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Seven years of LifeGlobal® media experience: success rates improvements and perspectives.

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Rita Figueira, PhD, TS(ABB)

Assisted Reproductive Technologies
Latin American Registry (2012)

- Where are we?

Reproductive BioMedicine Online (2015) 30, 43–51

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www.sciencedirect.com
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ARTICLE

Assisted reproductive technologies in Latin America: the Latin American Registry, 2012

CrossMark

Fernando Zegers-Hochschild [a,b,*], Juan Enrique Schwarze [c], Javier A Crosby [a], Carolina Musri [a], Maria do Carmo Borges de Souza [d]

31,857 IVF-ICSI cycles

10,073 FETs cycles

5396 IVF-ICSI cycles with donated oocytes

1764 Fertility preservation cycles

Multinational data – Latin America

•155 institutions

•14 countries

47,326 Total cycles

21,452 Brazil (45%)

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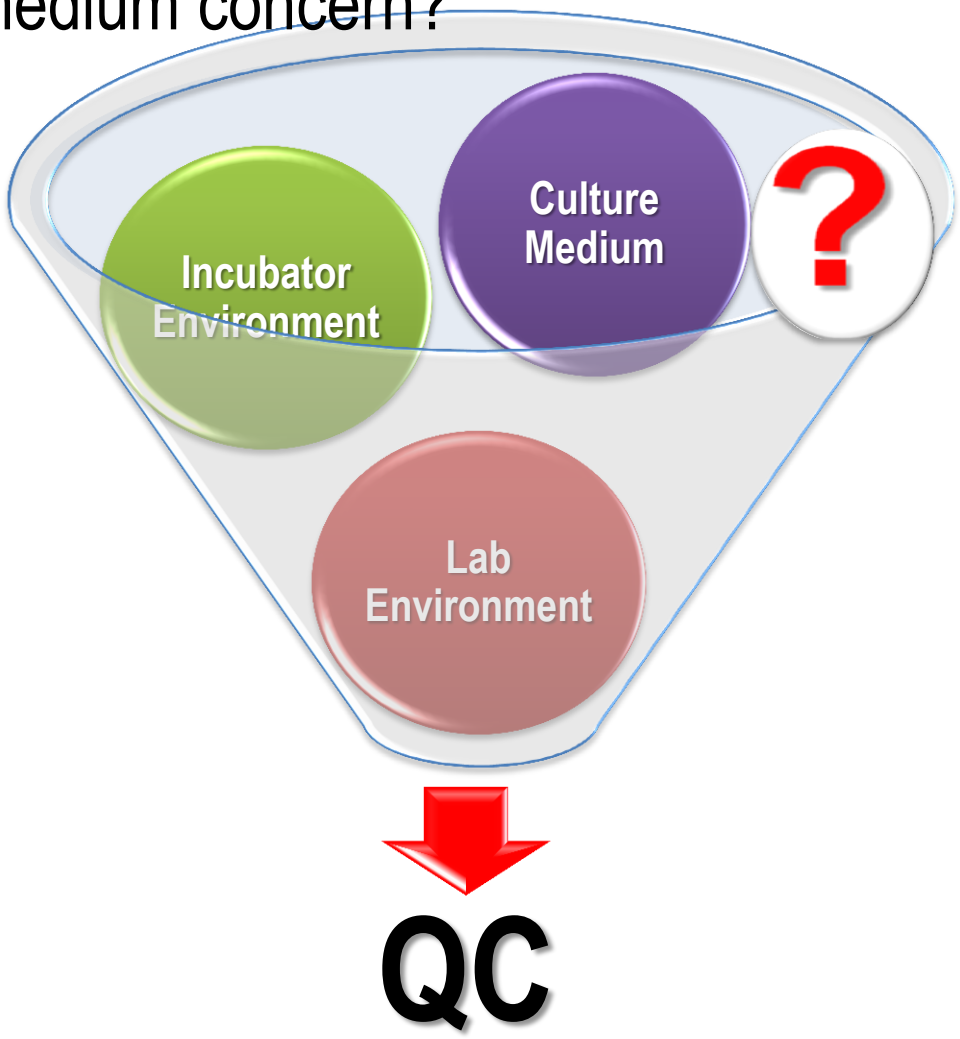
Assisted Reproductive Technologies
Quality Control (QC)

- Why culture medium concern?



Quality Control (QC)
Air Quality – ISO class 5

Reproductive BioMedicine Online (2013) 26, 9–21

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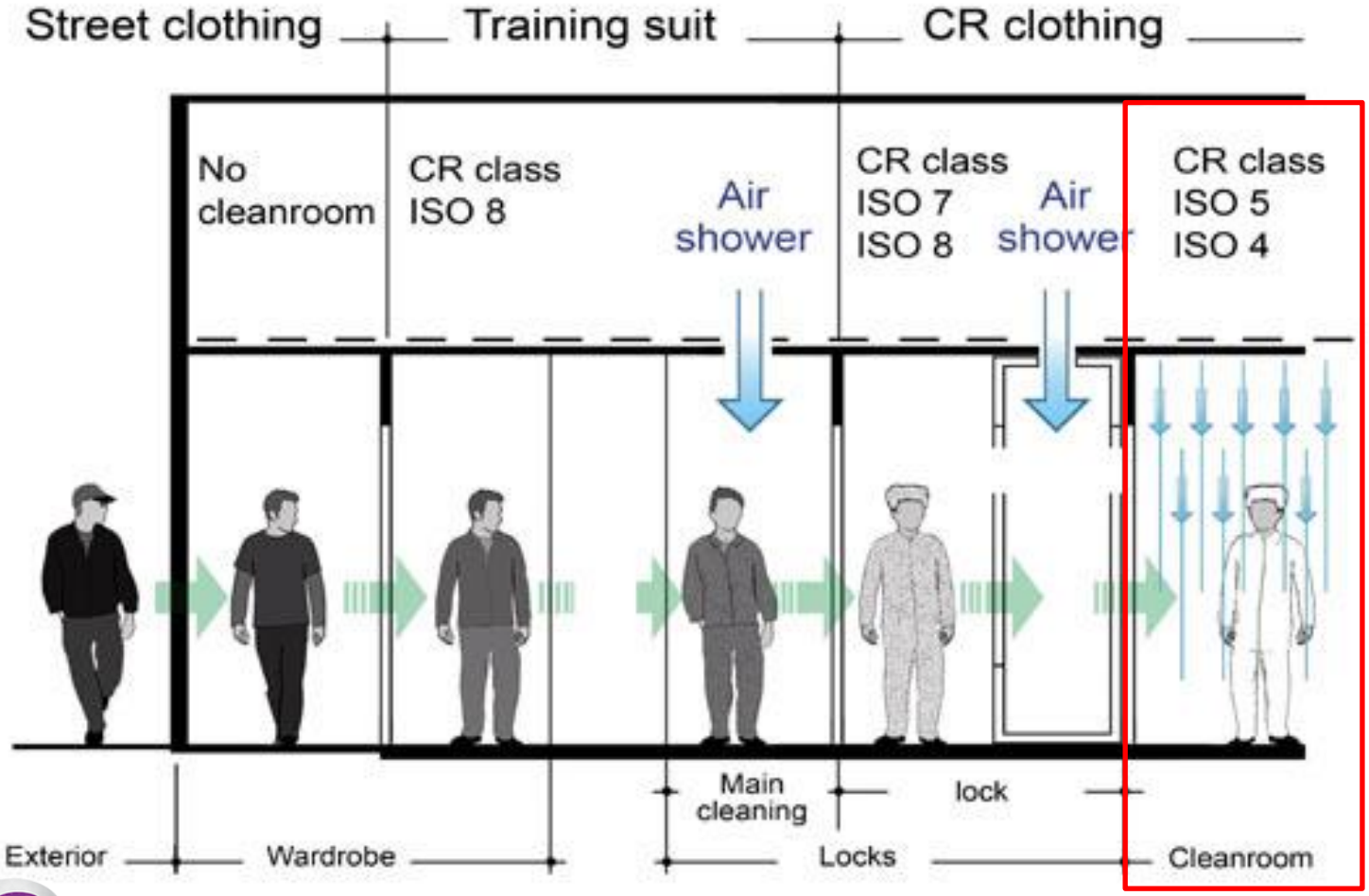
ARTICLE

Implementation of air quality control in reproductive laboratories in full compliance with the Brazilian Cells and Germinative Tissue Directive

Sandro C Esteves *, Fabiola C Bento



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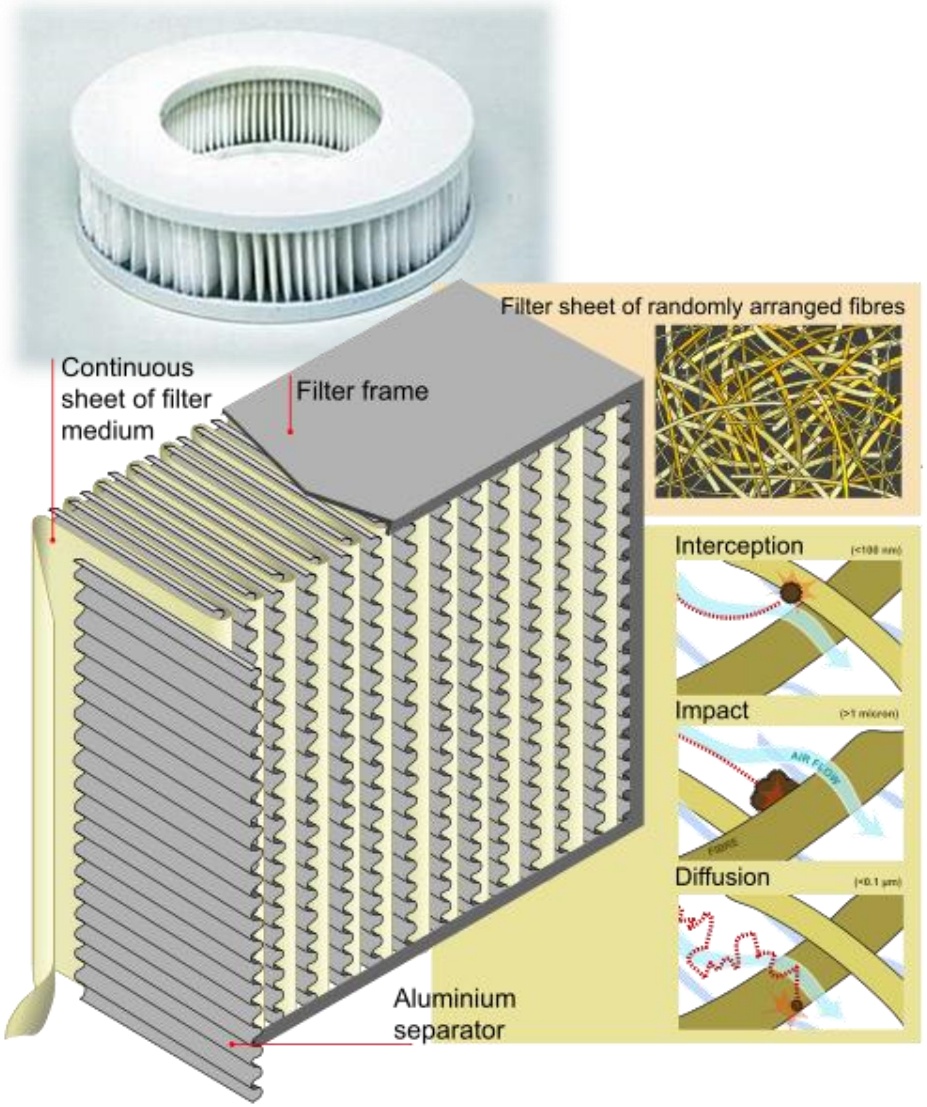
Quality Control (QC)
Air Quality – Incubators



Human Reproduction, Vol.25, No.5 pp. 1317–1324, 2010
Advanced Access publication on March 13, 2010 doi:10.1093/humrep/deq021

human reproduction ORIGINAL ARTICLE *Reproductive epidemiology*

Effect of air quality on assisted human reproduction†

Richard S. Legro[1,*], Mark V. Sauer[2], Gilbert L. Mottla[3], Kevin S. Richter[3], Xian Li[4], William C. Dodson[1], and Duanping Liao[4]

[1]Department of Obstetrics and Gynecology, Pennsylvania State University College of Medicine, 500 University Drive, H103, Hershey, PA 17033, USA [2]Department of Obstetrics and Gynecology, Columbia University College of Physicians and Surgeons, New York, NY 10032, USA [3]Shady Grove Fertility, Rockville, MD 20850, USA [4]Department of Public Health Sciences, Pennsylvania State University College of Medicine, Hershey, PA 17033, USA

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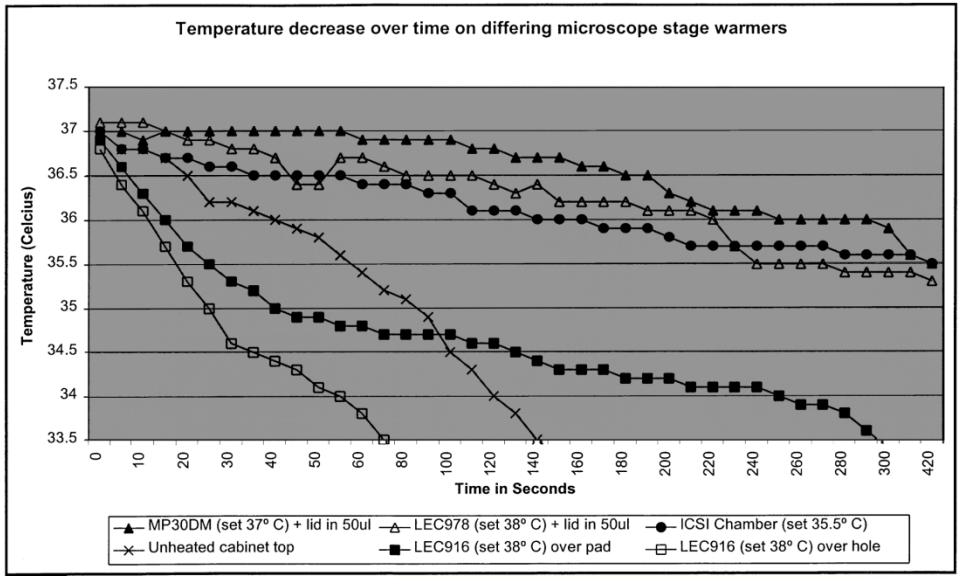
Quality Control (QC)
Lab Environment

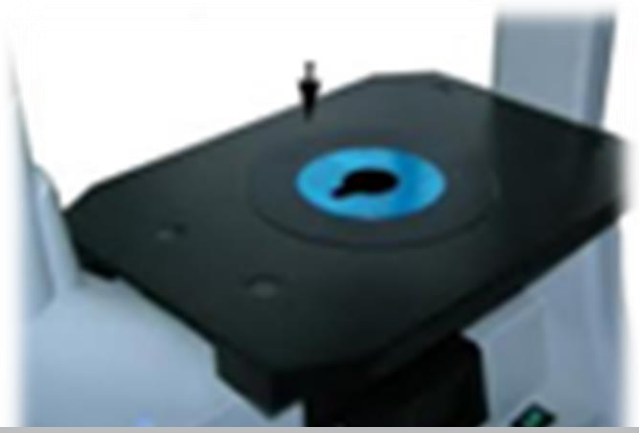
Journal of Assisted Reproduction and Genetics, Vol. 19, No. 8, August 2002 (© 2002)

Clinical Assisted Reproduction

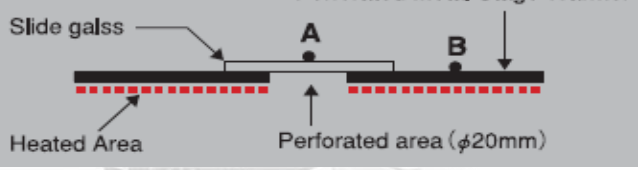
Objective Assessments of Temperature Maintenance Using In Vitro Culture Techniques[1]

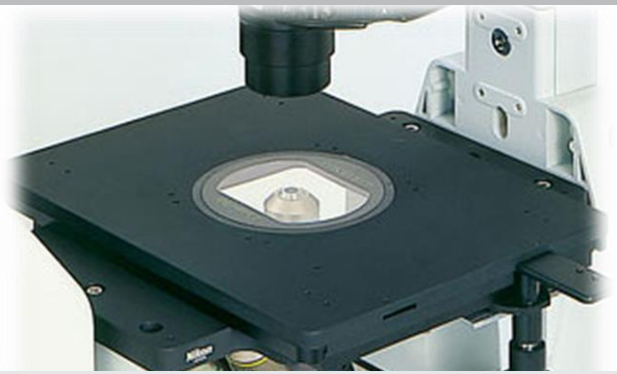
Simon Cooke,[2,5] John P. P. Tyler,[3] and Geoff Driscoll[3,4]



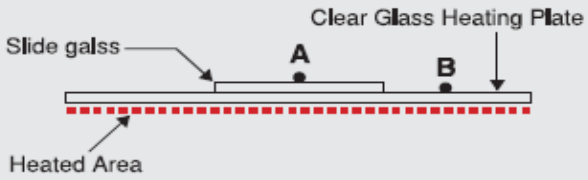


Point A: 32.9℃
Point B: 37.0℃
B — A = 4.1℃





Point A: 36.8℃
Point B: 37.0℃
B — A = 0.2℃



Quality Control (QC)
Incubators Environment

Reproductive BioMedicine Online (2014) 28, 535–547

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SYMPOSIUM: QUALITY MANAGEMENT IN ASSISTED REPRODUCTIVE TECHNOLOGY

Decisions for the IVF laboratory: comparative analysis of embryo culture incubators

Jason E Swain

Gas monitoring and recovery

Temperature

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Quality Control (QC)
Culture Medium

Reproductive BioMedicine Online (2010) 21, 6–16

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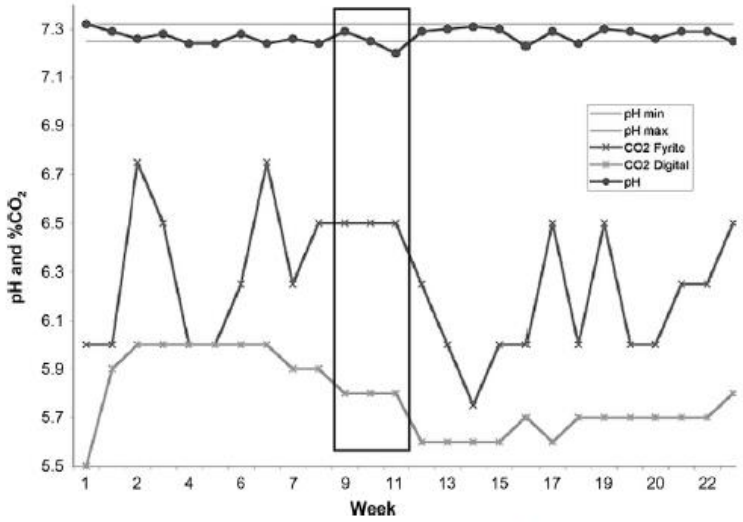

Figure 4 Demonstration of the fluctuation and inaccuracy of fyrite as an indicator of pH (adapted from Pool (2004)).

REVIEW

Optimizing the culture environment in the IVF laboratory: impact of pH and buffer capacity on gamete and embryo quality

Table III Recommended pHe values for various commercial IVF media (adapted from Swain, 2010).

Company	Medium	Recommended pHe
Cook	Sydney IVF Cleavage	7.3–7.5
	Sydney IVF Blastocyst	7.3–7.5
	Sydney IVF Fertilization	7.3–7.5
FertiPro	FertiCult™ IVF	7.2–7.6
	FertiCult™ G3	7.3–7.6
Gynemed	GM501 Basic	7.2–7.45
	GM501 Cult	7.2–7.45
InVitroCare	IVC-ONE™	7.25–7.45
	IVC-TWO™	7.25–7.45
	IVC-THREE™	7.25–7.45
Irvine	PI®	7.27–7.32
	ECM®	7.2–7.25
	SSM™	7.28–7.32
	MultiBlast®	7.3–7.4
	HTF	7.2–7.3
Life Global	global®	7.2–7.4[a]
	global® for Fertilization	7.2–7.4[a]
	Blastocyst	7.2–7.4[a]
	HTF	7.2–7.4[a]
	HTFxtra	7.2–7.4[a]
Origio	Universal IVF	7.3–7.4
	ISM1™	7.2–7.3
	ISM2™	7.35–7.45
	EmbryoAssist™	7.2–7.3
	BlastAssist®	7.35–7.45
	EmbryoGen®	7.2–7.3
Sage	Quinns Advantage® Fert	7.3 ± 0.1
	Quinns Advantage® Cleavage	7.2 ± 0.1
	Quinns Advantage® Blastocyst	7.3 ± 0.1
Vitrolife	G-IVF™ (G5-Series)	7.35 ± 0.1
	G-1™ (G5 Series)	7.27 ± 0.07
	G-2™ (G5 Series)	7.27 ± 0.07

[a]Company recommends 7.3.

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Assisted Reproductive Technologies
Quality Control (QC)

Fertility and Sterility® Vol. 94, No. 4, September 2010

What do consistently high-performing in vitro fertilization programs in the U.S. do?

Bradley J. Van Voorhis, M.D.,[a] *Mika Thomas, M.D.,*[b] *Eric S. Surrey, M.D.,*[c] *and Amy Sparks, Ph.D.*[a]

[a] Department of Obstetrics and Gynecology, University of Iowa Carver College of Medicine, Iowa City, Iowa; [b] Dallas-Fort Worth Fertility Associates, Dallas, Texas; and [c] Colorado Center for Reproductive Medicine, Lone Tree, Colorado

Título:	Resolução RDC n° 23, 27 de maio de 2011
Ementa:	Dispõe sobre o regulamento técnico para o funcionamento dos Bancos de Células e Tecidos Germinativos e dá outras providências.
Publicação:	D.O.U. – Diário Oficial da União; Poder Executivo, de 30 de maio de 2011
Órgão emissor:	ANVISA – Agência Nacional de Vigilância Sanitária
Alcance do ato:	Federal – Brasil
Área de atuação:	Sangue, outros Tecidos, Células e Órgãos

TABLE 2

Common clinical and laboratory practices among high-performing IVF programs: reported by at least 7 of 10 programs.

