

## **Modern Methods of Early Detection of Endometrial Cancer on the Example of “Pipelle” Urogenital Probe**

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### **ABSTRACT**

Today, at a time when cancer is developing rapidly, a number of scientific studies are being conducted worldwide in the field of early detection, prevention and treatment of the disease. A number of new methods are being recommended by experts to put into practice, which is convenient, effective, rapid, uncomplicated and painless methods of early detection of tumor diseases especially uterine cancer in women.

**KEYWORDS:** women, Cancer, diagnosis, Pipelle-urogenital, Pipelle, Atypic hyperplasia, Endometriosis

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### **INTRODUCTION**

Uterine cancer is one of the most dangerous and prevalent cancers in the world, and its most common symptom is pathological bleeding from the uterus [34]. Obesity, age  $\geq 40$  years, diabetes, hypertension, taking estrogen-containing drugs, treatment with tamoxifen, hereditary predisposition, insufficient physical activity are currently the most common causes of this pathology in the world [34,24]. Endometrial curettage is the most widely used and popular method in the medical institutions of our Republic for the detection of precancerous diseases that cause uterine cancer, uterine hyperplasia, atypical cellular hyperplasia and uterine endometrial polyps. Endometrial curettage is now rarely used worldwide. Because this method can cause many inconveniences and complications such as profuse bleeding, there is a need to resort to new effective methods [34].

Uterine cancer is the fourth most common cancer for women in the United States. The prevalence of endometrial cancer worldwide over the past years: In 2012 endometrial cancer [35,32] was diagnosed in 527,600 women in the globe with the mortality rate 1.7 to 2.4 per 100,000 women. In the United States EC incidence was 61,380 new uterine cancer cases in 2017, with almost 11,000 deaths from the disease [35, 32]. Up to now, the American Cancer Society has identified about 66,570 new cases of endometrial cancer

by 2021, of which about 12,940 have died from this diagnosis.

The most common complaint in women with endometrial cancer during menopause is bleeding, which makes diagnosis easier. Almost 75% of women who complain of acyclic bleeding during menopause are diagnosed with uterine cancer at an early stage [4,9,6], which further increases the effectiveness of treatment. Patients who complain of abnormal bleeding are first examined by ultrasound, endometrial thickness is assessed, and a histological sample is taken from the uterine endometrial layer to confirm the diagnosis, because the diagnosis of uterine cancer is based on endometrial sample results [24]. There are various methods of sampling the uterine endometrium in foreign countries, including diagnostic uterine incision, hysteroscopy, Pipelle-urogenital probe sampling, Vabra Z-sampler, Mi-Mark cell sampler, Isaacs cell sampler, Gynoscann device, Endorette, Tao Brush, SAP- 1 device and others have been used [27,20,23,15]. However, none of the methods listed above allowed a complete assessment of uterine endometrial tissue.

### **THE MAIN FINDINGS AND RESULTS**

The uterine cavity scrapings was developed by Recamier in 1840 and has been used for many years as the "gold standard" for endometrial sampling.(31) This method, which

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has been popular for about 176 years, has many complications, such as bleeding, uterine perforation (60% of cases) [14]. It was found to be an expensive procedure, especially in the USA, with a high rate of complications and significant social impact due to complications such as pain, risk of infection, and an increased likelihood of tumor cell proliferation [34]. Vacuum curettage the Vabra aspiration was introduced by Jensen in 1968 to assess endometrial status in uterine body diseases [18]. The Vabra aspiration system is a stainless steel cannula of 4.2 mm in diameter attached to a portable electric vacuum pump. Since its invention, there have been around 30 studies confirming excellent patient acceptance and diagnostic value with the Vabra aspirator [25]. However, later it was found that utilization of the Vabra method is not very good at detecting polyps and could miss early cancers [31]. Utilization of the Gynoscann method comprises a disposable, plastic curette of 3 mm in diameter, consisting of two flexible wings attached to the end of a flexible rod and contained in a thin tube [20,30]. There were many studies of the Gynoscann method and its effectiveness. However, according to comparative studies, Gynoscann cannot replace curettage without the risk of overlooking significant pathology [20].

