The Role of the Diagnostic Radiologist in the Diagnosis and Treatment of Breast Cancer

The role of the radiologist in the diagnosis and care of the breast cancer patient has changed dramatically over the past two decades. Imaging techniques have become increasingly important in early detection and diagnosis by percutaneous biopsy techniques. Imaging provides guidance for definitive surgical excisions, enables physicians to determine cancer stage or extent of disease, helps to evaluate the success of conservative and neo-adjuvant therapies, and is used to monitor for disease recurrence. Following a period of nearly 60 years with no change in the mortality rates for breast cancer in the US, a significant decrease of about 2.3% per year in mortality has been observed since 1990.1 This is generally acknowledged to be due to a combination of detecting the disease at an earlier stage through screening mammography, increased awareness, and improved treatments.

Our capabilities to detect breast cancer at a treatable stage have continued to improve over the past several decades. Along with cervical cancer, breast cancer is one of the few cancers that prove to be significantly impacted by mass population screening. Mammography has remained the mainstay, with screen-film image quality assurance having been significantly improved and standardized by the US Mammography Quality and Standards Act (MQSA), in effect since 1994. Almost all imaging now is rapidly becoming digital. The first digital mammography machines for clinical use received FDA approval in 2000. The mammography section at The University of Chicago Hospitals currently has two operating digital mammography machines out of a total of five mammography units; the remaining three have been fitted for digital mammography with a pre-FDA Fuji CR system for which the FDA observer trial was conducted here, ending in 2004. FDA approval for this system is expected by the end of 2005.

Having an all-digital capability is relatively rare. Once approved by the FDA, it will allow us to conduct studies that will lead to improved capabilities. At the end of 2004, a computer-aided detection (CAD) device (R2 Technology ImageChecker) was placed in the clinical area to assist radiologists in the interpretation of screen-film mammograms. In 2005, the Radiology Department plans to install the Radiology PACS system to aid in the interpretation of digital mammograms.

The Breast Diagnostic Program actively collaborates with the Kurt Rossmann Laboratories for Radiologic Research. For example, the R2 Technology device was a direct result of collaborative research conducted at The University of Chicago Hospitals. There are now over 1,400 such units throughout the world. Other collaborative efforts include imaging research involving multimodality, computer-aided diagnostic methods, which will soon be introduced into the diagnostic imaging area.

A few years ago, the Section of Breast Imaging expanded its ultrasound equipment to two dedicated units (Philips ATL 5000), and has recently installed a prototype whole-breast, automated ultrasound unit designed by Philips to conduct pilot studies (WhoBUS). This machine can provide 3-D breast images and may lead to a new way of screening the breast with ultrasound. Mammographic screening for women with dense breast tissue is limited since small cancers may be obscured; ultrasound screening of this population of women may prove very beneficial in the future.

The biggest change in breast imaging has been the introduction of breast magnetic resonance imaging (MRI) studies over the past three years. Breast MRI allows more precise determination of the extent of cancer within the breast, thus providing more accurate information for treating physicians. In 2000 and 2001, only a handful of such studies were performed here. In 2004, over 650 studies were conducted; and the projections are for increased utilization. Under the leadership of Dr. Gillian Newstead, breast MRI techniques have become an important addition to our methods of breast cancer detection. Breast MRI allows the detection of breast cancers that are occult by other screening methods. MRI of the breast has been documented in recent years to be the most sensitive method for detection of breast cancer. In 2004, a Dutch report, examining MRI versus mammography in high-risk patients, concluded that MRI is approximately twice as sensitive as mammography.7

With digital mammography, hand-held breast ultrasound, and dynamic breast MRI imaging, we have embarked on a prospective funded trial, led by Dr. Funmi Olopade, to screen high-risk patients identified in her clinic. To date, 85 patients have been enrolled, with three cancers found to be occult except on
MRI. This rate of about 35 cancers per 1,000 screened is in keeping with other similar studies, and is about ten times the rate found on mammography. This study will continue, in addition to other MRI studies involving clinical aspects of breast cancer care: staging at the time of initial diagnosis, identification of residual disease after surgery with close or positive margins, and distinguishing fibroadenomas [false positives] from cancers.

Now its use is routine, as only about 40% of MRI-detected lesions can be identified by doing additional work-up on mammography or ultrasound.

