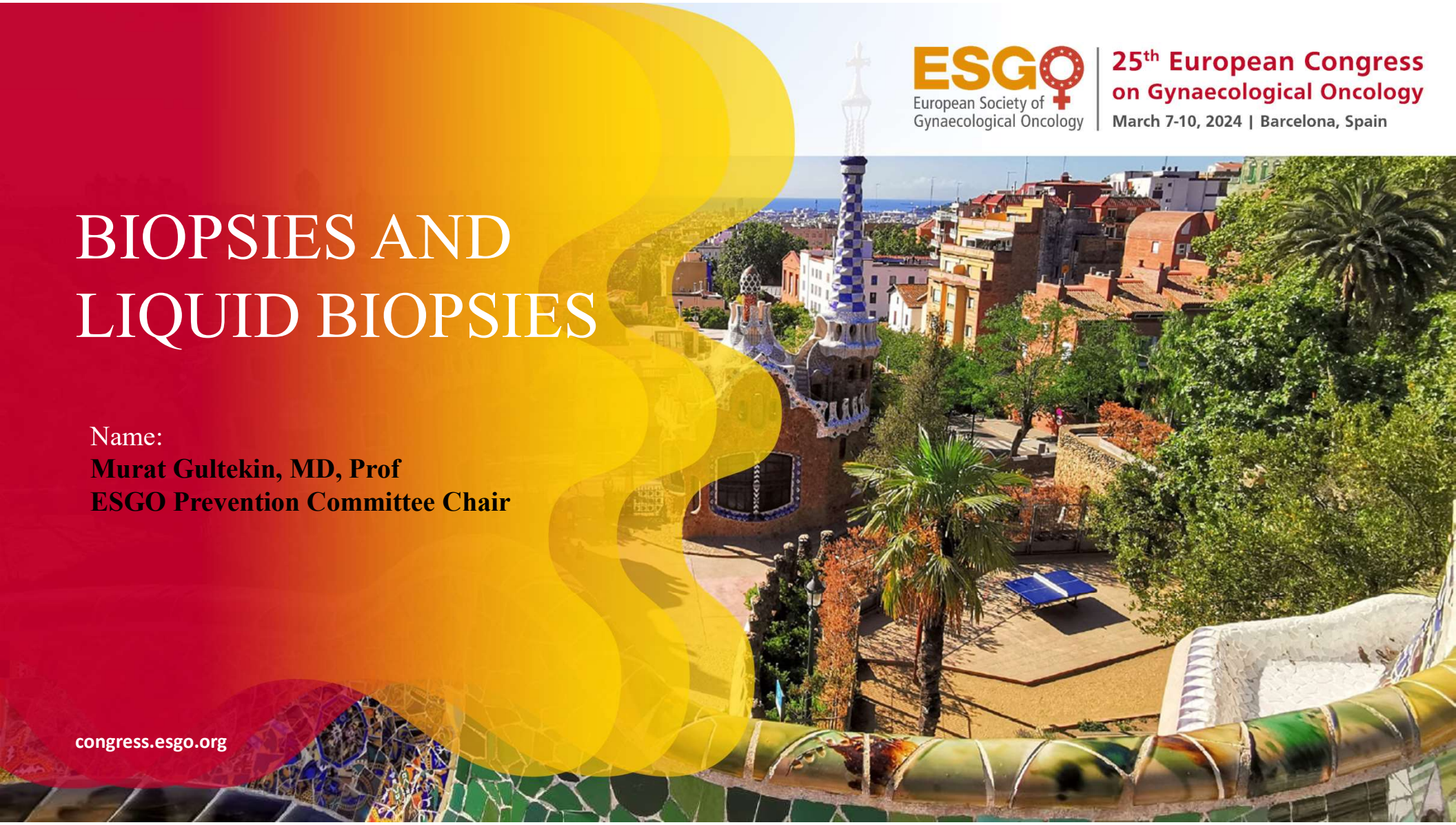
ESGO
European Society of Gynaecological Oncology

25th European Congress on Gynaecological Oncology
March 7-10, 2024 | Barcelona, Spain

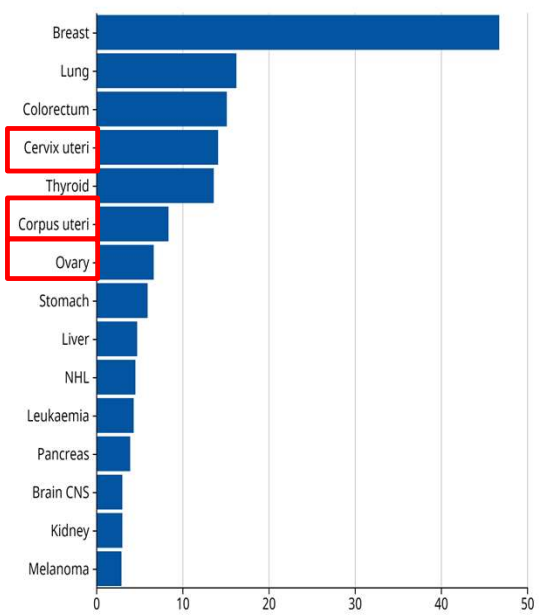
BIOPSIES AND LIQUID BIOPSIES



Name:
Murat Gultekin, MD, Prof
ESGO Prevention Committee Chair

WORLD

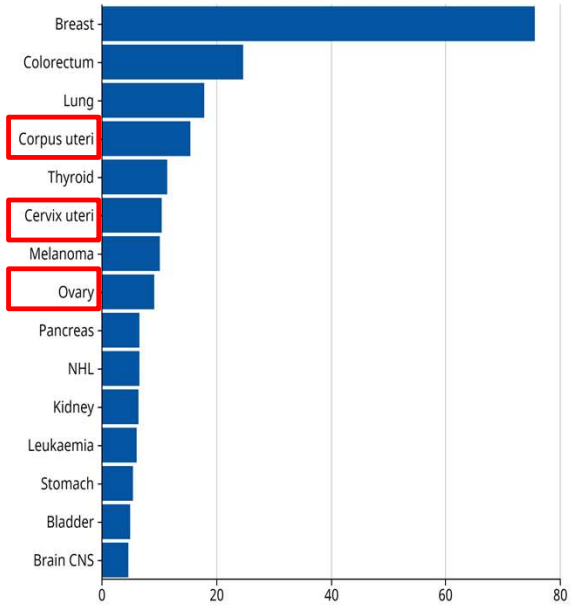
Age-Standardized Rate (World) per 100 000, Incidence, Females, in 2022
Continents
(Top 15 cancer sites)



Cancer TODAY | IARC - https://gco.iarc.who.int/today
Data version : Globocan 2022

EUROPE

Age-Standardized Rate (World) per 100 000, Incidence, Females, in 2022



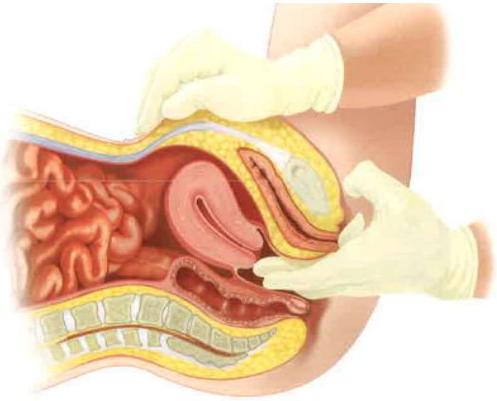
International Agency for Research on Cancer
World Health Organization
https://gco.iarc.who.int/today
2022
24

Gynaecological Procedures

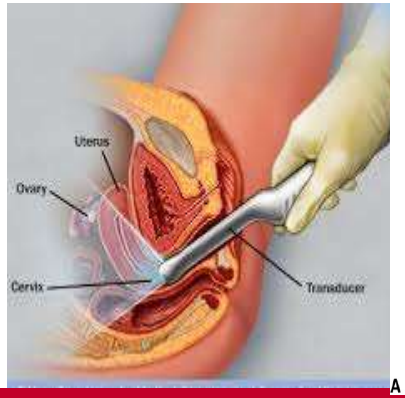
- Gynaecological exam
- Pap-Smear
- Transvaginal USG (tvUSG)
- Colposcopy
- Cervical Punch Biopsy
- Endocervical Curettage
- LEEP-LLETZ
- Conization

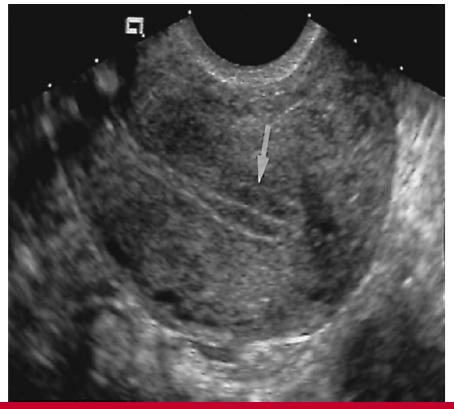
- Endometrial Biopsy
  - Pipelle
  - D&C
  - Fractionel Curettage
- Intra-uterine Device Implamentation
- Bartholine Cysts
- Vulvar Biopsy
- Histerescopy
- Laparoscopy

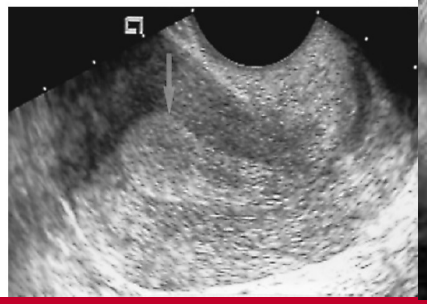
Gynaecological Exam

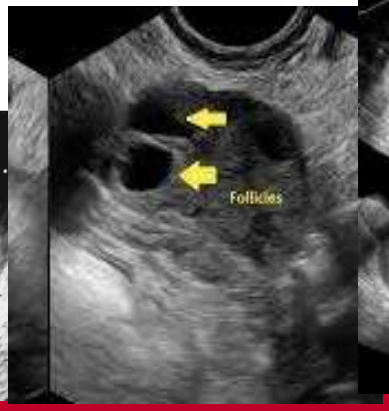


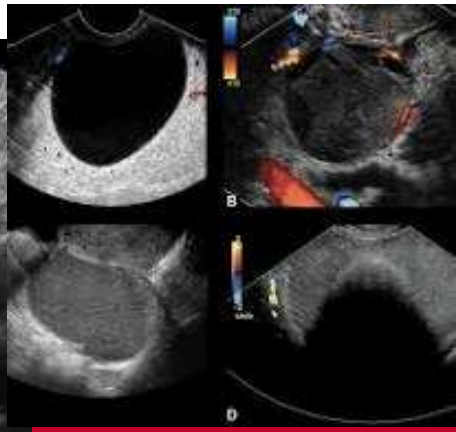
Transvaginal USG (tvUSG)





