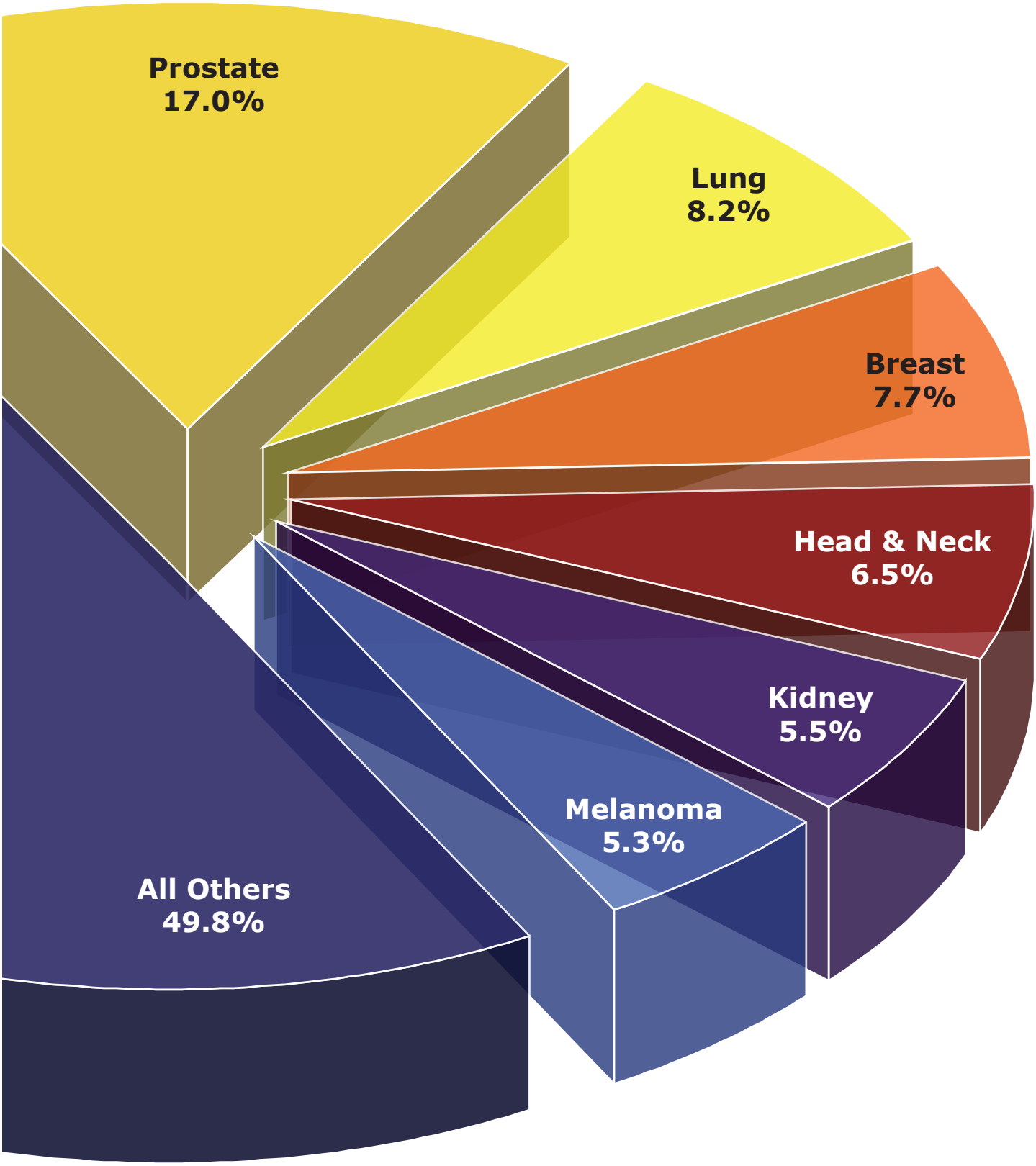
2007

cancer registry report

data from 2005 & highlighting head and neck cancers



Welcome

Mark C. Kelley, MD

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We are pleased to present this report of cancer registry data from 2005, including a selected site summary highlighting head and neck cancers. The number of new cases entered into the registry in 2005 represents a nearly 70 percent increase over 1999. Our new cancer cases represented 2,848 individuals from all 95 counties of Tennessee, as well as 970 patients from outside Tennessee.

Five primary sites (prostate, lung, breast, kidney and melanoma) represent 43% of our new cases in 2005. We are pleased to report five-year survival rates that are comparable – and in many cases, exceed – national benchmarks from the National Cancer Institute SEER database.

The Vanderbilt-Ingram Cancer Center remains committed to improving the quality of cancer care available to our patients and to patients treated elsewhere, through our translational research program and our collaborations with peers at other centers. In addition to recently receiving accreditation with commendation from the American College of Surgeons Commission on Cancer, Vanderbilt-Ingram is Tennessee's only NCI-designated Comprehensive Cancer Center and recently became the 21st member of the National Comprehensive Cancer Network.

We are currently engaged in developing a special section our website (www.vicc.org) to share more current Cancer Registry data for both consumer/patient audiences as well as for cancer professionals.

Please direct any questions inquiries about the data included in this report to our Cancer Registry at (615) 936-2282.

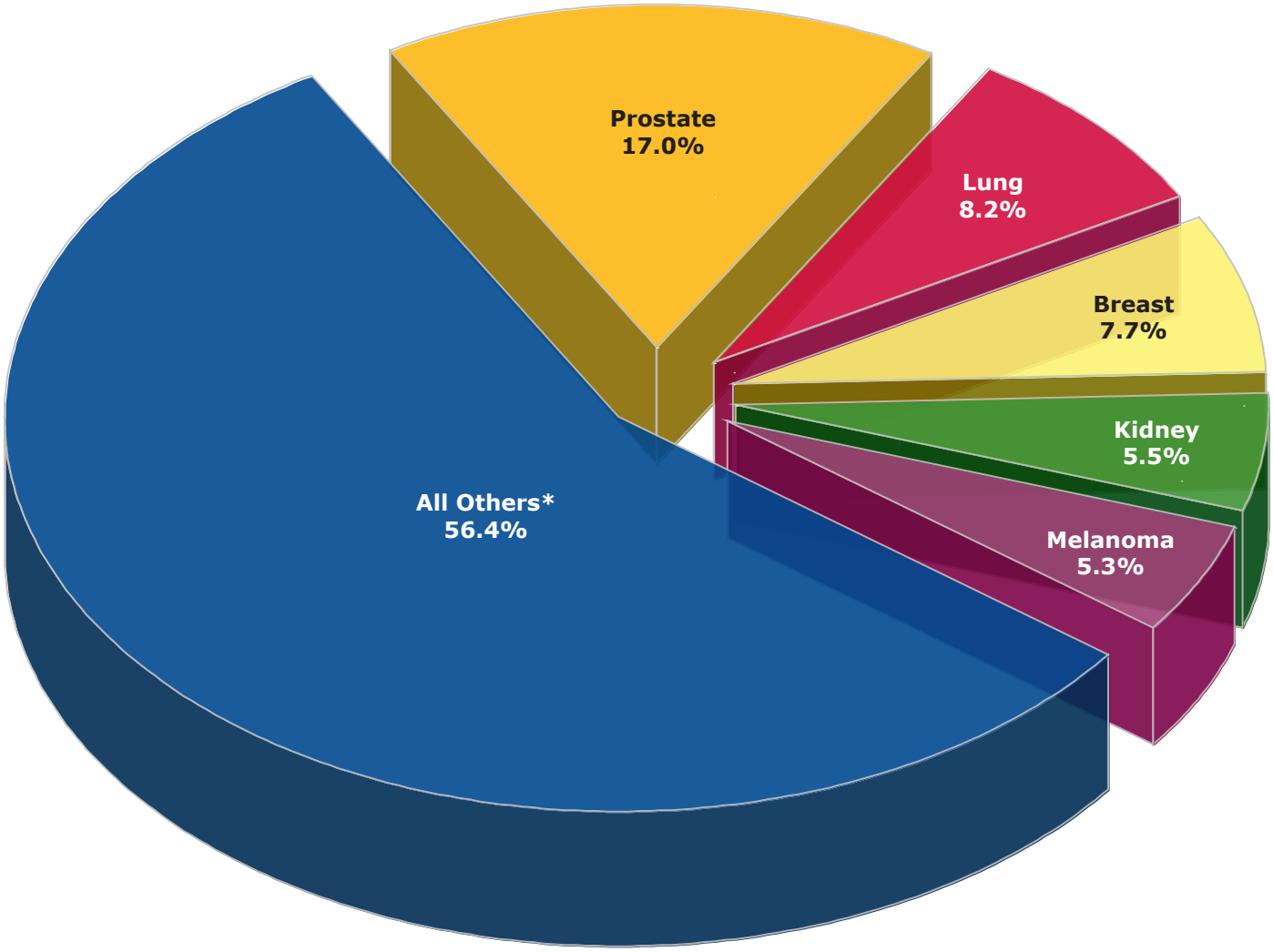
Mark C. Kelley, MD
Chair, Cancer Committee
Chief, Surgical Oncology