Laboratory practices
- Selective use of ICSI (median, 60% of cases; range, 42%–98%)
- Use of group culture of embryos in microdrops of media
- Adjustment of incubator % CO_2 based on media pH
- Selective use of assisted hatching (median rate, 10% in women aged ≤37 y) and PGS (median rate, 5% in women aged ≤37 y)
- Use of both cleavage stage (range, 17%–95%) and blastocyst (range, 5%–83%) ET

Laboratory environment
- Positive air pressure in the lab
- HEPA filtration of laboratory air
- Filtration of laboratory air for volatile and chemically active compounds
- Use of laminar flow hoods
- Use of heated microscope stages

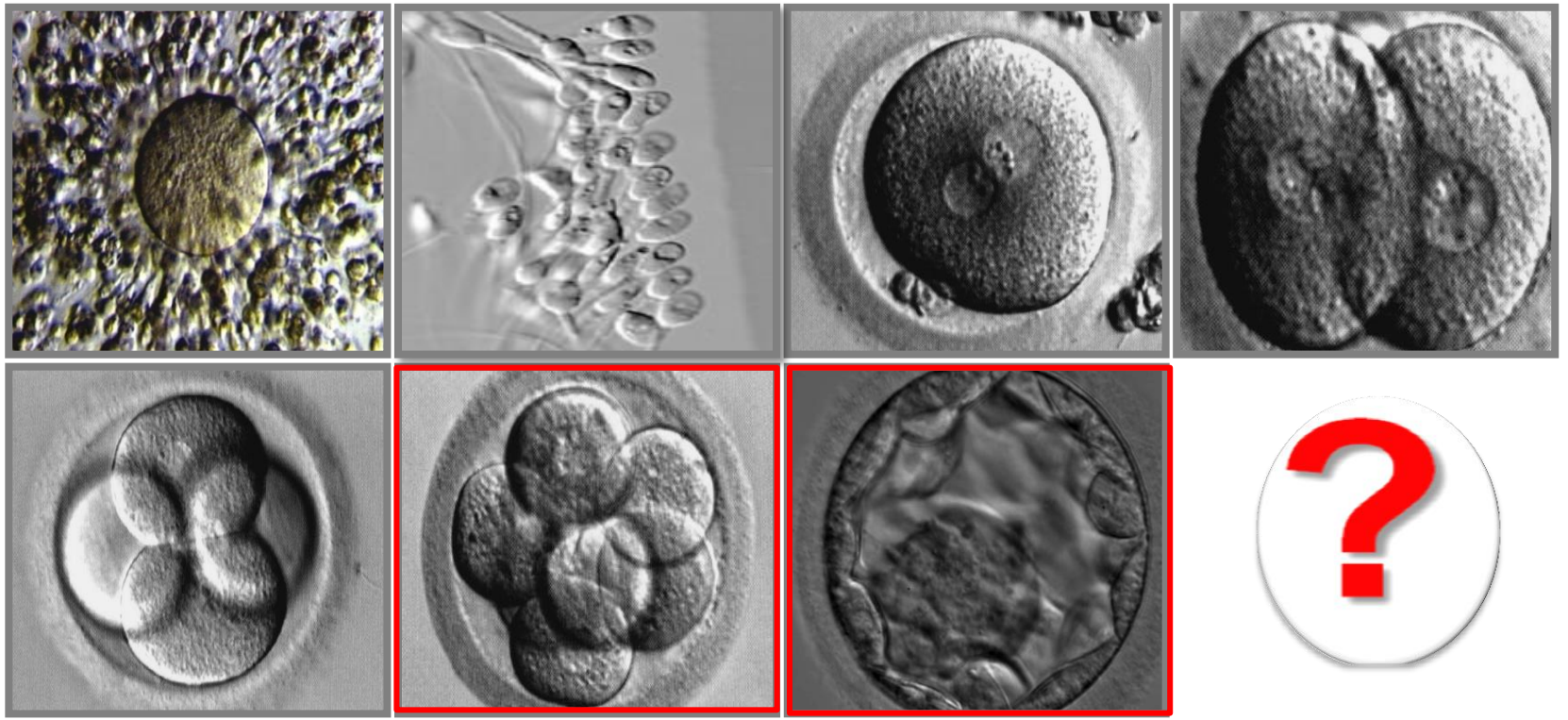
Quality Control (QC)
Day 5 transfer

Human Reproduction Vol.16, No.4 pp. 617–619, 2001

OPINION

To blastocyst or not to blastocyst? That is the question

Michael M.Alper[1,5], Peter Brinsden[2], Robert Fischer[3] and Matts Wikland[4]



Quality Control (QC)
Day 5 transfer

Human Reproduction Vol.16, No.4 pp. 617–619, 2001

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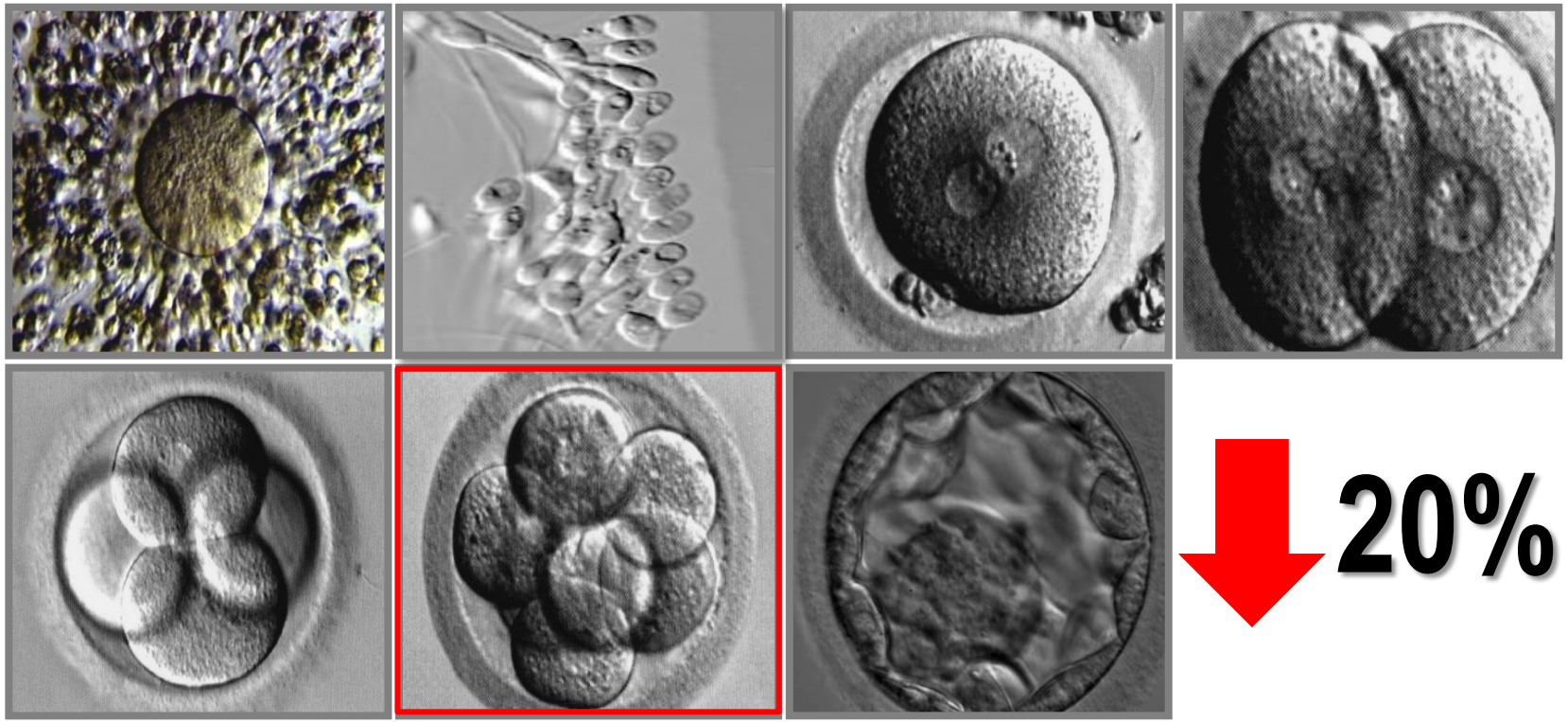

Quality Control (QC)
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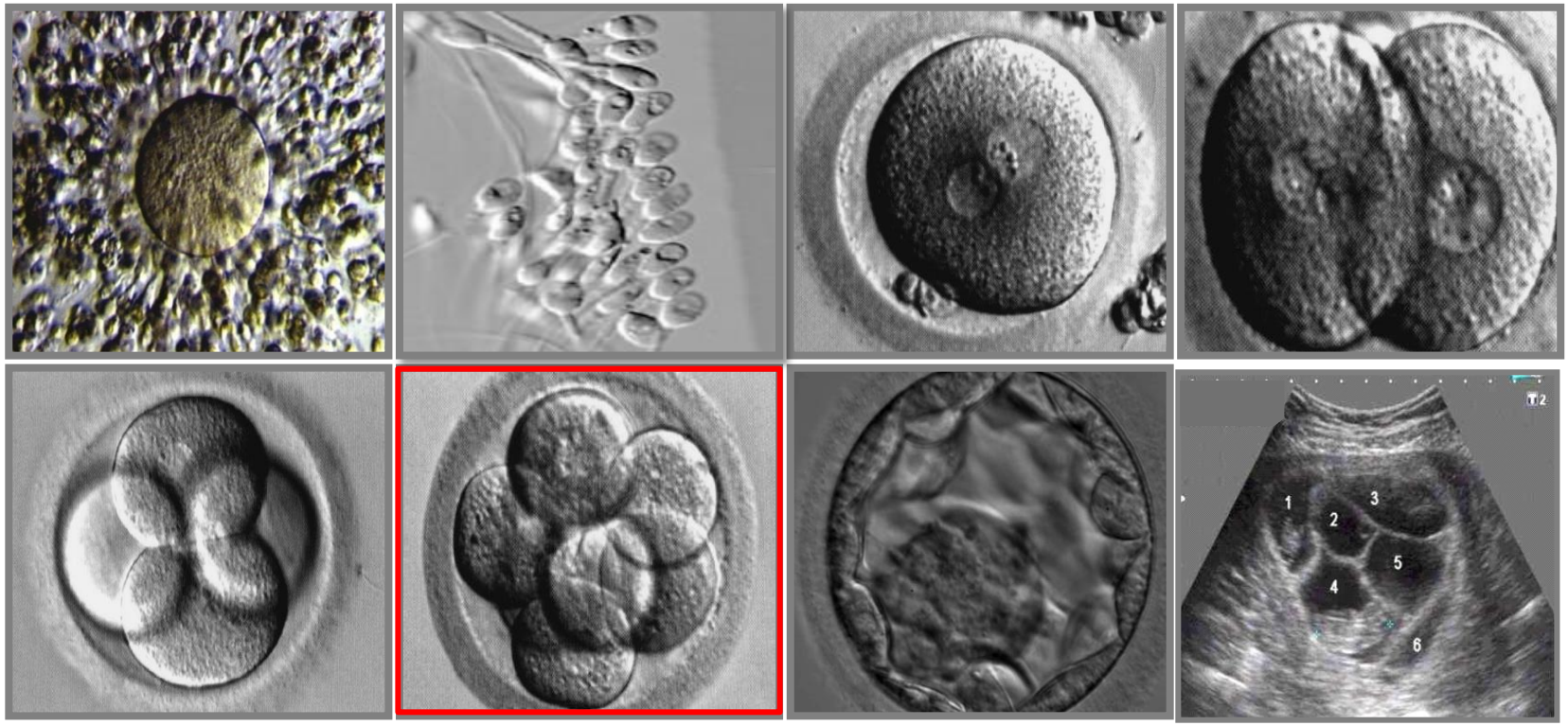

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Assisted Reproductive Technologies
Day 5 transfer

Fertility and Sterility® Vol. 99, No. 3, March 1, 2013

Blastocyst culture and transfer in clinical-assisted reproduction: a committee opinion

The Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology

American Society for Reproductive Medicine, Birmingham, Alabama

- Quality Control ✓
- Culture Medium
- Culture Systems: Low O_2
- Blastocyst Cryopreservation

Quality Control (QC)
Culture of the human embryo

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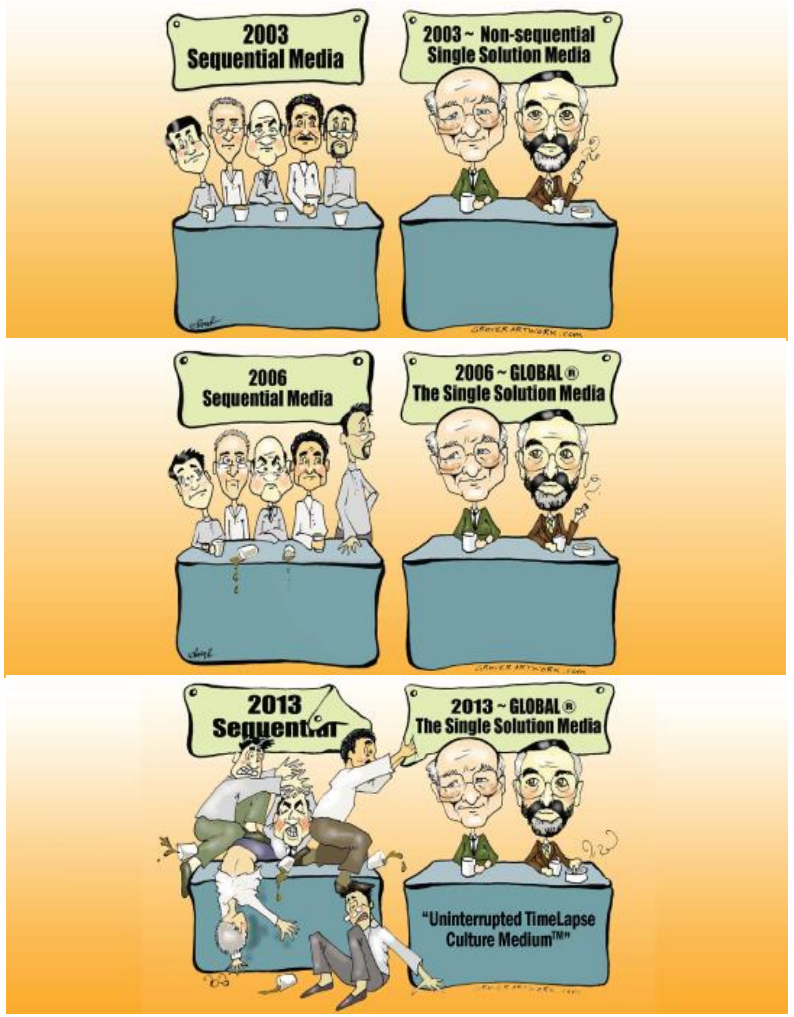
- Which media to use?
- Formulations Strategies

→ *Universal Media*

→ *Back to the Nature*

→ *Let the embryo choose*



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Assisted Reproductive Technologies
Day 5 transfer

Fertility and Sterility® Vol. 99, No. 3, March 1, 2013

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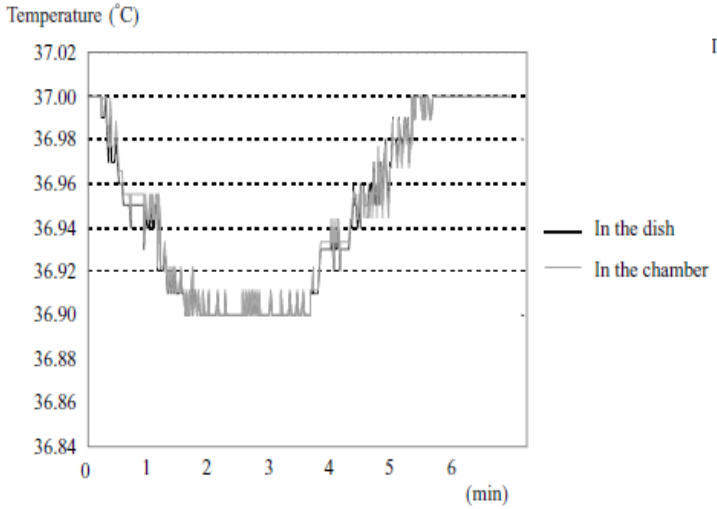
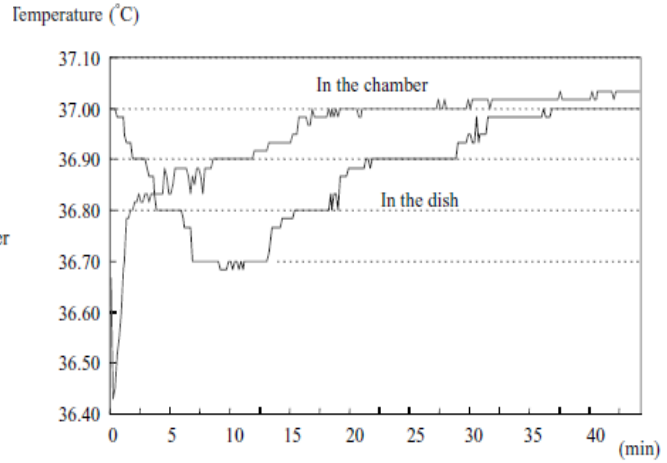
- Culture Systems: Low O_2
- Blastocyst Cryopreservation

Culture Systems: Low O_2

Benchtop Incubators

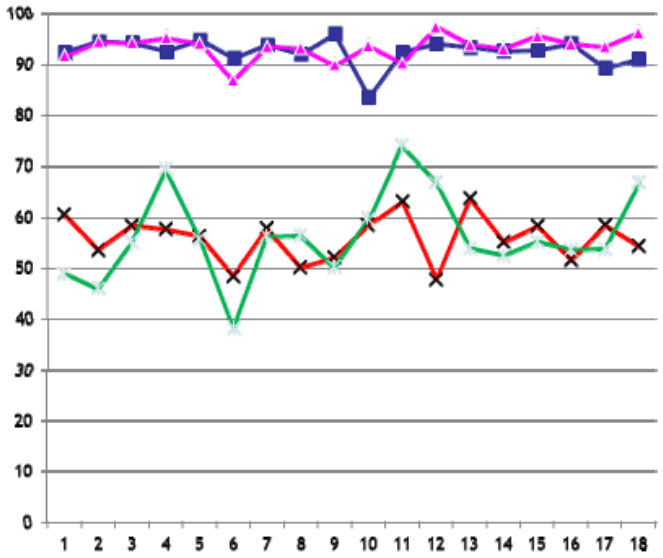




Fujiwara et al., 2007

Blastocyst Cryopreservation

Vitrification



Embryologist	N° vit. cycles	N°vit oocytes
1	54	634
2	128	1459
3	112	1211
4	44	475
5	362	4180
6	32	336
7	306	3562
8	15	171
9	31	362
10	27	367
11	30	374
12	27	348
13	63	737
14	397	4476
15	49	560
16	83	876
17	79	940
18	30	373

Ana Cobo, ALPHA 2012

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Assisted Reproductive Technologies

How to improve results?

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Assisted Reproductive Technologies
Current and future perspectives

Sperm

Oocyte

Embryo Day 1

Embryo Day 2

Embryo Day 3

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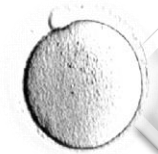
Assisted Reproductive Technologies
Current and future perspectives

Sperm



Oocyte

Embryo Day 1

Embryo Day 2

Embryo Day 3

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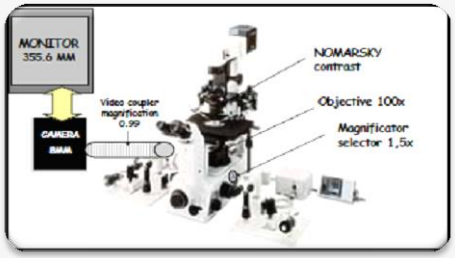
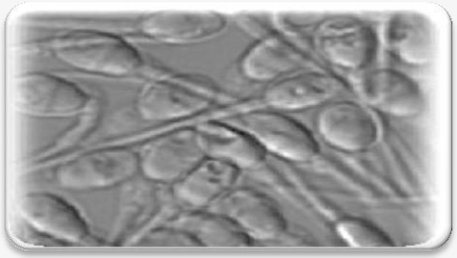
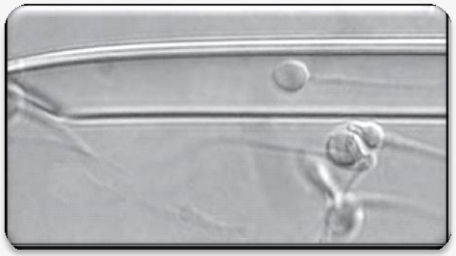
SPERM MORPHOLOGY

MSOME

Motile Sperm Organellar Morphology Examination







INVERTED LIGHT MICROSCOPE

DIC

REAL TIME SELECTION

VIABLE SPERM CELL AFTER EVALUATION

MAGNIFICATION

6000-13000x

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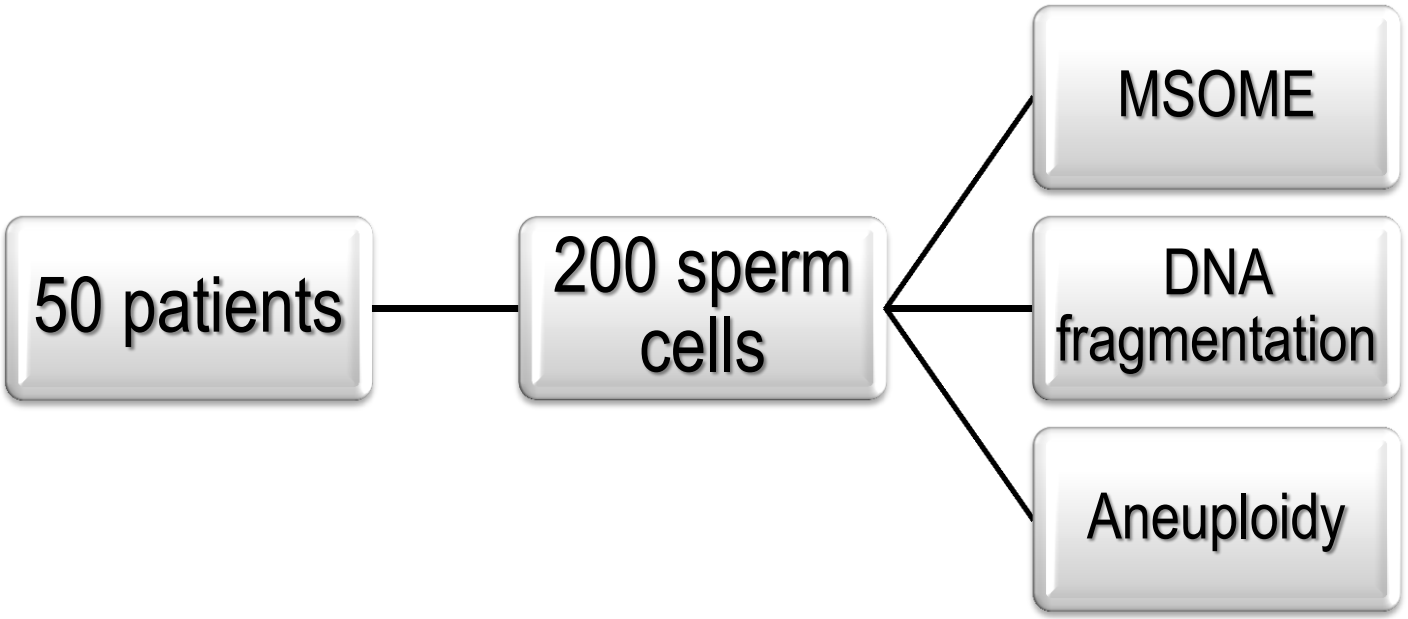
Sperm Organelle Morphologic Abnormalities: Contributing Factors and Effects on Intracytoplasmic Sperm Injection Cycles Outcomes



Edson Borges, Jr.

