



TechNote

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IMAGE-GUIDED VACUUM-ASSISTED BREAST BIOPSY FOR SUSPICIOUS, NON-PALPABLE BREAST LESIONS

Request: This response addressed a request for information from Alberta Health and Wellness. The objective is to inform on and describe the background and the current evidence on the use of image-guided vacuum-assisted breast biopsy (IGVB) for diagnostic sampling of suspicious, image-detected, non-palpable breast lesions or abnormalities.

BACKGROUND

Mortality rates associated with breast cancer have been steadily declining worldwide even though the incidence of breast cancer is increasing.¹⁻¹³ This likely reflects the impact of mammography screening and the improvements in the treatment options. The widespread usage of the screening mammography programs has increased the incidence of suspicious, image-detected, non-palpable breast lesions or abnormalities, which have resulted in an increase of the number of performed breast biopsies.

Although most of the image-detected breast lesions or abnormalities (60-85%) are not malignant, all of them cause anxiety.^{6-9,11,14-18} The diagnostic process should ideally be rapid, inexpensive, and accurate resulting in minimal patient discomfort or complications. Biopsy techniques need to ensure accurate histopathologic diagnosis of malignant lesions. By necessity, there has also been a need for a minimally invasive but accurate biopsy technique to reduce morbidity associated with the biopsy of benign lesions.

Technotes are brief reports, prepared on an urgent basis, which draw on limited reviews and analysis of relevant literature and on expert opinion and regulatory status where appropriate. They are not subject to an external review process.

Image-guided vacuum-assisted breast biopsy (IGVB) is one of the most recently developed image-guided percutaneous large core biopsy procedures. The focus of this paper is to summarize the most recently published scientific evidence on the safety and efficacy of IGVB as a diagnostic sampling technique for suspicious, image-detected, non-palpable breast lesions or abnormalities. The use of IGVB for other types of lesions or as a therapeutic option is beyond the scope of this review.

CLINICAL MANAGEMENT OF IMAGE-DETECTED NON-PALPABLE BREAST LESIONS

The traditional approach to biopsy suspicious, image-detected, non-palpable breast lesions has been open surgical biopsy.^{6,8,9,11,14-24} This procedure, while highly effective and accurate in experienced hands, is associated with a recognized rate of complications. The open surgical biopsy procedure requires operating room time, and general or local anesthesia. This procedure may also require post-operative hospitalization. Image-guided percutaneous breast biopsy has been developed and introduced with the aim of achieving accurate histologic diagnoses without the limitations and disadvantages associated with open surgical biopsy.

In comparison with open surgical biopsy, the image-guided percutaneous breast biopsy is faster to perform, provides greater patient's acceptance (less pain and discomfort, and improved cosmetics), causes minimal to no scarring on subsequent mammograms, and it is less expensive (can be performed under local anesthesia on an outpatient basis).^{9,11,14-18,21,22,25,26} Lesions that receive a benign diagnosis at image-guided percutaneous breast biopsy do not require surgical intervention. High-risk benign lesions or malignant lesions and those with an uncertain diagnosis would then undergo consideration for open surgical biopsy. This algorithm has been shown to significantly decrease morbidity and cost when compared to using only open surgical biopsy for all suspicious, image-detected lesions.

Current clinical management issues include patient selection, complete removal or sampling of the lesion, management after image-guided percutaneous breast biopsy, epithelial displacement, and equipment and technique.

Patient selection

Nearly all breast lesions or abnormalities that can be detected by mammography can be biopsied percutaneously.^{14-16,18,22,27-31} Lesions found at mammography are categorized according to the Breast Imaging Reporting and Data System (BIRADS) of the American College of Radiology (ACR) into: negative (Category 1), benign (Category 2), probably benign or equivocal finding (Category 3), suspicious abnormality (Category 4), and findings highly suggestive of malignancy (Category 5).

BIRADS Category 1 and 2 lesions constitute an indication for routine annual mammography follow-up but no additional tests are required.^{14-18,22,27,29-31} Lesions classified as Category 3 (including well-defined lesions, accumulation of uniform

microcalcifications, and asymmetric densities) are classified as low risk but may require further radiological investigation, or cytological or histopathological diagnosis. Category 4 abnormalities (including nodules not clearly defined, and non-uniform microcalcification) and Category 5 lesions require biopsy verification to facilitate further treatment.

Image-guided percutaneous breast biopsy is most often used for lesions classified as BIRADS Category 4, which have a reported malignancy rate of 33-50%.^{11,14-18,22,25,32} If the biopsy yields a benign diagnosis concordant with the imaging findings, the patient is usually spared the need for open breast surgery.

Approximately 75-90% of the lesions classified as BIRADS Category 5 are malignant and the utility of using image-guided percutaneous breast biopsy has been debated.^{11,15-17,22,25,32} Its use in this category of lesions depends on the clinical setting and the surgical treatment protocol that would otherwise have been used. For this category of lesions, image-guided percutaneous breast biopsy would be indicated to replace an open surgical biopsy when a second surgical procedure is planned (if carcinoma is found).

The likelihood of sparing a surgical procedure by using an image-guided percutaneous breast biopsy appears to be higher (76-77%) for Category 5 masses (usually representing invasive carcinoma) than for Category 5 calcifications (42-55%) (usually representing ductal carcinoma in situ).^{7,17,22,32}

Controversy exists regarding the role of image-guided percutaneous core biopsy in the evaluation of BIRADS Category 3 lesions ("probably benign"), which have a 0.5% to 2.0% frequency of carcinoma.^{11,14-17,20,22,25,32,33} Traditional management of these lesions is short-term follow-up mammography. However, biopsy may be considered in a subset of cases: when follow-up is unavailable or compromised, if a coexisting carcinoma is present, if the patient is at high risk for developing breast cancer, or if the patient's anxiety precludes short term follow-up.^{22,32}

Complete removal or sampling of the lesion

Some of the image-guided percutaneous breast biopsy techniques may remove the entire targeted lesion.^{15-18,20,22,25,32,34} However, the goal of this procedure is diagnosis and it is not indicated and approved for therapeutic purposes since complete removal of all imaging evidence of the lesion does not ensure the complete excision of the pathologic abnormality. Histopathologic examination of retrieved samples does not permit pathologic assessment of the biopsy excision margins, due to fragmented nature of the specimens. Complete removal of imaged evidence of the lesion does not obviate the need for excision.

Some clinical scenarios in which complete removal of the target lesion by image-guided percutaneous breast biopsy may be advantageous have been suggested.^{22,32} It may decrease the likelihood of subsequent tumor growth on follow-up. It may reduce some

of the limitations associated with the biopsy procedure. By allowing histologic analysis of larger volumes of lesion tissue, it may reduce the sampling error, with resultant decrease in the frequency of histologic underestimation, imaging-histologic discordance, and need for re-biopsy. Complete removal of the lesion may also decrease the patient's anxiety.

Management after breast biopsy

A second biopsy procedure (also referred to as repeat biopsy or re-biopsy) may be necessary to assure a complete and accurate pathologic diagnosis following image-guided percutaneous breast biopsy.^{8,12,15-20,22,25} In published series repeat biopsy has been recommended after image-guided percutaneous breast biopsy in 9% to 18% of cases. Reasons for re-biopsy include: pathology/histologic results that are discordant with the imaging findings, insufficient/inadequate specimens, and diagnosis of benign high-risk lesions.

Most repeat biopsies are performed for discordant results and diagnosis of high-risk lesions or lesions that are histologically heterogeneous (those containing atypical ductal hyperplasia and ductal carcinoma in situ or invasive carcinoma, and areas of ductal carcinoma in situ with coexistent invasive carcinoma).^{8,14-20,22,25,32} These lesions are usually found by mammography and undergo biopsy because of the presence of microcalcifications. They can be underestimated if tissue is only removed from the less aggressive area of the lesion, which makes it difficult to target the most aggressive site within the lesion.

A diagnosis of atypical ductal hyperplasia (ADH) at image-guided percutaneous breast biopsy is an indication for surgical excision because of the high prevalence of carcinoma in these lesions.^{12,15,17,22,25,32} Also, lesions yielding ductal carcinoma in situ (DCIS) at image-guided percutaneous breast biopsy may contain areas of invasive carcinoma at surgery.

Controversy exists regarding the need for surgical excision after image-guided percutaneous core biopsy diagnosis of other specific histologic results, including papillary lesions, radial scar, atypical lobular hyperplasia, and lobular carcinoma in situ.^{12,15-17,20,22,25,34}

Follow-up mammogram is recommended after a benign diagnosis at image-guided percutaneous breast biopsy.^{14,15,17,18,20,22,32} Several studies correlating results of stereotactic 14-gauge core needle biopsy with open surgical biopsy reported a cancer miss rate between 2.9% and 10.9% (average, 7.2%).^{17,22} In clinical follow-up studies after this procedure, the frequency of missed carcinomas averaged 2.8%. This rate is comparable to the cancer miss rate at open surgical biopsy (average of 2.0%). However, it indicates the possibility of a delay in the diagnosis and appropriate treatment of breast cancer.

The follow-up interval for lesions yielding benign diagnosis concordant with the imaging characteristics, has varied in different studies and it is not standardized.^{14,15,17,18,20,22,25,32} Some investigators suggested annual mammography if the percutaneous biopsy histologic diagnosis is specific and short-interval follow-up if the percutaneous biopsy histologic diagnosis is non-specific. Other investigators recommended that the first follow-up study be obtained 6 months after percutaneous biopsy for all lesions yielding benign findings concordant with imaging findings. Further work is necessary to determine the optimal follow-up protocol.

Epithelial displacement

All breast needling procedures (including image-guided percutaneous breast biopsy) can displace benign or malignant epithelium into tissue away from the target lesion.^{14,15,17,18,20,22,25,34} This can cause interpretive problems for the pathologist. To date only few studies addressed the issue of the biologic implications of epithelial displacement.^{15,17,20,22} The limited available data suggest that epithelial displacement does not contribute to local recurrence.

Equipment and technique

The currently available image-guided percutaneous breast biopsy modalities include fine needle aspiration biopsy (FNAB) and the conventional large core needle biopsy (CNB), which can be performed under stereotactic, ultrasound, or MRI guidance.^{6,7,9,11,14-18,25,32,34-37} FNAB is a well-established diagnostic sampling modality that is still often used as it has the advantages of decreased cost and a low complication rate. However, because of the nature of the specimen obtained, the accuracy of the technique can be limited and it requires expert cytopathologic assessment.

The CNB technique, introduced in the 1990s is technically similar to FNAB, but it has the advantage of the larger diameter of the needles used (18-, 16-, and 14-gauge) and the possibility of collecting tissue block, which enables histopathological assessment.^{3,6,9,11,15-18,20,22,32} Standard CNB comprises a spring-loaded gun together with a disposable core needle. The stereotactic 14-gauge CNB is the most commonly used technique to date, and it has been demonstrated to be effective in guiding further clinical management of breast disease and in reducing the number of patients requiring open surgical biopsy.^{3,6,9,11,15-20,22,25} However, it has several design limitations.