It is now usual for most patients without palpable breast cancer to have tissue diagnosis made prior to definitive surgical excision, by percutaneous core needle or FNA techniques aided by ultrasound or stereotactic guidance. A technique for ultrasound-guided core biopsy of axillary lymph nodes has been developed. At the 2004 meeting of the Radiological Society of North America (RSNA 2004), Dr. Hiroyuki Abe, working with Dr. Robert Schmidt, reported that this technique was highly sensitive and showed no significant complications. At this point, fifty patients have had this procedure; and its role in lymph node staging is still emerging. The most practical consequence is that many patients will be able to bypass even the newer method of sentinel lymph node biopsy, since positive nodes identified by this preoperative minimally invasive technique are an indication for axillary nodal dissection. This procedure can then be directly planned in conjunction with definitive surgery. Advanced breast cancer often requires more global imaging. In 2004, a PET/CT scanner became operational under the direction of Dr. Daniel Appelbaum, and is used when metastatic disease is suspected.

The diagnosis of breast cancer requires an integrated and multidisciplinary approach. New technology allows the radiologist to detect and evaluate breast cancer more effectively. The advent of digital mammography, advanced ultrasound techniques, computer-aided diagnosis, and magnetic resonance imaging provide enhanced methods for diagnosis.

At the University of Chicago Hospitals, a team of breast radiologists, including Drs. Gillian Newstead, Robert Schmidt, Charlene Sennett, Madonna Kral, James Chambless, and Hiroyuki Abe, provide a full range of diagnostic services to about 20,000 patients each year, and work closely with the other members of the multidisciplinary team.

New basic science involving MRI research techniques have been developed under the guidance of Dr Gregory Karczmar. A team of researchers includes physicists Milica Medved, Cheng Yang, Marta Zamora, and Sunny Arkani. The breast MRI research program is supported by a grant from the Segal Family Foundation. Other support from the National Institutes of Health and the American Cancer Society has been obtained. Programs currently include the investigation of high temporal resolution [HITS] techniques for the evaluation of ductal carcinoma in situ, and high spectral and spatial resolution [HISS] methods for evaluation of small breast lesions. Our clinical study data on nearly 1,500 patients indicate that up to 35% of patients with breast cancer have additional unsuspected disease identified by MRI compared to conventional studies, including contralateral breast cancers, ipsilateral breast cancers in a separate location in the affected breast, or extension of local disease not otherwise detected. This has a direct impact on surgical planning and staging. In order to fully utilize the capabilities of MRI in this regard, an MRI biopsy guidance system for lesions identified only on MRI has been acquired (Suros) this past year.


The Role of the Pathologist in the Diagnosis and Treatment of Breast Cancer

The role of the pathologist in the diagnosis and management of breast cancer has evolved to meet the needs of increasingly sophisticated breast imaging technology coupled with the desire of many patients for breast conservation surgery. Stereorecore, MRI, and ultrasound-directed needle biopsies accurately sample very small lesions, the former often targeted because of microcalcifications. In the past, the pathologist would have been required only to determine if the biopsy harbored a malignancy. Today, virtually all radiographically directed biopsies must detail not only pathologic tissue changes, but also correlate them carefully with the radiologic findings. For example, tissue calcifications are variably associated with either in situ or invasive carcinoma, but they may also be present in non-neoplastic proliferative breast disease. Since the nature and “mapping” of mammographically detected calcifications frequently determine whether an individual patient is a candidate for conservation surgery, it is critical that the pathologist communicate clearly to both the radiologist and the surgeon histologic alterations that accompany such calcifications. Similarly, radiographically detected solid or cystic masses, as well as areas of architectural distortion, must be accounted for in the pathologist’s needle core biopsy report in order to exclude necessity for further diagnostic open biopsy.