UROLOGY 78 (4), 2011

Sperm Organelle Morphologic Abnormalities: Contributing Factors and Effects on Intracytoplasmic Sperm Injection Cycles Outcomes

Table 1. Multivariate regression analysis of factors contributing to motile sperm organelle morphology defects incidence with variables including sperm DNA fragmentation percentage, patient's age, and sperm aneuploidy frequency

Predictor Variables	Response Variable MSOME	Slope	R^2	P
Percentage of sperm DNA fragmentation	Normal cells	−0.016	0.030	.145
	Abnormal shape	0.010	0.009	.411
	Abnormal size	0.004	0.189	<.001
	Large vacuoles	0.004	0.067	.029
	Small vacuoles	0.006	0.063	.034
Sperm aneuploidy	Normal cells	0.00291	0.009	.805
	Abnormal shape	0.00115	0.001	.960
	Abnormal size	0.08637	0.006	.528
	Large vacuoles	0.00291	0.009	.805
	Small vacuoles	0.00115	0.001	.960

Edson Borges, Jr.
UROLOGY 78 (4), 2011

Sperm Organelle Morphologic Abnormalities: Contributing Factors and Effects on Intracytoplasmic Sperm Injection Cycles Outcomes

Table 2. Multivariate regression analysis of factors contributing to the fertilization and implantation rates and binary logistic regression of factors contributing to pregnancy rate, with variables, including percentage of normal and abnormal cells according to motile sperm organelle morphology

Response Variable	Predictor Variables MSOME	Slope	R^2	*P*
Fertilization Rate	Normal cells	0.015	0.040	.0547
	Abnormal shape	−0.004	0.054	.2183
	Abnormal size	−0.002	0.116	.1231
	Large vacuoles	−0.019	0.012	.044
	Small vacuoles	−0.170	0.056	.005
Implantation rate	Normal cells	0.015	0.168	<.001
	Abnormal shape	−0.006	0.002	.290
	Abnormal size	−0.009	0.147	.004
	Large vacuoles	−0.013	0.139	.002
	Small vacuoles	−0.077	0.340	<.001
	MSOME	OR	CI	*P*
Pregnancy rate	Normal cells	1.158	0.783–1.711	.046
	Abnormal shape	0.860	0.628–1.178	.346
	Abnormal size	0.853	0.735–1.167	.032
	Large vacuoles	0.780	0.630–1.210	.043
	Small vacuoles	1.065	0.953–1.680	.103

J Assist Reprod Genet
DOI 10.1007/s10815-014-0326-9

GAMETE BIOLOGY

Sperm morphological abnormalities visualised at high magnification predict embryonic development, from fertilisation to the blastocyst stage, in couples undergoing ICSI

Amanda Souza Setti · Daniela Paes de Almeida Ferreira Braga · Livia Vingris · Thais Serzedello · Rita de Cássia Sávio Figueira · Assumpto Iaconelli Jr. · Edson Borges Jr.

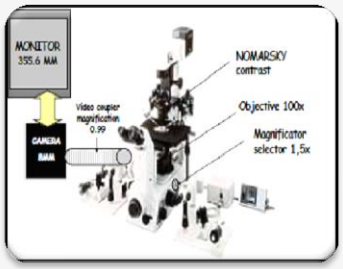
Table 3 Binary regression analysis of the embryo's characteristics that may be affected by the incidence of LNV sperm

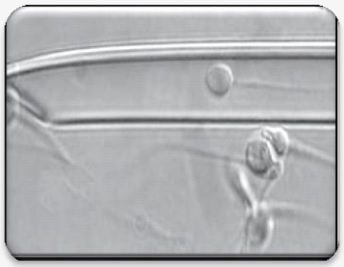
Predictor variable	Response variable		OR	CI	*p value*
Incidence of LNV sperm	**Day 1**	Zygote formation	0.98	0.95–1.01	NS
		Halo abnormality	1.00	0.94–1.05	NS
		PN size abnormalities	1.21	1.02–1.44	0.029
		PN position abnormality	1.17	1.02–1.36	0.034
		PN distance abnormality	1.27	1.04–1.54	0.022
		NPB number abnormality	1.26	1.16–1.52	0.017
		NPB distribution abnormality	1.29	1.25–1.62	0.015
	Day 2	Embryo cleavage	1.01	0.98–1.04	NS
		Normal number of blastomeres	0.78	0.69–0.87	<0.001
		Blastomere symmetry	0.96	0.92–1.01	NS
		Normal fragmentation	0.90	0.80–1.02	NS
		Blastomeres showing no visible nucleus	1.07	0.98–1.10	NS
		Multinucleated blastomere	1.05	0.95–1.13	NS
		High-quality embryo	0.99	0.95–1.03	NS
	Day 3	Normal number of blastomeres	0.75	0.68–0.88	<0.001
		Blastomere symmetry	1.00	0.96–1.03	NS
		Normal fragmentation	0.94	0.88–1.01	NS
		Blastomere showing no visible nucleus	1.04	0.98–1.08	NS
		Multinucleated blastomere	1.01	0.96–1.07	NS
		High-quality embryo	0.96	0.92–0.99	0.019
	Day 5	Blastocyst formation	0.90	0.87–0.94	<0.001
		Normal TE	0.84	0.79–0.89	<0.001
		Normal ICM	0.85	0.79–0.92	<0.001
		Grade of expansion	0.97	0.84–1.15	0.1278
		High-quality blastocyst	0.84	0.79–0.89	<0.001

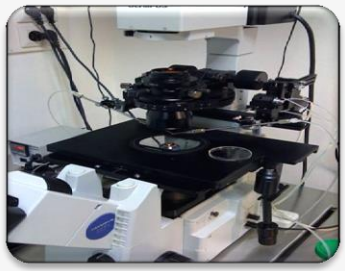
OR odds ratio; *CI* confidence intervals; *LNV* large nuclear vacuole; *PN* pronuclear; *NPB* nucleolar precursor bodies

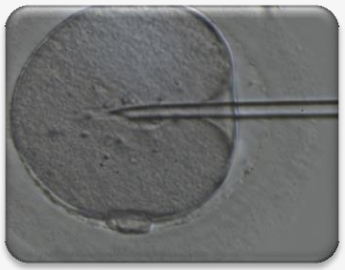
IMSI

Intracytoplasmic Morphologically Selected Injection









INVERTED LIGHT MICROSCOPE DIC	**MAGNIFICATION 6000-13000x**	**INVERTED LIGHT MICROSCOPE HOFFMAN**	**IMSI**

Reproductive BioMedicine Online (2010) 21, 450–455

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REVIEW

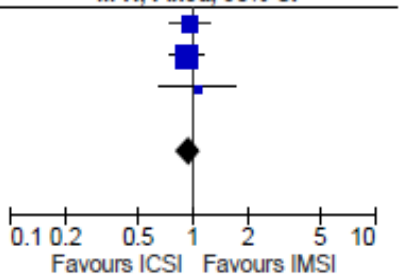
Intracytoplasmic sperm injection outcome versus intracytoplasmic morphologically selected sperm injection outcome: a meta-analysis

Amanda Souza Setti [a], Renata Cristina Ferreira [b], Daniela Paes de Almeida Ferreira Braga [a,b], Rita de Cássia Sávio Figueira [a,b], Assumpto Iaconelli Jr [b], Edson Borges Jr [a,b,*]

Fertilization

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Bartoov et al., 2003	341	530	334	510	37.3%	0.95 [0.74, 1.23]	2003
Berkovitz et al., 2006	528	784	514	744	52.9%	0.92 [0.74, 1.14]	2006
Antinori et al., 2008	624	658	605	640	9.7%	1.06 [0.65, 1.72]	2008
Total (95% CI)		1972		1894	100.0%	0.95 [0.81, 1.11]	
Total events	1493		1453				

Heterogeneity: Chi² = 0.27, df = 2 (P = 0.87); I² = 0%
Test for overall effect: Z = 0.69 (P = 0.49)

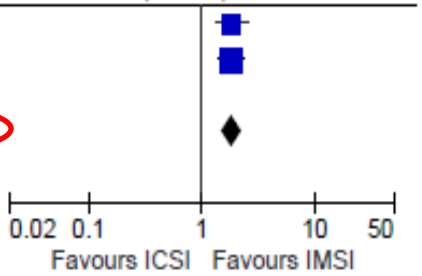


No significance

High-quality embryos

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Bartoov et al., 2003	154	341	103	334	41.0%	1.85 [1.35, 2.53]
Berkovitz et al., 2006	204	528	132	514	59.0%	1.82 [1.40, 2.37]
Total (95% CI)		869		848	100.0%	1.83 [1.50, 2.24]
Total events	358		235			

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.95); I² = 0%
Test for overall effect: Z = 5.86 (P < 0.00001)



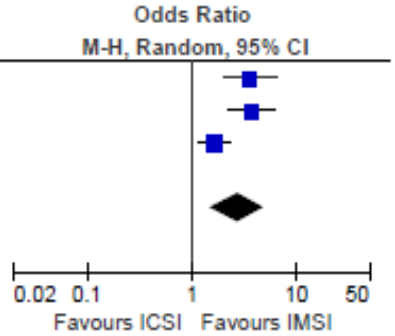
OR: 1.83 (1.50 – 2.24), p<0.001

FERTILITY MEDICAL GROUP

Implantation

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Bartoov et al., 2003	53	190	17	175	30.1%	3.60 [1.99, 6.50]	2003
Berkovitz et al., 2006	69	248	23	248	32.6%	3.77 [2.26, 6.29]	2006
Antinori et al., 2008	97	560	59	521	37.3%	1.64 [1.16, 2.32]	2008
Total (95% CI)		998		944	100.0%	2.72 [1.50, 4.95]	
Total events	219		99				

Heterogeneity: Tau² = 0.22; Chi² = 9.37, df = 2 (P = 0.009); I² = 79%
Test for overall effect: Z = 3.29 (P = 0.001)

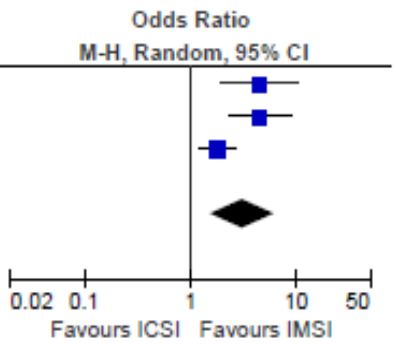


OR: 2.72 (1.50 – 4.95), p=0.001

Pregnancy

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Bartoov et al., 2003	33	50	15	50	27.7%	4.53 [1.95, 10.51]	2003
Berkovitz et al., 2006	48	80	20	80	32.3%	4.50 [2.29, 8.84]	2006
Antinori et al., 2008	89	227	58	219	40.1%	1.79 [1.20, 2.67]	2008
Total (95% CI)		357		349	100.0%	3.12 [1.55, 6.26]	
Total events	170		93				

Heterogeneity: Tau² = 0.27; Chi² = 7.48, df = 2 (P = 0.02); I² = 73%
Test for overall effect: Z = 3.19 (P = 0.001)

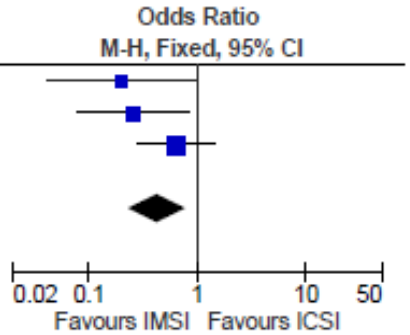


OR: 3.12 (1.55 – 6.26), p=0.001

Miscarriage

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Bartoov et al., 2003	3	33	5	15	20.8%	0.20 [0.04, 0.99]	2003
Berkovitz et al., 2006	7	48	8	20	32.2%	0.26 [0.08, 0.85]	2006
Antinori et al., 2008	15	89	14	58	47.0%	0.64 [0.28, 1.44]	2008
Total (95% CI)		170		93	100.0%	0.42 [0.23, 0.78]	
Total events	25		27				

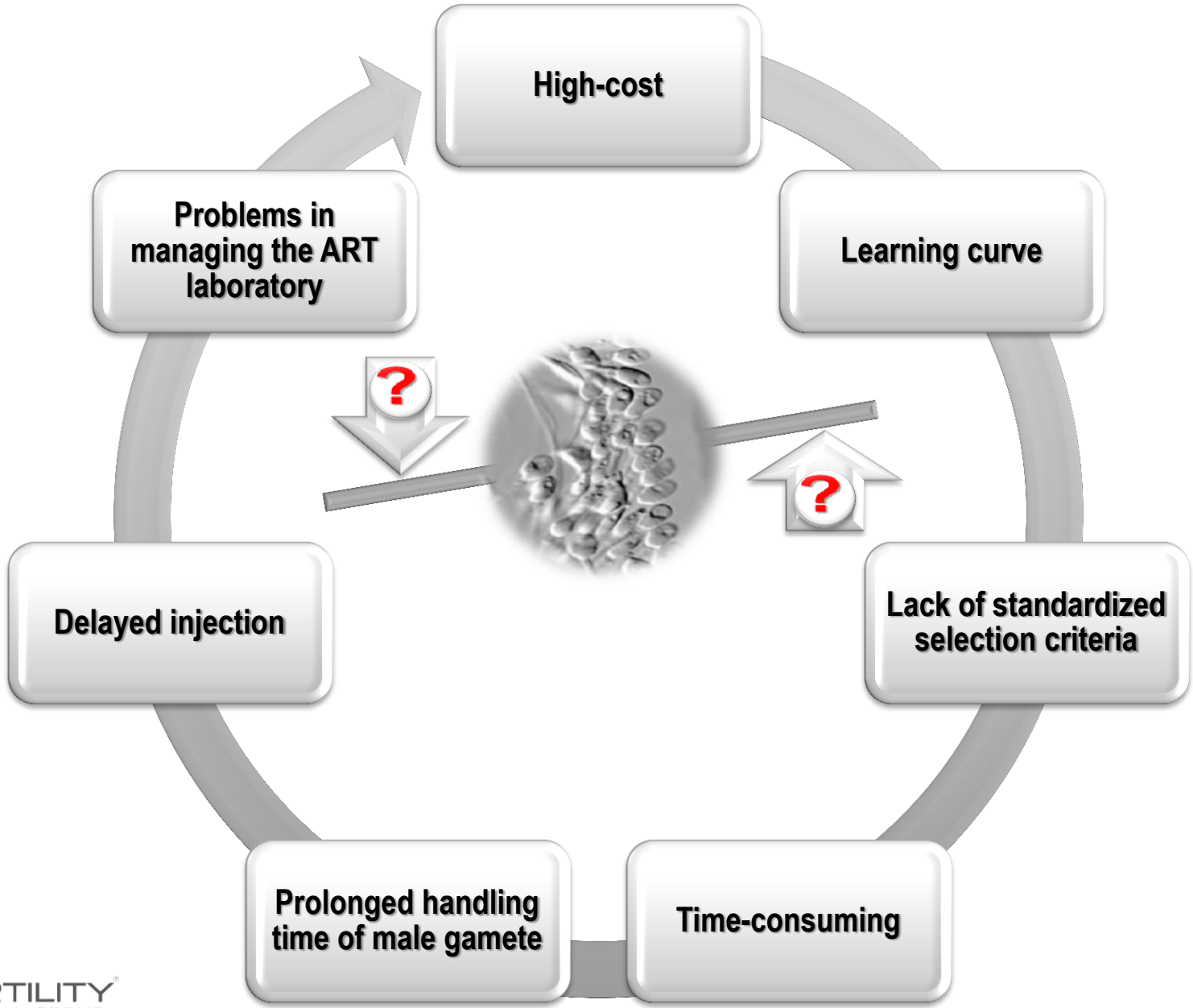
Heterogeneity: Chi² = 2.47, df = 2 (P = 0.29); I² = 19%
Test for overall effect: Z = 2.74 (P = 0.006)



OR: 0.42 (0.23 – 0.78), p=0.006

FERTILITY MEDICAL GROUP

IMSI – DRAWBACKS



FERTILITY MEDICAL GROUP

IMPLANTATION FAILURE

(Bartoov, 2002 e 2003; Junca, 2004; Berkovitz, 2006; Hazout, 2006; Antinori 2008; Nadalini, 2009; Cassuto, 2009; Wilding, 2011)

HIGH SPERM DNA FRAGMENTATION RATE

(Hazout, 2006; Wilding, 2011)

MALE FACTOR

(Balaban, 2010; Wilding, 2011, Setti, 2011)

LOW BLASTOCYST RATE

(Knez, 2012)

ADVANCED MATERNAL AGE

(Setti, 2013)

UNEXPLAINED INFERTILITY

(Setti, 2013 in press)

IMPLANTATION FAILURE

(Bartoov, 2002 e 2003; Junca, 2004; Berkovitz, 2006; Hazout, 2006; Antinori 2008; Nadalini, 2009; Cassuto, 2009; Wilding, 2011)

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UNEXPLAINED INFERTILITY

(Setti, 2013 in press)

