# Pain Experienced Using Two Different Methods of Endometrial Biopsy

## *A Randomized Controlled Trial*

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**OBJECTIVE:** To compare patient-reported pain, provider-reported ease of use, and tissue sampling adequacy between endometrial biopsy instruments.

**METHODS:** Women presenting for endometrial biopsy were randomized to either Pipelle or Explora curette. The primary outcome was patient-reported pain with biopsy as measured by a 100-mm visual analog scale. Secondary outcomes included the adequacy of biopsy sample and provider-reported ease of instrument use.

**RESULTS:** Groups were similar in respect to age, parity, ethnicity, level of dysmenorrhea, menopausal status, and biopsy indication. The most common indication for biopsy was abnormal uterine bleeding. Subject reported pain with biopsy was similar between groups (Pipelle, 6.21±2.41 cm; Explora, 6.91±2.88 cm; $P$=.14), as was provider-reported ease of use. Although procedure length was significantly shorter for patients in the Pipelle group (4.05±1.48 minutes compared with 5.27±2.53 minutes; $P$=.007), 38% of Pipelle procedures required two or more passes to obtain a sample compared with only 9% using the Explora ($P$=.004). The Explora group had a higher proportion of adequate samples (97% compared with 91%; $P$=.33).

**CONCLUSION:** Women's pain during endometrial biopsy does not differ by type of biopsy instrument used.

**CLINICAL TRIAL REGISTRATION:** ClinicalTrials.gov, www.clinicaltrials.gov NCT00613925.

*(Obstet Gynecol 2011;117:636–41)*
*DOI: 10.1097/AOG.0b013e31820ad45b*

**LEVEL OF EVIDENCE: I**

Outpatient endometrial biopsy is a widely accepted means of evaluating the endometrium.[1–3] In the outpatient setting, the ideal endometrial biopsy device is easy to use and efficiently procures an adequate endometrial sample without creating a painful experience for the patient. Currently, instrument selection is solely based on provider preference.

As the first disposable biopsy device available in the United States, the Pipelle de Cornier (Unimar) is the most studied biopsy device in the literature. It is a 23.5-cm-long, flexible, polypropylene sheath with an outer diameter of 3.1 mm and a single 2.4-mm opening on its distal end. An inner plunger is withdrawn, creating suction along a negative pressure gradient. The Pipelle since has been compared with numerous other biopsy devices. These studies all support the Pipelle as an adequate and equal, if not preferable, sampling device, particularly regarding decreased patient-reported pain.[3–12]

Little data exist comparing a relatively new device, the Explora curette (Milex)[7,13,14] with the Pipelle.[7] The Explora is slightly more rigid than the Pipelle and has a sharp, Randall-type cutting edge on one side of its distal end; it is 19.7-cm-long, with an outer diameter of 3.0 mm, and suction is created by pulling back on a locking syringe. A randomized study by Lipscomb et al[7] found similar pain scores and sample adequacy with the Pipelle and Explora sampling technique using a 10-point ordinal scale.

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*The authors thank the Women's Health Research Unit at Oregon Health and Science University for their donated administrative support.*

*Presented at the Oregon Section of the American College of Obstetricians and Gynecologists Annual Clinical Meeting, April 10, 2010, Bend, Oregon.*

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***Financial Disclosure***
*Dr. Morgan is funded by the Office of Research on Women's Health and the National Institute of Child Health and Human Development, Oregon, BIRCWH grant number HD043488-08. The other authors did not report any potential conflicts of interest.*


ISSN: 0029-7844/11

However, this study did not adjust for baseline pain, provider acceptability, or ease of use.[7] The purpose of this study was to compare two endometrial biopsy instruments (Pipelle and Explora curette) by objectively measuring patient-reported pain, provider-reported ease of use, and tissue sampling adequacy.

## MATERIALS AND METHODS

A prospective, blinded, randomized, clinical trial was conducted at Oregon Health and Science University in Portland, Oregon, from January 2008 to August 2009. The Oregon Health and Science University Institutional Review Board approved the study protocol, and all study participants submitted written informed consent.