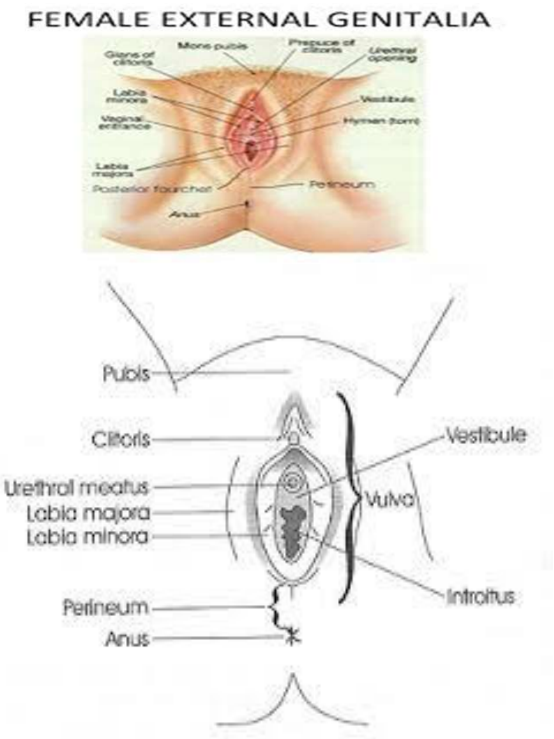


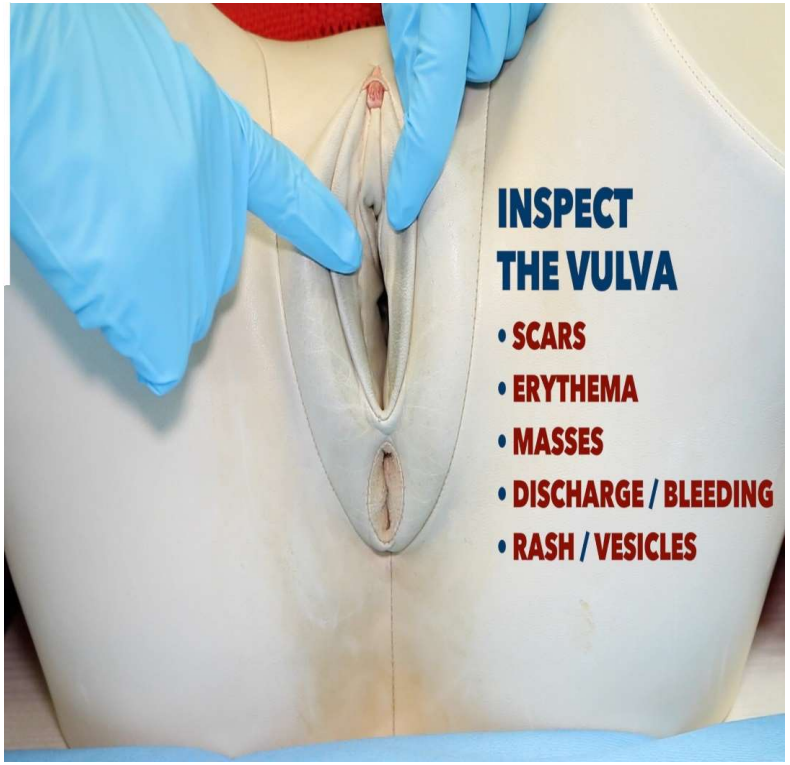


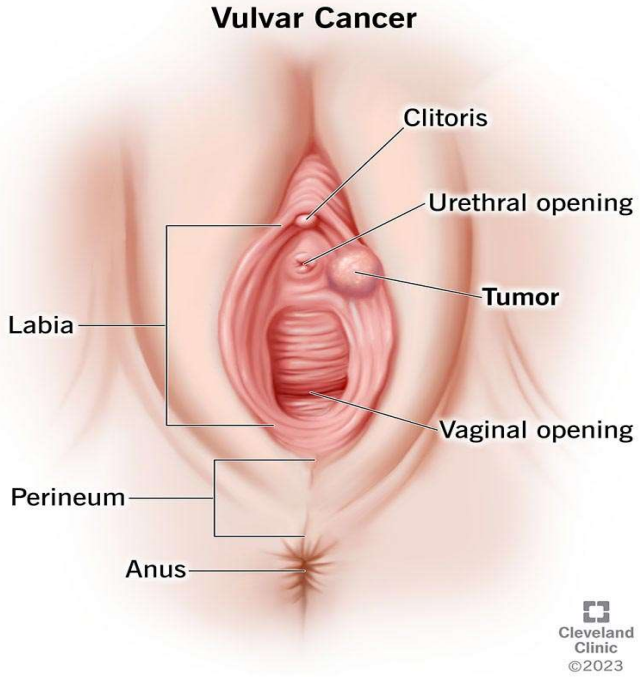


Pelvic Bimanuel Examination

Vulva

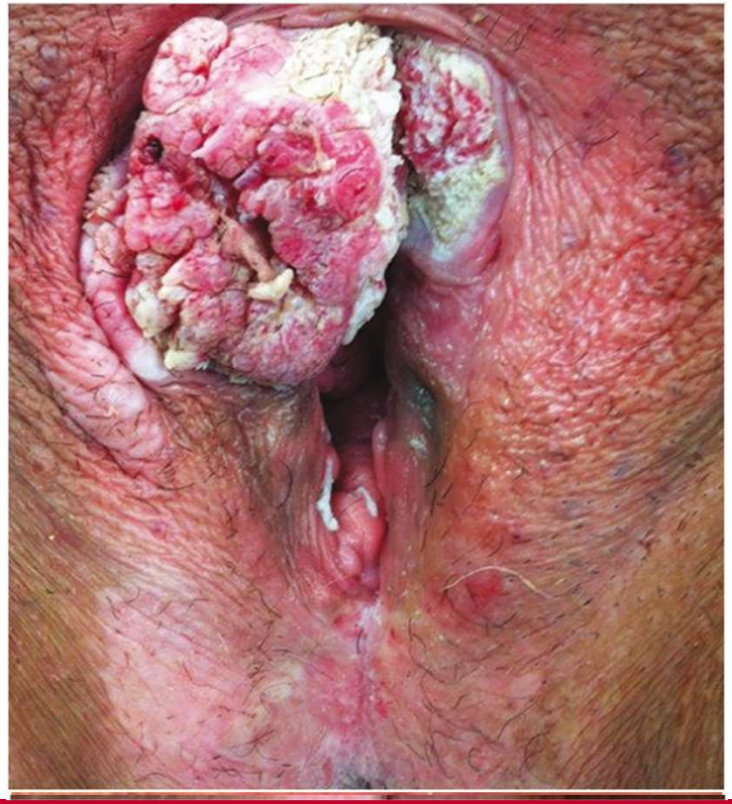


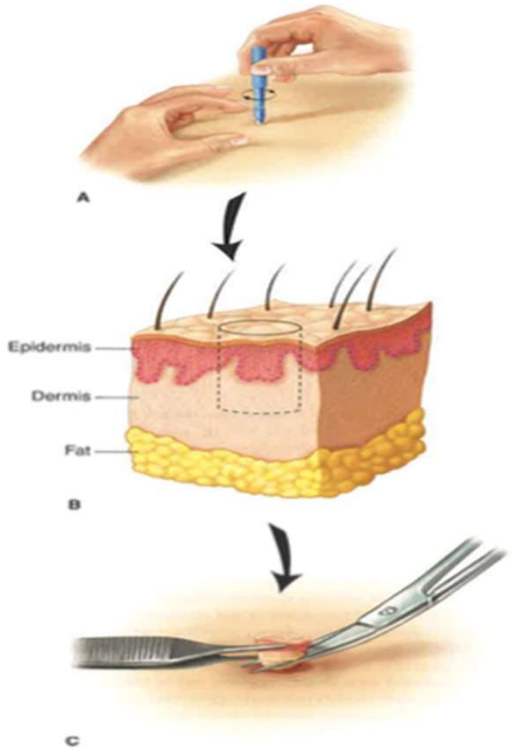




Vulvar Biopsies

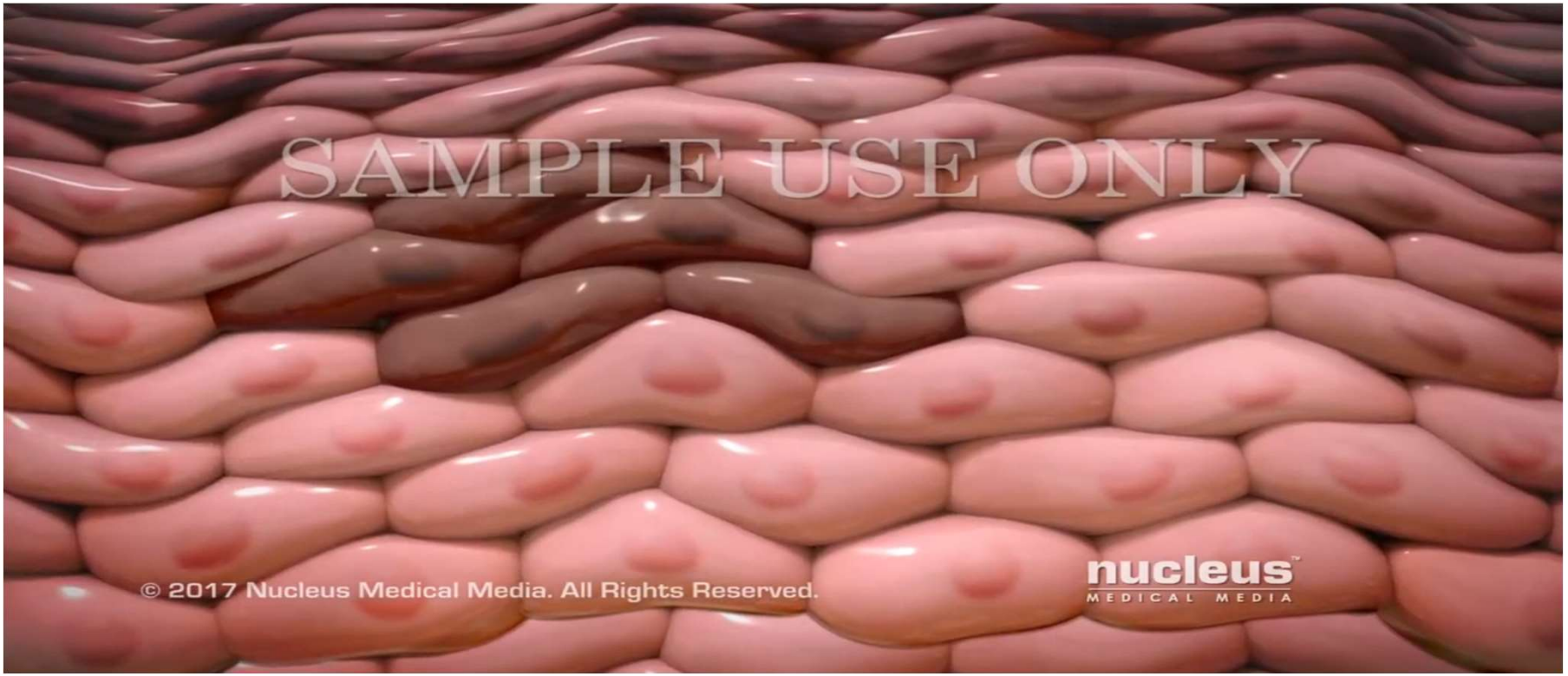
VULVAR BİOPSİES





Cervical Smear and Biopsies

Pap-Smear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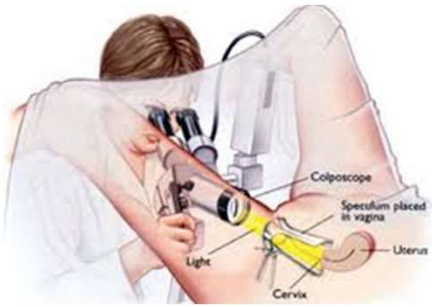
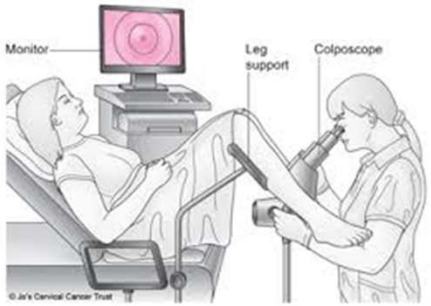
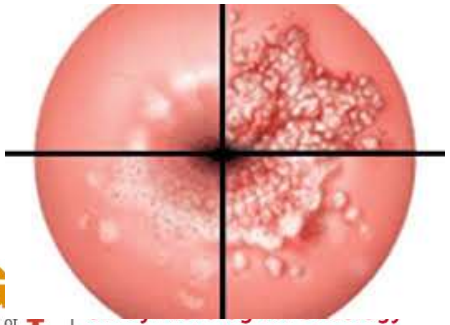
MEDICAL MEDIA

Colposcopy

- Vagen
- Vulva
- Cervix
  - Abnormal Smear
    - Normal, ASC-US, LSIL, HSIL, AGC
  - HPV 16/18
  - Other HPV (+) Abnormal Smear
- Colposcopic biopsy results
  - Normal, CIN 1-2-3, Cancer







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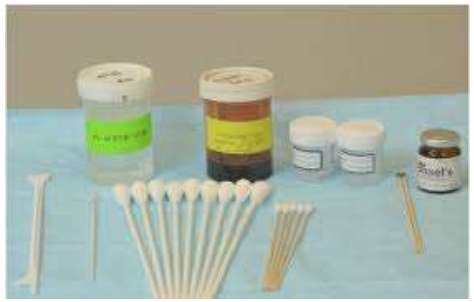
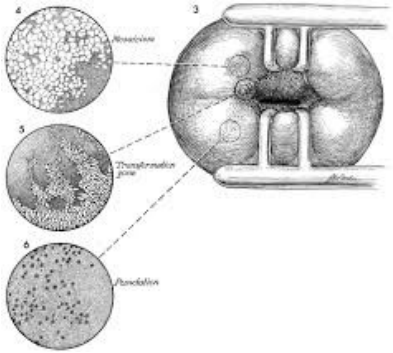
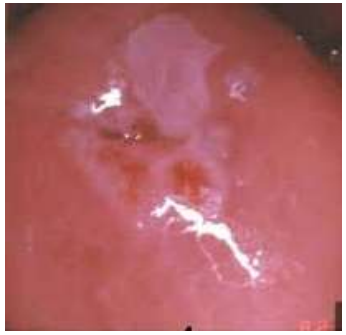
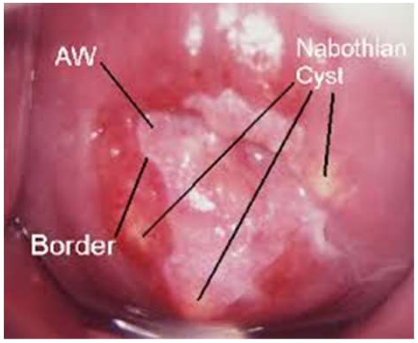
Abnormal Colposcopy





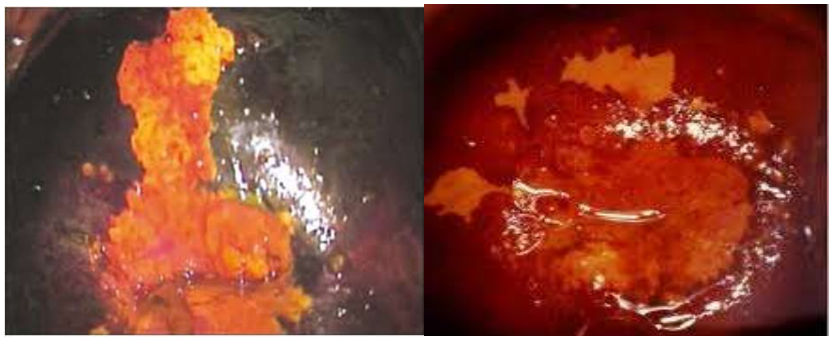




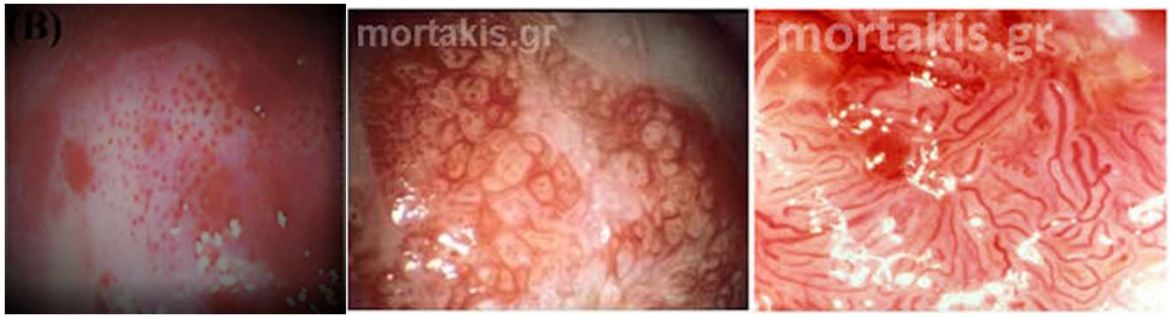
Aceto-White Epithelium

%3 or %5 Acetic Acid

Abnormal Colposcopy

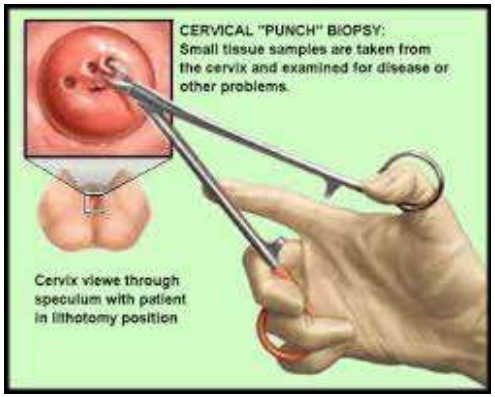


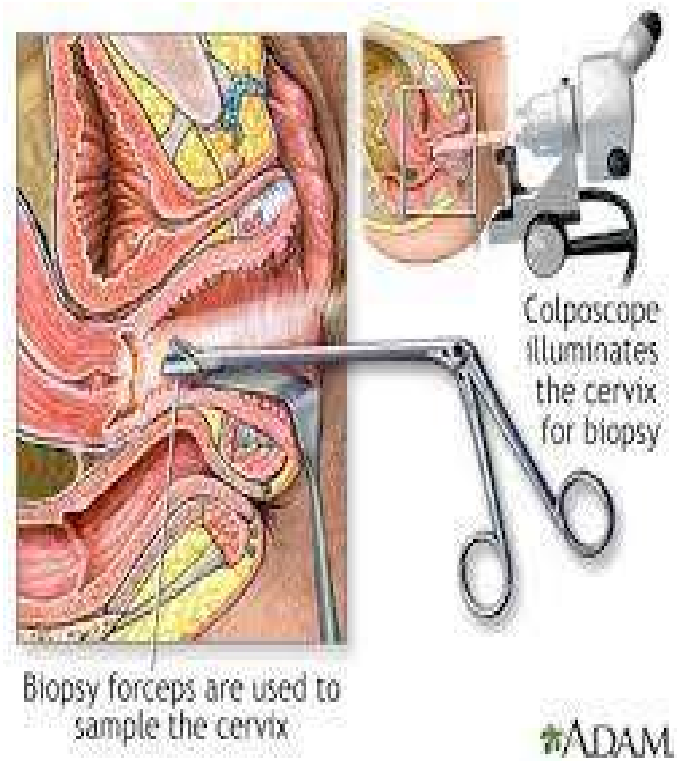
Lugol (-)
Schiller (+)

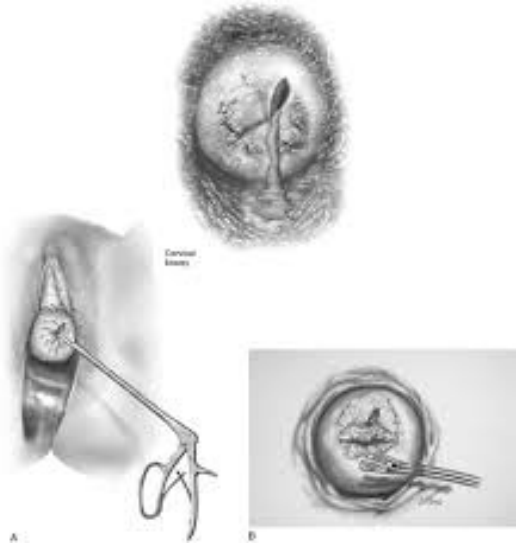


Abnormal Vascularization
- **Punctuation**
- **Mosaicism**
- **Abnormal Branches**

