Role of Combined Fine Needle Aspiration and Ultrasonography in the Diagnosis of Impalpable Lesions of the Breast

PICHET SAMPATANUKUL, MD, MSc*,
DARUNEE BOONJUNWETWAT, MD**,
PATCHARAJIREE PAK-ART, MD**

Abstract

Objective : To evaluate the efficacy of combined fine needle aspiration (FNA) and ultrasonography in the diagnosis of impalpable breast lesions.

Method : To analyze the diagnostic performance of the FNA cytology and ultrasound among female patients with impalpable breast lesions that were referred to the FNA clinic at King Chulalongkorn Memorial Hospital and Faculty of Medicine, Chulalongkorn University in Bangkok, Thailand during the period of July 2001 to June 2002. The final diagnoses employed surgical pathology and 6-month follow-up of the patients.

Result : In a-year-period of the studied frame, there were 57 studied cases (18.3% of the total FNA breast cases). To diagnose malignant lesions, FNA cytology achieved the sensitivity of 61 per cent and the specificity of 100 per cent, whereas, diagnostic radiology had a sensitivity of 100 per cent and specificity of 56.1 per cent. The FNA cytology was superior to ultrasound in the determination of inflammatory lesions while imaging was dominant in the hard-to-aspirate malignant lesions. Therefore, the combined cyto-radiology criteria could correctly diagnose malignancy in all cases (100% accuracy).

Conclusion : The efficacy of combined FNA and ultrasonography in the diagnosis of impalpable breast lesions was highly satisfactory. The accuracy of each technique enhanced each other and gave the correct diagnosis in all cases.

Key word : FNA, Impalpable, Nonpalpable, Breast Lesions, Ultrasound Guidance, ACR BI-RADS

**SAMPATANUKUL P,
BOONJUNWETWAT D, PAK-ART P
J Med Assoc Thai 2003; 86 (Suppl 2): S284-S290**

* Department of Pathology,
** Department of Radiology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

The triple test has been emphasized in the management for pre-operative diagnosis of breast lumps[1]. It consists of clinical feature, radiological imaging and cytology. The latter principally employs the fine needle aspiration (FNA) technique. Most carcinomas manifest palpable lumps. Nevertheless, mammographic and ultrasonographic breast screening can lead to detection of early non-palpable breast cancers but at the same time reveal a large number of worrisome lesions that challenge the diagnostic management[2]. This varies from open surgical biopsy under image-guided needle localization, core biopsy, fine-needle aspiration, just for observation, based on the Breast Imaging Reporting and Data System (BI-RADS)[3]. The role of FNA for palpable breast nodules has been widely accepted as the first-line diagnostic means as well as the most cost-effective tool to verify breast cancer[4]. However, FNA's role for non-palpable lesions has not been established. It is compromised by the difficulty of sampling in very small lesions. In some practices, particularly outside the United States, FNA biopsy continues to be widely used, and core biopsy is less frequently advocated[2]. With the stereotactic FNA, Azavedo et al described the results in 2,594 women with mammographically detected occult breast lesions[5]. However, real-time ultrasonography is, nowadays, a more efficiently guided tool[6]. The disadvantage of the direct ultrasound-guided FNA procedure is, that it is more time-consuming and complex compared to an indirect ultrasonographic guidance with skin localization for a separate FNA procedure. The latter has not been a well documented as the former[6]. In view of the simplicity, the authors have been using the ultrasound-guided skin localization technique to perform FNA in our patients since 2001. The authors reported herein the first year results on the efficacy of combined FNA and ultrasonography in the diagnosis of impalpable breast lesions.

MATERIAL AND METHOD

During the period of July 2001-June 2002, the consecutive breast cases in the record file of single-unit approach FNA performed by the author's at King Chulalongkorn Memorial Hospital were analyzed. There were a total of 312 cases, 81.7 per cent of which had FNA by simple palpation at the OPD examination room. The rest which comprised 57 cases needed ultrasound guidance to perform the FNA biopsy.

The technique of aspiration has been fully described elsewhere[7]. Briefly, gauge 22 or 23 needles were used, attached to a 10-ml plastic syringe. When the needles were within the masses or lesions, negative pressure was applied to its full extent. The aspiration biopsy was in like a jerk movement and then the negative pressure was released before removal of the needles. Two to three passes were performed on each patient. The aspirates were pushed onto the slides and smears were made. Wet-fixed preparation and Papanicolaou stain were employed.

