BREAST BIOPSY:
OPPORTUNITIES FOR AN IMPROVED DIAGNOSIS
A major goal of modern breast medicine is to minimize the number of patients who undergo open surgical biopsies for diagnosis.


This supplement is sponsored by Intact Medical Corporation.

Founded in 1998 and based in Natick, Massachusetts, Intact Medical Corporation is a privately-held company focused on the design, development and marketing of innovative, minimally invasive systems for the volumetric excision of tissue for diagnostic and therapeutic applications in select cancer markets. The company’s lead product, the Intact™ Breast Lesion Excision System, received market clearance from the Food and Drug Administration in June 2001. Initial products are targeted at breast biopsy and the excision of high-risk lesions, potentially obviating the need for open surgical excisions. For more details on the company’s product family and services, visit www.intactmedical.com.

Faculty Disclosures

The contents of this supplement were based on comments solicited from the Faculty attending a roundtable discussion sponsored by Intact Medical Corporation, a privately-held company focused on the design, development, and marketing of innovative, minimally invasive systems for the volumetric excision of tissue for diagnostic and therapeutic applications in select cancer markets.

The faculty participants received honoraria for their attendance at this meeting. The following individual has a financial interest, arrangement, or affiliation with the manufacturer of the products discussed in this supplement: Larry K. Killebrew, MD.

The following individuals are on the Scientific Advisory Board for Intact Medical Corporation: Edward P. Dalton, MD; Thomas B. Julian, MD; Larry K. Killebrew, MD; Michael D. Lagios, MD; William R. Poller, MD; Lowell W. Rogers, MD; Jean F. Simpson, MD; Pat W. Whitworth, MD.

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BREAST BIOPSY is a complex, evolving, and controversial topic. In the last 30 years, there has been a gradual evolution in the management of breast disease toward more conservative and less invasive techniques.\(^1\) Surgeons are applying advanced biopsy procedures necessitating an adjustment by pathologists to the receipt of specimens that represent these new surgical techniques. As breast biopsy technology evolves, it is being embraced by some and being questioned by others.

Regardless, the goal remains the same — to minimize the number of patients who require open biopsy for diagnosis and to provide the most definitive diagnosis with the least invasive approach.\(^2\)

Statistics indicate a woman has a 1 in 8 chance of developing breast cancer in her lifetime but that more than 60% of women will develop some type of benign breast disease.\(^3\) Screening mammography is performed in asymptomatic women with the goal of discovering invasive breast cancer at an early, curable stage. Professional organizations recommend that women aged 40 to 50 have a screening mammography every 1 to 2 years.\(^4\) There will be more than 33.5 million screening mammograms performed this year, of which 5% to 10% will be abnormal.\(^5\) An estimated 1.4 million breast biopsies will also be performed and the majority (80%) of these lesions will prove to be benign.\(^6,7\)

Mammographic screening now identifies breast lesions that are too small to palpate. There is an increasing trend for patients to present with smaller and smaller lesions as imaging improves and screening becomes more routine.\(^6\) Using samples from percutaneous, large-core, needle biopsy, pathologists can diagnose most benign lesions accurately.\(^8\)

The most common and worrisome mammographic findings that require further evaluation are masses and calcifications. The sheer number of possible diagnoses makes the pathologist’s job very complex. Cancers must be excised but benign tumors may or may not require removal, sparing these women considerable trauma and expense.\(^5\) Benign lesions that become symptomatic causing pain, uncomfortable feelings of weight and asymmetry, and discomfort and irritation when wearing underclothing are candidates for removal. The emotional trauma associated with having a breast mass alone may warrant its excision.\(^3\) Often, follow-up procedures are required to reach a definitive diagnosis. There are situations where a percutaneous intact excisional biopsy may be appropriate initially and as follow-up to benign findings on core or needle biopsy.

On January 28, 2006, a scientific advisory board composed of radiologists, pathologists, and surgeons met to discuss the current challenges in diagnosing breast disease. This discussion focused on the current state-of-the-art, new technological advances in breast biopsy and the types of patients and situations that are best served by a percutaneous intact excisional biopsy. Case studies were presented where the Intact™ Breast Lesion Excision System (BLES) was used to obtain an intact specimen. This supplement summarizes the discussions that occurred during this roundtable meeting.

FIGURE 1. Gross pathology of core biopsy segments obtained with a 14-gauge percutaneous core biopsy needle, which will require evaluation of multiple histological levels to determine an accurate diagnosis.
surgical biopsy is reserved for instances when a large enough sample of tissue is not obtainable with percutaneous methods to assess prognostic and predictive factors.

There is continuing opportunity to educate all of our pathology colleagues when defining the gray zone between ADH and proliferative disease. I think that extent criteria are compromised with the smaller core biopsies.”

Lowell W. Rogers, MD
Long Beach Memorial Medical Center

Prior to the introduction of image-guided needle and core biopsy, open surgical biopsy was the only option. Open surgical biopsy typically yields an intact specimen of the entire mammographic lesion and surrounding breast tissue. It offers the possibility of removing the entire lesion with a clear margin. A surgical biopsy also enables a more comprehensive pathological review.