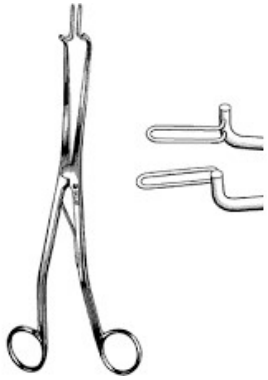
Cervical Punch Biopsy







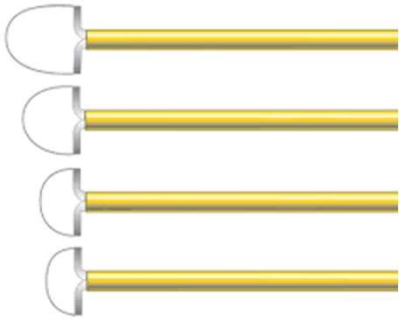
Endocervical Curettage (ECC)

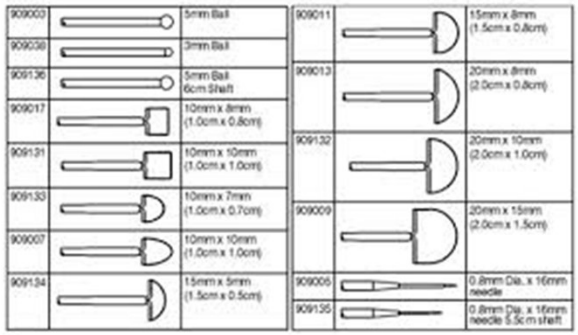


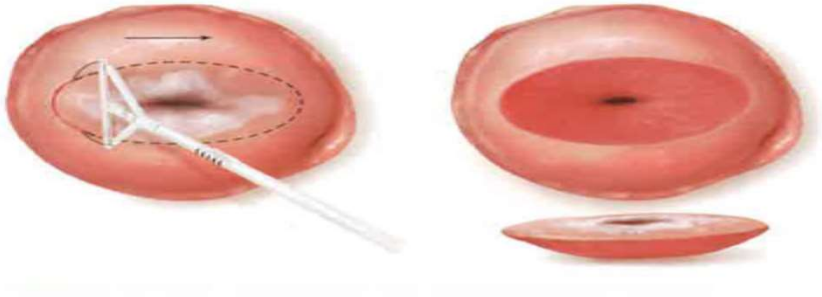
Indications

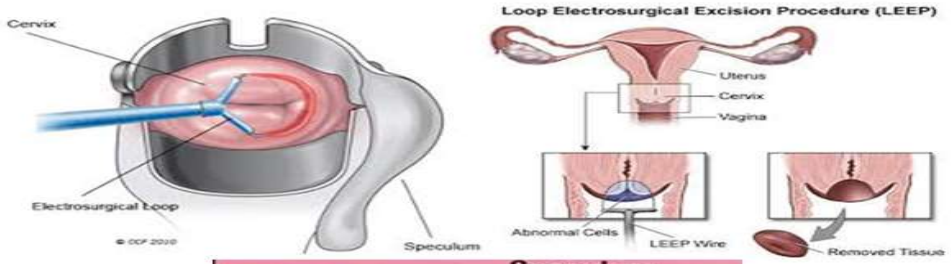
- Lesions extending in to ECC
- AGC
- Abnormal Uterine Bleeding

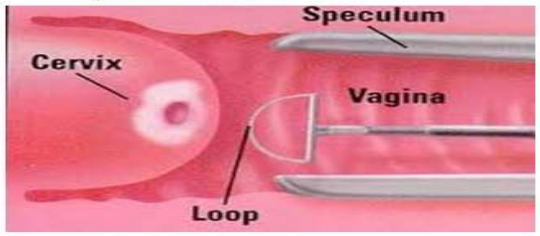
LEEP: Local Electro-Surgical Excision Procedure or LLETZ: Large Loop Excision of the Transtion Zone





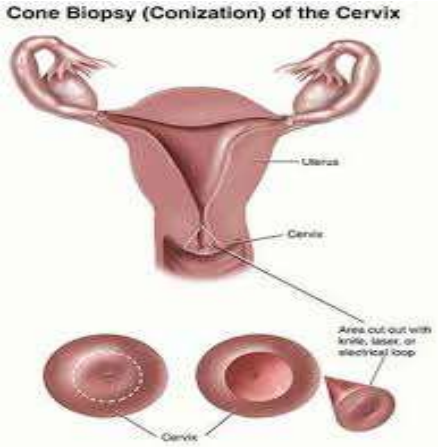


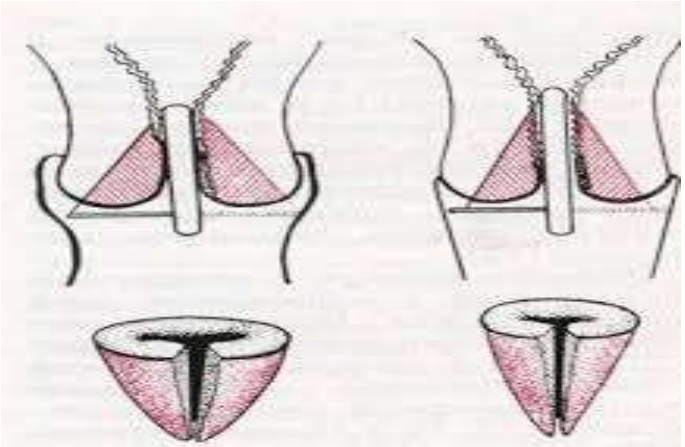


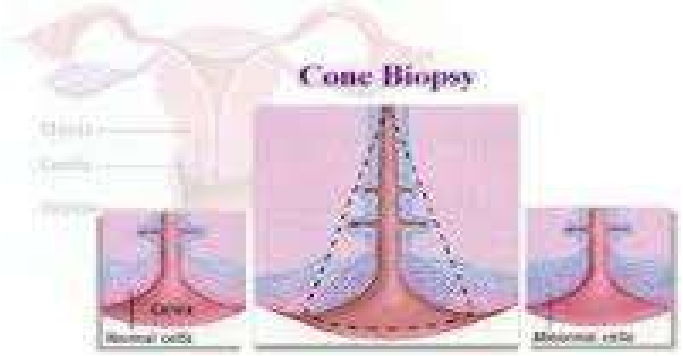


Single vs. Multiple Pass

Conization
(Cold Knife/ Co2 Laser/ Laser Diathermy/ LEEP)



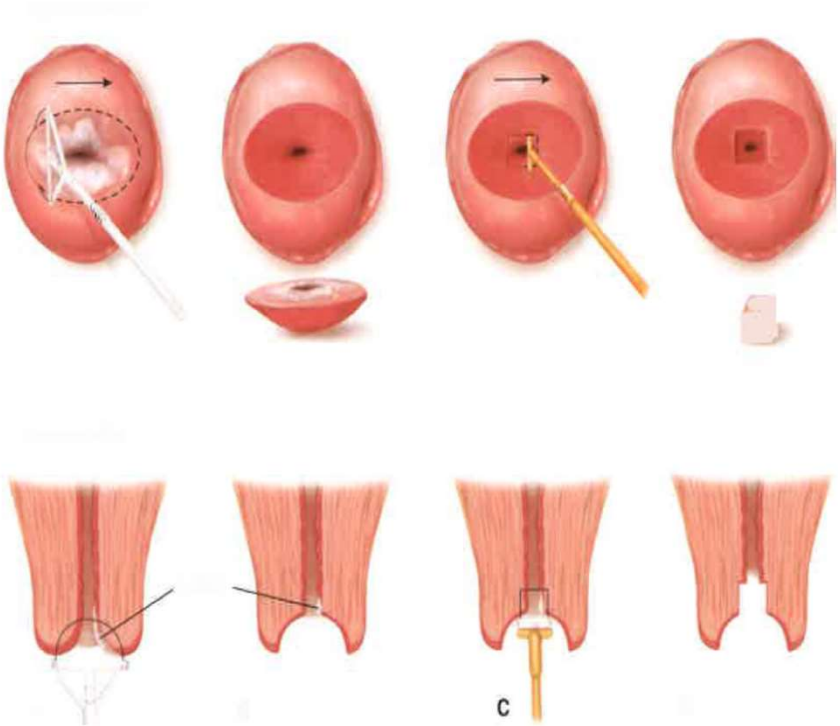




Indications

- ECC (+)
- Cytologic Abnormality not consistent with tissue diagnosis
- Unsatisfactory colposcopy
- Microinvasion on biopsy R/O invasive cancers
- Adenocarcinoma in situ

Conization by LEEP
(Cold Knife/ Co2 Laser/ Laser Diathermy/ LEEP)



Loop electrosurgical excision procedure (LEEP) "**top hat**" cervical conization procedure
transverse (upper row) and coronal (lower row) views,
A. Excision of ectocervical portion of lesion.
B. Appearance of cervix following ectocervical excision. C. Excision of endocervlcal portion of lesion,
D. Appearance of cervix upon procedure completion.

Endometrial Biopsies

Endometrial Biopsy Indications

- **Abnormal Bleeding**
- **Bleedings with High Risk Factors**
- **Post-Menapousal Bleeding**
- **Tamoxifen Users Bleeding**
- **Endometrial Thickness Increase**
  - **Postmenapousal >4-5 mm**
  - **Pre-menapousal : No Consensus**
    - **4-5 / 10/ 16 mm**
- **Cancer Screening (HNPCC)**
- **Follow up of Endometrial Hyperlasia**
- **Evaluation of uterine response to hormone therapy**
- **Abnormal Pap-smear with atypical cells favoring endometrial origion**

Endometrial Biopsy Types

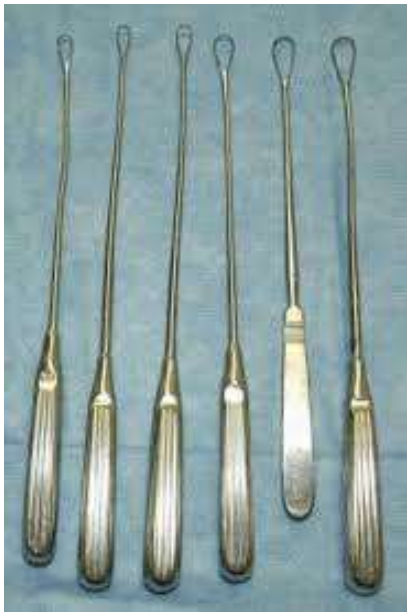
- Dilitation and Curettage (D&C): Sharp Curettage
- Fractionel Curettage (D&C + ECC)
- Pipelle Biopsy with Karman Aspirator (Suction Curettage)
- Hysteroscopic Biopsy

Endometrial Sampling Type	Sensitive
D&C	> %90
Aspiration Biopsy	%90 ~
Pipelle Biopsy	%83-97
Hysteroscopic Biopsy	%98 ~

Dilatation & Curettage (D&C): Sharp Curettage

Teneculum
Weighted Speculum,
Sim Speculum (Vaginal Retractor)
Histerometer (Sims Uterine Sound)

Dilatation & Curettage (D&C): Sharp Curettage



Hegar / Pratt/ Hank Dilatators

Uterine Curettes

Karman or Pipelle Aspiration Biopsy

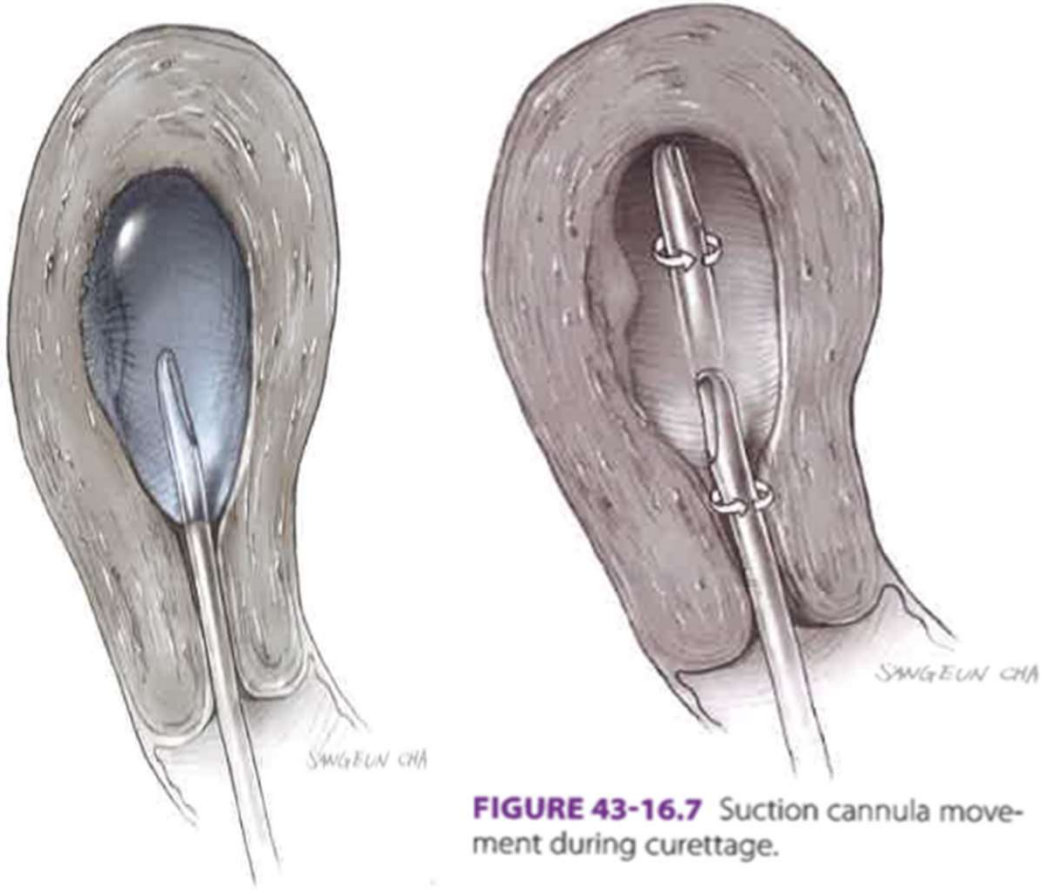


FIGURE 43-16.7 Suction cannula movement during curettage.

