Oocyte Freezing and Ovarian Tissue Cryopreservation: Comparing Results of These Two Methods in One Program

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Conflict of interest

I declare that I have no commercial or financial interests pertaining to the subject of this presentation or its content

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Introduction

- Higher cancer survival rates
- Fertility preservation(FP) should be beyond discussion
- FP ⟹ Holistic management of oncologic patients:
  - Established methods: Embryo / Oocyte vitrification
  - Experimental methods: Ovarian cortex cryopreservation
  - Complementary methods: IVM, GnRH agonists

Loren et al. JCO, 2013; Kim et al. JARG 2012; PC ASRM F&S 2013; Leturneau et al. Cancer 2012

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Introduction

- Established Method: **OV**
  - Data from oocyte donation
  - Data from infertile patients
  - Data from social freezing
- Experimental method: **OCT**
  - Around 100 live births
  - Publication bias

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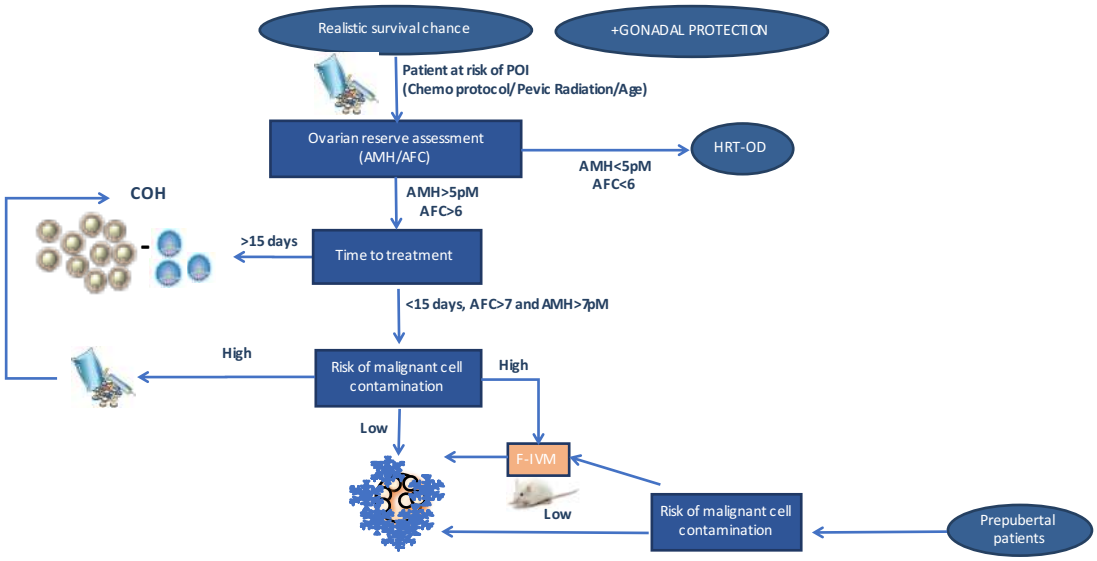
Management algorithm



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Objective

Compare the efficacy of OV with that of OCT in women undergoing gonadotoxic treatments

Live birth rate

Clinical pregnancy rates

Characteristics of the patients

Description of the procedures

Per patient

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Study design

FERTILITY PRESERVATION CANDIDATES

PATIENTS REQUIRING GONATOXIC TREATMENTS

UNDERWENT FERTILITY PRESERVATION

OVARIAN CORTEX CRYOPRESERVATION

OOCYTE VITRIFICATION

USED THE CRYOPRESERVED TISSUE/OOCYTES

Tissue Thawing + Reimplantation

Oocyte Warming + IVF

INCLUSION CRITERIA

- Reasonable prognosis
- High risk of infertility
- Patients undergoing OCT
- Patients undergoing OV

EXCLUSION CRITERIA

- Age >40 years old*
- Prepubertal patients
- Both techniques
- Embryo vitrification
- OCT for endocrine function preservation
- Patients not undergoing any technique

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Methods

FP PROGRAM

- Free access
- Nationwide coverage
- Same management algorithm
- **OOV: Multicentric**
- **OCT: Centralized**

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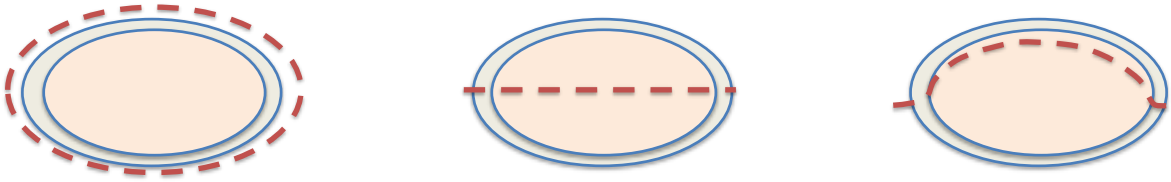
OCT