FERTILITY MEDICAL GROUP

IMSI – MALE FACTOR

Fertility and Sterility® Vol. 95, No. 8, June 30, 2011 2711

Edson Borges Jr., M.D., Ph.D.[a,b,c]
[a] Sapientiae Institute–Educational and Research Center in Assisted Reproduction, São Paulo, Brazil
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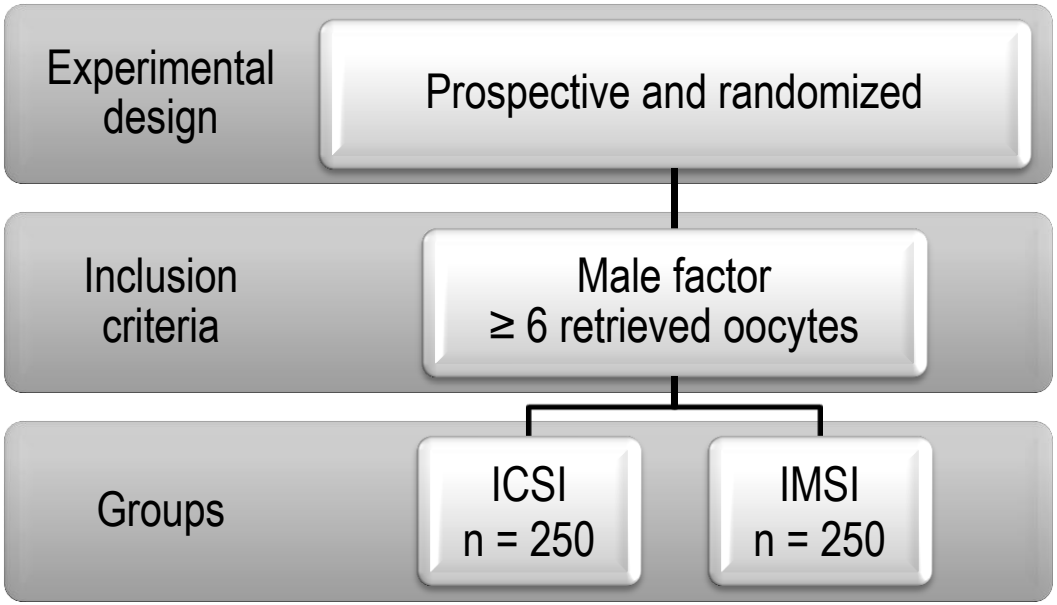
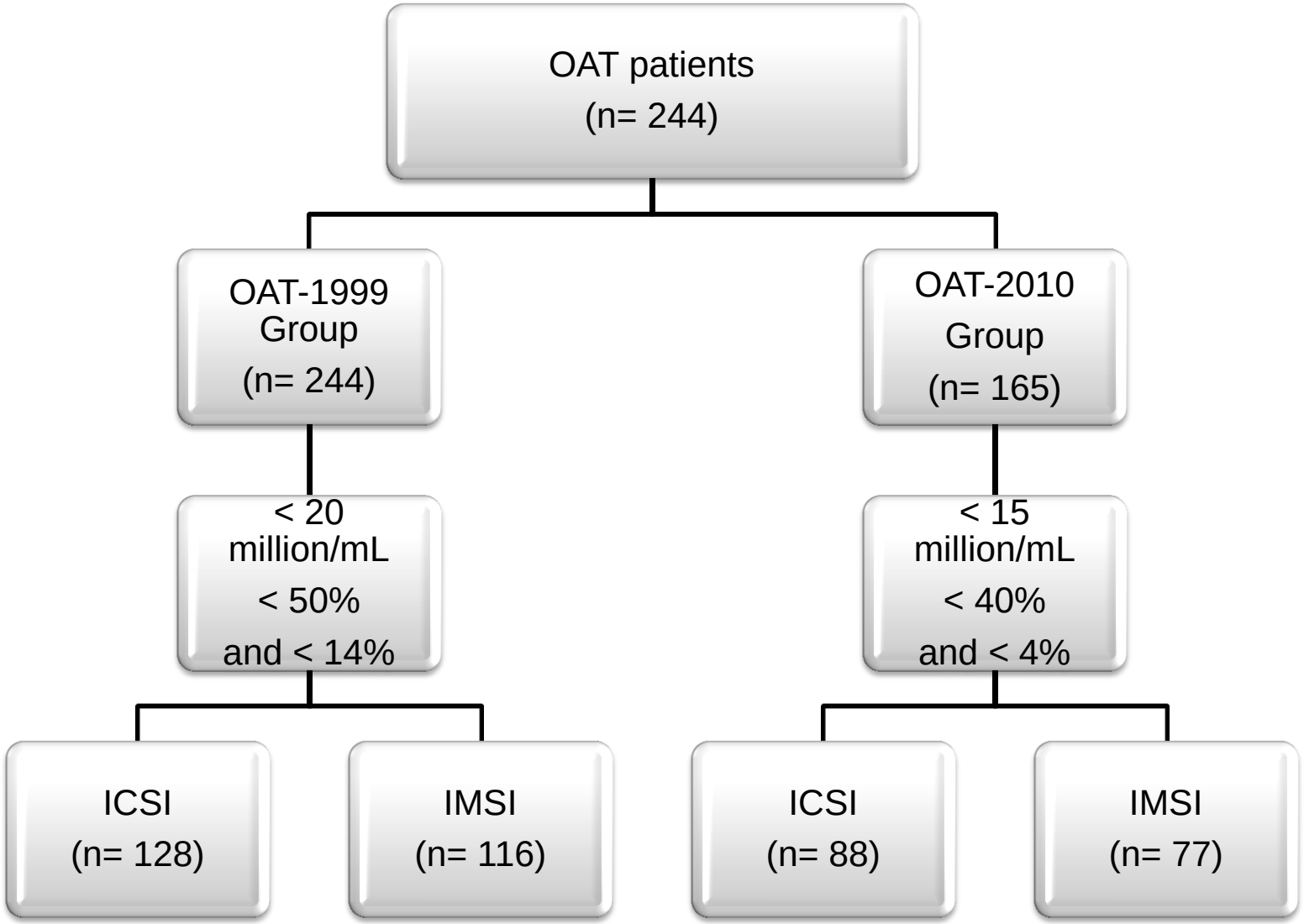
Intracytoplasmic morphologically selected sperm injection benefits for patients with oligoasthenozoospermia according to the 2010 World Health Organization reference values



FERTILITY MEDICAL GROUP

IMSI – MALE FACTOR



IMSI – MALE FACTOR

IMSI efficacy ➡ OAT-2010 Group

Outcome	OR	CI	P value
Fertilization	4.3	2.2 – 6.4	0.004
Top quality embryos	0.87	0.6 – 1.8	0.784
Pregnancy	1.67	1.2 – 3.0	0.045
Implantation	2.6	1.2 – 5.7	0.013
Miscarriage	1.2	0.6 – 1.6	0.487

IMPLANTATION FAILURE

(Bartoov, 2002 e 2003; Junca, 2004; Berkovitz, 2006; Hazout, 2006; Antinori 2008; Nadalini, 2009; Cassuto, 2009; Wilding, 2011)

HIGH SPERM DNA FRAGMENTATION RATE

(Hazout, 2006; Wilding, 2011)

MALE FACTOR

(Balaban, 2010; Wilding, 2011, Setti, 2011)

LOW BLASTOCYST RATE

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ADVANCED MATERNAL AGE

(Setti, 2013)

UNEXPLAINED INFERTILITY

(Setti, 2013 in press)

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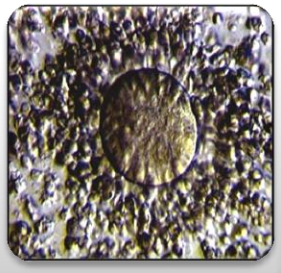
journal homepage: www.elsevier.com/locate/ejogrb

Intracytoplasmic morphologically selected sperm injection is beneficial in cases of advanced maternal age: a prospective randomized study

A.S. Setti [a,b], R.C.S. Figueira [b], D.P.A.F. Braga [a,b], T. Aoki [c], A. Iaconelli Jr.[a,b], E. Borges Jr.[a,b,*]

[a] Instituto Sapientiae – Centro de Estudos e Pesquisa em Reprodução Humana Assistida, Rua Vieira Maciel, 62, 04503-040 São Paulo, SP, Brazil
[b] Fertility – Centro de Fertilização Assistida, Av. Brigadeiro Luis Antonio, 4545, 01401-002 São Paulo, SP, Brazil
[c] Faculdade de Ciências Médicas da Santa Casa de São Paulo, Rua Dr. Cesário Motta Junior, 61, 01401-002 São Paulo, SP, Brazil

OOCYTE REPAIR



Clinic appointment

Eligible

Not eligible

Discuss trial, invite patient to participate

Standard care

Agree to participate

Does not agree to participate

Consent

Randomization

IMSI
N = 33

ICSI
N = 33

FERTILITY MEDICAL GROUP

IMSI – MATERNAL AGE

Variable	IMSI group (n=33)	ICSI group (n=33)	*p* value
Fertilization rate (%)	67,1	69,7	0,727
High-quality embryos rate on D3 (%)	48,5	44,3	0,615
Cycles with embryo transfer (%)	30/33 (90,9)	29/33 (87,9)	0,688
Miscarriage rate (%)	6/18 (33,3)	0/4 (0,0)	0,540

- **IMPLANTATION FAILURE**
  (Bartoov, 2002 e 2003; Junca, 2004; Berkovitz, 2006; Hazout, 2006; Antinori 2008; Nadalini, 2009; Cassuto, 2009; Wilding, 2011)
- **HIGH SPERM DNA FRAGMENTATION RATE**
  (Hazout, 2006; Wilding, 2011)
- **MALE FACTOR**
  (Balaban, 2010; Wilding, 2011, Setti, 2011)
- **LOW BLASTOCYST RATE**
  (Knez, 2012)
- **ADVANCED MATERNAL AGE**
  (Setti, 2013)
- **UNEXPLAINED INFERTILITY**
  (Setti, 2013 in press)

IMSI – UNEXPLAINED INFERTILITY

Variable	IMSI group (n=36)	ICSI group (n=36)	p value
High-quality embryos rate on D3 (%)	53,5	59,6	0,412
Mean number of transferred embryos	2,8 ± 0,5	2,7 ± 0,6	0,546

FERTILITY MEDICAL GROUP

(Setti, in press)

INTRACYTOPLASMIC MORPHOLOGICALLY SELECTED SPERM INJECTION RESULTS IN IMPROVED CLINICAL OUTCOMES IN COUPLES WITH PREVIOUS ICSI FAILURES OR MALE FACTOR INFERTILITY: A META-ANALYSIS.

A. S. Setti,[a,b] D. P. A. F. Braga,[a,b] R. C. S. Figueira,[a] A. Iaconelli, Jr,[a,b] E. Borges, Jr.[a,b] [a]Fertility - Centro de Fertilização Assistida, São Paulo, SP, Brazil; [b]Instituto Sapientiae - Centro de Estudos e Pesquisa em Reprodução Assistida, São Paulo, SP, Brazil.

ejog European Journal of Obstetrics & Gynecology and Reproductive Biology

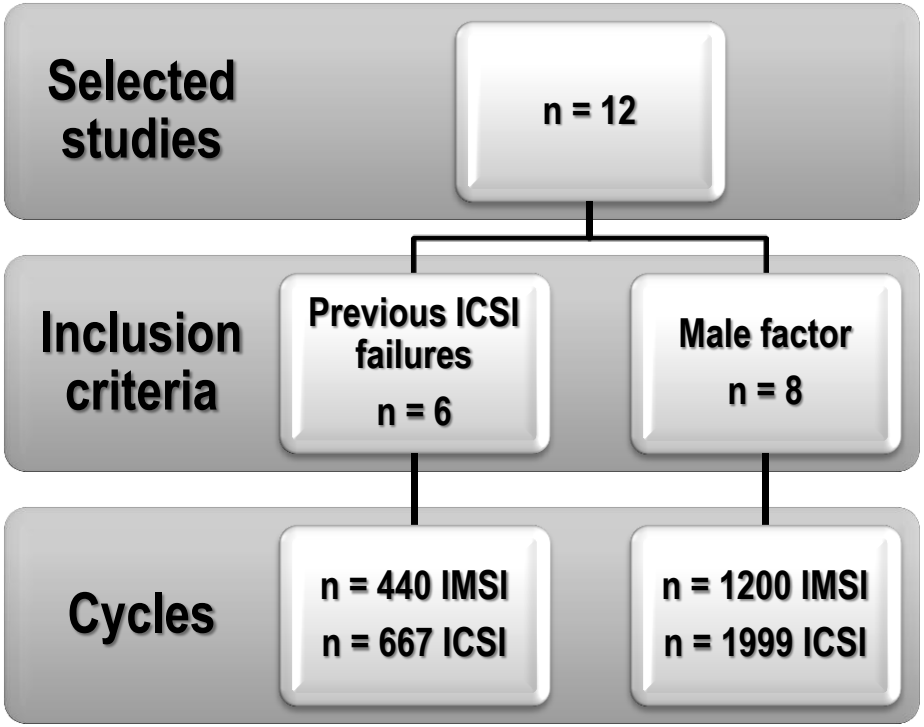
December 2014 Volume 183, Pages 96–103

MEDLINE
April 2013

- **Articles ICSI x IMSI**

Keywords

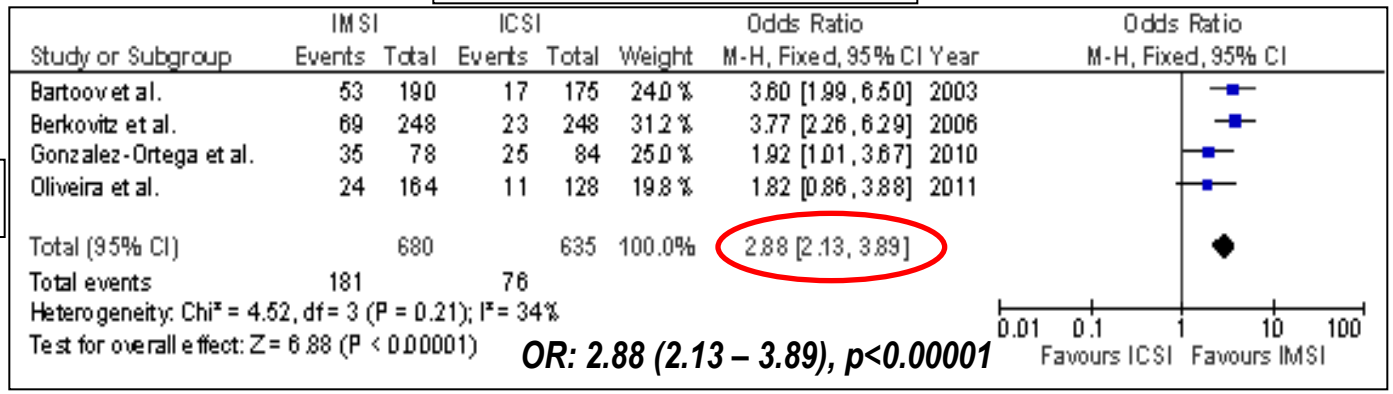
- **"ICSI", "IMSI", "MSOME", "high magnification IMSI"**



FERTILITY MEDICAL GROUP

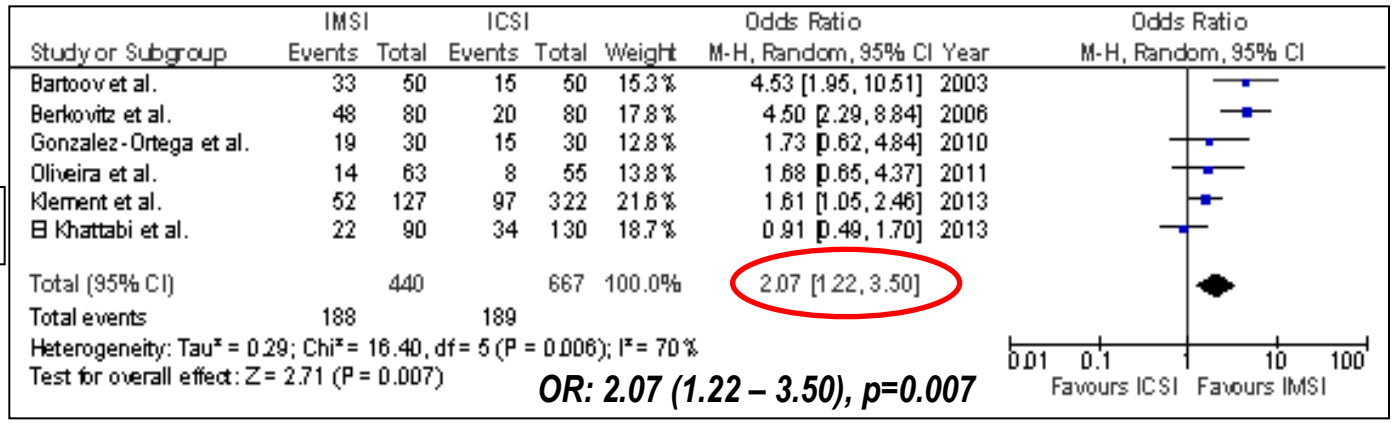
Previous ICSI failures

IR



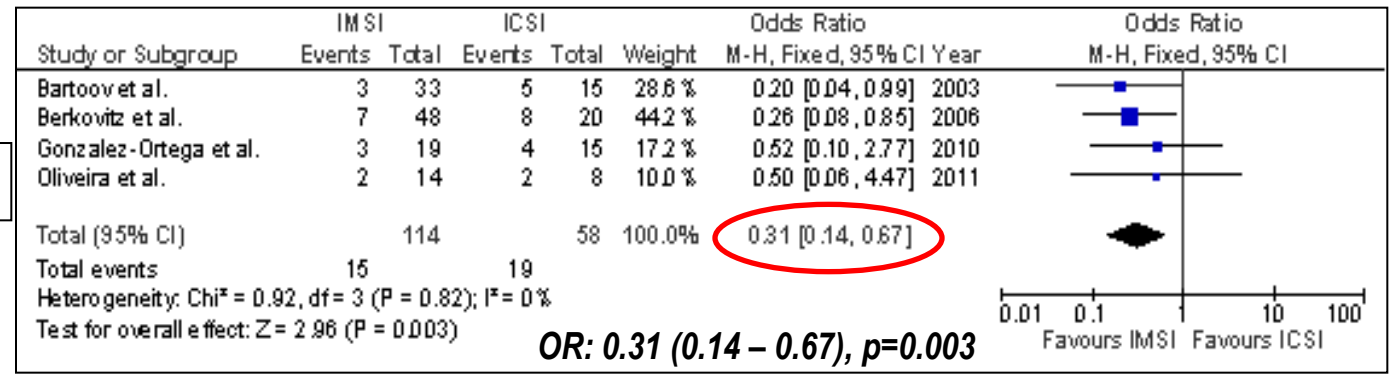
OR: 2.88 (2.13 – 3.89), p<0.00001

PR



OR: 2.07 (1.22 – 3.50), p=0.007

MR



OR: 0.31 (0.14 – 0.67), p=0.003

FERTILITY MEDICAL GROUP

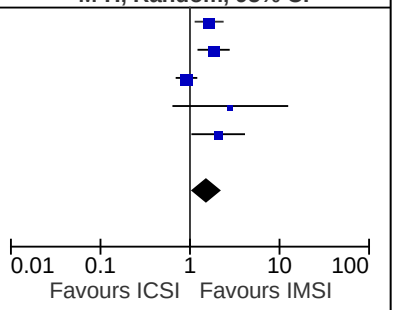
Male factor

IR

Study or Subgroup	IMSI Events	IMSI Total	ICSI Events	ICSI Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Antinori et al.	97	560	59	521	25.4%	1.64 [1.16, 2.32]	2008
Wilding et al.	86	355	48	324	24.1%	1.84 [1.24, 2.72]	2011
Setti et al.	158	664	156	613	27.9%	0.91 [0.71, 1.18]	2011
Knez et al.	6	35	3	44	5.9%	2.83 [0.65, 12.24]	2011
Knez et al.	27	93	19	115	16.7%	2.07 [1.06, 4.02]	2012
Total (95% CI)		**1707**		**1617**	**100.0%**	**1.54 [1.04, 2.28]**	
Total events	374		285				

Heterogeneity: Tau² = 0.13; Chi² = 14.98, df = 4 (P = 0.005); I² = 73%

Test for overall effect: Z = 2.13 (P = 0.03)



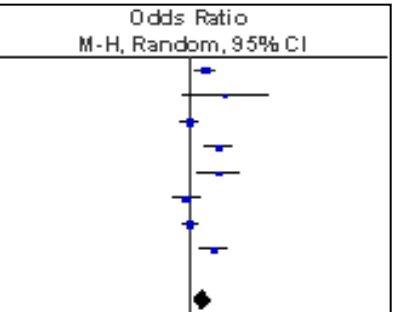
OR: 1.54 (1.04 – 2.28), p=0.03

PR

Study or Subgroup	IMSI Events	IMSI Total	ICSI Events	ICSI Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Antinori et al.	89	227	58	219	14.9%	1.79 [1.20, 2.67]	2008
Knez et al.	5	20	3	37	3.9%	3.78 [0.80, 17.89]	2011
Setti et al.	93	250	92	250	15.5%	1.02 [0.71, 1.46]	2011
Wilding et al.	80	122	44	110	12.9%	2.86 [1.68, 4.87]	2011
Knez et al.	25	52	17	70	9.7%	2.89 [1.34, 6.24]	2012
De Vos et al.	43	125	51	139	13.3%	0.90 [0.55, 1.50]	2013
Klement et al.	126	269	473	1033	16.8%	1.04 [0.80, 1.37]	2013
El Khattabi et al.	61	132	33	126	13.0%	2.42 [1.43, 4.09]	2013
Total (95% CI)		1197		1984	100.0%	1.63 [1.15, 2.30]	
Total events	522		771				

Heterogeneity: Tau² = 0.17; Chi² = 27.85, df = 7 (P = 0.0002); I² = 75%

Test for overall effect: Z = 2.77 (P = 0.006)



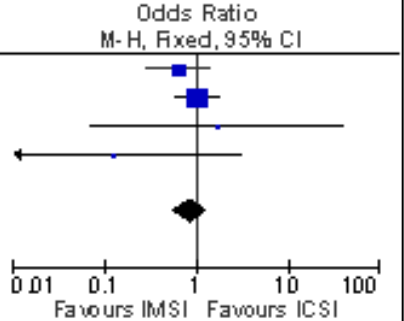
OR: 1.63 (1.15 – 2.30), p=0.006

MR

Study or Subgroup	IMSI Events	IMSI Total	ICSI Events	ICSI Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Antinori et al.	15	89	14	58	35.5%	0.64 [0.28, 1.44]	2008
Setti et al.	29	158	28	156	57.9%	1.03 [0.58, 1.82]	2011
Wilding et al.	1	80	0	44	1.6%	1.68 [0.07, 42.09]	2011
Knez et al.	1	5	2	3	5.0%	0.13 [0.00, 3.22]	2011
Total (95% CI)		332		261	100.0%	0.85 [0.54, 1.35]	
Total events	46		44				

Heterogeneity: Chi² = 2.40, df = 3 (P = 0.49); I² = 0%

Test for overall effect: Z = 0.68 (P = 0.50)



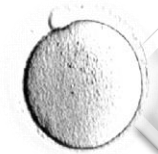
OR: 0.85 (0.54– 1.35), p=0.5

FERTILITY MEDICAL GROUP

Assisted Reproductive Technologies

Current and future perspectives

Sperm



Oocyte

Embryo Day 1

Embryo Day 2

Embryo Day 3

FERTILITY MEDICAL GROUP

OOCYTE MORPHOLOGY

Cytoplasmic features

*-Diffuse cytoplasmic granularity (**A**)*

*-Centrally located cytoplasmic granular area (**B**)*

-Dark garnular cytoplasm

*-Smooth endoplasmic reticulum clusters (**C**)*

*-Vacuoles (**D**)*

-Cytoplasmic inclusions

Extracytoplasmic features:

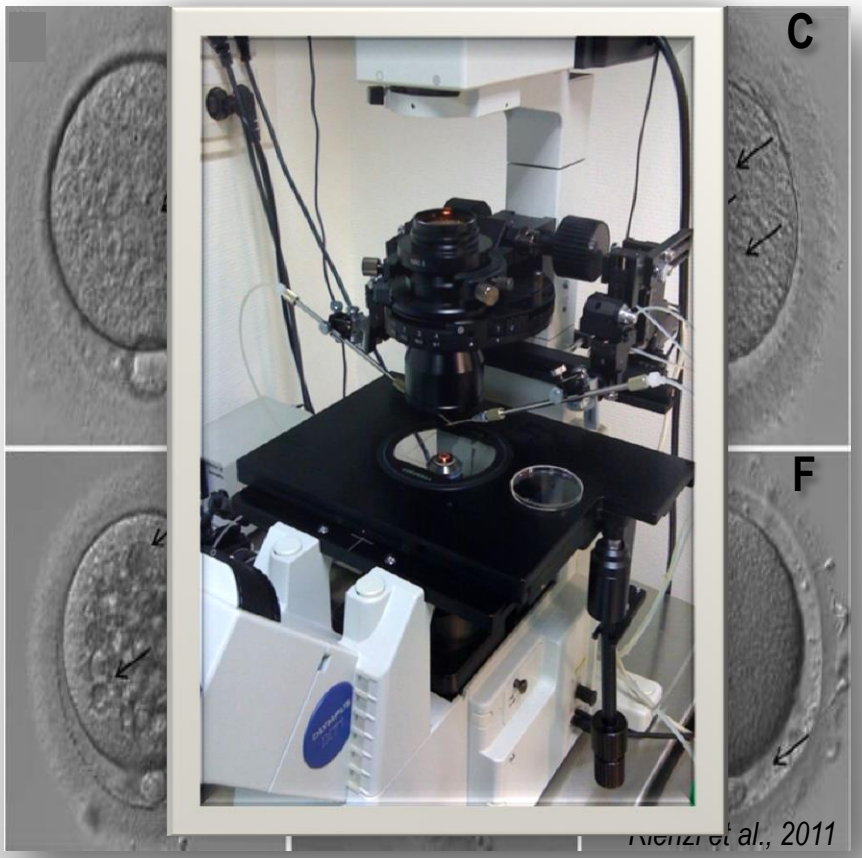
-Large I Polar body

*-Abnormal zona pellucida shape or color (**E**)*

*-Perivitelline space granularity (**F**)*

*-Large perivitelline space (**F**)*

-Abnorma shape of the oocyte



Rienzi et al., 2011

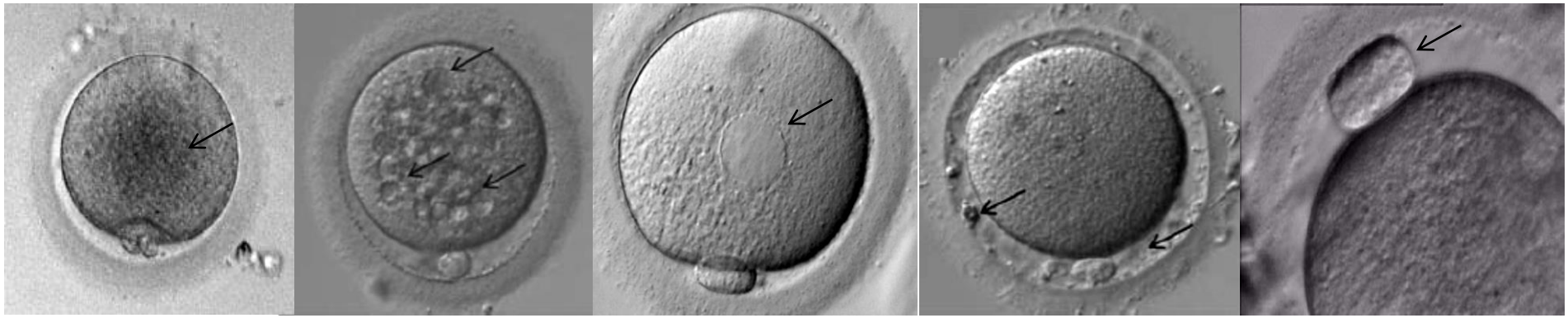
FERTILITY MEDICAL GROUP

Figueira et al.,2010; Rienzi et al., 2011; Setti et al., 2011

OOCYTE MORPHOLOGY

Contributing factors: ?

PATIENT AGE | **FSH TOTAL DOSE** | **ASPIRATED FOLLICLES** | **OOCYTE YIELD** | **MII RATE**

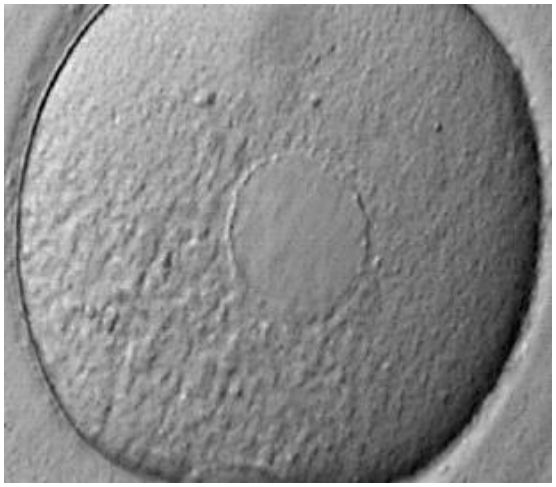
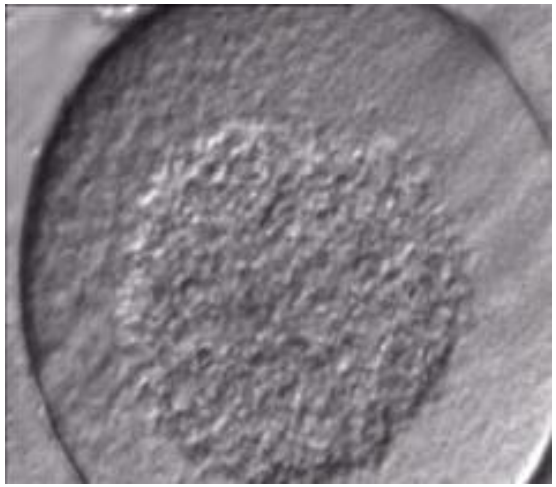


ICSI outcome effects: ?

FERTILIZATION **EMBRYO QUALITY**

Figueira et al., Fertil Steril 2010

OOCYTE MORPHOLOGY


Metaphase II human oocyte morphology: contributing factors and effects on fertilization potential and embryo developmental ability in ICSI cycles

Figueira et al., Fertil Steril 2010

3148 oocytes → 60.2% at least one morphologic abnormalitie

TABLE 1

General characteristics of stimulation ICSI cycles.

Cycles (n)	350
Age (yrs)	34.2 ± 4.7
Total gonadotropin dose (IU)	2,480 ± 756
E_2 concentration on hCG day (pg/mL)	1,705 ± 1,420
Aspirated follicles (n)	16.9 ± 13.2
Retrieved oocytes (n)	11.8 ± 9.2
Retrieved oocytes/no. of follicles (%)	69
MII oocytes (n)	8.7 ± 6.9
MII oocytes/total no. of retrieved oocytes (%)	71.2
Normal fertilization rate (%)	68.7
Rate of high-quality embryos (%)	62.1

Note: Values expressed as mean ± SD. MII = metaphase II.

Figueira. Correspondence. Fertil Steril 2009.

OOCYTE MORPHOLOGY

Contribuiting factors and effects on oocyte morphology	Odds ratio (95% CI)	*P* value
Maternal age		
Large perivitelline space size	1.09 (1.07 - 1.11)	<0.001
Perivitelline space granularity	1.03 (1.01 - 1.05)	<0.001
Vacuoles	1.07 (1.04 - 1.11)	<0.001
GnRH agonist protocol*		
Large perivitelline space size	1.83 (1.49 - 2.25)	<0.001
Perivitelline space granularity	1.23 (1.02 - 1.48)	0.034
Total dose of FSH*		
Perivitelline space granularity	1.10 (1.00 - 1.20)	0.040
Number of aspirated follicles*		
Increased cytoplasmic granularity	1.02 (1.01 - 1.02)	<0.001
Oocyte yield (no. of retrieved oocytes/no. follicles)*		
Increased cytoplasmic granularity	1.01 (1.00 - 1.01)	0.016
Perivitelline space granularity	1.02 (1.01 - 1.02)	0.016
MII oocyte rate (no. of MII oocyte/number of retrieved oocyte)*		
Fragmented first polar body	1.01 (1.00 - 1.01)	0.013

Figueira et al., Fertil Steril 2010

OOCYTE MORPHOLOGY

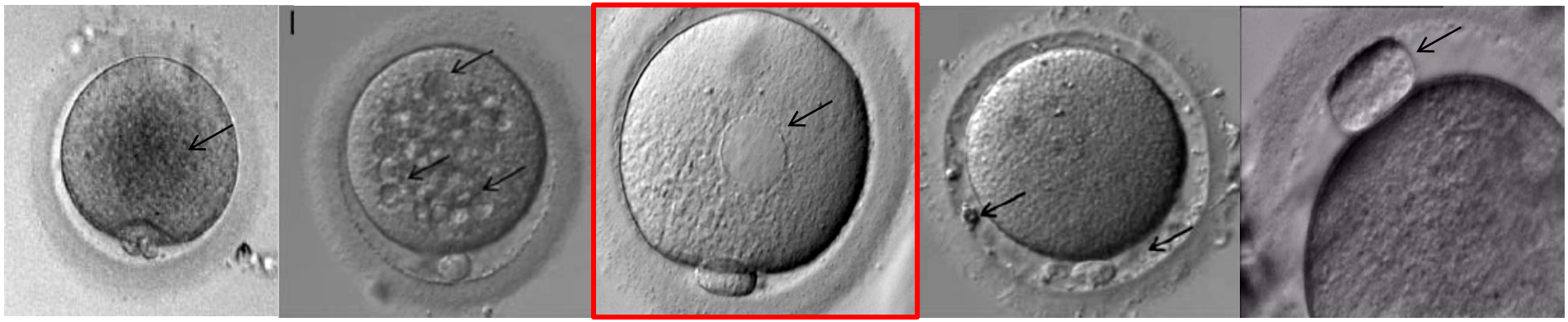
Oocyte abnormalities effects on fertilization and embryo quality	Odds ratio (95% CI)	*P* value
Fertilization rate		
Increased cytoplasmic granularity	1.22 (1.02 - 1.45)	0.010
Vacuoles	1.46 (1.02 - 2.10)	0.031
Large perivitelline space size	1.24 (1.02 - 1.52)	0.004
Embryo quality on the third day of development		
Perivitelline space granularity	1.32 (1.04 - 1.69)	0.023

Figueira et al., Fertil Steril 2010

OOCYTE MORPHOLOGY

Contributing factors:

PATIENT AGE | **FSH TOTAL DOSE** | **ASPIRATED FOLLICLES** | **OOCYTE YIELD** | **MII RATE**



ICSI outcome effects:

Human Reproduction, Vol.26, No.6 pp. 1270–1283, 2011
Advanced Access publication on April 18, 2011 doi:10.1093/humrep/der037

human reproduction ORIGINAL ARTICLE *ESHRE pages*

The Istanbul consensus workshop on embryo assessment: proceedings of an expert meeting†

Alpha Scientists in Reproductive Medicine and ESHRE Special Interest Group of Embryology

Figueira et al., Fertil Steril 2010

OOCYTE MORPHOLOGY

European Journal of Obstetrics & Gynecology and Reproductive Biology 159 (2011) 364–370

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European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Relationship between oocyte abnormal morphology and intracytoplasmic sperm injection outcomes: a meta-analysis

Amanda S. Setti [a], Rita C.S. Figueira [b], Daniela P.A.F. Braga [b], Simone S. Colturato [b], Assumpto Iaconelli Jr. [a,b], Edson Borges Jr. [a,b,*]

[a] *Sapientiae Institute – Educational and Research Center in Assisted Reproduction, Rua Vieira Maciel, 62, São Paulo, SP, Zip 04503-040, Brazil*
[b] *Fertility – Assisted Fertilisation Center, Av. Brigadeiro Luis Antonio, 4545, Sao Paulo, SP, Zip 01401-002, Brazil*

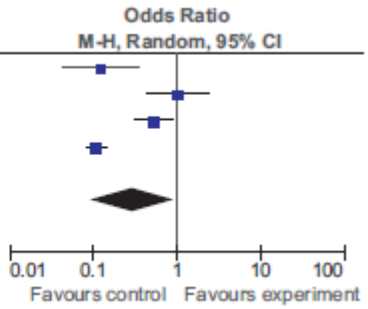
Condensation

Our meta-analysis demonstrates that the probability of an oocyte becoming fertilised is significantly reduced by the presence of intracytoplasmic inclusions and extracytoplasmic dysmorphisms.

Effect of large IPB on fertilization rate

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Ebner et al.	9	18	155	174	22.5%	0.12 [0.04, 0.35]	2000
De Santis et al.	15	25	202	340	24.1%	1.02 [0.45, 2.35]	2005
Fancsovits et al.	31	62	468	714	26.2%	0.53 [0.31, 0.89]	2006
Navarro et al.	75	363	967	1366	27.2%	0.11 [0.08, 0.14]	2009
Total (95% CI)		468		2594	100.0%	0.29 [0.09, 0.90]	
Total events	130		1792				

Heterogeneity: Tau² = 1.22; Chi² = 46.71, df = 3 (P < 0.00001); I² = 94%
Test for overall effect: Z = 2.13 (P = 0.03)

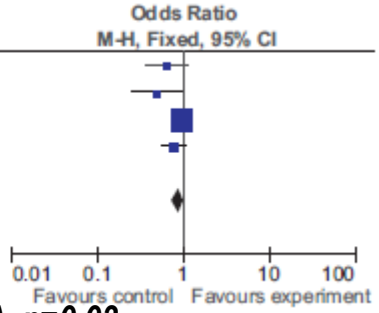


OR: 0.29 (0.09 – 0.90), p<0.00001

Effect of large PVS on fertilization rate

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
De Sutter et al.	39	66	135	194	7.2%	0.63 [0.35, 1.13]	1996
Xia	70	96	107	126	6.4%	0.48 [0.25, 0.93]	1997
Balaban et al.	620	864	1589	2180	65.4%	0.95 [0.79, 1.13]	1998
Ten et al.	108	176	975	1446	21.0%	0.77 [0.56, 1.06]	2007
Total (95% CI)		1202		3946	100.0%	0.86 [0.74, 0.99]	
Total events	837		2806				

Heterogeneity: Chi² = 5.68, df = 3 (P = 0.13); I² = 47%
Test for overall effect: Z = 2.12 (P = 0.03)

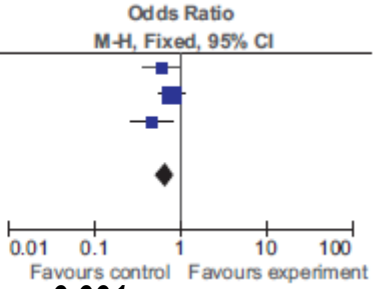


OR: 0.86 (0.74 – 0.99), p=0.03

Effect of refractile bodies on fertilization rate

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
De Sutter et al.	57	98	135	194	26.2%	0.61 [0.37, 1.01]	1996
Balaban et al.	113	167	1589	2180	50.5%	0.78 [0.56, 1.09]	1998
Ebner et al.	58	84	249	300	23.3%	0.46 [0.26, 0.79]	2000
Total (95% CI)		349		2674	100.0%	0.66 [0.51, 0.84]	
Total events	228		1973				

Heterogeneity: Chi² = 2.72, df = 2 (P = 0.26); I² = 27%
Test for overall effect: Z = 3.29 (P = 0.001)

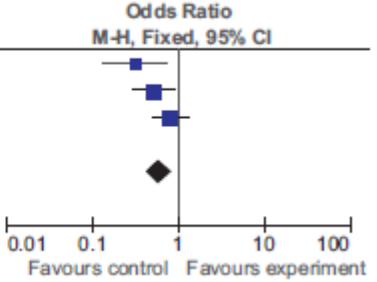


OR: 0.66 (0.51 – 0.84), p=0.001

Effect of vacuoles on fertilization rate

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
De Sutter et al.	10	24	135	194	21.5%	0.31 [0.13, 0.74]	1996
Ebner et al.,	23	47	752	1151	37.3%	0.51 [0.28, 0.91]	2005
Ten et al.	42	68	1040	1554	41.3%	0.80 [0.48, 1.32]	2007
Total (95% CI)		139		2899	100.0%	0.59 [0.42, 0.83]	
Total events	75		1927				

Heterogeneity: Chi² = 3.72, df = 2 (P = 0.16); I² = 46%
Test for overall effect: Z = 3.05 (P = 0.002)



OR: 0.59 (0.42 – 0.83), p=0.002

Fertility and Sterility® Vol. 100, No. 3, September 2013 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2013.05.021

Influence of oocyte dysmorphisms on blastocyst formation and quality

Daniela Paes Almeida Ferreira Braga, D.V.M., M.Sc.,[a,b] Amanda S. Setti, M.Sc.,[a,b] Rita de Cássia S. Figueira, M.Sc.,[a] Rogério Bonassi Machado, M.D., Ph.D.,[c] Assumpto Iaconelli Jr., M.D.,[a] and Edson Borges Jr., M.D., Ph.D.[a,b]

Ordinal regression analysis of oocyte dysmorphisms that may affect the blastocysts' degree of expansion and hatching status.

Response variable	Predictor variable	*P* value	OR	CI: lower	CI: upper
Degree of expansion and hatching status	Cytoplasmic granularity	.084	1.33	0.96	1.84
	Cytoplasmic color	.083	1.88	0.92	3.82
	Vacuoles in the ooplasm	.178	1.21	0.92	1.60
	Aggregates of smooth ERC	.020[a]	0.61	0.40	0.93
	Large PVS	< .001[a]	0.80	0.71	0.91
	PVS granularity	.955	1.45	1.22	0.91
	ZP abnormalities	.235	0.84	0.64	1.12
	Shape abnormalities	.002[a]	0.75	0.24	0.95

[a] Statistically significant.

Braga. Oocyte defects and blastocyst quality. Fertil Steril 2013.

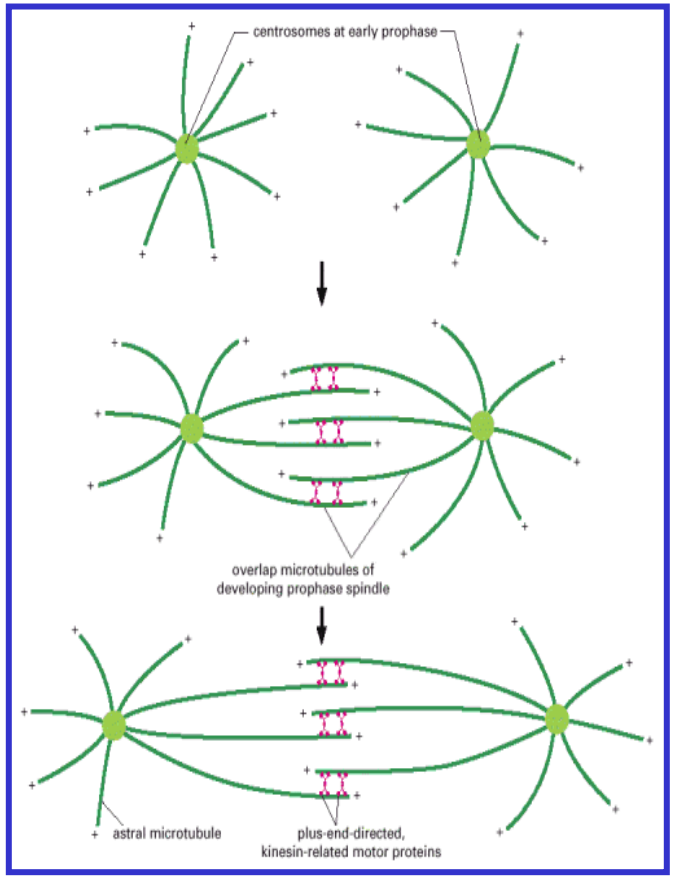
Binary regression analysis of oocyte dysmorphisms that may affect the blastocysts' inner cell mass and trophectoderm quality.

Response variable	Predictor variable	*P* value	OR	CI: lower	CI: upper
ICM quality	Cytoplasmic granularity	.998	1.15	0.95	2.15
	Cytoplasmic color	.708	1.87	0.92	2.68
	Vacuoles in the ooplasm	.983	1.01	0.31	3.28
	Aggregates of smooth ERC	.005[a]	0.65	0.12	0.85
	Large PVS	.045[a]	0.85	0.63	0.98
	PVS granularity	.158	0.53	0.22	1.28
	ZP abnormalities	.122	2.09	0.82	2.35
	Shape abnormalities.	.763	0.74	0.10	3.01
TE cell quality	Cytoplasmic granularity	.075	0.50	0.24	0.98
	Cytoplasmic color	.153	0.24	0.03	1.71
	Vacuoles in the ooplasm	.746	0.92	0.57	1.49
	Aggregates of smooth ERC	.731	1.13	0.55	2.33
	Large PVS	< .001[a]	0.50	0.36	0.71
	PVS granularity	.210	1.15	0.93	1.42
	ZP abnormalities	.333	1.27	0.79	1.42
	Shape abnormalities.	.618	0.84	0.41	1.70

[a] Statistically significant.

Braga. Oocyte defects and blastocyst quality. Fertil Steril 2013.

