Fertilite Koruyucu Laparoskopik Cerrahi

- Over Transpozisyonu
- Over Dokusu İmplantasyonu

Dr. L. Cem Demirel

Memorial Ataşehir IVF

Strategies for fertility preservation

1. Reducing toxicity

2. Cryopreservation

3. Conservative surgery

Fertility sparing surgery

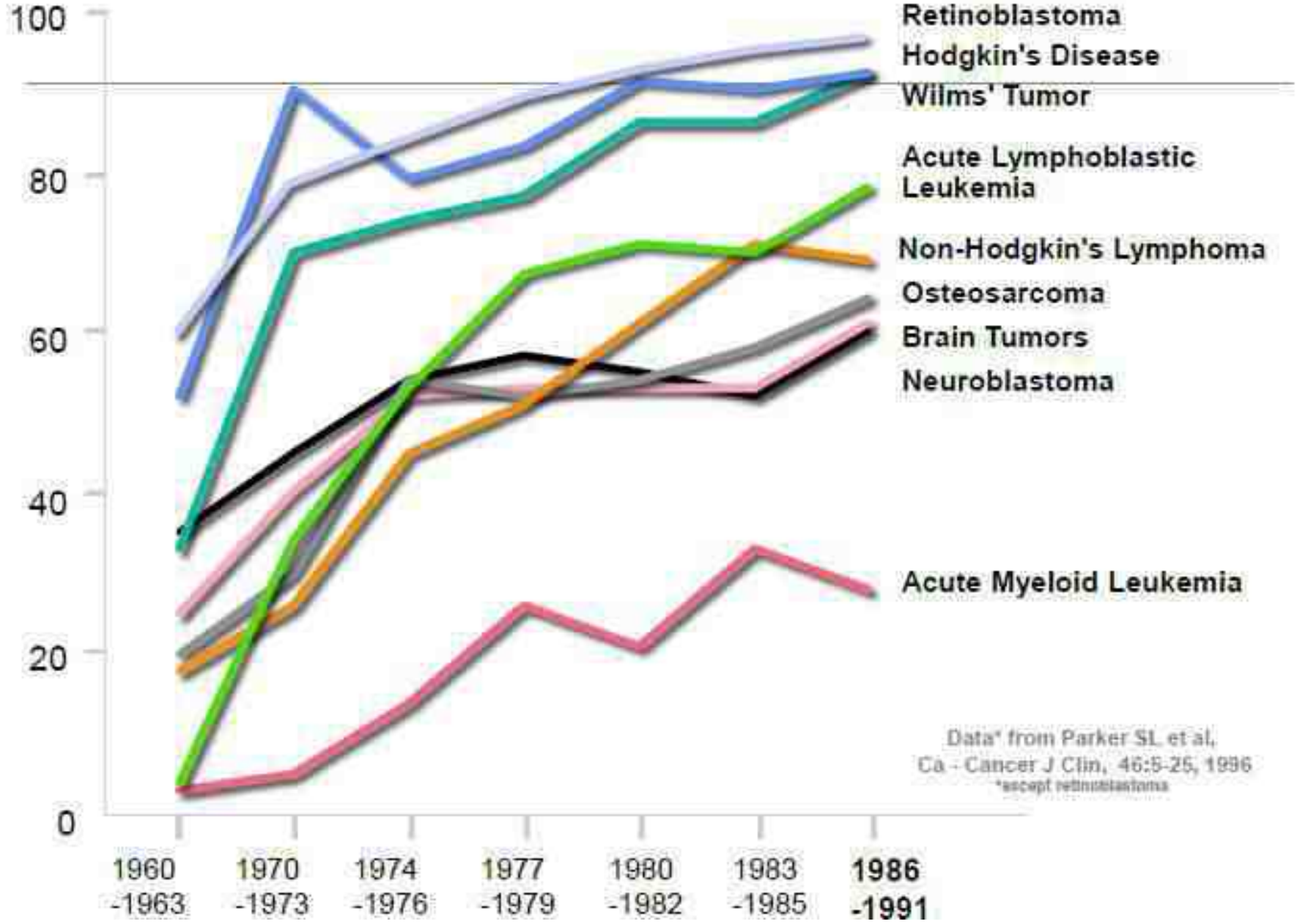
1. Ovarian cancer :
   - Borderline tumours
   - Invasive carcinoma stage Ia G1

2. Endometrial cancer: stage Ia G1,

3. Cervical cancer: < 2 cms, stages Ia – Ib1,

Querleu D et al, Bull Cancer 2008
Gurgan T et al, Placenta 2008
Fujiwara H et al, Hum Rep 2009
Koskas et al. Fertil Steril 2012

% Survival in Common Pediatric Cancers



ASSESSMENT OF RISK OF SUBFERTILITY AFTER TREATMENT FOR COMMON CANCERS IN CHILDHOOD AND ADOLESCENCE

Low risk <20%	Acute lymphoblastic leukemia
	Wilm's tumor
	Soft-tissue sarcoma: stage I
	Germ cell tumors (with gonadal preservation and no radiotherapy)
	Retinoblastoma
	Brain tumor: surgery only, cranial irradiation <24 Gy
Medium risk	Acute myeloblastic leukemia
	Hepatoblastoma
	Osteosarcoma
	Ewing's sarcoma stage II or III
	Neuroblastoma
	Non-Hodgkin lymphoma
	Hodgkin's disease: alternating treatment
	Brain tumor: craniospinal radiotherapy, cranial irradiation >24 Gy
High risk >80%	Whole-body irradiation
	Localized pelvic radiotherapy
	Chemotherapy conditioning for bone-marrow transplantation
	Hodgkin's disease: treatment with alkylating drugs
	Soft-tissue sarcoma: stage IV
	Metastatic Ewing's sarcoma