Over the past several years, the role of MRI has become increasingly important both in detecting lesions which are not visualized with conventional mammography or ultrasound, and also in “staging” the extent or presence of other abnormal masses within the breast which further helps to better select patient candidates for conservative surgery. The addition of MRI diagnostics, however, has greatly increased the complexity of the pathologist’s assessment of breast resections where two or more geographically separate lesions may have to be identified, either by using multiple needles to bracket the imaged area of concern in relatively larger lumpectomy specimens, or by performing separate needle localized sections for diagnosis. As with small needle cores, these larger needle localization biopsies again require the pathologist to correlate the histologic findings with the specimen x-rays provided by the radiologist, while simultaneously evaluating the resected margins so that both the surgeon and radiation oncologist are assured that complete excision of any detected malignancy within the specimen has been achieved. Surgeons use standard suture tags to orient large lumpectomy-type specimens; and it is critical that the pathologist maintain the orientation of all resection lines because if malignancy is discovered in a small inked area of a relatively large specimen, the precise location of the involved tissue may enable the surgeon to re-excise a limited amount of additional breast, preserving the patient’s expressed option for breast conservation. Large breast excisions, especially those submitted with identifying x-rays, needles and other markers, are most often hand delivered by the surgeon to the surgical pathology gross room. This direct communication between pathologist and surgeon further ensures that identifying clips, suture tags and special areas of surgical concern, will be addressed during tissue sectioning and subsequent histologic evaluation. While the nature of breast conserving surgery has made the excision of in-situ and invasive breast cancer an increasingly labor intensive activity for the pathologist, the standard use of sentinel node biopsy for the majority of patients, although requiring intraoperative frozen section diagnosis of one or more nodes, has greatly reduced the number of formal axillary dissection specimens received in the pathology laboratory.

Complete renovation of the entire Surgical Pathology area, providing an expanded and modern working facility, was instituted by Dr. Thomas Krausz after his appointment in 2000 as Surgical Pathology Director and Chief of Anatomic Pathology. The addition of two full-time Pathology Assistants greatly facilitated the section’s ability to keep up with the ever-increasing workload of our clinical breast group. Using a new specimen x-ray machine to examine resections harboring small or elusive calcifications, which in the past would have required much more extensive tissue sampling, has also facilitated examination of breast specimens. Currently two full-time attending faculty in the Section of Surgical Pathology participate in the weekly multidisciplinary breast oncology meetings, review all outside slides from patients seeking second opinions, and will be providing all necessary pathology support for various ongoing or newly proposed clinical and investigative projects in breast cancer.
The Role of the Surgeon in the Diagnosis and Treatment of Breast Cancer

I recently operated on an 80-year-old woman. In speaking to her 90-year-old husband post-operatively, I discovered that his first wife had died of breast cancer in 1950, six months after a radical mastectomy. He seemed to expect a similar outcome following the wire-localization lumpectomy and sentinel node biopsy that I had just completed. This led me to reflect on the incredible progress that has been made in treating breast cancer in the last fifty years, and on how much the prognosis has improved. There have also been immense improvements made in quality of life issues for breast cancer survivors.

Breast cancer remains a disease that presents in a variety of ways. A palpable mass is present in up to 65% of women, but many patients present with non-palpable abnormalities that are discovered only at the time of breast imaging. Once a suspicious lesion has been identified on either physical exam or on imaging, a tissue diagnosis is the next critical step. While in the past excisional biopsy for diagnosis was a common practice, it is now preferred to obtain a percutaneous biopsy, with palpable guidance or image guidance (with mammography, ultrasound, or MRI-guidance). A pre-operative confirmation of malignancy allows for definitive planning of surgical therapy, with attention to both the primary tumor and to lymph node assessment. It should be considered standard of care to obtain a pre-operative diagnosis, using fine needle aspiration (FNA), core needle biopsy, or vacuum-assisted biopsy.

Surgical therapy for breast cancer should be thought about in terms of options for the breast and options for the axilla. For early stage breast cancer, most women can be treated with breast conserving therapy, which consists of a negative-margin lumpectomy or partial mastectomy, followed by external beam radiation therapy to the breast. Mastectomy remains an option, but there is now over twenty years of follow-up data on patients from randomized trials showing no survival advantage to mastectomy. For this reason, most women will choose a breast conserving approach. For patients who either require or choose a mastectomy, reconstruction options have improved immensely. Immediate reconstruction using a skin-sparing approach has proved safe, with no increased incidence of local recurrence. The immediate or delayed use of autologous tissue in the form of a TRAM flap (transverse rectus abdominus myocutaneous flap) has expanded the options greatly. A spectrum of options including free flaps such as SIEP (superficial inferior epigastric perforator) and DIEP (deep inferior epigastric perforator) flaps and hybrid flaps that combine various techniques are now routinely used, decreasing abdominal wall morbidity and helping to speed recovery. Plastic surgeons are crucial members of the breast cancer care team, both in the setting of mastectomies and in post-lumpectomy breasts with unsatisfactory cosmetic outcomes.