Open biopsy methods require a skin incision, suture and anesthesia, and are associated with significant cosmetic defects and morbidity.10,11 The disadvantages of this invasive technique include postoperative hematoma, infection, and scarring which may have an effect on future mammographic imaging. Today the role of open definitive targeting, minimal risk of hematoma (vs. surgery), increased sampling accuracy, and the avoidance of, and costs for, operating room procedures.12,13

DEFINITIONS:

Core Needle Biopsy—a biopsy method used to obtain tissue cylinders from a target organ, via a large bore needle, for paraffin embedding and histological processing. This technique can be performed with and without vacuum-assisted sources. Core needle biopsy products include Mammotome® (Ethicon Endo-Surgery), Vacora® (C.R. Bard, Inc.), ATEC® (Suros Surgical Systems), EnCore™ (SenoRx) and Cassi™ (Sanarus).

Percutaneous Intact Excisional Biopsy—a biopsy method used to obtain large (10 mm to 20 mm) intact samples for paraffin embedding and histological processing and also having the potential to completely excise the lesion. Products include Site Select® (Site Select Medical Technologies), Encapsule™ (Rubicor) and the Intact™ Breast Lesion Excision System (Intact Medical Corporation).

Underestimates—The rate at which findings from biopsy specimens miscalculate the severity of a breast lesion, measured against open surgical excision—the gold standard. For example, ADH underestimates are calculated at the rate at which the histopathological diagnosis of the stereotactic biopsy specimen was atypical ductal hyperplasia and the histopathological diagnosis of the subsequent surgical excision was either ductal carcinoma in situ (DCIS) or infiltrating cancer. Similarly, DCIS underestimates are the rate at which the histopathological diagnosis of the stereotactic biopsy specimen was DCIS and the histopathological diagnosis of the subsequent surgical excision was infiltrating cancer.14

Concordance—an agreement in findings that support the accuracy of a particular diagnosis; more specifically, the level or percent agreement between mammographic findings and pathological reports or between the results of two comparative biopsy procedures and histopathological findings from surgical specimens.
LIMITATIONS OF CURRENT METHODS

FINE NEEDLE aspiration, often used, has been replaced with vacuum-assisted core biopsy and is now reserved for a limited number of cases due to its unreliability in making a definitive diagnosis of benignity. Core biopsy allows pathologists to accurately diagnose and classify carcinomas as well as establish hormone receptors and other biomarker status. A major diagnostic limitation of core needle biopsy is its inability to definitively establish a diagnosis when it reveals a high-risk lesion such as ADH, ALH/LCIS, radial scar, etc. Such biopsies inherently do not permit evaluation of the spatial relationships, extent and margins of the lesion because it is sampled in multiple cores which have an unknown relationship to one another (See Table 2).

The multiple cores obtained from the target make evaluation of margins impossible, and the inability to evaluate the spatial relationships of the foci of high-risk lesions within the cores makes decisions about the likelihood of a complete excision or diagnostic upgrade speculative at best.

Although mammographic-pathologic correlation is required for all image-directed biopsies, establishing concordance is more difficult when the target is disrupted by the biopsy procedure rather than removed intact as in most surgical needle localizations and percutaneous intact devices.

TABLE 2. Limitations and Problems with Core Needle Biopsies

- Loss of spatial orientation: inability to establish margin and extent
- Standard requirement of multiple levels to achieve adequate examination and establish concordance
- Requirement for open excision of all high-risk lesions (ADH, ALH/LCIS, radial scars, papillary lesions, and CAPSS with hyperplastic and/or atypical features)
- Increased time and costs for pathologist and hospital: reduced net reimbursement per procedure
- Artifacts: tissue fragmentation, epithelial implantation and benign transport which can create dangerous diagnostic dilemmas (misdiagnoses)
- Increased difficulty in establishing mammographic-pathologic correlation and concordance

There are limitations with the current technologies. Most rely on multiple cores, either with a 14-gauge gun or an 11- or 8-gauge vacuum-assisted procedure. A major disadvantage is the loss of spatial orientation. With multiple samples, the pathologist is not able to establish margins to establish the extent of the disease. This makes mammographic/pathologic correlation very difficult and it requires a great deal of effort to do this.

Michael D. Lagios, MD
The Breast Cancer Consultation Service
Technical Difficulties: Needle and core biopsies can underestimate the presence of invasive disease due to sampling error. Inadequate sampling and an inability to demonstrate calcifications within the excised tissue may occur. Microclips may be required to guide further procedures; however, significant clip migration has been reported. Various step levels are required for pathological evaluation. Poor sampling technique and incorrect needle placement can lead to false positives or false negative results. Breast lesions diagnosed using large-core biopsy as ADH or ductal carcinoma in situ must still undergo surgical excision to exclude the presence of a higher grade lesion that may have been missed because of sampling error. Underestimates using various vacuum-assisted devices have been reported to range from 9.5% to over 50% of cases. Removal of most of a malignant lesion by vacuum-assisted biopsy may lead to difficulties in estimating the true size of the tumor at excision, which would be an important indicator for adjuvant therapy.