Data Charts

Top Five Primary Sites - 2005 Analytic Cases

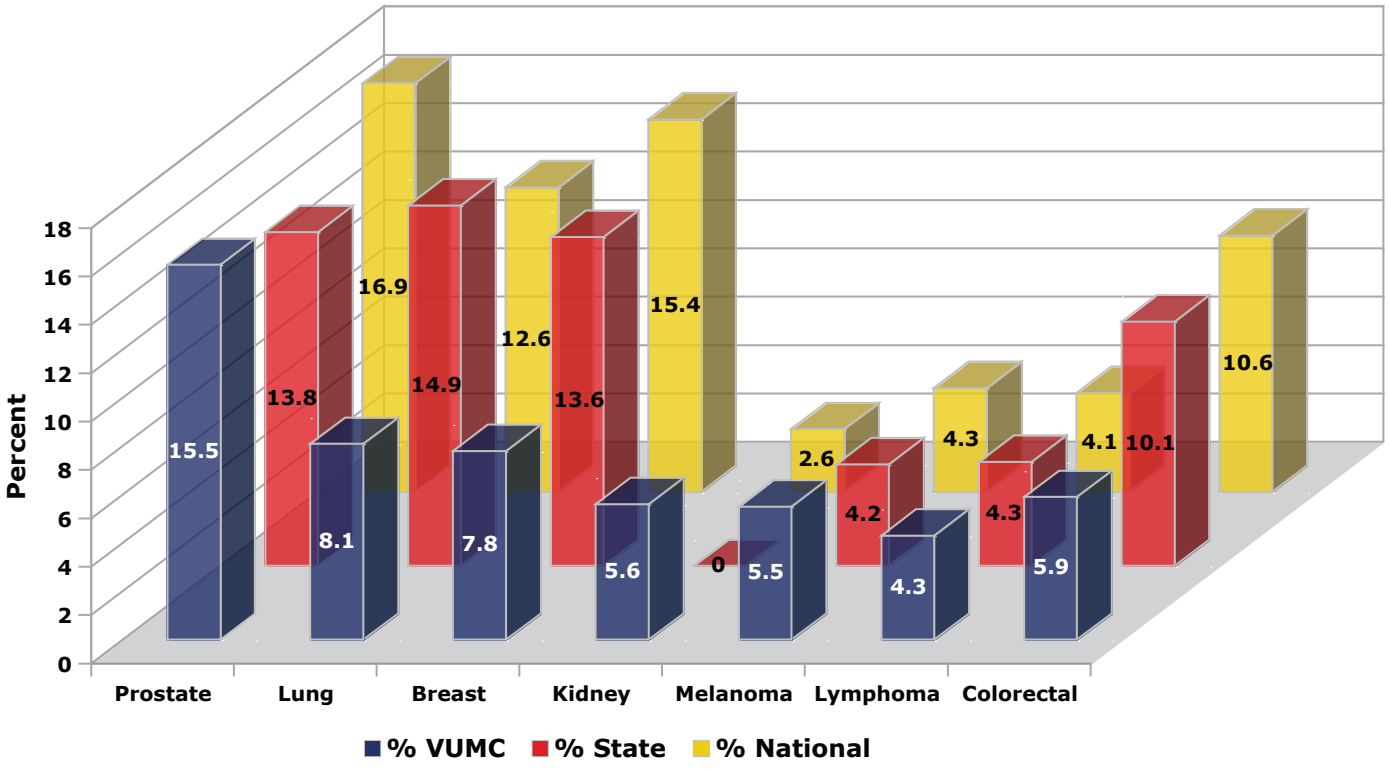
Prostate	17.0%
Lung	8.2%
Breast	7.7%
Kidney	5.5%
Melanoma	5.3%
All Others*	56.4%
Total Cases	**100.0%**

* Includes head & neck cancers



Comparison at Incidence for Selected Primary Sites
All Cases 2005 with Estimated New Cases
for Selected Sites by State, U.S., 2005

Site	% VUMC	% State	% National
Prostate	15.5	13.8	16.9
Lung	8.1	14.9	12.6
Breast	7.8	13.6	15.4
Kidney	5.6	N/A	2.6
Melanoma	5.5	4.2	4.3
Lymphoma	4.3	4.3	4.1
Colorectal	5.9	10.1	10.6



Comparison Age at Diagnosis
All Class of Case (2001-2005)

Age Range	2001	2002	2003	2004	2005
0 - 17	4.3%	2.8%	3.8%	3.9%	3.8%
18 - 29	5.1%	5.3%	3.7%	4.7%	3.8%
30 - 39	7.9%	7.1%	5.5%	6.7%	5.9%
40 -49	14.0%	13.6%	15.0%	13.4%	14.7%
50 - 59	23.6%	25.2%	24.1%	26.6%	24.6%
60 -69	24.9%	25.3%	26.1%	24.2%	27.1%
70 -79	15.5%	16.3%	16.8%	15.3%	15.2%
80 - 89	4.3%	4.3%	4.5%	5.1%	4.5%
> = 90	0.4%	0.2%	0.5%	0.2%	0.3%
Total Cases	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**

Comparison Case Counts Primary System
All Class of Case (1999-2005)

PRIMARY SYSTEM	1999	2000	2001	2002	2003	2004	2005
Head and Neck	103	134	160	149	154	172	174
Digestive System	300	356	411	441	409	405	490
Respiratory System	327	338	380	366	329	388	401
Bone, Skin/Soft Tissue	267	267	272	261	305	348	361
Breast, female & male	237	280	285	248	263	257	296
Reproductive Organs	200	257	246	280	187	188	192
Male Sites	255	320	390	421	436	491	617
Urinary System	179	241	261	300	318	372	406
Central Nervous System	75	72	90	79	75	81	104
Endocrine System	36	69	83	98	88	114	150
Lymphatic System	144	173	192	177	175	170	196
Hematopoietic	115	144	207	212	234	288	249
Other & ill-defined sites	0	1	0	1	2	0	2
Unknown primary	27	32	53	44	45	39	36
Benign/borderline brain,cns	N/A	N/A	N/A	N/A	N/A	117	144
Total Cases	**2265**	**2684**	**3030**	**3077**	**3020**	**3430**	**3818**

Comparison of All Case Counts (1999-2005)

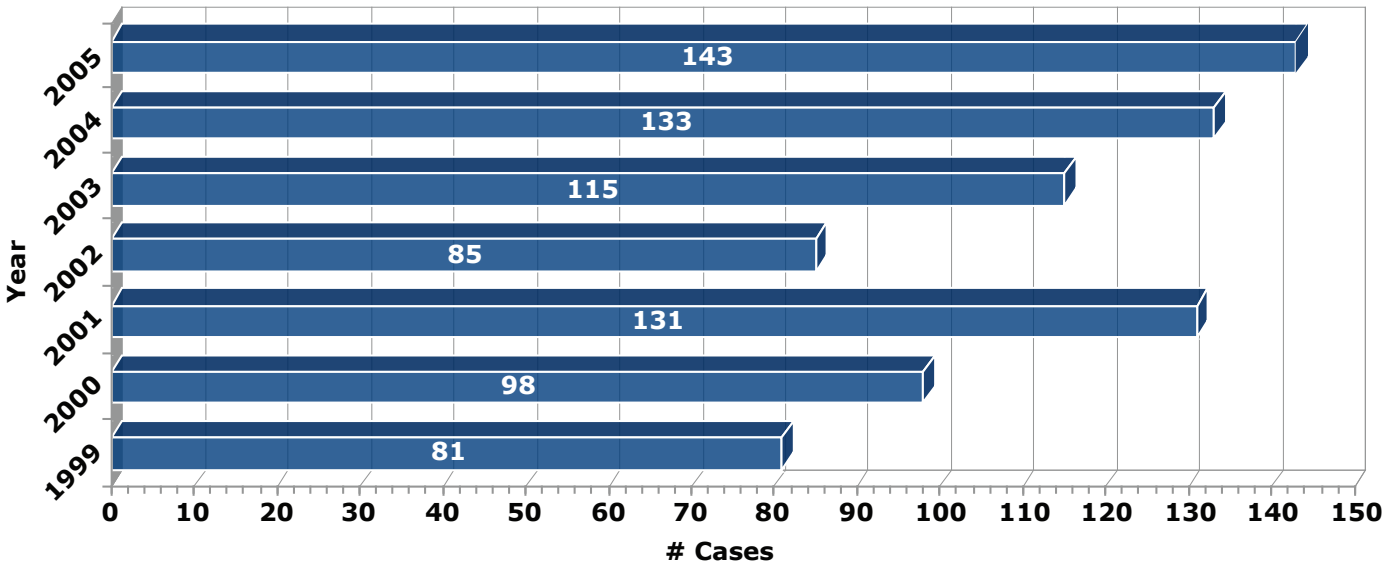
CANCER SITE	1999	2000	2001	2002	2003	2004	2005
Lip	1	2	4	6	3	3	7
Tongue	25	40	47	40	50	62	52
Salivary glands	10	12	14	19	10	10	14
Gum & hard palate	18	14	21	18	10	20	18
Floor of mouth	5	9	12	6	6	16	9
Buccal mucosa	6	9	9	9	12	8	9
Oropharynx	21	29	26	38	36	31	45
Nasopharynx	5	6	10	6	12	12	7
Hypopharynx	11	7	15	5	11	9	9
Other oral cavity	1	6	2	2	4	1	4
Esophagus	28	37	31	30	31	39	38
Stomach	22	18	25	24	14	19	34
Small Intestine	3	9	13	15	13	10	15
Colon	101	115	122	146	111	95	129
Rectum/Anus	53	50	53	78	62	79	98
Liver	26	48	54	49	54	72	68
Gallbladder	15	14	17	11	24	14	20
Pancreas	44	57	74	76	87	60	71
Other digestive tract	8	8	22	12	13	17	17
Nasal cavities, sinuses, ear	15	6	12	21	13	14	16
Larynx	70	51	60	51	44	74	73
Trachea, bronchus, lung-small	31	39	29	27	44	36	41
Trachea, bronchus, lung-NSC	202	236	259	255	223	259	263
Other respiratory	9	6	20	12	5	5	8
Bone	25	40	26	34	44	45	55
Connective & soft tissue	56	83	69	63	77	84	86
Malignant melanoma	111	120	153	143	174	206	213
Other skin	75	24	24	21	10	13	7
Breast, female & male	237	280	285	248	263	257	296
Cervix	64	80	85	107	46	32	40