Lymph node status remains the most important prognostic factor in early stage breast cancer. Pre-surgical evaluation of the axilla includes thorough physical exam, imaging of the axilla on mammography, and routine ultrasound of the axilla. Suspicious axillary nodes are biopsied percutaneously, either by palpation or with ultrasound guidance. For clinically positive axillae, the standard of care remains a complete axillary node dissection, which achieves both accurate staging and excellent local control. In patients with a clinically negative axilla, assessment of axillary node involvement has been revolutionized in the last decade by sentinel node biopsy. Performed with both pre-operative lymphoscintigraphy and intra-operative blue dye injection, sentinel node biopsy is now routinely done, sparing many women the morbidity of a complete axillary lymph node dissection.

While results of a large U.S. randomized sentinel node trial are pending, an Italian trial which randomized women to sentinel node biopsy with completion dissection only for positive nodes vs. sentinel node and complete dissection in all patients showed no difference in survival, a low rate of axillary recurrence, and a much lower rate of complications in the sentinel node only group. At present, a histologically negative sentinel node is accepted as evidence of a tumor-free axilla and completion dissection is not recommended. A sentinel node that is positive by routine staining reflects an involved axilla, and the current standard of care is to complete the axillary dissection. Currently, other options for the sentinel node positive axilla are being investigated, including axillary radiation and observation. Indications for sentinel node biopsy continue to expand, with the technique now routinely used for multicentric disease, for T3 tumors (>5 cm), and in cases of extensive DCIS requiring mas-
tectomy. Long-term studies of sentinel node biopsy reveal very low morbidity, with lymphedema rates of two to three percent at five years, as opposed to 20-25% with complete axillary dissection, and very low local recurrence rates.

Neoadjuvant chemotherapy is utilized much less frequently in breast cancer than in other malignancies. Routine indications for neoadjuvant therapy include inflammatory breast cancer and other locally advanced breast cancers, where mastectomy is not possible at presentation. The role of neoadjuvant chemotherapy in patients with operable breast cancer is the subject of ongoing investigation and is of great interest. A large randomized trial showed no overall survival advantage in patients with operable breast cancer who were treated with upfront chemotherapy. However, the same trial revealed that more patients were able to undergo a breast conserving procedure in the neoadjuvant group. At present, neoadjuvant therapy is offered to women who desire breast conservation, but who would require a mastectomy at initial presentation.

Surgeons play an important part in the long-term follow-up of breast cancer patients. The surgeon’s role in follow-up includes thorough physical exam of the affected breast/chest wall and axilla, the contralateral breast, and the neck nodes. Post-treatment mammograms are reviewed, with the conserved breast undergoing imaging every six months for the first two to three years and the contralateral breast undergoing annual imaging. Systemic issues such as weight loss, energy level, and bone pain are monitored. Many patients with early stage breast cancers, which are estrogen and/or progesterone receptor positive, will be on anti-estrogen therapy following radiation. Systemic hormonal therapy is frequently prescribed and monitored by breast surgical oncologists. In the past, treatment with five years of Tamoxifen was routine, but with the advent of the aromatase inhibitors, anti-estrogen therapy has become more complex. In post-menopausal women, data supports the use of aromatase inhibitors such as anastrozole (Arimidex®), letrozole (Femara®), and exemestane (Aromasin®) as adjuvant therapy, with improved disease free survival and decreased rates of contralateral breast cancers when compared to Tamoxifen in a variety of sequencing and duration settings. No overall survival benefit has been shown yet. This class of drugs was recently endorsed as part of the standard of care for post-menopausal women with ER+/PR+ breast cancers. While this makes discussion of options and decisions more complex, the rewards in terms of improved outcomes are evident.

