Genomic Summit
Juntos fazemos o amanhã

Timelapse e IA na avaliação embrionária: Como interpretar os resultados e melhorar as chances de gestação

Edson Borges Jr.

Fertility Medical Group

Instituto Sapientiae

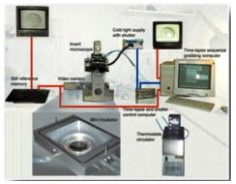
FERTILITY

Ausência de Conflito de Interesse

Resolução do Conselho Federal de Medicina nº 1.595/2.000

FERTILITY

History
of « modern » TLT



Single-point morphological assessment

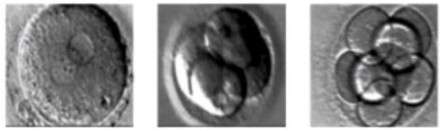
1997[1]

2011[2]

2020

D3 culture

Blastocyst culture



[1]Payne et al. *Hum Reprod*. 1997;**12**:532–541.
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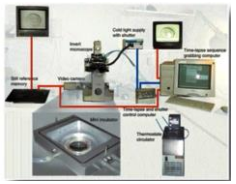
History of « modern » TLT



Single-point morphological assessment

Continuous embryo monitoring

1997[1]

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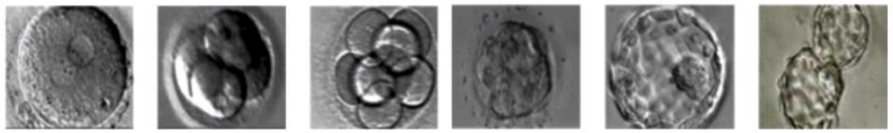

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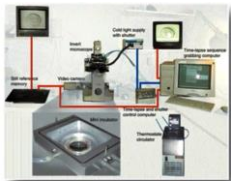
History
of « modern » TLT



Single-point morphological assessment

Continuous embryo monitoring

Manual algorithms

1997[1]

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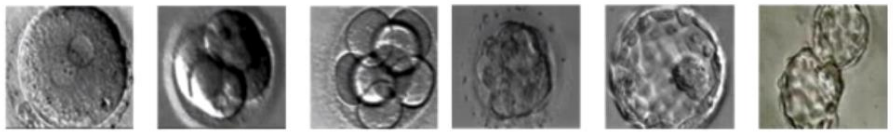

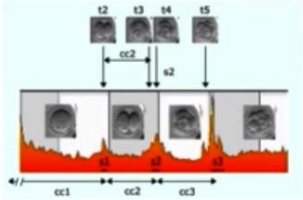

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History
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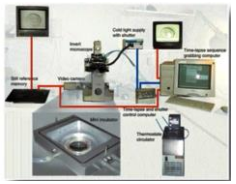


Single-point morphological assessment

Continuous embryo monitoring

Manual algorithms

Automated image analysis platforms

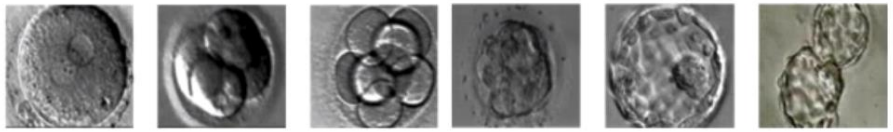
1997[1]

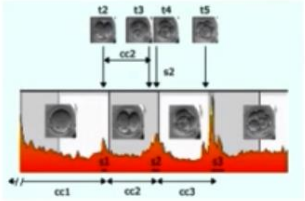
2011[2]

2020

D3 culture

Blastocyst culture





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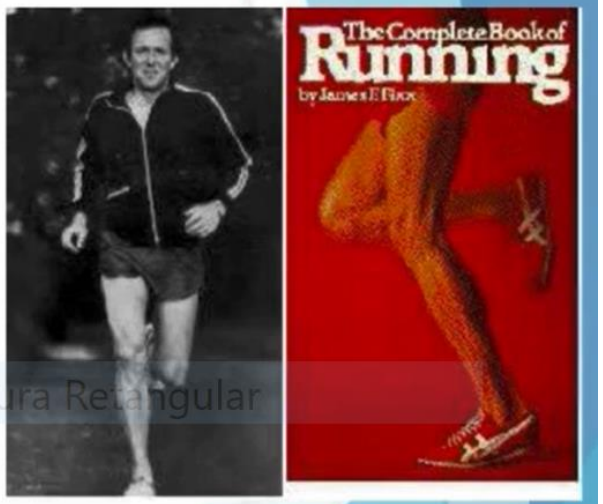
Morphokinetics and what we do not see!

- Winston Churchill
- Drank
- Smoked Cigars
- Overweight

- Roger Bannister
- The first man to run the 4 minute mile
- Exercised frequently

- Jimmy Fixx
- Started America's fitness revolution, popularizing running



Captura Rectangular

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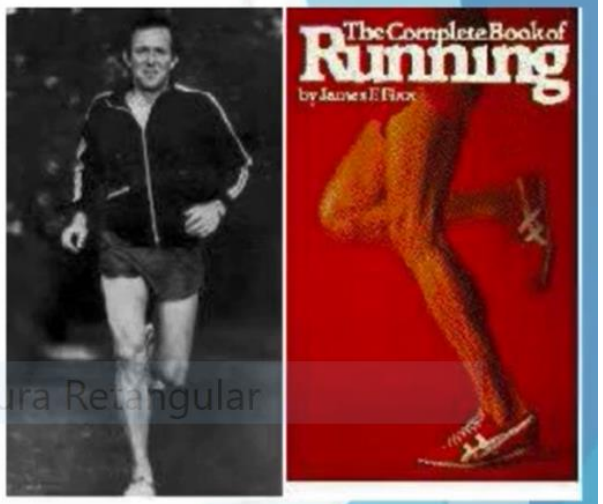

Who lived the longest?

Morphokinetics and what we do not see!