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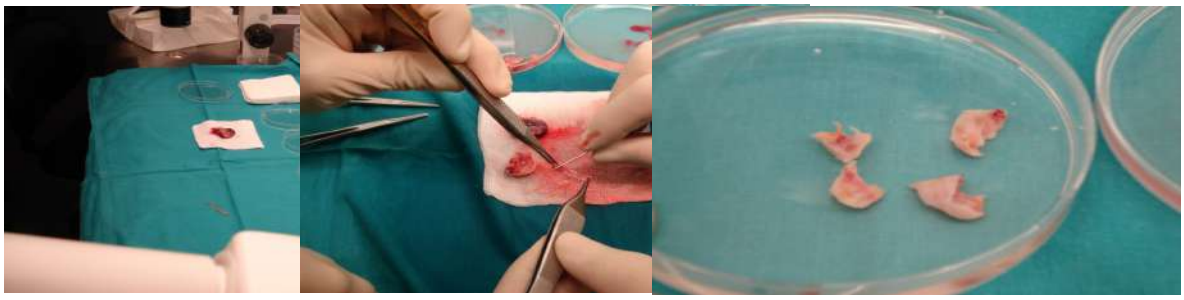
OCT



Ovarian strips

Slow freeze

SSS, 15min
12.5% DMSO

EVA bags

Herraiz et al. F&S, 2013

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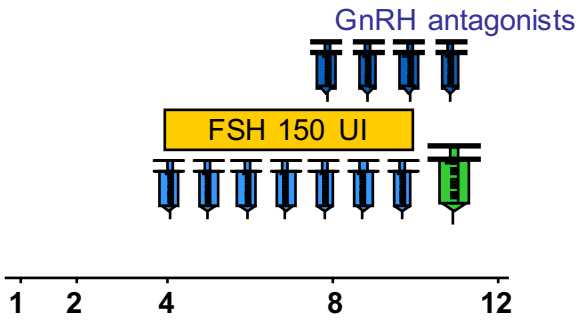
COH

STANDARD



- GnRH Antagonists, follicles ≥14 mm.
- GnRH agonist when 19-21 mm

Domingo et al. F&S, 2012

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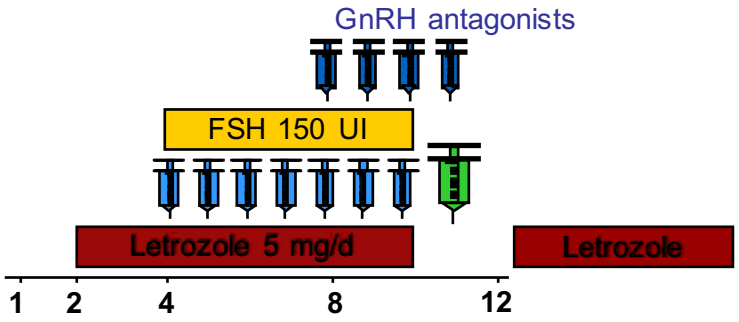
COH

HORMONE-DEPENDENT CONDITIONS



- GnRH Antagonists, follicles ≥14 mm.
- GnRH agonist when 19-21 mm

Oktay et al. JCEM, 2006

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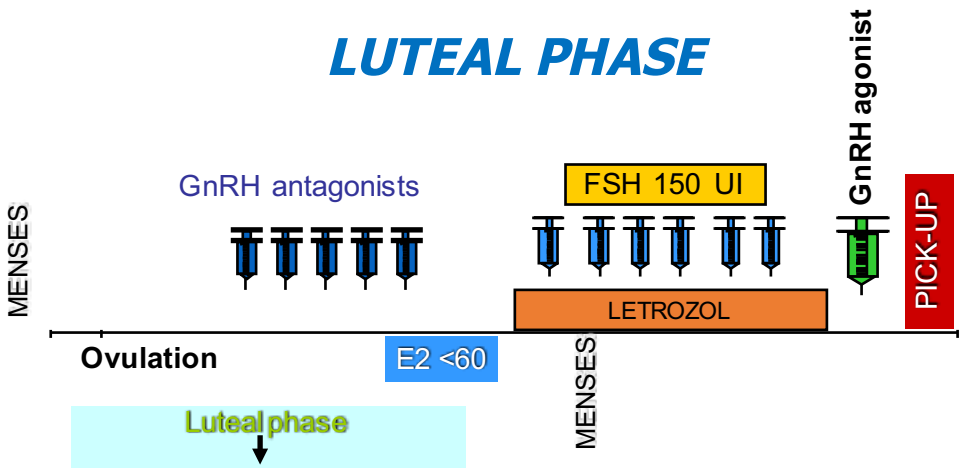
LUTEAL PHASE