CANCER SITE	1999	2000	2001	2002	2003	2004	2005
Endometrium (corpus uteri)	52	79	76	67	56	72	70
Ovary	40	49	40	54	43	43	48
Other female genital organs	44	49	45	52	42	41	34
Prostate	211	288	341	387	397	451	589
Testis	31	27	40	25	27	36	21
Other male genital organs	13	5	9	9	12	4	7
Bladder	91	124	124	146	142	165	162
Kidney	70	97	117	138	167	183	215
Other urinary organs	18	20	20	16	9	24	29
Eye	2	1	6	2	6	2	2
Brain	68	67	80	73	65	73	91
Other CNS	5	4	4	4	4	6	11
Thyroid	33	57	74	94	80	103	135
Other endocrine	3	12	9	4	8	11	15
Hodgkin's	32	32	21	35	38	29	33
Non-Hodgkin's Lymphomas	112	141	171	142	137	141	163
Plasma cell tumors	24	29	39	44	55	60	66
Lymphocytic leukemias	34	44	38	51	52	62	56
Myeloid leukemias	45	49	77	67	70	89	73
Other leukemias	7	14	15	11	9	7	8
Myeloprolif. & myelodysplas	0	0	24	19	32	49	25
Other hematopoietic diseases	5	8	14	20	16	21	21
Other & ill-defined sites	0	1	0	1	2	0	2
Unknown primary	27	32	53	44	45	39	36
Benign/borderline brain, cns	0	0	0	0	0	117	144
Total Cases	**2265**	**2684**	**3030**	**3077**	**3020**	**3430**	**3818**

State of Residence at Diagnosis (2005, All Cases)

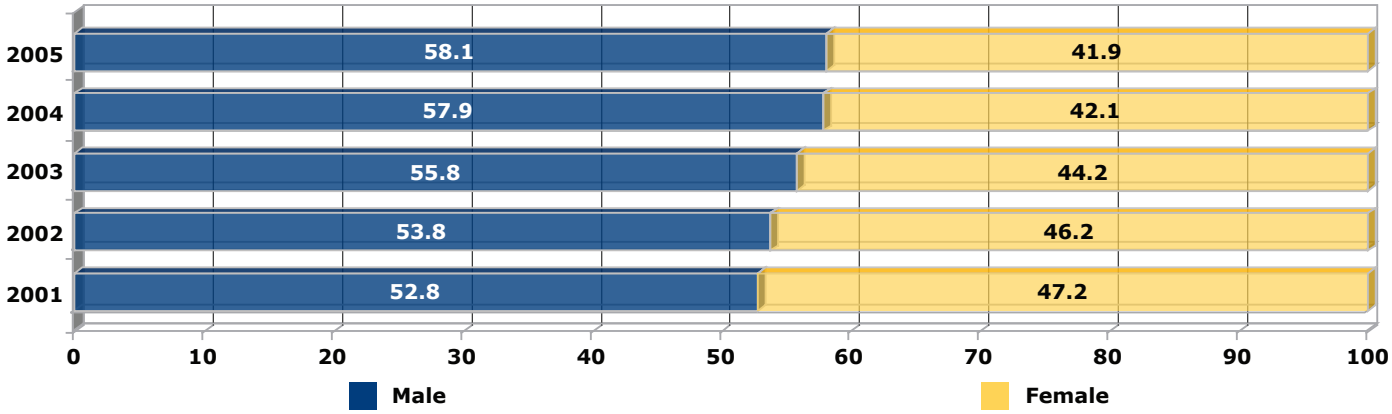
State	# Cases	State	# Cases	State	# Cases
Alaska	2	Michigan	4	Puerto Rico	1
Alabama	96	Minnesota	1	South Carolina	13
Arkansas	9	Missouri	2	Tennessee 2	2858
Colorado	1	Mississippi	28	Texas	4
Florida	17	North Carolina	16	Utah	1
Georgia	47	Nebraska	1	Virginia	31
Iowa	1	New Jersey	1	Washington	1
Illinois	26	New Mexico	2	West Virginia	2
Indiana	29	New York	5	Outside No. America	1
Kentucky	608	Ohio	3		
Maryland	3	Oklahoma	1		
Maine	1	Pennsylvania	2	**Total Cases**	**3818**

Vanderbilt Childhood Cancer Program (All Cases)



A program of Vanderbilt-Ingram and the Monroe Carell, Jr. Children's Hospital at Vanderbilt

Comparison by Gender (All Classes, 2001-2005)

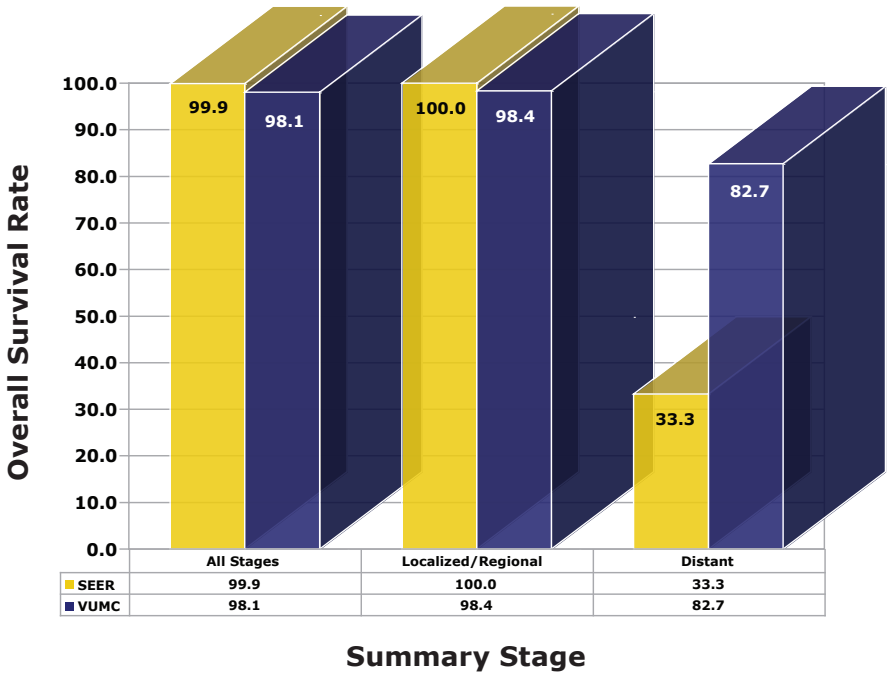


County at Diagnosis, All Pediatric Cases (2005)

County	# Cases	County	# Cases
Bedford	2	Maury	2
Blount	1	Montgomery	4
Cannon	1	Obion	1
Coffee	2	Pickett	1
Cumberland	1	Putnam	1
Davidson	21	Robertson	1
DeKalb	1	Rutherford	15
Dickson	2	Sevier	1
Fentress	1	Shelby	1
Franklin	1	Smith	2
Hamilton	6	Stewart	1
Henry	1	sullivan	1
Hickman	3	Sumner	7
Jackson	1	Tipton	1
Knox	1	Warren	2
Lake	1	White	3
Lewis	1	williamson	8
Lincoln	1	Wilson	7
Loudon	2	Out of State	30
Marshall	4	**Total Cases**	**143**

Survival Data

Overall Comparison 5-YR Survival Rate - Prostate Cancer
VUMC (1997-2002) and SEER* (1996-2002)

