ÜREME TIBBI VE CERRAHİSİ DERNEĞİ
İnfertilite Tedavisinde Güncel Yaklaşımlar Toplantısı
Ankara, 21.12.2014

Embriyo Kriyoprezervasyonu

Dr. Sinan Özkavukcu
Ankara Üniversitesi Tıp Fakültesi
ÜYTE Merkezi Laboratuvar Sorumlusu

Sunu Planı

1. Dondurmak eğlenceli, bakalım faydalı mı?
2. Bu işin yolu yordamı nedir?
3. Tartışmalı konular aramızı bozmasın
4. Yeni ve ilginç yaklaşımlar uzak mı?

Tarihçe

Nature **305**, 707-709 (20 October 1983) | doi:10.1038/305707a0; Accepted 26 August 1983

Human pregnancy following cryopreservation, thawing and transfer of an eight-cell embryo

Alan Trounson & Linda Mohr

1. Department of Obstetrics and Gynaecology, Monash University, Queen Victoria Medical Centre, Melbourne, Australia 3000

İlk gebelik 1983'te enfeksiyona bağlı düşükle sonuçlandı

İlk doğum 1984'te Hollanda'da gerçekleşti

Fertil Steril. 1984 Aug;42(2):293-6.

Two pregnancies following transfer of intact frozen-thawed embryos.

Zeilmaker GH, Alberda AT, van Gent I, Rijkmans CM, Droqendijk AC.

Fertil Steril. 1990 Mar;53(3):469-72.

Survival and pregnancy outcome after ultrarapid freezing of human embryos.

Gordts S[1], Roziers P, Campo R, Noto V.

Vitrifikasyonun ilk başarısı (1990)

Kriyoprezervasyon

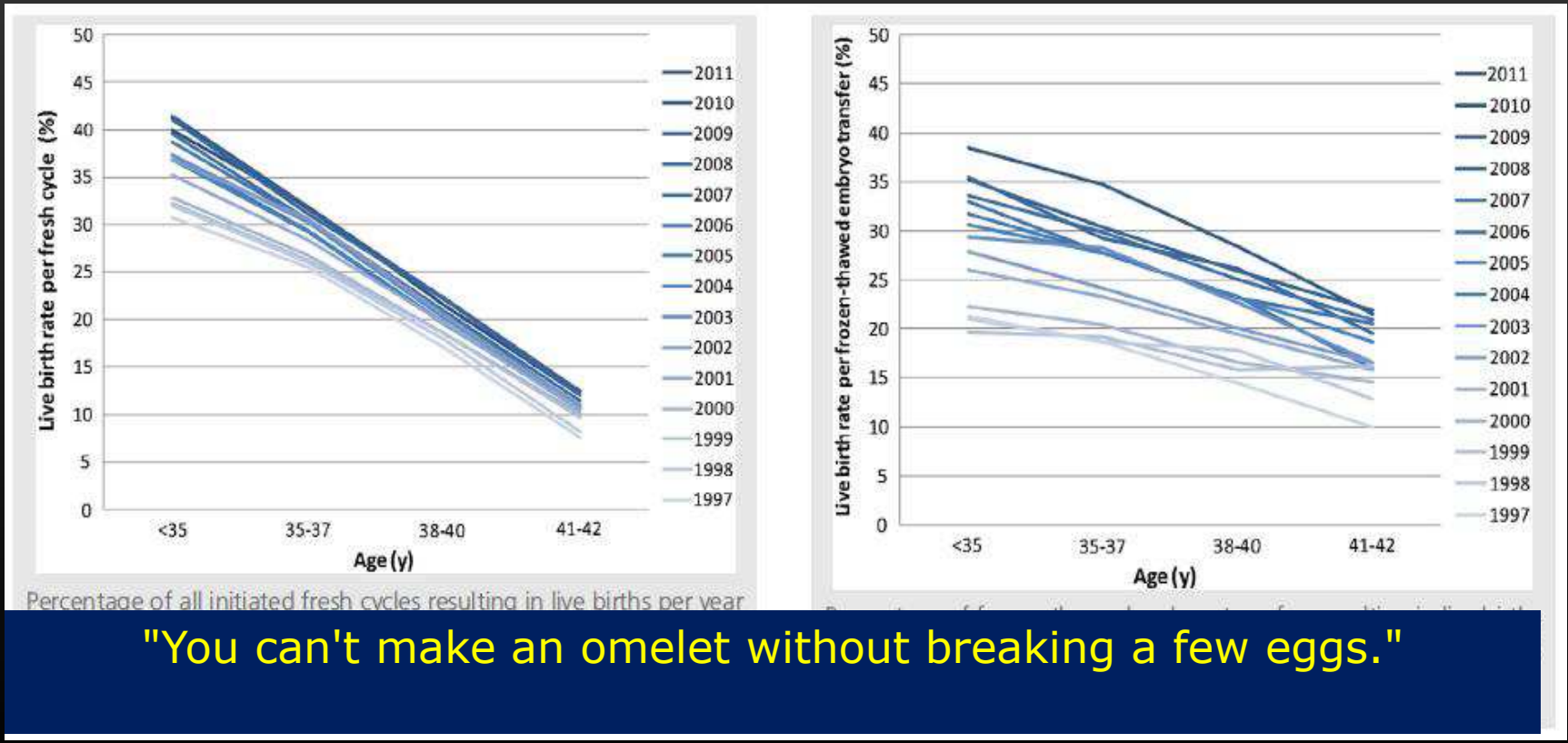
- Bulunduğu ortamda donma sıcaklığını düşüren maddelerin (kriyoprotektan ajanlar) katkısıyla hücre zarları ve içeriğine zarar vermeden, tüm metabolik aktivitenin durduğu düşük sıcaklıklara hücreleri indirip, daha sonra aynı şekilde fizyolojik sıcaklıklara döndürme işlemidir.