Lutealphase
↓
Use antagonists until E2<60
↓
Start stimulation

Domingo et al. F&S, 2012

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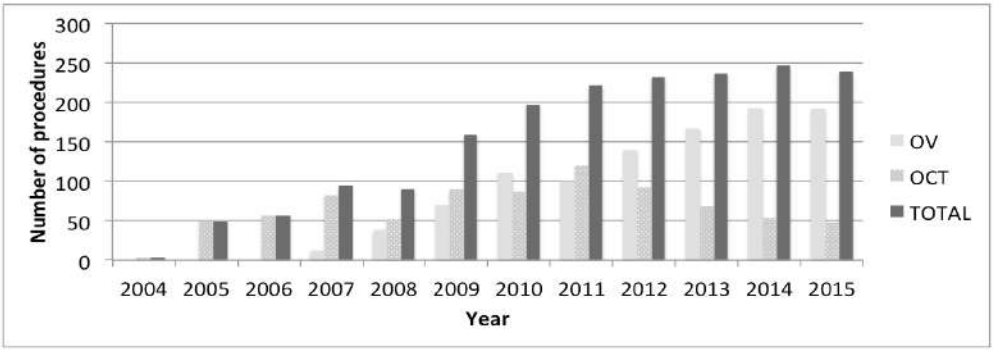
Number of procedures stratified by fertility preservation technique and year



n=1024 OV
n=800 OCT

57%
72%

Activity in Spain

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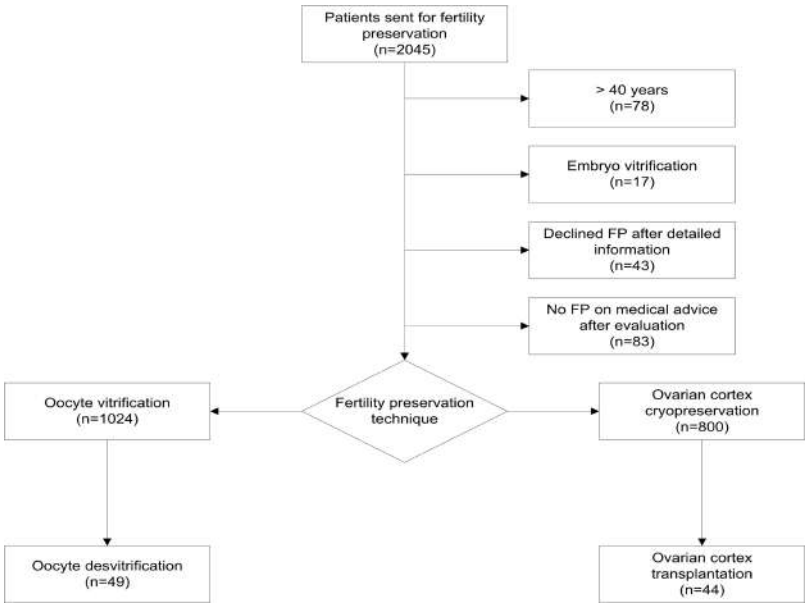
Patients´ flow chart



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Baseline characteristics of the patients

		Oocyte vitrification, n=1024 (%)	Ovarian cortex transplantation, n=800 (%)	P value
Age (years)		31.7 (6.4)	28.2 (7.3)	p< 0.001
BMI (kg/m²)		22.5 (3.6)	21.8 (3.5)	ns
AMH (pM)		11.6 [5.4-24.7]	11.8 [6.4-21.9]	ns
Nulliparous		952 (89.8)	722 (90.2)	ns
Duration of the FP procedure (days) *		24.0 (6.2)	4.5 (4.1)	p< 0.001
Conditions motivating FP	Breast	618 (60.3)	431 (53.9)	p< 0.001
	HL	145 (14.2)	159 (19.9)	
	NHL	61 (6.0)	24 (3.0)	
	Gynecological	44 (4.3)	25 (3.1)	
	Sarcoma	16 (1.6)	52 (6.5)	
	Leukemia	12 (1.2)	54 (6.7)	
	Autoimmune disease	8 (0.8)	20 (2.5)	
	Other solid organ tumors	120 (11.7)[a]	35 (4.4)[b]	