For ultrasound guidance, the indirect guide or skin localization of the lesion was employed. The radiologist (DB) made a mark on the skin that was perpendicular to the lesion and then measured for the span of depth as well as the distance perpendicularly from the skin. The aspirator (PS) performed the needle aspiration biopsy as the patient lay in a still position using the same technique as described above. The entering portion of the needle was estimated from the whole length of the needle minus the length of the portion above the skin. After the aspiration biopsy, the radiologist checked the needle tracts by ultrasound.

The radiologists (DB and PP) made the agreement on the radiologic imaging report in each case according to the Breast Imaging Reporting and Data System (BI-RADS) established by the American College of Radiology[8]. The FNA cytology was rendered by the author (PS), conforming histopathological terminology. The final diagnoses were retrieved from the file of the surgical pathology records of the Hospital for the subsequent excision or specific treatment. For the benign cases that did not receive surgery, a 6-month follow-up to confirm the innocence of the lesions was obtained.

RESULTS

There were 255 cases that were classified as palpable and 57 cases classified as impalpable lesions. The patients' ages ranged from 19-85 years (the median age was 42 years).

Of the 255 palpable breast mass cases, there were 2 false negative cases (0.8%) and no false positive cases.

Of the 57 cases with impalpable breast lesions, the patients' ages ranged from 21-85 years (the median age was 47 years) and the greatest dimensions of the masses ranged from 0.4-10 cm (median = 1 cm). The radiology reports were BI-RADS 2 = 11

cases, BI-RADS 3 = 14 cases, BI-RADS 4 = 16 cases, and BI-RADS 5 = 16 cases. Fig. 1. shows the frequency and true malignancy that ocurred in each BI-RADS category. The final diagnoses showed all cases of BI-RADS 2 and 3 were benign conditions. Five and 13 malignant cases were from BI-RADS 4 and 5 categories respectively. Considering BI-RADS 4 and 5 as a positive test by radiology, the sensitivity achieved 100 per cent and the specificity was 56.1 per cent. The benign cases of the BI-RADS 4 included fibroadenoma, ductal hyperplasia, apocrine cyst and inflammatory cyst (Fig. 2), whereas, benign cases of the BI-RADS 5 turned out to be inflammatory lesion and organizing abscess (Fig. 3).

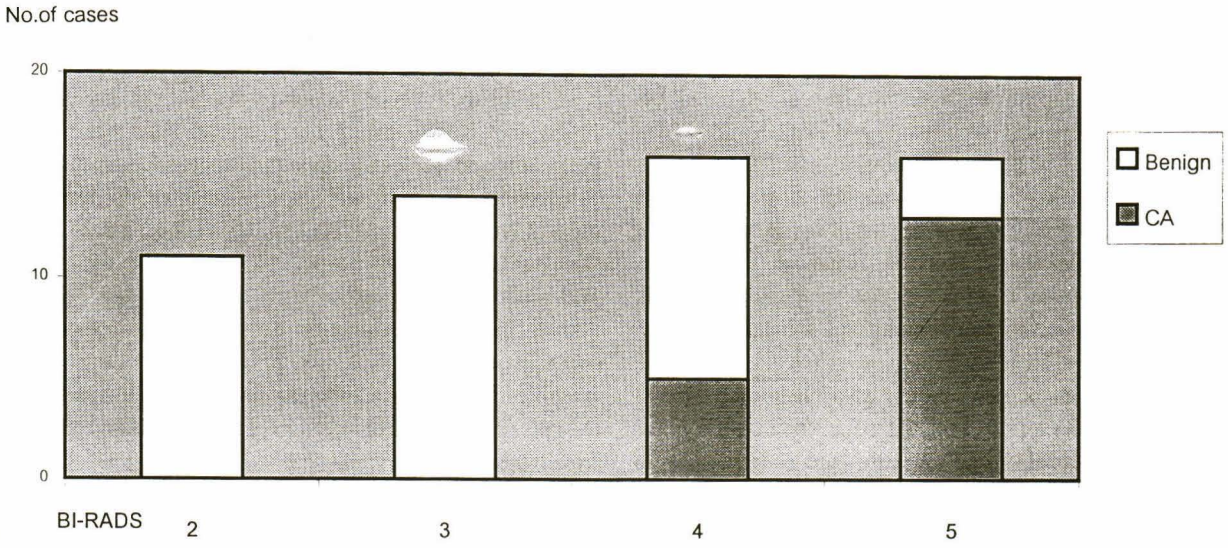


Fig. 1. Bar-graph demonstrates the number of cases and carcinoma cases belonging to each BI-RADS category of the studied population.