Nonpregnant literate women older than 18 years presenting with an indication for an endometrial biopsy were recruited from the Center for Women's Health at Oregon Health and Science University. Women were excluded if they had cervical stenosis, uterine anomalies or leiomyomas that distorted the cavity, clotting disorder, history of uterine or cervical surgery, current sexually transmitted infection, purulent cervicitis, puerperal or postabortion sepsis, or pelvic inflammatory disease within the past 3 months.

After consent, eligible participants were randomly assigned to a biopsy device (Pipelle or Explora curette) through a computer-generated randomization scheme controlled by off-site research staff and not accessible to study providers. Whereas the providers could not be blinded to the device allocation, study participants were blinded to group allocation. Patients were not shown the device and references to the type of device were not made. The randomization key was provided to research investigators only after data analysis. Demographic information was collected from the participants before the procedure. Women who were not using a reliable form of contraception or who were premenopausal menopausal underwent a urine pregnancy test before their biopsy. The endometrial biopsy was performed in a standardized fashion, which included speculum placement, cervical preparation, local anesthetic spray to the face of the cervix (no paracervical block), tenaculum placement, and biopsy. The number of curette passes through the cervix to subjectively obtain an adequate sample was at the discretion of the provider.

Participants completed visual analog scales at the following time points: before speculum placement (positioning), during speculum placement, during endometrial biopsy, and 5 minutes after the procedure. The primary outcome for this study was patient-reported pain at the time of biopsy. Secondary outcomes included provider-reported ease of the procedure and histopathological adequacy of the biopsy sample by routine hematoxylin-eosin-stained histologic sections. Sample adequacy was defined as the presence of both endometrial glands and stroma. Ease of use was rated using a 5-point Likert scale (1=easiest, 5=most difficult). The adequacy of the biopsy samples was determined by a single pathologist with expertise in gynecologic pathology blinded to group allocation. Additionally, uterine size (by bimanual examination and sounding), number of curette passes (insertion of the sampling device through the internal os to the fundus and complete removal of the device from the external os), procedure length (speculum placement to speculum removal, including all passes if more than one), need for dilation, need for additional pain medication or paracervical block, and adverse events were recorded.

We hypothesized that there would be less pain reported by participants in the Pipelle group (more flexible, no cutting edge, and less negative pressure). Because this research was performed as part of a resident research requirement and funds were limited, a one-sided sample size analysis was used to keep the sample to a reasonable number. To demonstrate a 20-mm decrease in pain on a 100-mm visual analog scale, a sample size of 35 women per group was calculated (80% power, $\alpha=0.05$, assuming a standard deviation of approximately 30 mm; PASS 2005 Software).[15] Mean visual analog scale pain scores for both groups were compared at each time point using nonparametric testing (Mann Whitney *U* test) or, if normally distributed, by an independent sample *t* test. Categorical data were analyzed by Fisher exact test. All statistics were performed according to intent to treat, except when noted and analyzed using SPSS software.

## RESULTS

Of the 70 women who enrolled in the study, 69 completed all study procedures. Study flow is documented in Figure 1. There were no statistically significant differences in baseline characteristics between the two study arms, including race, gravidity, parity, menopausal status, and characterization of menstrual periods (Table 1). The majority of the participants in both groups were premenopausal. The most common indication for biopsy was abnormal uterine bleeding, followed by postmenopausal bleeding (Table 1).

Attending physicians performed the majority of the procedures, with no differences in provider level of experience between the groups (Table 2). Although the estimation of uterine size by bimanual examina-