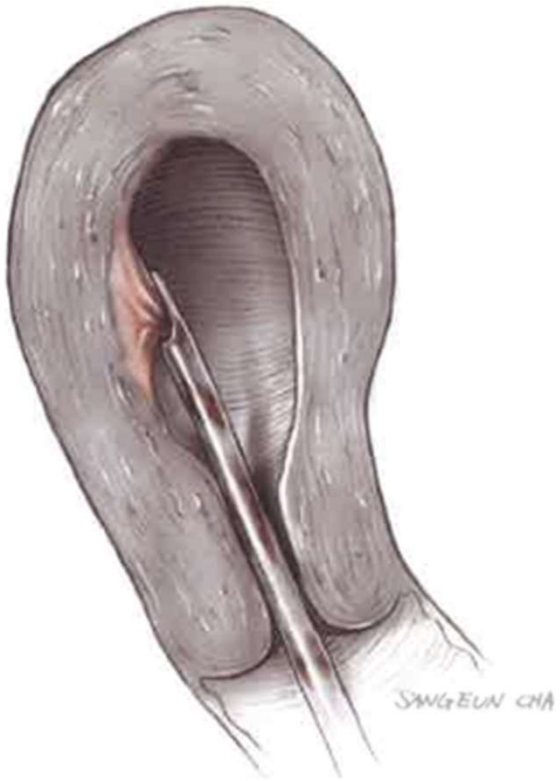
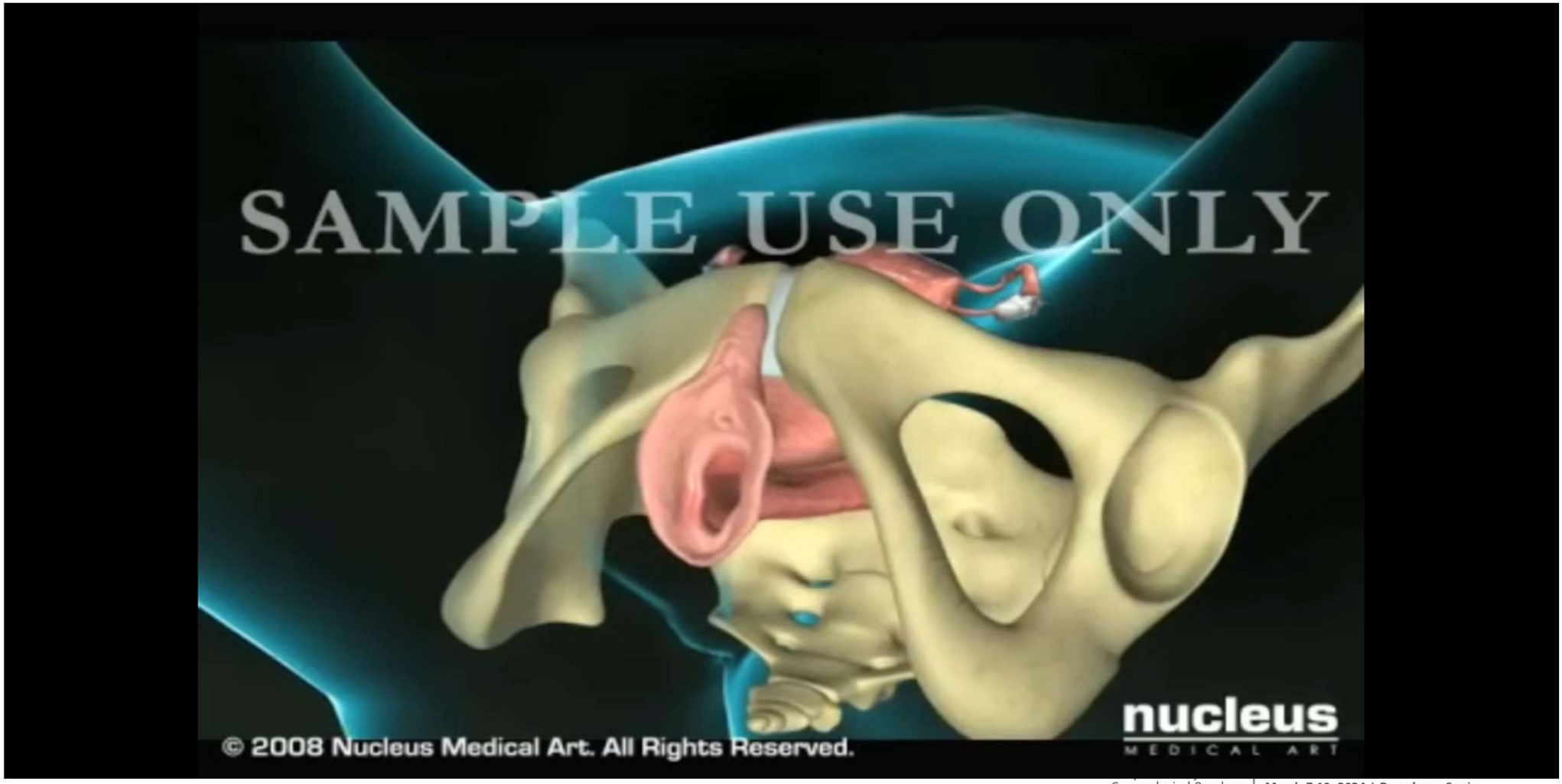


FIGURE 43-16.8 Removal of uterine contents.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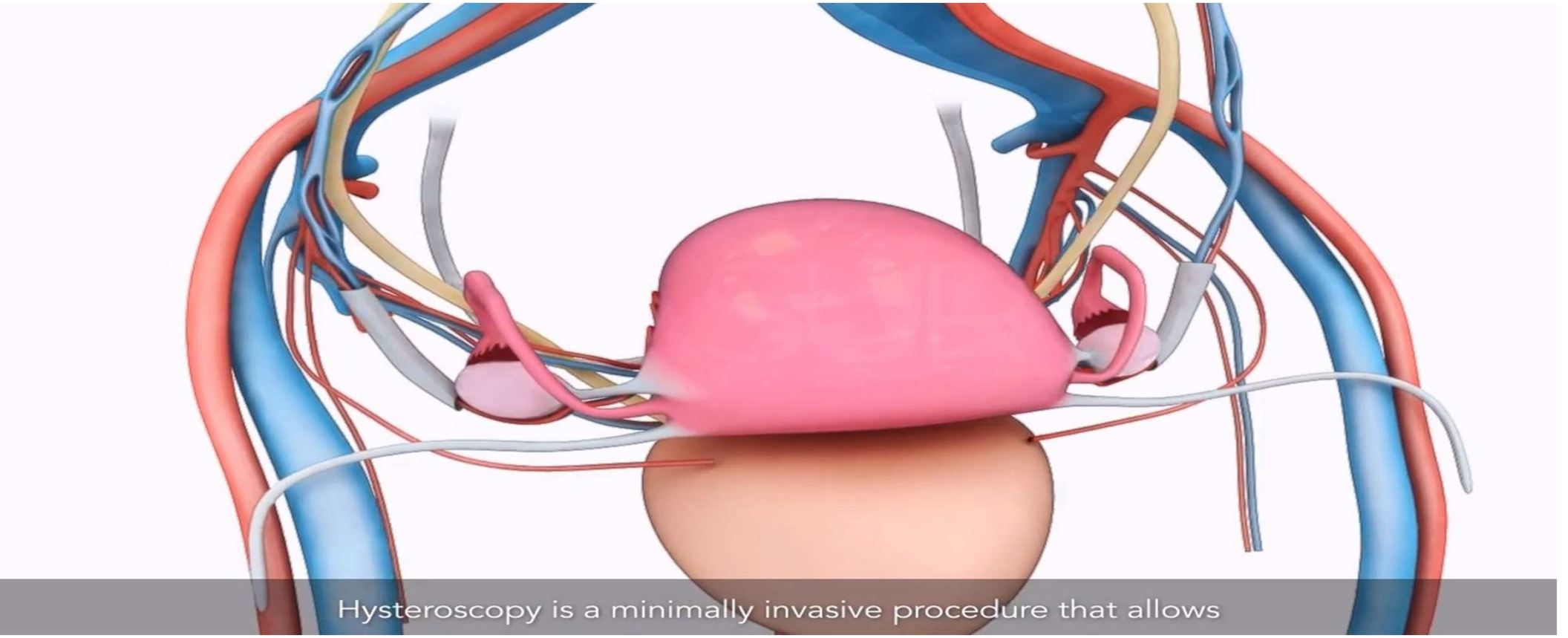
MEDICAL ART

Hysteroscopy (H/S)

- **Hysteroscopic Devices**
  - **Diagnostic**
    - **Rigid or Flexible**
  - **Resectoscope**

Hysteroscopy (H/S)

- Hysteroscopy= **Hysteroscope + Light source + Uterine distention medium**+ **Video camera system**. Most hysteroscopes consists of a 3- to 4-mm-diameter endoscope surrounded by an outer sheath.
  - **Diagnostic hysteroscopes** offer a small diameter, which provides an adequate endometrial cavity view yet requires minimal if any cervical dilatation.
  - **Operative hysteroscopes** have sheaths that increase the overall diameter and necessitate cervical dilation in most cases. Thus, cases requiring operative hysteroscopes are best managed under general or regional anesthesia in the operating room for patient comfort and safety.


Hysteroscopy is a minimally invasive procedure that allows

Resectoscope

- Consists of inner and outer sheaths.
- The inner sheath houses a 3- to 4-mm-diameter endoscope and a channel for fuid medium inflow.
- The 8- to 10-mm outer sheath contains an electrosurgical resection loop and allows fluid egress from the uterus through a series of small holes near the sheath's distal end.
- By means of a spring mechanism the resection loop can be extended and than retracted to shave off contacted tissues. Through ist central cannula, larger instruments that are energy based for tissue resection can be passed such as roller bar, vaporising electrodes (unipolar, bipolar, laser), hot scalpel and motorized morcellator.

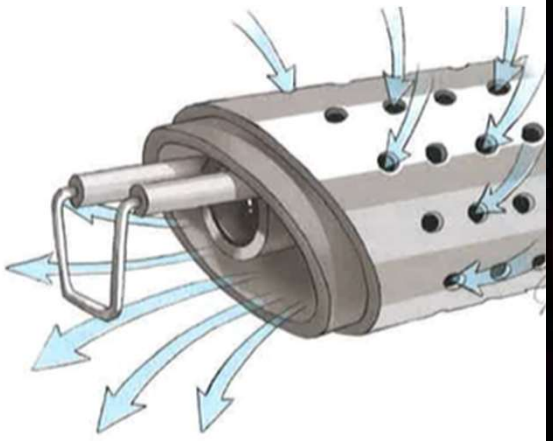
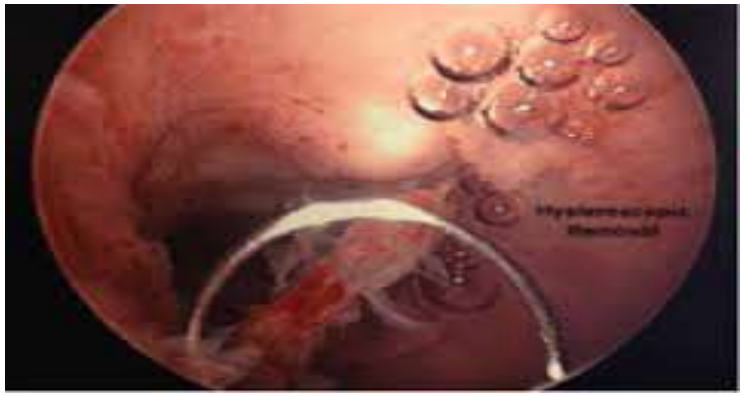
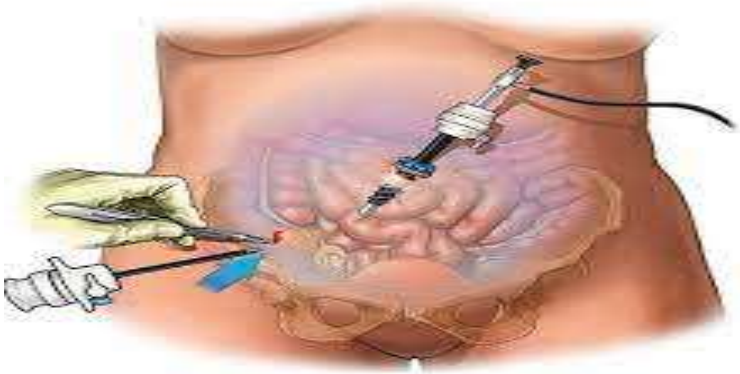


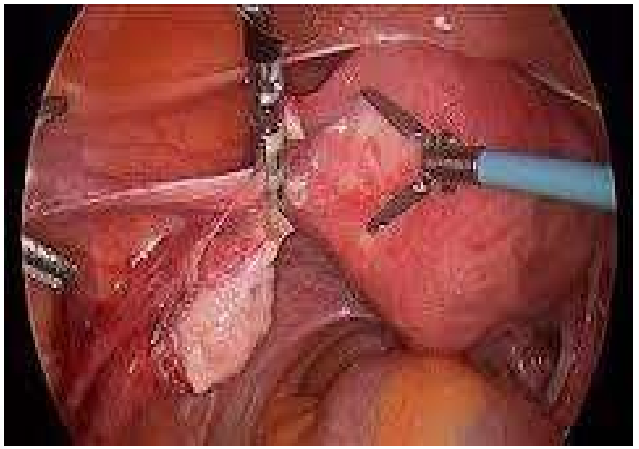
FIGURE 41-38 Distention medium flow through resectosco