The most recent from the above-mentioned techniques, SAP-1 device, was patented and approved to be used in China in 2001 [15]. The sheath of this device is 25 cm in length and 3 mm in diameter. SAP-1 is becoming a reliable method for screening EC and its precursors, especially as it shows high reliability: sensitivity 73%, specificity 95.8%, positive predictive value (PPV) 75% and negative predictive value (NPV) 95.3% [15,36]. The challenges in this procedure encouraged physicians to find and implement a safer, less invasive, more accurate, and easier-to-use method for endometrial sampling. Such methods have been tested in practice for years, The most popular vacuum aspiration device for office sampling

procedure is the “Pipelle” device invented in 1984 by Cornier E., Paris, France [11,27]. Moreover, Eddowes in 1990, Youssif and Mcmillan in 1995. Leng in 2013, Fakhar et al. in 2008; Elsandabesee and Greenwood in 2005; Machado et al., in 2003; Dijkhuizen et al., in 2000; Sundsbak and Jebsen in 1994; Zorlu et al. In 1994; Sanam and Majid in 2015; Ben-Baruch et al. in 1994; In 2011, Leclair conducted various scientific studies on the method of sampling the endometrial part of the uterus using the “Pipelle” urogenetic probe [14,27].

There are several types of “Pipelle” urogenetic probe such as:

1. “The Pipelle de Cornier” is a flexible polypropylene tube, with an external diameter of 3.1 mm and an internal diameter of 2.6 mm. The sheath measures 23.5 cm in length and has a soft endouterine end. There is a perforation, 2.4 mm in diameter, near the endouterine end of the sheath [11]. During the removal of an internal piston, negative pressure is created and endometrial tissue comes into the cannula. . 2. “Pipelle H” has the same outer and inner diameters as “Pipelle de cornier” and is 50 cm long [12]. “Pipelle H” device was developed at the Royal Free Hospital in London for histological sampling during routine hysteroscopies. [22,26]. “Pipelle Mark II” (Laboratoire CCD, Paris, France) is the only device providing samples for both histology and cytology in one single attempt/procedure; and it is a possible explanation of its high efficacy [28].

“Pipelle” urogenetic probe biopsy is superior to other methods in detecting endometrial cancer and atypical hyperplasia. “Pipelle” urogenetic probe accuracy is relatively high in postmenopausal and premenopausal women (Cancer 2000; 89: 1765-72. © 2000 American Cancer Society). This method is very popular because it is convenient and simple, painless, and less invasive. It allows you to take a sample of 4-10% of the endometrial surface and obtain data with a sensitivity of up to 97% [19].



Figure-1. Type “C” urogenetic probe “Pipelle”.

### Sampling technique with “Pipelle” urogenetic probe.

“Pipelle” Sampling with a urogenetic probe does not require special training. For women planning a pregnancy, it is recommended to carry out the procedure on days 8-9 of the menstrual cycle. Any woman of reproductive age or woman who can become pregnant should have a documented pregnancy test before treatment. Pre- and post-

menopausal women do not need to choose a separate day. Just before the day of sampling, the doctor will review the level of cleanliness of the vagina and advise not to use suppositories, tampons, or similar materials the day before the procedure. The procedure is minimally invasive and very convenient without the use of any analgesics [19,34, 15]. If

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the procedure methodology is fully followed, no complications will be observed when using this method.

### Indications for “Pipelle” biopsy:

- Endometrial hyperplasia
- To assess the condition of the uterus in infertility after hormonal therapy
- To assess the condition of the endometrium in cases of infertility and miscarriage
- In order to assess the planned dynamic monitoring of the effectiveness of hormone therapy
- Atypic hyperplasia
- Endometriosis
- When bleeding during menopause and bleeding on the background of hormonal contraceptives
- In uterine fibroids
- Endometrial polyps
- In order to determine the causes of menstrual disorders
- When uterine cancer is suspected
- (in vitro fertilization) in stage 1 of IVF [1, 34, 15,5].