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Results of ovarian stimulation in fertility preservation patients

Duration of stimulation (days)	10.6 (3.0)
Doses of FSH (UI)	1611 (845)
E2 day of triggering (pg/mL)	
Hormone-sensitive*	371 (498)
Non-hormone-sensitive	1290 (1258)
Number of retrieved oocytes	11.6 (8.6)
Number of vitrified MII oocytes	8.1 (6.6)
Cancelled cycles, n (%)**	11/1024 (0.01)

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Results OV vs OCT

		OV (n=49)	OCT (n=44)	P value
Status of the patient	Amenorrhea > 1 year	9 (18.4)	20 (45.5)	p=0.04
	POI without amenorrhea	34 (69.4)	21 (47.7)	
	No POI	6 (12.2)	3 (6.8)	
Age at retrieval		35.2 (3.1)	34.3 (7.2)	n.s.
Age at utilization		39.0 (3.8)	38.9 (4.1)	n.s.
Type of cancer	Breast	38 (77.5)	31 (70.4)	p=0.04
	Hodgkin lymphoma	2 (4.1)	9 (20.4)	
	Non-Hodgkin lymphoma	3 (6.1)	0 (0)	
	Other	6 (12.2)*	4 (9.1)#	
Storage time (years)		3.9 (2.0)	5.5 (1.8)	n.s.
Number of pregnancies		21 (42.9)	15 (34.0)	n.s.
Number of live births		17 (34.7)	10 (22.7)	n.s.

* Includes the following cancers: 2 endometrium, 1 rectum, 1 myeloma, 1 Sarcoma, 1 Acute myeloid leukemia
# Includes the following cancers: 2 rectum, 1 medulloblastoma, 1 persistent trophoblastic disease

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Per-Patient Analysis

	OV (n=49)	OCT (n=44)
	PATIENTS WITH CLINICAL PREGNANCIES	
Pregnant	20 **(40.8%)**	12 **(27.3%)**
Non-Pregnant	29 (59.2%)	32 (72.7%)
	PATIENTS WITH LIVE BIRTHS	
Live birth	16 **(32.6%)**	8 **(18.2%)**
No Live birth	32 (67.4%)	36 (81.8%)

p = n.s.

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Fertility results after utilization of vitrified oocytes or cryopreserved ovarian tissue

	BREAST		p	HODGKING LYMPHOMA		p	NON-HODGKIN LYMPHOMA		p	OTHER CONDITIONS		p	ALL		p
	OV (n=38)	OCT (n=31)		OV (n=2)	OCT (n=9)		OV (n=3)	OCT (n=0)		OV (n=6)	OCT (n=4)		OV (n=49)	OCT (n=44)	
Status of patient at reimplantation			ns			ns			-			ns			0.04
-Amenorrhea >1 year	5 (13.2)	11 (35.5)		1 (50.0)	7 (77.8)		1 (33.3)	-		2 (33.3)	2 (50.0)		9 (18.4)	20 (45.4)	
-POI without amenorrhea	30 (78.9)	19 (61.3)		0 ()	2 (22.2)		2 (66.7)			2 (33.3)	0 (0)		34 (69.4)	21 (47.8)	
-Regular menstruations	3 (7.9)	1 (3.2)		1 (50.0)	0 (0)		0 (0)			2 (33.3)	2(50.0)		6 (12.3)	3 (6.8)	
Age at retrieval (years)	35.5 (3.1)	35.8 (3.3)	ns	32.5 (4.9)	27.1 (3.7)	ns	34.5 (2.1)	-	-	34.2 (3.7)	29.5 (0.2)	ns	35.2 (3.1)	34.3 (7.2)	ns
Age at reimplantation (years)	40.0 (3.3)	41.0 (2.4)	ns	33.5 (3.5)	33.8 (3.1)	ns	39.0 (1.0)	-	-	37.0 (4.2)	32.9 (1.7)	ns	39.0 (3.8)	38.9 (4.1)	ns
AMH before reimplantation (pM)	0 [0-1.33]	0 [0-0]	ns	2.1 [0-4.2]	0 [0-1.00]	ns	0 [0-0]	-	-	0 [0-1.26]	0.37 [0-1.47]	ns	0 [0-1.29]	0 [0-0.30]	ns
Number of pregnant patients	13 (34.2)	5 (16.1)	ns	1 (50.0)	5 (55.5)	ns	2 (66.7)	0	ns	4 (66.7)	2 (50.0)	ns	20 (40.8)	12 (27.3)	ns
Number of patients with live births	11 (28.9)	2 (6.4)	ns	1 (50.0)	4 (44.4)	ns	2 (66.7)	0	ns	2 (33.3)	2 (50.0)	ns	16 (32.6)	8 (18.2)	ns