Embriyo Kriyoprezervasyonu

- Bir embriyoloji laboratuvarı için rutin bir işlem haline gelmiştir.
- Son dekatta artan oranda dondurma-çözme döngüleri gerçekleştirilmekte ve çözme sonrası transferlerden elde edilen gebelikler artmaktadır.
- IVF kümülatif başarı şansını artırmak
- çoğul gebeliği önlemek
- OHSS
- endometriyumun uygunsuzluğu
- doğurganlığın korunması

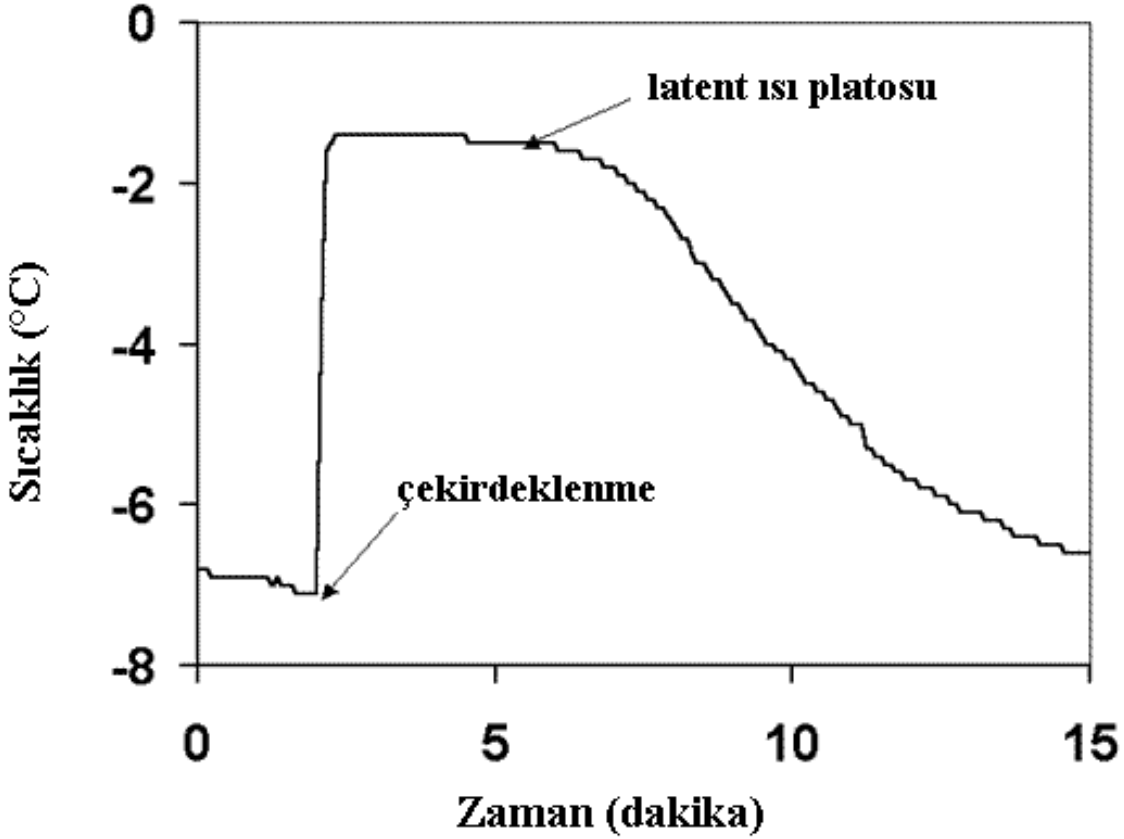
IVF sikluslarına katkısı

- Amerika CDC verileri 1997-2011
- Taze sikluslarda başarı %29 artmışken (31 → 40)
- FET sikluslarında başarı %86 artmış (21 → 39)

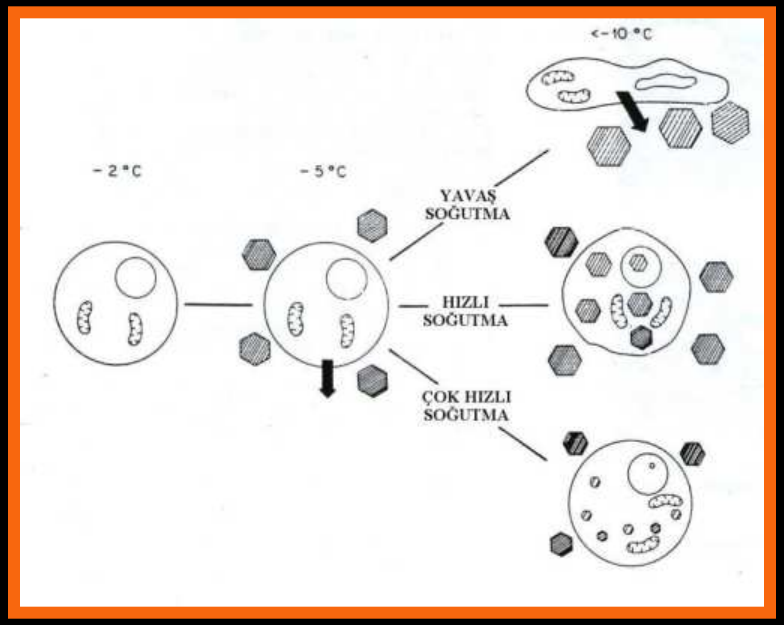


"You can't make an omelet without breaking a few eggs."