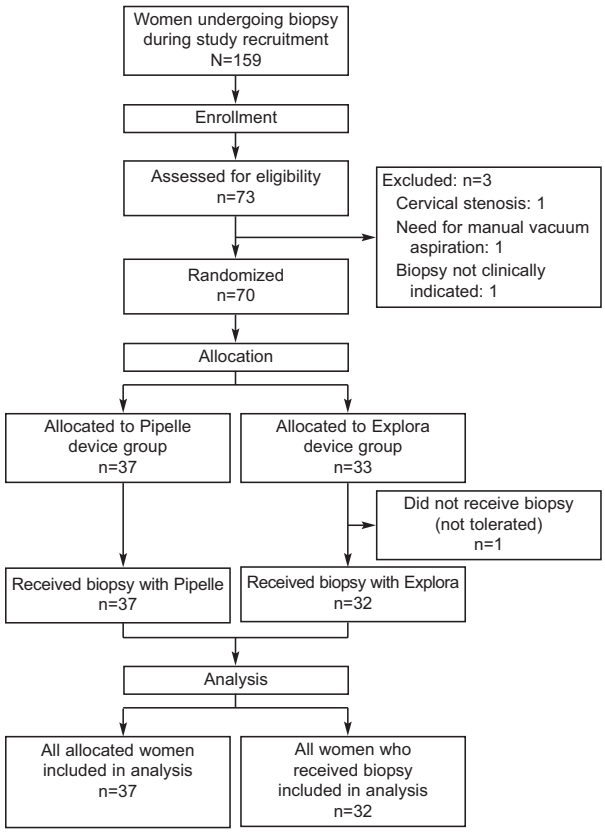


**Fig. 1.** Study flow.
*Leclair. Pipelle or Explora for Endometrial Biopsy. Obstet Gynecol 2011.*

tion was the same between groups, uterine size by uterine sound was slightly larger in the Explora group, but this was not statistically significant (range, 5–12 cm compared with 6–10.5 cm; *P*=.08; Table 2).

Providers had no clear preference for either device according to ease of use measurements (Fig. 2), and this was not influenced by provider experience level (attending compared with resident). Slightly more providers rated the Pipelle "easiest" or "easy," whereas the Explora was more often rated "average" or "hard," but this was not statistically significant. Although the majority of samples were obtained with only one pass from either device (n=52 of 69), a significantly greater number of procedures performed with the Pipelle required two or more passes (14 compared with 3; *P*=.004). Procedure length was significantly shorter in the Pipelle group (4.1±1.5 minutes compared with 5.3±2.5 minutes; *P*=.007; Table 2). When participants requiring multiple passes were excluded in a subanalysis, procedure length was still significantly shorter in the Pipelle group. The significant differences in biopsy passes and procedure time were not influenced by provider experience level or specific individual providers. Seven patients required dilation (Pipelle, n=3; Explora, n=4) to complete their biopsies. Excluding these participants in a subanalysis did not alter the difference in procedure time found between the groups.

Histologic analysis did not reveal any samples with hyperplasia or malignancy. Although not statistically significant, the Explora group had a higher proportion of adequate samples (96.8% compared with 91.2%; *P*=.33; Table 2).

There were no significant differences in pain scores at the time of endometrial biopsy (Pipelle, 6.21±2.41 cm; Explora, 6.91±2.88 cm; *P*=.14) or at any other time point except at baseline, with participants in the Explora group demonstrating significantly more pain (Pipelle 0.35±0.74 cm compared with Explora 1.12±1.59 cm; *P*=.01; Fig. 3). Analyzing the procedure-related pain scores as the change in pain from baseline did not reveal any significant differences in pain scores between the two groups. Additionally, there were no significant differences in premedication between groups. Excluding the premedicated participants in a subanalysis did not alter any of the outcomes measured.

## DISCUSSION

In this randomized comparison trial of the Pipelle and Explora endometrial biopsy devices, no significant differences were demonstrated in patient-reported pain or provider-reported ease of use. Some advantage may be afforded to the Pipelle because procedure length was slightly shorter (1 minute), but almost 40% of Pipelle biopsies required more than one pass through the cervix. This was an unexpected finding of our study, and it is unclear whether this is a result of provider preference, patient tolerance, or necessity for tissue adequacy. Nonetheless, this study was powered to identify only if use of the Explora curette was more painful than use of the Pipelle, and we found that patients reported a similar pain experience between the two instruments.