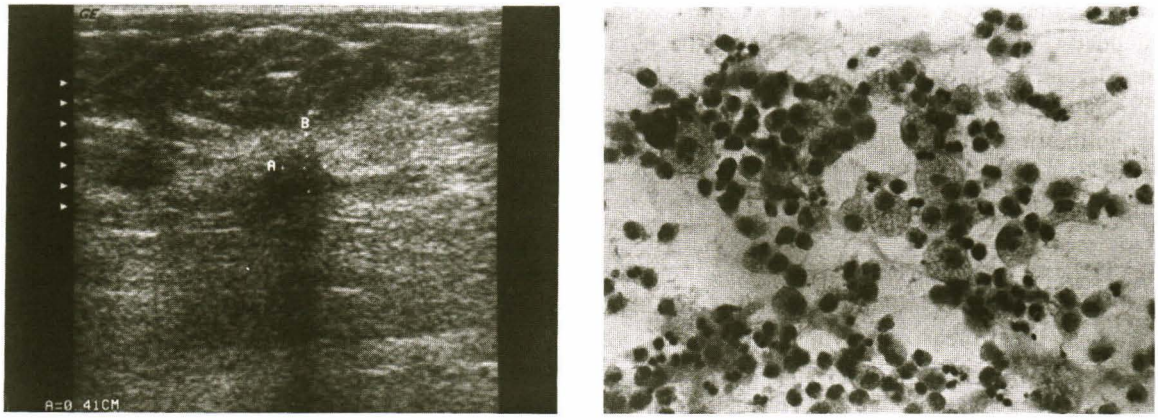


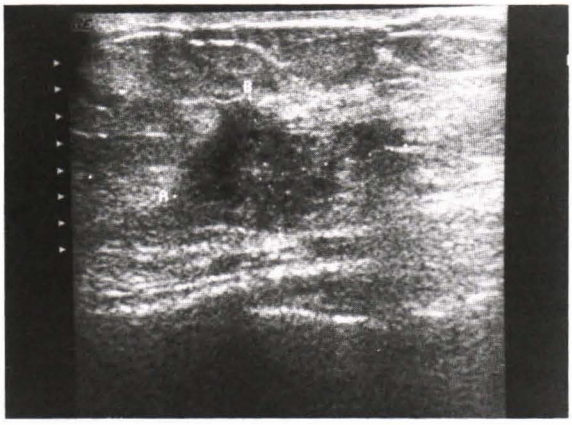
Fig. 2. Inflammatory cyst. Ultrasound illustrates an ill-defined hypoechoic mass with shadow, 4 mm in size (BI-RADS 4). Cytologic smear shows a lot of inflammatory cells and histiocytes. (Papanicolaou, original magnification x 400.)

FNA could make correct diagnosis in 11 out of the 18 carcinomas. Fig. 4. demonstrates one such case that imaging showed a small mass with microlobulation (BI-RADS 4). No false positive cases occurred. The pitfalls of the false negative were from relatively bland-looking appearance of the small carcinoma and scirrhous components. The sensitivity of cytology test for impalpable lesion was 61 per cent and specificity was 100 per cent.

With consensus results from the two diagnostic means, that is to diagnose malignancy needs the combined criteria, the accuracy achieved 100 per cent (Table 1).

DISCUSSION

The terms described as "palpable" and "impalpable" are based on clinical examination. The influencing factors involve size, superficial or deep location, as well as surrounding texture of the masses. In general, a breast mass less than 1 cm in size at its greatest dimension and not located superficially is hard to palpate. When a mass is deeply seated, if it