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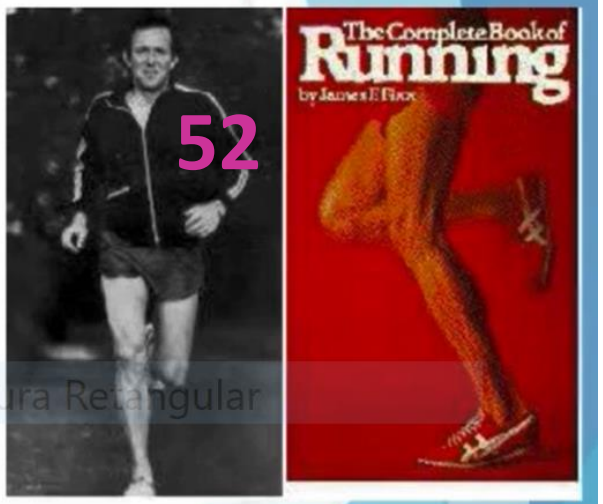
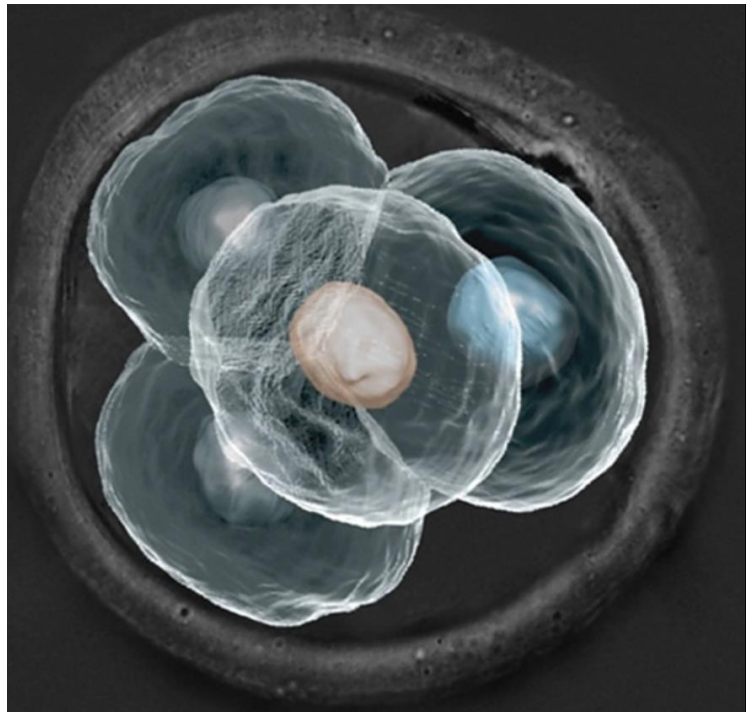


Who lived the longest?

IA and deep learning – embryo evaluation



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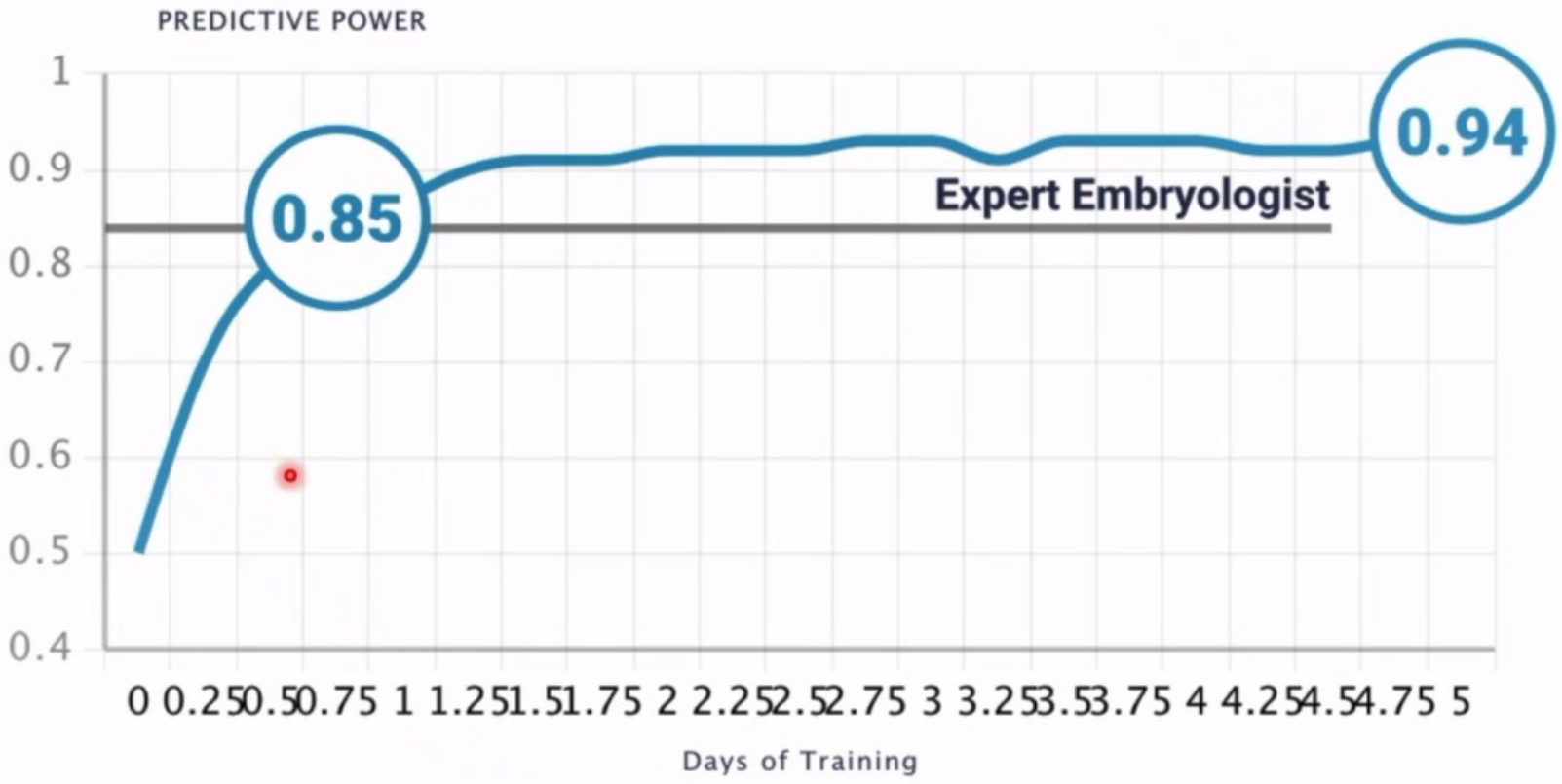
AI technology **exceeded expert human embryologists after only one day** of training