Cost and Time Implications: Adequate examination of multiple levels of multiple fragments or cores per cassette is time-consuming, difficult and expensive. Currently, the majority of core biopsies are performed with devices of 11-gauge or larger, corresponding to minimal core diameters of 3 – 5 mm. In order to detect a randomly distributed high-risk lesion of 1 – 1.5 mm size within such a core, multiple step-levels are required to adequately sample the full depth of the core. For example, an 11-gauge, 3 mm diameter core will require step-levels spaced approximately 0.4 – 0.5 mm apart. This results in 5 – 6 histologic slides, each representing a specific step-level or as many as 12 slides per biopsy, requiring 2 cassettes to process. In contrast, with percutaneous intact excisional biopsy, the entire imaged abnormality can be excised intact and examined completely in only 1 – 2 blocks without step-levels (i.e., 1 – 2 slides).

A recent cost comparison analysis of vacuum-assisted core needle to percutaneous intact excisional biopsy in a pathology consulting service setting is presented in Table 3. The profit margin for both the physician component and the hospital component was substantially higher for the Intact BLES procedure compared to that of conventional vacuum-assisted devices, which actually lost money billing under a CPT code of 88305.

### Table 3. Cost Comparison of Two Breast Biopsy Procedures*

<table>
<thead>
<tr>
<th></th>
<th>Physician Component</th>
<th>Hospital Component</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Core Needle:</strong></td>
<td>$47.25</td>
<td>$35.70</td>
</tr>
<tr>
<td>11-gauge x two</td>
<td>Report, edit: 6 min.</td>
<td></td>
</tr>
<tr>
<td>six levels</td>
<td>@ $6.00 each: $72.00</td>
<td></td>
</tr>
<tr>
<td>Total Time:</td>
<td>Report: $10.00</td>
<td></td>
</tr>
<tr>
<td>Total Cost:</td>
<td>Total Cost: $82.00</td>
<td></td>
</tr>
<tr>
<td>Profit/Loss:</td>
<td>Profit/Loss: ($46.30)</td>
<td></td>
</tr>
<tr>
<td><strong>Interpretation:</strong></td>
<td>12 slides</td>
<td></td>
</tr>
<tr>
<td>18 min.**</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Report:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total Cost:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Profit/Loss:</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **Percutaneous Intact Excisional Biopsy:** | $29.25 |
| 15 mm basket one level                     |        |
| Interpretation: 3 min.**                   | 2 slides|
| Report, edit: 6 min.                       | @ $6.00 each: $12.00 |
| Total Time: 9 min.                         | Report: $10.00 |
| Total Cost: $18.00 †                      | Total Cost: $22.00 |
| Profit/Loss: ($0.75)                       | Profit/Loss: ($13.70)|

* Ductal carcinoma in situ, intermediate grade (NG II with zonal necrosis), cribriform pattern with associated microcalcifications

** Calculated as a mean of 1.5 minutes per slide

† Calculated as 18/60 x $ 120 per hour

‡ Calculated as 9/60 x $ 120 per hour

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One of the distinguishing criteria between ADH and low grade DCIS is evaluating the extent of the lesion. When the lesion is disrupted, you cannot evaluate its extent. Regardless of how well educated the pathologist, when the criterion is extent and it has been disrupted, by definition you can’t distinguish extent.

Jean F. Simpson, MD
Vanderbilt University Medical Center
NEW TECHNOLOGICAL ADVANCES

BENEFITS OF MINIMALLY-INVASIVE PROCEDURES

The goal of minimally-invasive breast biopsy procedures is to limit the physical impact on the patients by reducing the invasiveness of the procedure and to reduce the procedural costs without sacrificing accuracy.\(^3\) Percutaneous intact excisional biopsy is a new category of devices. They remove a single, large block of tissue with one small incision. Their main advantage is complete excision of an intact lesion. Subsequently, the pathologist can provide a diagnosis, and also confirm that the entire lesion has been removed in one piece. The advantages these systems provide are precise targeting, tissue conservation, and cost savings from avoiding operating room charges. Table 4 outlines several other benefits that radiologists, surgeons, and pathologists have identified with percutaneous intact excisional biopsy, specifically from their practical clinical experience with the Intact Breast Lesion Excision System.

Although use of these types of systems is becoming more and more common, care is still required in selecting patients appropriate for these less invasive modalities.

The Intact BLES is an innovative breast biopsy system whereby a large, intact, specimen is removed percutaneously under ultrasound or stereotactic image guidance. A small incision (6 to 8 mm) is made in the breast to accommodate the wand’s shaft; however, the tissue retrieved is far larger than this incision. The RF energy cauterizes a channel to the lesion. When the lesion is reached, five struts open to a maximum of 20 mm to circumscribe the entire lesion. The Intact BLES captures a specimen in one pass within 10 seconds or less. Since no breast tissue is removed from the channel, it collapses upon itself after removal of the lesion and heals normally. The RF energy allows easy passage through a variety of tissue types, including dense breast tissue. The incision is closed with a SteriStrip or liquid bandage; no stitches are required. Experience has shown that less bleeding occurs with the Intact BLES compared to conventional core needle biopsies. A variety of capture basket sizes (10 mm, 12 mm, 15 mm, 20 mm) are available.