For some lesions with histologic heterogeneity, such as calcifications and lesions containing ADH and DCIS or DCIS and invasive carcinoma, CNB may provide incomplete characterization of the histologic findings (referred to as histologic underestimates).^{9,11,14-17,20,25,32,38} Because most lesions containing ADH or DCIS contain calcifications, histologic underestimates are most often encountered in calcific lesions.

Image-guided vacuum-assisted breast biopsy (IGVB) was recently introduced on the market (at the end of the 1995) as a minimally invasive alternative to open surgical biopsy to facilitate and improve the ease and accuracy of image-guided percutaneous

breast biopsy. It represents a mechanical improvement compared to conventional CNB devices, aiming to overcome the inadequate tissue sampling and sampling errors by modification of the core biopsy collection technique.

IMAGE-GUIDED VACUUM-ASSISTED BREAST BIOPSY (IGVB)

With IGVB, each tissue core or sample is evacuated from the needle or probe by vacuum suction into a drainage system.^{1,9,11,14-18,25,26,39} The vacuum device is connected to the centre of the probe, designed to pull tissue into the cutting edge. The vacuum draws tissue into a side hole in the probe, and a rotating cutter advances over the tissue, cuts a core from the breast, and withdraws the specimen. The vacuum can be used to suction the blood out of the biopsy cavity during and at the end of the procedure. Tissue adjacent to the probe can be sequentially removed by rotating the probe 360°. The probe only needs to be inserted once into, or immediately adjacent to, the lesion and multiple specimens can be obtained from a single insertion.

IGVB devices are available with 14-gauge, 11-gauge, and 8-gauge probes.^{1,9,11,14-20,22,23,25,26,39} The volume of tissue removed through these probes varies. The reported average specimen weight is 34 mg with a 14-gauge IGVB probe, 100 mg with an 11-gauge probe, and much greater with an 8-gauge probe (between 250 mg and 300 mg). The number of retrieved specimens can vary (between 10 and 20) depending on the type and diameter of the lesion(s). The adequacy of sampling can be assessed immediately following the procedure and for microcalcifications mammography of the tissue samples can be performed to verify the result.

IGVB has the ability to remove smaller lesions completely (especially those <1cm) with larger probes (such as the 11-gauge probe).^{1,9,11,14-16,19,20,22,39} In cases where the whole or a high proportion of the image-detected lesion has been removed, a small metal marker clip is introduced through the biopsy probe and deployed at the biopsy site so the lesion can be localized in the event that surgical removal of the area is necessary. The clip placement provides the ability to characterize the biopsy site on follow-up mammograms more carefully. However, because clip migration has been reported in up to 20% of cases^{15,16}, immediate post-biopsy mammograms are needed to facilitate proper understanding of the relationship of the biopsy site to the clip if subsequent needle localization and excision is needed.¹⁹

IGVB can be carried out on an outpatient basis with local anesthesia after the imaging work-up has been completed.^{1,8,9,11,15-17,20,23,40,41} The small incision utilized with IGVB devices, which amounts to a 3-4 mm skin cut, does not require sutures. The patient is discharged with a bandaid/dressing and can usually return to normal activity shortly after IGVB.

Imaging modalities

IGVB can be done under guidance of various imaging modalities including stereotactic, ultrasound and MRI. However, IGVB under stereotactic guidance is currently the most commonly used technique in the investigation of suspicious non-palpable lesions.

The sensitivity of stereotactic biopsy is a function of the lesion type and number of samples taken.^{1,7,9,15-21,25,26,30,32,34,42,43} It can be used for all types of mammographic lesions (solid masses or calcifications). Although stereotactic guidance is the preferred guidance technique for calcifications, calcifications that are too widely dispersed are difficult to target by this method. Inadequate sampling with stereotactic guidance is more common for calcifications than for masses, because of the potential for coexistent benign and malignant processes in up to 35% of cases.

The lesions that are very superficial or retro-areolar or lesions located in the very back of the breast may not be suitable for stereotactic biopsy because of technical limitations.^{14-17,20,22,25,32} Calcifications that are scattered rather than closely clustered may also be difficult to sample accurately.¹⁴ Also, lesions that are too vaguely defined to generate useful coordinates for needle placement should not be sampled stereotactically. Technical success is also a function of the operator's experience.^{19,22,31,32,42,43}

Stereotactic IGVB can be performed using an upright or a dedicated prone unit with digital imaging capabilities.^{1,7,9,15-21,25,26,30,32,34,36,42,43} The main disadvantage of this method is the expense of the dedicated equipment.

The use of sonography to localize and permit biopsy of non-palpable breast lesions has become more popular in the last decade.^{1,7,11,14-17,19,20,22,29,31,34,44,45} It has several advantages as a guidance technique including lack of ionizing radiation, use of readily available non-dedicated equipment, real time visualization of the needle/probe and multi-directional sampling. The ultrasound-guided biopsy is quicker, simpler, and cheaper than stereotactic biopsy. In addition, it allows for biopsy of lesions not accessible to stereotactic biopsy such as deeply located (close to chest wall) or immediately retroareolar lesions.

The main disadvantage of ultrasound-guided biopsy is that the lesion(s) must be sonographically visible to undergo ultrasound-guided breast biopsy.^{1,7,15,16,18,24-26,29,31,32,34,44,45} Many mammographic abnormalities are not seen by ultrasound-guided, particularly lesions that manifest primarily as calcifications for which biopsy by stereotactic guidance is preferred. Additionally some operators find the IGVB probes and their attached cables awkward to use with ultrasound guided biopsy.¹⁸

The breast size, and the type of breast tissue may determine what image guidance modality to use.^{1,7,9,14-18,24-26,34,42,44} Small, dense breasts are best imaged with ultrasound-guided biopsy, while large fatty breasts should undergo mammography.^{1,7,9,14-18,24-26,34,42,44} In some patients, breast tissue may be difficult to

transverse because of dense fibrosis and a co-axial system can facilitate biopsy in these patients.

Contrast-enhanced MRI is increasingly used as a complementary method in detecting early stage breast malignancies, which cannot be detected by clinical examination and conventional imaging methods such as mammography.^{1,16-19,26,32,35,36,46-50} Among the MRI-detected lesions 50% to 80% are found to be benign. To avoid open surgical biopsy, various percutaneous breast biopsy techniques using MRI guidance have been developed for the histologic work-up of suspicious and undefined lesions that are only MRI-detected.

Currently most MRI-guided breast biopsies are performed on closed magnet systems.^{14-16,18,19,32,35-37,49,51} This method requires a dedicated breast coil and poses several challenges including the necessity to remove the patient from the magnet to perform the biopsy, limited access to the medial breast tissue, and the transient nature of the contrast enhancement. Other limiting factors include the inability to document lesion removal with specimen radiography and distortion of localization coordinates by the magnetic field. MRI-guided biopsy also presents special problems in verifying that the target lesion has been sampled successfully since tissue samples do not enhance *ex vivo*.^{18,32}

The MRI-guided biopsy differs from stereotactic- and ultrasound-guided biopsy in several ways.^{15-19,32,35-37,49,51} MRI-guided biopsy expertise and equipment are not widely available. It is more time consuming and the imaging costs are higher. It requires that intravenous access be obtained and contrast enhancement material be injected at least once. While stereotactic- and ultrasound-guided biopsy are usually performed for lesions detected at screening mammography, MRI-guided biopsy is used for lesions detectable only on MRI. This method requires MRI-compatible tissue sampling equipment, which is costly for IGVB.

Safety

The reviewed literature suggests that IGVB is safe with a low complication rate.^{1,8,14-20,22,23,25,42,44,52} Minor reported complications include bleeding, hematoma, and vasovagal reactions. The risk of bleeding and resulting hematoma appears to be less than 1% and major hematomas are rarely seen (1 in 1000). Infection at the probe insertion site is also possible, but the probability of infection requiring antibiotic therapy appears to be less than 1 in 1000.

IGVB under stereotactic guidance was reported as a cause of Mondor's disease (a very rare condition characterized by thrombophlebitis of the superficial veins of the breasts and chest wall).^{53,54}

Any type of breast biopsy procedure may damage a breast implant.^{1,3,34} Positioning problems, difficulties viewing lesions, bleeding, and suboptimal tissue samples have been reported in patients with breast implants who underwent stereotactic biopsy.

Although there are no absolute contraindications to IGVB, certain medical conditions may be considered as contraindications for this procedure.^{1,8,15-18,20,22,25,29-31,34,44,55}

Relative contraindications include the patient's inability to lie prone for 30-60 minutes (i.e., patients with severe arthritis in the neck, back, or shoulders and those with severe obstructive lung disease) and patient's inability to stay immobile (i.e., patients with neuromuscular disorders).

Prior to the procedure, the patient should be asked about use of medications such as aspirin or anticoagulants, or a history of bleeding disorders.^{1,8,15-17,20,22,25,29-31,34,44,55} In patients with coagulopathy it may be advisable to delay performance of biopsy until the coagulopathy can be corrected.²⁵ Patients should also be asked about allergies, as allergic reaction to lidocaine or other medications or materials used during the biopsy can occur.³⁴ In pregnant or lactating women a milk fistula may form after biopsy, especially if the lesion is centrally located and deep in the breast.³⁴

Indications

IGVB is intended to provide diagnostic sampling of breast tissue for histologic examination with partial or complete removal of the imaged abnormality.^{1,17,20,22,56} The main application is in sampling of suspicious, image detected, non-palpable breast lesions. It also has been used in the biopsy of small, indefinite/unclear lesions, particularly those occurring in association with surgical scarring, fibrosis, or prosthetic implants.⁵⁶

Complete removal of breast lesions has been reported with IGVB although it is only indicated for diagnosis purposes and not for therapeutic purposes.^{1,9,14-17,19,22,23,26,33} The reviewed literature cautions that at least in cases of diagnosed malignancy, the disappearance of the radiographic lesion should not be taken as evidence that the lesions had been completely excised. Therefore the IGVB procedure should not be considered as a therapeutic option for these patients.

Available IGVB systems

Seven IGVB systems are currently available on the market in North America.^{1,9,18,23,26,55,57} (<http://www.fda.gov/>), (<http://www.mdall.ca>). The most popular system is the Mammotome® Breast Biopsy System, commercially introduced in 1995, which is manufactured and distributed worldwide by Ethicon Endo-Surgery Inc.^{1,40,55,57} (<http://www.fda.gov/>). The system may be used with ultrasound or stereotactic guidance and it is available in a hand held configuration or can be mounted on an articulated support arm or on a stereotactic table.

The Automated Tissue Excision and Collection (ATEC®) Vacuum Assisted Core Biopsy System was commercially introduced in 2002 and is manufactured by Suros Surgical Systems Inc.^{1,58-61} (<http://www.fda.gov/>). It may be used with ultrasound or

stereotactic guidance and, because of its pneumatic (air-powered hand piece), it is the first IGVB system also compatible with MRI.