### Contraindications:

- With severe inflammation of the cervix and vagina (possibly after treatment)
- Pregnancy
- With blood coagulation pathology

### Equipment for “Pipelle” biopsy:

1. Gynecological room for procedure
2. Vaginal speculum
3. Medical gloves
4. Clamp and tweezers
5. Sterile wipes and tampons
6. 70% Isopropyl Alcohol
7. “Pipelle” urogenetic probe
8. Sol. NaCl 0.9% -5-6ml
9. 10% Neutral buffered formalin (NBF)
10. Container with a volume of 5-10ml [1, 34, 15,5,3].

When the patient is ready for the procedure, a speculum is placed in the vagina. The cervix is examined and cleaned with sterile gauze soaked in alcohol. “Pipelle” Sol urogenetic probe. NaCl is extracted from 0.9% -5-6 ml (depending on the volume of the uterus) and is slowly introduced into the body of the uterus through the cervical canal. "In the third part of the pipette there is a hole with a diameter of 2.4 mm, from which the liquid enters the uterine cavity when the piston is pushed. [1, 34, 15.5]. When the fluid enters the body of the uterus, the probe is gently turned, and when negative pressure is generated, the endometrial tissue fills the cannula, so that the biomaterial is easily removed and introduced for cyto- and histological examination [1,3].

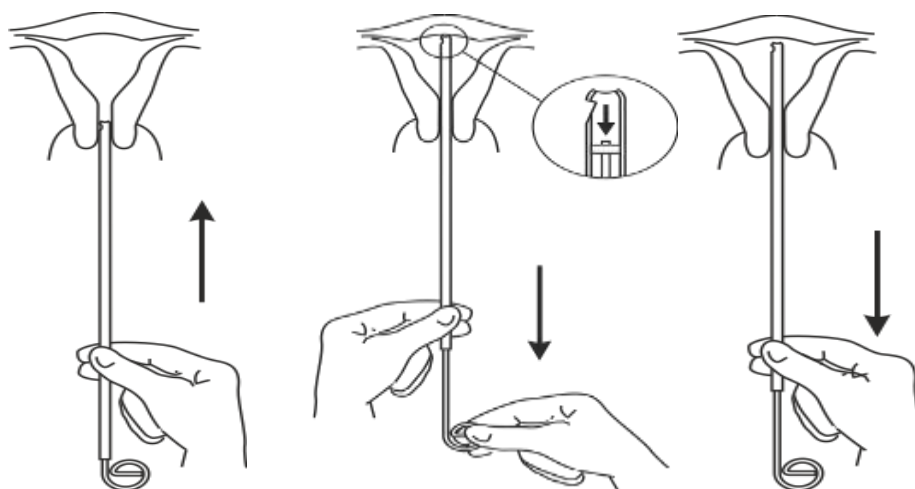


Figure-2. Method of obtaining biomaterial from the body of the uterus using the device “Pipelle” [1].

A number of scientists have conducted research on the extraction of biomaterial from the body of the uterus using the urogenetic probe “Pipelle”, including: Caravaca de la Cruz Murica (Spain) in the Department of Obstetrics and Gynecology at the Comarcal del Noroeste Hospital. Machado F and Moreno J conducted a case-control study in pre- and postmenopausal women with abnormal bleeding to assess the accuracy of endometrial biopsy with the “Pipelle” device. Of these, 1535 samples were taken with “Corner Pipelle”. Subsequently, curettage and hysterectomy were performed in 168 patients. The histological data were

compared and, according to the report, the sensitivity of Corner Pipelle was 84.2%, specificity 99.1%, accuracy 96.9%, positivity 94.1%, the study material was insufficient. It was estimated at 16.09% [21]. The experimental results proved that the biomaterial obtained with the Pipelle device can be used in practice as an understandable, convenient and economical method for the treatment of endometrial cancer and atypical hyperplasia.

