



2009 Cancer Program Annual Report

with Statistical Data from 2008

and a special report on Breast Cancer

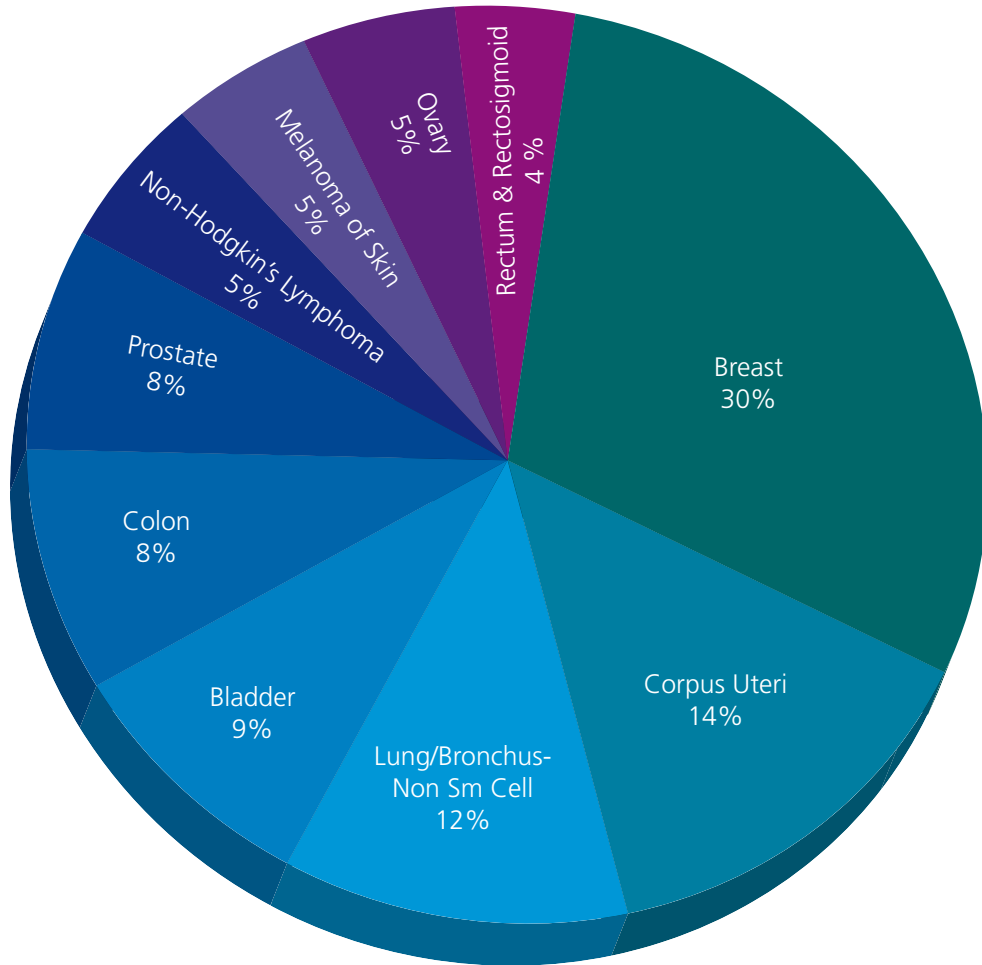


NORTHWEST HOSPITAL
& MEDICAL CENTER

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TOP TEN CANCER SITES FOR 2008



SITE	Total Cases
Breast	161
Corpus Uteri	74
Lung/Bronchus-Non Small Cell	63
Bladder	48
Colon	44
Prostate	42
Non-Hodgkin's Lymphoma	29
Melanoma of Skin	27
Ovary	27
Rectum & Rectosigmoid	22

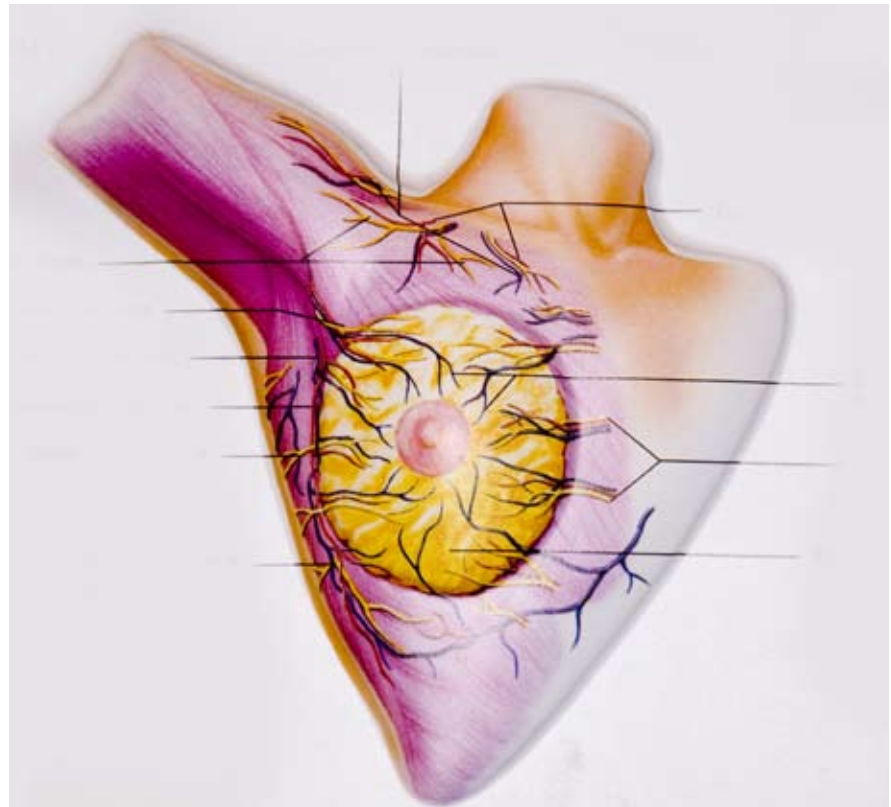
Breast cancer is not one disease.

If there is one refrain which keeps recurring throughout the research results of the last decade it is this: breast cancer comprises an array of subtypes which cannot be treated the same way. "One size fits all" has been replaced by meticulous analysis of any given cancer down to the molecular level if at all possible - with the presumption that treatment can be matched to that cancer with ever increasing specificity.

For every new diagnosis of breast cancer the next question should therefore be: "Which one?"

Oncologists have known from the early days of breast cancer research that multiple variables existed for this disease. Cancers in premenopausal women seemed to behave differently from those of postmenopausal patients. Some cancers expressed the estrogen receptor, some did not. Some cancers were more likely to be bilateral, others more difficult to detect on breast imaging.

It was then that two new variables began to populate research publications. *Prognostic factors* were those that could help identify those cancers with good outcome versus those less favorable. Although helpful to physician and patient alike, identifying a poor-prognostic factor in an individual's cancer highlighted the problem, but not the answer. What was needed was a type of factor which would help guide treatment choices. Indeed, *predictive factors* were those characteristics which in fact allowed physicians to confidently



“..breast cancer comprises an array of subtypes which cannot be treated the same way.”

estimate high likelihood of response to a given treatment.

What followed has been a flourishing of breast cancer research of immense importance. The identification of a prognostic factor in most cases has been quickly followed by a treatment which keys on that same factor. In other words, the very determinant that sets apart the prognosis of and therefore defines a specific subset of breast cancer patients has become the target for intensive research on how to use the uniqueness of that determinant as a lever with which to destroy the cancer. Awareness of the aforementioned estrogen receptor, for example, has led to the develop-

ment of the drug Tamoxifen, which homes in on and blocks the estrogen receptor on susceptible cancers, leading to cancer shrinkage in up to 65% of cases. Likewise, identification of the Her2 gene has led to the development of trastuzumab (Herceptin), a monoclonal antibody which targets cancers over-expressing this gene product. Are estrogen receptor-expressing cancers the same as Her2-overexpressing cancers? Usually not. Identification of these two subpopulations of breast cancer patients has led to two distinct treatment strategies which do not often overlap. This “divide-and-conquer” strategy has great appeal. Thus prognostic and predictive fac-

tors often become one and the same. The key continues to be the high level of innovation which inevitably follows the discovery of a specific prognostic factor, hopefully leading to a treatment strategy based on that factor within a few years.

This same degree of variation can be seen in all aspects of breast cancer care. There are now three distinct ways to image breast cancer, three ways to biopsy breast cancer, two ways to apply surgery to remove breast cancers, and several ways to apply radiation. Systemic therapy of breast cancer can include hormone manipulation, chemotherapy, targeted biological therapy, or a combination of all three. Depending on the type of cancer identified, the pathway from screening to diagnosis

to treatment can take any number of directions.

Picking one's way through this maze requires the participation of highly trained physician specialists in each phase or discipline involved and the constant communication of specialists with each other and with the patient so that the very best choices are made for each aspect of the patient's care. The goal continues to be maximization of the prospects for cure.