Biomedizinische-Instrumente & Produkte, GMBH (BIP) Inc. manufactures the VacuFlash® Biopsy System, commercially introduced in 2002 (<http://www.fda.gov/>). This system may be used under ultrasound, stereotactic, computed tomography (CT), or MRI guidance. It is equivalent to and has similar indications and technological characteristics as the Mammotome® and the ATEC® systems available on the market (<http://www.fda.gov/>). The patient contact components and component materials for obtaining core biopsy samples in the VacuFlash®, Mammotome®, and ATEC® systems are equivalent. The hand-held or mounted biopsy device used with or without imaging modalities for these systems provides for the diagnostic removal of breast tissue with fluid management through a combination of vacuum and radial cutting functions.

VACORA® Vacuum Assisted Breast Biopsy System was also recently introduced on the North American market (<http://www.crbard.com>) (<http://www.fda.gov/>). This system, manufactured by C. R. Bard Inc., can be used with stereotactic x-ray, ultrasound and MRI. The Vacora® system is compact and portable and it requires no external vacuum carts, generators, external tubing, wires, cables and foot pedals.

SenoRx, Inc. manufactures two breast biopsy systems, EnCor® and SenoCor®, introduced on the market in 2002 (<http://www.fda.gov/>), (<http://www.senorx.com>). EnCor® is a programmable, automated, closed biopsy system for MRI, stereotactic, and ultrasound-guided imaging modalities. SenoCor® features a circumferential biopsy system for sampling masses utilizing ultrasonography and may be used under ultrasound guidance.

Another IGVB system introduced in 2002 is the En-Bloc® system manufactured by Neothermia Corporation (<http://www.fda.gov/>), (<http://www.neothermia.com>). The En-Bloc® system can be used under ultrasound guidance to remove tissue by automated electro-surgical cutting and simultaneous capture of an incised tissue volume. The probe contains two sets of active electrodes.

Cost

The IGVB procedure is less expensive than open surgical biopsy but more expensive than standard CNB^{1,3,23,40,43,52} (<http://imaginis.com>). The open surgical biopsy can cost up to \$5000 USD, while the standard CNB costs approximately \$1500 USD and the IGVB (using the Mammotome®) costs approximately \$2000 USD. In terms of equipment costs, the Mammotome® biopsy system costs up to \$30,000 USD, depending on the configuration and features.

Other cost factors include follow-up procedures, staffing, and disposable supplies. The disposables used for IGVB are more expensive than those used for standard CNB.^{18,23,34,43,52,56,62} The Mammotome® probe costs about \$215 USD and the ATEC®

probe costs about \$275 USD.¹⁸ In comparison, the needles used for CNB cost about \$14 to \$24 USD each.¹⁸ Costs were not available for the other systems.

In Alberta it has been estimated a cost of \$300 CAD for the disposable probes and a capital or fixed cost of \$25,000 to \$30,000 CAD for the probe driver and vacuum suction.⁶³ Each IGVB procedure would cost a total of \$1059.92 CAD. The capital cost for equipment, including the dedicated table and probe driver, was estimated at \$300,000 CAD.

Cost savings due to successful use of the IGVB may result from avoidance of open surgical biopsy^{17,18,22,25,40,64} (<http://imaginis.com>). One study of 200 consecutive solitary non-palpable lesions that had stereotactic 11-gauge vacuum assisted breast biopsy found that the procedure spared a surgical biopsy in 76% of cases, decreasing the cost of diagnosis by 20%.⁶⁴ However, the stereotactic 14-gauge CNB spared a surgical procedure in 76-85% of cases, decreasing the cost of diagnosis by 40-56%.⁶⁴

Regulatory status

A search of the Health Canada Medical Device Active License Listing database found the following IGVB systems: the Mammotome[®] and the Mammotome[®] Handheld systems, the Vacora[®] system, the En-Bloc[®] system, and SenoCor[®] biopsy device (<http://www.mdall.ca>). These systems are licensed for diagnostic sampling of breast abnormalities during a biopsy procedure (Health Canada, personal communication).

Currently there are 30 Mammotome[®] sites in Canada: three in British Columbia, four in Alberta, two in Manitoba, seven in Ontario, and 14 in Quebec (Johnson & Johnson Medical Products, personal communication). In Alberta there are two Mammotome[®] sites at the Lendrum Breast Centre and the Cross Cancer Institute in Edmonton, one at the Grace Womens' Hospital-Foothills Hospital in Calgary, and one at the Lethbridge Regional Hospital.

The EnCor[®], VacuFlash[®], and ATEC[®] systems are not licensed for diagnostic breast biopsy in Canada (Health Canada, personal communication). Suros Surgical Systems, Inc. is currently awaiting approval from Health Canada for commercial sale of the ATEC[®] system in Canada (Suros Surgical Systems, Inc, personal communication). The approval is for use of the ATEC[®] system to perform diagnostic breast biopsy and tissue sampling of breast abnormalities as well as partial or complete removal of visible evidence of benign breast disease. Two ATEC[®] systems are currently installed in Canada, one in Manitoba (Winnipeg) and one in Ontario (Toronto).

The IGVB systems that received clearance for marketing from the United States Food and Drug Administration (FDA) to be used for diagnostic biopsy of breast abnormalities include: the VacuFlash[®] system, the ATEC[®] system, the SenoCor[®] biopsy device, the En-Bloc biopsy system[®], the Mammotome[®] system, the Mammotome[®] Handheld system, and the Mammotome[®] Handheld system with 8-gauge probe (<http://www.fda.gov/>).

Coverage

In Canada there is significant variation in the claims made for IGVB.^{63,65} This procedure is not included as a specific item in the healthcare plans of the Canadian provinces.⁶³ The only biopsy code in Canada was originally designed for Spring Loaded Core biopsy (Suros Surgical Systems, Inc., personal communication).

In Quebec the IGVB procedure is likely billed under an existing code.^{63,65} In Ontario the procedure is used in some centres^{63,65} (Suros Surgical Systems, Inc., personal communication) but the physicians performing it receive no reimbursement (Suros Surgical Systems, Inc., personal communication). In British Columbia all costs associated with the Mammotome[®] procedure are reportedly covered by the British Columbia Cancer Agency or by hospital allocations with no fee-for-service billings.⁶⁵

In Alberta, procedures done at the Grace and Lethbridge Regional Hospitals would be covered by their respective health authorities and those performed at the Cross Cancer Institute in Edmonton by the Alberta Cancer Board.⁶⁵ Procedures performed at the Lendrum Breast Centre Imaging in Edmonton would likely be billed under an existing code for core biopsy.^{63,65}

In the United States the IGVB with stereotactic and ultrasound guidance is reimbursed by Medicare for non-palpable lesions and those lesions classified as BIRADS Category 3, Category 4, and Category 5.^{1,66-68} IGVB using the Mammotome[®] is reimbursed by Medicare and almost all commercial and private health insurance plans in the United States.¹ The Excellus Health Plan (independent licensees of the BlueCross BlueShield Association)⁶⁹ considers the IGVB using the Mammotome[®] (under stereotactic or ultrasound guidance) as medically appropriate for diagnostic evaluation of nonpalpable breast abnormalities. The procedure is not considered medically necessary when used for therapeutic purposes (such as complete excision of a lesion or lumpectomy).

CIGNA HealthCare covers the use of IGVB (Mammotome[®] device) as a minimally invasive breast biopsy procedure.⁷⁰ The Aetna Insurance Company considers it as a medically necessary procedure and alternative to needle localization core surgical biopsy in members with breast abnormalities identified by mammography that are non-palpable or difficult to palpate (i.e., because they are deep, mobile, small (< 2 cm), or are composed of clustered microcalcifications).⁷¹

Training and standards for performance

The IGVB procedure can be performed by a radiologist or surgeon.^{1,14-17,24} This procedure can be performed in a radiology department, women's health centre, outpatient surgical centre, or physician's office.

Training

According to the manufacturer, the Mammotome[®] system should be used only by physicians trained in percutaneous needle techniques for tissue sample collection.¹

As specific cautions apply when percutaneous breast biopsy procedures are undertaken, those who perform these biopsies must be aware of the close association of some benign findings with malignant ones.^{7,14-17,20,24,29-31} Concurrence between the microscopic findings and the imaging findings is crucial, especially when a benign diagnosis is rendered, to be certain that a malignant focus has not been overlooked. Image findings should be available to the pathologist. A review of the imaging findings with the microscopic findings by the radiologist is required to ensure that the sample of tissue obtained is representative of the imaging findings.

Interpretive experience in screening and diagnostic mammography and ultrasound imaging is essential for those performing image-guided percutaneous interventional procedures (including IGVB).^{7,14,23,24,29-31} Radiographic equipment used for these procedures should be operated by a radiologic technologist or a physician who meets certain qualifications.

As new breast imaging modalities and percutaneous breast interventional techniques are developed, additional clinical training, under supervision and with proper documentation, should be obtained before radiologists interpret or perform such examinations or procedures independently.^{14,24,29-31}

In Canada, the additional training must meet with pertinent provincial/regional regulations.²⁹ Continuing professional development must meet with the requirements of the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada.

Quality assurance

As with mammography programs, the establishment of a quality assurance program for IGVB is useful to determine the level of care delivered by a facility and its individual physicians, to ensure the equipment is functioning properly, and to help recognize problems as they arise so that they can be corrected. Quality control tests to be performed by a qualified specialist and a radiologic technologist, have been described by different organizations including the American College of Radiology (ACR), the Canadian Association of Radiologists (CAR), and the European Society for Mastology.^{14-16,29-31,72}

In addition to quality control testing, a complete quality assurance program should also collect outcome data on the procedures.^{14-16,29-31,72} Data should be collected on the number of performed procedures, number of diagnosed carcinomas, number of reported or observed complications, and the number of lesions requiring repeat biopsy (re-biopsy) and the reasons why. All these data should lead to an adequate accreditation program as already established by ACR and CAR.

ACR and CAR established accreditation programs for stereotactic- and ultrasound-guided percutaneous breast biopsy.²⁹⁻³¹ The programs address physician qualifications, equipment performance, quality assurance/control procedures, and

clinical image quality. Accreditation by these programs requires that personnel involved in these procedures meet initial and continuing training requirements and that they perform a minimum number of procedures annually. Additionally, a facility must have a quality control program in place and collect outcome data on the performance of these procedures at the time of application.

The American College of Surgeons published a statement on physician qualifications for stereotactic biopsy.¹ The American Society of Breast Surgeons offers a certification program in breast ultrasound for surgeons. The program addresses issues similar to those of the ACR accreditation program.

In Alberta no accreditation program is offered for image-guided vacuum-assisted breast biopsy procedures (College of Physicians and Surgeons, personal communication).