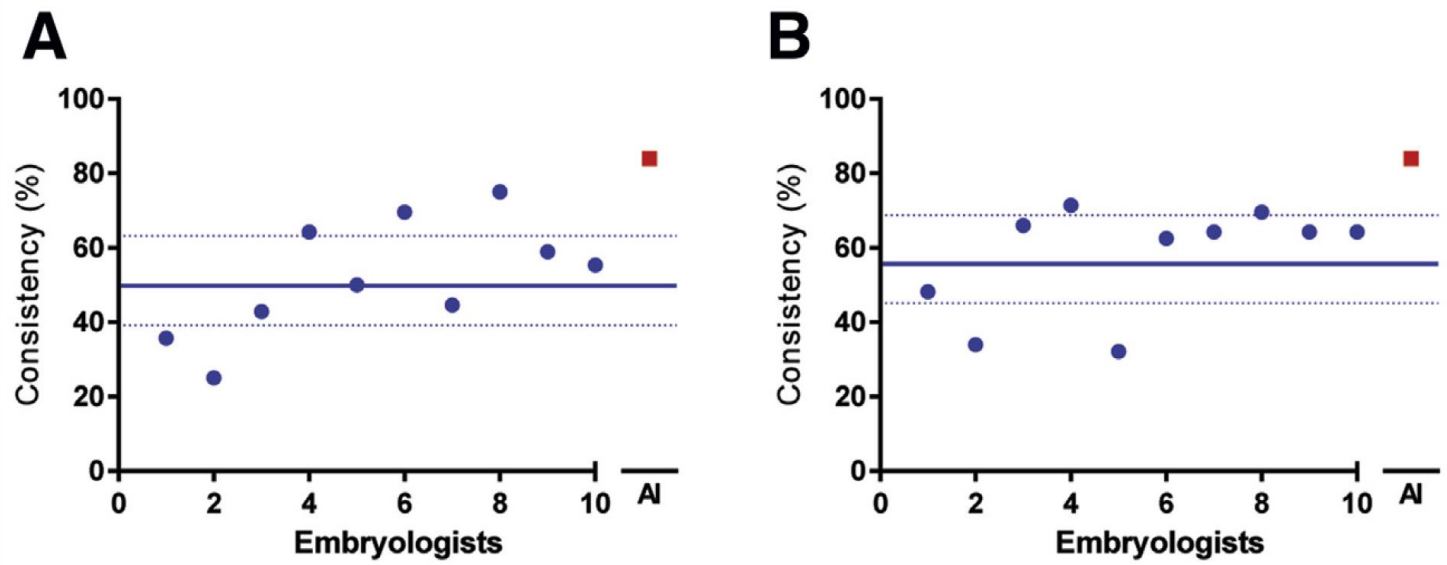
FERTILITY

Consistency and objectivity of automated embryo assessments using deep neural networks

Charles L. Bormann, Ph.D.,[a,b] Prudhvi Thirumalaraju, B. Tech,[c] Manoj Kumar Kanakasabapathy, M. Tech,[c] Hemanth Kandula, B. Tech,[c] Irene Souter, M.D.,[a] Irene Dimitriadis, M.D., Ph.D.,[a,b] Raghav Gupta, B. Tech,[c] Rohan Pooniwala, B. Tech,[c] and Hadi Shafiee, Ph.D.[a,b]

Fertility and Sterility® Vol. 113, No. 4, April 2020

Either discarding or selecting embryos for biopsy for cryo-preservation



Variability *(%CV averages)*:

- Embryologist: *82.84% for 70 hpi and 44.98% for 113 hpi*
- Neural Network: 16,08%

FERTILITY

EMBRYOSCOPE - KIDSCORE

KIDSCORE D3

Well	Dec.	Current score	NOT2PN	tPNf	t2	t3	t4	t5	t8	cells66	Last stage	Morph. grade	Last image
AA-1	❄	3	●	23.1	26.3	40.0	40.8	40.8	60.3	8.0	B	4CC D6	
AA-2	❄	4	●	24.9	27.6	39.0	39.2	57.3	69.5	7.0	B	5BA D6	
AA-3	❄	4	●	23.7	26.3	40.2	40.5	56.4	68.8	7.0	B	4CC D6	
AA-4	✕	5	○	22.2	24.9	36.5	37.2	51.1	56.6	9.0	B	4CC D6	
AA-5	✓	5	●	24.9	27.6	40.5	41.2	56.1	58.8	8.0	B	3BA D5	
AA-6	❄	5	●	21.1	24.1	35.6	36.3	49.6	52.4	8.0	B	4BB D5	
AA-7	❄	1	●	26.1	28.8	31.0	41.0	41.0	55.8	8.0	B	4AA D5	
AA-8	❄	1	●	31.5	33.6	36.5	47.4	48.1	65.3	8.0	B	3BB D5	
AA-9	✓	5	●	22.7	25.3	37.0	37.0	49.4	52.6	8.0	B	4AA D5	
AA-10	❄	1	●	21.4	23.7	24.8	33.6	33.8	46.4	8.0	B	5AA D5	