In the past few years, this process of responding to the specific biology of the cancer with biology-specific treatment has become known as *Personalized Oncology*. This report endeavors to describe this process in greater detail from the standpoint

of each specialty involved in breast cancer care. It is hoped that as the concept of Personalized Oncology is further developed in the future, current strategies will be augmented by newer, more novel ways of not only defining more breast cancer subsets, but also developing new treatment modalities which target those subsets. The tantalizing hope going forward is that in the future, all new diagnoses of breast cancer will slot easily into a pre-existing array of breast cancer subsets, each with its own highly individualized and successful treatment strategy. With such progress, the dream of cure for all patients with breast cancer will be one step closer to reality. ●

BREAST MRI: CURRENT ROLE IN SCREENING FOR BREAST CANCER | KATHERINE DEE, MD & CRAIG HANSON, MD

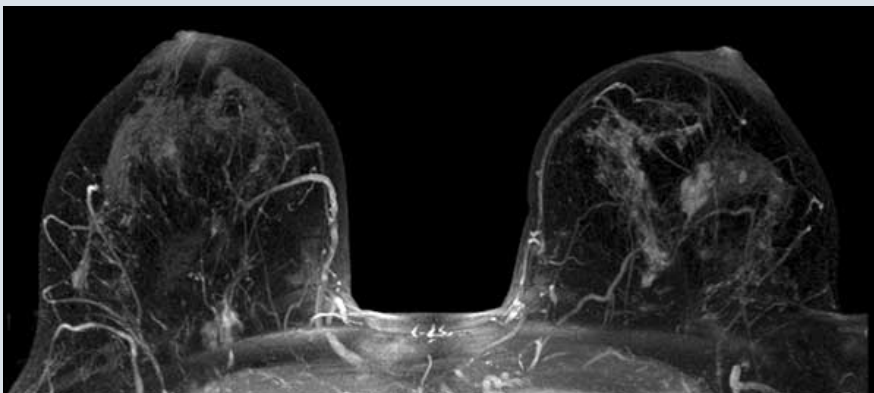
Dynamic contrast-enhanced breast MRI has matured into an imaging technique that is invaluable in the preoperative assessment of patients with newly diagnosed breast cancer.

It is also useful in the assessment of response to neoadjuvant chemotherapy, in patients with positive margins after a surgical biopsy with inadequate pre-surgical imaging, and in

patients who present with metastatic axillary lymphadenopathy with a suspected occult breast primary.

Although breast MRI may occasionally be helpful as an adjunct to mammography and/or ultrasound in certain challenging diagnostic cases, it is important to note that MRI is not a substitute for biopsy of a suspicious finding, including those detected clinically.

The role of breast MRI for screening women at high risk is now well established. In April of 2007 the American Cancer Society (ACS), based on a



meta-analysis of the medical literature and expert consensus, endorsed breast MRI for high risk screening. In fact, breast MRI is the most sensitive detection method currently available, with a reported sensitivity for detection of invasive breast cancers as small as 5 mm in the 90-95% range.

In order to identify those patients who should undergo screening with breast MRI one must define risk. The ACS currently recommends annual screening breast MRI, in addition to annual mammography, beginning at age 30 for women who meet one of the following criteria:

1. BRCA 1 or 2 mutation carrier
2. First degree relative of BRCA mutation carrier, untested
3. Lifetime risk of 20-25% or greater based on accepted risk assessment tools
4. Chest radiation at age 10-30
5. Carrier or has a first-degree relative who carries a genetic mutation in the TP53 or PTEN genes (Li-Fraumeni syndrome and Cowden and Bannayan-Riley-Ruvalcaba syndromes)

Most women at high risk do not have known susceptibility genetic muta-

tions, but do have familial clustering and/or other significant risk factors that place them at high risk. Various risk assessment models are available, including the Gail Model, Claus Model, BRCAPro Model, Tyrer-Cuzick Model and Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA). Unfortunately, the most readily available and easy to use model, the Gail Model, does not include important risk factors such as age at the time of diagnosis of first degree maternal relatives or the ability to document the paternal family history.

As importantly, none of the commonly available risk models incorporate radiographic breast density, which based on at least 15 large studies using quantitative techniques has been documented as a moderate to strong independent risk factor (relative risk 3-5). Furthermore, dense breast tissue, as defined by a fibroglandular density of 50% or greater relative to fat, significantly lowers the sensitivity of mammography.

It is likely that in the relatively near future, following validation studies, quantitative breast density will be available at those facilities performing digital mammography and that breast density will be incorporated into many risk assessment models, including the Gail Model.

Currently, recommendations for breast MRI screening in those patients considered at intermediate risk remain controversial. This includes patients with an estimated lifetime risk of 15-20% and those who have a personal history of breast cancer, LCIS or atypical hyperplasia. The Breast Cancer Multidisciplinary Team at NWH&MC recommends consideration for breast MRI screening in those patients who have any of the above criteria and who also have dense breasts. In fact, it is likely that when breast density is eventually incorporated into available risk assessment tools many women currently considered at intermediate risk will be assessed as high risk.

For those women who undergo breast MRI screening a protocol consisting of annual breast MRI alternating every 6 months with annual mammography is recommended. Breast MRI screening is not recommended for women at average risk.

In conclusion, breast MRI is firmly established for screening women at high risk regardless of breast density. It should also be strongly considered in women at intermediate risk who have dense breast tissue. ●

Breast cancer surgery at first glance would seem straight forward to the point of being simple: choose mastectomy versus lumpectomy with radiation, and choose full axillary lymph node dissection versus sentinel lymph node surgery, with full dissection only if the sentinel node is positive for cancer. Experience has shown, however, that each patient is different, and each new case of breast cancer needs to be evaluated fully in order to make wise, informed choices regarding surgical care. The following case studies illustrate the need for a Personalized Care approach regarding surgical oncology for breast cancer patients:

CASE 1: AM is a 43 year old patient diagnosed with ductal carcinoma in situ (DCIS) after mammography disclosed a new cluster of suspicious microcalcifications. She expressed interest in breast conservation, however MRI revealed that the area of concern was actually 7 cm in size. Biopsies performed at the outer extent of the lesion unfortunately confirmed DCIS. Our recommendation changed to that of mastectomy. She explored several reconstruction options and ultimately decided upon mastectomy followed by immediate ipsilateral tissue expander reconstruction plus contralateral breast reduction.

CASE 2: BA is a 73 year old woman diagnosed on biopsy with a high-grade infiltrating ductal carcinoma, measuring 1.5 cm on imaging. The small size of the tumor initially engendered high hopes of a straightforward treatment plan, but the cancer was found to be “triple-nega-



“tive”, that is, negative for ER, PR, and Her2. After meeting with her medical oncologist, the patient elected to receive neo-adjuvant (pre-operative) chemotherapy with AC followed by T (adriamycin, cyclophosphamide, Taxol). She required initial surgery for placement of a Portacath, at which time sentinel nodes were removed. Five nodes were recovered, all negative for cancer. Subsequent pre-operative chemotherapy was carried out in Maui (AC) and Seattle (Taxol), with a good tumor shrinkage documented on breast imaging. The patient subsequently underwent lumpectomy and radiation.

CASE 3: JU is a 56 year old female with a weak family history of breast cancer diagnosed on initial core biopsy with an intermediate grade infiltrating ductal cancer plus associated high-grade DCIS. The infiltrating tumor was ER-PR- but Her2-

positive. Total size by MRI was approximately 2.5 cm. Although the tumor seemed relatively small, it was located far medially and the patient’s breasts were quite petite. Both factors gave rise to doubts about the efficacy and cosmetic outcome of lumpectomy, and mastectomy was strongly considered. Neo-adjuvant chemotherapy was carried out, followed by mastectomy. After surgery, she received Herceptin for nearly one year. Toward the end of that year, she opted to have prophylactic mastectomy of the opposite breast. She will soon undergo bilateral tissue expander placement, with possible conversion to free graft reconstruction from inner thigh musculature (transverse upper gracilis, or TUG) in the future.

As one can see from these examples, no two women are alike, nor are their options for breast cancer treatment. There is also a tremendous variety in

the emotional response of any given patient to a new diagnosis of breast cancer. Many patients understandably do not absorb all of the information relayed by their physician(s) on the first visit, and must return for several follow up appointments, hopefully with friends or family members accompanying them. Some patients wish to go through the decision-making process very rapidly, to “get that cancer out of me” as soon as possible. Others seek opinions from multiple specialists and do a great deal of reading and soul searching before settling on a plan. Some patients desire that their physicians be quite directive, formulating a plan

which can be followed by the patient in a straight-forward manner, while others become immersed in research papers and desire to be randomized in a pertinent clinical trial. Some patients wish to be treated with a care plan that is not standard-of-care or mainstream. Some come to the office with multiple family members and friends, while others prefer to face cancer alone in order to maintain privacy.

Our office offers a calm, caring setting for all breast cancer patients. We collaborate closely with our colleagues in the multiple other disciplines taking part in breast cancer

management: diagnostic radiologists, pathologists, medical and radiation oncologists, reconstructive (plastic) surgeons, pharmacists, and the Lymphedema Team of physical and occupational therapists here at Northwest Hospital. We work with patients to allay their fears, assuring them that most newly-diagnosed breast cancers are very treatable. We commonly order breast MRI, arrange for patients to meet with other associated specialists, present each new patient’s case at our weekly Breast Conference, and individualize a treatment plan specifically and optimally for each patient. ●

BREAST CANCER SCREENING GUIDELINES

Screening guidelines are related to the patient’s risk. Risk can be assessed by various models, the most common being the Gail model, which can be readily accessed at the following Website: www.cancer.gov/bcrisktool.

Of note, the Gail model does not take into account second- or third-degree family members, or the age at time of diagnosis. It also does not take into account mammographic breast density, which is now considered a significant independent risk factor.

Screening guidelines for average risk and high risk patients are well established and are endorsed by the American Cancer Society. Guidelines for moderate risk patients are less well established, particularly with respect to breast MRI screening.

Average Risk (Less than 15% estimated lifetime risk)

Recommended Screening: **Annual mammograms starting at age 40.**

A baseline mammogram at age 35 is no longer recommended.

High Risk (20% or greater estimated lifetime risk):

- Strong family hx (particularly if premenopausal)
- Known BRCA gene carrier
- History of chest radiation age 10-20
- Li-Fraumeni, Cowden, or Bannayab-Riley-Ruvalcaba syndromes

Recommended Screening: **Annual mammography and annual breast MRI, regardless of breast density.**

Alternate these exams every 6 months. For those with a strong family history of premenopausal breast

cancer, screening should start at least 10 years earlier than the age at time of diagnosis of the patient’s first-degree relative(s).