**TABLE 4. Advantages of Percutaneous Intact Excisional Biopsy Techniques**

- Preservation of spatial relationships: ability to establish margins and extent
- No standard requirement of levels: most biopsies can be processed in 2 cassettes without levels
- Avoidance of open excision for high-risk lesions in which pathologic and mammographic evaluation establish excision and concordance
- Decreased cost and time required for pathologist and hospital: increased reimbursement per procedure
- Elimination of artifact of tissue fragmentation, epithelial implantation and benign transport
- Greater ease in establishing mammographic-pathologic correlation and concordance

“We perform about 1,500 biopsies per year. Over the last 15 years, we have used Vacora, Mammotome, Intact, and Bard systems. We now prefer the Intact Breast Lesion Excision System and use it in about three-fourths of our biopsy patients. I prefer catching microcalcifications with a basket instead of a spear.”

Larry K. Killebrew, MD
Oklahoma Breast Care Center
FACULTY

MODERATOR:

MICHAEL D. LAGIOS, MD
The Breast Cancer Consultation Service

A San Francisco native, Michael D. Lagios, MD, has been active in clinical breast cancer research since his discharge from the U.S. Army Medical Corps in 1972. His group pioneered breast conservation therapy without irradiation for ductal carcinoma in situ at a small community hospital, publishing the first results in 1982, research which initiated a paradigm shift in the treatment of that disease. Subsequently, his team developed nuclear grading as a basic method of risk classification and refined methods of tissue processing for both ductal carcinoma in situ and mammographically-directed biopsies. Dr. Lagios is currently Medical Director of the Breast Cancer Consultation Service in Tiburon, California, Director of Breast Services at St. Mary’s Hospital and Medical Center, and holds academic appointments at both Stanford University and the University of California, San Francisco. Dr. Lagios writes extensively on breast cancer pathology and treatment, having authored or co-authored numerous original papers, editorials, clinical reviews, and chapters. He received his undergraduate degree from the University of California, Berkeley, and his MD from the University of California, San Francisco School of Medicine.

PARTICIPANTS:

EDWARD P. DALTON, MD, FACS
Elliot Breast Health Center

Edward P. Dalton, MD, maintains a clinical practice at the Elliot Breast Health Center in Manchester, New Hampshire, where he specializes in breast surgery and breast problem solving. He focuses his clinical interests on challenges related to breast cancer diagnosis and surgery. The goal of placing screening and problem solving under one roof at the Center will be achieved in 2006. Dr. Dalton was previously Chief of Surgery at Elliot Hospital in Manchester, New Hampshire. He is a Fellow of the American College of Surgeons and is active in a number of professional societies, including the American Cancer Society, the American Society of Breast Surgeons, and the National Consortium of Breast Centers, where he served as both Trustee and President. Dr. Dalton is a graduate of St. Louis University School of Medicine and did postgraduate training at the University of Michigan and the State University of New York at Buffalo. He has been in private practice since 1977, with a breast specialization for almost 20 years.

THOMAS B. JULIAN, MD, FACS
Allegheny General Hospital

Thomas B. Julian, MD, is an accomplished breast cancer surgeon, researcher, and educator, currently serving as Associate Director of the Allegheny Breast Center, Staff Surgeon in the Division of Surgical Oncology at Allegheny General Hospital, both located in Pittsburgh, Pennsylvania, and Associate Professor of Human Oncology at Drexel University College of Medicine in Philadelphia. He has been a principal investigator for numerous breast cancer pre- and post-launch clinical trials studying topics such as primary systemic combination drug therapy in postmenopausal hormone-receptor-positive breast cancer patients, the GeneSearch™ breast lymph node assay for intraoperative molecular testing, digital mammography imaging, and MRI evaluation of the contralateral breast in recently diagnosed female breast cancer patients, among others. Together with colleagues Yoed Rabin, PhD, and Norman Wolmark, MD, Dr. Julian was awarded two U.S. patents for developing new methods and equipment for use in cryosurgery. From 2002 through 2005, he has been the Protocol Officer for three breast cancer trials conducted by the National Surgical Adjuvant Breast and Bowel Project (NSABP), for which he serves as Associate Director of Medical Oversight. Dr. Julian’s research has been widely published; appearing in over 120 articles, reviews, book chapters, audiovisual displays, abstracts, and scientific exhibits. He completed his undergraduate work in chemistry at Ohio State University and the University of Pittsburgh and obtained his MD degree from the University of Pittsburgh School of Medicine.

LARRY K. KILLEBREW, MD
Oklahoma Breast Care Center

Larry K. Killebrew, MD, founded the Oklahoma Breast Care Center in 1985. The Center has achieved many historical milestones over the years, with Dr. Killebrew serving as Medical Director. It was the first breast center in the state to receive accreditation from the American College of Radiology and the first to provide a successful statewide mobile imaging program (with two mobile coaches), which also provides no-cost and low-cost screenings to indigent patients. In 1992, Dr. Killebrew pioneered the minimally invasive stereotactic biopsy in Oklahoma as an option to surgical biopsy, a procedure that has since become the standard of care throughout the United States; he also became the first to introduce the Intact™ Breast Lesion Excision System (BLES) in the southern United States. Dr. Killebrew’s body of work is reflected in many original articles published in several journals. He co-authored with Dr. Steve Parker the landmark study that established stereotactic biopsy use, published in Radiology (The Grey Journal) in 1994. Other articles have appeared in the Journal of the American Medical Association (JAMA), Medical Economics, and The Breast Journal.