SCORE

KIDSCORE D5

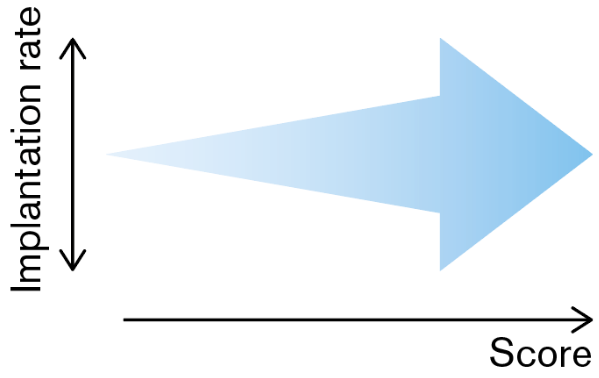
Well	Dec.	Current score	NOT2PN	t2	t3	t4	t5	tB	TE	Last stage	Morph. grade	Last image
AA-1	❄	2.3	●	26.3	40.0	40.8	40.8	136.7	C	B	4CC D6	
AA-2	❄	4.9	●	27.6	39.0	39.2	57.3	118.5	A	B	5BA D6	
AA-3	❄	4	●	26.3	40.2	40.5	56.4	113.4	C	B	4CC D6	
AA-4	✕	2.9	○	24.9	36.5	37.2	51.1	127.3	C	B	4CC D6	
AA-5	✓	6.5	●	27.6	40.5	41.2	56.1	112.2	A	B	3BA D5	
AA-6	❄	6.5	●	24.1	35.6	36.3	49.6	111.7	B	B	4BB D5	
AA-7	❄	3.6	●	28.8	31.0	41.0	41.0	107.5	A	B	4AA D5	
AA-8	❄	3.3	●	33.6	36.5	47.4	48.1	114.9	B	B	3BB D5	
AA-9	✓	7.8	●	25.3	37.0	37.0	49.4	104.7	A	B	4AA D5	
AA-10	❄	3.9	●	23.7	24.8	33.6	33.8	94.8	A	B	5AA D5	

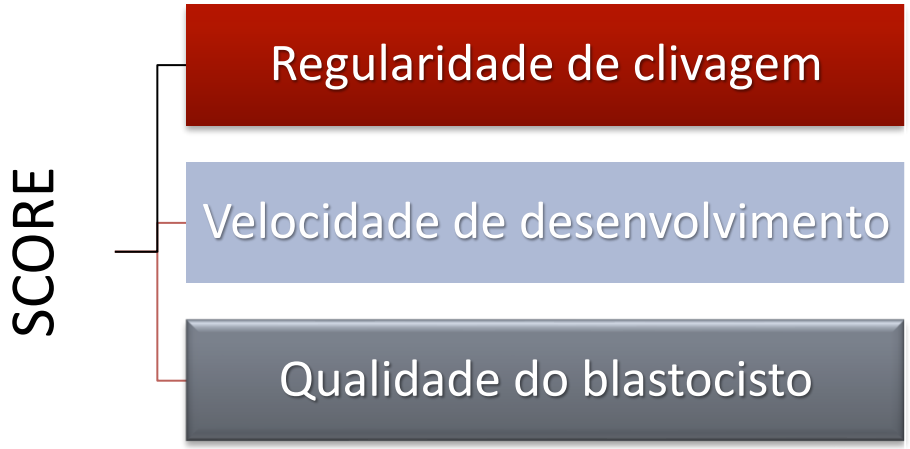
FERTILITY

EMBRYOSCOPE – KIDScore D5

O KIDscore D5 é baseado nas informações do desenvolvimento embrionário até o dia 5, de aproximadamente 1100 embriões com status de implantação conhecido.

Score: 1 a 9,9 (de acordo com a chance de implantação)