Moderate Risk (15-20% estimated lifetime risk):

- Personal history of breast cancer
- One first-degree relative with breast CA, particularly if premenopausal
- Multiple non first-degree relatives, particularly if premenopausal
- Hx of ADH, ALH, LCIS

*Patients with more than one of the above will usually be at high risk.

Recommended Screening: **If the patient has dense breasts on mammography and one of the above risk factors, strongly consider the high risk guideline.** Otherwise, use the average risk guideline.

Radiotherapy is the use of ionizing radiation to eradicate cancer. Over the past century, it has evolved from a crude, poorly understood treatment to a sophisticated discipline tailored specifically to individual patients and diagnoses.

The History of Radiotherapy

Within four years of Roentgen’s discovery of x-rays in 1895, external beam radiation was used to cure cancers. The first reported case is illustrated in figure 1.

In the early years, radiotherapy devices were primitive and dosing was arbitrary and unscientific. Over ensuing decades, technologic improvements allowed safer, more precise delivery of radiation. In the 1950’s, cobalt radiotherapy units (figure 2) and medical linear accelerators were introduced, providing better penetration of radiation to cancers deep in the body. Simultaneously, uniform methods of calculating delivered dose were developed. Over the next decades, radiobiologists studied and determined how different cancers and normal tissues responded to radiotherapy. This facilitated the development of optimal dose-fractionation schemes, which yielded better cure rates with fewer complications.

The invention of computerized tomography (CT) in the 1970’s paved the way for computerized 3-dimensional planning of radiation delivery. In 3-D planning, a truly personalized “virtual” patient is reconstructed digitally, and a treatment plan is developed for each patient, taking into account variations in patient size

and anatomy. In a more sophisticated variation called IMRT (intensity modulated radiotherapy), the amount of radiation delivered across multiple intersecting radiation fields is modulated. A custom computerized plan is developed for each patient, insuring that the target is uniformly covered, while the nearby normal tissues are spaced (see figure 3).

The Newest Developments in Radiotherapy

3-D conformal radiotherapy and IMRT are capable of delivering uniform radiation doses to targets deep in the patient. However, targeted

cancers are not static: patients and targeting reference points on the skin are not stable, and internal organs can move considerably (e.g., with respiration or with bowel peristalsis). To account for target motion and set-up uncertainty, radiation oncologists must treat both the cancer and a margin of normal tissue around it.

Image guidance refers to the use of x-ray or other imaging modalities to determine prior to treatment the exact location of a patient’s cancer. This is another example of personalized therapy: in this case, treatment is personalized for each patient through

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Figure 1

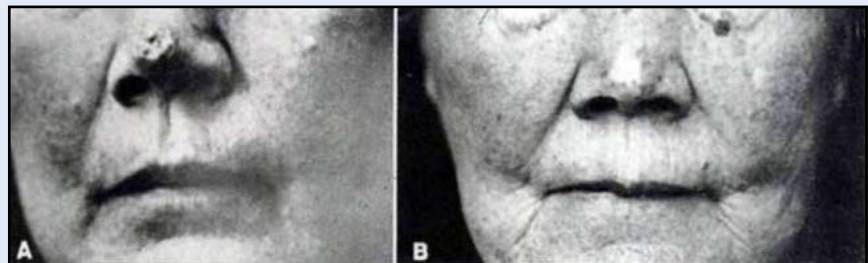


Figure 2

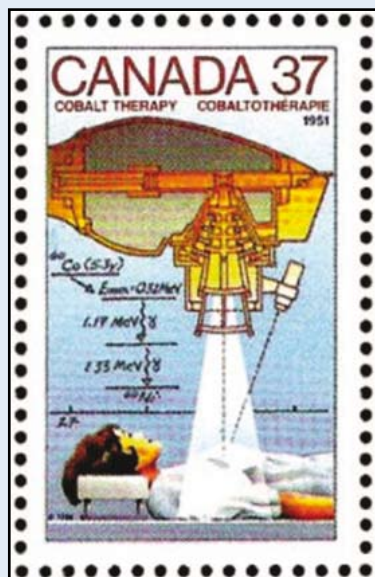


Figure 1: In 1899, Tor Stenbeck, a Swedish physician, treated this basal cell cancer (A) with external beam radiotherapy.; 30 years later (B), the cancer remained controlled.

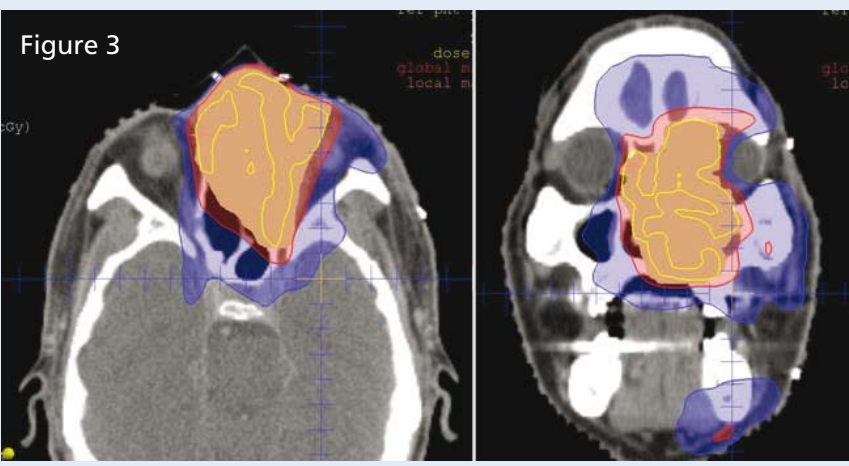
Figure 2: This Canadian stamp commemorates the first Co-60 external beam machine, developed in 1951.

time. Variations in target position are corrected before each fraction of radiation is delivered. This more precise delivery of radiation allows radiation oncologists to treat a smaller margin of normal tissue around the cancer, which reduces potential side effects. An example of image guidance is illustrated in figure 4.

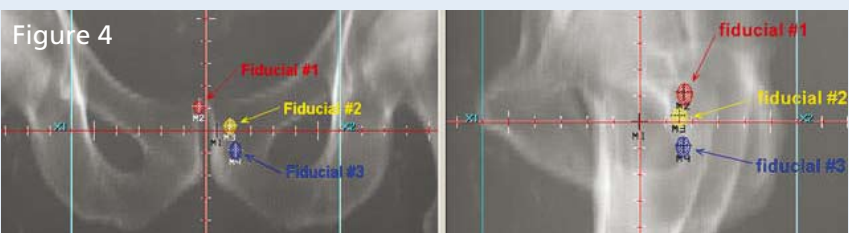
Adaptive radiotherapy refers to modifying treatment to account for changes in tumor size or location during the course of treatment; again, radiotherapy is personalized for the patient through time. Tumors often shrink during the 7-weeks required to complete therapy. In the past, the same treatment plan was used throughout this course. By re-imaging and repeating a treatment plan partway through a course, a smaller tumor can be targeted. This reduces radiation delivered to surrounding normal tissues, which can reduce side effects.

Conclusion

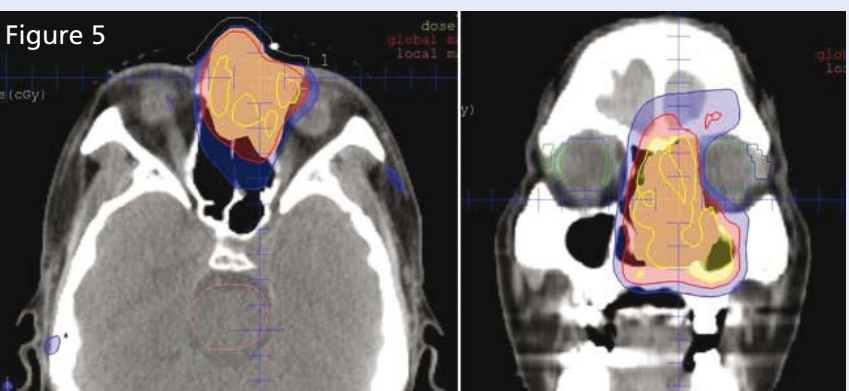
Advancements in x-ray, imaging, and computer technology have greatly changed the practice of radiation oncology over the past century. We can now safely deliver radiation to most parts of the body, while sparing adjacent normal tissues. CT imaging allows us to develop personalized treatment plans for every patient. Image-guidance permits varying treatment delivery to account for changing patient and tumor location. Adaptive radiotherapy permits personalizes treatment as a function of tumor response. These advances promise to reduce side effects from treatment, and potential yield improved rates of tumor control. ●



This treatment plan illustrates how IMRT delivers uniform dose to the target (nasal cavity and paranasal sinuses), while limiting dose to the eye, optic nerve/chiasm, and brain. The solid-colored tan region represents the cancer being targeted. The red region receives full dose (>55Gy); the dose has fallen off to 41Gy at the blue line – a dose which is safe for the brain and optic chiasm.



Prior to each treatment, an x-ray is taken using the linear accelerator, and gold fiducials within the prostate are identified. The patient position is adjusted based on fiducial location.



Same patient as illustrated in Fig. 3 after 4 weeks of external beam radiation and concomitant cis-platinum chemotherapy. The radiation plan is adapted to treat the now considerably smaller tumor (solid-colored tan). Smaller IMRT fields are used for the final portion of the treatment course; this will reduce radiation dose delivered to surrounding normal tissues, and should reduce the chance for side effects. Note that less of the left eye is in the high-dose region.

PATHOLOGY: OBTAINING DATA FOR PERSONALIZED TREATMENT OF BREAST CANCER | ELIZABETH SCHMIDT, MD

Breast cancers demonstrate wide diversity when analyzed in the pathology laboratory. Many breast tumor characteristics are determined under the lens of a microscope. Newer tools identify molecular and genetic differences among breast cancers. The particular combination of these tumor characteristics is used by the patient and her physicians to choose among treatment options and devise a personalized plan for treatment.