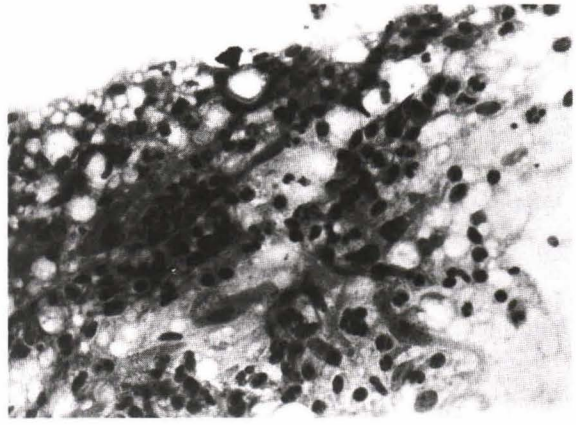
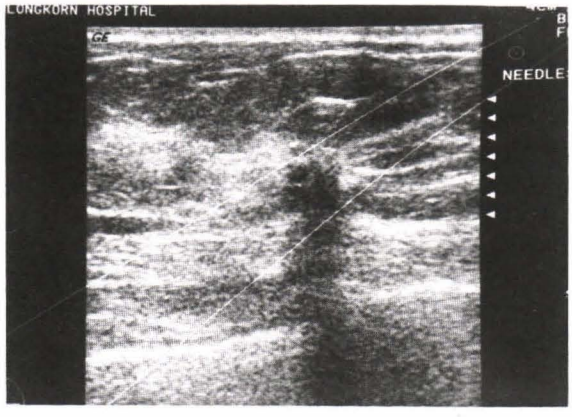


Fig. 3. Organizing abscess. Ultrasound elicits an irregular hypoechoic mass, 10 x 7 mm in size (BI-RADS 5). Cytologic smear displays mixed inflammatory cells and fibroblasts. (Papanicolaou, original magnification x 400.)



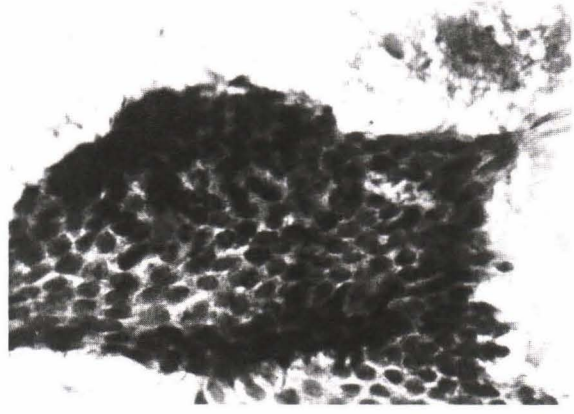


Fig. 4. Carcinoma. Ultrasound reveals a microlobulated hypoechoic mass, 5 mm in size (BI-RADS 4). Cytologic smear exhibits microfragments of malignant neoplastic cells and necrotic debris. (Papanicolaou, original magnification x 400.)

Table 1. Diagnostic performances of the radiology, cytology and combined tests in diagnosis of malignancy of the 57 studied impalpable breast lesion cases.

Diagnostic mean and criteria	Sensitivity %	Specificity %
Radiology (Ultrasound) "BI-RADS 4 and 5"	100	56.1
Cytology (FNA) "malignancy"	61	100
Combined Cytology and Radiology "any BI-RADS with cytologic malignancy OR BI-RADS 5 without cytologic inflammatory lesions"	100	100

is not large enough, it cannot be palpated or is only vaguely palpable. Texture is another character that is important. If a mass is merged with dense fibrous, even it is superficial, sometimes it is difficult to feel the actual lump. To perform an aspiration on breast lumps, the palpable character is pertinent to the aspirator[9]. For vague masses and mammographically or ultrasound demonstrated impalpable masses, imaging guidance is needed. Therefore, the meaning of impalpable masses is those that need FNA performed under ultrasound guidance

Ultrasound is suitable imaging guidance for FNA and can either directly or indirectly guide the needle into the mass. The former is usually performed by skillful radiologists who do the ultrasound[6]. The shadowy echo of the running needle can be demonstrated in real time *via* the monitor. Therefore, it ensures the aspiration point within the mass, however, it is more complex and time-consuming than the latter which radiologists do for skin localization. The mark should be perpendicular to the mass and the depth span as well as the perpendicular distance from the skin to the center of the mass is measured. When the patients lies still on the bed, the aspirator will do the aspiration biopsy with the same technique as for the palpable one. One case can be performed within 15 min with indirectly guided FNA by ultrasound compared with more than 30 min per case when performed with direct guidance. To ensure that the needle is placed within the mass, an immediate post aspiration ultrasound is conducted to check the needle signal.

The first line role of the FNA to diagnose and plan management for any palpable breast lump is accepted nowadays in the hands of an experienced aspirator[10]. This can give a high accuracy as well as the most cost-effectiveness[4,11]. False negative rate is low and usually is due to small lesions and/or desmoplastic stroma, though some cases occur because of cytomorphologic resemblance to benign entities[12]. False positive is aimed at zero. In the present study, the authors achieved this goal. Two false negative cases occurred, both were because of subtle atypia of the tumor cells. No false positive cases were present. Furthermore, in this era of neoadjuvant therapy for locally advanced breast carcinoma, FNA biopsy is often adequate for providing tissue for the biomarkers analysis.