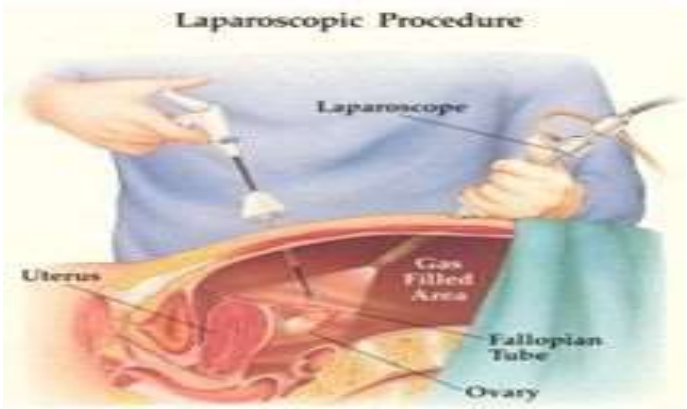


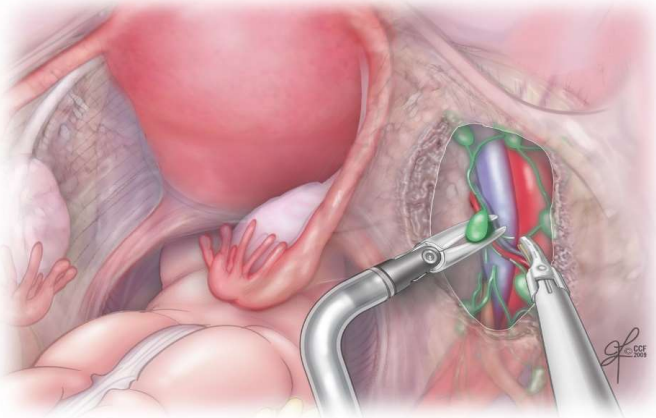
Ovarian Biopsies

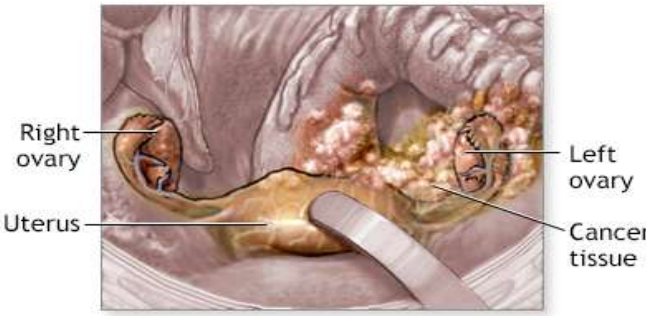
LAPAROSCOPY



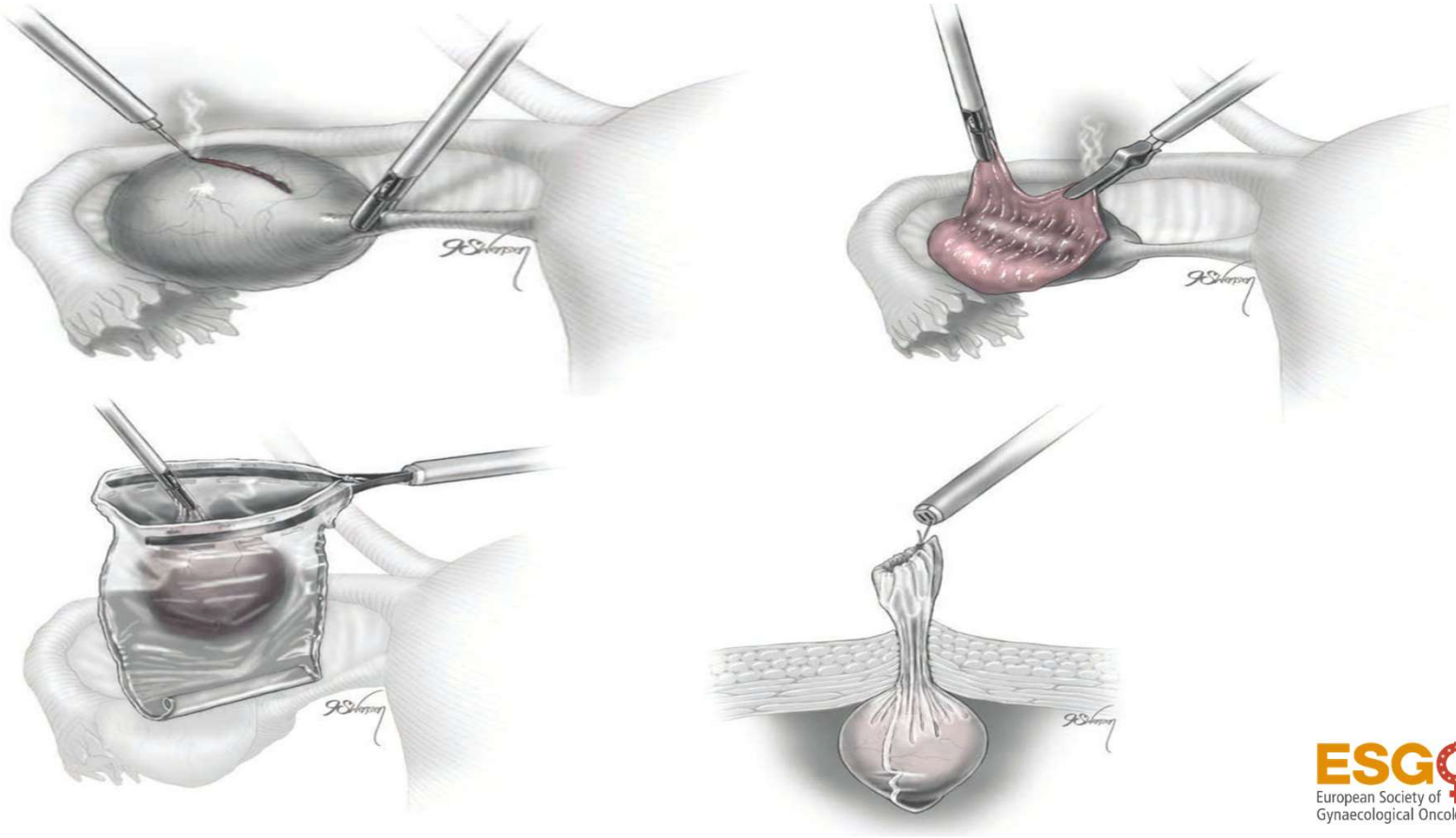


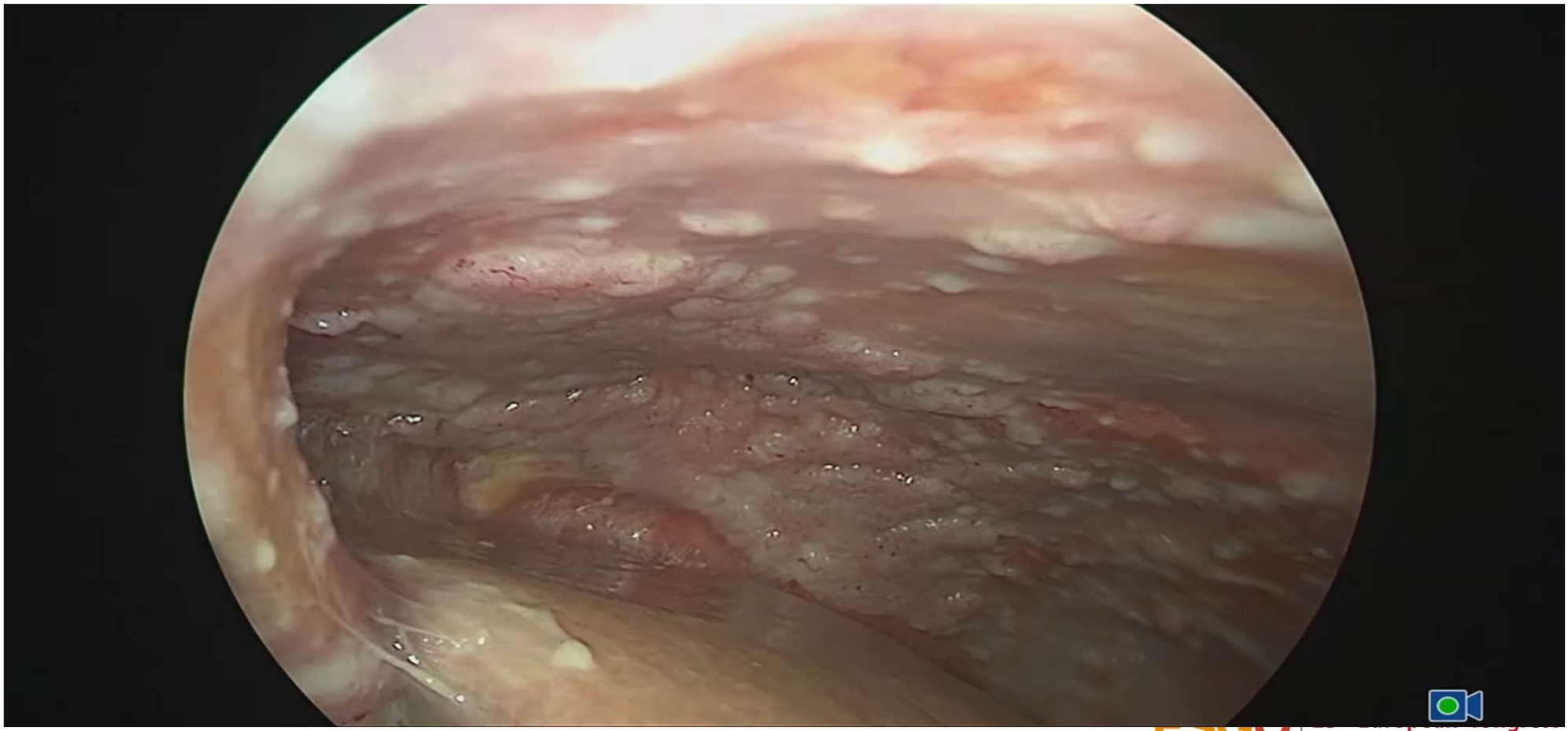




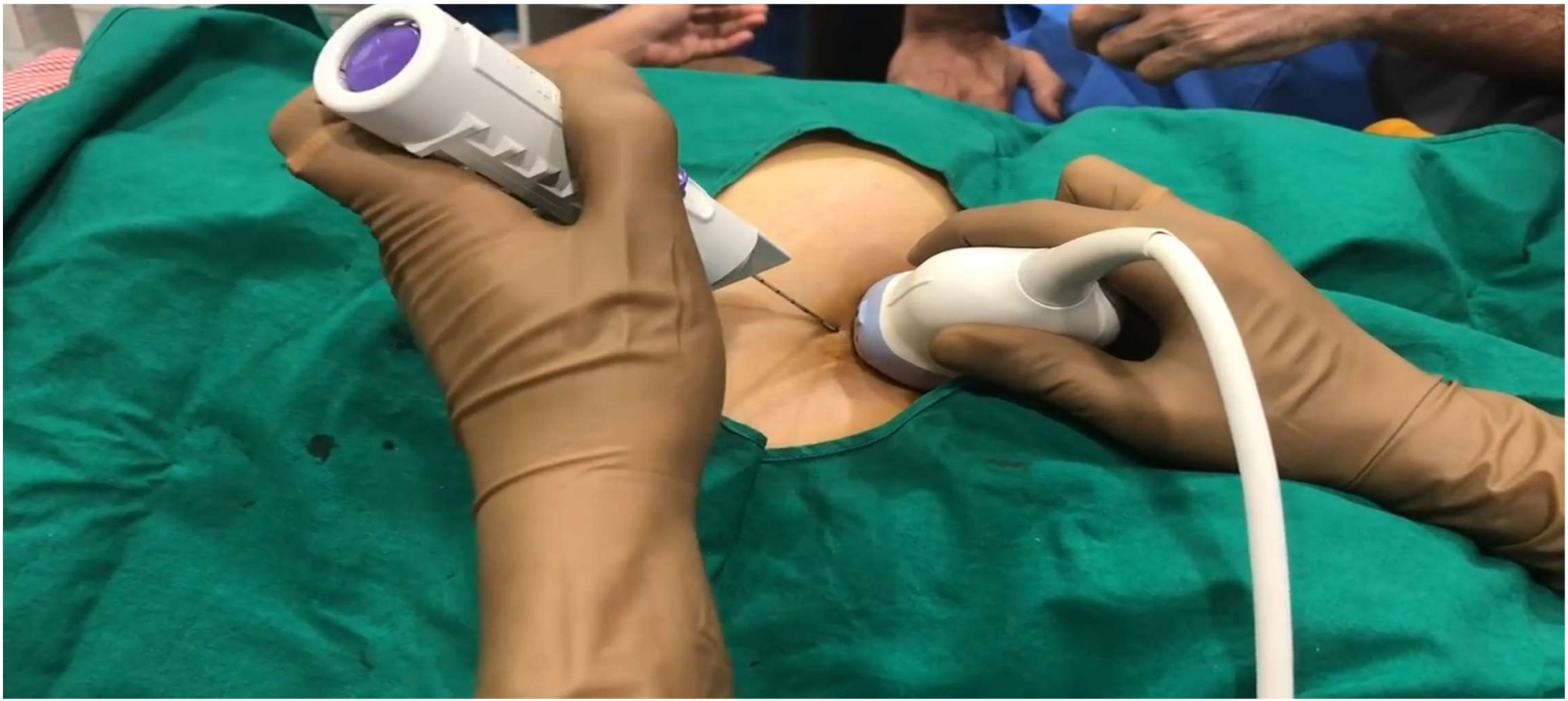


LAPAROSCOPY





LAPAROSCOPİC BIOPSY



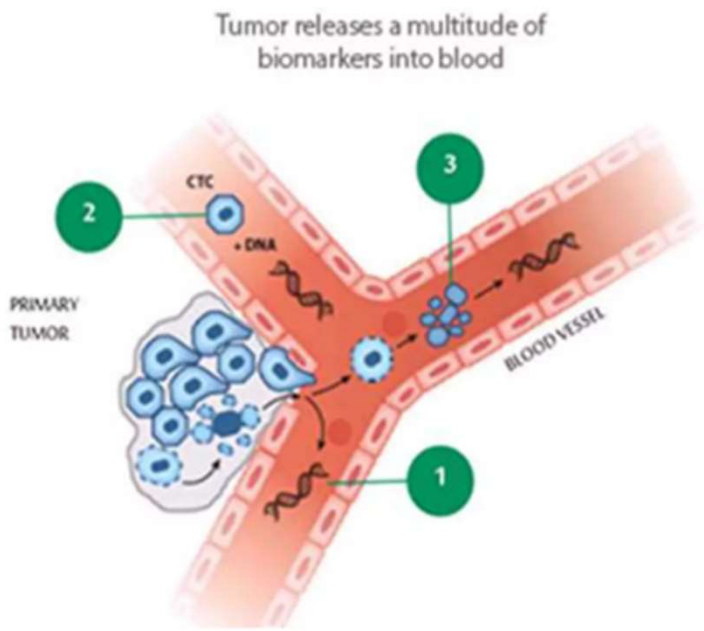
ESGO European Society of Gynaecological Oncology
25th European Congress on Gynaecological Oncology
March 7-10, 2024 | Barcelona, Spain

USG GUIDED BIOPSY

FUTURE

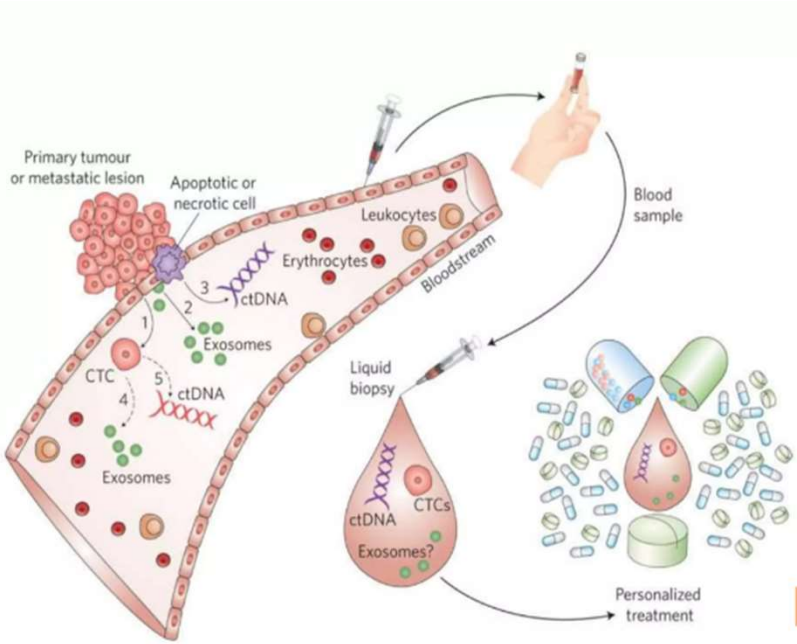
- LIQUID BIOPSIES
- ERA PerMed-CytoMARK PROJECT

LIQUID BIOPSIES

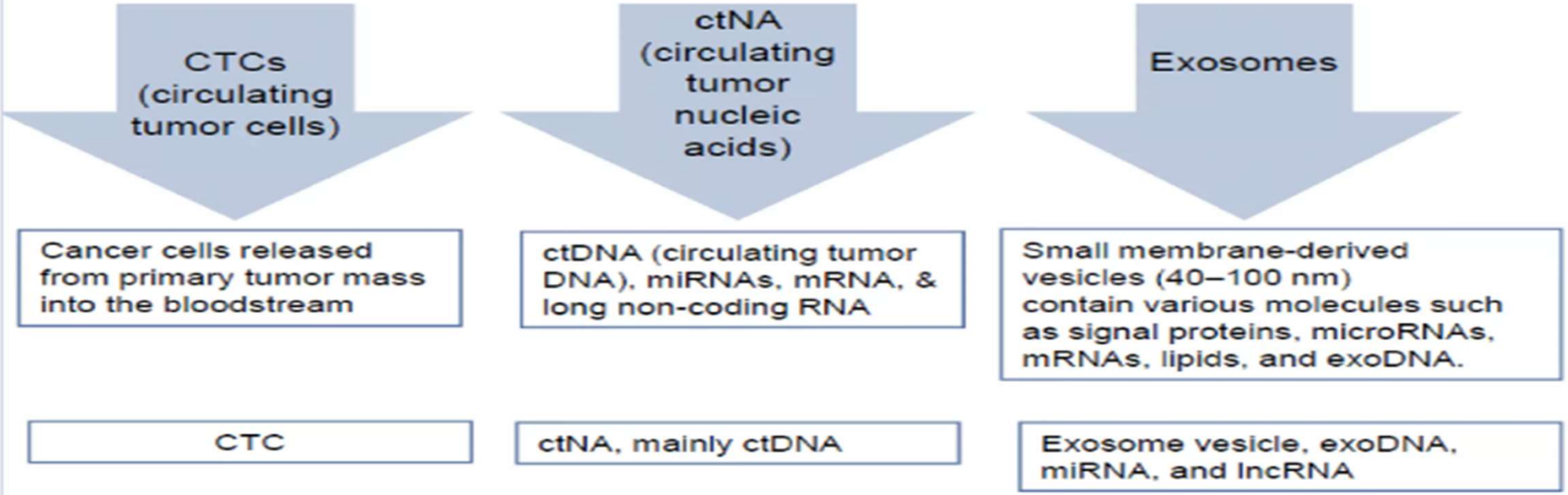


Tumor biomarkers in blood

1. Cell-free DNA (cfDNA)
2. Circulating tumor cells (CTCs)
3. Exosomes & micro vesicles



Liquid biopsies



Samples: blood, serum/plasma, urine, CSF, saliva

Uterine Aspirates

Cervical Cancer Detection and Prognosis

Table 1 Studies using cell-free DNA as a biomarker for the detection of cervical cancer