Bir Çözeltinin Konvansiyonel Donma Eğrisi
Yavaş Dondurma Donma Mekaniği



Hücreleri Soğukta Koruma Yöntemleri



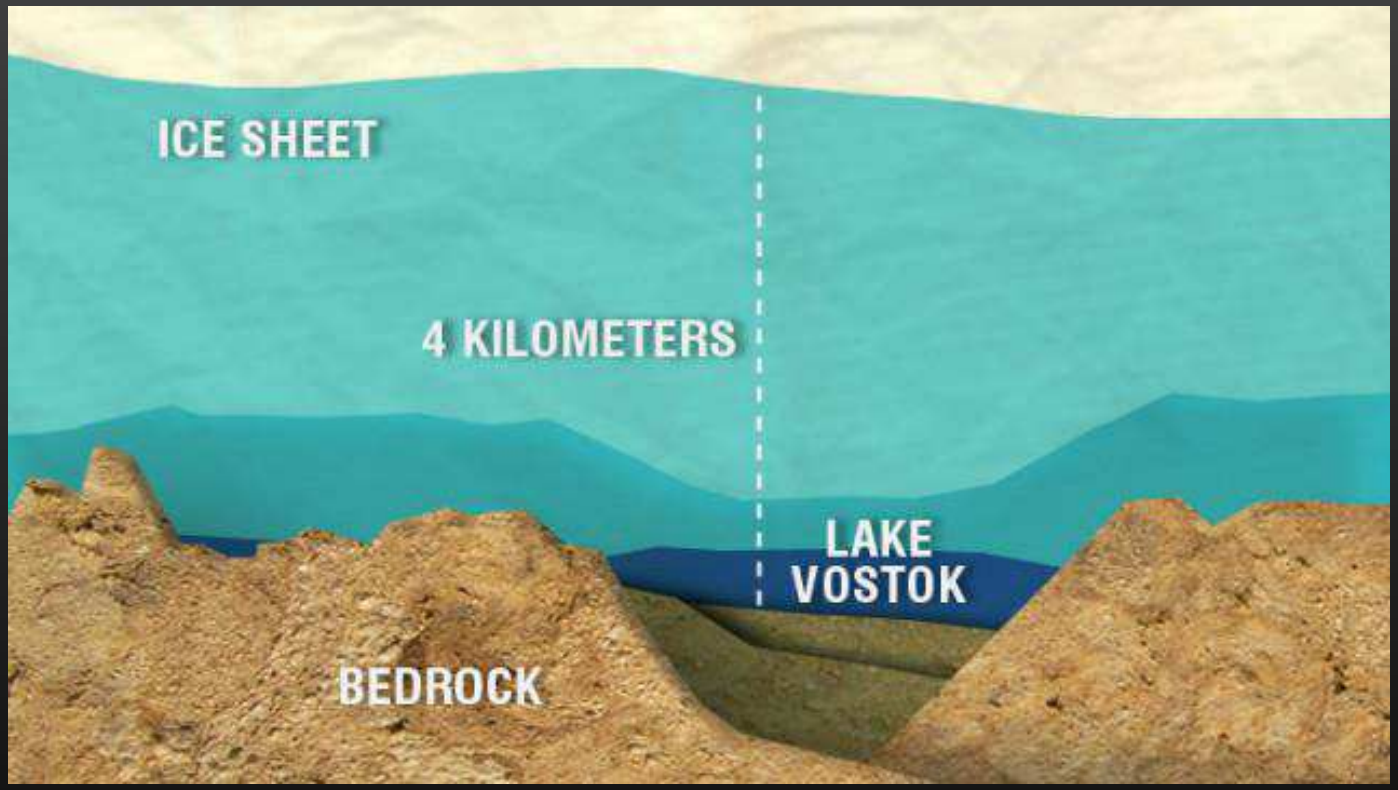
Ara hızdaki soğutmayla ilgili tüm çalışmalarda hücre içi buz oluşumu nedeniyle ağır hücre hasarı ve kaybı bildirilmiştir.

Hc. içi buz oluşumuna bağlı asıl hasar çözme sırasında meydana gelmektedir.

Yavaş Dondurma vs. Vitrifikasyon

- İşlem uzun
- Kullanıcıdan bağımsız teknik
- Yavaş dondurma cihazına ihtiyaç
- Düşük toksisite
- Buz kristali oluşumu

- İşlem kısa
- Başarı operatör tecrübesine bağımlı
- Yüksek toksisite
- Buz kristali oluşumu gerçekleşmez

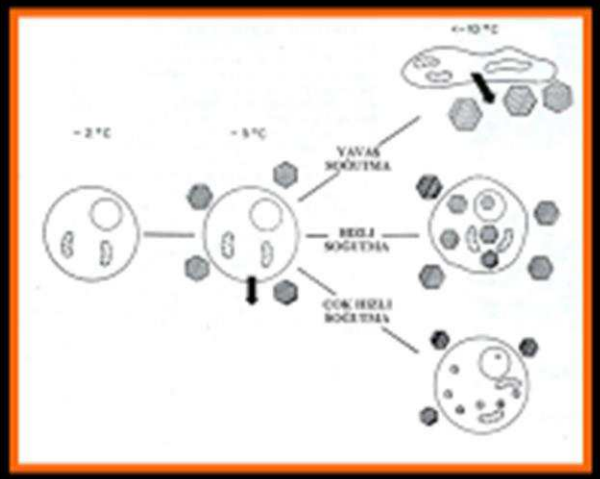


%41-50 propanediol içeren sıvının heterojen çekirdeklenme ısısı, vitrifikasyon ısısının altındadır. Bunun anlamı vitrifikasyon sıcaklığında buz kristalleri oluşmamasıdır.

Slow freezing, vitrification and ultra-rapid freezing of human embryos: a systematic review and meta

Faten F Abde
Tommaso Fal

Hücreleri Soğukta Koruma Yöntemleri



Ara hızdaki soğutmayla ilgili tüm çalışmalarda hücre içi buz oluşumu nedeniyle ağır hücre hasarı ve kaybı bildirilmiştir.
Hc. içi buz oluşumuna bağlı asıl hasar çözme sırasında meydana gelmektedir.

Techniques f

217

Study
or sub-categ

01 Ultra-Rap
Mauri 2001
Subtotal (95
Total events
Test for hete
Test for ove

02 Vitrificati
Li 2007
Bernal 2008
Kim 2006
Subtotal (95
Total events
Test for hete
Test for ove

Clinical outcomes following cryopreservation of blastocysts by vitrification or slow freezing: a population-based cohort study

Z. Li[1,2], Y.A

[1]School of Women's an
University of Technolog
Wales, Sydney 2031, A
Gynaecology, University

Table III Pregnancy outcomes following transfer of fresh, slow frozen and vitrified blastocysts, Australia and New Zealand, 2009–2011.

	Fresh (n = 46 890)	Slow freezing (n = 11 644)	Vitrification (n = 19 978)
Clinical pregnancies	16 845	2766	6537
Miscarriage	3022	589	1314
Reduction or termination	113	21	47
Ectopic or heterotopic pregnancy	213	17	60
Live deliveries	13 049	2065	4955
	% per thaw cycle		
Clinical pregnancies	n.a.	21.5	31.3
	n.a.	4.6	6.3
	n.a.	0.2	0.2
	n.a.	0.1	0.3
	n.a.	16.1	23.7
	% per embryo transfer cycle		
	35.9	23.8	32.7
	6.4	5.1	6.6
	0.2	0.2	0.2
	0.5	0.1	0.3
	27.8	17.7	24.8
	% per clinical pregnancy		
	17.9	21.3	20.1
	0.7	0.8	0.7
	1.3	0.6	0.9
	77.5	74.7	75.8

Table IV Adjusted relative risk for pregnancy outcomes following transfer of slow frozen and vitrified blastocysts, Australia and New Zealand, 2009–2011.

	Slow freezing	Vitrification ARR (95% CI)
Thawed cycles result in transfer[a]	Ref	1.05 (1.03, 1.08)*
Pregnancy outcomes[b]		
Clinical pregnancies/thaw cycle[a]	Ref	1.43 (1.37, 1.50)*
Clinical pregnancies/embryo transfer	Ref	1.38 (1.32, 1.45)*
Live deliveries/thaw cycle[a]	Ref	1.47 (1.39, 1.55)*
Live deliveries/embryo transfer	Ref	1.41 (1.34, 1.49)*
Live deliveries/clinical pregnancy	Ref	1.02 (0.97, 1.08)
Miscarriage/clinical pregnancy	Ref	0.91 (0.82, 1.01)
Perinatal outcomes[b]		
Perinatal mortality	Ref	1.10 (0.64, 1.89)
Preterm delivery	Ref	0.97 (0.75, 1.25)
LBW births	Ref	1.08 (0.89, 1.31)
SGA births[c]	Ref	0.88 (0.70, 1.10)
LGA births[c]	Ref	0.89 (0.78, 1.02)

Fresh vs SF vs VF

Table VI Adjusted relative risk for pregnancy outcomes and perinatal outcomes following transfer of fresh, slow frozen and vitrified blastocysts, Australia and New Zealand, 2009–2011.