OOCYTE SUBCELLULAR STRUCTURES

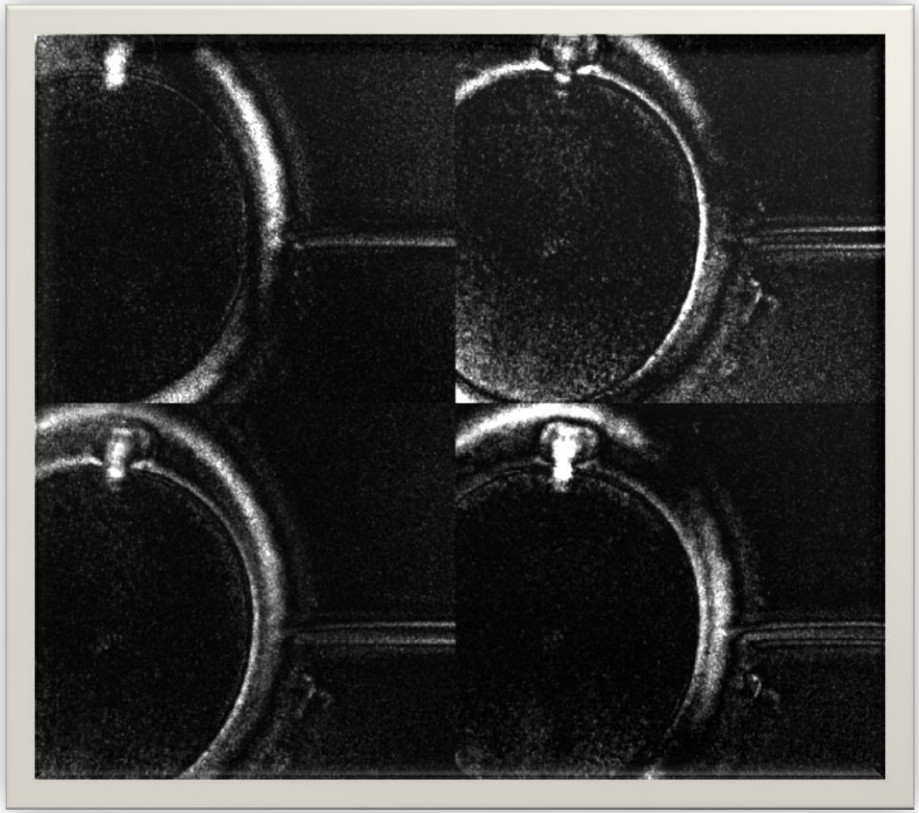


Human Reproduction Update, Vol.17, No.5 pp. 654–666, 2011
Advanced Access publication on April 29, 2011 doi:10.1093/humupd/dmr016

human reproduction update

Gamete competence assessment by polarizing optics in assisted reproduction

Markus Montag[1,2,*], Maria Köster[1], Katrin van der Ven[1], and Hans van der Ven[1]



Spindle imaging: a marker for embryo development and implantation

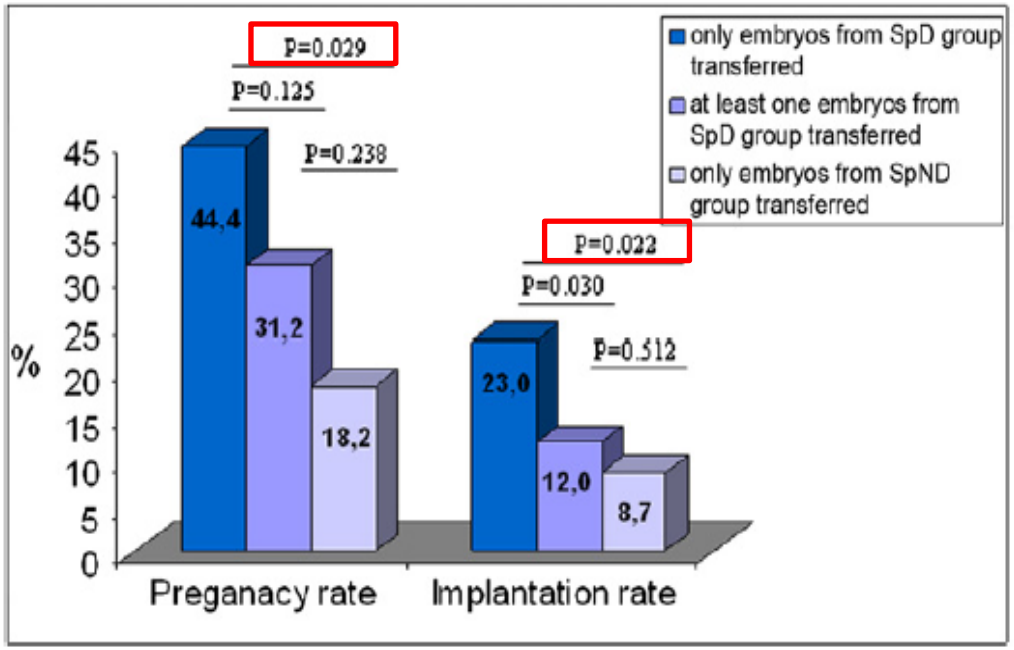
Camila Madaschi, B.Sc.,[a] *Tatiana Carvalho de Souza Bonetti, M.Sc.,*[b] *Daniela Paes de Almeida Ferreira Braga, M.Sc.,*[a,b] *Fabio Firmbach Pasqualotto, M.D., Ph.D.,*[c] *Assumpto Iaconelli, Jr., M.D.,*[a,b] *and Edson Borges, Jr., M.D., Ph.D.*[a,b]

[a] Fertility–Assisted Fertilization Center, São Paulo; [b] Sapientiae Institute, São Paulo; and [c] Institute of Biotechnology, University of Caxias do Sul, Caxias do Sul, Brazil

Fertility and Sterility® Vol. 90, No. 1, July 2008

FIGURE 2

Pregnancy and implantation rates of the three different transfer sets.



Madaschi. Spindle imaging and embryo development. Fertil Steril 2008.

FERTILITY MEDICAL GROUP

OOCYTE SUBCELLULAR STRUCTURES

Zona pellucida birefringence score and meiotic spindle visualization in relation to embryo development and ICSI outcomes

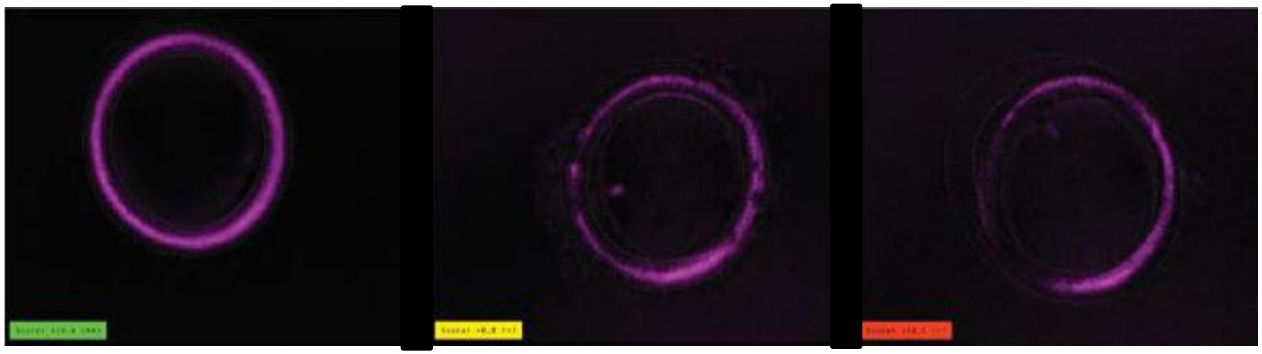


Table 3. Implantation, pregnancy and miscarriage rates in the three different transfer groups.

Groups	*HB transfer*	*Combined transfer*	*LB transfer*	P-*value*
n	20	74	36	
Implantation rate[a] (%)	32.2[a]	23.2[a,b]	12.6[b]	0.041
Pregnancy rate (%)	60.0 (12/20)[a]	50.0 (37/74)[a,b]	25.0 (9/36)[b]	0.004
Miscarriage rate (%)	0 (0/0)[a]	18.9 (7/37)[a,b]	33.3 (3/9)[b]	0.021

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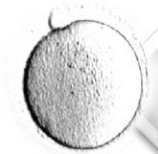
Madaschi et al., RBMOnline, 2009

Assisted Reproductive Technologies
Current and future perspectives

Sperm



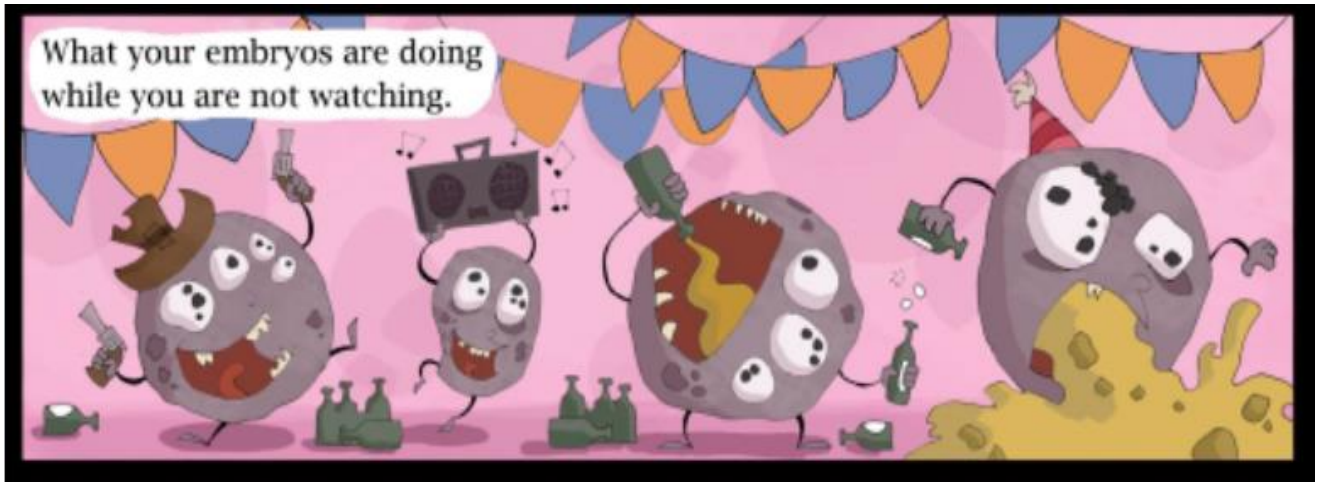
Oocyte

Embryo Day 1

Embryo Day 2

Embryo Day 3

EMBRYO MORPHOLOGY



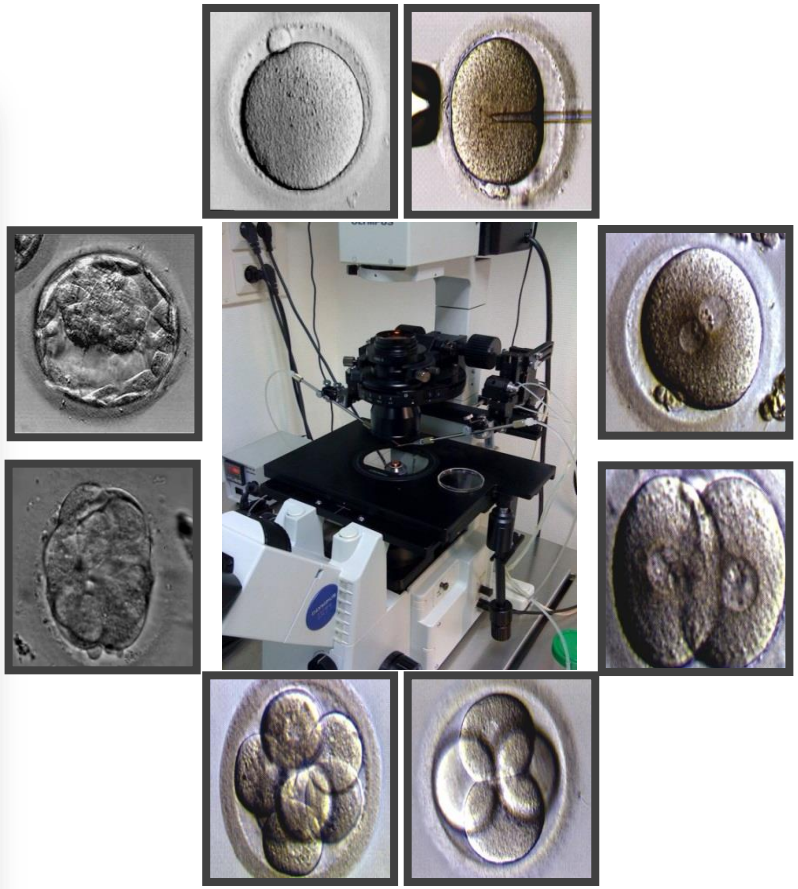
Human Reproduction, Vol.26, No.6 pp. 1270–1283, 2011
Advanced Access publication on April 18, 2011 doi:10.1093/humrep/der037

human reproduction ORIGINAL ARTICLE *ESHRE pages*

The Istanbul consensus workshop on embryo assessment: proceedings of an expert meeting†

Alpha Scientists in Reproductive Medicine and ESHRE Special Interest Group of Embryology

Type of observation	Timing (hours post-insemination)	Expected stage of development
Fertilization check	17 ± 1	Pronuclear stage
Syngamy check	23 ± 1	Expect 50% to be in syngamy (up to 20% may be at the 2-cell stage)
Early cleavage check	26 ± 1 h post-ICSI 28 ± 1 h post-IVF	2-cell stage
Day-2 embryo assessment	44 ± 1	4-cell stage
Day-3 embryo assessment	68 ± 1	8-cell stage
Day-4 embryo assessment	92 ± 2	Morula
Day-5 embryo assessment	116 ± 2	Blastocyst



FERTILITY MEDICAL GROUP

Assessing fertilization and zygotes

-Two pronuclei and two polar bodies

Pronuclear (PN) morphology

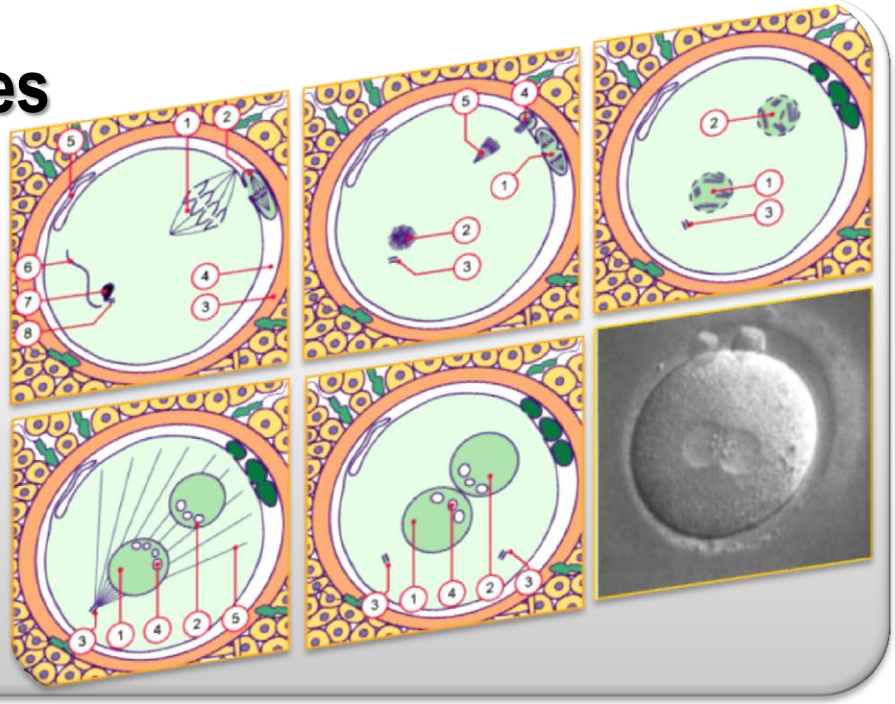
-PN size and position

-Nucleolar precursor bodies (NPBs) number

-NPBs relative position

-Cytoplasmic halo presence

-Vacuoles presence



Tesarik et al., 1999; Scott et al., 2000; Montag et al., 2001; Rienzi et al., 2002; Brezinova et al., 2009

Assessing cleavage-stage embryos

Blastomere number and cleavage rate

-No. of cells on day 2

-No. of cells on day 3

-Completely arrested

-Arrested in one blastomere

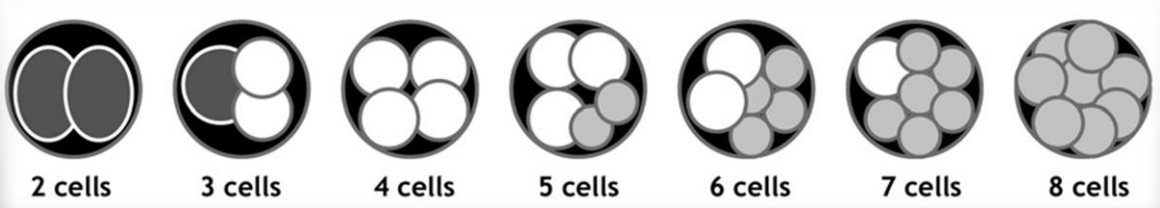
Racowsky et al., 2003; Magli et al., 2007; Racowsky et al., 2011; Kroener et al., 2014

Assessing cleavage-stage embryos

Uneven cell size

-Symmetrical blastomeres

-Asymmetrical blastomeres



Hardarson et al., 2001; Racowsky et al., 2003; Racowsky et al., 2011

Fragmentation

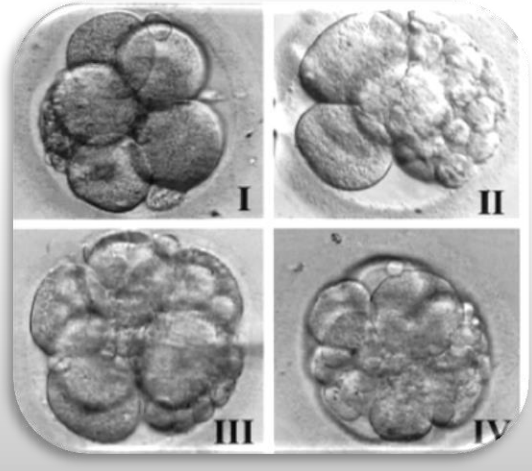
Quantitative description:

-Relative proportion

-<10% fragmentation - negligible

Qualitative description (Alikani et al., 1999):

-Size and distribution



Munne et al., 1998 ; Alikani et al., 1999; Magli et al., 2007; Stensen et al., 2015

Multinucleation

-No. of interphase nucleus in each blastomere

-No. of multinucleated blastomeres

Meriano et al., 2004; Moriwaki et al., 2004; Rienzi et al., 2005; Magli et al., 2007

FERTILITY MEDICAL GROUP

J Assist Reprod Genet
DOI 10.1007/s10815-013-0073-3

ASSISTED REPRODUCTION TECHNOLOGIES

The combination of pronuclear and blastocyst morphology: a strong prognostic tool for implantation potential

Daniela Paes Almeida Ferreira Braga · Amanda S. Setti · Rita de Cássia S. Figueira · Assumpto Iaconelli Jr · Edson Borges Jr

Table 1 Binary regression analysis of the pronuclear morphological characteristics that may affect the blastocyst morphological factors

Response variable	Predictor variable	P	OR	CI: Lower	CI: Upper
ICM alteration	Halo normality	0.513	2.33	0.19	9.25
	PN size	0.562	0.46	0.03	6.3
	PN position	0.649	1.63	0.2	3.28
	Number of NPB	**0.035**	2.51	1.2	3.34
	Size of NPB	0.997	1.76	0.65	3.43
	Distribution of NPB	0.185	0.18	0.01	2.27
TE alterations	Halo normality	0.434	1.43	0.58	3.51
	PN size	0.127	2.27	0.79	6.51
	PN position	**0.049**	2.38	1.31	4.05
	Number of NPB	0.196	0.86	0.21	1.55
	Size of NPB	0.236	0.754	0.34	1.14
	Distribution of NPB	**>0.001**	6.03	2.31	15.77

Bold numbers are statistically significant

J Assist Reprod Genet (2014) 31:1105–1110
DOI 10.1007/s10815-014-0266-4

EMBRYO BIOLOGY

The importance of the cleavage stage morphology evaluation for blastocyst transfer in patients with good prognosis

Daniela P. A. F. Braga · Amanda S. Setti ·
Rita C. S. Figueira · Assumpto Iaconelli Jr. · Edson Borges Jr.