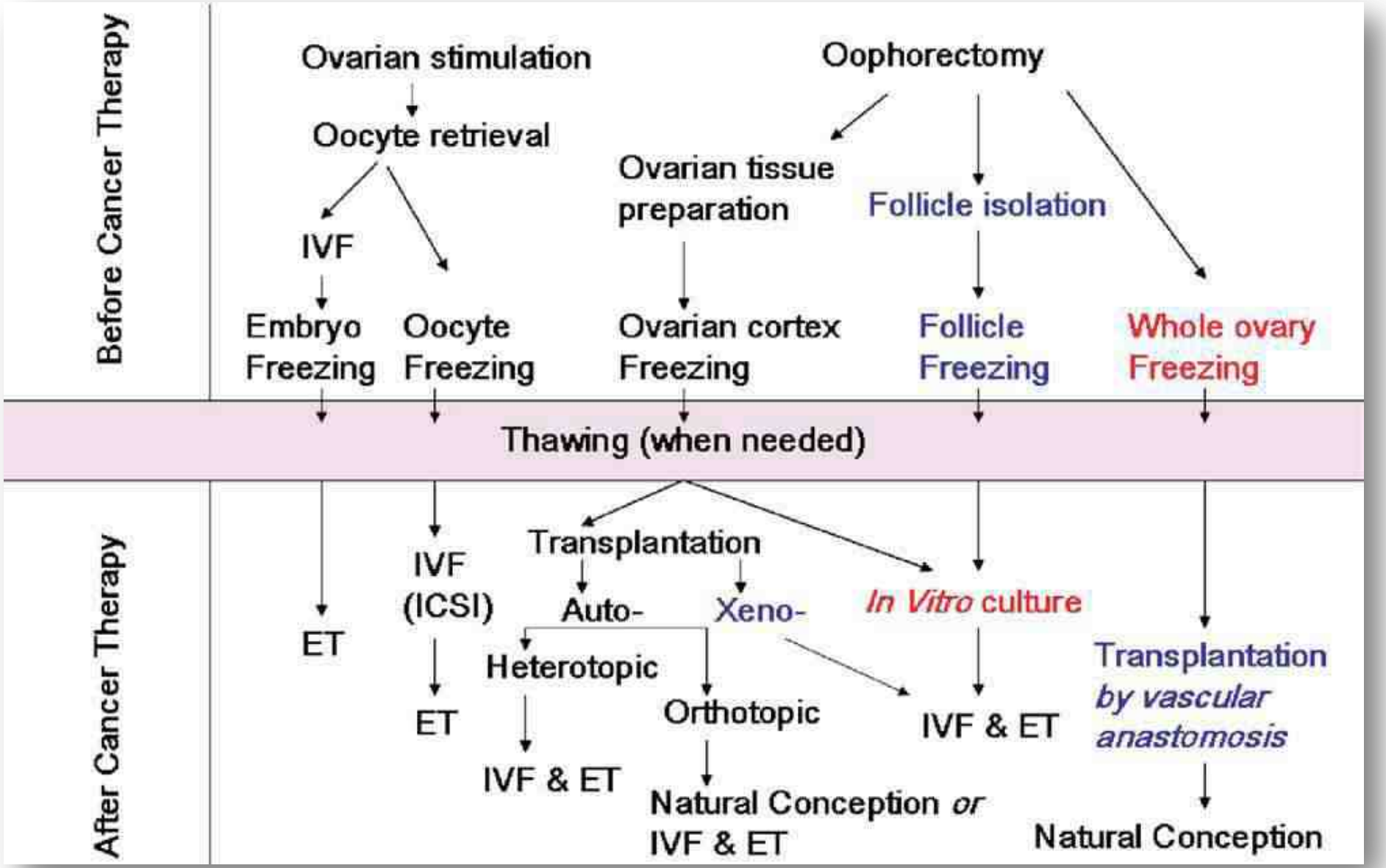
WALLACE et al 2005

NON-MALIGNANT PATHOLOGIES WITH RISK OF POF

- Bone-marrow transplantation
  - Sickle cell anemia
  - Thalassemia major
  - Aplastic anemia
  - Autoimmune diseases unresponsive to immunosuppressive therapy
- Autoimmune diseases requiring chemotherapy
  - Systemic lupus erythematosus
  - Rheumatoid arthritis
  - Behcet's disease
  - Wegener's disease
  - Multiple sclerosis
- Ovarian pathologies
  - Recurrent ovarian cysts
  - Ovarian torsion
- Endocrine or genetic diseases
  - Turner syndrome
  - Galactosemia
  - Family history of premature ovarian failure
- Sex reassignment surgery in transsexuals

Modified from P. JADOUL et al (2010)

Human Reproduction Update 16-6, 617-630


Before Cancer Therapy
Ovarian stimulation
Oocyte retrieval
IVF
Embryo Freezing
Oocyte Freezing
Oophorectomy
Ovarian tissue preparation
Follicle isolation
Ovarian cortex Freezing
Follicle Freezing
Whole ovary Freezing
Thawing (when needed)
After Cancer Therapy
ET
IVF (ICSI)
ET
Transplantation
Auto-
Xeno-
Heterotopic
IVF & ET
Orthotopic
Natural Conception or IVF & ET
In Vitro culture
IVF & ET
Transplantation by vascular anastomosis
Natural Conception