	Fresh	Slow freezing ARR (95% CI)	Vitrification ARR (95% CI)
Pregnancy outcomes[a]			
Clinical pregnancies/embryo transfer	Ref	0.62 (0.59, 0.64)*	0.85 (0.82, 0.87)*
Live deliveries /embryo transfer	Ref	0.58 (0.55, 0.61)*	0.81 (0.79, 0.84)*
Live deliveries/clinical pregnancy	Ref	0.94 (0.90, 0.99)*	0.97 (0.93, 1.00)*
Miscarriage/clinical pregnancy	Ref	1.31 (1.19, 1.44)*	1.16 (1.09, 1.24)*
Perinatal outcomes[a]			
Perinatal mortality	Ref	0.87 (0.53, 1.42)	0.92 (0.67, 1.27)
Preterm delivery	Ref	0.80 (0.68, 0.96)*	0.86 (0.77, 0.96)*
[illegible]ths	Ref	0.66 (0.53, 0.82)*	0.67 (0.58, 0.78)*
[illegible]A births[b]	Ref	0.64 (0.53, 0.78)*	0.60 (0.53, 0.68)*
LGA births[b]	Ref	1.77 (1.57, 2.00)*	1.54 (1.40, 1.69)*

[a]Maternal age, cause of infertility, parity, number of embryo transferred, IVF/ICSI were adjusted in multivariable regression analysis.
[b]20–42 weeks gestation with known baby sex.
ARR, adjusted relative risk; CI, confidence interval; LBW, low birthweight; SGA, small for gestational age; LGA, large for gestational age; Ref, reference category.
*, significant at the 0.05 level.

Cryopreservation of human embryos by vitrification or slow freezing: a systematic review and meta-analysis

Kalliopi E. Loutradi, M.Med.Sc., Efstratios M. Kolibianakis, M.D., Ph.D., Christos A. Venetis, M.D., M.Sc., Evangelos G. Papanikolaou, M.D., Ph.D., George Pados, M.D., Ph.D., Ioannis Bontis, M.D., Ph.D., and Basil C. Tarlatzis, M.D., Ph.D.

Unit for Human Reproduction, 1st Department of Obstetrics and Gynaecology, Papageorgiou General Hospital, Thessaloniki, Greece

Odds ratio of postthawing survival rate of cleavage stage embryos after vitrification and slow freezing.

Study	Vitrification n/N	Slow freezing n/N	OR (random) 95% CI	Weight %	OR (random) 95% CI
Rama Raju	121/127	72/120		34.00	13.44 [5.48,32.98]
Zheng	46/49	8/52		28.71	84.33 [21.01, 338.51]
Kuwayama	879/897	857/942		37.28	4.84 [2.89, 8.12]
Total (95% CI)	1073	1114		100.00	15.57 [3.68, 65.82]

Total events: 1046 (Vitrificati

Test for heterogeneity: Chi^2 =

Test for overall effect: Z = 3.

Loutradi. Techniques and Instrumenta

Odds ratio of postthawing survival rate of blastocysts after vitrification and slow freezing.

Study	Vitrification n/N	Slow freezing n/N	OR (fixed) 95% CI	Weight %	OR (fixed) 95% CI
Huang	68/81	41/72		21.41	3.95 [1.86, 8.41]
Kuwayama	5695/6328	131/156		78.59	1.72 [1.11, 2.65]
Total (95% CI)	6409	228		100.00	2.20 [1.53, 3.16]

Total events: 5763 (Vitrification), 172 (Slow freezing)

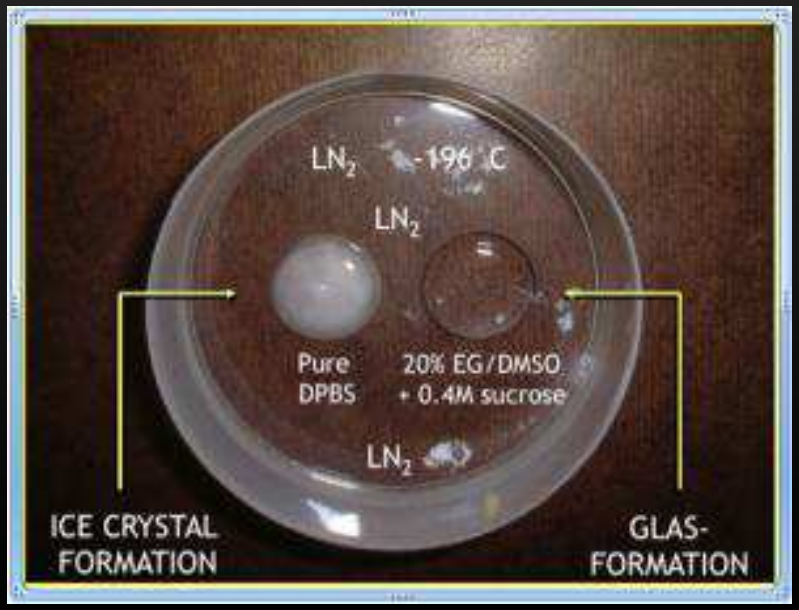
Test for heterogeneity: Chi^2 = 3.56, df = 1 (P = 0.06)

Test for overall effect: Z = 4.25 (P < 0.0001)

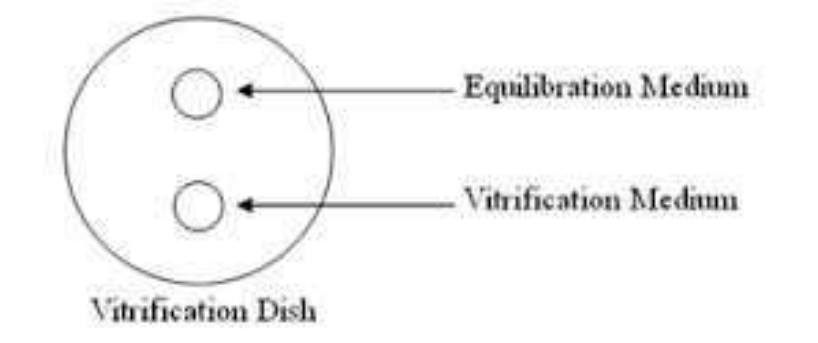
Loutradi. Techniques and Instrumentation. Fertil Steril 2008.