FERTILITY

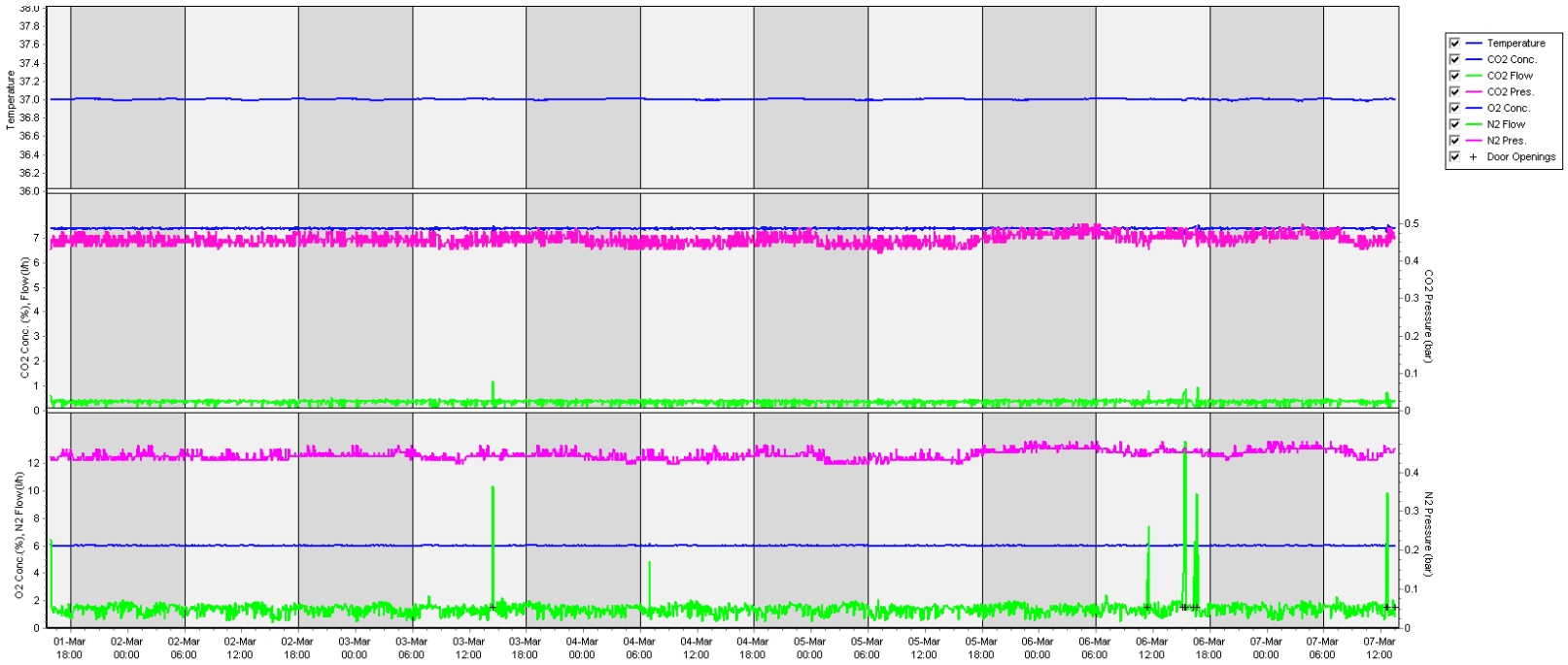
EMBRYOSCOPE *plus*

- Incubadora CO_2 / O_2
- Capacidade: 15 pacientes com 16 embriões (total 240 embriões)
- Ar purificado por carvão ativado e filtro HEPA
- Tempo total de exposição à luz: <40 seg/dia (por embrião)
- Óptica de contraste de modulação Hoffman de alta qualidade
- Tempo entre as aquisições de imagens: 10 minutos
- Aquisição de imagem em múltiplos planos focais
- Incubação seca

FERTILITY

EMBRYOSCOPE - INCUBAÇÃO

AMBIENTE DE CULTIVO SEGURO PARA OS EMBRIÕES

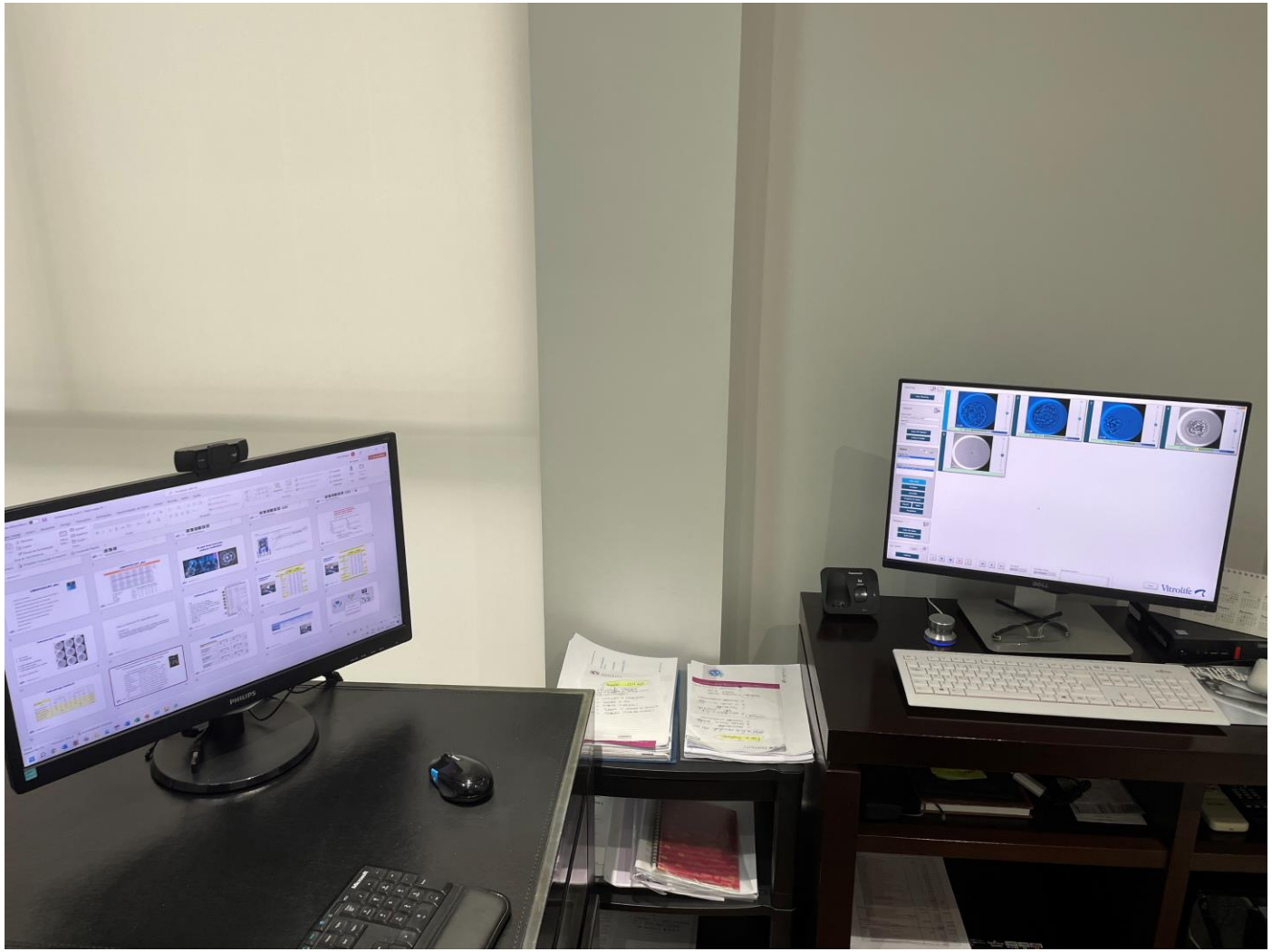


- Temperatura
- CO_2 / O_2
- pH
- VOC
- Coleção de imagens
- Alarme

Summary | Alarms | Warnings | Log | Other

Variable	Unit	Average	Min	Max	StdDev	Set-Point
Temperature	C	37.00	36.98	37.02	0.007	37.0
CO2 Concentration	%	7.38	7.25	7.46	0.032	7.4
CO2 Flow	l/h	0.36	0.01	0.60	0.096	0.0
CO2 Pressure	bar	0.46	0.42	0.50	0.016	0.0
O2 Concentration	%	6.01	5.97	6.15	0.011	6.0
N2 Flow	l/h	1.38	0.45	6.45	0.361	0.0
N2 Pressure	bar	0.44	0.42	0.48	0.013	0.0