Moradan Sanam and Mir Mohammad Hani Madjid at the Center for the Study of Abnormal Uterine Bleeding in Iran have a pathology of the uterus over the age of 35 years.

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In 130 patients with hemorrhage, biomaterial was obtained from the uterine body using Pipelle without any analgesia and without dilation of the cervical canal, and then in the same patients, both biomaterials were obtained from the uterine body by diagnostic curettage using general anesthesia and sent to the same pathologist. The diagnostic values are compared. The diagnostic accuracy of “Pipelle” was more than 97% compared with curettage, a mismatch less than 5%, 100% accuracy, 100% specificity, and 90% susceptibility have been reported for endometrial proliferation, secretory endometrium, simple hyperplasia without atypia, and cancer [29].

Shazia Fakhra, Gulshan Saeed and others at the Shifa Medical College, Department of Obstetrics and Gynecology, Islamabad, Pakistan, performed endometrial sampling on 100 patients using a “Pipelle” urogenital probe and then performed a diagnostic incision using a standard curette. The Pipelle device had a sensitivity, specificity, and a positive prognostic value of 100% for the diagnosis of endometrial carcinoma, hyperplasia, and secretory endometrium. High diagnostic sensitivity for atypical and normal hyperplasia of “Pipelle” was found to be 100%, specificity 98%, specificity for endometrial proliferation 94 and 93%, and negative prognostic value for endometritis 97%. Only endometrial polyps were found to be insufficient for evaluation. In conclusion: “Pipelle” is a highly sensitive, specific, and very convenient, safe instrument for the diagnosis of urogenital probe endometrial hyperplasia and cancer [16].

At the Department of Obstetrics and Gynecology, Faculty of Medicine, Isfahan University of Medical Sciences, 87 patients with postmenopausal bleeding Fariba Behnamfar and Elham Arshad received endometrial material from the uterine body in an outpatient setting using a “Pipelle” device and compared the results with diagnostic curettage in the operating room. The results of hysterectomy were also compared with the results of “Pipelle” and diagnostic curettage. Results obtained using the “Pipelle” urogenital probe: 94.1% of malignant tumors were diagnosed and 100% malignant tumors were detected in the sample obtained by curettage. The sensitivity and specificity of “Pipelle” to curettage are 94.12% and 100%, respectively, for the diagnosis of malignant tumors. The results confirmed “Pipelle” safe, cost-effective, and rapid method, and concluded that diagnostic curettage was preferable to cutting [7].

Ibrahim Anwar Abdelazim, Amro Aboelezz and Amr Fati Abdulkarim at the Department of Obstetrics and Gynecology, Ain Shams University, Faculty of Medicine practice was conducted and the results were compared. Diagnostic incision using conventional diagnostic curettage revealed endometrial proliferation in 37 out of 140 samples, secretory endometrium in 33 samples, endometrial hyperplasia in 49 samples (45 without atypia and 4 with atypia), endometritis in 8 samples, and endometrial polyps

in 3 samples. In this study, the Pipelle device had 100% sensitivity, 100% specificity, and 100% accuracy for the diagnosis of endometrial hyperplasia, endometrial carcinoma, proliferative, and secretory endometriosis. It also has a sum of 88.9% sensitivity and 99.2% negative prediction value. The results show that the “Pipelle” endometrial sampling method is a safe, accurate and low-cost outpatient method that can detect malignant and benign uterine tumors with general sensitivity and accuracy without general and local anesthesia [2].