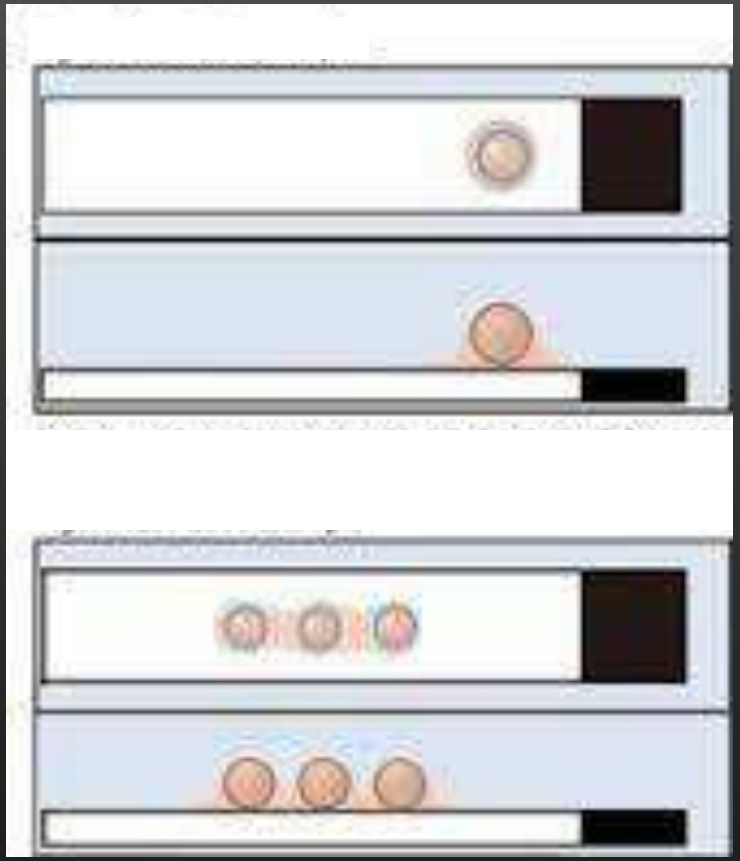
Vitrifikasyon İçin Olmazsa Olmaz

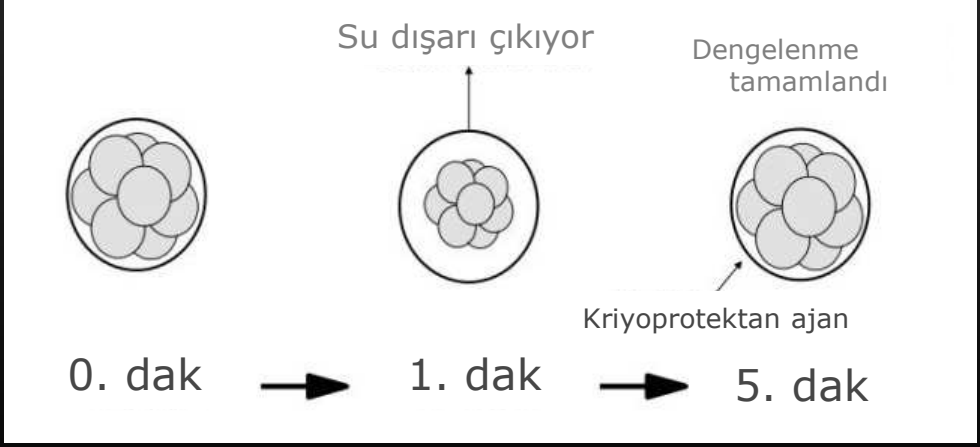
1. Yüksek CPA konsantrasyonu
2. Düşük hacimle çalışma
3. Yüksek soğutma hızı
4. Yüksek çözme hızı

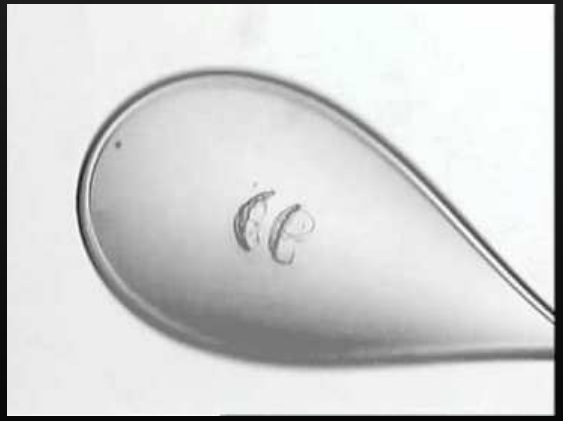


Vitrifikasyon









Su çıkışı ve dengelenme fazı oosit ve blastokist için daha zor/uzun olabilir

f blastocoeles using either
ser pulse prior to the coolin
mproves survival rate and
f vitrified human blastocysts

ome of vitrified blastocyst transfer with art

	Study group
Number of initiated vitrified blastocyst cycles	
Number of cycles with vitrified blastocyst transfer	266
Clinical pregnancies (%)	160 (60.2)
Number of implantation	209
Implantation rate (%)	46.7
Number of cycles miscarried (%)	35 (21.9)
Number of birth	57
Boy	41