Fertility Preservation in Cancer Patients

1st choice

OOCYTE CRYOPRESERVATION

- Women willing to conceive
- Oncologist consultation and approval
- Does not exclude ovarian cortex removal

Concerns:

- Cross-contamination

OVARIAN CORTEX CRYOPRESERVATION

- Girls
- Contraindication for ovarian stimulation
- Oncologist disapprove stimulation
- No time for ovarian stimulation

Concerns:

- Leukaemia
- Cross-contamination

The risk of ovarian metastasis according to cancer types

- Cancers with low risk of ovarian involvement
  - Wilm's tumour
  - Ewing's sarcoma
  - Breast cancer
    - Stage I-III
    - Infiltrative ductal histological subtype
  - Non-Hodgkin's lymphoma
  - Hodgkin's lymphoma
  - Non-genital rhabdomyosarcoma
  - Osteogenic sarcoma
  - Squamous cell carcinoma of the cervix
- Cancers with moderate risk of ovarian involvement
  - Adenocarcinoma/adenosquamous carcinoma of the cervix
  - Colon cancer
  - Breast cancer
    - Stage IV
    - Infiltrative lobular histological subtype
- Cancers with high risk of ovarian involvement
  - Leukaemia
  - Neuroblastoma
  - Burkitt lymphoma

M. Sonmezer and K. Oktay 2004

Human Reproduction Update, 10-3 : 251-266

AUTOTRANSPLANTATION OF CRYOPRESERVED OVARIAN TISSUE IN CANCER SURVIVORS AND THE RISK OF REINTRODUCING MALIGNANCY: A SYSTEMATIC REVIEW

L. Bastings et al.

Methods: A systematic review of literature

Results: A total of 289 studies were included

Conclusions: It is advisable to refrain from ovarian tissue autotransplantation in survivors of leukaemia. With survivors of all other malignancies, current knowledge regarding the safety of autotransplantation should be discussed. The most reassuring data regarding autotransplantation safety were found for lymphoma patients.

Human Reproduction Update 19-5:483-506 (2013)

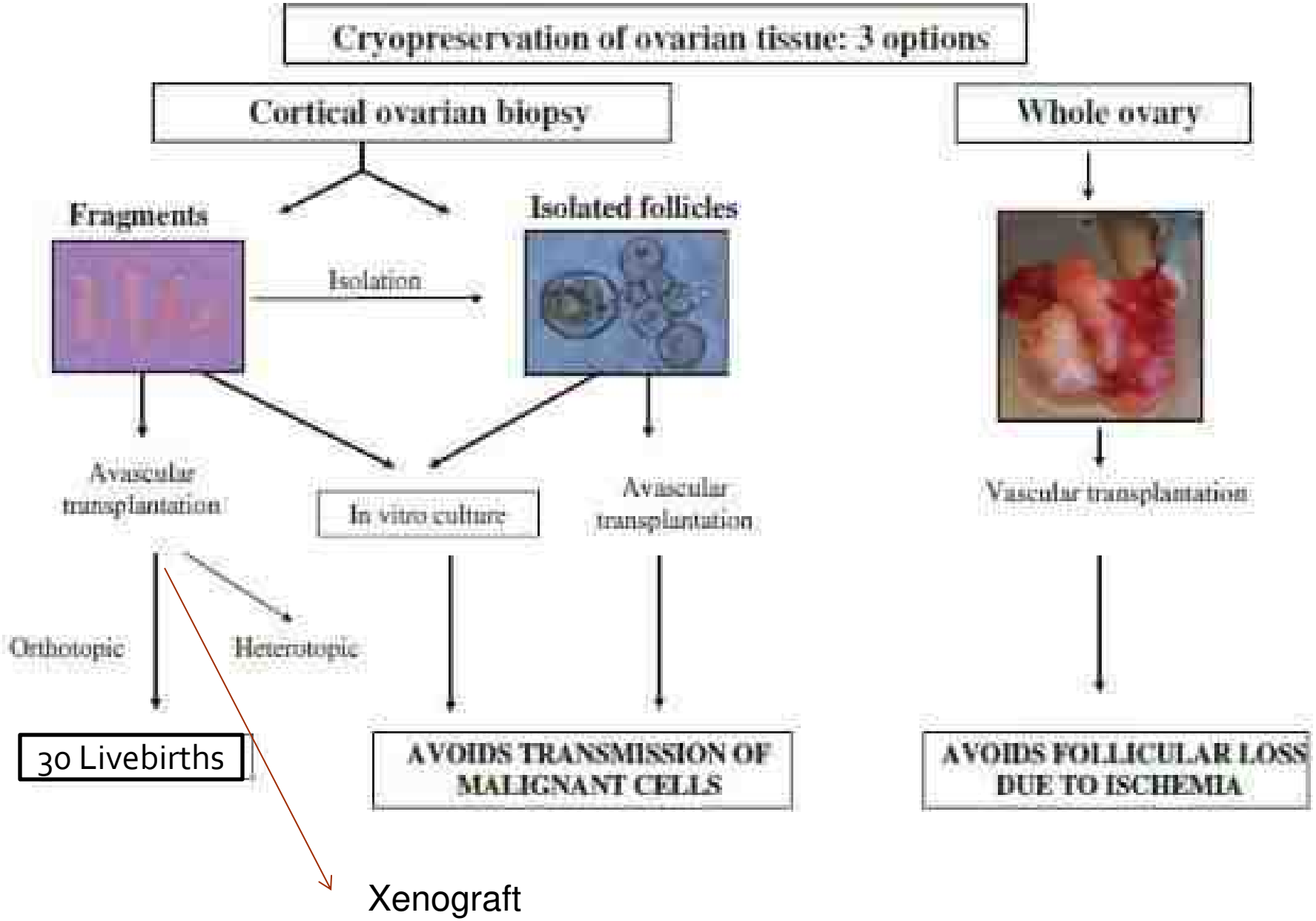
CRYOPRESERVATION	CHARACTERISTICS
Embryos	**9.5 ± 2.33 days** HUQD, 2013
Oocytes	
Ovarian tissue	Minimum a surgical intervention No need for ovarian stimulation . No time limitation Risk of reimplanting malignant cells (minimal in breast cancer) Graft survival?