On the contrary, the role of FNA on impalpable small lesions is less than established. One must question the real usefulness of FNA or even core needle biopsy. The argument is that when any suspicious lesions on imaging are coped with, the lesions need removal. Nevertheless, as evident in this study, 18 of the 32 cases (56.1%) that showed BI-RADS 4 or 5 imaging were actual carcinoma. Three cases of BI-RADS 5 which were highly suggestive of cancer turned out to be inflammatory lesions. Therefore, to operate on all suspicious imaging lesions may not be efficient. Two of the three inflammatory cases in the present study recovered with medication without surgery. The inflammatory cyst was cured after aspiration (Fig. 2). On the other hand, FNA in the present study could not rely on its negative test because the sensitivity was 61 per cent but when it reported carcinoma, it was true.

The authors propose the criteria for malignancy from the combined cytology and radiology means (cyto-radiology criteria) which include 2 categories. The first category criterion is any BI-RADS with cytologic malignancy and the second category criterion is BI-RADS 5 without cytologic diagnosis as an inflammatory lesion. With regard to the cyto-radiology criteria, all of the 18 carcinoma cases were correctly diagnosed. Furthermore, the coupled test

will make use of the FNA since FNA alone often gives insufficient samples[13]. On the other hand, the cytologic features were proven diagnostically when sufficient samples were present[14]. These observations were recognized by the authors too and, therefore, the complement of both means in the diagnosis and management for impalpable breast lesions are emphasized.

In conclusion, either ultrasound or FNA cytology has advantages and pitfalls in diagnosing impalpable breast lesions. Ultrasound provides a high sensitivity but modest specificity. It cannot reliably distinguish inflammatory lesions from malignancy. FNA cytology, on the other hand, achieves high specificity but modest sensitivity. The combined ultrasound and FNA cytology result (cyto-radiology criteria) has proven the most accurate. The technique to perform FNA under ultrasound-guided skin localization has verified its simplicity, feasibility and is less time-consuming.

(Received for publication on April 26, 2003)

REFERENCES

1. Silverman JF, Lanin D, O'Brian K, et al. The triage role of fine needle aspiration biopsy of palpable masses. Acta Cytol 1987; 31: 731-6.
2. Dershaw DD. Stereotactic breast biopsy. In: Singletary SE, Robb GL eds. Advanced therapy of breast disease. Hamilton: BC. Decker Inc; 2000: 89-98.
3. Singletary SE, Bevers T, Dempsey P, et al. NCCN practice guidelines: Screening for and evaluation of suspicious breast lesions. Oncology 1998; 12: 89-138.
4. Layfield LJ, Chrischilles EA, Cohen MB, Bottles K. The palpable breast nodule: A cost-effectiveness analysis of alternate diagnostic approaches. Cancer 1993; 72: 1642-51.
5. Azavedo E, Svane G, Auer G. Stereotactic fine-needle biopsy in 2,594 mammographically detected non-palpable lesions. Lancet 1989; 1: 1033-6.
6. Fornage BD. Ultrasound-guided percutaneous needle biopsy of nonpalpable breast masses. In: Singletary SE, Robb GL eds. Advanced therapy of breast disease. Hamilton: BC. Decker Inc; 2000: 99-111.
7. Sampatanukul P. Fine needle aspiration cytology services at Chulalongkorn Hospital. Chula Med J 1992; 36: 311-7.
8. American College of Radiology. Breast imaging reporting and data system (BI-RADS). Reston (VA): American College of Radiology; 1993: 2-3.
9. The uniform approach to breast fine needle aspiration biopsy. A synopsis. Developed and approved at an NCI-sponsored conference, Bethesda, MD, Sep. 9-10, 1996. Acta Cytol 1996; 40: 1120-6.
10. Dabbs DA, Silverman JF. Breast. In: Geisinger KR, Silverman JF eds. Fine needle aspiration cytology of superficial organs and body sites. New York: Churchill Livingstone; 1999: 51-84.
11. Layfield LJ. Can fine needle aspiration replace open biopsy in the diagnosis of palpable breast lesions? Am J Clin Pathol 1992; 98: 145-7.
12. Rogers LA, Lee KR. Breast carcinoma simulating fibroadenoma or fibrocystic change by FNA: A study of 16 cases. Am J Clin Pathol 1992; 98: 155-60.
13. Pisano ED, Fajardo LL, Tsimikas J, et al. Rate of insufficient samples for fine-needle aspiration for nonpalpable breast lesions in a multicenter clinical trial. Cancer 1998; 82: 679-88.
14. Bibbo M, Scheiber M, Cajulis R, et al. Stereotaxic fine needle aspiration cytology of clinically occult malignant and premalignant breast lesions. Acta Cytol 1988; 32: 193-201.