Prognostic versus predictive factors

Tumor characteristics of breast cancers have two main functions: prognostic and predictive. Prognostic factors are those that predict the aggressiveness of the disease if left untreated. Predictive factors are those that assess the likelihood that the tumor will respond to interventions such as chemotherapy, radiation therapy, and targeted therapy. Many breast cancer characteristics have both prognostic and predictive value.

Macroscopic and microscopic breast cancer characteristics

1. Invasive vs. in situ carcinoma: Tumors that are confined within the breast ductal system (“in situ” carcinomas) have a different path of spread than tumors that are invasive into the surrounding connective tissue of the breast, and are thus managed differently. Surgery is the primary method for treatment of in situ carcinoma; more extensive in situ disease requires a larger procedure (mastectomy vs. “lumpectomy”). Invasive tumors are more

- likely to spread via lymphatic and blood vessels; assessment of the regional lymph nodes is important. Pre-operative (“neo-adjuvant”) chemotherapy may be considered for invasive tumors.
- 2. Size of tumor: Tumor size is an important prognostic factor for breast cancer. The larger the tumor, the higher the likelihood it has metastasized and the more tissue that must be removed for local control of the tumor. The amount of tumor remaining in a post-neo-adjuvant surgical specimen is also prognostic for long-term survival.
- 3. Histologic type: There are many histologic types of breast cancer with somewhat different clinical implications. Lobular carcinomas are more often bilateral than ductal carcinomas and may be more extensive than suspected by mammogram. Thus knowing the type of histology may influence the amount of tissue that the surgeon decides to remove.
- 4. Histologic grade: The Nottingham grading system used for invasive breast carcinomas. This system classifies the tumor into low-grade, intermediate-

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Table 1: Examples of treatment choices based on breast tumor characteristics	
Invasive vs. In Situ	Extent of surgery Type of axillary lymph node assessment Radiation therapy choices
Tumor Size	Extent of surgery Type of axillary lymph node assessment Radiation therapy choices Neo-adjuvant vs. adjuvant chemotherapy
Histologic Type	Extent of surgery Type of diagnostic imaging evaluation
Histologic Grade	Neo-adjuvant vs. adjuvant chemotherapy Type of chemotherapy
Lymph Node Status	Extent of surgery Type of chemotherapy Radiation therapy choices
Estrogen & Progesterone Receptors	Type of chemotherapy and/or hormonal therapy Neo-adjuvant vs. adjuvant chemotherapy
HER-2 Oncogene/Oncoprotein	Type of chemotherapy Use of targeted therapy
Gene Expression Profiling	Type of Chemotherapy

grade, or high-grade. The Nottingham grade is prognostic for disease-free and overall survival. The grade of the tumor may also influence the choice of chemotherapy agents and whether neo-adjuvant chemotherapy is administered.

1. **Lymph node status:** The number of lymph nodes involved by metastatic carcinoma is another traditional prognostic factor. Large tumors are treated with complete axillary dissection to assess the number of nodes involved. The sentinel lymph node procedure, a limited node dissection technique, has become widely used for smaller-sized invasive carcinomas. This procedure identifies the first node(s) to which the tumor drains. These nodes are examined more extensively in

the Pathology laboratory, with multiple levels and immunostains. The absence of metastasis in the sentinel node allows the patient to forgo a full axillary dissection and decreases the risk of lymphedema.

Molecular characteristics of breast cancer

1. **Hormone receptors (ER and PR):** Estrogen Receptor (ER) and Progesterone Receptor (PR) are nuclear transcription factors involved in the regulation of growth and differentiation (ER) or proliferation (PR) of breast epithelial cells. These protein receptors may be functional to varying degrees in breast cancers. They are weakly prognostic factors but are strongly predictive for response to hormonal therapies such as tamoxifen.

2. **HER-2 oncogene/oncoprotein:** A more recently identified, and highly significant, breast cancer biomarker is the proto-oncogene Her-2, located on chromosome 17. It encodes a tyrosine-kinase protein on the outer cell membrane which is involved in regulating many cell functions including proliferation, survival, and apoptosis. The HER-2 gene is amplified in 15-30% of invasive breast carcinomas. It is currently assayed by one of two methods: immunohistochemistry to detect overexpression of the HER-2 oncoprotein (see picture), and fluorescence in situ hybridization (FISH) to identify amplification of the HER-2 oncogene.

HER-2 status is predictive for response to some types of cytotoxic chemotherapy.

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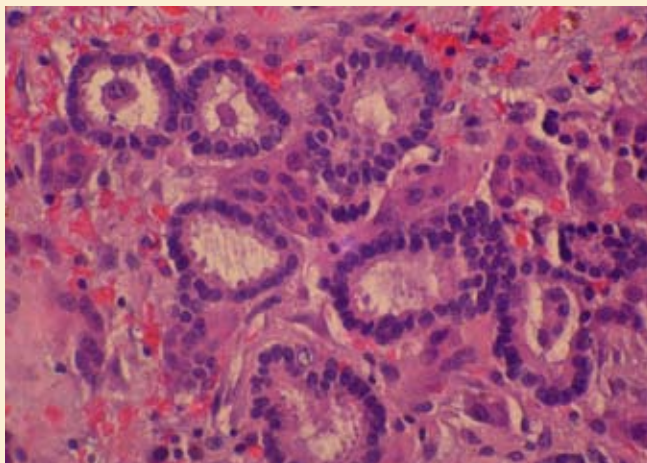


FIGURE 1 Low histologic grade vs high histologic grade: Grading is based on how closely the tumor resembles normal breast ducts.

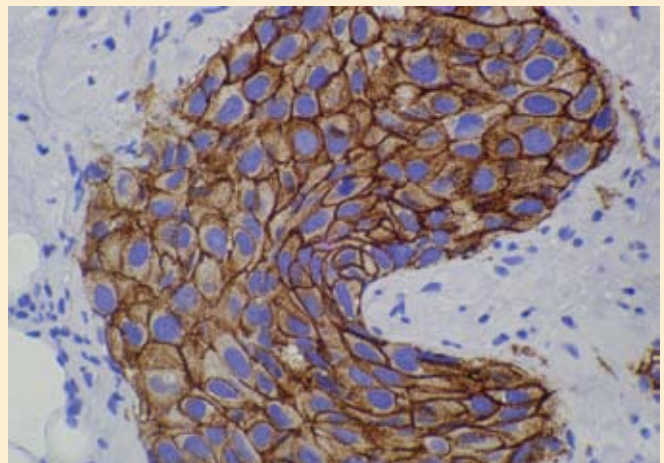


FIGURE 2 HER2 oncoprotein overexpression: Strong staining of cell membranes by immunostaining on tumor cells indicates overexpression of the HER2 oncoprotein and predicts responsiveness of the tumor to targeted antibody treatment.

therapies and also for new antibody-based therapies which specifically target the HER-2 protein, such as trastuzumab. These new targeted therapies promise exciting improvements in breast cancer survival.

Gene expression profiling

A new tool for analyzing breast cancers is gene expression profiling, or gene arrays. These are groups of genes that have statistical significance in assessing prognosis and/or predicting response to various treatment modalities for breast cancer. Several gene expression profiles have been reported to have prognostic and/or predictive value for breast cancer patients. Two are currently commercially available, one using a 21-gene profile (OncotypeDX) that provides a recurrence score in the subset of ER-positive, node-negative patients, and one using a 70-gene

array (Mammaprint) that identifies patients with good and poor prognostic signatures.

Combining data to define subgroups of breast cancers

ER, PR, and HER2 data may be used to subdivide breast cancers into groups with similar prognostic and/or predictive profiles. Thus, tumors with the combination of ER positive, PR positive, HER-2 negative profile tend to be lower histologic grade, slower growing, and more responsive to hormone therapy but less responsive to trastuzumab. ER negative, PR negative, HER-2 positive tumors are more likely high grade, are less responsive to hormone therapy but do respond to trastuzumab. "Triple negative" cancers (ER negative, PR negative, HER-2 negative) tend to be high histologic grade, more rapidly growing, poorer prognosis and less

responsive to hormone or trastuzumab therapy.

Putting it all together

When the various data for an individual tumor have been determined, the patient and her physicians can discuss treatment options. The multidisciplinary breast cancer conference is a mechanism for the many professionals involved in breast cancer treatment to meet together to review the diagnostic imaging and pathology data, discuss pros and cons of the many available choices for treatment, and coordinate care for an individual patient. Northwest Hospital medical staff members are welcome to attend these weekly conferences at 7 am on Wednesday mornings in the MOB Cancer Conference Room. ●

HORMONE-BASED ADJUVANT TREATMENT OF BREAST CANCER | DOUGLAS LEE, MD

Adjuvant therapy in early, curable breast cancer centers on enhancing the chance of cure. It has long been known that approximately 75% of breast cancers possess estrogen and/or progesterone receptors (ER/PR+) which, when occupied by the corresponding hormone, stimulate cancer growth and progression. Likewise, when such receptor-hormone interaction is inhibited, long-term survival improves.

The prototype for hormone-based treatment of breast cancer has been

Tamoxifen, which competitively inhibits occupation of the estrogen receptor. This "wooden nickel" approach does result in some estrogen-like effects such as maintenance of bone density and increased thromboembolic disease, but does not stimulate cancer progression. On the contrary, 5 years of Tamoxifen exposure is associated with a 5 to 11% absolute increase in survival in early breast cancer patients with 10 years of follow-up (Early Breast Cancer Trialists Group, Lancet 1998, May 16;351 (9114):1451-67).



Tamoxifen benefits both premenopausal and postmenopausal patients. Toxicity includes increased incidence of deep vein thrombosis and uterine cancer.