Comparison to alternatives

IGVB currently competes with standard CNB as a minimally invasive alternative to open surgical biopsy.^{1,14-18,20,22,25} IGVB has higher equipment and supply costs than CNB but has several advantages as a diagnostic sampling method.^{14-18,20,22,25}:

- The needle is placed in the breast only once and tissue from around the probe, not just in the line of fire, can be obtained. This may be advantageous when performing biopsy of small clusters of microcalcifications as less exact positioning of the needle in relation to the target cluster is required.
- With the IGVB, multiple tissue cores can be obtained in a circumferential manner and larger volume of tissue is removed. This can provide more complete sampling and better characterization of the lesions, potentially reducing the number of unsatisfactory biopsies and the frequency of repeat biopsies.
- Vacuum can be used to suction the blood out of the biopsy cavity during and at the end of the procedure.
- IGVB allows placement of a marker clip to localize the biopsy site when complete removal of the targeted lesion results, should subsequent surgical excision be required.
- Because its probe does not need to be fired in the breast, superficial lesions and lesions in thin breasts may be amenable to IGVB.

Results reported by several published series and validation studies have suggested that IGVB under stereotactic guidance may be superior to stereotactic CNB in several clinical scenarios.^{1,14-18,20,22,25} Calcification retrieval can be improved by using IGVB. Because of the larger size of the retrieved tissue sample, IGVB may result in a more accurate characterization of histologically heterogeneous lesions. This, in turn, may reduce the frequency of ADH underestimates (defined as the biopsy diagnosis of ADH in a lesion

that has DCIS) and DCIS underestimates (defined as the biopsy diagnosis of DCIS in a lesion that has invasive carcinoma) as compared to CNB.

The frequency of epithelial displacement may be lower with IGVB as compared with CNB.^{15,17,18,20,22,25} One of the explanations would be that the step during the procedure that most likely would result in epithelial displacement is probably firing the needle through the carcinoma, which is not necessary when using IGVB. With IGVB, larger volumes are retrieved so displaced cells are more likely to be retrieved. Also, the use of vacuum tends to pull cells into the probe rather than displace them from the biopsy site.

However, complete removal is also more likely after stereotactic IGVB than after stereotactic CNB.^{1,14-18,20,22,23,25} In case of microcalcifications, it has been emphasized the possibility that specimen may be aspirated into the debris canister, thus compromising the accuracy of the histologic diagnosis, hence reinforcing the unsuitability of this procedure as a treatment for malignant lesions.²³

AVAILABLE EVIDENCE

This TechNote response is based on a review of systematic reviews conducted on the use of IGVB for diagnosing suspicious, image-detected, non-palpable breast lesions or abnormalities. Selected for data extraction were only published reports of systematic reviews that, by virtue of design and quality of reporting⁷³⁻⁷⁵ were most likely to provide high level of evidence. Individual randomized or non-randomized controlled trials or comparative studies published subsequent to the selected systematic reviews are not included.

Only two reviews^{27,39} met the inclusion criteria as described in the methodology section (see Appendix B). Both examined the use of IGVB with stereotactic guidance for diagnostic sampling of suspicious breast lesions. The following commentary summarizes the reported findings. Details of these studies (study's characteristics, reported main results and conclusions, and the study's objective and methodology) are provided in Table C1 and Table C2 (Appendix C).

Systematic reviews

Hetnal et al.²⁷ conducted a systematic review to compare the clinical efficacy and safety of FNAB, CNB and mammotomy (which is an IGVB procedure using the Mammotome® system) in referral to the gold-standard (open surgical biopsy and/or mammography follow-up) for secondary diagnostics of non-palpable breast lesions in women. Three of the studies reviewed by **Hetnal et al.**²⁷, compared mammotomy (using stereotactic guidance) with the gold standard. The exclusion criteria used for study selection are not clearly stated in the reviewed version of this systematic review. Also, the reviewers did not clearly specify the design of the three selected studies. All mammotomy biopsies performed in these studies, which included a total of 792 cases of non-palpable breast lesions, resulted in "diagnostically competent histological material".

Meta-analysis results obtained by **Hetnal et al.**²⁷ for the diagnostic parameters of mammotomy indicated a pooled sensitivity of 97.9%. This would suggest that out of 1000 subjects with malignant breast lesion(s) confirmed by the gold standard, mammotomy detected malignant lesion(s) in 979 patients and the remaining 21 patients would be misdiagnosed as having benign lesions, resulting in false negatives. Pooled specificity of mammotomy was 100%, suggesting that in all subjects with a confirmed benign lesion by the gold standard, there was concurrence.

The positive predictive value (PPV) calculated for mammotomy was 100% suggesting that all subjects with detected malignant lesions really have malignant lesions.²⁷ The estimated negative predictive value (NPV) of mammotomy was 99.3%. This would suggest that out of 1000 subjects, in whom this procedure showed a benign lesion, the gold standard confirms the diagnosis in 993 and the remaining seven subjects would have malignant lesions (false positives).

The reported high value (259.3) for the positive likelihood ratio (LR+) and the low value (0.033) for negative likelihood ratio (LR-) value would indicate the power of the mammotomy results in determining the presence of a malignant lesion with the positive result and exclusion of a malignant lesion with a negative result.²⁷ The reported percentage of true results (99.5%) and the value of the diagnostic odds ratio (8530.8) would indicate that the use of mammotomy is characterized by high accuracy.

The comparative analyses of mammotomy, CNB, and FNAB as optional biopsy methods for non-palpable breast lesions, showed statistically significantly higher sensitivity, specificity, PPV, NPV, and accuracy value (percentage of true positive results) for mammotomy (see Table 1).

Table 1: Summary of the diagnostic parameters for mammotomy, CNB and FNAB (modified from Hetnal et al.²⁷)

Diagnostic parameter	Mammotomy	CNB	FNAB
Percentage of non-diagnostic biopsies	0%	3.8% [CI _{95%} 3.10-4.45]	11.2% [CI _{95%} 10.60- 11.86]
Sensitivity	97.9% [CI _{95%} 94.7-99.4]	88.3% [CI _{95%} 86.6-89.9]	82.5% [CI _{95%} 81.0- 83.9]
Specificity	100.0% [CI _{95%} 99.4-100]	98.8% [CI _{95%} 98.3- 99.1]	97.9% [CI _{95%} 97.6-98.2]
Positive predictive value	100% [-]	97.42% [CI _{95%} 96.86-97.99]	92.35% [CI _{95%} 91.79- 92.91]
Negative predictive value	99.34% [CI _{95%} 98.69- 99.99]	94.20% [CI _{95%} 93.37-95.04]	94.76% [CI _{95%} 94.30- 95.23]
Accuracy	99.49% [CI _{95%} 98.93- 100]	95.20% [CI _{95%} 94.44-95.97]	94.26% [CI _{95%} 93.77-94.74]
Positive likelihood ratio	259.32 [CI _{95%} 52.52- 1280.2]	55.28 [CI _{95%} 25.51- 119.77]	33.3 [CI _{95%} 21.35- 51.93]
Negative likelihood ratio	0.033 [CI _{95%} 0.007-0.165]	0.120 [CI _{95%} 0.075- 0.192]	0.168 [CI _{95%} 0.128- 0.22]
Diagnostic odds ratio	8530.8 [CI _{95%} 644.14-112978.2]	471.00 [CI _{95%} 208.99-1061.5]	248.73 [CI _{95%} 140.54- 440.22]

CI95% - 95% confidence interval

The comparative analysis of the results obtained for mammotomy and CNB (see Table 1) showed statistically significantly higher sensitivity ($p < 0.001$), specificity ($p = 0.003$), PPV ($p = 0.01$), NPV ($p < 0.001$), and accuracy ($p < 0.001$) for mammotomy.²⁷ In comparison with CNB, mammotomy also had higher values for the diagnostic odds ratio, LR+ and LR-. These differences were found statistically significant in Kruskal-Wallis test (non-parametrical ANOVA, $p < 0.05$). However, the reviewers could not draw conclusions regarding the statistical significance of the differences between the meta-analysis results (pooled values) for these parameters.

In the group of patients diagnosed by mammotomy no cases of non-diagnostic biopsies were observed, while in the group diagnosed by CNB 115 cases of non-diagnostic biopsies (4%) were observed (see Table 1).²⁷ The difference was found statistically significant (*p-value not mentioned in the reviewed version of the published report*) with a number needed to harm value of 26.5 [95% Confidence Interval 22.5 - 32.3]. This would suggest that for every 27 non-palpable lesions undergoing CNB instead of mammotomy, one non-diagnostic biopsy will be obtained.

The comparative analysis of the diagnostic efficacy of mammotomy and FNAB (see Table 1), showed statistically significant higher sensitivity ($p < 0.001$), specificity ($p < 0.001$), accuracy ($p < 0.001$), PPV ($p < 0.001$), and NPV ($p < 0.001$) for mammotomy.²⁷ In comparison with FNAB, mammotomy was also characterized by statistically significantly higher diagnostic odds ratio and LR+ values (“significance for meta-analysis results”; *p-value not mentioned in the reviewed version of the published report*). Although the LR- value calculated for mammotomy was also higher than that calculated for FNAB, the difference between the estimated values was not statistically significant for meta-analysis results (pooled values) (*p-value not mentioned in the reviewed version of the published report*).

In the group of patients diagnosed by FNAB, 1083 cases of non-diagnostic biopsies (11%) were observed (see Table 1).²⁷ The estimated number needed to harm of 8.9 [95% Confidence Interval 8.43; 9.43] would suggest that for every nine non-palpable lesions subjected to fine needle aspiration biopsy instead of mammotomy, one non-diagnostic biopsy will be obtained.

Hoorntje et al.³⁹ conducted a critical review of the literature published on the accuracy of IGVB with stereotactic guidance and compared it with published data on the accuracy of 14-gauge CNB. Twenty-two primary research studies on the use of IGVB with stereotactic guidance were included in the review (*information on the type of system used and/or manufacturer was not provided in the reviewed version of this systematic review*). According to the reviewers, most of these studies provided limited data on patient selection and, in many studies, it was not clear whether the patients enrolled were those with non-palpable breast lesions or if consecutive patients were included. The prevalence of carcinoma varied largely between the studies, which might indicate patient selection for the vacuum-assisted procedure.

Seven studies reported on the number of inconclusive diagnoses (*the reviewers did not clearly specify the design of these studies*).³⁹ The proportion of these lesions varied from 0.5% to 9.% (median 1.2%) and in three of 28 (11%) cases that were followed by surgical excision, a malignancy was found.

Fifteen studies contributed data to the combined high-risk underestimate rate for the stereotactically-guided 11-gauge vacuum-assisted breast biopsy procedure (*the reviewers did not clearly specify the design of these studies*).³⁹ Homogeneity testing of the high-risk underestimate rate for each study showed that they did not differ statistically significantly ($p>0.25$). A total of 416 high-risk lesions were detected in these 15 studies. However, 57 lesions did not have definitive diagnosis and they were excluded from the analysis. Of the remaining 359 high-risk lesions, 57 were proven to be malignant, with a combined high-risk underestimate rate of 16%.

