplies. Any dexterity problems or other life style issues are assessed at this meeting to eliminate or decrease the patient's anxiety about the ostomy care.

The abdomen is assessed with a wafer, with the patient lying, sitting, and standing to find the *best site* externally to place the stoma so the wafer will adhere with no to minimal problems. The wafer needs to be on a flat plane when the patient sits, and stands, and the site needs to avoid the umbilicus and the belt line. The stoma site needs to be in the patient's field of vision so self care is successful. Once the site is marked, it is covered with a clearfilm so the

patient can take a bath without the mark washing off. Prior to surgery, the surgeon will assess the stoma site to ensure it is the correct surgical site. It is explained to the patient that the surgeon will try to place the stoma at this site, if it is possible, following the internal surgical site assessment. Usually the stoma is placed at the marked site.

Once the patient has surgery, ET Services assesses the new stoma and the surrounding skin site and selects the best appliance for the patient to successfully care for the ostomy. Before discharge the appliance will be changed one to two times with the patient and significant other during a teaching session. The stoma is measured and a pattern is made for the patient to use when he/she cuts the wafer for the next appliance change. Each step of self-care is reviewed multiple times before discharge, including: how to remove the old wafer and prepare the skin to receive the new wafer, how to prepare the new wafer and place over the stoma, and how to attach the pouch and clip. A prescription for the needed ostomy supplies is provided and key issues such as where to purchase replacement supplies or understanding insurance coverage are discussed.

When patients want to try other ostomy products, beside what the hospital currently has available, arrangements are made to have samples sent to the patients' home.

Depending on the patient's situation, home care may be supported by home health or through outpatient ET service. Sometimes the patient will develop skin irritation under the wafer, leaking problems, or other problems with the ostomy wafer or pouch weeks, months, or years after their ostomy surgery. ET Services provides outpatient services to help assist in these situations. As not all patients know ahead of the surgery that they will have an ostomy, ET Services works with these patients and significant others to help them adjust to the situation and introduce the patient of ostomy care into their expected recovery period.

ET Services is always available to talk with the patient or family to answer questions, or just to listen to the concerns. ET Services works closely with the surgeons to make sure the patient, while hospitalized or once discharged, has every opportunity to have a smooth transition to return to their normal lifestyle.

CANCER SERVICES

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