LONG-TERM DURATION OF FUNCTION OF OVARIAN TISSUE TRANSPLANTS: CASE REPORTS

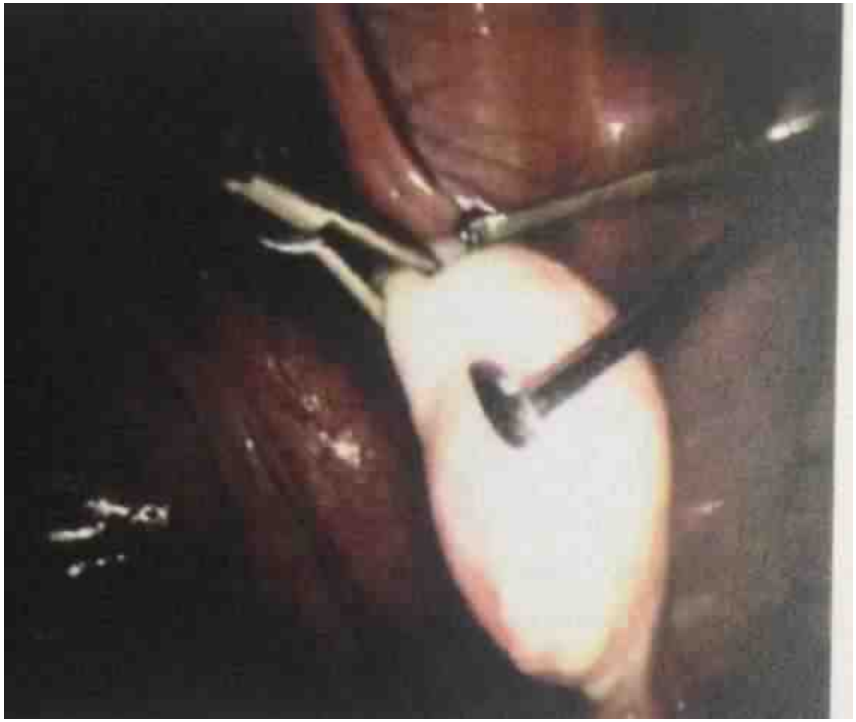
Claus Y. Andersen et al

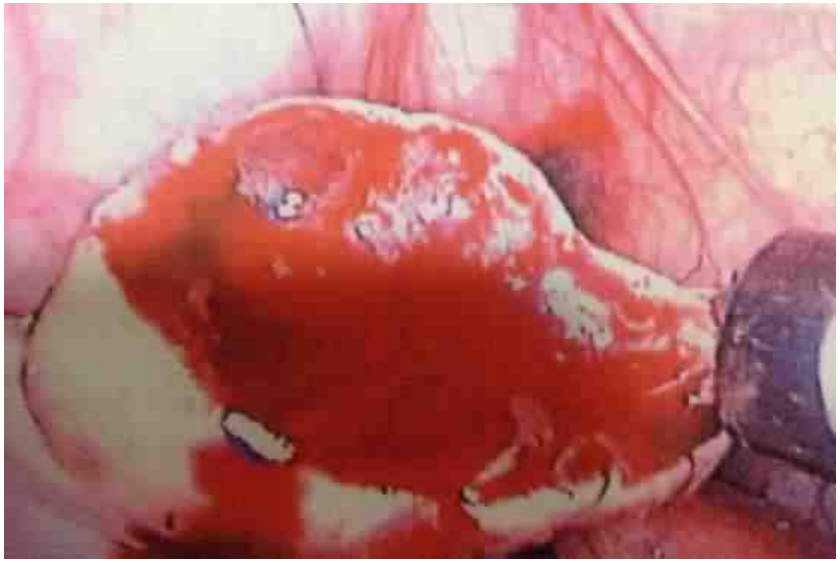
These three case reports describe the long-term duration of function of ovarian cortical tissue grafts among patients in a university fertility preservation programme in Europe and in a private practice programme in the USA. One woman underwent sterilizing cancer treatment and had frozen ovarian tissue transplanted, and two women underwent fresh ovarian tissue transplants. The function of ovarian cortical strips has continued for more than 7 years in these three women, with the birth of eight healthy babies following a single graft per patient.