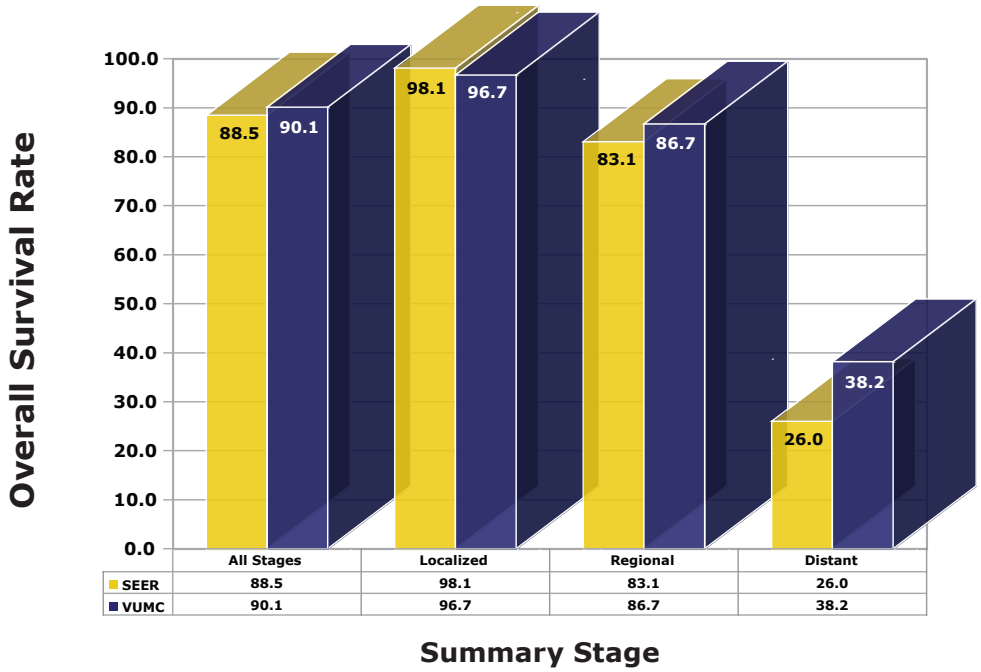


Source: **SEER Cancer Statistics Review 1975-2003**
SEER Table XXIII-5

National Cancer Institute
Prostate Cancer (Invasive)

* "A continuing project of the NCI, the SEER Program collects cancer data on a routine basis from designated population-based cancer registries in various areas of the country. With respect to selected demographic and epidemiologic factors, the areas are reasonably representative subsets of the US population."

Overall Comparison 5-YR Survival Rate - Breast Cancer
VUMC (1997-2002) and SEER (1996-2002)

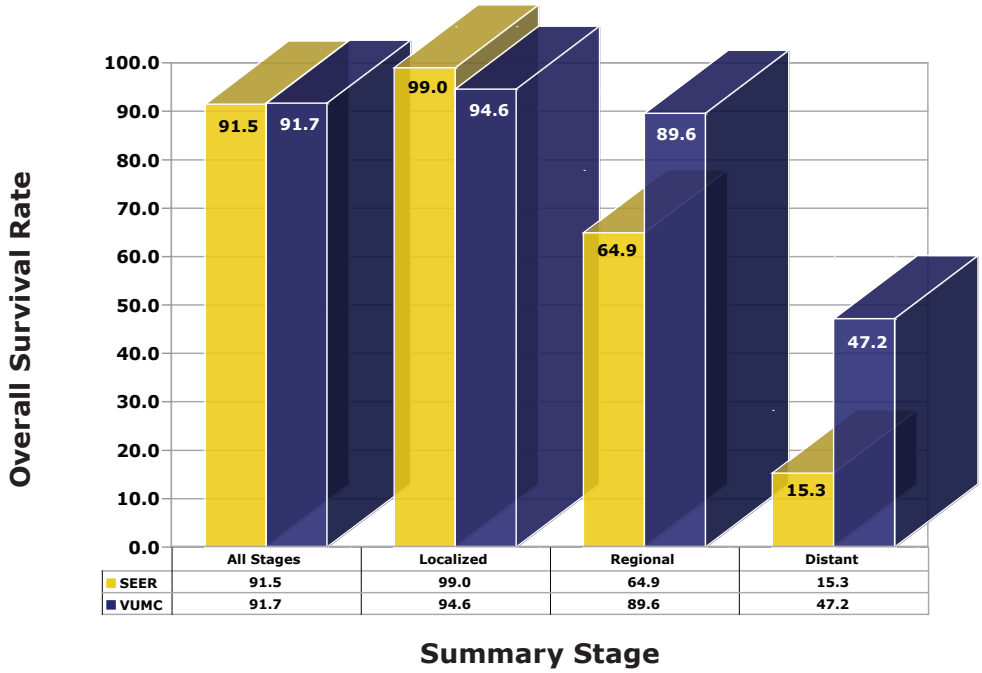


In situ cases are not included in the All Stages group.

Source: **SEER Cancer Statistics Review 1975-2003**
SEER Table IV-10

National Cancer Institute
Female Breast Cancer (Invasive)

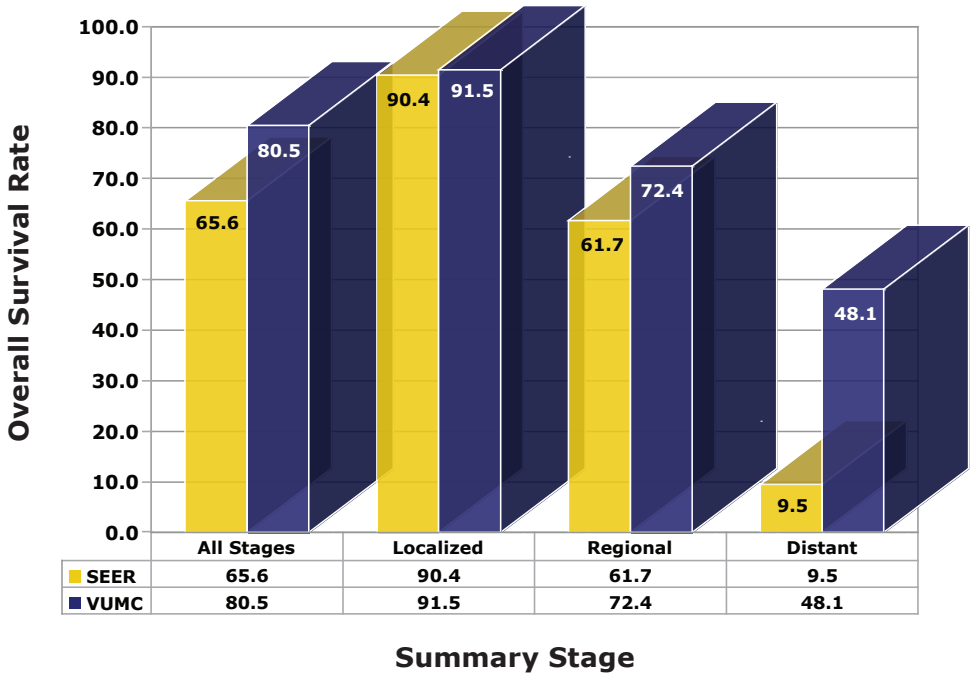
Overall Comparison 5-YR Survival Rate - Melanoma of the Skin
VUMC (1996-2002) and SEER (1997-2002)



Source: **SEER Cancer Statistics Review 1975-2003**
SEER Table XVI-5

National Cancer Institute
Melanoma of the Skin (Invasive)

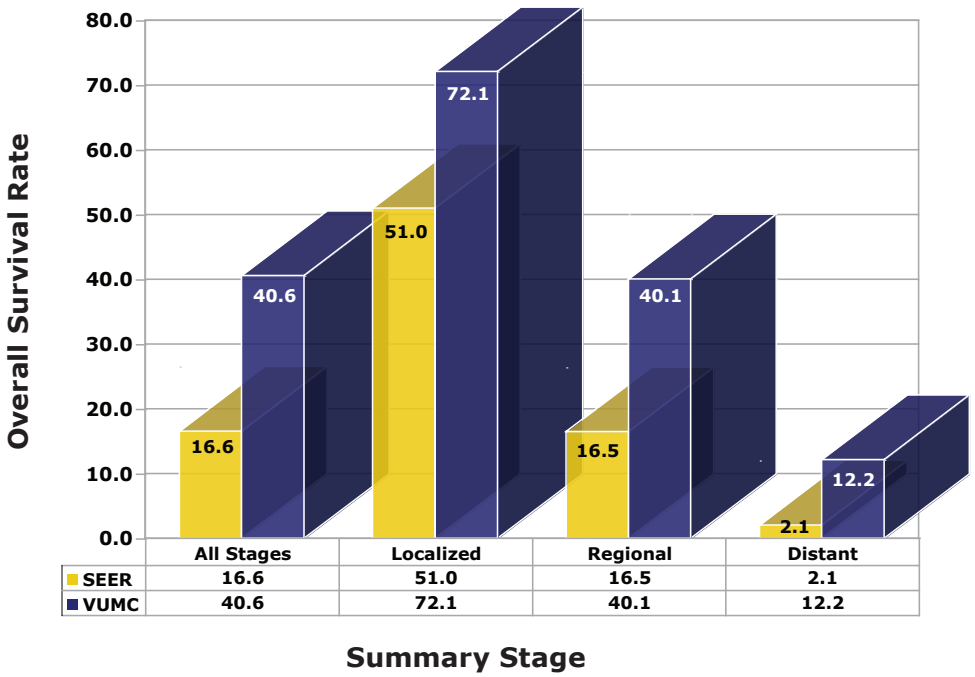
Overall Comparison 5-YR Survival Rate - Kidney and Renal Pelvis Cancer VUMC (1996-2002) and SEER (1997-2002)