In vit
by las

Hiroshi I
Masanori

J Assist Rep

ycles

Çözme

Açık ya da kapalı sistem

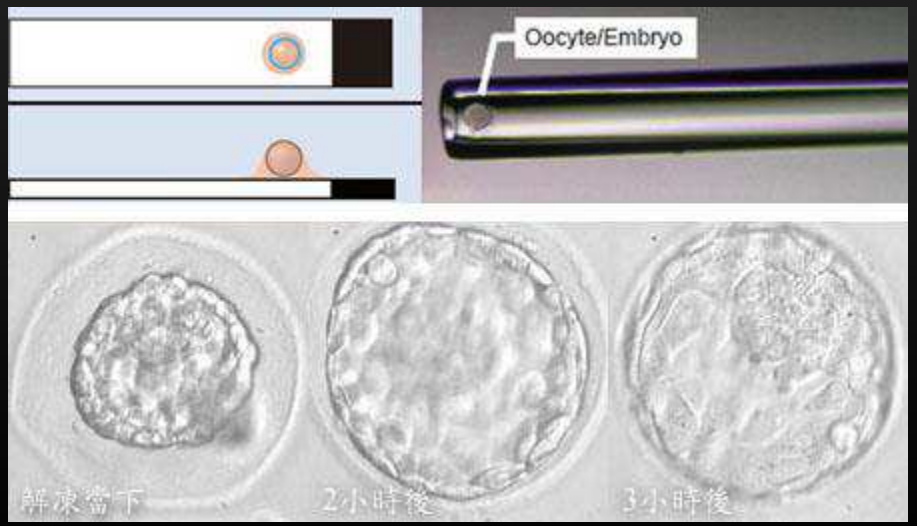
Yavaş dondurma ya da vitrifikasyon

Kullandığınız medyum ya da hangi sıcakta dengeleme yaptığınız

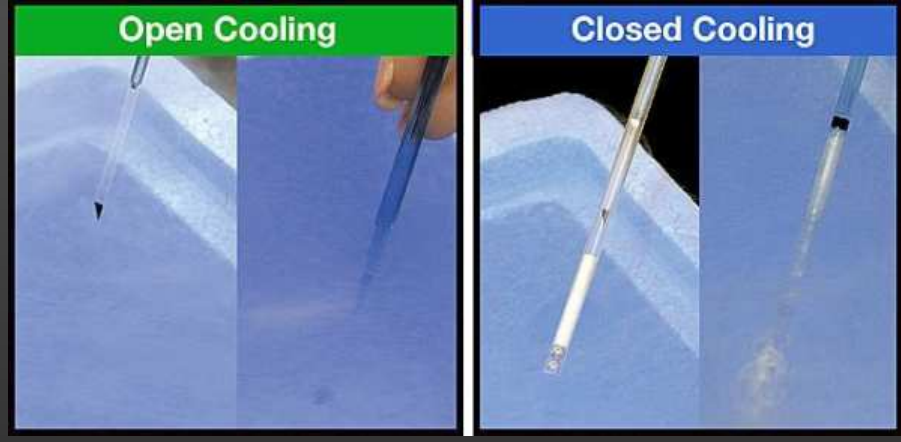
Kullandığınız taşıyıcı

FARKETMEZ

Her zaman süper hızlı çözme yapmalısınız



Dondurma-Saklama ve Kontaminasyon



Risk of contamination of germplasm during cryopreservation and cryobanking in IVF units

A. Bielanski[1,4] and G. Vajta[2,3]

Human Reproduction, Vol.24, No.10 pp. 2457–2467, 2009

Deneysel olarak sıvı azottan biyolojik materyallere bulaş gösterildi

Denekler arası bulaş bildirilmedi

Kullandığımız sıvı azot, depo ve taşıma tankları STERİL DEĞİL

Table I Microbial contamination of embryos and semen during storage in liquid nitrogen (adapted from Bielanski et *al.*, 2003)

Sample tank	Identified microbial contamination			Years of storage	Total no. of stored samples
	Liquid nitrogen	Semen	Embryos		
Research					
Laboratory tanks					
1	*Staphylococcus auricularis*	Nd	Nd	20	580
2	*Bacillus licheniformis*, *Bacillus* spp.	*Stenotrophomonas maltophilia*, *Staphylococcus sciuri*	Nd	15	840
3	CDC group IVc-2, *Alcaligenes faecalis*	*Proteus vulgaris*	Nd	8	460
4	*Brevundimonas vesicularis*	*E. coli*	Nd	15	1350
5	*Stenotrophomonas maltophilia*	—	Nd	12	650
6	*Staphylococcus capitis*, unidentified Gram-negative rod, *Comamonas acidovorans*	*Morganella morganii*, *Gemella morbillorum*, *Stenotrophomonas maltophilia*, *Citrobacter koseri*	*Bacillus subtilis*, *Ochrobactrum anthropi*, *Staphylococcus epidermidis*	15	1200
7	*Stenotrophomonas maltophilia*, *Comamonas testosteroni*	*Stenotrophomonas maltophilia*, *Citrobacter koseri*	*Stenotrophomonas maltophilia*, *Bacillus* spp., *Pseudomonas fluorescens*, *Acinetobacter lwoffi*	18	1480
8	*Bacillus pumilus*, *Eikenella corrodens*	—	*Stenotrophomonas maltophilia*, *Bacillus* spp., unidentified Gram-negative rod	10	960
Commercial tanks					
9	Nd	Nd	—	10	58 456
10	Nd	*Aspergillus* spp.	—	30	138 430
11	*Aspergillus* spp.	*Corynebacterium xerosis*, *Bacillus sphaericus*	—	30	34 962
12	Nd	*Stenotrophomonas maltophilia*	—	35	150 000
13	Nd	*Stenotrophomonas maltophilia*	—	15	280 864
14	*Aspergillus* spp.	*Photobacterium damsela*	—	15	260 912
15	Nd	*Bacillus sphericus*, *Corynebacterium* spp., *Staphylococcus sciuri*	—	12	262 642
16	*Stenotrophomonas maltophilia*	*Ralstonia pickettii*	—	12	404 955

Nd, not detected; —, not available for testing.

Kontaminasyonu önlemek için…

- Aynı tip enfeksiyon taşıyıcıları için ortak saklama tankı
- Tankların belli aralıklarla temizlenmesi (?)
- Sıvı azotun filtrasyonu ya da UV sterilizasyonu
- Kapalı sistem embriyo vitrifikasyon taşıyıcıları kullanmak
- Buhar fazında saklama yapabilen depo tanklarının kullanımı

Hangi gün donduralım?

Outcomes of vitrified early cleavage-stage and blastocyst-stage embryos in a cryopreservation program: evaluation of 3,150 warming cycles

Ana Cobo, Ph.D., María José de los Santos, Ph.D., Damià Castellò, Ph.D., Pilar Gámiz, Ph.D., Pilar Campos, M.L.T., and José Remohí, M.D.

IVI-Valencia, Institut Universitari IVI, Valencia, Spain

Overall outcome according to developmental stage at vitrification.