Table 1 Binary regression analysis of the influence of embryo quality on days two or three on blastocyst formation and implantation chance

Predictor variable	Response variable	P	OR	CI: Lower	CI: Upper
Embryo quality on day two	Blastocyst formation	0.001	0.82	0.73	0.92
	Blastocyst implantation	<0.001	0.58	0.43	0.77
Embryo quality on day three	Blastocyst formation	<0.001	0.69	0.61	0.78
	Blastocyst implantation	0.001	0.63	0.48	0.83

OR: odds ratio. and *CI*: confidence interval

MULTIVARIABLE PREDICTION MODEL

Study Population

743 ICSI Cycles

583 Patients

5850 Embryos

Morphological Evaluation

D+0

D+1

D+2

D+3

Parameters evaluated

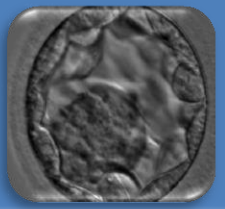
- Oocyte dysmorphisms

- Number and size of pronuclei
- Number of nucleolar precursor bodies (NPB)
- NPB distribution in each pronucleus

- Number of blastomeres
- Blastomeres uniformity
- Fragmentation degree
- Multinucleated blastomeres
- Cleavage rate

End points

- Blastocyst rate



- Implantation rate

FERTILITY MEDICAL GROUP

Figueira et al.,2015 unpublished data

Ranking embryos based on their blastocyst achievement potential

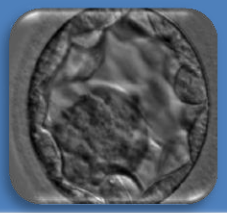
		Potential predictive factors	*P*	OR	CI (Lower-Upper)
1		Maternal age	<0.001	0.959	0.943-0.975
2		Oocytes retrived (%)	0.003	0.994	0.990-0.998
3		Oocyte perivitelline space alteration	<0.001	0.668	0.556-0.804
4		Slow cleavage	<0.001	0.608	0.474-0.780
	Day 2	Fast cleavage	<0.001	0.351	0.271-0.453
5		Asymmetric blastomeres	<0.001	0.663	0.568-0.773
6		Multinucleation	0.021	0.660	0.464-0.939
7		Multinucleation (more than 25% of embryo blastomeres)	0.001	0.560	0.392-0.801
8		Anucleated blastomeres	<0.001	0.619	0.525-0.730
9		Number of cells	<0.001	1.244	1.145-1.351
10		Slow cleavage	<0.001	0.465	0.351-0.616
	Day 3	Fast cleavage	<0.001	0.504	0.370-0.687
11		Asymmetric blastomeres	<0.001	0.676	0.575-0.795
12		0-10% Fragmentation	0.001	0.430	0.261-0.709
		0-20% Fragmentation	<0.001	0.283	0.155-0.514
13		Multinucleated blastomeres	0.006	0.786	0.663-0.933
14		Anucleated blastomeres	0.010	0.891	0.815-0.973

Ranking embryos based on their implantation potential

		Potential predictive factors	*P*	OR	CI (Lower-Upper)
1		Maternal age	<0.001	0.878	0.833-0.925
2	Day 2	Asymmetric blastomeres	0.046	0.624	0.393-0.992
3		Multinucleation	0.011	0.254	0.088-0.732
4		Anucleated blastomeres	0.029	0.451	0.221-0.923

End points

- Blastocyst rate



- Implantation rate

FERTILITY MEDICAL GROUP

Figueira et al.,2015 unpublished data

Molecular Human Reproduction, Vol.16, No.8 pp. 513–530, 2010
Advanced Access publication on June 10, 2010 doi:10.1093/molehr/gaq041

MHR NEW RESEARCH HORIZON *Review*

OMICS in assisted reproduction: possibilities and pitfalls

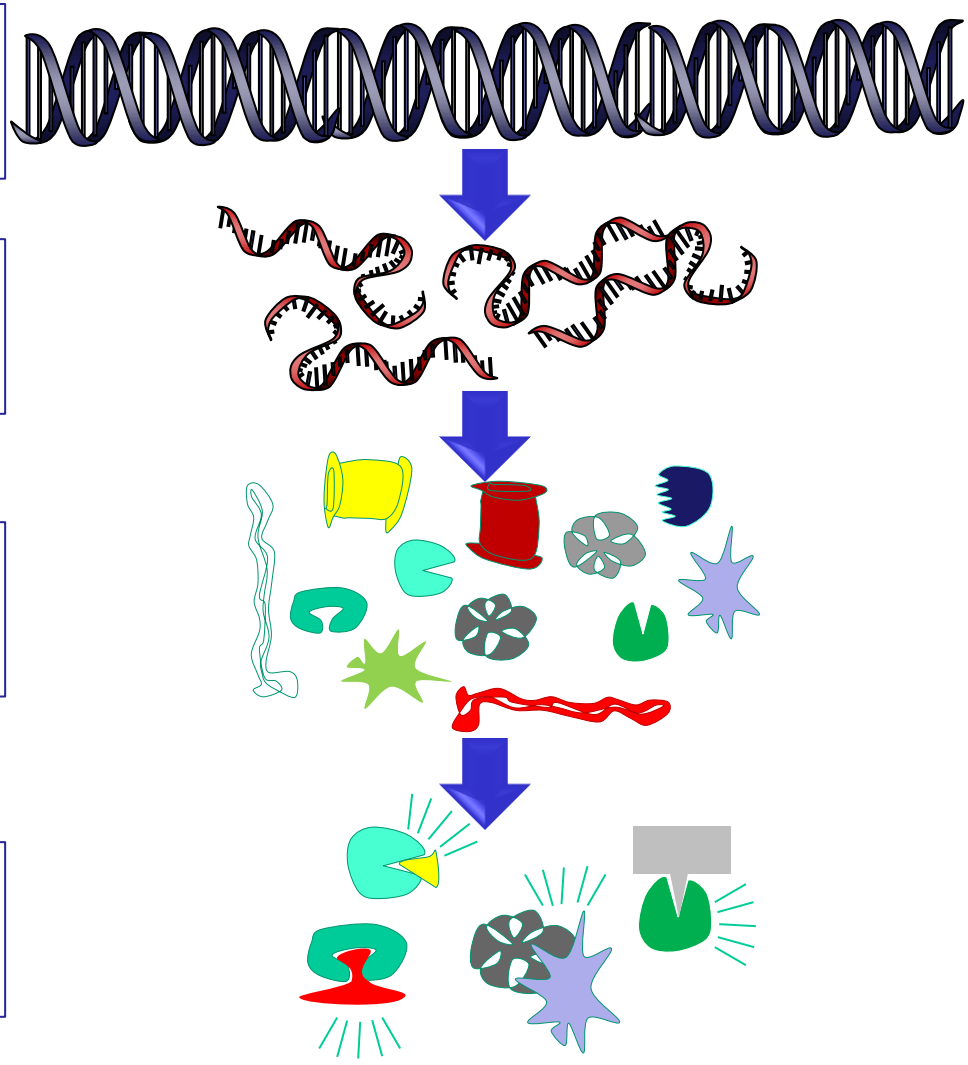
Emre Seli[1], Claude Robert[2], and Marc-Andre Sirard[2,*]

GENOME
~25,000 GENES

TRANSCRIPTOME
~100,000

PROTEOME
~1,000,000

METABOLOME
~2,500

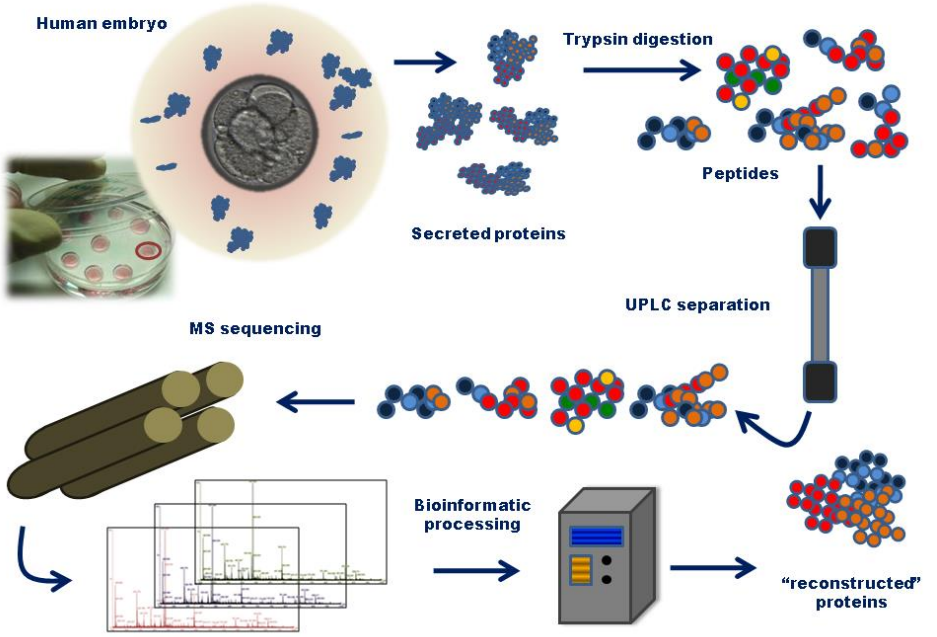


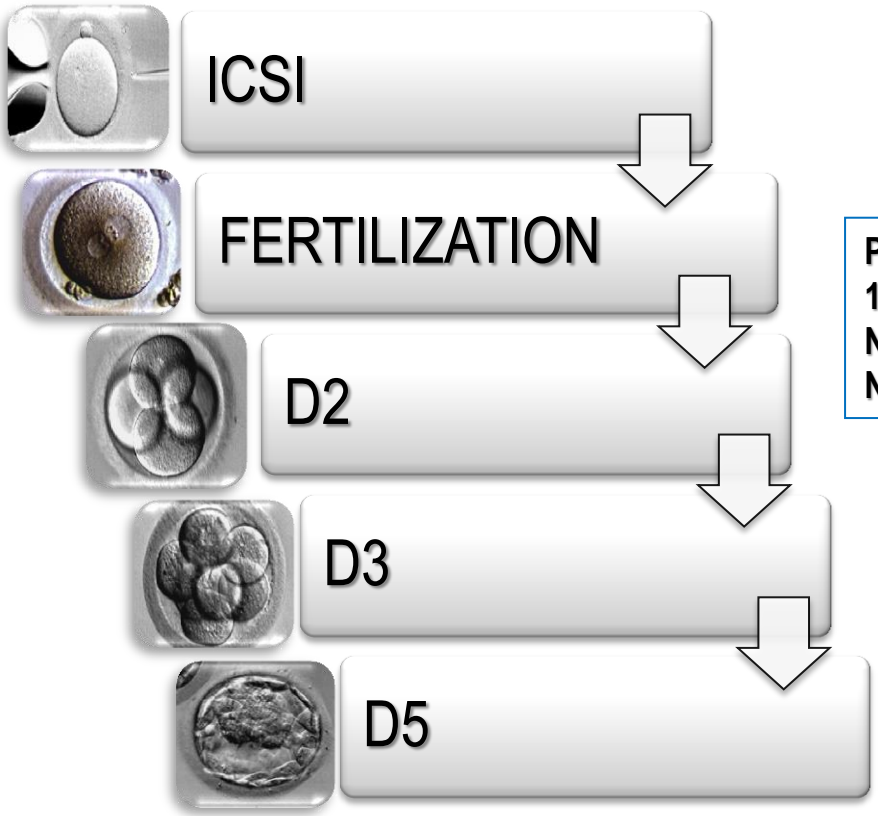
FERTILITY MEDICAL GROUP

Secretome of the preimplantation human embryo by bottom-up label-free proteomics

Anal Bioanal Chem (2011) 401:1331–1339

Sylvia S. Cortezzi · Jerusa S. Garcia · Christina R. Ferreira · Daniela P. A. F. Braga · Rita C. S. Figueira · Assumpto Iaconelli Jr · Gustavo H. M. F. Souza · Edson Borges Jr · Marcos N. Eberlin





POSITIVE PREGNANCY POOL
100% IMPLANTATION
N= 4 COUPLES
N= 8 EMBRYOS

NEGATIVE PREGNANCY POOL
0% IMPLANTATION
N= 4 COUPLES
N= 8 EMBRYOS

FERTILITY MEDICAL GROUP

Secretome of the preimplantation human embryo by bottom-up label-free proteomics

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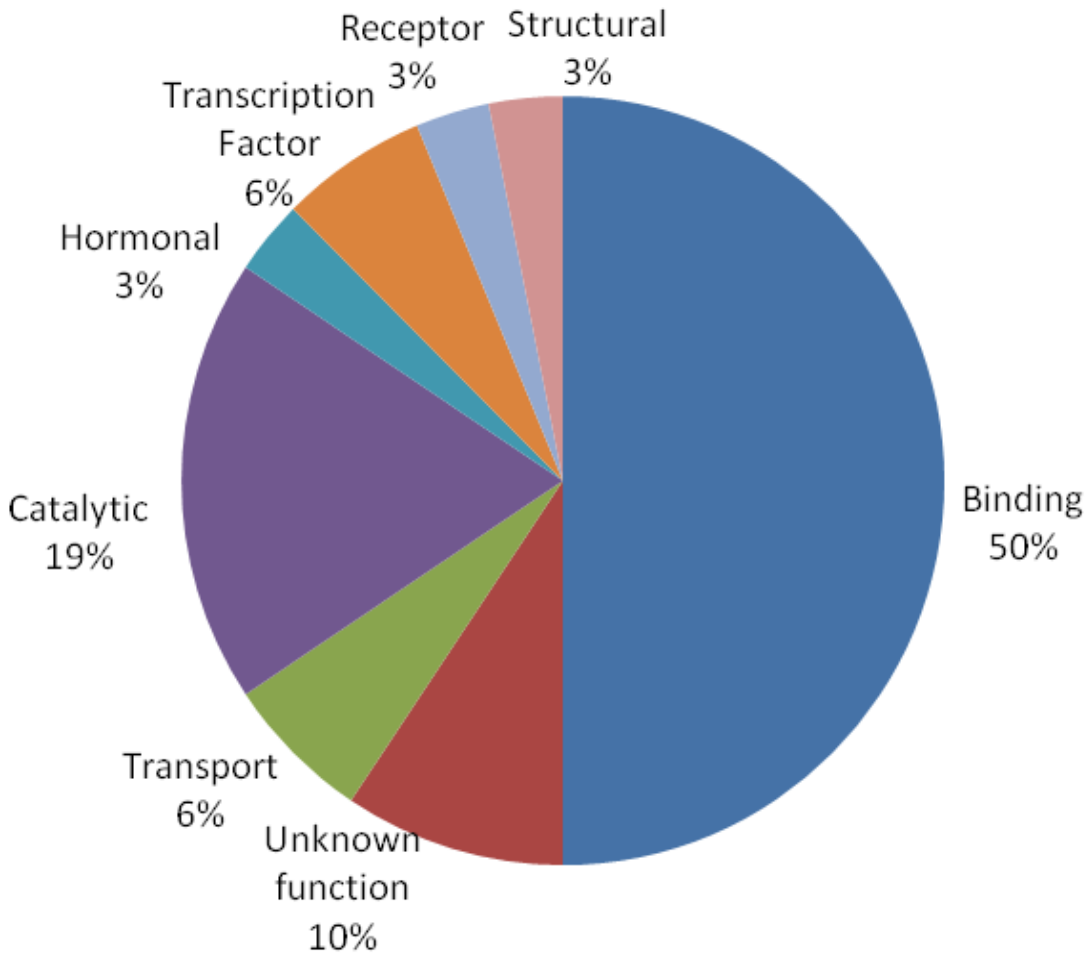
25 PROTEINS

Positive Group: 15

Negative Group: 10

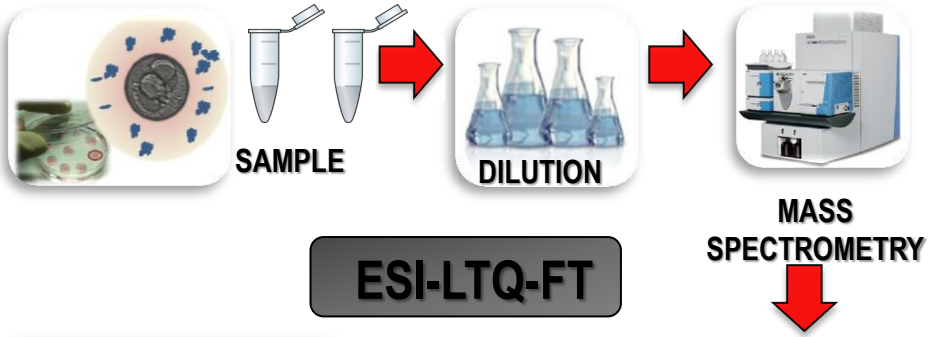


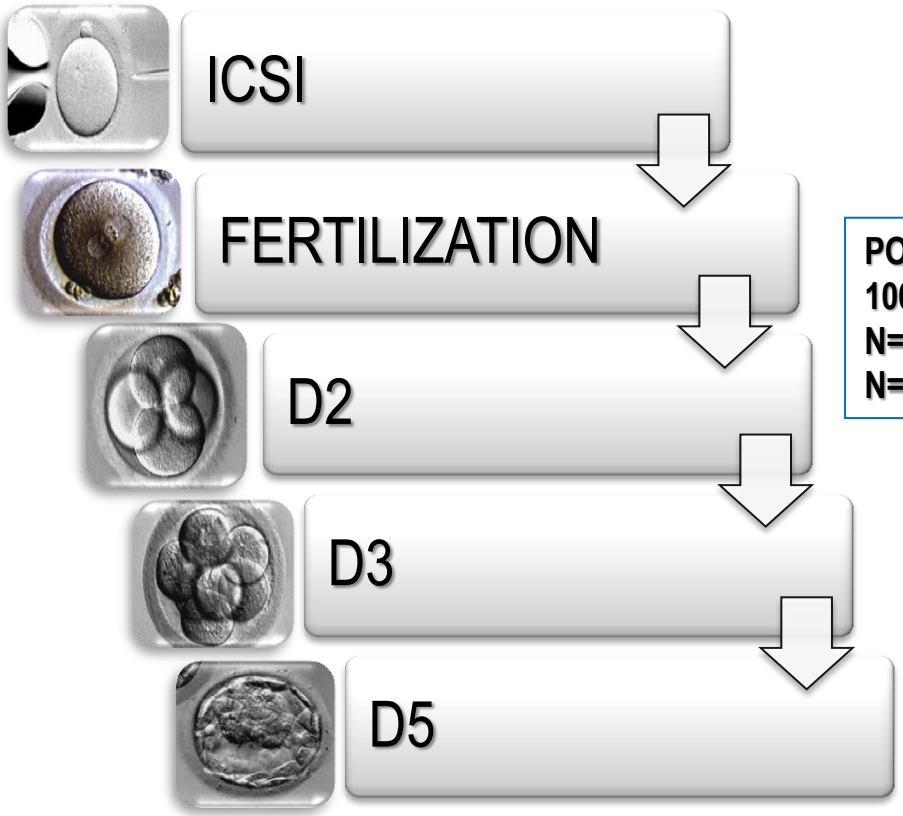
FERTILITY MEDICAL GROUP

Prediction of embryo implantation potential by mass spectrometry fingerprinting of the culture medium

Reproduction (2013) **145** 453–462

Sylvia Sanches Cortezzi[1], Elaine Cristina Cabral[2], Marcello Garcia Trevisan[3,4], Christina Ramires Ferreira[2], Amanda Souza Setti[1,5], Daniela Paes de Almeida Ferreira Braga[1,5], Rita de Cássia Sávio Figueira[5], Assumpto Iaconelli Jr[1,5], Marcos Nogueira Eberlin[2] and Edson Borges Jr[1,5]





POSITIVE PREGNANCY POOL
100% IMPLANTATION
N= 15 COUPLES
N= 29 EMBRYOS

NEGATIVE PREGNANCY POOL
0% IMPLANTATION
N= 40 COUPLES
N= 84 EMBRYOS

FERTILITY MEDICAL GROUP

Prediction of embryo implantation potential by mass spectrometry fingerprinting of the culture medium

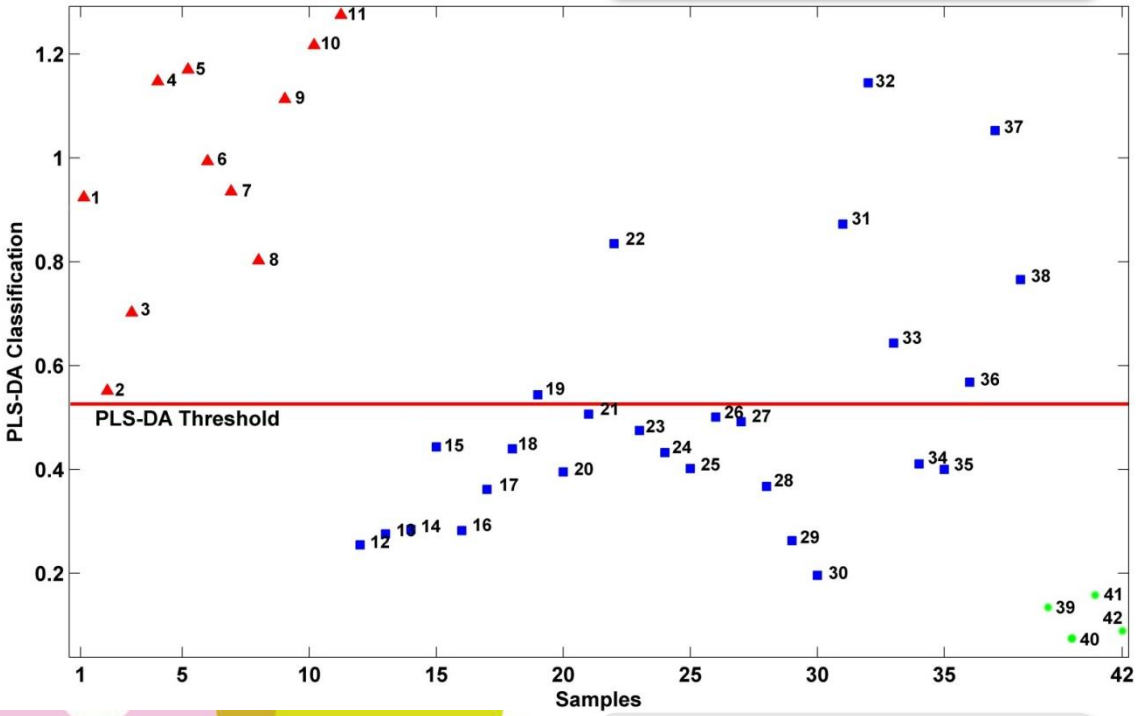
Reproduction (2013) **145** 453–462

Sylvia Sanches Cortezzi[1], Elaine Cristina Cabral[2], Marcello Garcia Trevisan[3,4], Christina Ramires Ferreira[2], Amanda Souza Setti[1,5], Daniela Paes de Almeida Ferreira Braga[1,5], Rita de Cássia Sávio Figueira[5], Assumpto Iaconelli Jr[1,5], Marcos Nogueira Eberlin[2] and Edson Borges Jr[1,5]

Positive: 100%

VALIDATION – 38 samples

100% x 0%
IMPLANTATION



Negative: 70%

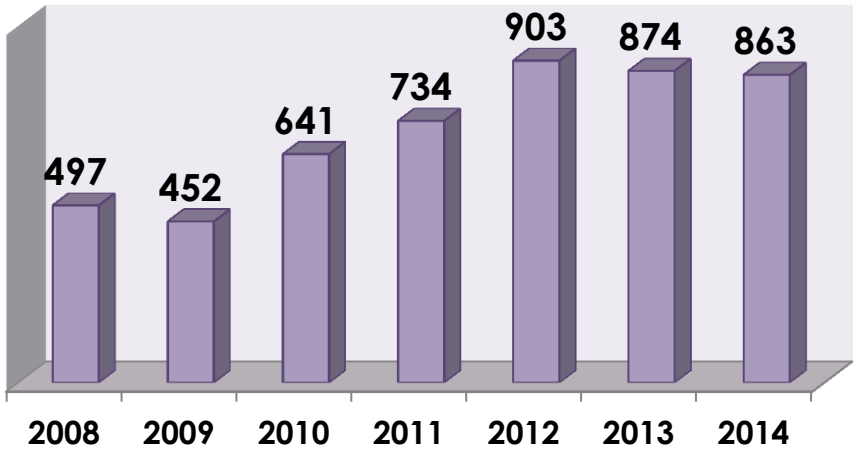
NON-INVASIVE PREDICTION OF EMBRYO IMPLANTATION POTENTIAL AND CULTURE MEDIA QUALITY CONTROL BY MASS SPECTROMETRY FINGERPRINTING - GFI 2012