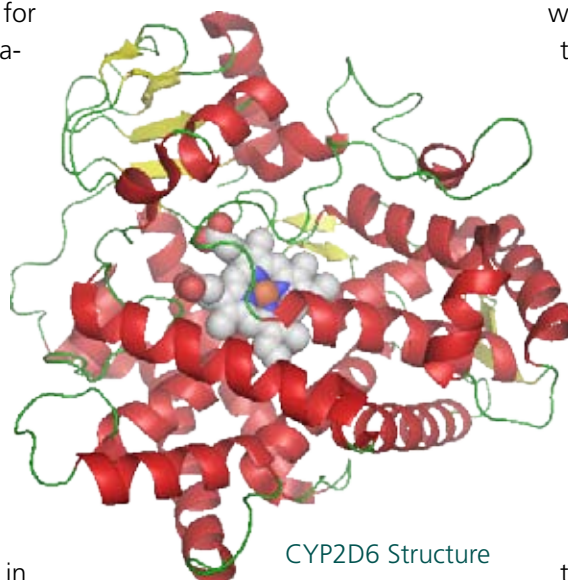
While other types of hormone manipulation techniques exist for breast cancer treatment, Tamoxifen has been the mainstay of such treatment for decades. In addition, other than determination of tumor ER/PR status,

there has been little data regarding which patients might respond to Tamoxifen and which patients would not. This has led to a “one size fits all” strategy.

However, in the last few years, another class of hormone-based treatment has emerged for postmenopausal patients. These drugs, collectively called aromatase inhibitors, work by inhibiting aromatase, the enzyme chiefly responsible for catalyzing the formation of estradiol in tiny amounts in postmenopausal women from androgen precursors. At this time there are three commercially available drugs in this class: Anastrozole, Letrozole, and Exemestane. Clinical trials have not been completed comparing the relative efficacy of these drugs. All of them, however, have demonstrated superiority to Tamoxifen in enhancing disease-free survival in early breast cancer patients either in head-to-head studies or in sequential studies in which several years of Tamoxifen are followed by several years of aromatase inhibitor therapy, versus 5 years of Tamoxifen. Side-effects included severe myalgias, hot flashes, and loss of bone density. It should be re-emphasized that this therapy has no role in patients unless they are postmenopausal.

Recent data has also modified guidelines for the use of adjuvant Tamoxifen. Tamoxifen is known to be metabolized to its more active metabolite Endoxifen by a specific cytochrome P450 class enzyme coded for by the

gene CYP2D6. Patients on Tamoxifen who take certain Selective Serotonin Reuptake inhibitor (SSRI) antidepressants such as Paroxetine and Fluoxetine often exhibit lower serum levels of Endoxifen than patients not taking these antidepressants (Jin et al, JNCI 2005 97:30-39). Of the SSRI agents now available, only Venlafaxine does not inhibit the metabolism of Tamoxifen to Endoxifen.



Similar studies also noted the existence of mutated CYP2D6 alleles in some patients which, if homozygous, are associated with significantly lower serum Endoxifen levels than those of Tamoxifen users possessing wild-type alleles. Fortunately, chemical assays are now commercially available to allow characterization of any given patient's CYP2D6 status, and if a “poor metabolizer” is identified, the likelihood of Tamoxifen efficacy in that individual may be prohibitively low (Aubert et al; JCO Vol 27 No 18@, Part II or II, 2009: LBA4009).

Thus the indications for adjuvant Tamoxifen can be refined to include those patients who do not have “slow metabolizer” alleles for CYP2D6 and who are not on SSRI agents, with the exception of Venlafaxine. It is intriguing to speculate on the outcome of a clinical trial comparing adjuvant aromatase inhibitors and Tamoxifen in postmenopausal patients if only CYP2D6 “normal metabolizers” and those not on SSRI antidepressants were to be included. Would aromatase inhibitor therapy remain superior to Tamoxifen?

An ongoing controversy in the adjuvant treatment of premenopausal breast cancer patients is the role of ovarian suppression, in that the induction of menopause in such patients might increase their freedom from relapse and increase overall survival. Thus far, prospective randomized trials have not addressed whether standard chemotherapy + Tamoxifen adjuvant therapy in such individuals would be enhanced by either oophorectomy or the use of LHRH agonists. Ongoing clinical studies such as the SOFT trial will hopefully answer this important question.

Even if a premenopausal breast cancer patient were to be made functionally postmenopausal, would Tamoxifen or an aromatase inhibitor be the more appropriate partner? If trial data regarding postmenopausal women older than age 50 provides a guide, one would predict that aromatase inhibitor therapy would be superior to Tamoxifen in

these patients. Interestingly, Austrian Breast and Colorectal Cancer Study Group Trial 12 (N Engl J Med 2009; 360 (22) 2367) studied more than 1800 premenopausal patients rendered functionally postmenopausal by the use of LHRH agonist Gosere- lin, randomizing between Tamoxifen and the aromatase inhibitor Anastro- zole. Contrary to expectation, there was no difference in disease-free sur- vival between the two groups.

Traditionally, premenopausal patients have been treated in the adjuvant setting with a combination of che- motherapy and Tamoxifen. This prac- tice followed the release of the Early Breast Cancer Trialists Group meta- analysis (Lancet 2005; 365 (9472): 1665) indicating an additive effect for chemotherapy and endocrine treat- ment. Newer research work utilizing genetic micro-arrays of the breast cancer itself have helped identify

cancers which demonstrate excellent response to hormone-based therapy and, more importantly, no additional improvement with chemotherapy. Such patients can safely be treated with hormone-based therapy alone and thus be spared the toxicity of chemotherapy altogether. The advan- tages of personalized treatment in these patients is amply illustrated. ●

ADJUVANT CHEMOTHERAPY AND BIOLOGICAL TREATMENT OF BREAST CANCER | DOUGLAS LEE, MD

Personal Oncology Care in breast cancer is increasingly evident in the selection of adjuvant chemotherapy and biological therapy. Formerly, decisions regarding the use of che- motherapy depended on large meta- analyses of available published lit- erature and the use of online tools such as "Adjuvant! Online" to assess risk and benefit. Many premeno- pausal and more limited numbers of postmenopausal patients were recommended to take adjuvant che-

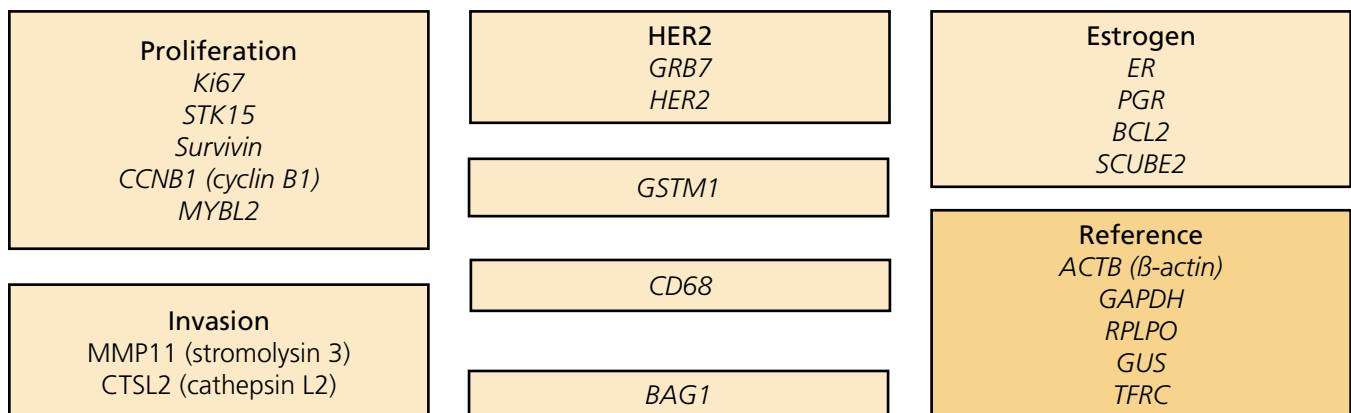
motherapy based on such empiric observable trends analysis. Landmark information derived from bench research and incorporated into clini- cal trials has modified this practice in significant ways.

Individual Tumor Micro-array Analysis: Chemotherapy or Not?

The mapping of the entire human genome has facilitated the ability to evaluate certain genes within any given breast tumor itself to derive

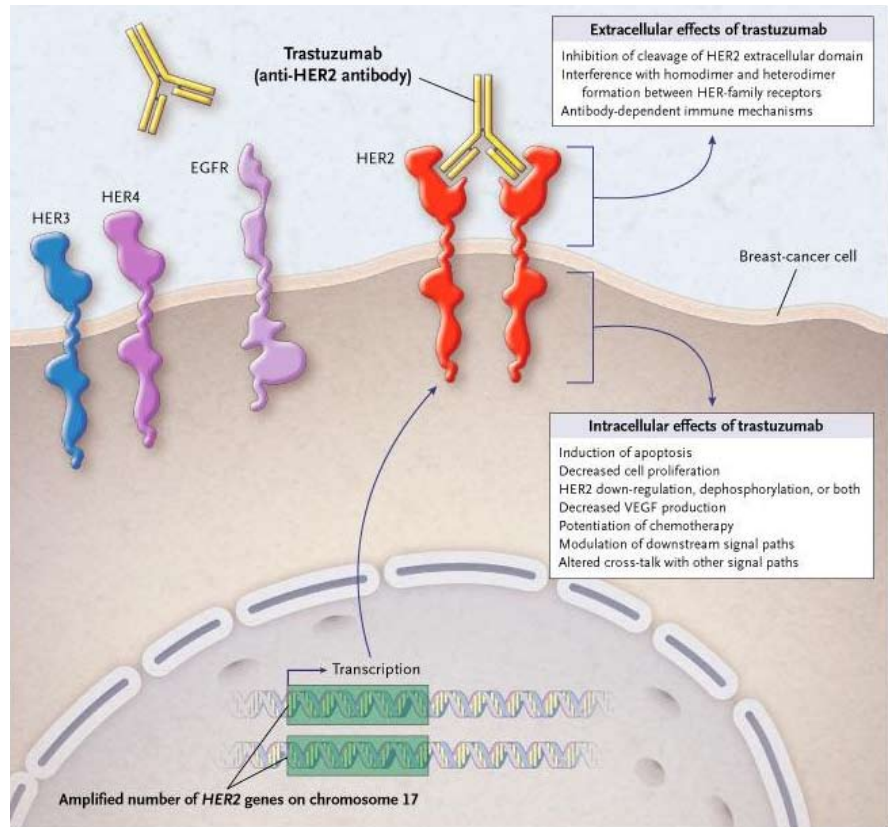
both prognostic and predictive infor- mation for that tumor. Multiple assays exist for this analysis. The Oncotype Dx assay, a RT-PCR analysis of 21 selected genes, became com- mercially available after demonstrat- ing high accuracy in predicting which node-negative, hormone receptor- positive breast cancers required hor- mone adjuvant therapy alone and

CONTINUED ON PAGE 16



which cancers additionally required chemotherapy. Ongoing trials are in progress to apply similar technology to node-positive breast cancer patients. Such assays have the groundbreaking effect of identifying patients whose cancers do not benefit from adjuvant chemotherapy, thus freeing them from the obligation to take chemotherapy at all.