REPRODUCTIVE BIOMEDICINE ONLINE (2012) 25, 128-132

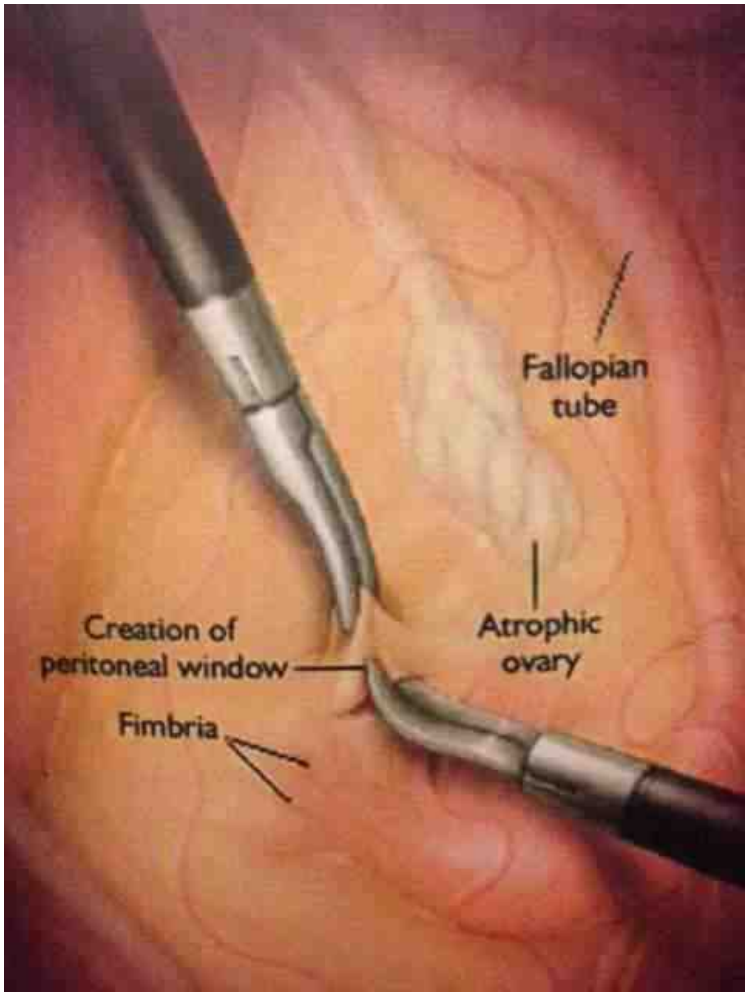

Cryopreservation of ovarian tissue: 3 options
Cortical ovarian biopsy
Whole ovary
Fragments
Isolated follicles
Isolation
Avascular transplantation
In vitro culture
Avascular transplantation
Vascular transplantation
Orthotopic
Heterotopic
30 Livebirths
AVOIDS TRANSMISSION OF MALIGNANT CELLS
AVOIDS FOLLICULAR LOSS DUE TO ISCHEMIA
Xenograft