Source: **SEER Cancer Statistics Review 1975-2003**
SEER Table XI-5

National Cancer Institute
Kidney and Renal Pelvis Cancer (Invasive)

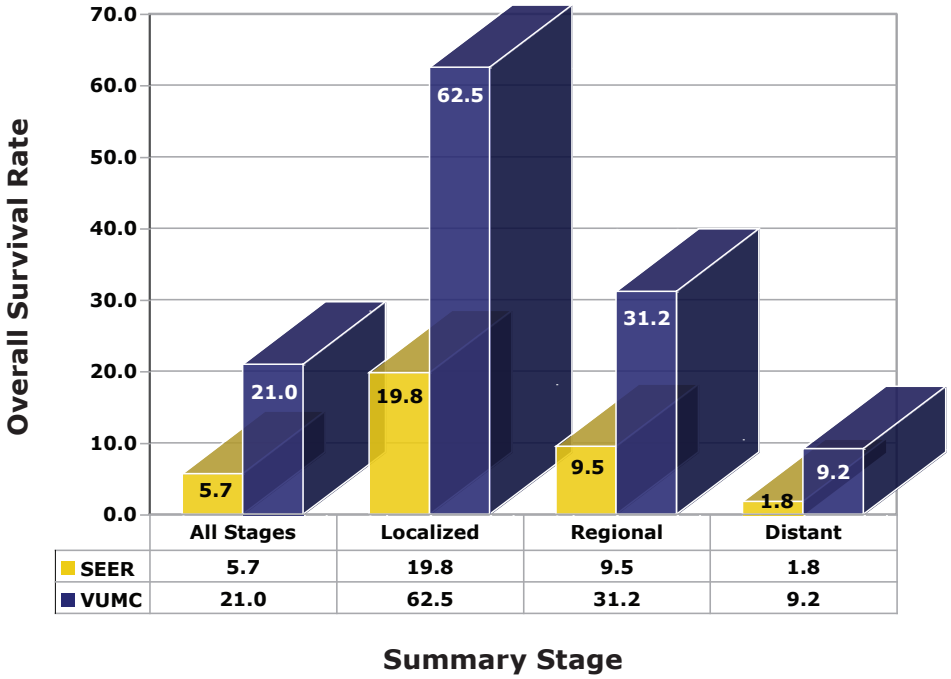
Overall Comparison 5-YR Survival Rate - Non-Small Cell Lung and Bronchus Cancer Analytic Cases, SEER (1996-2002) and VUMC (1997-2002)



Source: **SEER Cancer Statistics Review 1975-2003**
SEER Table XV-11

National Cancer Institute
Non-small Cell Lung and Bronchus Cancer (Invasive)

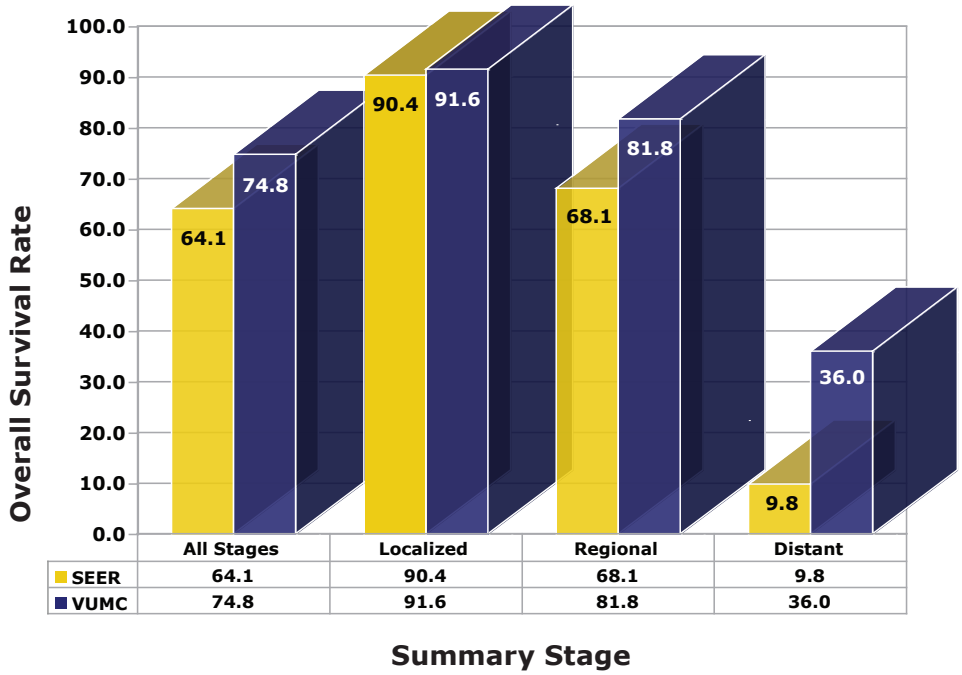
Overall Comparison 5-YR Survival Rate - Small Cell Lung and Bronchus Cancer Analytic Cases, SEER (1996-2002) and (VUMC 1997-2002)



Source: **SEER Cancer Statistics Review 1975-2003**
SEER Table XV-10

National Cancer Institute
Small Cell Lung and Bronchus Cancer (Invasive)

Overall Comparison 5-YR Survival Rate - Colon and Rectum Cancer SEER (1996-2002) and VUMC (1997-2002)



Source: **SEER Cancer Statistics Review 1975-2003**
SEER Table VI-9

National Cancer Institute
Colon and Rectum Cancer (Invasive)

Selected Site Summary

Head and Neck Cancer

By **Wendell G. Yarbrough, M.D., F.A.C.S.**
Ingram Professor of Cancer Research
Associate Professor of Otolaryngology and Cancer Biology

Vanderbilt-Ingram's Head & Neck Cancer Team

Head and neck cancers include tumors that arise in structures or derivatives of the upper aerodigestive tract including the oral cavity, pharynx, larynx, nasal and sinus cavities, and salivary glands. Some clinicians suggest that thyroid cancer should also be grouped with head and neck cancer because the thyroid is an embryologic derivative of the tongue base; however, thyroid cancer has distinct histology and treatment regimens. Excluding thyroid, the most common histological type of cancer observed in the head and neck is squamous cell carcinoma, which accounts for more than 90% of cancers of the oral cavity, larynx, and pharynx. Head and neck squamous cell carcinoma (HNSCC) is a devastating disease because of its unacceptable cure rate (less than 50% for Stage III and IV) and because of its location within structures critical for verbal communication and swallowing.

The American Cancer Society (ACS) estimated that close to 50,000 people in the United States were diagnosed with head and neck cancer in 2005. Data on head and neck cancer has traditionally been kept in such a way that obtaining true estimates of incidence and mortality his been difficult. For instance, the ACS divides head and neck cancer into seven categories, while the American College of Surgeons (ACOS) divides head and neck cancer into 12 categories. Although incidence of head and neck cancer in Tennessee is difficult to determine, data suggests that the southern part of the United States, including Tennessee, suffers with a disproportionate burden of this disease. In fact, at Vanderbilt, head and neck cancer has been one of the three most common cancers treated over the last several years. Because of divisions in reporting and lack of widespread media coverage for HNSCC, it is considered the "forgotten cancer" among many health care providers.

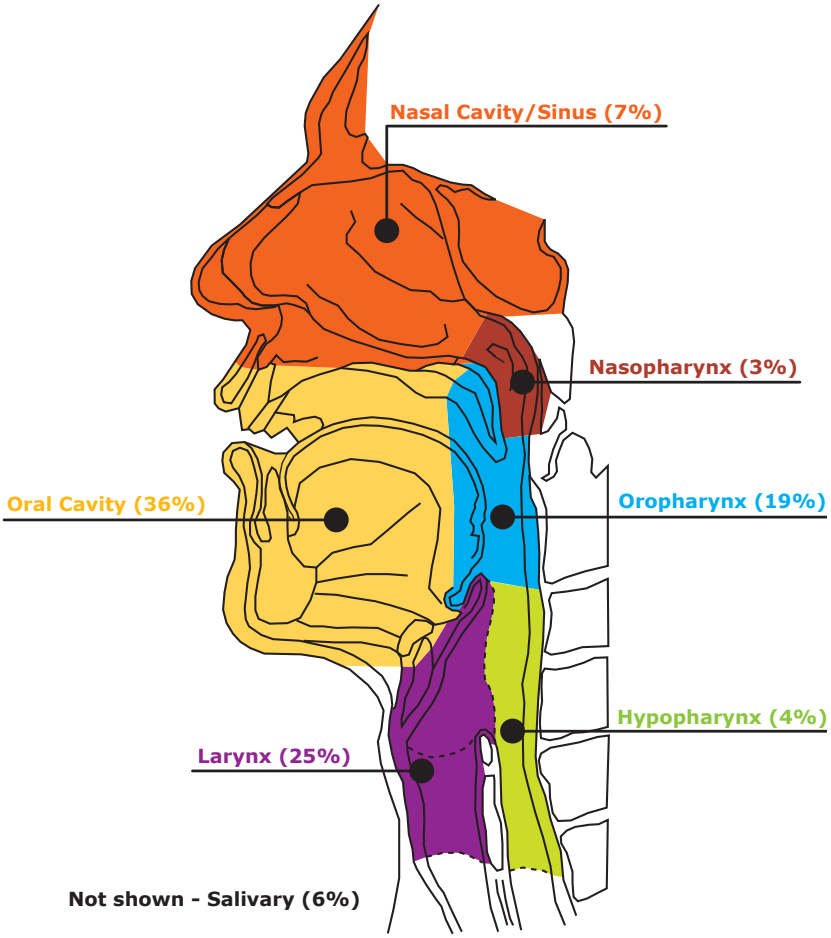
Prevalence, Etiology and Failure Pattern

HNSCC arises from the epithelial lining of the upper aerodigestive tract. These areas are exposed to carcinogens from tobacco smoke, alcohol consumption (ethanol), smokeless tobacco, and human papilloma virus (HPV). It has been estimated that approximately 75% of HNSCC is directly attributable to tobacco consumption. Although ethanol exposure alone is associated with the risk of developing HNSCC, ethanol combined with tobacco dramatically increases risk due to the synergistic interaction between the two.