No	Study	Year	Method	Target gene	Sample	Sensitivity (%)	Specificity (%)	Patient population	Metastatic vs non-metastatic
1	Pornthanakasem et al[71]	2001	qPCR	HPV DNA	Plasma	12.00	100	63	Non-metastatic (stage I–IV)
2	Dong et al[72]	2002	qPCR	HPV DNA	Plasma	64.30	98.33	232 patients and 60 normal controls	Non-metastatic patients (carcinoma in situ and advanced) and normal controls
3	Hsu et al[73]	2003	qPCR	HPV DNA	Serum	24.10	100	112 patients and 40 controls including patients with cervical carcinoma in situ or benign disease	Stage 1B and IIA
4	Campitelli et al[74]	2012	DIPS- PCR	HPV DNA	Serum	86.00	No controls	16	IB–IVA and one case was a pelvic relapse of cervical SCC
5	Zhang et al[75]	2016	RT-qPCR	*BMI1* mRNA	Plasma	69.70	95.90	109 patients with LICC, 138 patients with CIN and 80 healthy volunteers	Stage I–IV
6	Jeannot et al[37]	2016	ddPCR	HPV DNA	Plasma	83.00	100	47 cases of cervical cancer and 18 cases of CIN	Stage I–IV
7	Kang et al[76]	2017	ddPCR	HPV DNA	Serum	100	100	19 patients and 45 healthy controls	Metastatic
8	Chung et al[40]	2017	ddPCR	*PIK3CA*	Plasma	22.2	No controls	170	Stage I–IV
9	Cheung et al[39]	2019	ddPCR	HPV DNA	Plasma	61.6	No controls	138	Non-metastatic (mostly stage IB–II)
10	Cabel et al[38]	2021	ddPCR	HPV DNA	Serum/ plasma	69	No controls	55	Locally advanced cervical cancer
11	Leung et al[42]	2021	NGS	HPV DNA	Plasma	100	88	17 patients with cervical cancer, 13 with HPV positive oropharynx cancer, 50 controls (21 female, 29 male)	Non-metastatic

CIN, cervical intra-epithelial neoplasia; ddPCR, droplet digital PCR; HPV, human papillomavirus; NGS, next generation sequencing; PCR, polymerase chain reaction; qPCR, quantitative PCR; RT-qPCR, reverse transcription quantitative PCR; SCC, squamous cell carcinoma; UCC, uterine cervical cancer.

Table 2 Selected studies validating cfDNA as a prognostic marker in cervical cancer

Study	Patient population	No of patients	Time of blood sample collection	Key findings
Kang et al (2017)[76]	Metastatic cervical cancer	19	Pre- and post-treatment time points	HPV cfDNA represents a promising tumor marker for non-invasive HPV genotyping and may be used in selecting patients for HPV type-specific T cell-based immunotherapies
Han et al (2018)[57]	Stage IB–IVA cervical cancer	23	At baseline, end of CRT, 3 months after CRT, and at recurrence	3-month plasma HPV DNA level is more accurate than 3-month FDG–PET imaging in detecting residual disease
Tian et al (2019)[61]	Different stages of cervical cancer (stages I–IV)	57	Blood samples available at various time points (once, twice or thrice randomly)	The decrease in values of cfDNA AFD was directly associated with reduction of tumor mass. Targeted deep sequencing of cfDNA along with genomic DNA may help in prediction of treatment response and relapse in cervical cancer
Lee et al (2020)[58]	Different stages of cervical cancer (stages I–IV)	4 for treatment monitoring	1 week prior to primary treatment and three times during the treatment	RNF213 mutation could be potentially used as a monitoring marker for response to chemo- and radiotherapy
Jeannot et al (2021)[36]	HPV16- or HPV18-positive cervical cancer patients	94	At baseline, at the end of treatment and during follow-up visits at 6, 12, and 18 months	HPV ctDNA detection in serum sample was associated with high FIGO stage and para-aortic lymph node involvement
Cabel et al (2021)[38]	Cervical cancer at any stage	55	At baseline (before treatment), days 7, 21 and 35 during CRT and then at 2, 6, 12, 18 and 24 months	Residual HPV ctDNA at the end of CRT or during follow-up could help to identify patients more likely to experience subsequent relapse
Tian et al (2021)[62]	Locally advanced or metastatic relapsed cervical cancer	82	Before and, when possible, during therapy	Five genes which are significantly associated with metastasis were identified. Reduction in mutations in these genes post therapy was associated with stable disease or partial remission
Kim et al (2022)[59]	Patients with pathologically proven uterine cervical cancer who had completed planned radical RT and 4 patients without distant metastasis	25	Before RT (visit 1), during RT (especially before brachytherapy, visit 2), and 3 months after RT (visit 3)	HPV cfDNA ratio outperforms tumor markers in treatment monitoring and may be considered as a valuable tool for monitoring and predicting treatment responses
Mittelstadt et al (2023)[63]	Advanced-stage disease (n=17, FIGO IB3–IVB) and patients with early-stage disease (n=9, FIGO IA–IB2)	26	Before and after therapy at different time points (8 patients followed for therapy monitoring)	HPV-cfDNA is a potential marker for treatment response monitoring in cervical cancer patients

Continued

Endometrial Cancer: Early Detection, Therapy Response and Prognostic

Table 1. Summary of studies characterizing circulating biomarkers to monitor EC.

Biomarker	Stage	Clinical Significance	Type of Sample	Cohort	Technology	References
HE4 and CA125	Early stages	Prognosis and recurrence monitoring	Serum	174	Enzyme immunoassay	[48]
cfDNA content	Early and advanced stages	Diagnostic, prognostic, potential application to therapy response	Plasma	$n = 109$; 31 FIGO I, 59 FIGO II, 19 FIGO III	PCR-RFLP	[96]
cfDNA content	Early stages	Prognostic predictor	Serum	$n = 88$	Alu-qPCR	[54]
ctDNA	Early and advanced stages	Prognostic, therapy response	Plasma	$n = 199$; 12 G1, 30 G2, 18 G3	ddPCR (*PIK3CA, KRAS*)	[79]
cfDNA and cfmtDNA	Early and advanced stages	Diagnostic, prognostic, potential application to therapy management	Serum	$n = 81$; 12 G1, 30 G2, 17 G3	Rf-qPCR	[52]
ctDNA	Early and advanced stages	Prognostic, therapy response	Tissue, serum	$n = 44$; 17 uterine cancer cases)	WES, ddPCR	[57]
ctDNA	Localized and advanced stages	Disease monitoring	Uterine aspirates, plasma	$n = 60$	ddPCR	[44]
ctDNA	Localized and advanced stages	Disease monitoring	Plasma	$n = 13$	NGS	[59]
ctDNA	Localized stages	Disease monitoring	Plasma	$n = 9$	ddPCR	[60]
miR-135b, miR-205 and miR-30a-3p	Localized stages	Diagnostic and post-surgery monitoring	Plasma	$n = 24$	Rf-qPCR	[69]
CTCs	Advanced stages	Therapy response	Whole blood	$n = 30$	CellSearch	[81]

Ovarian Cancer: Early detection and follow-up

Table 1
Characteristics of the main studies included [cmiRNA: Circulating miRNA; CT: chemotherapy; CTC: Circulating Tumor Cells; ctDNA: Circulating tumor DNA; ddPCR: droplet digital PCR; DFS: disease-free survival; iCTC: invasive subpopulation of CTCs; MSP: Fluorescent methylation-specific PCR; Multiplex RT-PCR: multiplex reverse transcriptase-polymerase chain reaction; NA: Not applicable; NR: Not reported; PFS: progression-free survival; PPV: positive predictive value; OS: overall survival; TP53MAF: TP53 mutant allele fraction; ttd: time from first relapse to death; TTP: time to progression; WES: whole- exome sequencing; RCT: randomized clinical trial].

Authors	Country	Study design	No. of cases	Stage	Liquid biopsy (genes-proteins analyzed)	Tool	Detection rate	Results
Zhang 1994 (Van Berchelaer et al., 2018)	China	Prospective observational	109	Stage I-IV	CTC (peripheral blood)	Multiplex RT-PCR	90%	OS shorter in CTC +
Marth 2003 (Pearl et al., 2014)	Austria/ Norway	Prospective observational	90	Stage I-IV	CTC (peripheral blood - bone marrow)	Immuno-cytochemistry	• Bone marrow 21% • Peripheral blood 12%	OS shorter in CTC + bone marrow
Judson 2003 (Liu et al., 2018)	USA	Prospective observational	64	Stage I-IV	CT (peripheral blood)	Tumor-enriched immunocytochemical assay	18,7%	PFS and OS No differences
Gifford 2004 (Cohen et al., 2018)	UK	Phase III RCT	128	Stage Ic- IV	DNA methylation (hMLH1 CpG)	MSP of hMLH1 CpG island.	• Pre-CT 12% • Relapse 33%	TTP shorter in Methylation of hMLH1
Ibanez De Caceres 2004 (Wang et al., 2018)	USA	Retrospective	50	Stage I-IV	DNA methylation (BRCA, RASSF1A) (Serum - peritoneal fluid)	MSP of BRCA1 and RASSF1A	• BRCA1 24% • RASSF1A 50%	Sensitivity: 82% Specificity: 100%
Fan 2009 (Bianci et al., 2018a)	USA	Prospective observational	71	Stage I-IV	CTC (peripheral blood)	Immuno-cytochemistry	60.6%	DFS shorter in CTC+
Resnick 2009 (Fabbri, 2018)	USA	Retrospective case control	28	Stage I-IV	cmiRNA	single step Trizol method + RT-PCR (TaqMan Array Human MicroRNA panel)	NR	miRNAs-21, – 92, – 93, – 126 significantly over expressed in OC miRNAs – 127, 155, – 99b significantly under expressed in OC
Aktas 2011 (Judson et al., 2003)	Germany	Prospective Observational	122	Stage I-IV	CTC (peripheral blood - bone marrow)	AdnaTest BreastCancer Followed by Multiplex RT-PCR	• Bone marrow 35% (before surgery) 21% (after CT) • Peripheral blood 19% (before surgery) 27% (after CT)	OS and DFS shorter in CTC + before surgery, shorter in CTC – after surgery

Authors	Country	Study design	No. of cases	Stage	Liquid biopsy (genes-proteins analyzed)	Tool	Detection rate	Results
Zhang 2013 (Taechaudeli et al., 2009)	China	Retrospective	87	Stage I-IV	DNA methylation (APC, RASSF1A, CDH1, RUNX3, TFF12, SFRP5 e OPCML)	Multiplex-MSP assay	NR	Early vs Advanced stages: same specificity, lower sensitivity in early stage
Zhang 2013 (Wang et al., 2017)	China	Retrospective, nested case-control	360	Stage I-IV	cmiRNA	TaqMan low-density array + RT-PCR	• miRNA over-expressed miR-205 • miRNAs under-expressed let-7 f	PFS: 100 months (all stages) PFS: 100 months (stages II-IV)
Pearl 2014 (Bekhukhi et al., 2011)	USA	Retrospective	129	Stage I-IV	iCTC (peripheral blood)	Multi-parameter flow cytometry (FACSCalibur and AIRIA, BD Biosciences)	68.6%	PPV: 77.8% (stage I-II) PPV: 97.3% (all stages)
Pereira 2015 (Barbosa et al., 2018)	USA	Prospe ctive observ ational	44	Stage I-IV	ctDNA	WES and targeted gene sequencing + ddPCR	93.8%	ctDNA (on the paired CT scan): high sensitivity ctDNA (tumor at the time of surgery): high specificity
Meng 2015 (Pandey et al., 2019)	Germany	Retrosp ective case-control	190	Stage I-IV	cmiRNA	TaqMan PCR microRNA assays	• miRNAs over-expressed - miR-7, – 429 • miRNAs under-expressed - miR-25, – 93	miR-7, – 25, – 93, – 429 have high sensitivity and specificity
Parkinson 2016 (Forshew et al., 2012a)	UK	Retrospective	40	Stage I, II, IV	ctDNA (TP53MAF)	Microfluidic digital PCR	82%	PPV: 6 months (TP53MAF decrease ≤ 60% after 1 cycle CT) PPV: 6 months (TP53MAF decrease > 60% after 1 cycle CT)
Flanagan 2017 (Phallen et al., 2017)	UK	Phase III RCT	247	Stage Ic-IV	DNA methylation (MLH1)	Illumina 450k methylation array	NR	DNA methylation at time of relapse following chemotherapy is related to ttd

