

Value of Four-dimensional Ultrasonography in Sonohysterography-Guided Biopsy of Focal Endometrial Lesions A Preliminary Clinical Experience

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INTRODUCTION

Three-dimensional ultrasonography (3-D US) with either multiplanar reconstruction or volume-rendering techniques can provide imaging planes not available with 2-D US. It also allows visualization of the surface area of the pathology and their topographical orientation. Reports with the use of 3-D imaging have shown promising results. 3-D sonohysterography offers a comprehensive overview of relationship between lesions and uterine cavity. Thus, it could help to reinforce the diagnostic impression based on 2-D sonohysterography in the detection and depiction of the uterine pathology.

There have been previous studies using 3-D US as guidance in the biopsy procedure. It provided additional spatial information by nature of its ability to simultaneously show structures in 3 orthogonal planes. 3-D US guidance for biopsy offers advantages over current 2-D US guided biopsy technique: Lesion and needle position relative to each other are far more easily understood; There is no worry of losing track of where the lesion is by moving the probe and needle position; The misleading artifactual appearance of correct needle placement when it is positioned at the edge of the lesion seen by the planar nature of 2-D US can be overcome. However, currently published studies used static 3-D imaging as an adjunct to 2-D US guidance.

Four-dimensional US (4-D US) is a new recent technology capable of showing real-time 3-D US imaging instead of static images. It can also be used in the guidance of biopsy to provide real-time 3-D visualization of the exact 3-D relationships of the biopsy device and target lesion. Thus, it has the potential to facilitate more accurate placement of the device within the target lesion in 3-D space during procedure. In addition, sampling error due to lateralization phenomenon whereby the width of the US beam is wider than the width of the needle tip itself seen with 2-D US scanning can be avoided.

Recently, endometrial biopsies can be successfully performed under continuous ultrasound guidance during sonohysterography and its results may be fairly comparable to those of hysteroscopic biopsy. Therefore, the use of 4-D US guidance technique may potentially improve the efficacy of the sonohysterography-guided biopsy of the focal endometrial lesions.

PURPOSE

The purpose of this study was to present the efficacy of four-dimensional ultrasonography in performing sonohysterography-guided biopsy of focal endometrial lesions.

SUBJECTS AND METHODS

SUBJECTS

Twenty-four patients with focal endometrial lesions detected on baseline SH were enrolled prospectively for a six-month period, from July to December 2005. The average patient age was 37.8 years (range 23-53 years).

4-D US GUIDANCE FOR SONOHYSTEROGRAPHIC BIOPSY

8-F Foley balloon catheter and a 5-F Goldstein sonohysterography catheter (Cook OB/GYN, USA) were used for sonohysterography. 3.1 mm flexible or semi-rigid Pipelle endometrial sampler with an inner piston (CooperSurgical, USA) was used as the primary biopsy device. 3-F or 5-F flexible cup biopsy forceps, or 3.0 mm endometrial sampling catheter with a twist-and-Lock syringe (Marina, USA) were also used in a few cases.

TECHNIQUES OF SH-GUIDED BIOPSY

Procedure was performed with written informed consent from the patients. The patients were prepared using antibiotics and analgesics. SH was performed as a baseline before the procedure (Fig. 1). Biopsy device was inserted through the cervical canal into the uterine cavity, right beside the Foley catheter with inflated or deflated balloon. It is then advanced and placed within the target lesion under real-time 4-D US guidance. The device position within the lesion was confirmed. Sampling the tissue specimen was done as withdrawing the inner piston to create a negative pressure, then twirled the catheter while moving slowly back and forth. Suction aspiration technique with a vacuum syringe or aspirator could also be used instead. Multiple sampling of a single lesion or biopsy of multiple lesions was performed by an experienced operator. The average time duration of the procedure was about 20 minutes.

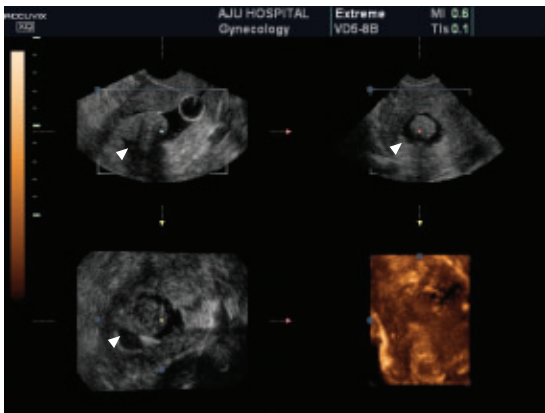


FIGURE 1.
3-D sonohysterographic, multiplanar images and the surface-rendered image of the uterine cavity show polypoid lesion (arrowheads) in the fundus.