In India, where oral cavity cancer is one of the most prevalent forms of cancer, combinations of lye,

tobacco and the betel nut have been implicated.

Like many tobacco-related cancers such as lung and esophageal squamous cell carcinoma, the incidence of HNSCC has been decreasing over the last several years. This is likely attributable to the success of programs to decrease smoking that started in the 1970s and 1980s. Ironically, risk for HNSCC seems to be increasing among one subgroup – young non-smokers. Although the reasons are not fully understood, this increase may be in part due a newly defined role of HPV infection as an etiologic agent of HNSCC. There are many types of HPV and for years, HPV types 16, 18, and 31 have been associated with uterine cervical cancer. HPV is thought to cause cancer primarily by expressing two genes – E6 and E7 – that inactivate the human tumor suppressor genes p53 and retinoblastoma. In HNSCC, up to 50% of oropharyngeal cancers and 25% of oral cavity cancers have been found to contain HPV sequences, almost all being type 16. HPV that causes HNSCC can be considered a sexually transmitted disease just as with the HPV types that cause uterine cervical cancer.



Distribution of head and neck cancers by subsite

Within the upper aerodigestive tract, there is a predisposition for some sub-sites to be more commonly involved with HNSCC. The likelihood of a subsite being affected can be predicted based in part on carcinogen exposure. Laryngeal cancers are rare with smokeless tobacco consumption but frequent among smokers. Even within the oral cavity, sites with more or longer exposure are at increased risk. For example, the floor of mouth and the tongue, where carcinogens mixed with secretions tend to linger, are more often affected than sites such as the palate or upper alveolus. For partially unexplained reasons, HPV has a tendency to cause cancers of the oropharynx and is particularly associated with squamous cell carcinoma of the tonsil.

Prevention & Early Detection

Cancer deaths among men decreased for the first time ever from 1996 to 1997, largely due to decreased deaths from tobacco-related cancers, including head and neck squamous cell carcinoma. Decreased tobacco consumption will continue to have the single greatest impact on prevention of head and neck cancer. Many efforts to educate the public about the risk of tobacco use have been buoyed by the national tobacco settlement that provided funds for education and imposed limitations on advertisements, especially those directed at children. The ACS with its "Campaign for Tobacco-free Kids" and many other groups have focused on educating children on the hazards of tobacco. Combined efforts have led to rules or legislation that has rendered many workplaces, restaurants, sporting venues, and public buildings smoke-free. Currently, the Tennessee Legislature is considering a ban on indoor smoking in public buildings.

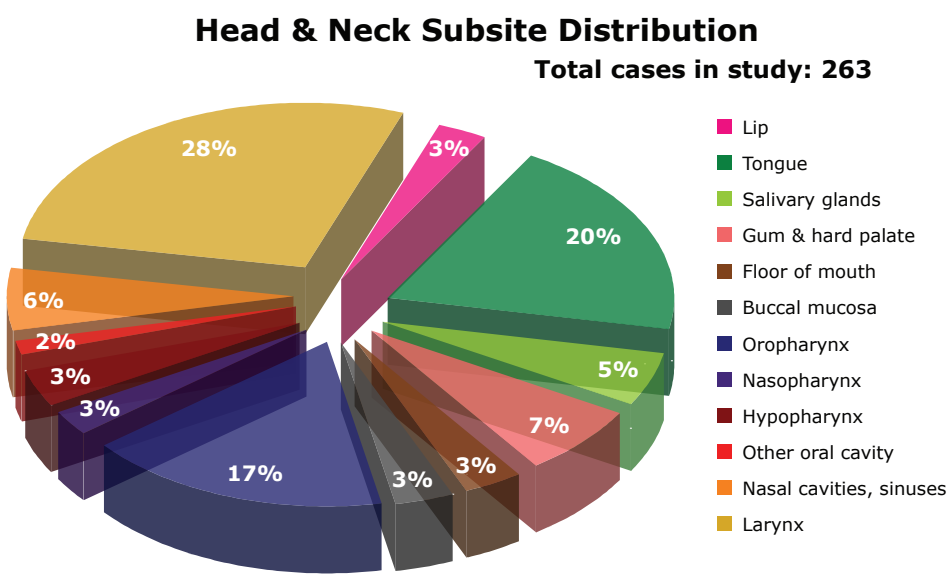
Early detection efforts have been centered on increasing public awareness of signs and symptoms of head and neck cancer. The Yul Brynner Foundation has pioneered this effort through creation of a national head and neck cancer awareness week each April. The Vanderbilt Head and Neck Oncology Team participates in this effort, including a free screening day at both Vanderbilt University Medical Center and the Nashville Veterans Administration Medical Center. Early detection efforts have also focused on education of health care providers, including physicians and dentists, to increase frequency of oral examinations and to increase awareness.

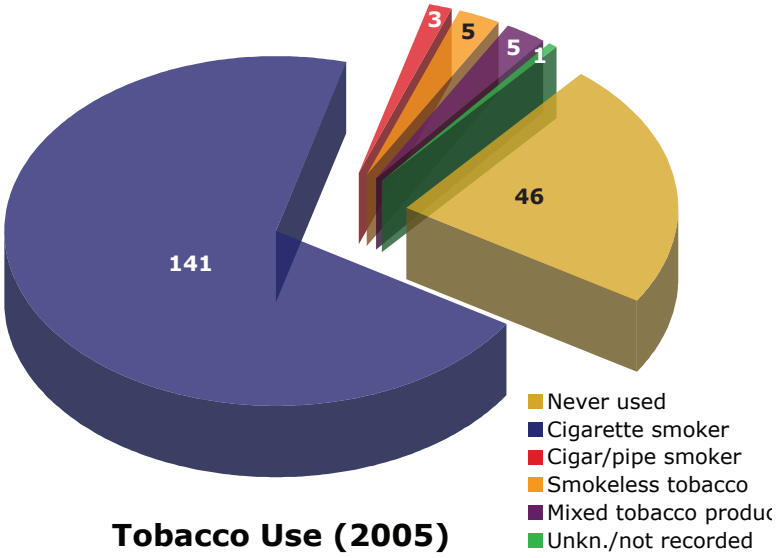
Detection of head and neck cancer frequently relies on specialized equipment for visualization of the upper aerodigestive tract or imaging studies such as CT or MRI. Serum markers indicating presence of cancer are a valuable clinical tool to assist in early detection and are currently used for many cancer types including prostate and thyroid. Like many cancers, head and neck cancers have very high cure rates if detected very early during their development. Additionally, early detection allows treatment with a single modality, either surgery or radiation, and minimizes treatment-associated morbidity. Researchers are actively pursuing identification of serum and salivary biomarkers to assist with early detection of head and neck cancer, but to date there are no reliable markers that are clinically useful.

Staging and Current Therapy

Staging of head and neck squamous cell carcinoma is based on the size of the primary tumor or critical structures that are invaded by the primary cancer (T stage), the number and size of cervical lymph nodes that contain cancer cells (N stage), and the presence or absence of distant metastases (M stage). The TNM categorization then determines an overall stage. Stages I and II HNSCC are considered early while stage III and IV are considered late. This system is far from perfect, but yields the most accurate prediction of outcome and is one of the factors considered when selecting therapy. Accurate clinical staging typically requires an endoscopic evaluation, as well as an imaging evaluation of both the primary tumor and cervical lymph nodes. HNSCC patients seen by the head and neck team at Vanderbilt are frequently Stage III or IV with close to half suffering from second primary cancers or persistent/recurrent disease at presentation.

As with most solid tumors, detection of HNSCC at early stages is associated with increased survival and decreased treatment morbidity. Stage I and II patients have cure rates of approximately 90% with a single treatment modality, typically surgery or radiation. In contrast, late stage patients have survival of less then 50% even following aggressive multi-modality therapy (concurrent chemotherapy and radiation with or without surgery). The emergence of chemotherapy as a radiation sensitizer has dramatically altered therapy of HNSCC over the past 15 years. Some patients with advanced laryngeal cancers are candidates for voice-sparing partial laryngectomy; however, concurrent chemo/radiation therapy is now standard for many advanced cancers of the larynx, hypopharynx and oropharynx.