Diagnosis and treatment of breast cancer is a truly multidisciplinary undertaking, in which mammographers, surgeons, pathologists, nuclear medicine physicians, medical oncologists, radiation oncologists, social workers and many specialized nurses all join together to address a single disease. It is a privilege and a constant learning experience to be part of the talented team of doctors and healthcare professionals who make up the multidisciplinary breast cancer team at The University of Chicago Hospitals.
The Role of the Plastic Surgeon in the Treatment of Breast Cancer

Plastic surgery has traditionally held a prominent role in the multidisciplinary approach to the treatment of breast cancer. Specifically, plastic surgeons are involved in the care of breast cancer patients in three areas. Immediate breast reconstruction after mastectomy can be the most beneficial to patients as the psychological trauma of losing one’s breast(s) can be tempered by a reconstructed one. Multiple methods of reconstruction are available to most patients including using one’s own tissues as well as implants.

Secondly, plastic surgeons play an integral role in the complete treatment of breast cancer. After a mastectomy is performed and chemotherapy and radiation therapy is completed, reconstructive options are plenty for the recovering patient. Typically, one’s lower abdominal area is used to reconstruct breasts as this area most closely matches the shape and appearance of the natural breast. However, other methods of reconstruction for patients who have healed form their mastectomy abound. Options include implants as well as back muscle and skin.

Finally, an emerging field of reconstruction for those patients who opt for breast conservation therapy (lumpectomy and radiation) is becoming popular. Lumpectomy or partial mastectomy has been touted as a way to save most of one’s natural breast tissue; however, the results after breast conservation can be aesthetically displeasing. A newer method of using one’s own breast tissue for immediate and delayed reconstruction of lumpectomy sites is becoming popular. Early detection and treatment of breast cancer not only improve survival rates, but also make less radical surgical treatment possible; and with plastic surgery, an aesthetically acceptable reconstruction can also be achieved.

David H. Song, MD
Assistant Professor,
Section Chief,
Plastic & Reconstructive Surgery

The University of Chicago Hospitals and Health System = Cancer Program Annual Report
The Role of the Medical Oncologist in the Diagnosis and Treatment of Breast Cancer

At The University of Chicago, a team of medical oncologists works diligently to reduce breast cancer risk, promotes early detection, develops better modes of treatment, and educates medical students about the role of the medical oncologist in the diagnosis and treatment of breast cancer patients. Dr. Fleming directs the breast medical oncology program. Dr. Olopade runs the cancer risk program and manages a large laboratory investigating the genetics of the aggressive form of breast cancer often found in young African-American women. Dr. Conzen leads a laboratory dissecting the signaling pathways by which cells become malignant and evade chemotherapy. Dr. Mauer works as executive officer for Cancer and Leukemia Group B (CALGB), a national clinical trials group that includes several breast cancer clinical trials. Much of this type of research and practice is forwarded on to medical students at the University of Chicago through the teachings of Dr. Hoffman.

Patient diagnoses and potential treatments are discussed weekly at the Breast Cancer Multidisciplinary Group. This meeting includes medical oncologists, breast surgeons, plastic (reconstructive) surgeons, radiation oncologists, pathologists, social workers, genetic counselors, nurses, and radiologists (who interpret mammograms and breast MRIs). All new cases of nonmetastatic breast cancer diagnosed at the University of Chicago are discussed at this conference, often several times, to help the patient select the best treatment options and to coordinate care. Most breast tumors are diagnosed when small in size in which surgery will be the first treatment. For larger tumors, hormonal therapy or chemotherapy may be given before surgery, and may sometimes help avoid a mastectomy. Surgery, radiation therapy, and systemic therapy, including both hormonal (or “anti-hormonal”) therapy and chemotherapy are all used in the treatment of breast cancer.

The medical oncologist is generally responsible for the administration of systemic therapy, both in the adjuvant setting (before the cancer has spread, in an attempt to prevent distant metastases) and in the setting of metastatic disease.

Over the past decade, death rates from breast cancer in the U.S. have declined, despite the fact that the incidence of breast cancer has increased. Mammography and early detection may well have played a part in this, but death rates in young women, who are usually too young to have had a mammogram, are declining as well as those in older patients. This is probably due in large part to the widespread use of systemic chemotherapy and hormonal therapy to prevent the spread of disease.

Depending on the circumstance, systemic therapy may reduce the relative risk of death from breast cancer by 30% or more. On-line programs are now available with graphic representations to help patients and their physicians estimate how much each individual woman will benefit from chemotherapy and/or hormonal therapy.

The University of Chicago is very active in research. Fifteen to twenty clinical trials in the systemic therapy of breast cancer are available to our patients. We partici-