Chulalongkorn University, Faculty of Medicine, Department of Obstetrics and Gynecology S. Bunyavejchevin, S. Triratanachat and others divided 30 patients who complained of pathological bleeding from the uterus from June 1 to December 31, 1997 into 2 groups. In-group A, the removal of endometrial tissue was performed for the first time by a “Pipelle” device. Group B patients received a diagnostic incision from the uterine body using a curette. The results showed that histological sampling using the “Pipelle” device was found to be absolutely painless compared to curettage, and the sensitivity of the “Pipelle” device was 87.5 and 100%. In summary, endometrial sampling with a “Pipelle” device is a less painful, simple, easy, and cost-effective method than a diagnostic uterine incision. It should be used with caution in cancer [10].

In the Department of Obstetrics and Gynecology at the University of Tennessee, Memphis, Stovall TG, Photopoulos GJ, and others sampled the uterine body to determine the reliability of the “Pipelle” device in 40 patients, the mean age of the patients was 62 years (40-83). Discomfort was noted by the patient as mild, moderate, or severe, and severe pain was noted in only 2 patients (5.0%). No complications were reported after endometrial sampling on the Pipelle device. Endometrial carcinoma was confirmed in 3 out of 40 samples. The endometrial sample obtained using the “Pipelle” device was the same at 29 (74.4%) compared with post-hysterectomy histology. On the Pipelle, 5 (12.8%) showed a high level difference and 5 (12.8%) showed a low level. No residual tumor was detected in histology after 1 hysterectomy (2.5%) [33].

From October 2007 to November 2009, Fuat Demirkiran, Evrim Yavuz and others at the Department of Obstetrics and Gynecology, Istanbul University, Cerrahpasa Medical Faculty, performed 478 “Pipelle” and Curettage Endometrial Circumcision on 673 patients, 212 “Pipelle” and 16 Hysterectomy. Endometrial incision was performed using hysterectomy and curettage. The results obtained were compared with each other. The results of endometrial incision obtained using Pipelle and curettage were consistent. The compatibility rate between Pipelle and Hysterectomy was 67% and that of endometrial specimen using Hysterectomy and Curettage was 70%. The sensitivity of Pipelle biopsy in the detection of hyperplasia and atypical cells is 67 and 75%. The sensitivity of endometrial incision results obtained by curettage in the

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detection of hyperplasia and atypical cells is 62 and 83%. “Pipelle” biopsy has almost the same success rate as diagnostic endometrial incision. However, both biopsy methods are not perfect, but it has been concluded that “Pipelle” biopsy is cheaper and easier than curettage [13].

In 2009-2011, Gungorduk, Ascioglu, and others performed “Pipelle” on 78 out of 267 patients with normal uterine bleeding and 189 on regular curettage. The results were compared with the histology of patients who underwent hysterectomy. The compatibility rate between “Pipelle” biopsy and hysterectomy was 62%, hysterectomy and diagnostic curettage was 67%, “Pipelle” biopsy and diagnostic curettage for hyperplasia was 47.1% and 45%, and atypical cell detection was 71.4% in both techniques. All other indicators were the same in both groups. Thus, “Pipelle” biopsy was concluded to be a reasonably cost-effective, mini-invasive, and cost-effective method prior to hysterectomy [17].

### CONCLUSION

In summary, “Pipelle” biopsy is the most harmless method of examining uterine endometrial tissue using a special probe, which allows direct sampling of the endometrial portion and detects atypical cells with high sensitivity to endometrial curettage. In general, “Pipelle” biopsy is an improved method of curettage that allows vacuum aspiration to scrape away the tissue of the inner mucosa. In addition, “Pipelle” biopsy is a painless, reliable method of endometrial curettage that reduces the risk of various infections of the external and internal genitalia in women, prevents the spread of tumor cells, and relieves depression in women due to severe pain. does not require much time for practice, does not require dilation of the cervical canal as in diagnostic curettage. Painkillers are not used. Even at the planning stage of pregnancy, this practice allows early and harmless detection of various pathologies, reduces the risk of bleeding from the female genitals, various postoperative complications are prevented and the patient does not incur financial costs to treat postoperative complications after sampling.

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