Targeting Her2. The generation of a specific antibody targeting the extracellular domain of the protein coded for by the her2-neu gene has revolutionized adjuvant therapy for patients whose cancers over-express this protein. This antibody, called Trastuzumab (Herceptin), has been evaluated in adjuvant clinical trials combined with chemotherapy in patients with so-called her2-positive breast cancer. The BCIRG 006 trial randomized over 3,200 patients to standard anthracycline- and taxane-containing chemotherapy versus chemotherapy plus Trastuzumab (Robert et al; JCO Vol 25, no 18s (June 20 supplement), 2007:19647)). Chemotherapy in the Trastuzumab arms included an anthracycline-containing arm and a non-anthracycline-containing arm. The most recent analysis of BCIRG 006 revealed an approximately 36% reduction in relapse and an absolute 5-6% increase in overall survival for the Trastuzumab arms over the chemotherapy-alone arm. Trials of Lapatinib, a drug which targets both extra-cellular and intra-cellular aspects of Her2-neu gene product, have also demonstrated high levels of activity in her2-positive patients, mostly in the metastatic setting. Trials of Lapatinib in adjuvant breast cancer patients are underway. Only



about 20-25% of newly diagnosed breast cancers exhibit over-expression of her2, however it is certain that the prognosis of this group of patients has been radically improved through the use of targeted therapy.

Targeted Therapy in BRCA-1 and Triple-negative Breast Cancer.

Another small subset of breast cancer patients is defined by mutations in their BRCA-1 and BRCA-2 genes. Such mutations confer a high risk of breast cancer and ovarian cancer in affected individuals, along with slightly higher risks of other cancers as well. Mutated genes can be passed on to offspring with all of the associated risks. Breast malignancies associated with mutations of BRCA-1 make up approximately 10% of all breast cancers. These tumors tend to be so-called triple-negative tumors

in that they do not express estrogen-receptors, progesterone receptors, or over-expression of her2-neu. The triple-negative phenotype is associated with more aggressive behavior and higher rates of relapse. BRCA-1 mutations are also associated with inherent defects in the repair of single-stranded DNA breaks, making such cancer cells 1) more dependent on alternative pathways of DNA repair such as the poly (ADP-ribose) polymerase-1 (PARP-1) pathway and 2) more susceptible to DNA-damaging agents such as Cisplatin. Highlighted abstracts at the 2009 American Society of Clinical Oncology Annual Meeting included a study by O’Shaughnessy et al (JCO Vol 27, No 18S part II:793s) showing a marked improvement in survival in metastatic triple-negative patients when PARP-1 inhibitor BSI-2101 was added to che-

motherapy, while a trial reported by Gronwald et al (JCO Vol 27. No 15S, Part I: 7s) documented a 72% pathologic complete response rate when single-agent Cisplatin was given pre-operatively to BRCA-1 early breast cancer patients. These data serve to illustrate that strategies which target distinguishing characteristics of defined subpopulations of breast cancers can be highly successful.

Anthracyclines, Yes or No? Adjuvant therapy of breast cancer has included anthracyclines such as Doxorubicin and Epirubicin since the 1970s. Regimens containing these drugs have been associated with a reduction in breast cancer recurrence of 11.2% compared to traditional non-anthracycline programs such Cyclophosphamide, Methotrexate,

and 5-FU ((Lopez-Tarruella and Martin, Breast Cancer Research 2009, 11:204; 2009). Unfortunately, toxicities of this class of agents include cardiomyopathy (1-4%), extravasation risk, and secondary leukemias (0.5%). Recent studies comparing taxanes with anthracyclines raise the question of whether anthracyclines are necessary. For example, Jones et al (J Clin Oncol, 2009 Mar 10; 27(8): 1177-83) recently published 7-year follow-up data concerning US Oncology Research Trial 9735, in which early breast cancer patients were randomized to receive adjuvant Doxorubicin and Cyclophosphamide versus Docetaxel and Cyclophosphamide. The Docetaxel arm was associated with a significant overall survival advantage (87% versus 82%, $p = .032$), which was unaffected by age,

hormone receptor status, or her2-neu status. A more ambitious US Oncology trial comparing Docetaxel and Cyclophosphamide with Docetaxel, Cyclophosphamide, and Doxorubicin for higher risk early breast cancer patients is nearing completion. Significantly, in BCIRG 006 (discussed above), her2-neu overexpressing cancer patients receiving Doxorubicin versus Docetaxel in their adjuvant chemotherapy had equal disease-free survival, however there was a significant increase in cardiomyopathy associated with the Doxorubicin arm. These trials allow clinicians to have viable options when selecting adjuvant chemotherapy regimens which minimize cardiac side-effects, particularly for patients who have pre-existing cardiomyopathies. ●

TREATMENT OF METASTATIC BREAST CANCER | DOUGLAS LEE, MD

The use of hormone-based treatment (for hormone receptor-positive disease) and chemotherapy for patients with metastatic breast cancer is well-established. Patients whose cancers over-express her2-neu can experience significant increases in progression-free survival with Trastuzumab and Lapatinib therapy. As previously stated, bone metastases are routinely treated with IV bisphosphonates such as Zoledronic Acid.

Bevacizumab (Avastin) is a humanized monoclonal antibody which binds to and inhibits Vascular Endothelial Growth Factor (VEGF). VEGF is a key protein in angiogenesis, the

generation of new blood vessels feeding breast cancer cells. Clinical trial E2100 (Miller et al, N Eng J Med Vol 357:2666-2676) compared single agent Taxol combined with Bevacizumab with Taxol alone in patients with metastatic disease. The combined arm showed a 5-month improvement in progression-survival but no significant improvement in overall survival. Patients and clinicians alike have pondered the utility of such agents, which provide freedom from cancer progression but do not lengthen life span.

Clinical trials utilizing a Personalized Care objective are increasingly



dependent on biomarker analysis of individual tumors, often using gene micro-arrays. Such analyses have generated a catalog of subsets of breast cancer, each revealing specific mechanisms by which progression

and growth are mediated. Research into these mechanisms and pathways provides opportunities to target those pathways at critical junctures in the cancer cell life cycle.

For example, in the 2009 ASCO Educational Session, Dr. Stephen Johnston highlighted the phosphatidylinositol 3-kinase (PI3K)/Akt/mammalian target of rapamycin, or “mTOR” pathway (ASCO Educational Booklet 2009:20-28). This mTOR pathway is de-regulated in some hormone receptor-positive breast cancers, rendering them more likely to develop

resistance to standard hormone treatment. Clinical trials studying mTOR Inhibitors such as Temsirolimus and Everolimus have revealed promising results when these agents are combined with Aromastase Inhibitors in postmenopausal metastatic breast cancer patients with Estrogen receptor-positive disease. It is hoped that such drugs, which block downstream steps in the mTOR pathway, can modify the de-regulated pathway of affected cells in such a manner as to decrease resistance to hormone therapy and provide meaningful remissions in these patients.

As elucidation of other critical pathways and biomarkers proceeds, breast cancer patients will be provided increasing amounts of information regarding the specific subset of breast cancer they are dealing with. Specific targeted therapy for that subset will increasingly become available. Personalized Care for breast cancer shows considerable promise in accurately matching the best treatment to the individual patient so as to maximize success and minimize treatment-related side-effects. ●

LYMPHEDEMA TEAM SUPPORTS CASTING CALL PARTICIPANTS | JEAN GRANTHAM

The lymphedema team at Northwest Hospital plays an active role in Northwest Casting Call Fly Fishing Program. The therapists teach warm up and cool down stretches and breathing exercises tailored to meet the needs of each participant during the classroom training. Breast cancer patients prepare to take to their boats on the Yakima River. The aim is to show participants how they can safely engage in challenging activities, despite lymphedema or other impairments that may result from breast cancer. Participants learn to balance activity with rest, as well as

self-monitoring skills. These skills can then be translated to everyday life with confidence, says lymphedema therapist, MaryAnne Church Trettennero, OTR/L. “It is amazing to see the personal transformations that took place between the classroom session and our fishing trip.”

Patient Karen Flowers agrees. She says that after initially believing that cancer would end her life, Casting Call changed her mind. “That program gave me hope that not only could I expect to return to doing what I could do before cancer,”

Karen says, “but I can also expect to do new and exciting things that I had not even considered possible before.” “I have also gained a whole new community of comrades-in arms, both professionals and fellow survivors, who have become good friends and resources for managing my health long past the year of cancer treatments.” ●

“That program gave me hope that not only could I expect to return to doing what I could do before cancer,” Karen says, “but I can also expect to do new and exciting things that I had not even considered possible before.”