WILLIAM R. POLLER, MD, FACR
Allegheny Cancer Center

William R. Poller, MD, specializes in breast imaging, which captured his interest.
while reading mammograms for a national screening project in the early 1980s. An accomplished clinician, researcher, author, and educator, he is Associate Director of Radiology at Drexel University and Associate Director of the Breast Care Center, Division of Breast Imaging, at Allegheny General Hospital in Pittsburgh. He attended the University of Pittsburgh, where he obtained his Bachelor of Science in Biology and MD from the same medical school. He completed his Radiology Residency at the Albert Einstein College of Medicine in New York City. Dr. Poller’s recent research has concentrated on such topics as CAD techniques, digital imaging, whole breast ultrasound and breast biopsy (e.g., selective lymphadenectomy, sentinel node, stereotactic, and minimally invasive). His research has been widely presented in numerous articles and scientific exhibits, seven of which won “first place” or “excellent” recognition. Dr. Poller’s state-of-the-art breast cancer center, equipped with four full field digital mammography units, two stereotactic tables, and two ultrasound units, participates in the American College of Radiology Imaging Network (ACRIN) trials related to breast imaging. For demonstrated excellence in the conduct of these clinical trials, he received the Network Chair’s Institutional Achievement Award at ACRIN’s 2005 Fall Meeting. A dedicated teacher, Dr. Poller has delivered or directed over 300 medical education courses and lectures.

LOWELL W. ROGERS, MD
Long Beach Memorial Medical Center

Lowell W. Rogers, MD, is an accomplished surgical and anatomic pathologist, who has devoted most of his medical career to the study of solid tumors of the breast. He is Director of both the Anatomic Pathology and Breast Pathology Departments at California’s Long Beach Memorial Medical Center. Dr. Rogers also serves on the faculty of two medical schools, the University of California (Irvine) and Vanderbilt University Medical School (Nashville), where he teaches pathology and gynecology. A distinguished author, guest speaker, and international lecturer, Dr. Rogers has written or delivered over 45 papers and presentations on numerous breast cancer topics, including invasive lobular carcinoma of the breast, ductal carcinoma in situ of the breast, lobular neoplasia of the breast, the relationship between fibrocystic disease complex and breast cancer, ductal pattern lesions in biopsies as they relate to breast cancer risk, adjunctive use of ultrasound and core biopsy in diagnosis, and diagnostic aspects of stereotactic/percutaneous breast biopsy. He has also authored a textbook, Diagnostic Pathology of the Breast. Dr. Rogers received his BA in chemistry from the University of Arizona, and his MD from Johns Hopkins University School of Medicine, where he also completed his residency training. He was elected to both Phi Beta Kappa and Phi Kappa Phi and is a member of numerous hospital committees and professional societies.

JEAN F. SIMPSON, MD
Vanderbilt University Medical Center

Jean F. Simpson, MD, is a noted clinician, educator, and researcher in the fields of pathology and immunohistochemistry, with a special interest in the epidemiology and progression of breast tumors. Currently affiliated with Vanderbilt University in Nashville, Tennessee, she serves as professor of pathology and anatomic pathology, Director of Anatomic Pathology at the Medical Center, and interim Pathologist-in-Chief at Vanderbilt Children’s Hospital. Dr. Simpson has participated in breast cancer research funded by the City of Hope Cancer Center, the American Cancer Society and the National Institutes of Health, investigating such topics as molecular cytogenics and tumor progression in epithelial proliferative breast disease, breast tumor cell receptors, and the mechanisms of targeted anti-tumor strategies in breast cancer. A well-published writer, she has authored or co-authored over 100 scientific papers, books, and abstracts, and served on the editorial boards of Advances in Anatomic Pathology and Human Pathology. She also lectures extensively inside and outside the United States on subjects ranging from the role of breast pathology in risk assessment and molecular markers in premalignant breast disease to the histopathology of stereotactic core biopsy. Dr. Simpson obtained her MD from the Medical College of Georgia in Augusta, Georgia, and completed her residency and fellowship at Vanderbilt University.

PAT W. WHITWORTH, MD, FACS
Nashville Breast Center
Vanderbilt University

Pat W. Whitworth, MD, developed a passion for breast cancer research and education after completing the fellowship in surgical oncology at the M. D. Anderson Cancer Center in Houston, Texas, after completing his residency at the University of Louisville. Dr. Whitworth is now Director of the Nashville Breast Center. A dedicated researcher and educator, Dr. Whitworth holds numerous academic and medical appointments: Associate Clinical Professor of Surgery at Vanderbilt University in Nashville, Tennessee; longstanding membership on the American College of Surgeons ultrasound faculty; Vice-Chair of the Breast Organ Site Committee for the American College of Surgeons Oncology Group (ACOSOG); and Chairman of the Board of Directors for the American Society of Breast Surgeons (ASBS). Dr. Whitworth has compiled a long list of achievements in breast cancer research and education. He was one of 11 surgeons participating in the first national multi-institutional study to validate sentinel lymph node staging for breast cancer. In April 2002, he directed the ASBS sentinel lymph node staging course in Boston. He has authored and co-authored a number of publications on state-of-the-art, image-guided percutaneous breast biopsy with various technologies. In 2003, his Nashville Breast Center received an award from the American Society of Clinical Oncology for its work in ASOCOG clinical trials. Finally, as co-chair of the ASBS course in Oncoplastic Surgery, Dr. Whitworth is dedicated to helping the patients of all Society members secure access to state-of-the-art oncoplastic surgical therapies.
**COMPLETE REMOVAL OF MASSES OR CALCIFICATIONS**