FERTILITY



FERTILITY

Edson Borges Jr[1,2]

doi: 10.1017/S0967199422000077

Improved embryonic development and utilization rates with EmbryoScope: a within-subject comparison versus a benchtop incubator

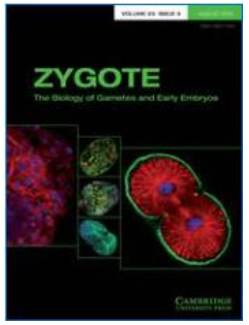


Table 2. Comparison of embryonic development between Control and TLI groups using GzLM followed by Bonferroni post hoc test

Variables	Control group ($n = 71$)	TLI group ($n = 71$)	*P*-value
Normal fertilization (%)	74.8 ± 2.7 (69.6–80.1)	77.4 ± 2.7 (72.2–82.6)	0.499
Abnormal fertilization (%)	6.2 ± 1.5 (3.1–9.2)	6.8 ± 1.5 (3.8–9.8)	0.767
Non-fertilization (%)	16.8 ± 2.1 (12.7–20.8)	11.9 ± 2.1 (7.8–15.9)	0.098
Oocyte degeneration post injection (%)	2.2 ± 1.3 (0.22–4.7)	3.9 ± 1.3 (1.4–6.3)	0.352
Day-2 non-cleavage (%)	3.8 ± 0.2 (3.3–4.3)	1.1 ± 0.1 (0.9–1.3)	<0.001
Cleavage (%)	85.3 ± 1.2 (83.0–87.7)	84.2 ± 1.3 (81.7–86.8)	0.521
Day-5 embryos (%)	62.4 ± 1.0 (60.5–64.3)	86.4 ± 1.1 (84.2–88.6)	<0.001
Blastocyst development (%)	40.9 ± 1.1 (38.8–43.1)	55.6 ± 1.3 (53.1–58.1)	<0.001
Frozen blastocyst (%)	31.8 ± 0.8 (30.3–33.3)	37.0 ± 0.9 (35.2–38.9)	<0.001
OUR	40.7 ± 1.0 (38.8–42.7)	50.2 ± 1.1 (48.0–52.4)	<0.001
EUR	52.4 ± 1.1 (50.3–54.7)	66.6 ± 1.2 (64.3–68.9)	<0.001

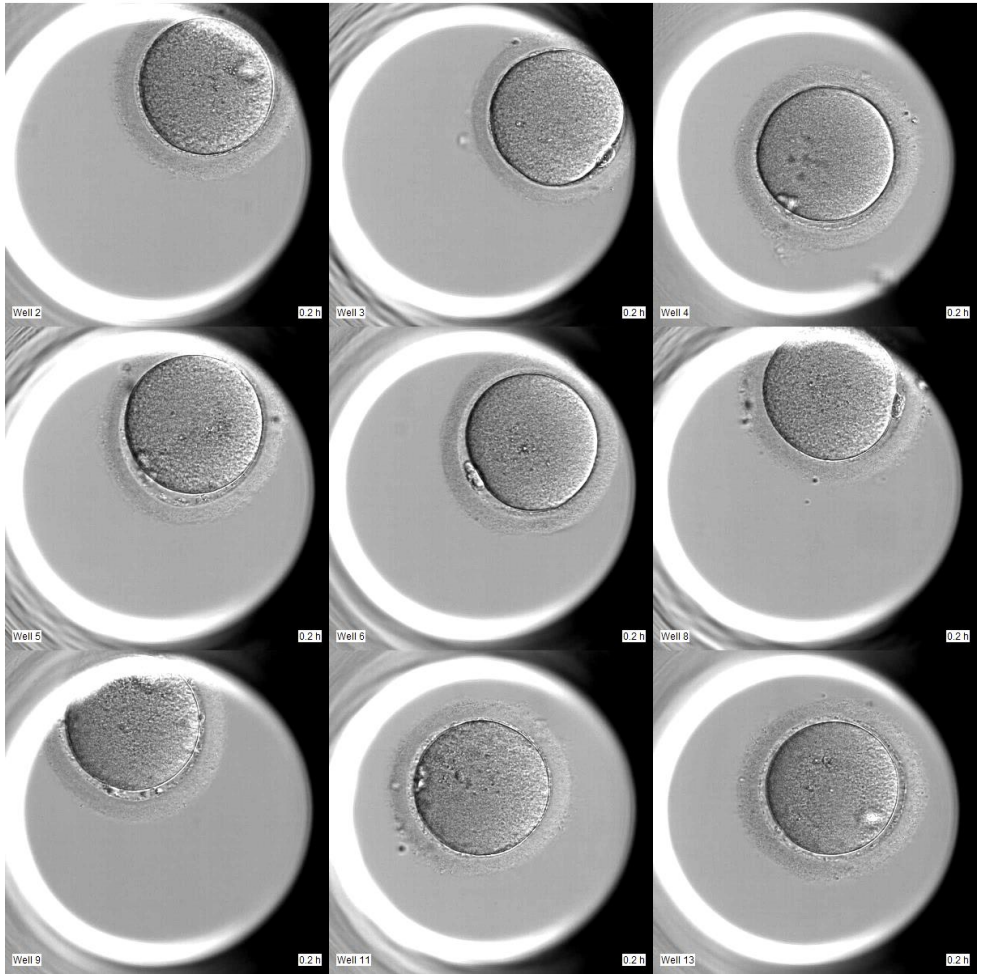
Note: Values are means ± standard error (95% confidence interval). EUR: embryo utilization rate; GzLM: generalized linear models; OUR: oocyte utilization rate; TLI: time-lapse imaging.