4-D US GUIDANCE

3-D and 4-D volume data set were acquired with the use of a 5-8 MHz, endovaginal curved mechanical array volume transducer and Accuvix XQ 3-D US system (Medison, Seoul, Korea). For the standard display method of real-time guidance during the biopsy procedure, Multi Slice views of 3 orthogonal image planes with a 3-D rendering in the surface mode were used. The 3-D rendered image as well as all 3 orthogonal planar views portrayed simultaneously on the ultrasonographic screen were constantly updated in real-time manner. So the movement of the needle tip and placement could be always seen in the during the procedure. We used a 7 cm depth, a 5x7 cm size of the render box, and a 45-50° angle of volume acquisition. The frame rate was 5 frames per second. The cut depth of slice was ranged from 0.5 mm to 5 mm.

We selected the viewing perspective of Multi Slice views in 3 orthogonal planes and the optimal setting of 3-D rendering that maximize the visibility of the biopsy needle and maintains a good depiction of the target lesion. For Multi Slice views of 3 orthogonal image planes, multiple section slice images in the sagittal plane were favored for displaying the relationship between lesion and biopsy device than the single section images of 3 orthogonal planes. For the 3-D rendering method, the shaded or smooth surface mode in sagittal plane was selected after various rendering techniques were evaluated in pilot study. This rendered image corresponded to the view-point of conventional sagittal 2-D ultrasonographic scanning. Finally, the single-section view in 3 orthogonal planes plus a sagittal surface-rendering view (Fig. 2) and/or the multi-section views in sagittal plane (Fig. 3) were used for real-time guidance during the procedure.

3-D volume scans were obtained and a multiplanar analysis with 3-D cine display were performed during procedures as following: An initial scan before the needle was advanced, a prebiopsy scan after the needle was placed within or near the target lesion, to confirm the optimal position of the device tip, and a postbiopsy scan. Volume acquisition is performed and the acquired 3 perpendicular planes of the volumes are fan-shaped with a maximum angle of 80° render box size of 5x7 cm ,

and depth of 7 cm. This size is sufficient to include the entire uterine cavity. During procedure, repeated 3-D volume dataset were acquired to check continuously the exact position of the needle. Within approximately 0.3 seconds the system acquires the entire 3-D volume dataset and displays the information in a multiplanar imaging mode.

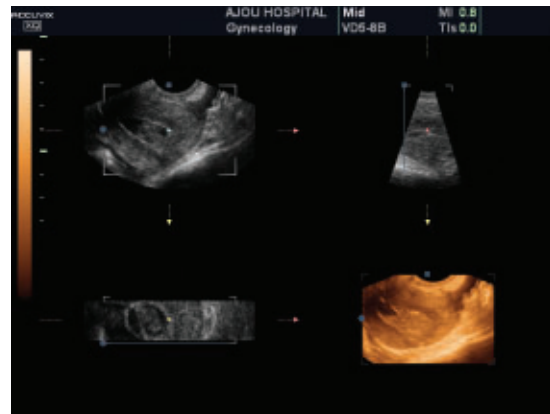


FIGURE 2.
4-D SH multiplanar images and the surface-rendered image. 3 orthogonal real-time planes are perpendicular to one another: The top left image is a source image in sagittal orientation; The top right image is axial planar; The bottom left image is coronal planar. The biopsy device is imaged in each plane simultaneously and in real time. The bottom right image is a real-time 3-D volume-rendered image in the surface mode that is set as a sagittal plane. It provides more constant visualization of the advancement of the biopsy device.

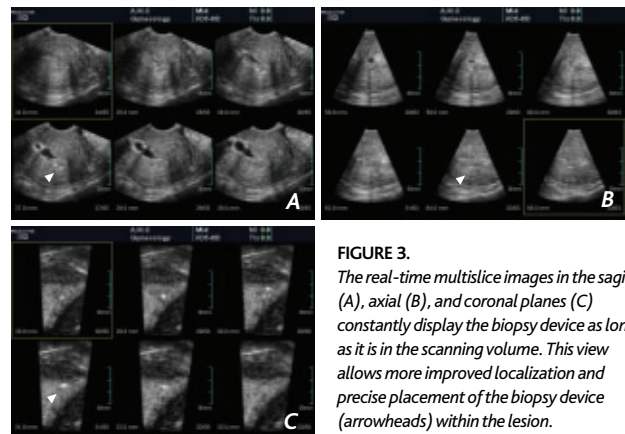


FIGURE 3.
The real-time multislice images in the sagittal (A), axial (B), and coronal planes (C) constantly display the biopsy device as long as it is in the scanning volume. This view allows more improved localization and precise placement of the biopsy device (arrowheads) within the lesion.