Data on the high-risk underestimate rate for the 14-gauge IGVB with stereotactic guidance was reported by 3/15 studies.³⁹ Homogeneity testing showed these studies did not differ statistically significantly ($p>0.1$) and the combined high-risk underestimate rate was 24%. The difference between results obtained with the 11-gauge and 14-gauge systems was not statistically significant ($p>0.05$).

Three of the 15 studies conducted on the use of the 11-gauge IGVB with stereotactic guidance reported on lesions consisting of calcifications only.³⁹ In these studies, 12 malignancies were diagnosed in 83 patients with surgery or adequate follow-up. The combined high-risk underestimate rate was 15%.

Thirteen studies reported on the ductal carcinoma *in situ* (DCIS) underestimate rates for the stereotactically guided 11-gauge vacuum-assisted breast biopsy procedure (*the reviewers did not clearly specify the design of these studies*).³⁹ Homogeneity testing of each study's results did not show any significant differences ($p>0.1$). A total of 1157 DCIS lesions were diagnosed in these studies and 52% of them were detected in one multi-institutional study (which described results obtained in 16 centres). One hundred and twenty-two lesions showed invasive cancer at surgery. The combined DCIS underestimate rate was 11%.

Four of the above mentioned studies also reported on the DCIS lesions detected with a stereotactically guided 14-gauge vacuum-assisted breast biopsy system.³⁹ The homogeneity testing showed significant differences between the results reported by these studies ($p<0.01$) and the calculated combined DCIS underestimate rate was 13% (which, according to the reviewers, should be regarded with caution).

Two of the 13 studies conducted on the use of stereotactically guided 11-gauge vacuum-assisted breast biopsy reported DCIS underestimate rates for lesions appearing as calcifications only and they were 5% and 8%, respectively.³⁹

The finding of benign lesions detected by stereotactic 11-gauge IGVB with at least some follow-up was described in seven studies (*the reviewers did not clearly specify the design of*

these studies).³⁹ However, follow-up of these lesions was considered as inadequate according to the preset inclusion criteria (surgery of follow-up for 90% of patients for at least 2 years). In one of the seven studies, 12 of the 491 patients with benign lesions had adequate follow-up. Two of these patients underwent excision (which showed a malignancy) and 10 had unchanged and unsuspecting mammograms 2 years after vacuum-assisted breast biopsy. In two other studies, 1/61 and 4/120 benign lesions diagnosed with stereotactic 11-gauge IGVB had been excised, but no malignancies were found.

Due to incomplete or non-reported follow-up of the benign lesions that were not surgically removed (also referred to as “a verification problem”) in all studies, **Hoorntje et al.**³⁹ were unable to calculate the miss-rate and thus the sensitivity rate. The reviewers concluded that the “miss-rate for 14-gauge automate biopsy is 3%, and it is not clear from the available data in this study that this rate is lower when using vacuum biopsy”.

The review by **Hoorntje et al.**³⁹ showed that stereotactic 11-gauge IGVB results in a high-risk underestimate rate and a DCIS underestimate rate of 16% and 11% respectively. To estimate the benefit of this procedure over stereotactic 14-gauge automated needle biopsy, the reviewers calculated the number of preventable underestimated diagnoses in a representative, non-selective population of patients with non-palpable breast lesions. The underestimate rates computed in the review by **Hoorntje et al.**³⁹ were used as data for the stereotactic IGVB and as data for stereotactic 14-gauge automated needle breast biopsy, the investigators used the data reported in the meta-analysis conducted by the Verkooijen et al.⁷⁶

The published data reported for the high-risk and DCIS underestimate rates with stereotactic 14-gauge automated needle breast biopsy were 40% and 15%, respectively.³⁹ When these rates were compared with those estimated by **Hoorntje et al.**³⁹ for the stereotactic 11-gauge IGVB, a significant decrease in the high risk underestimate rate (difference of 24%; $p < 0.05$) and a not statistically significant decrease in the DCIS underestimate rate (difference of 4%; $p > 0.05$) were found.

Hoorntje et al.³⁹ also used data from a recently conducted multicentre trial in the Netherlands which included women referred for a biopsy of a suspicious non-palpable breast lesion to estimate the number of preventable underestimated diagnoses. In this population of 858 women, a total of 20 high-risk lesions and 158 DCIS lesions were diagnosed by surgery. The reviewers found that if IGVB was used in these women, 9/858 (1%) women would have been spared a high-risk underestimate diagnosis and 11/858 (1.3%) would have been spared a DCIS underestimate diagnosis. The total decrease in the underestimated diagnoses would have been 20/858 (2.3%) when using the IGVB method instead of the automated needle biopsy in this well-defined population.

Hoorntje et al.³⁹ looked at lesions consisting only of calcifications to determine whether the selective use of the IGVB procedure for lesions for which 14-gauge automated biopsy is less accurate (such as calcifications), would be another option that could be further explored. They found that, although the number of lesions was very low, the combined high-risk underestimate rates (14.5%) and DCIS underestimate rates (6.1%) were comparable to the rates estimated in studies describing all lesions.

GUIDELINES AND CONSENSUS STATEMENTS

An interdisciplinary consensus on the use and technique of IGVB with stereotactic guidance was achieved based on the literature published until December 2001 and the experience gained by users of the Mammotome® systems.⁷² Represented were disciplines involved in diagnosis, radiology, pathology, and gynecology. The consensus incorporated the literature on IGVB with stereotactic guidance, the data and consensus statements on the histopathological assessment and recording of percutaneous biopsy material, the clinico-pathological correlation of percutaneous biopsies, as well as expert opinion.

This consensus includes protocols for establishment of an indication, performance indicators, interdisciplinary interpretation and therapeutic recommendation, documentation, and follow-up. The consensus has been limited to “indications for which sufficient experience exists and the protocols are in place for satisfactory assessment”. Asymmetrical changes, extensive areas of microcalcifications or palpable lesions (“all of which are generally much larger than the area that can be obtained by vacuum-assisted biopsy”) were not included in the list of indications.

The consensus⁷² suggests that IGVB with stereotactic guidance should only be indicated after the completion of imaging and clinical assessment, in compliance with the current standards. Indications included microcalcifications and small non-palpable breast lesions, which should belong to BIRADS Category 4 (requiring clarifications) or BIRADS Category 5 (highly suspicious). In individual cases this procedure may also be appropriate for BIRADS Category 3 lesions. Lesions very close to the skin and architectural distortions (“suspected radial scar”) were considered as “suitable only under certain conditions or unsuitable”.

According to this consensus⁷², acquisition of >20 cores (using 11-gauge probe) should be routinely attempted. The goal is the diagnostic removal of small lesions as far as this is possible, thereby increasing diagnostic confidence and reducing the so-called “underestimates”. However, the IGVB should be regarded as a diagnostic procedure. The procedure should not be regarded as a therapeutic method in case of malignancy or pre-invasive neoplasia (invasive carcinoma, atypia, DCIS, or lobular carcinoma in situ LCIS). Surgical excision with a therapeutic objective is required in these cases.⁷²

The pre/post insertion and post-biopsy stereotactic images and a post-biopsy mammogram must be documented.⁷² After IGVB, specimen radiography must be

carried out in at least all cases with microcalcifications, which should be sent to the pathologist together with the specimens. A control mammogram shall be taken after IGVB or on a following working day to confirm the correct sampling depth.

All cases with no or uncertain histopathological correlation require discussion in a regular interdisciplinary conference and a documented consensus concerning further work-up or therapy.⁷² Providers should collect data relating to the findings before and after the examination, the procedure, complications, histopathologic findings and therapeutic recommendation, and findings of follow-up mammography.

Standardised documentation of the primary findings and follow-up mammography after 3-9 months is requested.

In 2003, at the American College of Surgeons annual spring meeting, a panel of breast cancer experts encouraged physicians to perform minimally invasive breast biopsy rather than traditional open surgical breast biopsy to detect malignancies whenever possible.²⁴ The panel recommended IGVB over other biopsy techniques as the procedure increases the size of the specimen for analysis (which may help pathologists make a more reliable lesion categorization) and it can remove image-detected evidence of lesions and microcalcifications.

Guidelines for non-operative diagnostic procedures produced by the Royal College of Pathologists in the United Kingdom⁷⁷ recommend that the choice of the sampling method in any centre should be determined by:

- the sensitivity and specificity of the technique in the centre;
- the diagnostic information required for malignant lesions;
- patient comfort;
- cost;
- the availability of staff skilled and experienced in using the procedures.

Consideration of the likely underlying histological nature of the lesion from the imaging features should also be taken into account when deciding on the sampling method to be used.⁷⁷ For certain types of mammographic abnormality, such as moderate to low level suspicion microcalcification, when the use of conventional FNAB or 14-gauge CNB carries a risk of an equivocal result, use of larger volume sampling techniques such as IGVB may increase the accuracy of biopsy.

EXPERT OPINION

Advice was obtained from four Canadian specialists who have expertise in using IGVB for diagnostic sampling of suspicious, image-detected, non-palpable lesions or abnormalities. The following commentary summarizes the advice received.

The IGVB procedure is considered the standard of care in many countries in Europe, Australia, and North America. The consensus among the radiologists performing IGVB, pathologists evaluating the retrieved samples, and the surgeons making the treatment decisions based on the biopsy results, is that the procedure is an accurate diagnostic tool, with high sensitivity and specificity in diagnosing breast disease, with a very low false negative rate. IGVB is also considered as a safe procedure, characterized by a very low complications rate. The most frequently observed complications include bleeding (in approximately 1% of cases), reaction to local anaesthetics (in approximately 0.5% of cases), and infection (very rare).

In Canada there is no standard biopsy procedure for diagnostic sampling of suspicious non-palpable breast lesions and there are no written clinical practice guidelines for performing image guided biopsy. However, it is generally accepted that if a suspicious mass is visible by both mammography and ultrasound, the mass should be biopsied under ultrasound guidance. The ultrasound imaging modality is generally considered as faster, cheaper, and more comfortable for the patient than using stereotactic guidance.

Both image-guided large core (14-gauge) automated gun-needle (spring loaded) biopsy and IGVB procedures are used in Canada for diagnostic sampling of masses and microcalcifications (BIRADS Category 4 and 5 lesions). A diagnostic sample of an ultrasound visible mass can usually be obtained by using a 14-gauge spring loaded needle biopsy under ultrasound guidance. Microcalcifications can be successfully biopsied using the stereotactic 14-gauge spring loaded needle biopsy procedure. However, the procedure is associated with a high false negative rate, when no calcifications are retrieved within the core, or the pathologists underestimate the breast disease due to the small core size.

The generally accepted and preferred practice in Canada is to perform IGVB under stereotactic guidance for clusters of microcalcifications as well as mammographic non-calcified lesions, which cannot be reliably identified by ultrasound. Although it is more expensive than the 14-gauge spring loaded CNB, the IGVB is preferred for these cases because it is considered as highly effective (provides better sampling, with very, very low false negative and complications rates) and it is easier to use.