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Outcomes stratified by age

	Pregnancy			Live birth		
OV (n=49)	**YES**	**NO**	**p-value**	**YES**	**NO**	**p-value**
Age >36	6	8	n.s.	6	8	n.s.
Age≤36	14	21		10	25	
OCT (n=44)	**YES**	**NO**	**p-value**	**YES**	**NO**	**p-value**
Age >36	0	8	0.04	0	8	n.s.
Age≤36	12	24		8	28	

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Efficiency of oocyte vitrification and ovarian cortex cryopreservation and transplantation in fertility preservation

	OV patients (n=49)
Warmed oocyte/patient	5.1 (3.5)
Oocyte survival rate (%)	77.3%
Nº ET (Fresh - frozen)	68
Surplus embryos/patient	2.7 (2.2)
Warmed embryo/patient	2.0 (1.7)
Embryo survival rate (%)	91.7%
Nº Embryos transferred	1.42
Clinical pregnancy rate/ fresh cycle	14/51 (27.4)
Live birth rate/ fresh cycle	11/51 (21.6)
Clinical pregnancy rate/transfer	20/55 (36.4%)
Live birth rate/transfer	16/55 (29.1%)
Number of pregnancies	21 (42.9)
Number of live births	17 (34.7)
Number of pregnant patients	20 (40.8)
Number of patients with live births	16 (32.6)

	OCT Patients, n=44 (%)
Surgical approach	
-Laparoscopy	1 (2.3)
-Laparotomy	41 (93.2)
Surgical technique/sites	
-Subcortical pouches	24 (54.5)
-Cortical microsurgical sutures	26 (59.1)
-Subperitoneal pouches	27 (61.4)
Ovarian function after graft	43 (97.7)
CPR after spontaneous pregnancy	7 (15.9)
LBR after spontaneous pregnancy	5 (11.4)
Number of patients undergoing IVF	28
CPR after IVF	8 (18.2)
LBR after IVF	5 (11.4)

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Conclusions

- Useful information to counsel patients and oncologists
- Both methods are effective in preserving fertility
- There is a trend to higher CPR and LBR in the OV group
- OCT allows for natural pregnancy and restores ovarian function

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Thank you

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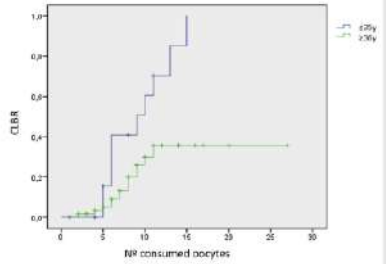
Oocyte vitrification

Efficacy

FIGURE 2

CLBR according to age (≤35 vs ≥36) and Nº oocytes consumed



≤35 years old		≥36 years old	
Nºoocytes	CLBR (IC95%)	Nºoocytes	CLBR (95% CI)
5	15,4 (-4,2-35,0)	5	5,1 (-0,6-10,7)
8	40,6 (13,2-68,4)	8	19,9 (8,7-31,1)
9	50,6 (31,6-79,6)	9	25,8 (12,7-38,9)
10	60,5 (34,5-89,5)	10	29,7 (15,2-34,2)
15	85,2 (60,5-100)	11	35,6 (18,4-52,8)

Kaplan-Meier plotting of the cumulative live birth rates (CLBR) of at least one baby, depending on the total number of consumed oocytes and categorized by age (≤35 y and ≥36 y). Overall comparisons: log rank (Mantel-Cox); P=.003; Tarone-Ware; P=.011. The table shows the CLBRs and 95% confidence intervals (CI) when 5-15 oocytes were consumed, according to age.

Cobo. Oocyte vitrification for oocyte donation. Fertil Steril 2016.

Fertil Steril 2016; 105:755-764.

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RESULTS-UPDATE

OV

31/58 CPR per Patient: 53.4%

22/58 OPR per Patient: 37.9%

OCT

13/44 CPR per Patient: 29.5%

9/44 OPR per Patient: 20.5%

- March 2017

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Oocyte vitrification vs OTC

RECOMMENDATIONS

OOCYTE VITRIFICATION	OVARIAN TISSUE CRYO (OTC)
• Age >35 • Leukemia (and other high risk tumors) • Good ovarian reserve • Enough time for COS • Previous surgery or frozen pelvis • Post-pubertal status • BRCA carriers	• Age <36 • Willing natural conception • No time for COS • Without permission of the oncologist • Pre-pubertal status

They don't exclude each other

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Fertility Preservation decision tree