GFI Grant for Fertility

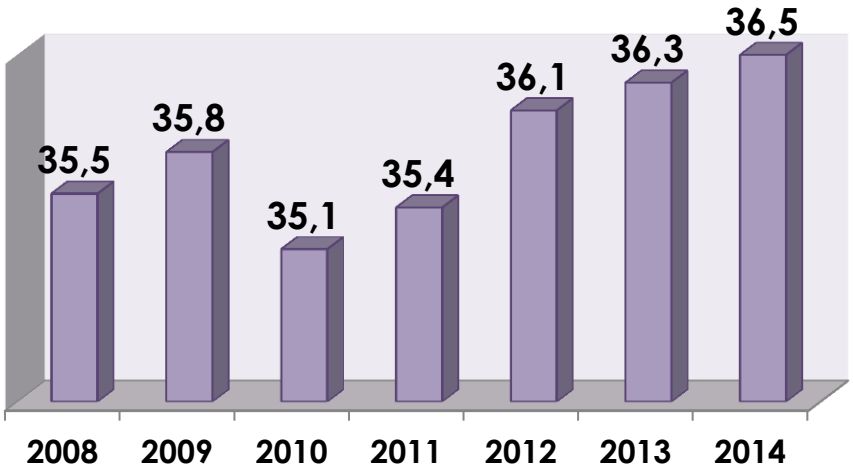
FERTILITY MEDICAL GROUP

Fertility Medical Group - Brazil
Results IVF –ICSI cycles

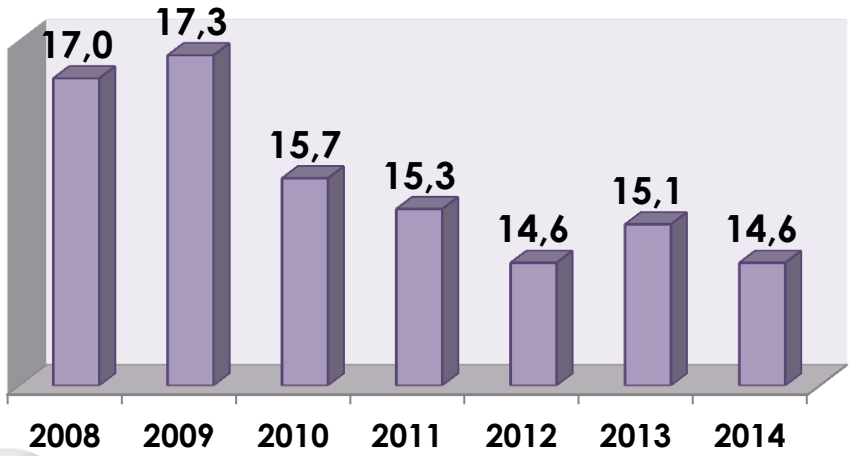
ICSI cycles



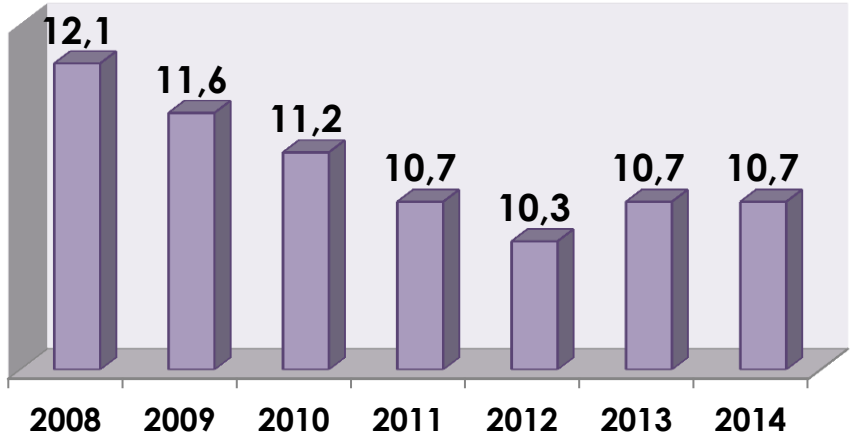
Maternal age



No. of aspirated follicles



No. of retrieved oocytes



FERTILITY
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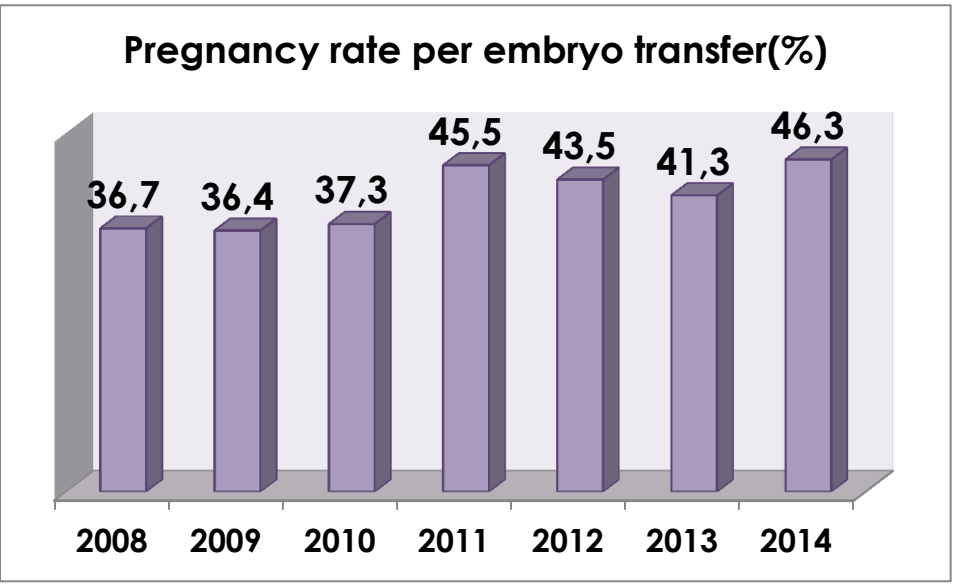
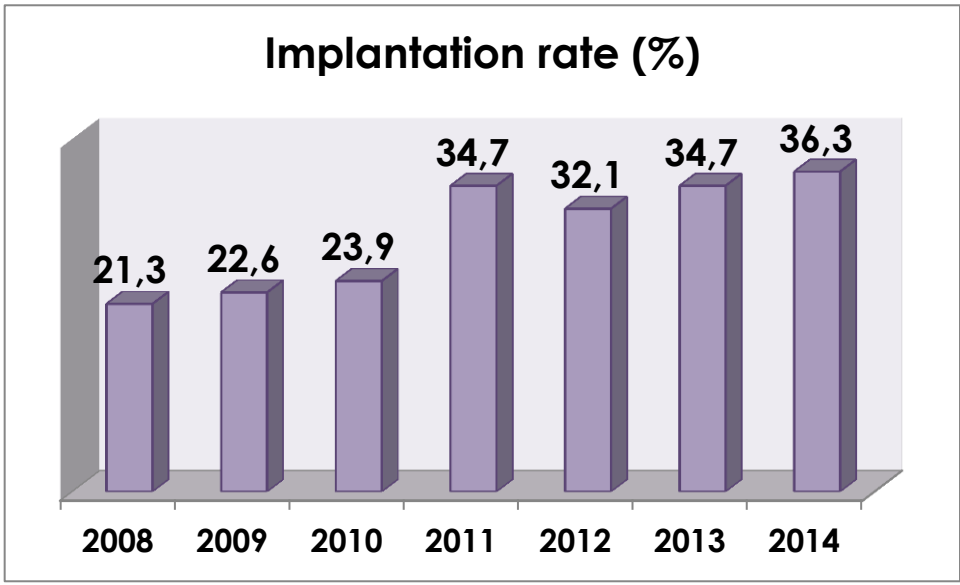
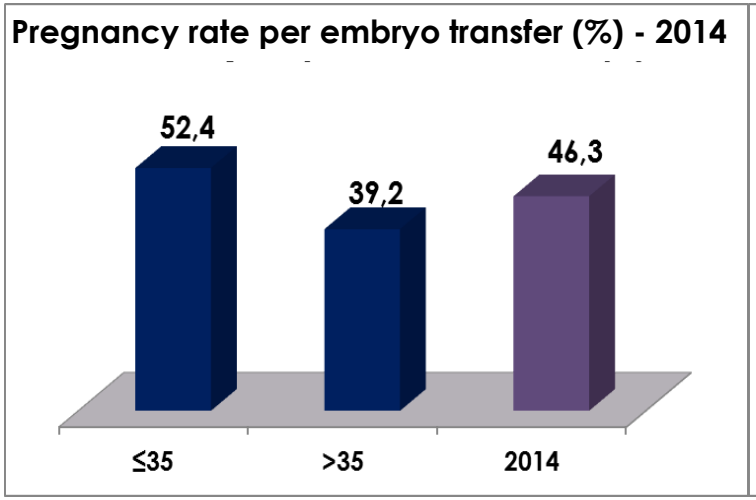
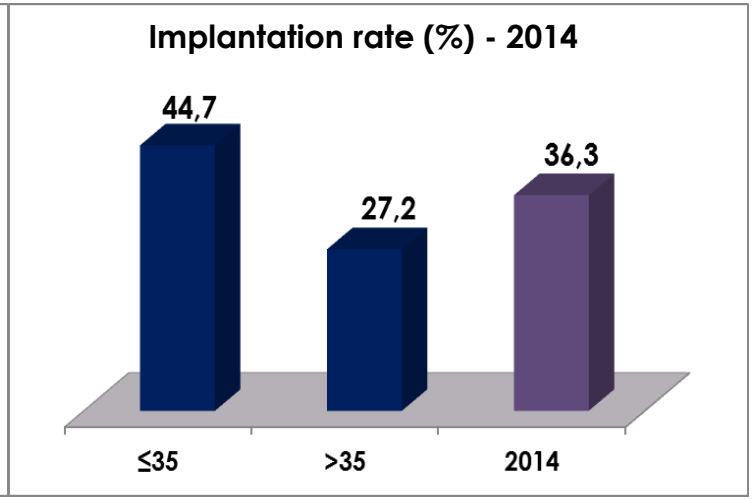
Fertility Medical Group - Brazil
Results IVF –ICSI cycles







Maternal age



Maternal age

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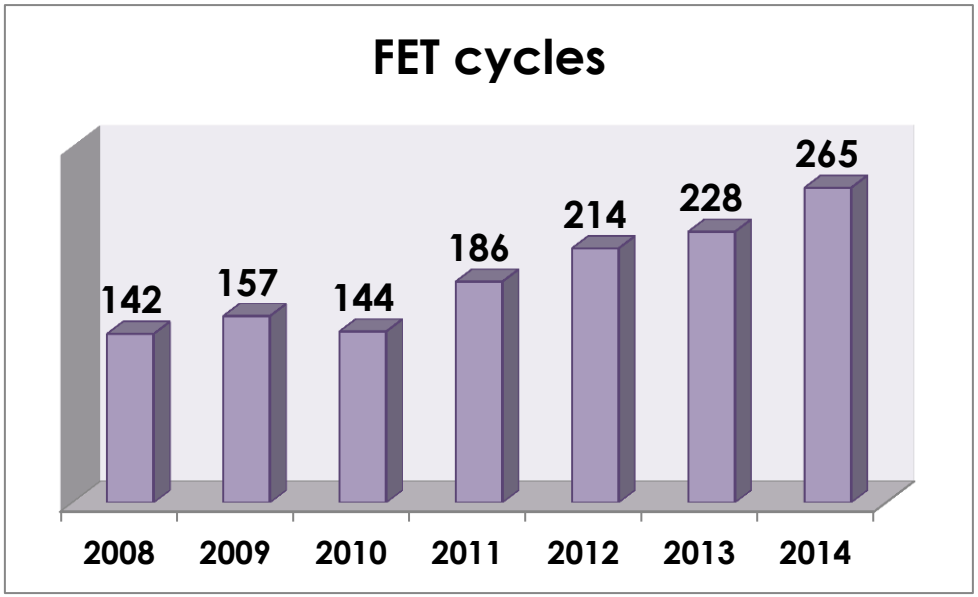
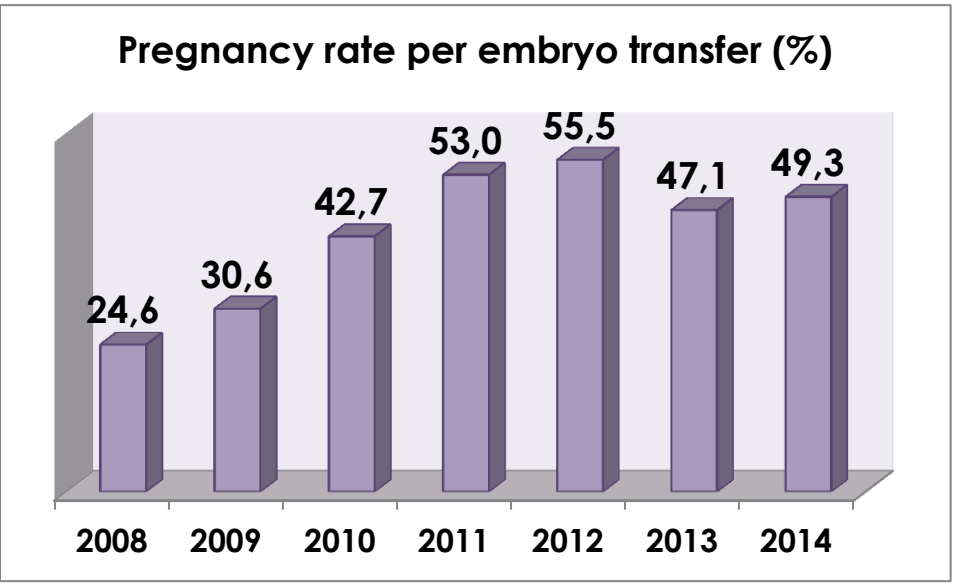
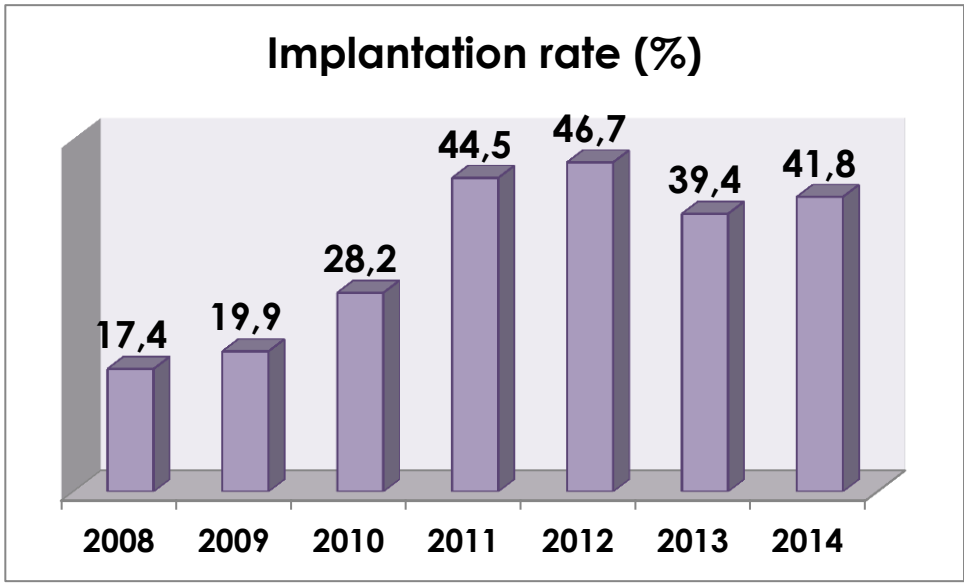
Fertility Medical Group - Brazil
Results FET cycles

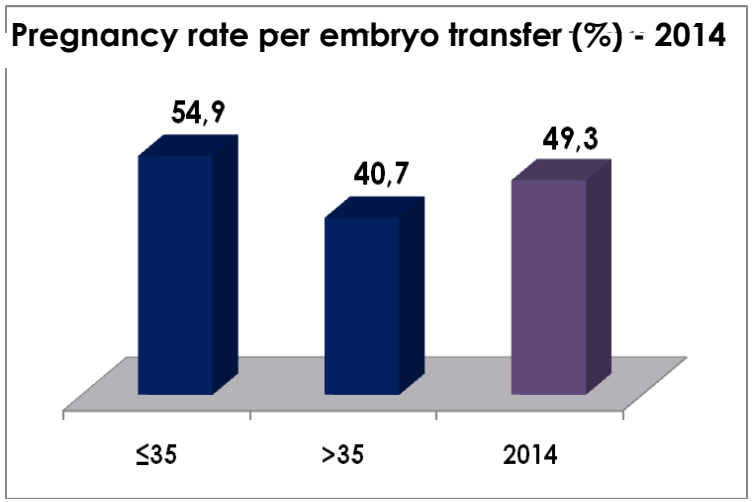


FERTILITY MEDICAL GROUP

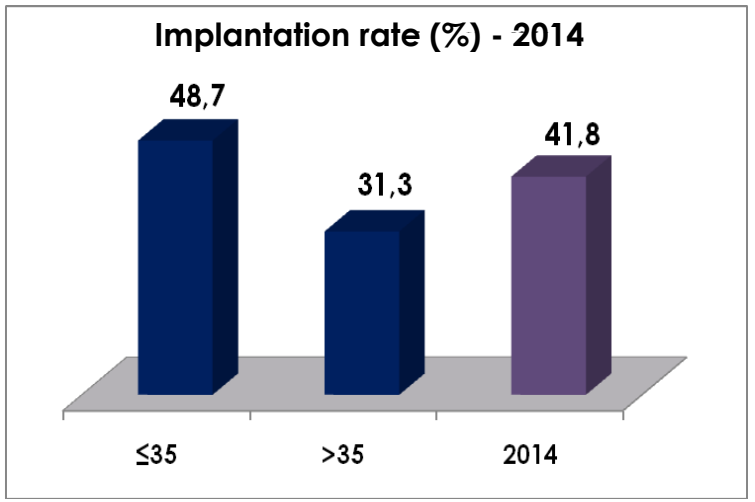
Fertility Medical Group - Brazil
Results FET cycles







Maternal age



Maternal age

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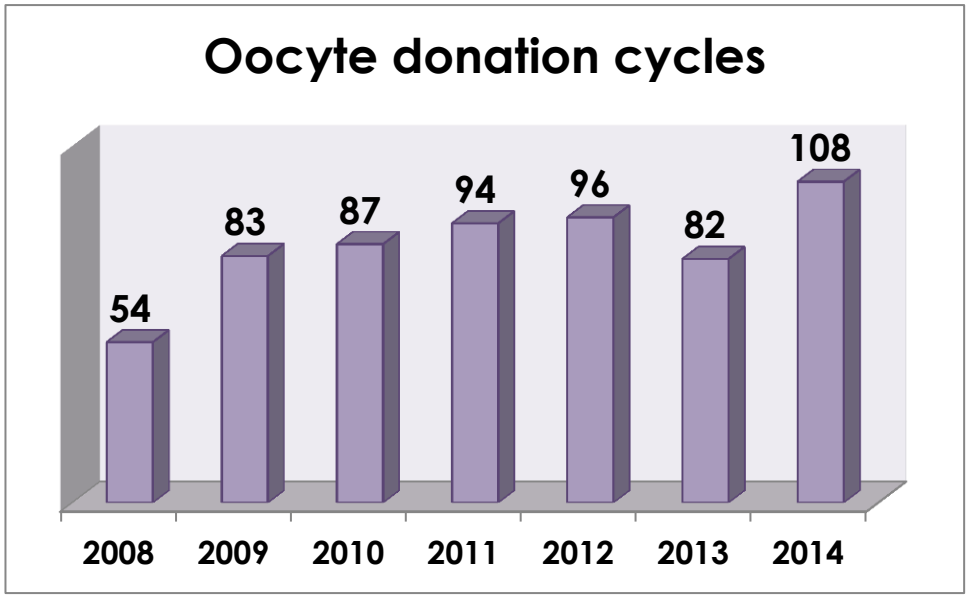
Fertility Medical Group - Brazil
Results Oocyte donation cycles



	Fresh oocytes	Oocyte Bank
Pregnancy rate per embryo transfer	55,6%	52,1%
Implantation rate	40,0%	39,0%

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CONCEPTIONS

Full in vitro fertilization laboratory mechanization: toward robotic assisted reproduction?

Marcos Meseguer, Ph.D.,[a] Ulrich Kruhne, Ph.D.,[b] and Steen Laursen, Ph.D.[c]

[a] Instituto Valenciano de Infertilidad, Universidad de Valencia, Valencia, Spain; [b] Center for Process Engineering and Technology, Technical University of Denmark, Lyngby, Denmark; and [c] IVF-SYD, Fredericia, Denmark

Human Reproduction, Vol.27, No.2 pp. 303–313, 2012

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human reproduction

OPINION

When and how should new technology be introduced into the IVF laboratory?

Joyce Harper[1,*], M. Cristina Magli[2], Kersti Lundin[3], Christopher L.R. Barratt[4], and Daniel Brison[5]

[1]UCL Centre for PG&D, Institute for Womens Health, UCL and Centre for Reproductive and Genetic Health, University College London Hospital, London, UK [2]SISMER, Reproductive Medicine Unit, Bologna, Italy [3]Reproductive Medicine, Sahlgrenska University Hospital, Institute for Clinical Sciences, University of Gothenburg, 413 45 Gothenburg, Sweden [4]Reproductive and Developmental Biology Group, Division of Medical Sciences, Ninewells Hospital, University of Dundee, Dundee, Scotland DD1 9SY, UK [5]Department of Reproductive Medicine, St Mary's Hospital, Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Sciences Centre, Oxford Road, Manchester M13 9WL, UK

*Correspondence address. joyce.harper@ucl.ac.uk

Thank you!

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