Ultrasound-guided CNB with a 14-gauge spring loaded needle is usually used in Canada to sample discrete soft tissue masses. However, IGVB under ultrasound guidance may be performed for a solid mass (identified by ultrasound) that is very small or very close to the chest wall (when it may not be safe to use a 14-gauge automated gun-needle biopsy).

IGVB under ultrasound guidance is less frequently performed for sampling of other solid masses (usually done with a 14-gauge) in Canada than in the United States because of the difference in the cost for disposables. The 14-gauge spring loaded Tru-Cut® biopsy needle costs approximately \$40 CAD, while a Mammotome®

disposable needle/probe costs approximately \$300 CAD, with an additional \$100 CAD for the marker clip, which is to be placed at the biopsy site if the whole lesion is likely to be removed during the procedure. It is also more difficult to push an 11-gauge Mammotome® needle/probe through a dense uncompressed breast for an IGVB with ultrasound guidance than a 14-gauge spring loaded needle. The SenoCor® system may be less difficult to perform for these cases as it uses a radiofrequency needle tip to cut through the tissue.

In Canada, the number of Mammotome® probes used in 2004 (up to November) was approximated at 2500 in the Province of Quebec, 924 in Ontario, 425 in Manitoba, 1120 in Alberta, and 365 in British Columbia. Although the Mammotome® is the most commonly used system, three SenoCor® biopsy systems are in use in Canada: one in Edmonton, one in Ottawa, and one in Montreal.

The procedure is most commonly performed by a radiologist working closely with a radiation technologist. Training for the radiologists and technologists on the IGVB procedure is provided by the vendor's application specialists. Training is also obtained by attending Continuing Medical Education courses in breast imaging, which are specifically geared to biopsy or which include biopsy among other topics. Many courses offer both didactic and hands-on training. The staff with experience and expertise in using IGVB for diagnostic sampling of image-detected breast lesions within the facility may train other staff members.

Although in Alberta there is no accreditation program for this procedure, since all facilities are accredited under the CAR program, the CAR standards would be applicable standards. In addition, there is a facility accreditation under the Alberta College of Physicians and Surgeons which looks at equipment, images, and reporting.

In British Columbia, Alberta, Ontario, and the Province of Quebec, if the IGVB procedure is performed in hospitals, it is covered through the hospital's budget. In Manitoba, if the procedure is performed at the Women's Health centre it is covered through a separate budget funded by the Government of Manitoba.

DISCUSSION

IGVB was introduced as a minimally invasive alternative to open surgical biopsy for the diagnostic sampling of suspicious, image-detected, non-palpable breast lesions. When used under stereotactic guidance, it appears to be as effective as open surgical biopsy in obtaining tissue samples for histopathologic analysis in the diagnosis of breast cancer.^{27,39} The correlation between stereotactic IGVB (particularly when using 11-gauge probes) and open surgical biopsy is high due to the size of the collected samples. IGVB is fast and simple to perform, with a very low complication rate and can reduce the overall costs of breast disease diagnosis when compared to open surgical biopsy.

Due to these advantages, IGVB has diffused rapidly during the last decade and is increasingly replacing standard CNB for diagnostic sampling of suspicious, image-detected, nonpalpable breast lesions. IGVB is a variant procedure of CNB, which acquires larger tissue samples by using a single insertion of the probe and more samples can be obtained in a short period of time. Although there are no studies directly comparing the diagnostic performance of these techniques^{27,39}, positive conclusions as to the safety and efficacy of stereotactic IGVB as an alternative to stereotactic CNB have been made.^{43,78}

Results reported by two systematic reviews^{27,39} and expert opinion suggest that, when used under stereotactic guidance, IGVB may be more effective in diagnosing suspicious, image-detected, non-palpable breast lesions than stereotactic CNB for several clinical scenarios. It appears to result in statistically significant improvement in the pre-operative diagnosis of lesions classified as BIRADS Category 4 and 5 (particularly when calcifications and small lesions are considered).³⁹ Mammotomy is characterized by statistically significantly higher sensitivity, specificity, accuracy, and positive and negative predictive values than the stereotactic CNB.²⁷ It allows more efficacious confirmation of the exclusion of malignant as well benign lesions.

Given its design advantages over standard CNB, IGVB is expected to decrease the number of high-risk and DCIS-underestimates. According to Hoorntje et al.³⁹, the underestimation of histopathologic findings is significantly reduced with stereotactic 11-gauge IGVB, which has better sensitivity for detecting DCIS and ADH when compared to 14-gauge stereotactic CNB.

A clinically important advantage of stereotactic IGVB would be to decrease the cancer miss-rates.¹⁴ Currently it is unclear whether IGVB has significant advantage in this regard. Based on the findings reported by the studies selected for their systematic review, Hoorntje et al.³⁹ were not able to determine whether stereotactic 11-gauge IGVB results in a reduced cancer miss-rate in comparison to stereotactic 14-gauge CNB.³⁹ False negative results could not be avoided even when 20 specimens per lesion were retrieved with IGVB^{15,16} and this procedure cannot avoid the need for subsequent open surgical biopsy in every case.¹⁴

The main disadvantage of IGVB is the cost associated with the disposable materials of the vacuum suction system, which is 10 times higher than that for the 14-gauge CNB. In addition to the cost of larger probes, the cost of the marker clip can also add to the expense of performing IGVB on smaller lesions. However, cost analyses have shown that cost savings per procedure are possible.^{1,23,64} A facility currently performing stereotactic CNB should evaluate the acquisition costs for IGVB along with the procedural volumes to determine whether adding IGVB is cost-effective. According to the ECRI the return on investment might be achieved when more than 100 procedures are performed annually.¹

Stereotactic 11-gauge IGVB may be used for lesions that are not amenable to stereotactic 14-gauge CNB (including small masses, undefined calcifications, superficial lesions, and those located in thin breasts) and those for which stereotactic 14-gauge CNB is less accurate (such as histologically heterogeneous lesions and those consisting of calcifications only). According to Liberman and Kaplan⁶⁴ the use of stereotactic 11-gauge IGVB for calcifications and for non-palpable masses not amenable to stereotactic 14-gauge CNB would yield annual savings exceeding \$50 million.

The advantage of stereotactic IGVB procedures for microcalcifications has demonstrated improved diagnostic accuracy because of the underestimation of lesions that manifest as microcalcifications.^{14-17,22,25,32} As insufficient samples and pathology under-classification are not issues with ultrasound guided biopsy^{7,34,45}, the advantages and role of IGVB under ultrasound-guidance, have yet to be demonstrated or established.

IGVB with MRI guidance is promising for lesions that are seen only on MRI. However, currently its use is limited by availability and technical issues of quality and specificity and it is not considered standard of practice.^{14,16-18,35,36} Economic considerations also preclude its use.

CONCLUSIONS

Facilities currently performing stereotactic CNB may consider IGVB under stereotactic guidance as an alternative for the diagnostic sampling of selected suspicious, image-detected, non-palpable breast lesions or abnormalities. The choice of the technique to use depends on the lesion and breast characteristics, as well as on the equipment availability, the expertise of the physician performing the biopsy, and cost considerations. Selective application of 11-gauge IGVB may be considered for calcifications and lesions not amenable to stereotactic 14-gauge CNB.

Currently it is still unclear whether the benefits of stereotactic 11-gauge IGVB outweigh its additional costs when compared to stereotactic 14-gauge CNB. Based on the results of two systematic reviews, stereotactic 11-gauge IGVB appears to diminish the shortcomings of the stereotactic 14-gauge CNB by reducing histologic underestimation and the need for repeat biopsy. However, the question on whether the miss-rate of cancer is lower when using stereotactic 11-gauge IGVB has yet to be answered. The histologic underestimation and the need for repeat biopsy have not been completely eradicated by using stereotactic 11-gauge IGVB.

False positive interpretations still occur with stereotactic IGVB and all cases should be subject to multidisciplinary review before definitive treatment. Potential candidates should be informed about the procedure and its risks.

An advantage of using IGVB under ultrasound guidance over ultrasound-guided CNB has yet to be established. Currently, the experience with IGVB under MRI guidance is

still limited. Further research is necessary to evaluate the utility and cost-effectiveness of these methods.

As for screening programs, quality control and quality assurance programs should be instituted for all IGVB techniques.

While FDA and Health Canada have approved several IGVB systems for diagnosis, none has been approved for treatment of breast cancer. Coverage for this procedure varies in North America.

This TechNote response is limited since it reports the results from two systematic reviews and recently published primary research studies (which may address some of the outstanding issues outlined below) are not included.

Further research is needed to define the definitive role of IGVB as a diagnostic sampling method. Consensus is needed on the adequate patient selection criteria and techniques to reduce the false positive and false negative rates as much as possible, as well on follow-up strategies. Further work should include evaluation of IGVB in direct comparison with CNB (using stereotactic, ultrasound, or MRI guidance) with respect to safety, diagnostic accuracy and cost effectiveness, and the evaluation of these methods with respect to optimisation of choice for different breast lesions. Long-term follow-up studies are also needed.

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Technotes are brief reports, prepared on an urgent basis, which draw on limited reviews and analysis of relevant literature and on expert opinion and regulatory status where appropriate. They are not subject to an external review process.

APPENDIX A: SEARCH STRATEGY

The literature search was conducted by the AHFMR Research Librarian between April 27th and May 17th date. Major electronic databases used include: The Cochrane Library, NHS Centre for Reviews and Dissemination (CRD Databases: NHS EED, HTA, DARE), PubMed and EMBASE, Web of Science, and CINAHL. In addition, relevant library collections, web sites of practice guidelines, regulatory agencies, evidence-based resources and other HTA related agency resources (AETMIS, CCOHTA, ECRI) were searched. Internet search engines were also used to locate grey literature.

Medical Subject Headings (MeSH) terms relevant to this topic are: Breast; Biopsy, Needle; Ultrasonography; Magnetic Resonance Imaging; Stereotaxic techniques; Vacuum; Keywords used: mammotome; MIBB; ABBI; ATEC; Vacora; VacuFlash; breast; biopsy; stereotactic; stereotaxic; ultrasound; image-guided; MRI; percutaneous; suction; image; large core; etc.