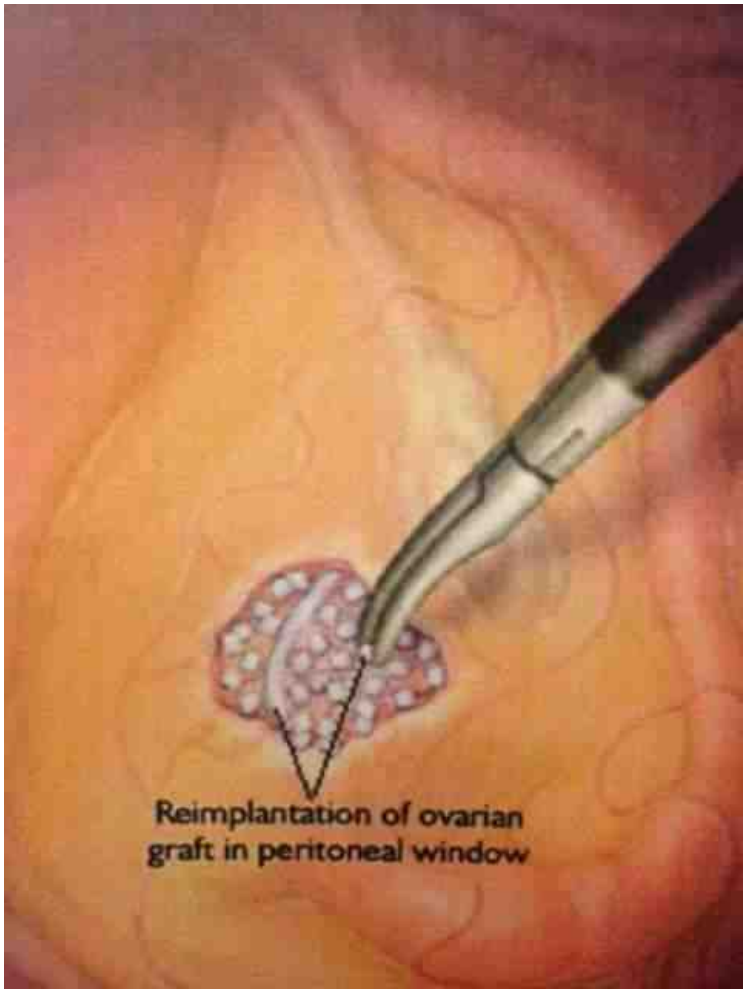
LS excision of ovarian tissue for cryo



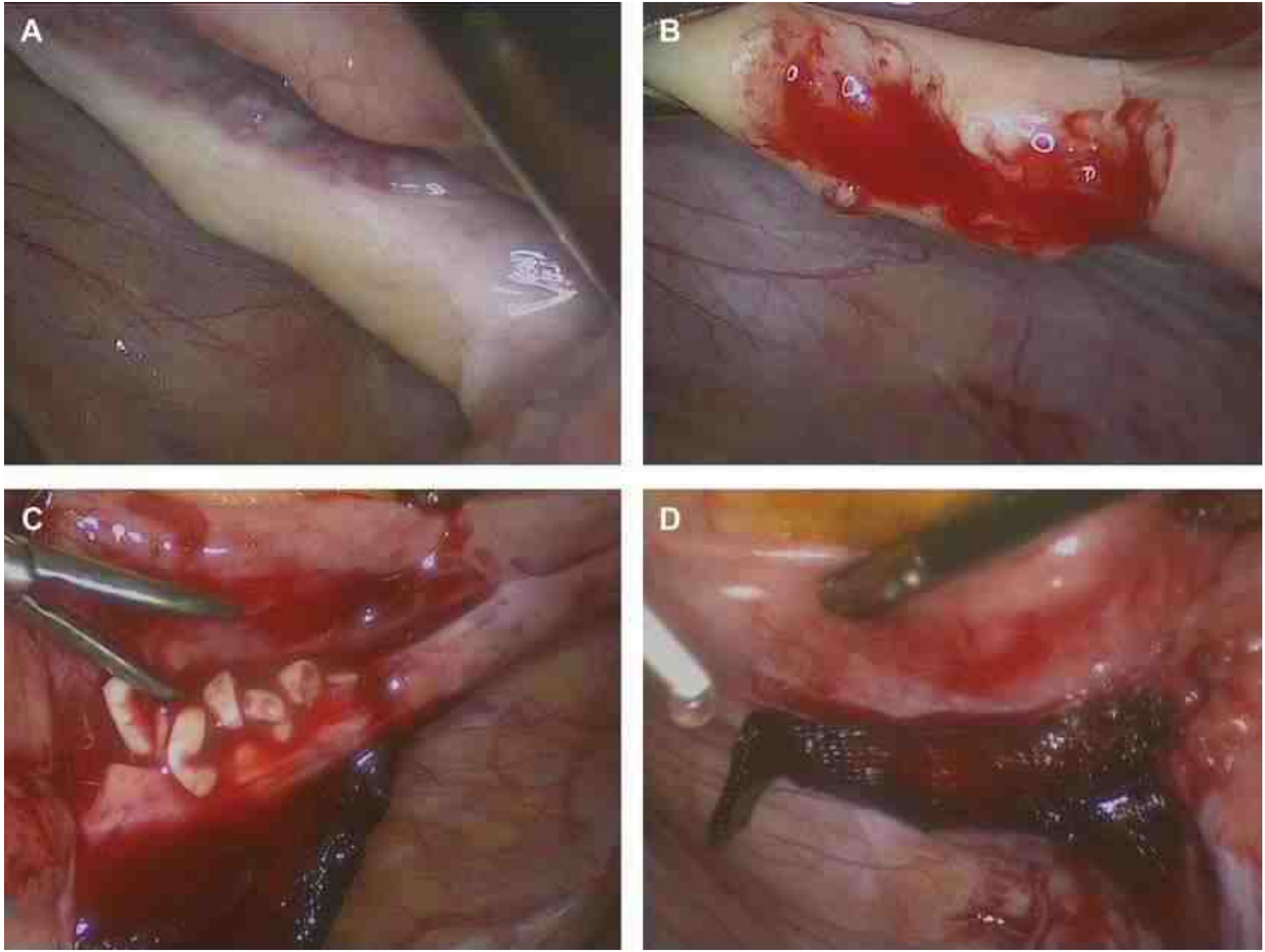


Reimplantasyon - I

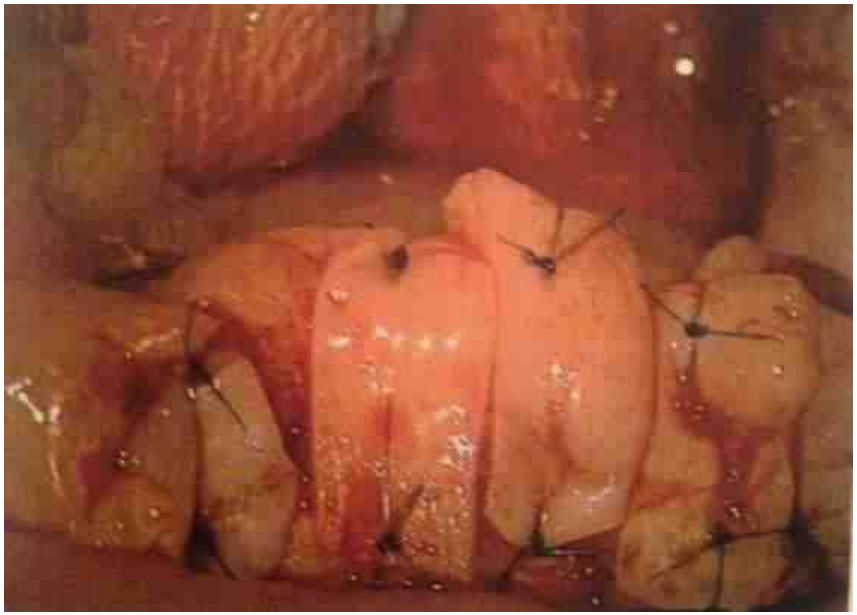




Reimplantasyon - II


A
B
C
D

Overin medullasına sütüre edilmiş dondurulmuş over dokusu parçaları



İskemi

- Primordial folliküllerin çoğu transplantasyon sonrası kaybedilir (survi:%5-50)
- Teorik olarak:antioksidan veya anti apopitotik kullanımı veya anjiogenez indüksiyonu (GT kullanımı)
- Anjiogenez 48 saat-7gün