ASSESSMENT OF CYTOHISTOLOGIC FINDINGS OF 4-D SH GUIDED BIOPSY

Cytologic results were classified as diagnostic and non-diagnostic aspirates. The findings of diagnostic aspirates were subdivided into benign pathology: proliferative or secretory endometrium; polyp; hyperplasia without atypia; placental polyp; DUB; atrophy; surface endometrium in submucosal lesion or malignancy/suspicious for malignancy: cancer; atypical hyperplasia.

CLINICAL OUTCOME AND DIAGNOSTIC ACCURACY OF 4-D SH GUIDED BIOPSY

Reference standard for the procedure was the final pathologic results by hysteroscopic procedures and hysterectomy, or office endometrial sampling results prior to or subsequent SH guided biopsy. 18 of total 24

patients were performed with surgical procedures: hysterectomy and hysteroscopic polypectomy, curettage, or myomectomy were performed in 6 and 12 patients, respectively. The final pathologic diagnosis of successful 21 patients, 3 failed patients, and 2 patients with non-diagnostic biopsy results were evaluated. We correlated the cytologic results of 4-D SH guided biopsy with the final pathologic diagnosis of endometrium obtained by surgical procedures in 19 patients. And thus we assessed the diagnostic accuracy of the technique.

RESULTS

4-D SH guided biopsies were successfully performed in 21(87.5%) of 24 patients. 3 patients could not undergo SH-guided biopsy due to failure to pass through the cervix or to reach a focal lesion from limited steerability of the biopsy device (n=1, Fig. 4) and inadequate uterine distension with cervical leakage of saline (n=2). For the 3 patients with failure of SH-guided biopsy, polyps were diagnosed with hysteroscopic polypectomy or curettage

Technical Result of 4-D SH Guided Biopsy

Success	87.5%
Failure	12.5%

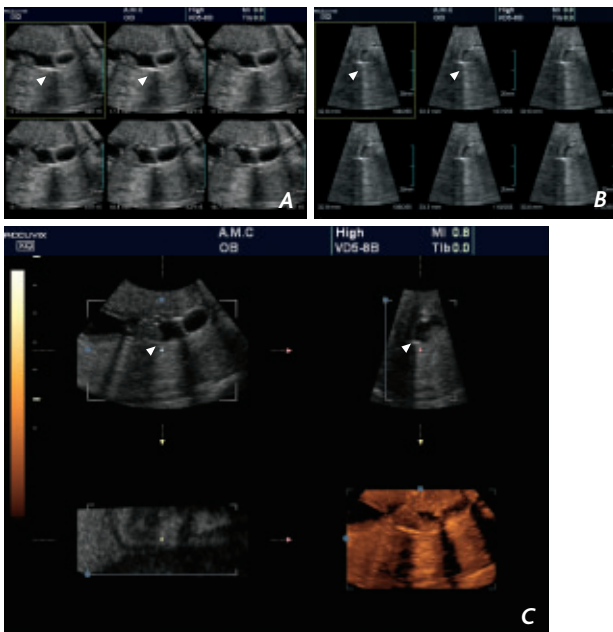


FIGURE 4. Perception of target failure in the real-time multislice SH images in the sagittal (A) and axial planes and 4-D SH multiplanar and the surface-rendered image (C). The biopsy needle (arrowheads) is directed to the mass in posterior wall on Multislice sagittal scan. However Multislice axial scan shows the biopsy needle placed out of position.

The histologic results of sonohysterography-guided biopsy were "Diagnostic" in 19 (90.5%) of 21 patients, with sufficient tissue and adequacy for histologic diagnosis. The results showed "Non-diagnostic" in 2 patients (9.5%) with endometrial polyps, lacking sufficient tissue with blood clot and indeterminate cellular features for histologic diagnosis.