Embryoscope FERTILITY

- 427 ciclos
- 372 pacientes

✓3.020 ovócitos cultivados
✓2.398 2PN (79,4%)
✓1.488 blastocistos: *62,1% 2PN*

❑ 2018: *49,9% 2PN*



Does a universal TLT algorithm exist?

- Probably not.
- Each laboratory should perform a proper validation, certifying the value of each variable introduced and the corrections for putative confounders that could influence the algorithms

FERTILITY

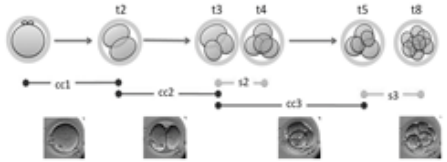
FERTscore FERTILITY

- **PN**
- pronuclei appearance **(tPNa)**
- timing to pronuclei fading **(tPNf)**
- timing to two **(t2)**, three **(t3)**, four **(t4)**, five, **(t5)**, six **(t6)**, seven **(t7)**, and eight cells **(t8)**
- timing to blastulation **(tB)**
- duration of the second cycle **(t3-t2) - cc2**
- duration of the third cycle **(t5-t3) - cc3**
- **(t2-tPNf) - s1**
- **(t4-t3) - s2**
- **(t8-t5) - s3**

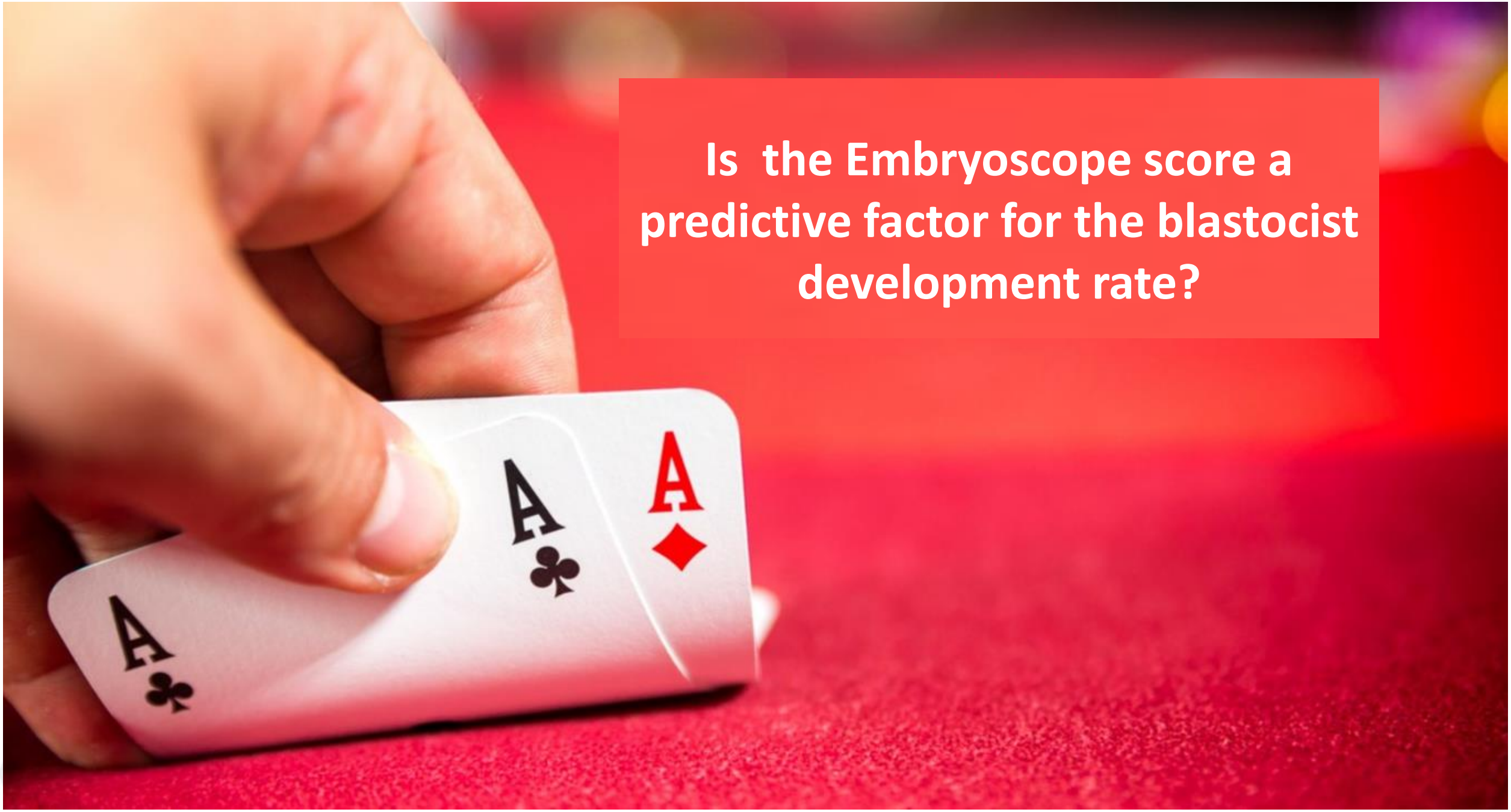
Parâmetros de Avaliação Embryoscope - Fertility