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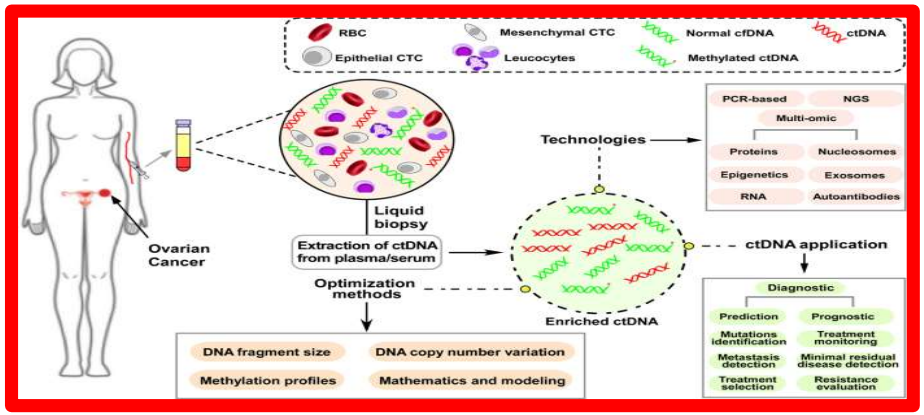
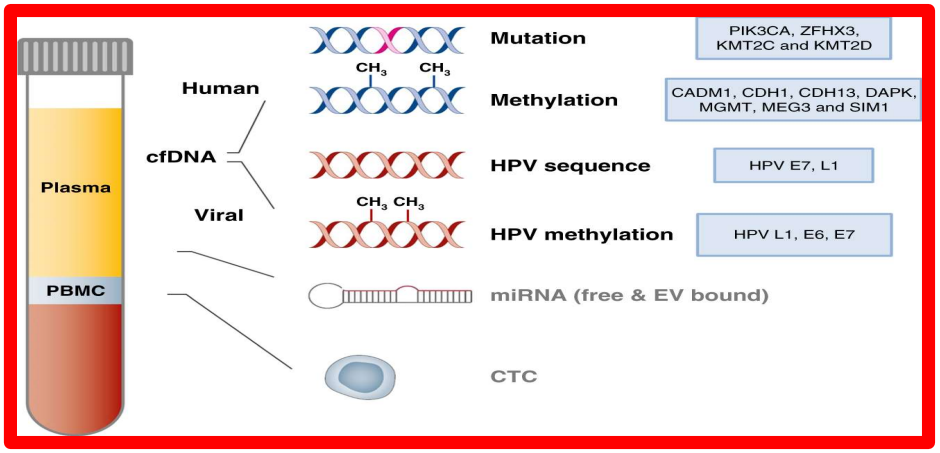
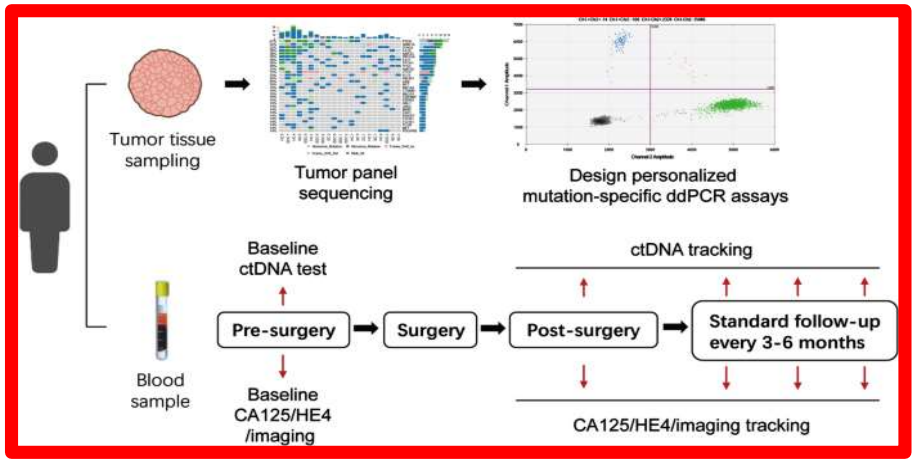
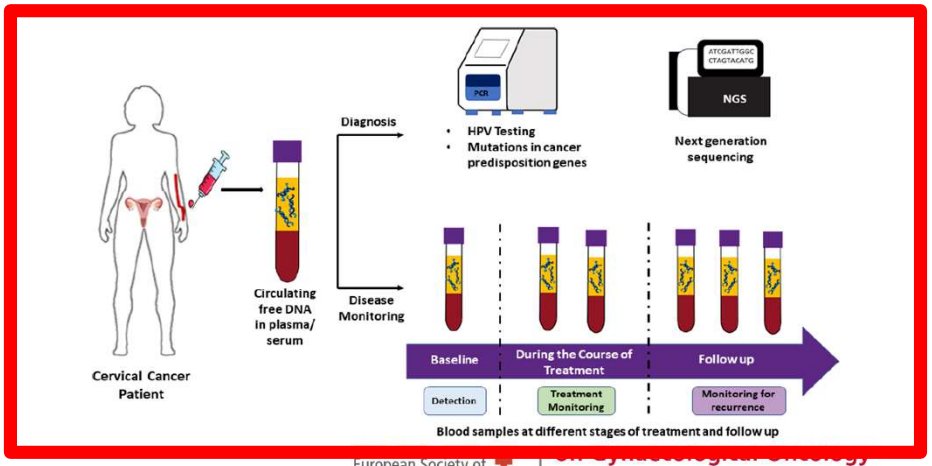

RBC
Epithelial CTC
Mesenchymal CTC
Leucocytes
Normal cfDNA
Methylated ctDNA
ctDNA
Ovarian Cancer
Liquid biopsy
Extraction of ctDNA from plasma/serum
Optimization methods
Technologies
PCR-based
NGS
Multi-omic
Proteins
Nucleosomes
Epigenetics
Exosomes
RNA
Autoantibodies
ctDNA application
Enriched ctDNA
Diagnostic
Prediction
Prognostic
Mutations identification
Treatment monitoring
Metastasis detection
Minimal residual disease detection
Treatment selection
Resistance evaluation
DNA fragment size
DNA copy number variation
Methylation profiles
Mathematics and modeling

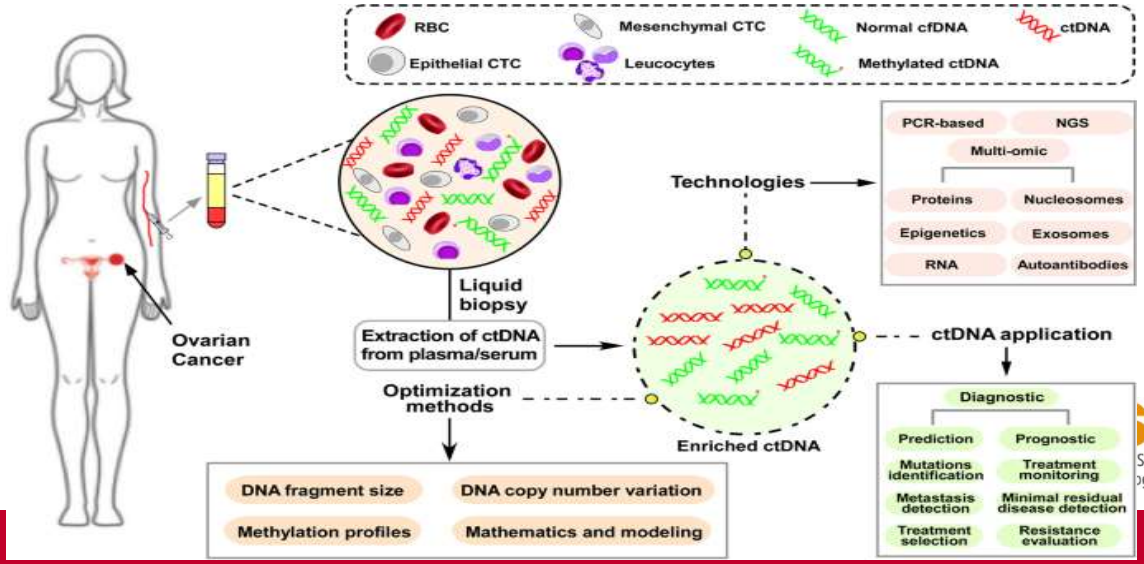

Plasma
PBMC
Human
cfDNA
Viral
Mutation
PIK3CA, ZFHX3, KMT2C and KMT2D
Methylation
CADM1, CDH1, CDH13, DAPK, MGMT, MEG3 and SIM1
HPV sequence
HPV E7, L1
HPV methylation
HPV L1, E6, E7
miRNA (free & EV bound)
CTC


Tumor tissue sampling
Tumor panel sequencing
Design personalized mutation-specific ddPCR assays
Baseline ctDNA test
ctDNA tracking
Pre-surgery
Surgery
Post-surgery
Standard follow-up every 3-6 months
Blood sample
Baseline CA125/HE4 /imaging
CA125/HE4/imaging tracking


Cervical Cancer Patient
Circulating free DNA in plasma/ serum
Diagnosis
Disease Monitoring
PCR
HPV Testing
Mutations in cancer predisposition genes
NGS
Next generation sequencing
Baseline
During the Course of Treatment
Follow up
Detection
Treatment Monitoring
Monitoring for recurrence
Blood samples at different stages of treatment and follow up

Cell free DNA (cfDNA)-Endometrial Cancer

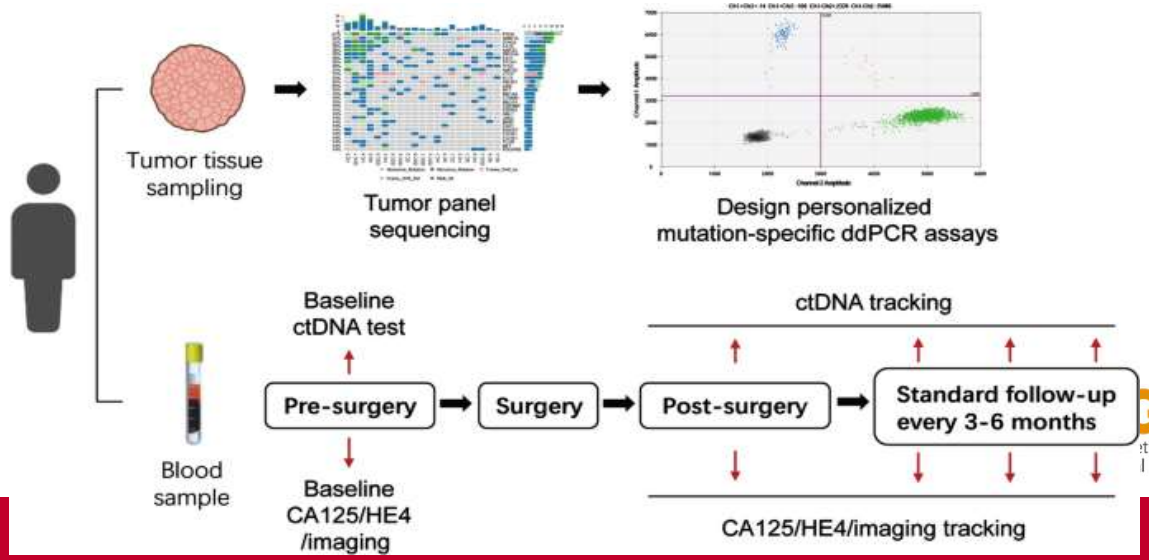
- Changes in circulating cell-free DNA (cfDNA) levels have been associated with cancer development and progression.
- A recent study found higher levels of total cell-free DNA (cfDNA) and mitochondrial cell-free DNA (cfmtDNA) in the blood of patients with endometrial cancer compared to non-cancerous conditions. The increase was notably more significant in cases of high-grade endometrial cancer.



Cell free DNA (cfDNA)-Endometrial Cancer

- ctDNA can better predict how well a treatment is working compared to standard blood tests and imaging scans.

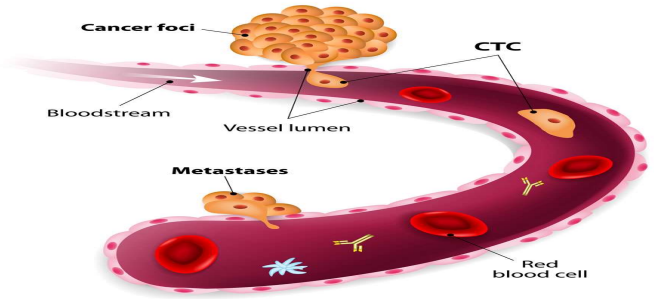
- ctDNA levels can provide effective prediction on survival.



Circulating Tumour Cells (CTCs), Endometrial Cancer

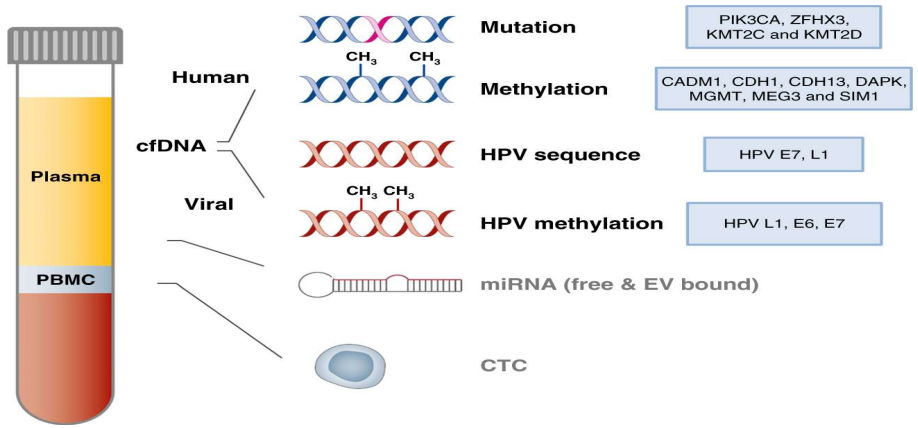
- The ENITEC (European Network for Individualized Treatment in EC) Consortium described a study with 22% (n= 32) CTC-positive high-risk EC patients.

- CTCs in the blood might be of help to determine the potential risk of recurrence and assess prognosis in endometrial cancer patients, but their use in clinical settings is still limited and inconclusive.



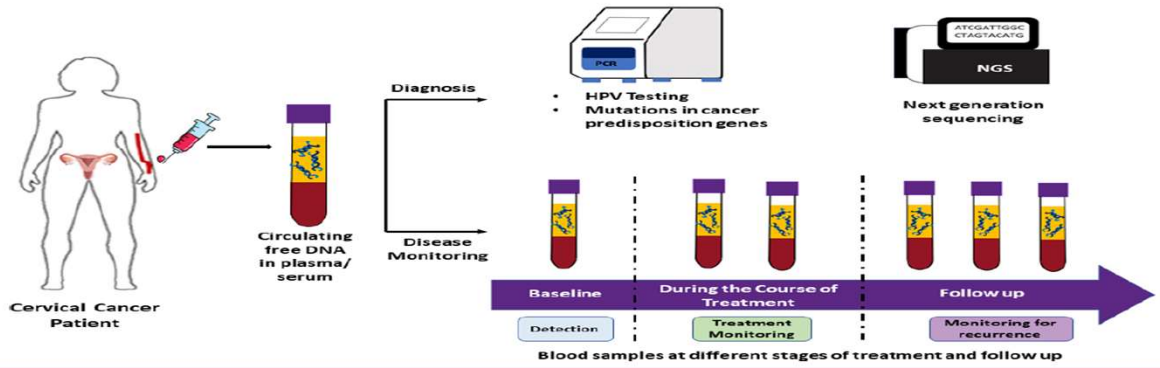
Cell free DNA (cfDNA)-Cervical Cancer

- The majority of cervical cancers are linked to high-risk HPV infections. Detecting HPV DNA in the blood can predict the possibility of cervical cancer metastasis within a year.
- However, the main issue was that the PCR technology in the early 2000s was not sufficient to detect minor variations and low copy numbers, rendering it ineffective.
- In recent years, with the advent of methods like Droplet Digital PCR (ddPCR), the specificity of the assay has reached 100%, with a sensitivity of around 90%.



Cell free DNA (cfDNA)-Cervical Cancer

- The Cancer Genome Atlas (TCGA) Research Network published one of the most extensive studies in cervical cancer in 2017.
- Identified previously unreported significantly mutated genes and other factors that make these tumors good targets for immunotherapy and targeted therapy based on their genetic profiles.
- Several studies have indicated that lower levels of circulating cell-free DNA (cfDNA) in patients are associated with a favorable response to treatment in various types of cancers.
- Conversely, higher levels of cfDNA typically signify a poor response to treatment and a lower progression-free survival (PFS) rate.

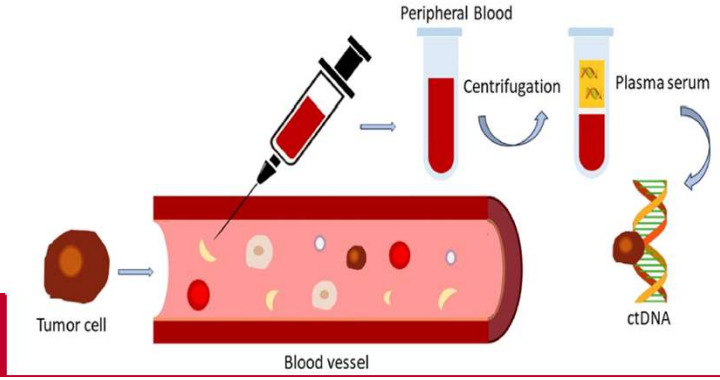


Cell free DNA (cfDNA)-Ovarian Cancer

- The findings suggest that circulating tumor cells (CTCs) can play a crucial role in early diagnosis, prognostic prediction, and treatment guidance for ovarian cancer (OC).