บทบาทของการเจาะดูดด้วยเข็มขนาดเล็กร่วมกับอุลตร้าซาวด์ในการวินิจฉัยรอยโรคที่คลำไม่ได้ของเต้านม

พิเชฐ สัมปทานุกุล, พบ, วทม,*
*ดรุณี บุญยืนเวทวัฒน์, พบ**, พัชราจิรี ภาคอรรถ, พบ***

วัตถุประสงค์ : เพื่อศึกษาประสิทธิภาพของวิธีการตรวจวินิจฉัยก้อนหรือรอยโรคทางรังสีวิทยาของเต้านมที่คลำไม่ได้ โดยการใช้อุลตร้าซาวด์ร่วมกับเซลล์วินิจฉัยของการเจาะดูดด้วยเข็มขนาดเล็ก

วิธีการวิจัย : ประเมินความถูกต้องของผลการวินิจฉัยด้วยวิธีการใช้อุลตร้าซาวด์ร่วมกับเซลล์วินิจฉัยของการเจาะดูดด้วยเข็มขนาดเล็ก ในกลุ่มผู้ป่วยหญิงซึ่งตรวจพบรอยโรคที่คลำไม่ได้ของเต้านม ที่ส่งปรึกษามาที่คลินิกเซลล์วินิจฉัย โรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย และคณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ตั้งแต่เดือนกรกฎาคม 2544 ถึงเดือนมิถุนายน 2545 โดยใช้ผลชิ้นเนื้อและการติดตาม 6 เดือนเป็นเกณฑ์ สำหรับการวินิจฉัยสุดท้าย

ผลการวิจัย : ในระยะเวลา 1 ปีที่กำหนด มีผู้ป่วยที่ศึกษาทั้งสิ้น 57 คน (คิดเป็นร้อยละ 18.3 ของผู้ป่วยโรคเต้านมที่มีการวินิจฉัยโรคที่คลินิก) พบว่าเซลล์วินิจฉัยมีความไวของการบอกว่าเป็นมะเร็งถูกต้องร้อยละ 61 ความจำเพาะร้อยละ 100 ขณะที่รังสีวินิจฉัยมีความไวร้อยละ 100 ความจำเพาะร้อยละ 56.1 ข้อเด่นของเซลล์วินิจฉัยคือการบอกภาวะอักเสบได้เหนือกว่า ขณะที่อุลตร้าซาวด์ให้การวินิจฉัยรอยโรคแทรกซึมของมะเร็งที่เจาะดูดได้ยากได้ดีกว่า ดังนั้นเมื่อใช้การพิจารณาผลร่วมกันของทั้งสองวิธีการ ผลวินิจฉัยจะถูกต้องทั้งหมด (ร้อยละ 100)

สรุปผลการวิจัย : การใช้อุลตร้าซาวด์ร่วมกับเซลล์วินิจฉัยของการเจาะดูดด้วยเข็มขนาดเล็กมีประสิทธิภาพสูงในการตรวจวินิจฉัยก้อนและรอยโรคทางรังสีวิทยาของเต้านมที่คลำไม่ได้ การใช้สองวิธีการร่วมกันสามารถเพิ่มประสิทธิภาพของการวินิจฉัยมะเร็งให้ได้ความถูกต้องทั้งหมด

คำสำคัญ : เซลล์วินิจฉัย, การเจาะดูด, อุลตร้าซาวด์, มะเร็งเต้านม, รอยโรคคลำไม่ได้

พิเชฐ สัมปทานุกุล, ดรุณี บุญยืนเวทวัฒน์, พัชราจิรี ภาคอรรถ
จดหมายเหตุทางแพทย์ ฯ 2546; 86 (ฉบับพิเศษ 2): S284–S290

* ภาควิชาพยาธิวิทยา,
** ภาควิชารังสีวิทยา, คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย, กรุงเทพ ฯ 10330