Cytologic Results Obtained by 4-D SH-Guided Biopsy

Diagnostic results	90.5%
Non-diagnostic results	9.5%

Three cases with failure of SH guided biopsy underwent a hysteroscopic polypectomy (n=2) or curettage (n=1). The two patients with non-diagnostic SH guided biopsy result required a subsequent surgical procedure for definite diagnosis by a hysteroscopic polypectomy. Among 19 patients with diagnostic biopsy results, 13 patients had subsequent surgical procedure. The remaining six patients were followed up.

The results of 4-D SH guided biopsy were well correlated in all of the 19 cases with the final pathologic diagnosis obtained at surgery.

Pathologic Diagnosis in Patients with Diagnostic and Non-diagnostic 4-D SH-Guided Biopsy results

Diagnosis	Diagnostic	Nondiagnostic
Endometrial polyp	8	2
Endometrial hyperplasia	3	
Endometrial carcinoma	2	
Placental polyp	1	
DUB	1	
Surface endometrium*	4	

*Evidence of typical surface endometrium overlying submucosal lesion only, but impossible diagnosis of submucosal lesion

DISCUSSION

The cause of abnormal uterine bleeding is mostly benign and functional. However, a reported incidence of cancer is 5%-17% in peri- and postmenopausal women with bleeding and incidence of cancer in high risk young patients is increasing. Therefore, tissue sampling is required to confirm the presence of cancer in the endometrial abnormalities to exclude endometrial carcinoma and precancerous lesions. Pipelle endometrial sampling is currently used for assessment of the endometrium in women with abnormal uterine bleeding. It is sensitive for detection of diffuse endometrial lesion, such as cancer and atypical hyperplasia, but has the risk of missing focal lesion. It also has a failure rate of 30% and non-diagnostic in 47% (2-28%) of cases. Endometrial sampling was missing 50% of polypoid lesion seen on SH, with a false negative rate of 5-15%. Hysteroscopic biopsy remains as the gold standard for diagnosis and treatment with sensitivity of 100%



and specificity of 80% for histologic conformation of focal endometrial lesions although its invasiveness and much cost.

Endometrial biopsies have been performed under continuous US guidance during sonohysterography. The results of recent reports show low feasibility and poor correlation with pathologic diagnosis: The failure rate is about 16-27% and high rate of insufficient or uninterpretable samples of 21-40%. However, our results suggest that sonohysterography-guided biopsy for suspected focal endometrial lesions are feasible in most patients with high success rate of 87.5%. And it is shown to be accurate for the diagnosis of focal endometrial lesions with high rates of diagnostic yield (90.5%). Thus, its results may be fairly comparable to those of hysteroscopic biopsies.

Recently, 4-D US imaging has been used to guide the invasive obstetric procedures and biopsy of focal hepatic masses. They have suggested that the real-time feature of 4-D US might be useful by enhancing depiction and better understanding of the geometric relationships of the biopsy devices to target lesions, and guiding the biopsy procedures successfully. To our knowledge, this is the first report to study the use of 4-D US guidance for sonohysterography-guided endometrial biopsy. In our study, this technique effectively guided advancement, targeting, and positioning of the biopsy device: It provides improved constant visualization of biopsy devices and more perceptible information on the spatial relationship between the lesion and the device. We suggest that mixing the single or multi-section views in 3 orthogonal planes and the surface-rendering mode is well suited to visualizing the biopsy device and target lesion simultaneously. Real-time 3-D visualization of the biopsy device with multiple imaging planes would allow improved localization of the biopsy device and accurate, rapid placement of the device tip within the lesion. Thus, 4-D US improves the safety and accuracy, and thereby increasing operator's confidence in performing sonohysterography-guided biopsy of focal endometrial lesions.

Limitations and pitfalls of sonohysterography-guided endometrial biopsy include: improvements of the device as well as aspiration technique; technical difficulties in cervical insertion of biopsy device, targeting, managing cervical leakage of saline and operator's technical inexperience; non-diagnostic, false-negatives results with insufficient tissue, indeterminate cellular specimen, or sampling errors; suboptimal quality of guiding imaging methods with 4-D US, low resolution of multiplanar reconstructed images and poor quality of images due to movement artifact and air shadowing in the endometrial surface.

CONCLUSIONS

4-D US guidance is easier and may improve the efficacy of the sonohysterography-guided biopsy of the focal endometrial lesions. With improvement in technology of 3-D or 4-D US, biopsy device, operator's technical experience, this technique could be more feasible alternative to hysteroscopic endometrial biopsy.

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