THE CONCEPT OF totally removing small lesions has been proven with large core needle biopsy devices. Others have reported that 90 to 96% of lesions under 1.5 cm could be completely eliminated, sparing a surgical procedure in most women. Removal of a larger, fully intact specimen takes this concept one step further allowing the pathologist to view the architecture of specimens with adequate spatial recognition of the extent of the lesion.

Sie, et al. (2004) conducted a retrospective, multicenter study in women who underwent stereotactic biopsy of the breast for mammographic lesions presenting as microcalcifications and classified as BIRADS IV or BIRADS V to determine whether biopsy of the breast using a percutaneous intact specimen-sampling device (Intact BLES) was more accurate than percutaneous biopsy using a vacuum-assisted core needle biopsy device (Mammotome®). Two groups of women consisting of 742 patients each were selected to represent each biopsy technique. The pathology distribution of the lesions retrieved by both biopsy techniques were comparable. After comparison to specimens retrieved surgically, underestimation of DCIS and ADH occurred significantly less frequently in the biopsy samples taken with the Intact BLES system compared to those taken with the Mammotome system (see Table 5). Complete excision of ADH at biopsy was twice as frequent with the Intact BLES than with the Mammotome device. These results confirm previously observed improvements in concordance with the Intact BLES than those seen with vacuum-assisted core needle biopsy.

The Intact BLES offers lower cost for preparation and review. Percutaneous stereotactic needle core biopsies have been reported to cut biopsy costs by more than half compared to open biopsy. The elimination of additional procedures by initially obtaining an intact specimen may cut costs even further.

**With the Intact Breast Lesion Excision System, a larger basket doesn’t mean a larger incision. The incision is the same for all patients. I am not going to put a suture in the breast, so patient comfort is enhanced.**

William R. Poller, MD, FACR

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**TABLE 5. Diagnostic Gauge Accuracy of Intact BLES Compared to 11-Gauge Vacuum-Assisted Core Biopsy**

<table>
<thead>
<tr>
<th></th>
<th>Intact BLES</th>
<th>VACB</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCIS</td>
<td>n=110</td>
<td>n=112</td>
<td>0.03</td>
</tr>
<tr>
<td>Underestimates</td>
<td>5 (4.6%)</td>
<td>15 (13.4%)</td>
<td></td>
</tr>
<tr>
<td>ADH</td>
<td>n=32</td>
<td>n=30</td>
<td>0.01</td>
</tr>
<tr>
<td>Underestimates</td>
<td>3 (9.4%)</td>
<td>11 (36.7%)</td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td>n=32</td>
<td>n=30</td>
<td>0.02</td>
</tr>
<tr>
<td>Excision of ADH</td>
<td>21 (65.6%)</td>
<td>10 (33.3%)</td>
<td></td>
</tr>
</tbody>
</table>

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"I am excited about the potential to reduce the number of surgical biopsies for patients with high risk lesions. This is currently being investigated in a large, multicenter clinical trial."

Pat W. Whitworth MD, FACS
Nashville Breast Center
PATIENT SELECTION ISSUES

WHEN IS AN Intact BLES procedure a good choice? Generally, it is appropriate in most cases as a first biopsy option. An Intact BLES procedure is appropriate when a lesion that appears benign is expected to require complete removal. This may be the case when a benign palpable mass is bothersome to the patient. It is a beneficial procedure for women who have masses or microcalcifications of a size or extent that can be encompassed by an Intact BLES capture basket. Approximately 10% of all mammographic or ultrasonographic targets will contain either ADH, lobular neoplasia (ACH, LCIS) or other purported high-risk lesions, such as radial scar, papilloma, complex sclerosing lesion and/or columnar alteration with atypia. Lesions graded as BIRADS IV or V, and of an appropriate size, are candidates for complete excision with an Intact BLES procedure reducing the need for re-excision. High-risk lesions, initially diagnosed using needle biopsy specimens, requiring re-excision are also candidates for an Intact BLES procedure if they meet the size requirements. Complete re-excision can be accomplished percutaneously — accurately and precisely — with less potential morbidity and cost. There are other scenarios where this option may be appropriate; suggested uses are listed in Table 6. The following case studies present evidence for the selection of excisional biopsy using an Intact BLES procedure. In most cases, surgical avoidance was, or would have been, the outcome.