More importantly, our limited results demonstrated that 97% of Explora samples were adequate compared with only 91% of Pipelle samples. Although not statistically significant, the difference in biopsy adequacy of this magnitude may be clinically important. However, great caution should be taken during interpretation of this finding because our study was not powered to determine this outcome (power=18%). Moreover, the majority of our participants were premenopausal, and concerns of specimen adequacy may be more important in postmenopausal

**Table 1. Demographic Information**

| | Pipelle | | | | Explora | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | n | # | % | Mean±SD | n | # | % | Mean±SD | *P* |
| Age (y) | 37 | | | 45.2±7.3 | 32 | | | 46.1±7.7 | .31* |
| Race | 37 | | | | 29 | | | | .31† |
| White | | 35‡ | 94.6 | | | 26§ | 89.7 | | |
| African American | | 1 | 2.7 | | | 2 | 6.9 | | |
| Asian | | 1 | 2.7 | | | 0 | 0 | | |
| More than one race | | 0 | 0 | | | 1 | 3.4 | | |
| Gravidity (1 or more) | 36 | 28 | 77.8 | | 30 | 21 | 70.0 | | .33‖ |
| Parity (1 or more) | 26 | 25 | 100 | | 21 | 19 | 90.5 | | .42‖ |
| Menstrual status | 35 | | | | 32 | | | | .47† |
| Premenopausal | | 19 | 54.3 | | | 18 | 56.3 | | |
| Perimenopausal | | 8 | 22.9 | | | 9 | 28.1 | | |
| Postmenopausal | | 8 | 22.9 | | | 5 | 15.6 | | |
| Characterization of menses | 24 | | | | 26 | | | | .34* |
| Easy | | 2 | 8.3 | | | 1 | 3.8 | | |
| Mild cramping, does not require medication | | 4 | 16.7 | | | 8 | 30.8 | | |
| Moderate cramping, requires over-the-counter medication | | 14 | 58.3 | | | 9 | 34.6 | | |
| Moderate cramping, requires prescription medication | | 2 | 8.3 | | | 5 | 19.2 | | |
| Severe cramping, interferes with work or school | | 2 | 8.3 | | | 3 | 11.5 | | |
| Hormones | 36 | | | | 30 | | | | .30‖ |
| None | | 31 | 86.1 | | | 23 | 76.7 | | |
| Vaginal estrogen | | 0 | 0 | | | 0 | 0 | | |
| Oral estrogen | | 1 | 2.8 | | | 2 | 6.7 | | |
| Oral progesterone | | 1 | 2.8 | | | 1 | 3.3 | | |
| Combination hormone replacement therapy | | 3 | 8.3 | | | 3 | 10.0 | | |
| Other | | 0 | 0 | | | 1¶ | 3.4 | | |
| Premedicated | 34 | 3 | 8.8 | | 32 | 2 | 6.3 | | .37‖ |
| Indication | 37 | | | | 32 | | | | .48† |
| Abnormal uterine bleeding | | 26 | 70.3 | | | 24 | 75.0 | | |
| Postmenopausal bleeding | | 5 | 13.5 | | | 4 | 12.5 | | |
| Cancer screening | | 1 | 2.7 | | | 1 | 3.1 | | |
| Previous diagnosis of endometrial hyperplasia | | 1 | 2.7 | | | 1 | 3.1 | | |
| Atypical squamous cells (atypical glandular cells of unknown significance) | | 1 | 2.7 | | | 2 | 6.3 | | |
| Other | | 3 | 8.1 | | | 0 | 0 | | |

SD, standard deviation.
* Mean scores or normally distributed ordinal data analyzed by independent sample *t* test.
† Ordinal data analyzed by nonparametric Mann Whitney *U* test.
‡ Includes five patients who identified as Latina or Hispanic.
§ Includes three patients who identified as Latina or Hispanic.
‖ Categorical data analyzed by a Fisher exact test.
¶ Mirena intrauterine device.

women. Specimen adequacy remains an unresolved issue with these devices and should be further assessed in future studies.

A major strength of our study design was the careful assessment of baseline pain. Although the typical demographic indicators (age, race, parity) demonstrated no significant differences between groups, influences on pain response are complicated and our randomization strata may not have equalized the groups as well as we had hoped. To compensate for this, we assessed baseline pain. Although the baseline pain scores were significantly higher in the Explora group, a significant difference did not persist at the other time points.