	D2		D3		D5		D6	
	n (%)	95% CI (%)	n (%)	95% CI (%)	n (%)	95% CI (%)	n (%)	95% CI (%)
No. of warming cycles	147		1,725		675		603	
No. of warmed embryos	497		3,491		1,079		952	
Age (y)	36.1 ± 4.0[a]	(35.6–36.4)	37.4 ± 5.4[a]	(36.7–37.8)	38.9 ± 5.5[b]	(38.5–39.3)	38.6 ± 5.5[b]	(38.2–39.0)
Survival rate	472 (94.9)[a]	(93.0–96.8)	3,289 (94.2)[a]	(93.4–94.9)	1,033 (95.7)[a]	(94.5–96.9)	929 (97.6)[b]	(96.9–98.6)
No. of embryo transfers (%)	135 (91.8)[a]	(87.4–96.2)	1,685 (97.6)[b]	(96.9–98.3)	649 (96.2)[b]	(94.7–97.6)	589 (97.6)[b]	(96.4–98.8)
No. of embryos replaced (mean ± SD)	280 (1.9 ± 0.8)[a]	(1.9–2.0)	3,057 (1.8 ± 0.6)[a]	(1.8–1.9)	1,008 (1.5 ± 0.6)[b]	(1.5–1.6)	919 (1.5 ± 0.6)[b]	(1.5–1.6)
Implantation rate	76 (27.2)[a]	(22.0–32.4)	1,058 (34.6)[b]	(32.9–36.3)	426 (42.3)[c]	(39.3–45.3)	390 (42.4)[c]	(39.2–45.6)
CPR/cycle	59 (40.1)	(32.2–48.0)	708 (41.0)	(38.7–43.3)	295 (43.7)	(40.0–47.4)	251 (41.6)	(37.7–45.5)
CPR/transfer	59 (43.7)	(35.3–52.1)	708 (42.0)	(39.6–44.4)	295 (45.5)	(41.7–49.3)	251 (42.6)	(38.6–46.6)
OPR/cycle	44 (29.9)	(22.5–37.3)	571 (33.1)	(30.1–35.3)	235 (34.9)	(31.3–38.5)	178 (29.5)	(25.8–33.1)
OPR/transfer	44 (32.6)	(24.7–40.6)	571 (33.9)	(31.6–36.1)	235 (36.2)	(32.5–39.9)	178 (30.7)	(27.0–34.4)
Miscarriage rate	15 (23.1)	(12.4–33.9)	123 (17.3)	(14.5–20.1)	56 (18.9)	(14.4–23.4)	73 (29)	(23.4–34.6)
DR/cycle	44 (29.9)	(22.5–37.3)	570 (33.0)	(30.9–35.3)	235 (34.8)	(31.2–38.4)	178 (29.5)	(25.9–33.1)
LBR/cycle	52 (35.3)[a]	(27.6–43.0)	677 (39.2)[a]	(36.9–41.5)	274 (40.6)[a,b]	(36.9–44.3)	196 (32.5)[a,c]	(28.8–36.2)

Note: CPR = clinical pregnancy rate; OPR = ongoing pregnancy rate; DR = delivery rate; LBR = live birth rate.

[a,b,c] Different superscripts in the same row indicate statistical difference ($P<.05$).

Cobo. Clinical outcomes of vitrified embryos. Fertil Steril 2012.

Embriyo seçimi lehine bir bias söz konusu

Hepsini Dondur Politikası

Dondurma-çözme sonrası embriyo sağ kalım oranları ve buna bağlı transferler sonrası gebelik oranları giderek artmaktadır.

Taze sikluslarda kullanılan kontrollü over stimulasyonu (KOS) elde edilen oosit miktarını arttırmaktaysa da, siklus içerisinde doğal hormonal durumdan büyük ölçüde sapmaları da beraberinde getirmektedir.

KOS, suprafizyolojik seviyelerin (E ve P) sonucu olarak endometriyumun morfolojisi, gen ekspresiyonu ve biyokimyasal fonksiyonlarında değişiklikler meydana getirebilmekte ve embriyo-endometriyum asenkronisi ortaya çıkmaktadır.

Çalışmalar suprafizyolojik dozlarda hormon seviyelerinin embriyo kalitesine olumsuz şekilde etki etmediklerini, yüksek progesteron seviyesinin oosit morfolojisini etkilemediğini göstermiştir.

KOS protokollerinde uterin kontraktilitede de artış saptanmıştır.

Hepsini Dondur Politikası

Geniş çaplı ve multisentrik randomize klinik çalışmalara ihtiyaç vardır.

Bu çalışmalarda hasta ve embriyo seçimi oldukça kritiktir.

Fertil Steril. 2013 Feb;99(2):389-92. doi: 10.1016/j.fertnstert.2012.09.044. Epub 2012 Oct 11.

Matched-cohort comparison of single-embryo transfers in fresh and frozen-thawed embryo transfer cycles.

Shapiro BS[1], Daneshmand ST, Restrepo H, Garner FC, Aguirre M, Hudson C.

⊕ Author information

Abstract

OBJECTIVE: To discern the potential effect of
blastocysts in fresh and frozen-thawed single-e

DESIGN: Matched cohort study.

SETTING: Private fertility center.

PATIENT(S): Ninety-three matched pairs of sin

INTERVENTION(S): Fresh and frozen-thawed e

MAIN OUTCOME MEASURE(S): Ongoing preg

RESULT(S): The fresh and frozen-thawed grou
patient age, use of genetic screening, or presen
thawed group than in the fresh group for transfe
56.5%, respectively). This resulted in the overa
(55.9% vs. 26.9%, respectively).

CONCLUSION(S): Autologous day 6 blastocys
morphologically equivalent embryos transferred
fresh transfers after ovarian stimulation, sugge
ovarian stimulation.

Fertil Steril. 2012 Dec;98(6):1490-4. doi: 10.1016/j.fertnstert.2012.07.1136. Epub 2012 Aug 25.

Frozen-thawed embryo transfer is associated with a significantly reduced incidence of ectopic pregnancy.

Shapiro BS[1], Daneshmand ST, De Leon L, Garner FC, Aguirre M, Hudson C.

⊕ Author information

Abstract

OBJECTIVE: To compare the incidence of ectopic pregnancy (EP) after fresh ET and thawed ET.

DESIGN: Retrospective cohort study.

SETTING: Private fertility center.

PATIENT(S): This retrospective study included 2,150 blastocyst transfers, including all 1,460 fresh autologous blastocyst transfers and all 690 transfers of autologous blastocysts derived from post-thaw extended culture of thawed bipronuclear oocytes in the 8-year study period 2004-2011.

INTERVENTION(S): None.

MAIN OUTCOME MEASURE(S): Visualized EP and treated persistent pregnancy of unknown location.

RESULT(S): The rate of visualized EP was 1.5% in pregnancies in fresh autologous cycles, which was significantly more than the rate of 0 with autologous post-thaw extended culture. The rates of treated persistent pregnancy of unknown location were 2.5% and 0.3% in these two groups, respectively, a difference that was also statistically significant (relative risk 7.3, 95% confidence interval 1.7-31.0).

CONCLUSION(S): Relative to fresh transfer, thawed ET was associated with significantly reduced incidence of EP. These findings are consistent with ovarian stimulation increasing the risk of EP.