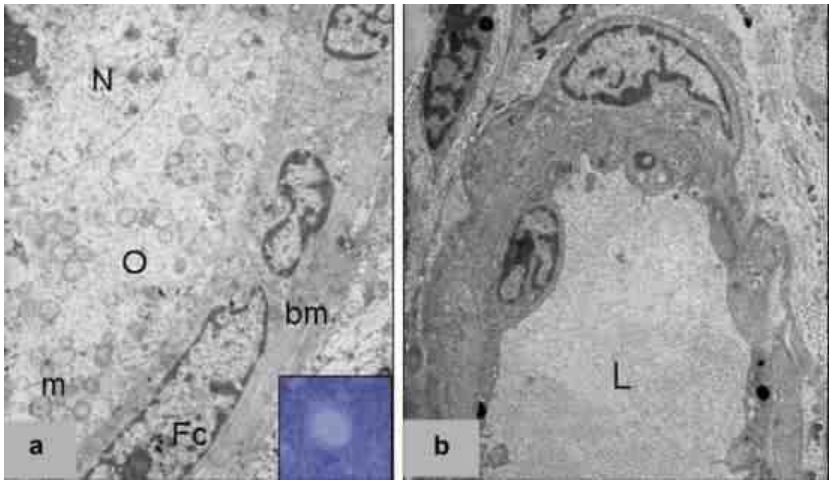


TABLE 1

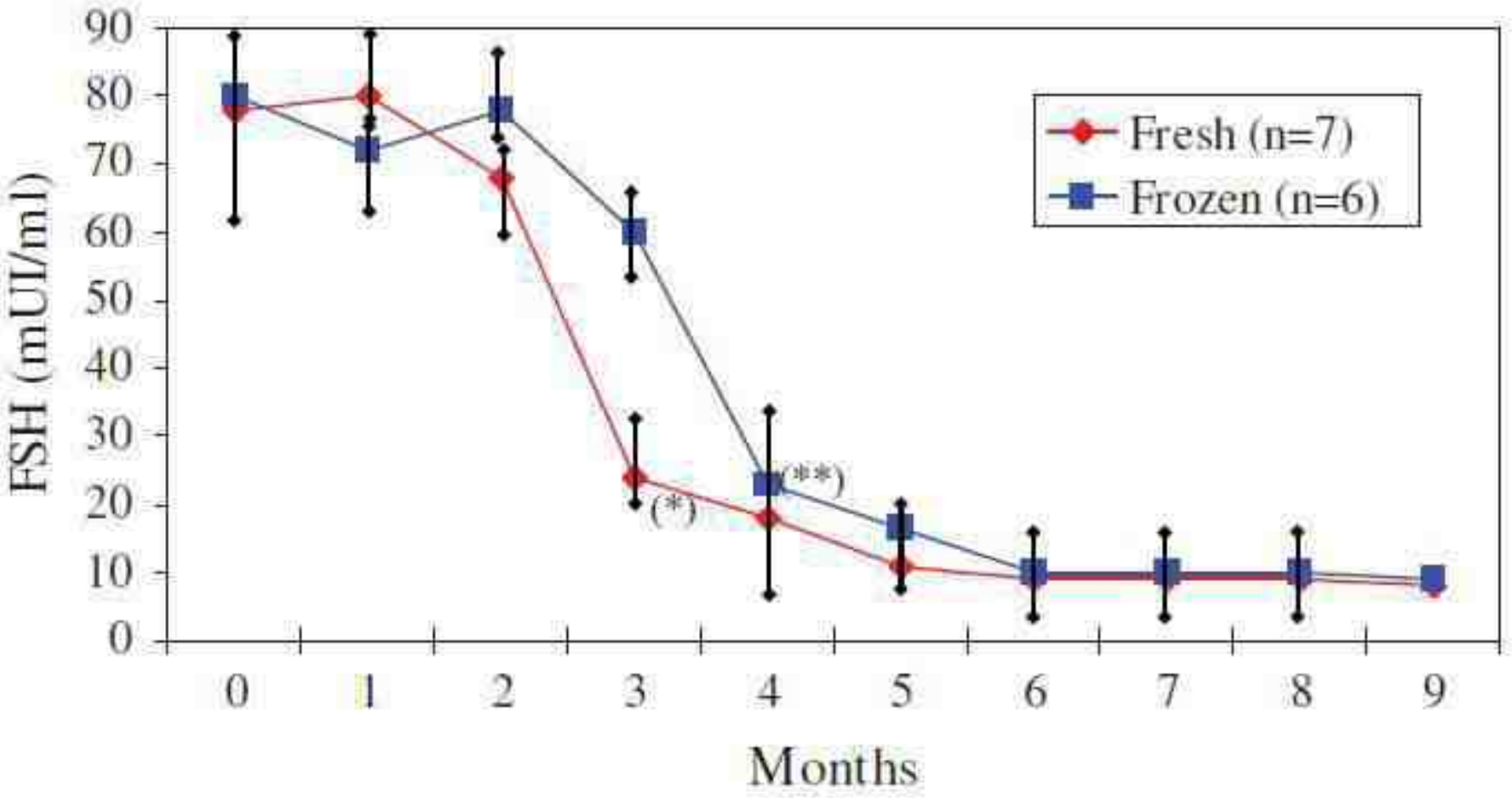
Follicular viability before and after freeze-thawing.