† See below for limits

Database	Platform	Edition or date searched	Search Terms ††
Core Databases			
The Cochrane Library	http://www.thecochrane.org	Issue 1, 2005 Searched May 17, 2005	“breast biopsy” OR “breast biopsies” OR mammotome OR MIBB OR minimally invasive breast biopsy OR ABBI OR advanced breast biopsy instrumentation OR ATEC OR Vacora OR VacuFlash
PubMed	www.pubmed.gov	Searched May 14, 2005	<ol style="list-style-type: none"> 1. mammotome OR mammotomy OR MIBB OR “Minimally invasive breast biopsy” OR ABBI OR “Advanced Breast Biopsy Instrumentation” OR ATEC OR Vacora OR VacuFlash 2. breast AND (biopsy OR biopsies) AND (vacuum OR suction OR “large core” OR percutaneous) AND (ultrasound OR image guided OR image OR imaged OR imaging OR stereotactic OR stereotaxic OR MRI) 3. #1 OR #2
CRD Databases (DARE, HTA & NHS EED)	http://www.york.ac.uk/inst/crd/crddbases.htm	Searched May 17, 2005	mammotome OR MIBB OR minimally invasive breast biopsy OR ABBI OR advanced breast biopsy instrumentation OR ATEC OR Vacora OR VacuFlash OR (breast AND (biopsy OR biopsies) AND (image guided OR stereotactic OR stereotaxic OR ultrasound OR MRI))

Database	Platform	Edition or date searched	Search Terms ^{††}
Core Databases (cont'd)			
EMBASE	Ovid Licensed Resource	Searched May 17, 2005	<ol style="list-style-type: none"> 1. mammotome OR MIBB OR minimally invasive breast biopsy OR ABBI OR advanced breast biopsy instrumentation OR ATEC OR Vacora OR VacuFlash 2. exp breast biopsy/ AND (vacuum OR suction OR large core OR percutaneous) AND (exp Ultrasound/ OR exp Stereotaxic Surgery/ OR stereotaxic OR stereotactic OR image guided OR exp Nuclear Magnetic Resonance Imaging/) 3. 1 or 2
Web of Science	ISI Licensed Resource	Searched April 27, 2005	<p>TS=(mammotome OR MIBB OR minimally invasive breast biopsy OR ABBI OR advanced breast biopsy instrumentation OR ATEC OR Vacora OR VacuFlash)</p> <p>OR</p> <p>TS=((vacuum OR suction OR image guided OR percutaneous) AND (breast SAME biops*) AND (image guided OR stereotactic OR stereotaxic OR ultraso* OR MRI))</p>
CINAHL	Ovid Licensed Resource	Searched May 17, 2005	mammotome OR MIBB OR minimally invasive breast biopsy OR ABBI OR advanced breast biopsy instrumentation OR ATEC OR Vacora OR VacuFlash OR (breast and exp Biopsy/ AND (vacuum OR suction OR large core OR percutaneous) AND (exp Magnetic Resonance Imaging/ OR exp Stereotaxic Techniques/ OR exp Ultrasonography/ OR stereotactic OR image guided OR exp Diagnostic Imaging/))
Library Catalogues			
NEOS (Central Alberta Library Consortium)	http://www.library.ualberta.ca/catalogue	Searched April 27, 2005	breast biopsy
Guidelines			
AMA Clinical Practice Guidelines	http://www.topalbertadoctors.org/guidelines/guidelinespdf.aspx	Searched April 27, 2005	breast cancer
CMA Infobase	http://mdm.ca/cpgsnew/cpgs/index.asp	Searched April 27, 2005	breast biopsy OR breast biopsies
National Guideline Clearinghouse	www.ngc.gov	Searched May 17, 2005	(image guided OR ultraso* OR stereota* OR MRI) AND breast AND biops*

Database	Platform	Edition or date searched	Search Terms ^{††}
Guidelines (cont'd)			
National Comprehensive Cancer Network	http://www.nccn.org/physician_gls/index.html	Searched April 27, 2005	breast cancer and diagnosis
Clinical Trials			
ClinicalTrials.gov	http://clinicaltrials.gov/	Searched May 17, 2005	breast, biopsy OR biopsies, vacuum; mammotome; MIBB; minimally invasive breast biopsy; ABBI; advanced breast biopsy instrumentation; Vacora; ATEC; VacuFlash
National Research Register	http://www.update-software.com/national/	Searched April 27, 2005	breast AND (biopsy OR biopsies) AND (vacuum OR stereotactic OR stereotaxic OR ultrasound OR image guided); mammotome OR ABBI OR MIBB
Coverage/Regulatory/Licensing Agencies			
Health Canada - Medical Devices Active Licence Listing	http://www.mdall.ca/	Searched May 17, 2005	mammotome; MIBB; ABBI; Vacora; ATEC; VacuFlash
FDA Center for Devices and Radiological Health	http://www.fda.gov/cdrh/	Searched May 17, 2005	mammotome; MIBB; ABBI; ATEC; Vacora; VacuFlash
Medicare Coverage Database	http://www.cms.hhs.gov/mcd/search.asp?	Searched April 28, 2005	breast biopsy
Evidence Based Medicine Resources			
ACP Journal Club	Ovid Licensed Resource	Searched May 17, 2005	(breast and biops\$) OR mammotome OR ABBI OR MIBB OR ATEC OR VacuFlash OR Vacora
Bandolier	http://www.jr2.ox.ac.uk/bandolier/	Searched April 27, 2005	breast biopsy
BestBETS	http://www.bestbets.org	Searched April 27, 2005	breast biopsy; breast biopsies
Clinical Evidence	http://www.clinicalevidence.com	Searched April 27, 2005	breast biopsy; breast biopsies

Database	Platform	Edition or date searched	Search Terms ^{††}
Grey Literature			
NELH	http://www.nelh.nhs.uk/	Searched April 28, 2005	breast biops%
Google	http://www.google.ca	Searched May 17, 2005	breast biopsy vacuum-assisted (stereotactic OR stereotaxic OR image guided OR ultrasound OR MRI); mammotome; “Minimally Invasive Breast Biopsy”; “Advanced Breast Biopsy Instrumentation”; ATEC breast biopsy; Vacora breast biopsy; VacuFlash breast biopsy
HTA Resources			
AETMIS	http://www.aetmis.gouv.qc.ca	Searched May 17, 2005	breast biopsy; breast biopsies; mammotome; ABBI; MIBB; ATEC; Vacora; VacuFlash
CCOHTA	http://www.ccohta.ca	Searched May 17, 2005	breast biopsy; breast biopsies; mammotome; ABBI; MIBB; ATEC; Vacora; VacuFlash
Institute for Clinical and Evaluative Sciences (ICES), Ontario	http://www.ices.on.ca/	Searched May 17, 2005	breast biopsy; breast biopsies; mammotome; ABBI; MIBB; ATEC; Vacora; VacuFlash
Health Technology Assessment Unit At McGill	http://www.mcgill.ca/tau/	Searched April 27, 2005	breast
Medical Advisory Secretariat	http://www.health.gov.on.ca/english/providers/program/mas/mas_mn.html	Searched April 27, 2005	breast and (biopsy or biopsies)
ECRI	http://www.ecri.org	Searched May 17, 2005	breast and biops* and vacuum; breast and biopsy and (MRI OR ultrasound OR stereotactic OR stereotaxic); breast and biopsy and image guided

Note:

[†] **Limits:** Searches were limited to **publication dates 2000-2005**; . This limit was applied in databases where such functions are available.

^{††} “*”, “#”, and “?” are truncation characters that retrieve all possible suffix variations of the root word e.g. surg* retrieves surgery, surgical, surgeon, etc.

; separates different searches performed on the same resource

In addition to the above-mentioned searches, the bibliographies and reference lists from the selected and retrieved articles were examined.

Canadian specialists in breast radiology and breast care were contacted for clinical input on the current status of using image-guided vacuum-assisted breast biopsy for the diagnostic sampling of suspicious, non-palpable breast lesions or abnormalities.

Manufacturers of the IGVB systems available on the market were contacted for information on regulatory status, availability, and coverage of their equipment for breast cancer diagnosis in Canada. At time of the completion of this report, such information was obtained only for the Mammotome® and ATEC® systems.

APPENDIX B: METHODOLOGY

Screening and reviewing the literature

The studies identified by the search strategy were retrieved, reviewed and assessed to determine the relevance of each study. One reviewer decided their inclusion/exclusion. Suitability for inclusion in the review was determined on the basis of a list of criteria developed for this study.

Considered for inclusion were published reports of systematic reviews (quantitative and/or qualitative) of primary research that evaluated the efficacy/effectiveness and safety of using IGVB for diagnostic sampling of diagnose suspicious, non-palpable, image-detected, breast lesions or abnormalities.

Using criteria from Cook et al.⁷⁴, **a review was considered to be systematic if** it met at least four of the following criteria:

- focused clinical question;
- explicit search strategy;
- use of explicit, reproducible and uniformly applied criteria for article selection;
- critical appraisal of the included studies;
- qualitative or quantitative data synthesis.

Published reports of systematic reviews **were excluded if** they focused on the use of IGVB systems as a therapeutic procedure.

Published reports of narrative and descriptive reviews, which summarized the research on the topic but lacked an explicit description of a systematic approach to the identification and interpretation of evidence, were excluded from data extraction. They were considered only as a source of background information.

Clinical reviews, commentaries and discussion papers on breast cancer, breast lesions, breast biopsy procedures, and/or on the use of IGVB for diagnostic sampling of suspicious, image-detected, non-palpable breast lesions or abnormalities were also included as a source of background information.

Published reports of primary research studies (such as randomized or non-randomized controlled trials), editorials, letters and technical reports **were excluded**.

Main characteristics, findings and, conclusions from published reports of the selected systematic reviews and details of their methodology were summarized in tabular form (Table C1 and Table C2 in Appendix C). The methodological quality of these studies was not critically appraised and no attempt was made to assess the validity of their findings.

For studies in which the reporting of the review methodology was unclear, their authors were contacted for further information. Contacted were only the authors who provided an e-mail address as contact information in the published reports of their studies.