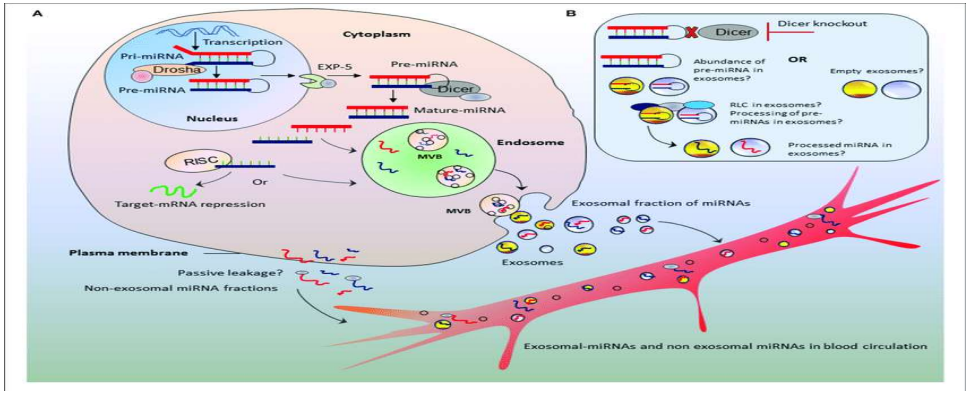
- Early-stage OC shows limited sensitivity and specificity in cfDNA analyses

- With the accumulation of data , liquid biopsy can use to help treat and follow-up of ovarian cancer.
- However, they still need to do more research and use the same methods for all patients



Circulating Exosomes/miRNAs (micro RNA)

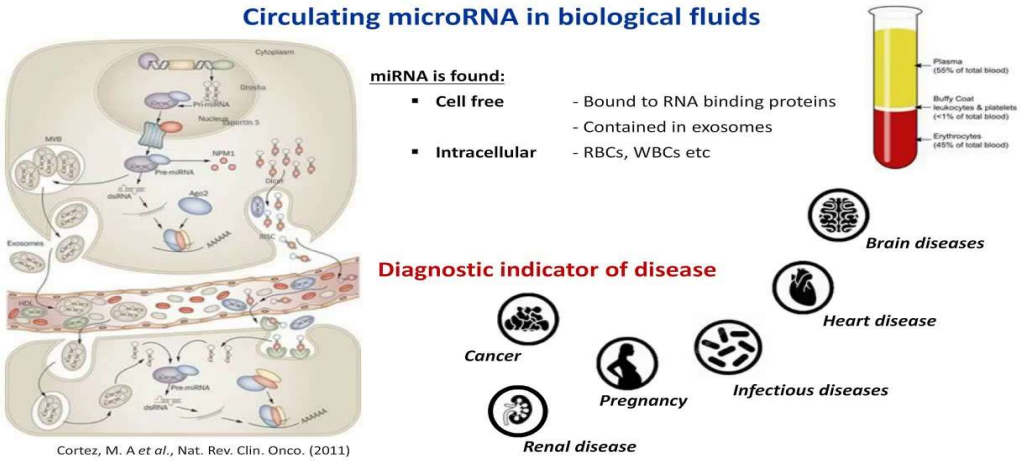
- Nanoparticle size structures called extracellular vesicles, which contain proteins, lipids, and DNA/RNAs and play a role in cell-to-cell communication, are considered as alternative forms of liquid biopsy.
- Not only do they appear in cancer cells, but they can also transfer tiny regulatory RNAs to cells called endometrial fibroblasts
- Plasma miR-99a/miR-199b resulted in 88% sensitivity and 93% specificity. (Good diagnostic potential).



Circulating Exosomes/miRNAs

- Evidence suggests that microRNAs increase more significantly in patients with gynecologic cancer compared to those with benign diseases and healthy controls.

- Great potential of miRNA signatures in liquid biopsies as valuable information in Gynecologic cancer.



Cortez, M. A *et al.*, Nat. Rev. Clin. Onco. (2011)

IDENTIFICATION OF NEW MOLECULER TARGET

BIOMARKERS ASSOCIATED WITH A HIGH RISK OF RECURRENCE

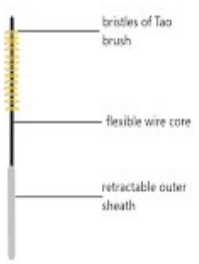
RESPONSE TO THERAPY AS VALUABLE TOOLS TO IMPROVE TREATMENT OF ADVANCED DISEASE

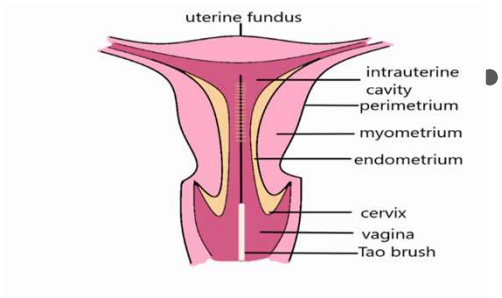
LOW QUANTITY OF TUMOUR MATERIAL PRESENT

MINIMAL DETECTİON OF RESIDUAL DISEASE

UTERINE ASPIRATES

- Pap brush, showed 81% (95% CI, 76–84%) of EC

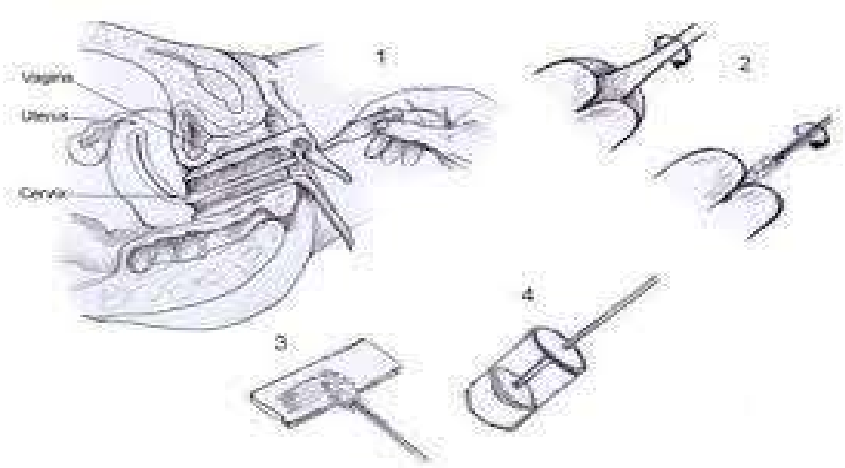


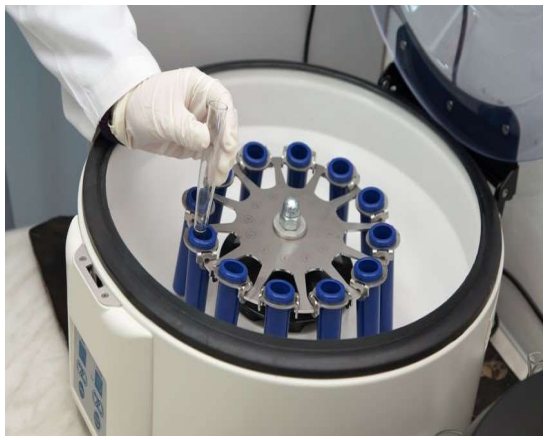


- Tao brush and endocervical sampling with a Pap brush,
- improved detection rate of 93% (95% CI, 87–97%) patients with endometrial cancer

ERA PerMed-CYTOMARK PROJECT

This funded project aims is to advance the development of a non-invasive, objective, and personalised diagnostic tool of endometrial cancer using cervical fluid protein biomarkers and clinical data.





SELF-EVALUATION QUESTIONNAIRE STAI Form Y-1

Please provide the following information:

Name_____ Date_____ S_____

Age_____ Gender (*Circle*) **M** **F** T_____

DIRECTIONS:

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you feel *right* now, that is, *at this moment*. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

	NOT AT ALL	SOMEWHAT	MODERATELY SO	VERY MUCH SO
1. I feel calm	1	2	3	4
2. I feel secure	1	2	3	4
3. I am tense	1	2	3	4
4. I feel strained	1	2	3	4
5. I feel at ease	1	2	3	4
6. I feel upset	1	2	3	4
7. I am presently worrying over possible misfortunes	1	2	3	4
8. I feel satisfied	1	2	3	4
9. I feel frightened	1	2	3	4
10. I feel comfortable	1	2	3	4
11. I feel self-confident	1	2	3	4
12. I feel nervous	1	2	3	4
13. I am jittery	1	2	3	4
14. I feel indecisive	1	2	3	4
15. I am relaxed	1	2	3	4
16. I feel content	1	2	3	4
17. I am worried	1	2	3	4
18. I feel confused	1	2	3	4
19. I feel steady	1	2	3	4
20. I feel pleasant	1	2	3	4

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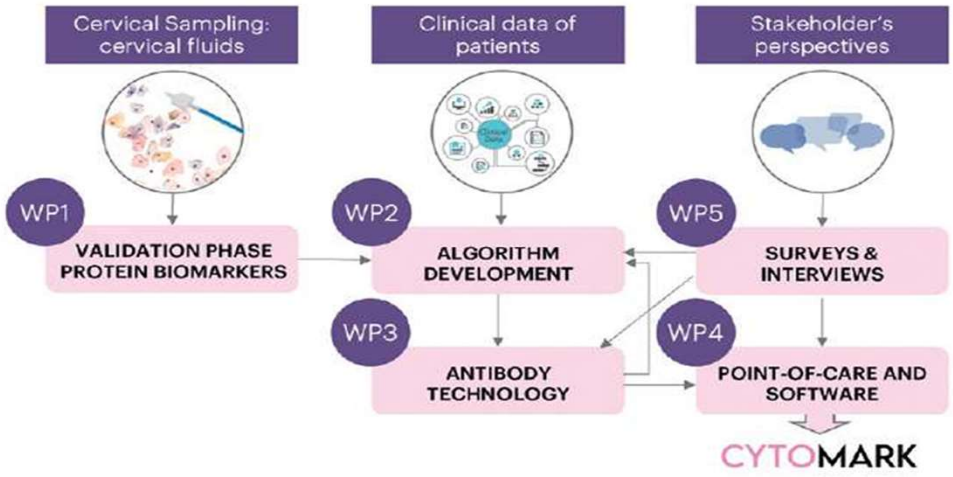
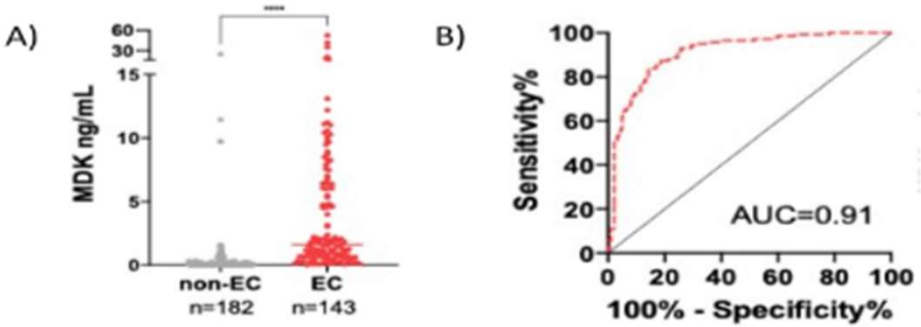


Partners:

1)Vall debron institute of research (VHIR), Spain
2)Luxembourg institute of health, Luxembourg
3)Universidad de santiago de compostela, Spain
4)Icosagen cell factory, Estonia
5)Hacettepe university hospitals, Turkiye
6)Solar biyoteknolojı ltd, Turkiye



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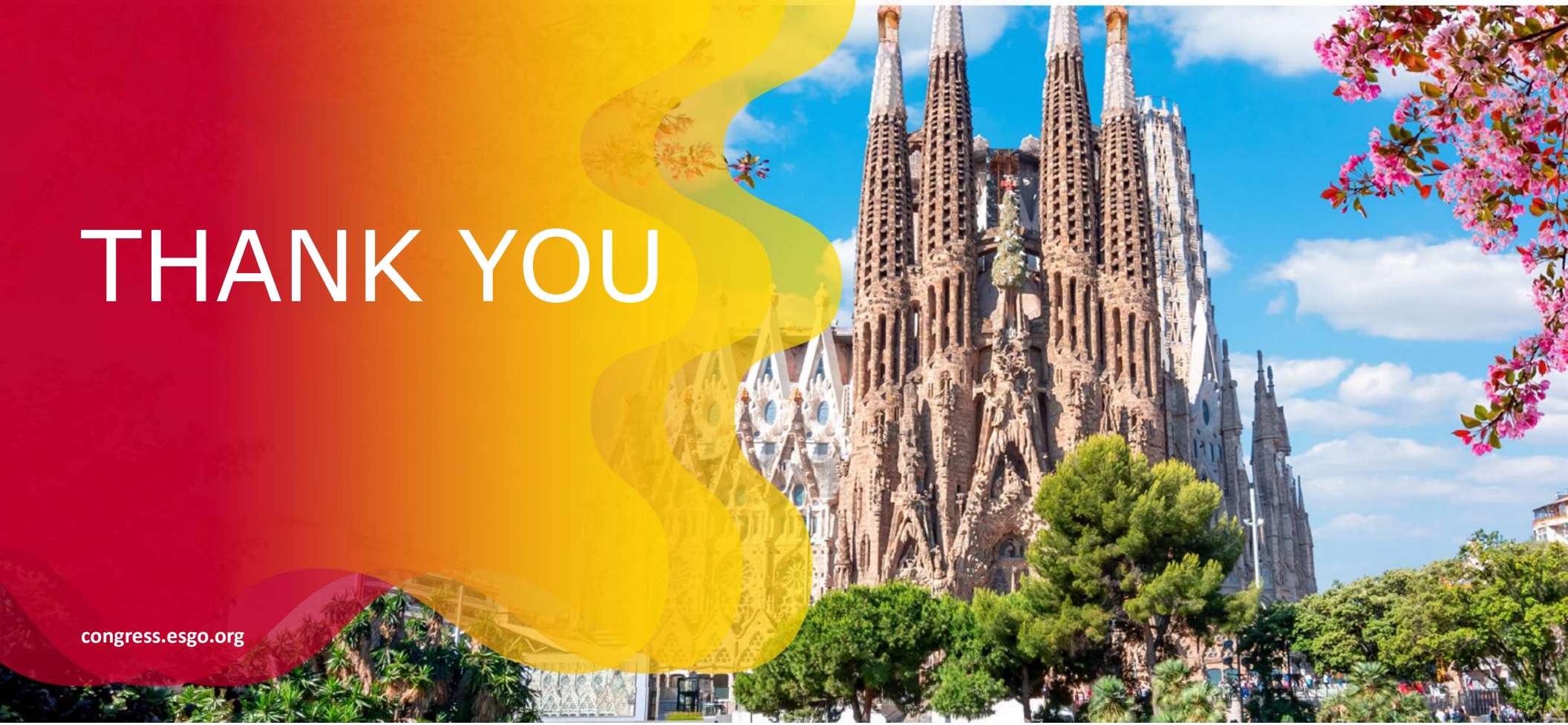

THANK YOU

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