Variable	Follicles in fresh ovary (n = 312)	Follicles in fresh ovary after DMSO exposure (n = 153)	Follicles in frozen-thawed ovary (n = 356)
% Live follicles	99.4 ± 1.0[a]	98.1 ± 3.2[a]	75.1 ± 1.9[b]
% Minimally damaged follicles	0.6 ± 1.0[a]	1.9 ± 3.2[a]	22.5 ± 2.2[b]
% Moderately damaged follicles	0 ± 0[a]	0 ± 0[a]	2.4 ± 1.1[b]
% Dead follicles	0 ± 0[a]	0 ± 0[a]	0 ± 0[a]

[ab] Within each row, values (mean ± SEM) with differing superscripts are significantly different ($P<.05$).

Martinez-Madrid. Freezing intact human ovary. Fertil Steril 2004.

Frozen vs Fresh ortotopik reimplantasyon



Donnez j, Annals of Medicine, 2011

Reimplantasyondan 4.5 ay sonra 14 mm lik folikül

Bir hafta sonra 21 mm lik korpus luteum ve eşlik eden 6.5 ng / mL P4 değeri

Gonadotoxic effect
Radiotherapy

- **Dose received**: in humans dose reducing follicular population to half is 2 Gy
- **Age**
- **Irradiation field**: probability of POF increases if corporal irradiation
- May have effects on **other structures**

RT doses and ovarian toxicity, according to age

Dose	Effect
60	no
60-150	>40: possible
250-500	15-40: 50% sterile
500-800	15-40: 75% sterile
>800	100% sterile

Wallace, 2005

Malign hastalıklarda ovarian transpozisyon endikasyonları

Jinekolojik maligniteler

- Erken servikal karsinom
- Erken vajinal karsinom
- Erken vulvar karsinom

Non-jinekolojik maligniteler

- Rektosigmoid tümör
- Pelvik ya da extrapelvik sarkoma
- Kemik kanseri (osteosarkoma, Ewing sarkomu)
- Lenfoma
- Medulloblastoma

Ovarian Transposition (Oophoropexia)

Objective:

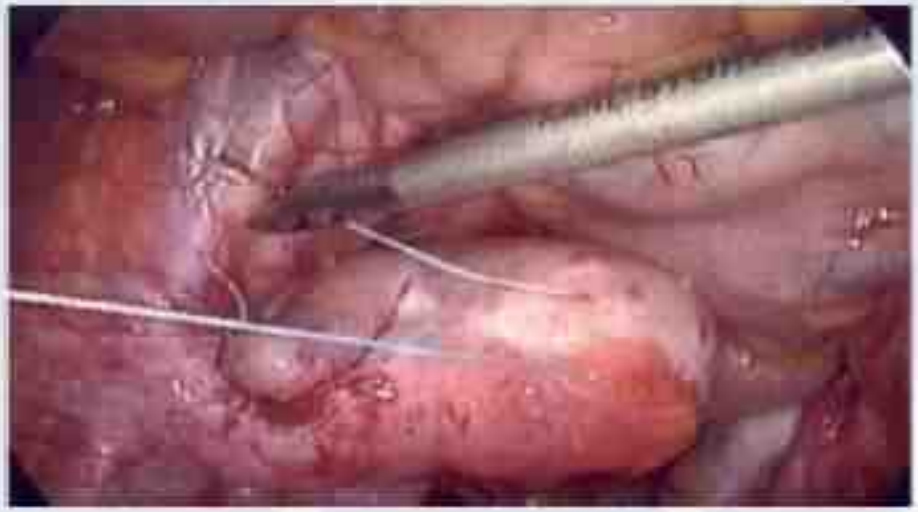
Move ovaries away from irradiation field to avoid direct exposition to radiotherapy

- Laparoscopy or laparotomy
- They can be fixed in the upper paracolic gutters or behind uterus
- Gonadal protection in 60% of the cases
- Ovarian function preservation in 83-88% of the cases
- Complications: vascular lesions, Fallopian tube infarct, cyst formation

Ovarian transposition

Objective:

To move the ovaries from the irradiation field before starting RT



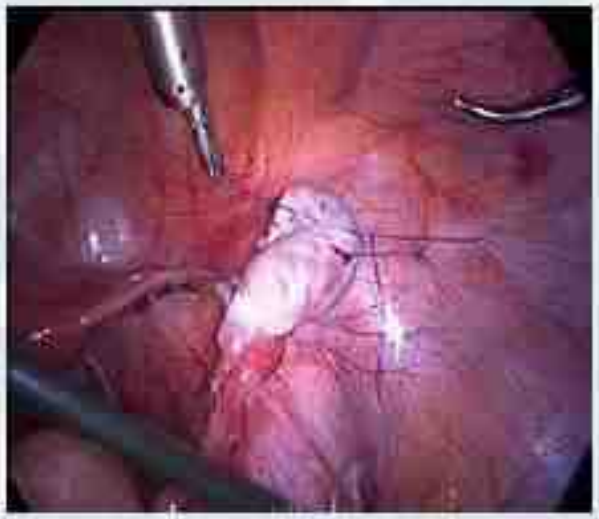
Indication:

Tumours requiring pelvic irradiation

Technique:

Laparoscopic / laparotomic

- **Medial**
- **Lateral**



Important:

- **Preserving ovarian vascularization**
- **Easy access for possible future OPU**
- **Cryopreserving ovarian fragments**

Tulandi et al, Obstet Gynecol Clin N Am , 2004

Teşekkür ederim.....