**TABLE 6. Patient Selection: Intact Breast Lesion Excision System**

<table>
<thead>
<tr>
<th>SUGGESTED USES</th>
</tr>
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<tbody>
<tr>
<td>Initial biopsy</td>
</tr>
<tr>
<td>Benign, palpable masses that are bothersome to the patient</td>
</tr>
<tr>
<td>Dense or fibrous breasts</td>
</tr>
<tr>
<td>Small, tightly clustered microcalcifications visualized on ultrasound or mammography</td>
</tr>
<tr>
<td>Small fibroadenomas</td>
</tr>
<tr>
<td>Radial scars</td>
</tr>
<tr>
<td>Lesions with mucus-like material on biopsy</td>
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<tr>
<td>Papillomas</td>
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<tr>
<td>Stereotactic-biopsy with ADH²</td>
</tr>
<tr>
<td>Lesions likely to be obliterated or missed with core biopsy</td>
</tr>
<tr>
<td>Fat necrosis, TRAM flaps</td>
</tr>
<tr>
<td>Small breast cancers in poor-risk women (co-morbid disease)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PATIENTS NOT SUITED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with:</td>
</tr>
<tr>
<td>Implants or pacemakers</td>
</tr>
<tr>
<td>Image abnormalities of an extent greater than available Intact BLES capture baskets, e.g., 25 mm</td>
</tr>
<tr>
<td>Lesions immediately behind the areola or in front of the chest wall (i.e., a stroke margin &lt; 6 mm)</td>
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</tbody>
</table>

**CASE STUDY 1: RADIAL SCAR WITH ALH**

**PATIENT HISTORY:**

**PATIENT:** Adult Female  
**AGE:** Unknown  
**INDICATION:** Clustered calcifications

**BIOPSY METHOD:**

- Intact BLES  
- 10 mm basket

**PATHOLOGY:**

- Radial scar with florid hyperplasia and small amount of calcification and incidental ADH

**DIAGNOSIS:**

- Radial scar with incidental atypical lobular hyperplasia  
- Calcifications present in enlarged lobular unit

**COMMENTS:**

- Surgical avoidance was recommended, but excision was performed anyway and proved negative.

Radial scar with florid hyperplasia and small amount of calcification.
CASE STUDY 2: ATYPICAL DUCTAL HYPERPLASIA

PATIENT HISTORY:
**PATIENT:** NN with a history of vernacular melanoma  
**AGE:** 67 years  
**INDICATION:** Screening mammogram revealed a new, small tight cluster of microcalcification within a fatty breast

BIOPSY METHOD:
- Stereotactic guidance
- 11-gauge Mamnotome

PATHOLOGY:
- Focal atypical ductal hyperplasia
- Intraductal papilloma with columnar cell change
- Fibrocystic disease and dystrophic calcification

CONFIRMING BIOPSY METHOD:
- Complete excision performed using the *Intact* Breast Lesion Excision System

DIAGNOSIS:
- Sclerosing adenosis
- Fibrocystic change
- Some microcalcifications
- No atypical ductal hyperplasia

COMMENTS:
- Surgical avoidance after excisional biopsy

CASE STUDY 3: INTRADUCTAL PAPILLOMA

PATIENT HISTORY:
**PATIENT:** JH  
**AGE:** 53 years  
**INDICATION:** History of intermittent nipple discharge, now bloody. Negative mammogram and CBE. Ultrasound showed solitary papillary lesion.

BIOPSY METHOD:
- Ultrasound guidance
- *Intact* BLES
- 20 mm basket

CONFIRMING BIOPSY METHOD:
- None needed

DIAGNOSIS:
- Benign papillary lesion

COMMENTS:
- Surgical avoidance of subareolar resection by excision of entire lesion on biopsy. Asymptomatic one year later

Histopathology showing full extent of a benign papillary lesion
CASE STUDY 4: POOR SURGICAL RISK

PATIENT HISTORY:
PATIENT: AL, wheelchair dependent, diabetic, hypertensive, post CVA with minimal residual
AGE: 77 years
INDICATION: Mammogram detected lesion in left breast

BIOPSY METHOD:
- Ultrasound guidance
- Intact BLES
- 20 mm basket

PATHOLOGY:
- Well differentiated invasive ductal carcinoma 0.7 cm
- DCIS absent
- Focally present at cauterized margin

CONFIRMING BIOPSY METHOD:
- None required

DIAGNOSIS:
- Invasive ductal carcinoma

COMMENTS:
- The Intact BLES sample made surgical avoidance possible in a poor-risk patient having a small mass because clear margins were visualized and adequate.
- Interval mammogram showed no evidence of recurrence.

PATHOLOGY of excised mass showing clear margins

CASE STUDY 5: ADH AND RADIAL SCAR

PATIENT HISTORY:
PATIENT: JS
AGE: 70 years
INDICATION: Subareolar mass 1.5 x 2 cm

BIOPSY METHOD:
- Intact BLES
- 10 mm basket

CONFIRMING BIOPSY METHOD:
- None required

DIAGNOSIS:
- Atypical ductal hyperplasia
- Radial scar

COMMENTS:
- Because an intact specimen includes the entirety of the lesion, the location and a definitive diagnosis of ADH could be confirmed.
- No upgrade needed
- A surgical excision was unnecessary, but was performed anyway

Histopathology of radial scar and ADH in radial scar. No malignancy observed.
The FDA Approved the Intact BLES for diagnostic sampling of breast abnormalities in 2001. The system proved to provide superior specimens for histological evaluation. Due to the intact nature of the tissue sampled, a more accurate diagnosis occurs, which minimizes the need for open surgical excision in many cases. In 2005, the FDA expanded indications for the system, for partial or complete removal of an imaged abnormality to obtain tissue samples for histological examination or partial removal of a palpable abnormality that has been classified as benign.