Riskler

Perinatal and neonatal outcomes of 494 babies delivered from 972 vitrified embryo transfers

Wenhao Shi, M.D., Xia Xue, M.D., Silin Zhang, M.D., Wanqiu Zhao, M.D., Shan Liu, Ph.D., Hanying Zhou, M.D., Min Wang, M.D., and Juanzi Shi, Ph.D.
Assisted Reproduction Center, Maternal and Child Health Care Hospital of Shaanxi Province, Xi'an, People's Republic of China

Comparison of obstetrical and neonatal outcomes between vitrified and fresh ETs.

	Singleton gestation		Multiple gestation	
Parameter	**Fresh**	**Vitrification**	**Fresh**	**Vitrification**
No. of vaginal deliveries (%)	76 (18.05)	34 (13.28)	21 (10.88)	11 (9.24)
No. of cesarean sections (%)	345 (81.95)	222 (86.72)	172 (89.12)	108 (90.76)
Mean gestational age, wk	38.85 ± 1.47	39.02 ± 1.67	36.67 ± 2.01	36.77 ± 1.56
No. of preterm deliveries (<37 wk) (%)	29 (6.89)	17 (6.64)	89 (46.11)	62 (52.10)
No. of very preterm deliveries (<32 wk) (%)	1 (0.24)	3 (1.17)	6 (3.11)	1 (0.84)
No. of cases of antenatal bleeding (%)	113 (26.84)	60 (23.44)	62 (32.12)	34 (28.57)
No. of cases of gestational diabetes (%)	14 (3.33)	6 (2.34)	12 (6.22)	5 (4.20)
No. of cases of pregnancy-induced hypertension (%)	16 (3.80)	10 (3.91)	17 (8.81)	19 (15.97)
Live birth	421	256	386	238
Male	197 (46.79)	126 (49.22)	178 (46.11)	107 (44.96)
Female	224 (53.21)	130 (50.78)	208 (53.89)	131 (55.04)
Mean birth weight, g	3,216.87 ± 451.30	3,337.44 ± 505.60[a]	2,435.23 ± 435.74	2,556.45 ± 432.91[a]
Mean Apgar score				
1 min	9.00 ± 0.07	8.91 ± 0.45[a]	8.91 ± 0.33	8.90 ± 0.39
5 min	9.91 ± 0.30	9.85 ± 0.47	9.36 ± 0.52	9.34 ± 0.56
10 min	9.92 ± 0.27	9.89 ± 0.37	9.45 ± 0.57	9.47 ± 0.56
Birth weight <1,500 g (%)	0	2 (0.78)	10 (2.59)	0[b]
Birth weight 1,500–2,499 g (%)	24 (5.70)	10 (3.91)	186 (48.19)	99 (41.60)[b]

LGA

Large baby syndrome in singletons born after frozen embryo transfer (FET): is it due to maternal factors or the cryotechnique?

A. Pinborg[1,*], A.A. Henningsen[2], A. Loft[2], S.S. Malchau[2], J. Forman[3], and A. Nyboe Andersen[2]

EPİGENETİK DEĞİŞİKLİKLER ?

Çeşitli Konular

Twice-frozen embryos are no detriment to pregnancy success: a retrospective comparative study

Juliette Koch, M.R.A.N.Z.C.O.G.,[a,b] Michael F. Costello, F.R.A.N.Z.C.O.G.,[a,b] Michael G. Chapman, F.R.A.N.Z.C.O.G.,[a,c] and Suha Kilani, Ph.D.[a]

Çok sayıda, birlikte dondurulmuş embriyolar çözüldüğünde ET için seçilip tekrar dondurulabilir.

The effect of modified quarter laser-assisted zona thinning on the implantation rate per embryo in frozen/vitrified-thawed/warmed embryo transfer cycles: a prospective randomized controlled trial†

S. Debrock*, K. Peeraer, C. Spiessens, D. Willemen, P. De Loecker, and T.M. D'Hooghe

FET siklusunda lazer ile AHA uygulamaları implantasyon oranlarını etkilemiyor

The time aspect in storing vitrified blastocysts: its impact on survival rate, implantation potential and babies born

B. Wirleitner[1,*], P. Vanderzwalmen[1,2], M. Bach[1], B. Baramsai[1], A. Neyer[1], D. Schwerda[1], M. Schuff[1], D. Spitzer[3], A. Stecher[1], M. Zintz[1], and N.H. Zech[1]

Saklama süresinin embriyo kalitesine gebelik oranlarına ve malformasyon görülme sıklığına etkisi görülmemiştir.

Konu hakkında en rafine ve kapsamlı bilgi ve KPI için…

Reproductive BioMedicine Online (2012) 25, 146– 167

www.sciencedirect.com
www.rbmonline.com

ELSEVIER

ARTICLE

The Alpha consensus meeting on cryopreservation key performance indicators and benchmarks: proceedings of an expert meeting

Alpha Scientists in Reproductive Medicine [1,*]

[1] Meeting participants: Başak Balaban (Assisted Reproduction Unit, American Hospital, Istanbul, Turkey), Veronica Bianchi (Tecnobios Procreazione, Bologna, Italy), Virginia Bolton (Assisted Conception Unit, Guy's Hospital, London, UK), Ana Cobo (Instituto Valenciano de Infertilidad, Valencia, Spain), Thomas Ebner (Kinderwunsch Zentrum Linz, Austria), David Edgar (Reproductive Services/Melbourne IVF, Royal Women's Hospital and Department of Obstetrics & Gynaecology, University of Melbourne, Victoria, Australia), Martin Greuner (Zentrum für gynäkologische Endokrinologie und Reproduktionsmedizin (IVF-SAAR), Saarbrücken, Germany), Stanley Leibo (Department of Biological Sciences, University of New Orleans, New Orleans, LA, USA), David Mortimer (Oozoa Biomedical Inc, West Vancouver BC, Canada), Zsolt Peter Nagy (Reproductive Biology Associates, Atlanta, GA, USA), Lodovico Parmegiani (Reproductive Medicine Unit-GynePro Medical Centers, Bologna, Italy), Tammie Roy (Genea, Kent Street, Sydney NSW, Australia), Alan Thornhill (The London Bridge Fertility, Gynaecology and Genetics Centre, London Bridge, UK), Lisbet Van Landuyt (Centre for Reproductive Medicine, University Hospital, Vrije Universiteit Brussel, Brussels, Belgium), Pierre Vanderzwalmen (IVF Centers Prof Zech – Bregenz, Austria and CHIREC, Braine-l'alleud, Belgium), Matthew (Tex) VerMilyea (Shady Grove Fertility Reproductive Science Center, Rockville, MD, USA), Maureen Wood (University of Aberdeen, Aberdeen, Scotland, UK)

* Corresponding author. *E-mail address:*alpha2@bluewin.ch (B Balaban)


Herkese mutlu yıllar
dilerim...