Tobacco Use (2005)

Recently, histologic features as a marker of clinical tumor behavior have been used to guide post-operative therapy. Cervical nodal metastases, growth pattern at the tumor periphery, perineural or perivascular spread have each been associated with decreased survival. Aggressive therapy with surgery followed by concurrent chemotherapy and post-operative radiation has been shown to provide a survival benefit for patients with histological features predicting poor outcome. Patients without indicators of biological aggressiveness can be safely spared the morbidity associated with combined chemo-radiation.

The strongest predictor of survival for HNSCC is the presence or absence of cervical nodal metastases. For some patients, the absence of clinical or radiographic evidence for cervical metastases can be misleading. In these patients, cervical lymph node dissection reveals metastatic disease in up to 30%. Nodal status plays such a critical role in determining treatment strategy that lymph node dissections are performed on many node negative patients to accurately determine if metastases exist. Accurate pathologic nodal staging is currently based exclusively on removal of all nodes from at risk areas of the neck. Recently, a study sponsored by the American College of Surgeons Oncology Group (ACOSOG) has examined the sentinel node technique to determine if it can replace node dissections for oral cavity cancer patients without clinical or radiographic evidence of metastases. The sentinel node strategy is already accepted and validated for melanoma and is based on tracing nodal distribution of a radionucleotide that is injected around the primary tumor. If validated, sentinel node sampling could obviate the need for neck dissection in a subset of patients.

Emerging therapies for HNSCC

Many new drugs have emerged that target specific molecules critical for tumor cell proliferation or survival. The most dramatic success has been related to the drug Gleevec to treat chronic myelogenous leukemia (CML). Gleevec targets and inhibits the oncogenic abl kinase in CML and has resulted in long term disease-free intervals for patients previously considered terminal. Compared to leukemias, solid tumors are less dependent on a single oncogenic stimulus and therefore acquire many molecular abnormalities that affect multiple pathways. Defects in HNSCC occur in pathways that regulate proliferation and apoptosis and present many potential targets. One limitation to the widespread use of targeted agents in HNSCC is our current inability to determine which agents will be most effective for a given tumor. Clinical trials are impractical or impossible to perform for all targeted agents as single therapy and trials are even less probable for combination of targeted therapy with standard chemotherapy or radiation.

Although many oncogenes are activated in HNSCC, the epidermal growth factor receptor (EGFR) has been the primary target of clinical trials because it is expressed in the vast majority of tumors and multiple inhibitors are clinically available. EGFR responds to extracellular growth factors by triggering intracellular signals that ultimately result in cellular proliferation and protection from apoptosis. Trials using EGFR inhibitors (EGFRi) as single modality therapy have had disappointing activity against HNSCC with response rates of 10% or less; however, combination of EGFRi with radiation has shown significant improvement in response to radiation. Studies are under way to compare EGFRi in combination with radiation to chemo-radiation.

Summary

Head and neck squamous cell carcinoma is a prevalent cancer that carries a poor prognosis if discovered at an advanced stage. HNSCC and its therapy exact a devastating toll on afflicted individuals by altering communication, swallowing, and facial appearance. Use of tobacco and ethanol, as well as sexual transmission of the human papilloma virus, are responsible for the majority of HNSCC, which further elevates the critical role of education, prevention, and early detection in controlling HNSCC. Surgery, with or without continued chemotherapy remain the mainstays of therapy, but targeted therapies offer promise for controlling HNSCC while limiting morbidity.

Selected Publications

2002

Chung CH, Bernard BS, Perou CM. Molecular portraits and the family trees of cancer. *Nature Genetics* 32 Suppl: 533-540, 2002.

Coleman SC, Stewart ZA, Day TA, **Netterville JL, Burkey BB, Pietenpol JA**. Analysis of cell-cycle checkpoint pathways in head and neck cancer cell lines: implications for therapeutic strategies. *Archives of Otolaryngology-Head and Neck Surgery* 128(2): 167-176, 2002.

Eichten A, Westfall MD, **Pietenpol JA**, Munger K. (2002) Stabilization and functional impairment of the tumor suppressor p53 by the human papillomavirus type 16 E7 oncoprotein. *Virology* 295(1): 74-85, 2002.

Goldstein RE, Netterville JL, Burkey BB, Johnson JE. Implications of follicular neoplasms, atypia, and lesions suspicious for malignancy diagnosed by fine-needle aspiration of thyroid nodules. *Annals of Surgery* 235(5): 656-64, 2002.

Moore BA, Duncan IM, **Burkey BB**, Day TA. Incidental metastatic papillary thyroid carcinoma in microvascular reconstruction. *Laryngoscope* 112(12): 2170-2177, 2002.

Sniezek JC, Matheny KM, **Burkey BB, Netterville JL, Pietenpol JA**. Expression of p63 and 14-3-3σ in normal and hyper-differentiated mucosa of the upper aerodigestive tract. *Otolaryngology- Head Neck Surgery* 126(6): 598-601, 2002.

2003

Abneth CC, Qiao Y-L, Dawsey SM, Buckman DW, Yang CS, **Blot WJ**, Dong Z-W, Taylor PR, Mark SD. Prospective study of serum retinol, ß-carotene, ß-cryptoxanthin, and lutein/zeaxanthin and esophageal and gastric cancers in China. *Cancer Causes and Control* 14(7): 645-655, 2003.

Barbieri CE, Barton CE, Pietenpol JA. DeltaNp63alpha expression is regulated by the phosphoinositide-3-kinase pathway. *Journal of Biological Chemistry* 278(51): 51408-51414, 2003.

Burkey BB. Section I: Head and Neck: Issues in Surgical Management. *Atlas of Cancer*. Ed. Maurie Markman. Philadelphia, PA: Lippincott Williams & Wilkins, 2003. 9-14.

Chung CH, Vokes EE. 49 year-old male with locally advanced squamous cell carcinoma of the head and neck: the case for sequential chemoradiotherapy programs - [Commentary]. *Clinical Advances in Hematology and Oncology* 1(1): 61-62, 2003.

Engel LS, Chow WH, Vaughan TL, Gammon MD, Risch HA, Stanford JL, Schoenberg JB, Mayne ST, Dubrow R, Rotterdam H, West AB, Blaser M, **Blot WJ**, Gail MH, Fraumeni JF Jr. Population attributable risks of esophageal and gastric cancers. *Journal of the National Cancer Institute* 95(18):1404-1413, 2003.

Jin YH, Clark AB, **Slebos RJC**, Al-Refai H, Taylor JA, Kunkel TA, Resnick MA, Gordenin DA. Cadmium is a mutagen that acts by inhibiting mismatch repair. *Nature Genetics* 34(3): 326-329, 2003.

Matheny KE, **Barbieri CE**, Sniezek JC, **Arteaga CL, Pietenpol JA** Inhibition of EGF receptor signaling decreases p63 expression in head and neck squamous carcinoma cells. *Laryngoscope* 113(6): 936-939, 2003.

Richards SV, Welch DC, Bayles SW, **Burkey BB**. Alveolar soft part sarcoma of the mandible. *Otolaryngology- Head and Neck Surgery* 128(1): 148-50, 2003.

Sinard RJ, Netterville JL, Ossoff RH. Squamous Cell Cancer of the Larynx. *The Larynx*. Ed. **Robert Ossoff**, Stanley Shapshay, Gayle Woodson, **James Netterville**. Philadelphia, PA: Lippincott Williams & Wilkins, 2003.

Sinard RJ, Nussenbaum B. Nonsquamous Cell Cancer of the Larynx. *The Larynx*. Ed. **Robert Ossoff**, Stanley Shapshay, Gayle Woodson, **James Netterville**. Philadelphia, PA: Lippincott Williams & Wilkins, 2003.

Sørensen HT, Friis S, Nørgård B, Mellemkjaer **L, Blot WJ, McLaughlin JK**, Ekbom A, Baron JA. Risk of cancer in a large cohort of nonaspirin NSAID users: a population-based study. *British Journal of Cancer* 88(11):1687-1692, 2003.

Stewart ZA, Westfall MD, **Pietenpol JA**. Cell cycle dysregulation and anticancer therapy. *Trends in Pharmaceutical Science* 24(3): 139-145, 2003.

Taylor PR, Qiao Y-L, Abnet CC, Dawsey SM, Yang CS, Gunter EW, Wang W, **Blot WJ**, Dong Z-W, Mark SD. Prospective study of serum vitamin E levels and esophageal and gastric cancers. *Journal of the National Cancer Institute* 95(18):1414-1416, 2003.

Wax MK, **Burkey BB**, Bascom DI, Rosenthal EL. The role of free tissue transfer in the reconstruction of massive neglected skin cancers of the head and neck. *Archives of Facial Plastic Surgery* 5(6): 479-82, 2003.

Westfall MD, **Mays DJ**, Sniezek JC, **Pietenpol JA**. The ΔNp63α phosphoprotein binds the p21 and 14-3-3σ promoters in vivo and has transcriptional repressor activity that is reduced by Hay-Wells syndrome-derived mutations. *Molecular and Cellular Biology*. 23(7): 2264-2276, 2003.