LYMPHEDEMA THERAPY: MAKING A DIFFERENCE THROUGH PERSONALIZED CARE | JEAN GRANTHAM

The Lymphedema therapists at NWH continue to play an integral role in providing personalized therapy services to patients with breast cancer. While not everyone with breast cancer will develop lymphedema, a small but significant fraction of patients do. In many cases, the presence of lymphedema can restrict range of motion, making it difficult for patients to perform activities of daily living (dressing, personal care, and housekeeping activities) and cause pain. The focus of the program is to educate all patients on how to recognize the signs and symptoms of lymphedema and how to integrate risk reduction techniques into

their daily life. For those who experience lymphedema, a comprehensive treatment approach is offered that addresses how to reduce and manage the swelling.

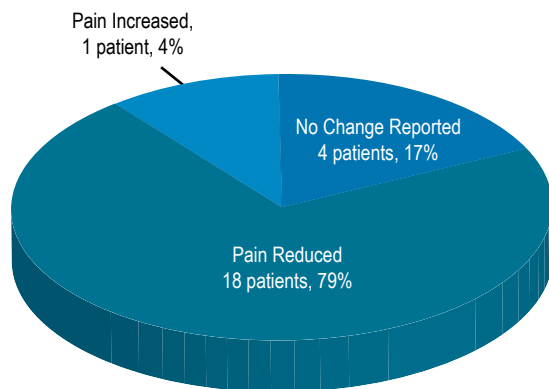
Of the 98 patients participating in the lymphedema program at Northwest Hospital, 58 had breast cancer. Thirty-three of those breast cancer patients attended three or more visits for lymphedema management, which included manual lymphatic drainage, garment fitting and ROM exercises. The remaining 25 breast cancer patients attended fewer than three visits and received training to recognize the signs and symptoms

of lymphedema as part of the early intervention Lymphedema Awareness Program.

Data was collected on changes in pain and Activities of Daily Living (ADL) in the 33 patients who were seen for 3 or more visits. Pain, measured on a 10-point scale, was a significant limitation to movement in 23 of these patients. By discharge, 18 of the 23 had reported pain reduction. ADL limitations, measured on a thirty six-point scale, were identified by 20 of the 33 patients. By discharge, 15 of the 20 reported improved ADL scores. ●

Pain With Motion

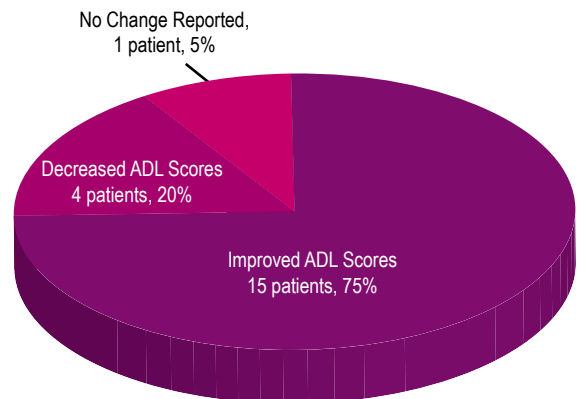
Outcome of breast cancer patients who reported pain with motion at admit 3+ visits.



Out of 33 breast cancer patients 23 reported pain with range of motion initially (70%). Of the patients who reported pain 78.3% (18/23) reported reduced pain at discharge.

Activities of Daily Living

ADL outcome of 20 breast cancer patients who reported deficit in ADL scores 3+ visits.



Out of 33 breast cancer patients, 20 patients reported deficits in Activities of Daily Living. Of the patients who reported deficits in ADL's 75% (15/20) reported improvement.

FIGO STAGING FOR FEMALE GENITAL TRACT CANCER - AN UPDATE | CHRISTINA ISACSON, MD

The International Federation of Gynecology and Obstetrics (FIGO) has issued new staging for uterine sarcomas and revised staging for carcinoma of the vulva, cervix and endometrium. These changes reflect the rapidly increasing knowledge about the biology, behavior and treatment of female genital tract cancer. Over the past three years, discussions have been held with international experts and societies to produce a consensus document that was approved by the International Union Against Cancer

(UICC), the American Joint Commission on Cancer (AJCC) and FIGO in 2008. This brief report summarizes the major changes.

Uterine sarcomas include leiomyosarcomas, endometrial stromal sarcomas, adenosarcomas, and carcinosarcomas. In the past, sarcomas were either not staged at all or were staged according to the 1988 FIGO criteria for uterine corpus carcinoma. The new classification recognizes that this group of malignancies is

heterogenous, with distinct clinical and pathologic characteristics (Tables 1 and 2). Leiomyosarcomas are the most common sarcoma and are separated from endometrial stromal sarcomas and adenosarcomas with respect to stage I – they are stratified by size rather than depth of myometrial invasion due to the fact that they arise within the myometrium, rather than from the endometrium. Carcinosarcomas (also called malignant mixed mullerian tumors, MMMT), have been recently reclassified as a

Table 1: Uterine Leiomyosarcoma

Stage I	Tumor limited to uterus
IA	<5 cm
IB	>5 cm
Stage II	Tumor extends to the pelvis
IIA	Adnexal involvement
IIB	Tumor extends to extrauterine pelvic tissue
Stage III	Tumor invades abdominal tissues (not just protruding into the abdomen)
IIIA	One site
IIIB	>one site
IIIC	Metastases to pelvic and/or para-aortic lymph nodes
Stage IVA	Tumor invades bladder and/or rectum
IVB	Distant metastasis

Table 2: Endometrial Stromal Sarcomas and Adenosarcomas

Stage I	Tumor limited to uterus
IA	Tumor limited to endometrium/endocervix with no myometrial invasion
IB	Less than or equal to half myometrial invasion
IC	More than half myometrial invasion
Stage II	Tumor extends to the pelvis
IIA	Adnexal involvement
IIB	Tumor extends to extrauterine pelvic tissue
Stage III	Tumor invades abdominal tissues (not just protruding into the abdomen)
IIIA	One site
IIIB	>one site
IIIC	Metastasis to pelvic and/or para-aortic lymph nodes
Stage IVA	Tumor invades bladder and/or rectum
IVB	Distant metastasis

“metaplastic” or “dedifferentiated” form of aggressive endometrial carcinoma and should now be staged as per carcinomas of the endometrium.

Vulvar cancer staging has undergone major changes based upon tumor size, extent of invasion and lymph node involvement characteristics (Table 3). Stage Ia remains unchanged due to their low risk of metastatic spread. Tumor size >2 cm with negative lymph nodes is no longer considered to be stage II as

these patients do as well as stage Ib vulvar cancer regardless of size. The new stage II was previously stage III - a tumor of any size with extension to adjacent perineal structures with negative nodes. Significantly, the number, size and presence of extracapsular spread of involved inguino-femoral lymph nodes creates three new subdivisions of Stage III. The bilaterality of positive nodes has been discounted. Stage IVA now includes fixed or ulcerated inguino-femoral lymph nodes. Accurate designation

of lymph node location, including gross clinical features and detailed pathologic characteristics are key to this revised staging system.

Cervical cancer is still clinically staged despite much debate. The major updates are as follows (Table 4): Stage 0 (carcinoma in-situ) has been deleted as it is a pre-invasive lesion. There were no changes in stage Ia (microinvasive carcinoma). Stage II now includes size with a cutoff of >4 cm in maximum tumor diameter

Table 3: Carcinoma of the Vulva

Stage I	Tumor confined to the vulva
IA	Lesions 2 cm in size, confined to the vulva or perineum and with stromal invasion ≤ 1.0 mm, no nodal metastasis
IB	Lesions >2 cm in size or with stromal invasion >1.0 mm, confined to the vulva or perineum, with negative nodes
Stage II	Tumor of any size with extension to adjacent perineal structures (1/3rd lower urethra, 1/3rd lower vagina, anus) with negative nodes
Stage III	Tumor of any size with or without extension to the adjacent perineal structures (1/3rd lower urethra, 1/3rd lower vagina, anus) with positive inguino-femoral lymph nodes
IIIA	(i) With 1 lymph node metastasis (5 mm), or (ii) 1-2 lymph node metastasis(es) (<5 mm)
IIIB	(i) With 2 or more lymph node metastases (5 mm), or (ii) 3 or more lymph node metastases (<5 mm)
IIIC	With positive nodes with extracapsular spread
Stage IV	Tumor invades other regional (2/3 rd upper urethra, 2/3 rd upper vagina), or distant structures
IVA	Tumor invades any of the following: (i) upper urethral and/or vaginal mucosa, bladder mucosa, rectal mucosa, or fixed to pelvic bone, or (ii) fixed or ulcerated inguino-femoral lymph nodes
IVB	Any distant metastasis including pelvic lymph nodes

distinguishing IIA1 from IIA2. Stages III and IV remain the same. Other important risk factors to take into account that are not included in the clinical staging include lymphovascular space invasion and lymph node status. This staging applies to both squamous cell carcinomas and adenocarcinomas of the cervix.

Surgical staging for endometrial cancer was first instituted 20 years ago and much outcome data has been accumulated. Due to the favorable prognosis for both stages IA (non-invasive) and IB (<50% myoinvasive), these two substages have been

merged into IA (Table 5). Stage IB now represents those tumors with invasion equal to or more than half of the myometrium. In addition, stage II now includes only endocervical stromal invasion; involvement of the endocervical glandular portion of the cervix is considered stage I. Stage III has undergone changes with respect to the significance of cytologic pelvic washings, parametrial involvement and the distinction of pelvic from para-aortic lymph node involvement. Due to its uncertain independent prognostic significance, pelvic washings have been thrown out, although still will be performed

and reported separately. Parametrial involvement is included with vaginal involvement for stage IIIB. Para-aortic lymph node metastases are a recognized predictor of poor outcome and subdivide IIIC into pelvic versus para-aortic lymph node metastases (IIIC1 vs IIIC2).