Therapeutic Potential?
The well-characterized, intact specimens provided by an Intact BLES procedure offer the option of surgical avoidance for high-risk lesions. The potential to obtain intact specimens with clear margins makes therapeutic applications an obvious expansion of the system's use.

Application of this instrumentation is still in its infancy; ongoing clinical trials will be needed to quantitatively assess its value in surgical avoidance for malignant lesions. It remains to be determined which histological parameters and mammographic concordance will be required to move from diagnostic applicability to a treatment modality.

Integrated Approach Needed
For breast biopsy to provide the most definitive diagnosis possible, an interdisciplinary approach must occur. Breast imaging, pathological diagnosis, and treatment decisions are an integrated function. There is a need to bring the specialties of radiology, pathology, and surgery together. Practice management and the business aspects of breast diagnosis and treatment call for breast programs with accountability from all aspects of the discipline. There is a need for these various specialties to embrace the changing trends in breast biopsy and become educated on new technological advances. It will also be important for physicians and their patients to readily accept more conservative treatment for benign tumors.

More concordance reporting is needed and direct communication between pathologists and other clinicians is essential because not all pathology reports contain the information needed for clinical decision making. An initiative that has worked at various centers is having a defined system to handle the need for reaching and reporting concordance between mammographic findings and breast biopsy. Individual centers will need to sort out the roles and responsibilities of the pathologist, the interventional radiologist, or a team encompassing various members of a review committee.

Financial Considerations
There is a need within the industry to resolve reimbursement issues. Currently, the reimbursement for breast biopsies has not kept up with the technology. A CPT code of 88305 currently covers biopsy procedures, including the percutaneous breast excision systems, for the tissue acquisition of skin, breast, or other diagnostic biopsies exclusive of cysts. Unfortunately, the collectable physician component and the hospital component do not cover actual costs for the complex nature of diagnosing breast tissues providing minimal profits and disincentives to diagnosticians. A more reasonable code for the newer technologies might be 88307, (breast excision of lesion surgical pathology requiring microscopic evaluation of margins), which is used to cover complete excision for a small mass. A redefinition of the scope and amount of work required to diagnose palpable masses in the breast is needed.

Breast programs, as a whole, when managed properly are very reasonable in terms of reimbursement. Rather than viewing the compensation and reimbursement for imaging or pathology as separate sectors, we must consider the income brought from therapy, and return a percentage back to the imaging centers and pathology.

The era of open biopsy has ended. Pathologists, radiologists, and surgeons must come together to understand and promote among themselves the appropriate use of needle, core, and large specimen capture devices and begin to supplant open biopsy as much as possible.

Towards Evidence-Based Medicine: Supporting the Use of Intact BLES for Surgical Avoidance

Jean F. Simpson, MD, from the Vanderbilt University Medical Center has conducted a Proliferative Lesion Trial: a retrospective review of cases looking at various patient types or disease entities, without mammographic evidence for context, where an Intact BLES procedure was performed followed by surgical incision. She presented her findings at the 2006 US and Canadian Academy of Pathology Congress. Preliminary results from this ongoing review have demonstrated that excised specimens obtained from the BLES procedure are able to definitively provide a diagnosis as well as provide a therapeutic option. Positive data (zero upgrades; n=40) obtained from the results of this retrospective trial have set the stage for a larger prospective trial: the Intact Percutaneous Excision Trial (i-PET).

The Percutaneous Excision Trial is designed to confirm that surgical intervention can be avoided by demonstrating that a definitive diagnosis can be made from the tissue sample collected using the Intact BLES. This prospective, multicenter trial will enroll up to 400 patients over the age of 18 who have a lesion that is likely to be entirely excised with the Intact BLES. The study design includes two arms: (1) patients previously having had a biopsy procedure and (2) patients not having a previous biopsy. A pathological diagnosis will be made and an evaluation of concordance with the radiologic findings will occur.
REFERENCES


24. Simpson JF. Intact™ Image-guided breast biopsy reduces need for subsequent open excision in benign proliferative lesions. Poster presented at the United States and Canadian Academy of Pathology Meeting. February 11-17, 2006; Atlanta, GA.
This is not a surgical sample.

Surprised?

In fact, this surgical-quality sample came from a **minimally invasive procedure**, using only local anesthesia and a 7mm incision.

Yet the **Intact™** Breast Lesion Excision System (BLES) lets you **remove the whole lesion**, intact, preserving its architectural integrity with excellent mammographic correlation. So you can clearly see and evaluate the lesion.

Confidently make the call. And avoid sending patients with high-risk lesions to surgery.

Learn more at [intactmedical.com](http://www.intactmedical.com) today. Or call: **(888) 430-4490**