2004

Becker MT, Shores CG, Yu KK, **Yarbrough WG**. Molecular assay to detect metastatic head and neck squamous cell carcinoma. *Archives of Otolaryngology- Head and Neck Surgery* 130(1):21-27, 2004.

Chung CH, Parker JS, Karaca G, Wu J, Funkhouser WK, Moore D, Butterfoss D, Xiang D, Zanation A, Yin X, Shockley WW, Weissler MC, Dressler LG, Shores CG, **Yarbrough WG**, Perou CM. Molecular classification of head and neck squamous cell carcinomas using patterns of gene expression. *Cancer Cell* 5(5): 489-500, 2004.

Grandis JR, **Pietenpol JA**, Greenberger JS, Mohla S. Head and neck cancer: meeting summary and research opportunities. *Cancer Research* 64(21): 8126-8129, 2004.

Lin DT, Coppit GL, Burkey BB, Netterville JL. Tumors of the accessory lobe of the parotid gland: a 10-year experience. *Laryngoscope* 114(9): 1652-1655, 2004.

Shores CG, Yin X, Funkhouser W, **Yarbrough WG**. Clinical evaluation of a new molecular method for detection of micrometastases in head and neck squamous cell carcinoma. *Archives of Otolaryngology- Head and Neck Surgery* 130(8):937-942, 2004.

Slebos RJC, Little RE, Umbach DM, Antipkin Y, Zadaorozhnaja TD, Mendel NA, Sommer CA, Conway K, Parrish E, Gulino S, Taylor, JA. Mini- and microsatellite mutations in children from Chernobyl accident cleanup workers. *Mutation Research* 559(1-2): 143-151, 2004.

Slebos RJC, Umbach DM, Sommer CA, Horner GA, Choi JY, Taylor JA. Analytical and statistical methods to evaluate microsatellite allelic imbalance in small amounts of DNA. *Laboratory Investigation* 84(5): 649-657, 2004.

Sniezek JC, Matheny KE, Westfall MD, **Pietenpol JA**. Dominant negative p63 isoform expression in head and neck squamous cell carcinoma. *Laryngoscope* 114(12): 2063-2072, 2004.

Westfall MD, **Pietenpol JA**. p63: Molecular complexity in development and cancer. *Carcinogenesis* 25(6): 857-864, 2004.

Ye W, Held M, Lagergren J, Engstrand L, **Blot WJ, McLaughlin JK**, Nyrén O. Helicobacter pylori infection, gastric atrophy: risk of adenocarcinoma and squamous-cell carcinoma of the esophagus and adenocarcinoma of the gastric cardia. *Journal of the National Cancer Institute* 96(5):388-396, 2004.

Zanation AM, Yin X, Shores C, **Yarbrough WG**. Phenotypic and microarray gene expression analysis of tri-dimensional raft modeled human head and neck squamous cell carcinoma. *Otolaryngology- Head and Neck Surgery* 131(5):577-84, 2004.

2005

Barbieri CE, Perez CA, Johnson KN, **Ely KA**, Billheimer D, **Pietenpol JA**. IGFBP-3 is a direct target of transcriptional regulation by delta-N-p63-alpha in squamous epithelium. *Cancer Research* 65(6): 2314-2320, 2005.

Cohen SM, Burkey BB, Netterville, JL. Surgical management of parapharyngeal space masses. *Head and Neck* 27(8): 669-675, 2005.

Hearnes JM, Mays DJ, Tang LJ, Schavolt KL, Jiang X, **Pietenpol JA**. A chromatin immunoprecipitation-based screen to identify functional genomic binding sites for sequence-specific transactivators. *Molecular and Cellular Biology* 25(22): 10148-10158, 2001.

Lin DT, Cohen SM, Coppit GL, Burkey BB. Squamous cell carcinoma of the oropharynx and hypopharynx. *Otolaryngology Clinics of North America* 38(1): 59-74, 2005.

Sinard RJ, Mickey BE, Roland PS. Anterior Cranial Base Surgery. SIPAC for the American Academy of Otolaryngology, First Edition, 2005.

Slebos RJC, Livanos E, Yim HW, Randell SH, Parsons AM, Detterbeck FC, Rivera MP, Taylor JA. Chromosomal abnormalities in bronchial epithelium from smokers, non-smokers and lung cancer patients. *Cancer Genetics and Cytogenetics* 159(2): 137-142, 2005.

Yom SS, Machtay M, Biel MA, **Sinard RJ**, El-Naggar AK, Weber RS, Rosenthal DI. Survival impact of planned restaging and early surgical salvage following definitive chemoradiation for locally advanced squamous cell carcinomas of the oropharynx and hypopharynx. *American Journal of Clinical Oncology* 28(4): 385-392, 2005.

2006

Barbieri CE, Brown KA, Johnson K, **Pietenpol JA**. Loss of p63 leads to increased cell migration and upregulation of genes involved in invasion and metastasis. *Cancer Research* 66(15): 7589-7597, 2006.

Barbieri CE, Pietenpol JA. p63 and epithelial biology. *Experimental Cell Research* 312(6): 695-706, 2006.

Chung CH, Ely K, McGavran L, Varella-Garcia M, Parker J, Parker N, Jarrett C, Carter J, **Murphy BA, Netterville JN, Burkey BB, Sinard RJ, Cmelak AJ**, Levy S, **Yarbrough WG, Slebos RJ**, Hirsch FR. Increased EGFR gene copy number is associated with poor prognosis in head and neck squamous cell carcinomas. *Journal of Clinical Oncology* 24(25): 4170-4176, 2006.

Chung CH, Johnson DH. Epidermal growth factor receptor: an overview of trials in head and neck and lung cancer- [Commentary]. *ONCOL 20*(2): 162, 166, 2006.

Chung CH, Levy S, Chaurand P, **Carbone DP**. Genomics and proteomics: emerging technologies in clinical cancer research. *Critical Reviews in Oncology and Hematology* 61(1): 1-25, 2006.

Chung CH, Levy S, **Yarbrough WG**. Clinical application of genomics in head and neck cancer. *Head and Neck* 28(4): 360-368, 2006.

Chung CH, Parker JS, **Ely K**, Carter J, Yi Y, **Murphy BA**, Ang KK, El-Naggar A, Zanation AM, **Cmelak AJ**, Levy S, **Slebos RJ, Yarbrough WG**. Gene expression profiles identify epithelial-to-mesenchymal transition and activation of nuclear factor-κB signaling as characteristics of a high-risk head and neck squamous cell carcinoma. *Cancer Research* 66(16): 8210-8218, 2006.

Mayne ST, Risch HA, Dubrow R, Chow WH, Gammon MD, Vaughan TL, Borchardt L, Schoenberg JB, Stanford JL, West AB, Rotterdam H, **Blot WJ**, Fraumeni JF Jr. Carbonated soft drink consumption and risk of esophageal adenocarcinoma. *Journal of the National Cancer Institute* 98(1): 72-75, 2006.

Murphy BA, Aulino JM, Chung CH, Ely KA, Sinard RJ, Cmelak AJ. Chapter 9: Esthesioneuroblastoma. *Textbook of Uncommon Cancer (Third Edition)*. Ed. Derek Raghavan, Martin L. Brecher, David H. Johnson, Neal J. Meropol, Paul L. Moots, Peter G. Rose, Ingrid A. Mayer. John Wiley & Sons, Ltd., 2006. 133-142.

Slebos RJC, Li M, **Evjen AN**, Coffa J, **Shyr Y, Yarbrough WG**. Mutagenic effect of cadmium on tetranucleotide repeats in human cells. *Mutation Research* 602(1-2): 92-99, 2006.

Slebos RJ, Yi Y, **Ely K**, Carter J, **Evjen A**, Zhang X, **Murphy BM, Cmelak AJ, Burkey BB, Netterville JL**, Levy S, **Yarbrough WG, Chung CH**. Gene expression differences associated with human papillomavirus status in head and neck squamous cell carcinoma. *Clinical Cancer Research* 12(3 Pt 1): 701-709, 2006.

Stacy DR, **Ely K, Massion PP, Yarbrough WG, Hallahan DE**, Sekhar KR, **Freeman ML**. Increased expression of nuclear factor E2 p45-related factor 2 (NRF2) in head and neck squamous cell carcinomas. *Head and Neck* 28(9): 813-818, 2006.

Wang J, He X, Luo Y, **Yarbrough WG**. A novel ARF-binding protein (LZAP) alters ARF regulation of HDM2. *Biochemical Journal* 393(Pt 2): 489-501, 2006.

Whigham AS, Netterville JL, Burkey BB, Sinard RJ, Chung CH, Slebos RJC, Yarbrough WG. Short-term culture and in vivo modeling of primary head and neck squamous cell carcinoma. *Archives of Otolaryngology- Head Neck Surgery* 132(8): 901-902, 2006.

Yarbrough WG, Slebos RJC, Liebler D. Proteomics: clinical applications for head and neck squamous cell carcinoma. *Head and Neck* 28(6): 549-558, 2006.

2007

Yim HW, **Slebos RJC**, Randell SH, Umbach DM, Parsons AM, Rivera MP, Detterbeck FC, Taylor JA. Smoking is associated with increased telomerase activity in short-term cultures of human bronchial epithelial cells. *Cancer Letters* 246(1-2): 23-33, 2007.