It is anticipated that the new/revised staging will be incorporated into the 7th edition of the AJCC/UICC Cancer Staging Manual and will begin to be utilized starting with the 2010 calendar year. ●

Table 4: Carcinoma of the Cervix Uteri

Stage I	The carcinoma is strictly confined to the cervix (extension to the corpus would be disregarded)
IA	Invasive carcinoma which can be diagnosed only by microscopy with deepest invasion 5 mm and largest extension 7 mm
IA1	Measured stromal invasion of 3.0 mm in depth and extension of 7.0 mm
IA2	Measured stromal invasion of >3.0 mm and not >5.0 mm with an extension of not >7.0 mm
IB	Clinically visible lesions limited to the cervix uteri or pre-clinical cancers greater than stage IA
IB1	Clinically visible lesion 4.0 cm in greatest dimension
IB2	Clinically visible lesion >4.0 cm in greatest dimension
Stage II	Cervical carcinoma invades beyond the uterus, but not to the pelvic sidewall or lower 3 rd of the vagina
IIA	Without parametrial invasion
IIA1	Clinically visible lesion 4.0 cm in greatest dimension
IIA2	Clinically visible lesion >4.0 cm in greatest dimension
IIB	With obvious parametrial invasion
Stage III	The tumor extends to the pelvic wall and/or involves the lower third of the vagina and/or causes hydronephrosis or non-functioning kidney
IIIA	Tumor involves lower third of the vagina, with no extension to the pelvic wall
IIIB	Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney
Stage IV	The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. Bullous edema, as such, does not permit a case to be allotted to Stage IV
IVA	Spread of the growth to adjacent organs
IVB	Spread to distant organs

Table 5: Carcinoma of the Endometrium

Stage I	Tumor confined to the corpus uteri
IA	No or less than half myometrial invasion
IB	Invasion equal to or more than half of the myometrium
Stage II	Tumor invades cervical stroma, but does not extend beyond the uterus
Stage III	Local and/or regional spread of the tumor
IIIA	Tumor invades the serosa of the corpus uteri and/or adnexae
IIIB	Vaginal and/or parametrial involvement
IIIC	Metastases to pelvic and/or para-aortic lymph nodes
IIIC1	Positive pelvic nodes
IIIC2	Positive para-aortic lymph nodes with or without positive pelvic lymph nodes
Stage IV	Tumor invades bladder and/or bowel mucosa, and/or distant metastases
IVA	Tumor invasion of bladder and/or bowel mucosa
IVB	Distant metastases, including intra-abdominal metastases and/or inguinal lymph nodes

CANCER CONFERENCE ACTIVITIES: THE TEAM APPROACH TO PATIENT CARE

Cancer conferences are meetings at which specialists from various areas of expertise discuss selected cancer patients. This provides a consultative service to the physicians treating the patient with input regarding further diagnostic work-up, staging, treatment and follow-up options. Radiology films and pathology slides for each case are also reviewed. Required attendance includes representatives from surgery, pathology, radiology, and medical and radiation oncology. The meetings are open to any health care professional that is involved in

CONFERENCE SCHEDULES:

- Breast Conference: Every Wednesday, 7-8am
- Chest Conference: 2nd & 4th Tuesdays, 7-8am
- General Cancer Conference: Every Wednesday, 12:30-1:30pm
- Gynecologic Oncology Conference: 1st & 3rd Tuesdays, 7-8am

All conferences are held in the Cancer Conference Room in the Medical Office building on the main campus.

caring for cancer patients, and often include plastic surgeons, physician assistants, nurses, patient and nurse

navigators, cancer registrars, physical therapists, and pharmacists. ●

2008 NEW CANCER CASES: SITE DISTRIBUTION REPORT

PRIMARY SITE	TOTAL	SEX		CLASS		DOMINANT AJCC STAGE GROUP						
		Male	Female	Analyt	NonAn	0	I	II	III	IV	None	Un-known
TONGUE	2	2	0	2	0	0	0	0	0	2	0	0
SALIVARY GLANDS, MAJOR	1	0	1	1	0	0	0	1	0	0	0	0
FLOOR OF MOUTH	1	0	1	1	0	1	0	0	0	0	0	0
MOUTH, OTHER & NOS	2	1	1	2	0	0	0	0	0	1	0	1
TONSIL	2	2	0	2	0	0	0	1	0	1	0	0
HYPOPHARYNX	1	0	1	1	0	0	0	0	0	1	0	0
PHARYNX & ILL-DEFINED	1	1	0	1	0	0	0	0	0	0	1	0
ESOPHAGUS	3	1	2	3	0	0	1	0	0	1	0	1
STOMACH	10	7	3	10	0	0	2	1	2	1	1	3
COLON	44	19	25	44	0	5	6	8	12	6	2	5
RECTUM & RECTOSIGMOID	22	11	11	22	0	1	3	6	4	4	0	4
ANUS,ANAL CANAL,ANORECTUM	6	3	3	6	0	0	2	0	1	0	0	3
LIVER	10	8	2	10	0	0	1	0	4	2	0	3
GALLBLADDER	1	0	1	1	0	0	0	0	0	1	0	0
BILE DUCTS	3	1	2	3	0	0	0	0	0	1	0	2
PANCREAS	8	3	5	8	0	0	0	0	0	7	0	1
RETROPERITONEUM	2	1	1	2	0	0	1	0	0	0	0	1
PERITONEUM,OMENTUM,MESENT	4	1	3	4	0	0	0	0	0	0	4	0
LARYNX	5	4	1	5	0	2	2	0	0	1	0	0
LUNG/BRONCHUS-SMALL CELL	9	5	4	9	0	1	0	1	0	5	0	2
LUNG/BRONCHUS-NON SM CELL	63	32	31	63	0	4	16	6	8	13	0	16
LEUKEMIA	10	7	3	10	0	0	0	0	0	0	10	0
MYELOMA	7	2	5	7	0	0	0	0	0	0	7	0
OTHER HEMATOPOIETIC	2	0	2	2	0	0	0	0	0	0	2	0
SOFT TISSUE	6	3	3	6	0	0	0	0	1	1	3	1
MELANOMA OF SKIN	27	12	15	27	0	7	4	2	2	2	0	10
BREAST	161	0	161	161	0	38	52	29	7	5	0	30
CERVIX IN SITU CA	3	0	3	3	0	3	0	0	0	0	0	0
CERVIX UTERI	13	0	13	13	0	0	7	2	1	0	0	3
CORPUS UTERI	74	0	74	74	0	2	44	3	10	4	2	9
OVARY	27	0	27	27	0	0	8	3	2	8	2	4
VAGINA	1	0	1	1	0	0	1	0	0	0	0	0
VULVA	9	0	9	9	0	1	3	2	0	1	0	2
OTHER FEMALE GENITAL	4	0	4	4	0	0	1	0	0	2	0	1
PROSTATE	42	42	0	42	0	0	0	17	2	4	0	19
TESTIS	4	4	0	4	0	1	3	0	0	0	0	0
BLADDER	48	29	19	48	0	28	4	6	1	3	1	5
KIDNEY AND RENAL PELVIS	11	6	5	11	0	0	5	1	0	1	0	4
URETER	1	1	0	1	0	0	0	0	1	0	0	0
BRAIN	17	9	8	17	0	0	0	0	0	0	17	0
OTHER NERVOUS SYSTEM	18	3	15	18	0	0	0	0	0	0	18	0
THYROID	7	4	3	7	0	0	1	2	1	0	0	3
OTHER ENDOCRINE	3	2	1	3	0	0	0	0	0	0	3	0
HODGKIN'S DISEASE	1	1	0	1	0	0	0	0	0	0	0	1
NON-HODGKIN'S LYMPHOMA	29	16	13	29	0	0	12	5	1	4	0	7
UNKNOWN OR ILL-DEFINED	9	3	6	9	0	0	0	0	0	0	9	0
TOTAL	734	246	488	734	0	94	179	96	60	82	82	141

CANCER COMMITTEE MEMBERS

J. Samuel Tolman, MD

Medical Oncology, Cancer Committee Chairman,
Coordinator-QA Cancer Registry Data

David D. Dong, MD, PhD

Medical Oncology, Past Cancer Committee Chairman

Rodney Kratz, MD

Colon and Rectal Surgery, ACoS Physician Liaison

Lorna Andrews, MBA, RN, CGRN

Director of Patient Care Services

Greg Bates, CNS

Psychiatric/Mental Health, Ad Hoc

George Birchfield, MD

Medical Oncology

Emily Bradley, MD

Urology

Jean Grantham, OTR

Rehabilitation

Karen Brandstrom, RN, MSN

Care Management/Social Services

Mark Cortezzo

Decision Support Manager

Paula Denevan, MD

General Surgery

Pat Fitch, RD, CD

Clinical Dietitian-Oncology/Surgery & ICU/
Telemetry, Ad Hoc

Judith Folks, MN

Performance Improvement

Erh Huang, PharmD

Pharmacy

Marc Jacobson, MD

Diagnostic Radiology

Douglas J. Lee, MD

Medical Oncology, Hospice, Pain Management

Robert Meier, MD

Radiation Oncology

Howard G. Muntz, MD

Gynecologic Oncology

Brad Nadir, CIS, CTR

Cancer Registrar

Christine Kellogg

Cancer Registry

Michelle Owen, RN, MPA

Nursing Unit Manager – 4th Floor

Mary Jo Sarver, ARNP, CNS, AOCN

Oncology/IV Therapy Clinical Nurse Specialist,
Coordinator – Community Outreach, ACS Representative

Charles R. Simrell, MD

Pathology

Sam Taagen, MD

Primary Care

Gayle Ward, RN

VP of Clinical Services/CNO

MISSION

Our mission is to raise the long-term health status of our community by providing personalized quality care with compassion, dignity and respect.

VISION

Northwest Hospital & Medical Center is a community of caring health professionals, valued and recognized for promoting wellness through early detection and prevention, minimally invasive interventions and innovative clinical practices.



**NORTHWEST HOSPITAL
& MEDICAL CENTER**

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