**Table 2. Provider Information**

| | Pipelle | | | | Explora | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | n | # | % | | n | # | % | | *P* |
| Provider level | 37 | | | | 32 | | | | .06 |
| Resident | | 10 | 27.0 | | | 16 | 50.0 | | |
| Fellow | | 1 | 2.7 | | | 0 | 0 | | |
| Attending | | 26 | 70.3 | | | 16 | 50.0 | | |
| Adequate sample | 34 | 31 | 91.2 | | 31 | 30 | 96.8 | | .33* |
| Uterine size (bimanual examination) | 34 | 7 (5–27) | | | 29 | 7 (5–24) | | | .44 |
| Uterine length (sound) | 36 | 8.0 (6–10.5) | | | 32 | 8.0 (5–12) | | | .083 |
| Passes | 36 | 1 (1–4) | | 1.53±0.77 | 31 | 1 (1–4) | | 1.16±0.58 | .004 |
| 1 | 22 | | | | 28 | | | | |
| 2 | 10 | | | | 2 | | | | |
| 3 | 3 | | | | 0 | | | | |
| 4 | 1 | | | | 1 | | | | |
| Procedure time (min) | 35 | | | 4.05±1.48 | 30 | | | 5.27±2.53 | .007 |

Data are median (range) or mean±standard deviation unless otherwise specified.
All *P* values were obtained using the nonparametric Mann Whitney *U* test, except for *when categorical data was analyzed by a Fisher exact test.

Additional limitations include the inherent bias that each provider may have had toward a particular biopsy instrument or the unfamiliarity with one device over the other, because providers could not be blinded to group allocation. These issues may have influenced the length of procedure time or the number of passes performed. For example, if providers think the Pipelle is better tolerated, then they might be more apt to perform a second pass to ensure sample adequacy. Nonverbal or verbal cues from the provider regarding the instrument also may have influenced the patient pain response.

Overall, the findings of this study are consistent with the body of literature on the Pipelle curette, which has shown that it is either equal or preferable to the comparator devices with respect to ease of use and patient tolerability. The strengths of our study include its randomized design, validated pain scales, and blinded analysis of specimen adequacy. Our study specifically corroborates findings from the only other study to directly compare the Pipelle to the Explora. Lipscomb et al[7] reported there were no statistically significant differences in pain with either biopsy device or in sampling adequacy. Although Lipscomb et al[7] did not find a significant difference in sampling adequacy, other studies[4,8,16] have found the Pipelle to be inferior in obtaining adequate tissue samples.

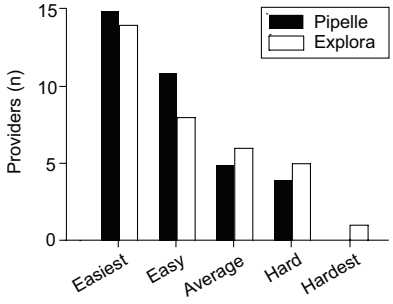


**Fig. 2.** Provider ease of use (Mann-Whitney *U*, *P*=.30).
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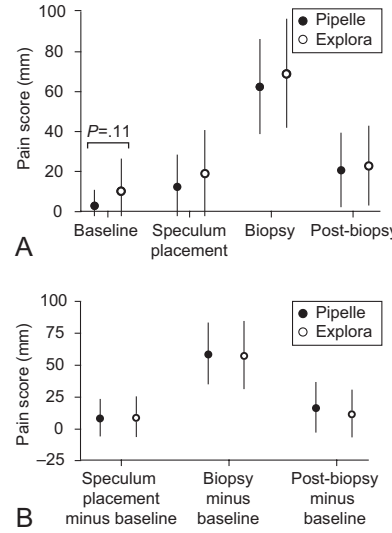


**Fig. 3. A.** Patient-reported mean visual analog scales pain scores (anchors: 0 mm=no pain, 100 mm=worst imaginable pain; Mann-Whitney *U*). **B.** Paired mean pain scores (baseline score subtracted from each time point; Mann-Whitney *U*).
*Leclair. Pipelle or Explora for Endometrial Biopsy. Obstet Gynecol 2011.*

In summary, our findings do not support that either the Pipelle or the Explora curette is a superior endometrial biopsy instrument from the patient perspective. Pain scores and ease of use were equal between groups, with no clear advantage of one over the other. Although biopsies performed with the Pipelle required less time but required more passes, neither of these findings likely has clinical significance.

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