APPENDIX C: RESULTS REPORTED BY SYSTEMATIC REVIEWS

Abbreviations

CI_{95%} - 95% confidence interval

CNB - core needle biopsy

DCIS - ductal carcinoma in situ

DOR - diagnostic odds ratio

FNAB - fine needle aspiration biopsy

LR - likelihood ratio

LR+ - positive likelihood ratio

LR- - negative likelihood ratio

NNTs - numbers-needed-to-treat

NNHs - numbers-needed-to-harm

NPV - negative predictive value

NSS - not statistically significant;

OBS - open surgical biopsy

PPV - positive predictive value

Sn - sensitivity

Sp - specificity

SPSS - the Statistical Package for Social Sciences

SS - statistically significant

Table C1: Selected systematic reviews (characteristics, main findings, and conclusions)

Study	Study's characteristics	Study's main findings* and conclusions**
Hetnal et.al. ²⁷ 2004 Poland	<p>Included studies: three clinical studies (information on the study design not provided);</p> <p>Excluded studies: studies on patients belonging to diagnostic sub-groups (limited to certain types of lesions).</p> <p>Participants: women with non-palpable breast lesions</p> <p>Intervention: mammotomy (vacuum-assisted core breast biopsy) with stereotatic guidance.</p> <p>Comparator(s): gold standard (OSB or mammography follow-up), CNB, FNAB</p> <p>Outcome(s) and outcome measures: Sn, Sp, PPV, NPV, accuracy, DOR, LR+, LR-, percentage of non-diagnostic biopsies (non-diagnostic samples taken), and complications.</p>	<p>Main Findings*</p> <p><u>Pooled sensitivity:</u> 97.9% [CI_{95%} 94.7- 99.4];</p> <p><u>Pooled specificity:</u> 100% [CI_{95%} 99.4- 100];</p> <p><u>PPV:</u> 100%;</p> <p><u>NPV:</u> 99.3% [CI_{95%} 98.69- 99.99];</p> <p><u>Pooled LR+:</u> 259.3 [CI_{95%} 52.53- 1280.2];</p> <p><u>Pooled LR-:</u> 0.033 [CI_{95%} 0.007- 0.165];</p> <p><u>Pooled DOR:</u> 8530.8 [CI_{95%} 644.14- 112978.2];</p> <p><u>Accuracy:</u> 99.5% (CI_{95%} 98.93- 100);</p> <p><u>Non-diagnostic biopsy:</u> no cases observed in the patients diagnosed by mammotomy</p> <p><u>Complications:</u> puncture site bleeding in 9/792 patients (1.1%), vasovagal reaction to local anaesthetics in 5/792 patients (0.6%), subcutaneous ecchymoses in 3/792 patients (0.4%), and seizures in 1 patient.</p> <p>Conclusions**</p> <p>"Based on the diagnostic efficacy and safety analysis conducted due to systematic review, it should be stated that mammotomy is the most efficacious diagnostic method of non-palpable breast lesions in women (apart from open surgical biopsy treated as the gold standard in clinical trials). It is characterised by the highest accuracy out of all analysed percutaneous biopsy methods."</p>

* Only main findings regarding the intervention of interest (image-guided vacuum-assisted core breast biopsy) are summarized;

** Summarized the conclusions stated by the author(s) or quoted them directly from the published report

Table C1: Selected systematic reviews (characteristics, main findings, and conclusions) (cont'd)

Study (authors, publication date, place)	Study's characteristics	Study's main findings* and conclusions**
<p>Hoorntje et al.³⁹ 2003 The Netherlands</p>	<p>Included studies: 22 clinical studies (information on the study design is not provided)</p> <p>Excluded studies: duplicated publications (where data were collected over the same period of time at the same centre), papers reporting on sonographically guided vacuum assisted breast biopsy, papers in which the diagnostic performance of the vacuum-assisted breast biopsy was not the object of study, studies in which the histological diagnoses from core biopsy and surgical excision or follow-up were not given, papers in which the absolute number of lesions (non-palpable) was not derivable, and papers in which information on follow-up was not available.</p> <p>Participants: patients with (non-palpable) breast lesions</p> <p>Intervention: vacuum assisted breast biopsy with stereotactic guidance</p> <p>Comparator(s): gold standard (surgical biopsy or adequate follow-up), stereotactic 14-gauge automated-needle biopsy</p> <p>Outcome(s) and outcome measure(s): proportion of inconclusive lesions, high-risk underestimate rate, DCIS underestimate rate, and miss-rate</p>	<p>Main Findings*</p> <p><u>Inconclusive biopsy:</u> data reported by seven studies - median value of the proportion of inconclusive lesions: 1.2%;</p> <p><u>High-risk underestimate rate:</u> data reported by 17 studies - for the 11-gauge probe (15 studies): combined high-risk underestimate of 15.9% [CI_{95%} 12.1-19.7%]; for lesions consisting of calcifications only (three studies), the combined high-risk underestimate of 14.5% [CI_{95%}: 7.7-23.9%] - for the 14-gauge probe (three studies): combined high-risk underestimate of 24 [CI_{95%} 19.1-31.5%]</p> <p>-NSS difference between 11-gauge and 14-gauge (p>0.05)</p> <p><u>DCIS underestimate rate:</u> data reported by 15 studies - for the 11-gauge probe (13 studies): combined DCIS underestimate rate was 10.6% [CI_{95%} 8.8-12.4%]; for lesions appearing as calcifications only (two studies): DCIS underestimate rates were 5% and 8% - for the 14-gauge (4 studies): homogeneity test was SS (p<0.01); combined DCIS underestimate of 12.7% [CI_{95%} 9.5-15.9%]</p> <p><u>Miss-rate:</u> due to incomplete follow-up of the benign lesions, the miss-rates and the sensitivity rate could not be calculated</p> <p><u>Complications</u> (three studies): bleeding or hematoma (n=4), vasovagal reaction (n=1), infection (n=1), seizure (n=1), and nausea (n=1).</p> <p>Conclusions**</p> <p>"In conclusion, the results of this review indicate that the vacuum-assisted breast biopsy, in comparison with the 14-gauge automated-needle biopsy, can decrease high-risk underestimate rates and DCIS underestimate rates but it is unclear whether it can decrease the miss-rate of cancer. Therefore at this time it is impossible to assess whether the benefits outweigh the additional costs of the procedure."</p>

* Only main findings regarding the intervention of interest (image-guided vacuum-assisted breast biopsy) are summarized;

** Summarized the conclusions stated by the author(s) or quoted them directly from the published report

Table C2: Objective(s) and methods of selected systematic reviews

Study (authors, publication date, place)	Study's objective(s) and methods
Hetnal et al. ²⁷ 2004 Poland	<p>Objective: to compare diagnostic efficacy and safety of selected methods used in diagnostics of non-palpable breast lesions and find answers to the following questions: 1) what is the accuracy of mammotomy, CNB, and FNAB in diagnostics of non-palpable breast lesions? and 2) what is the impact of the x-ray stereotactic or ultrasound imaging on the accuracy of biopsy? Diagnostic parameters of imaging methods were compared separately (stereotaxy vs. US).</p> <p>Methods:</p> <p>*A literature search for scientific reports pertaining to the diagnostics of non-palpable breast lesions was conducted, using the following sources: Medline (PubMed, Medscape), EMBASE, NHS-DARE, Online databases of medical journals (BMJ, JAMA, American Journal of Roentgenology, Radiology, RadioGraphics, Lancet, Archives of Surgery), CENTRAL, (The Cochrane Central Register of Controlled Trials), The Cochrane Database of Systematic Reviews; the bibliography listed in the identified scientific reports was also searched; the search was limited to studies conducted in humans; the used keywords included: 'vacuum-assisted', 'breast biopsy system', 'Mammotome', 'diagnos*', 'breast', 'lesion', 'cancer', 'palpable', 'non palpable', 'large-core', and 'female'.</p> <p>*RCTs and prospective clinical studies, comparing the specified procedures with gold standard (OBS and/or mammography follow-up for at least 10 months) were searched for; also searched for were case series (retrospective studies); targeted population included females with non-palpable breast lesions diagnosed by imaging methods; All patients included in the analysis were assessed with the gold standard or observed in follow-up.</p> <p>*Each diagnostic method was defined as a combination of 2 procedures: collection of biological material and imaging.</p> <p>*Primary endpoint: survival/mortality, complications, breast cancer detectability, QOL; Secondary endpoints: discomfort associated with the test, hospitalisation length, time to regain normal activity; parameters of diagnostic tests: Sn, Sp, PPV, NPV, LR, accuracy, and DOR.</p> <p>*Meta-analyses were carried out for all the above listed parameters (excluding NPV, PPV, and accuracy) with the use of Meta-Disc software. Patients with non-diagnostic biopsy results (non-diagnostic samples taken) were excluded from the analysis. With respect to the parameters of the diagnostic test the results were obtained from the meta-analyses, with the exception of DOR, LR+ and LR-. The Mann-Whitney U test was used for data not derived from meta-analyses but from rather from single clinical studies. The evaluation of the DOR, LR+ and LR- was carried out based on analysis of confidence intervals. When estimating the percentage of the non-diagnostic biopsies, the studies were not included in the analysis if non-diagnostic results were not reported.</p> <p>*Selected studies were subject to the evaluation of credibility based on the full text of scientific reports and they were included if they fulfilled pre-defined criteria. Two reviewers assessed each study. A third reviewer solved any disagreement or contradiction.</p> <p><u>Sensitivity</u> was defined as the capability of a test to detect disease in subjects where the disease is confirmed; <u>Specificity</u> was defined as the capability of a test to excluded disease in subjects with confirmed lack of disease; <u>PPV</u> was defined as the ratio of the number of truly ill subjects among those with positive test results to the number of subjects with positive results by the diagnostic test; <u>NPV</u> was defined as the ratio of the number of healthy subjects among subjects with negative test results to number of subjects with negative results by the diagnostic test; Likelihood ratio (<u>LR+ and LR-</u>) was defined as the capability of a test to change the likelihood before and after the test in order to aid the correct diagnosis; <u>Accuracy</u> was defined as the percentage of the true positive and true negative results in a sample; <u>DOR</u> was defined as the ratio of odds of a given disease occurrence in the group with positive results for a diagnostic test to the odds of occurrence of this disease in the group with negative results for that test.</p>

Table C2: Objective(s) and methods of selected systematic reviews (cont'd)

Study (authors, publication date, place)	Study's objective(s) and methods
Hoorntje et al. ³⁹ 2003 The Netherlands	<p>Objective: to assess the diagnostic performance of vacuum assisted breast biopsy and to evaluate its potential benefits over 14-gauge stereotactic automated needle breast biopsy.</p> <p>Methods:</p> <p>*The diagnostic performance of vacuum-assisted biopsy was evaluated by reviewing all available English-language literature published in Medline between 1995 and November 2001. Key words used: 'breast AND biopsy AND vacuum' or 'mammotome'</p> <p>*Publications were included in the review if: 1) all histological diagnoses of vacuum-assisted biopsy were confirmed either by surgical biopsy or adequate follow-up for 90% of patients for at least 2 years; 2) the absolute number of benign and malignant diagnoses was derivable; 3) the method of guidance was stereotactic; and 4) the size of the used vacuum probe was described.</p> <p>*The diagnostic performance of the vacuum-assisted breast biopsy was assessed using the method introduced by Burbank and Parker (the histological outcomes were classified according to 4 categories) and the proportion of inconclusive lesions, high-risk underestimate rate, DCIS underestimate rate and miss rate reported in each study were computed; if the study results were homogeneous a combined estimate was computed. *Statistics were performed using SPSS 9.0. For studies with more than 20 lesions, large-approximation 95% confidence interval (CI_{95%}) were calculated for all of the estimates. For studies including 20 or less lesions, exact CI_{95%} (binomial distribution) was used.</p> <p>The <i>inconclusive biopsy results</i> were defined as lesions for which re-biopsy is indicated, because a pathohistological diagnosis concordant with mammographical findings was not drawn from the vacuum-assisted breast biopsy.</p> <p>The <i>high-risk underestimate rate</i> was defined as the percentage of high-risk lesions on vacuum-assisted biopsy that was upgraded to DCIS or invasive cancer in the surgical specimen.</p> <p>The <i>DCIS underestimate rate</i> was defined as the percentage of DCIS lesions on vacuum-assisted biopsy upgraded to invasive cancer at the subsequent excision.</p> <p>The <i>miss-rate</i> was defined as the proportion of all carcinomas with a benign diagnosis on vacuum assisted biopsy.</p>

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