Variável	Descrição	Valores	Avaliação	Intervalo	Referência
PN	Quantidade de pronúcleos	Selecionar	Entre 16 - 18h após ICSI	-	-
tPNa	Tempo da inseminação até o aparecimento dos pronúcleos.	Horas	Anotar primeira imagem que **todos** os PNs podem ser observados.	9.16–9.64h	Aguilar 2014
tPNf	Tempo da inseminação até os pronúcleos desaparecerem	Horas	Anotar primeira imagem que todos os PNs desaparecem	>20h45m / 23.42–24.12h / 24.3 - 25.3h	Azarello 2012 / Aguilar 2014 / Desai 2014
t2	Tempo da inseminação até a completa divisão em 2 cel	Horas	No momento de divisão em 2cel	26.5 - 27.8 h	Desai 2014
t3	Tempo da inseminação até a completa divisão em 3 cel	Horas	No momento de divisão em 3cel	34-40h / 36.5 - 38.7 h	Basile 2015 / Desai 2014
t4	Tempo da inseminação até a completa divisão em 4 cel	Horas	No momento de divisão em 4cel	39.0 - 41.1 h	Desai 2014
t5	Tempo da inseminação até a completa divisão em 5 cel	Horas	No momento de divisão em 5cel	48.8 - 56.6 h / 50.8 - 53.2 h	Cruz 2012 / Desai 2014
t6	Tempo da inseminação até a completa divisão em 6 cel	Horas	No momento de divisão em 6cel	-	-
t7	Tempo da inseminação até a completa divisão em 7 cel	Horas	No momento de divisão em 7cel	-	-
t8	Tempo da inseminação até a completa divisão em 8 cel	Horas	No momento de divisão em 8cel	54.9 ± 5.2 h / 60.2 - 64.0 h	Dal Canto 2012 / Desai 2014
tB	Tempo da inseminação até a formação do blastocito	Horas	A última imagem antes do início da expansão (blastocito empurra a ZP)	120h / 103.8 - 106.6 h	Rubio 2014 / Desai 2014
ICM	Avaliação da Massa Celular Interna	A, B,C	classificar entre 115-120h (verificar ficha classificação D5)	-	-
TE	Avaliação do Trofectoderma	A, B,C	classificar entre 115-120h (verificar ficha classificação D5)	-	-

Legenda
Parâmetrar que geram o algoritmo
Parâmetrar que não geram o algoritmo



FERTILITY



Is the Embryoscope score a predictive factor for the blastocist development rate?

FERTscore FERTILITY

Análise discriminante de parâmetros associados à formação de blastocisto

		Não blastocisto (n=657)		Blastocisto (n=563)		
Cut-off	**Variável**	**Média**	**DP**	**Média**	**DP**	**p-value**
	tPNa	7,36	4,03	6,57	2,04	
	tPNf	24,35	5,24	22,90	6,02	
	t2	27,26	5,33	25,29	3,19	<0.001
	S1 (t2-tPNf)	19,90	3,68	18,71	2,82	
	t3	36,50	6,79	36,02	4,65	
	cc2 (t3-t2)	9,24	5,22	10,74	3,10	
	t4	39,74	7,29	37,46	4,43	
	s2 (t4-t3)	3,24	4,64	1,43	2,69	<0.001
	t5	48,30	9,59	48,77	7,15	
	cc3 (t5-t3)	11,80	6,68	12,75	4,62	
	t6	53,28	10,44	51,55	7,02	
	t7	57,34	11,62	54,21	8,40	<0.001
	t8	62,06	13,07	57,25	9,51	
	s3 (t8-t5)	13,75	10,05	8,48	7,84	<0.001

FERTILITY

FERTscore FERTILITY

Análise discriminante de parâmetros associados à formação de blastocisto

		Não blastocisto (n=657)		Blastocisto (n=563)		
Cut-off	**Variável**	**Média**	**DP**	**Média**	**DP**	**p-value**
	tPNa	7,36	4,03	6,57	2,04	
	tPNf	24,35	5,24	22,90	6,02	
26,27	t2	27,26	5,33	25,29	3,19	<0.001
	S1 (t2-tPNf)	19,90	3,68	18,71	2,82	
	t3	36,50	6,79	36,02	4,65	
	cc2 (t3-t2)	9,24	5,22	10,74	3,10	
	t4	39,74	7,29	37,46	4,43	
2,34	s2 (t4-t3)	3,24	4,64	1,43	2,69	<0.001
	t5	48,30	9,59	48,77	7,15	
	cc3 (t5-t3)	11,80	6,68	12,75	4,62	
	t6	53,28	10,44	51,55	7,02	
55,78	t7	57,34	11,62	54,21	8,40	<0.001
	t8	62,06	13,07	57,25	9,51	
11,12	s3 (t8-t5)	13,75	10,05	8,48	7,84	<0.001

76,1% de casos originais agrupados corretamente classificados

FERTILITY

Is the Embryoscope score correlated with pregnacy rate?

EmbryoScope FERTILITY

ICSI e OVODON					
Variáveis	Convencional (n=764)		Embryoscope (n=119)		p
	Média	DP	Média	DP	
Taxa de fertilização (%)	76,5	25,0	74,4	26,5	0,255
Taxa de blastocisto (%)	**59,2**	25,0	**66,0**	25,4	**0,003**
Embriões transferidos (n)	**2,0**	0,6	**1,2**	0,9	**<0,001**
Taxa de implantação (%)*	**24,5**	37,3	**36,4**	42,2	**0,006**
Taxa de gestação (%)*	**34,6**		**55,7**		**<0,001**
Taxa de aborto (%)*	**11,5**		**2,3**		**0,001**

FERTILITY

EmbryoScope FERTILITY

Resultado clínico estratificado por idade

Até 35 anos

	Convencional (n=182)		Embryoscope (n=181)		p
	Média	DP	Média	DP	
Taxa de implantação (%)	41.9	5.5	29.8	6.3	0.147
Taxa de gestação (%)	51.6		38.3		0.166
Taxa de aborto (%)	16.1		27.8		0.329

36 a 39 anos

	Convencional (n=182)		Embryoscope (n=275)		p
	Média	DP	Média	DP	
Taxa de implantação (%)	29.7	4.9	24.4	4.4	0.421
Taxa de gestação (%)	32.9		37.3		0.576
Taxa de aborto (%)	12.5		7.4		0.542

≥ 40 anos

	Convencional (n=140)		Embryoscope (n=225)		p
	Média	DP	Média	DP	
Taxa de implantação (%)	11.1	4.2	21.0	4.5	**<0.001**
Taxa de gestação (%)	14.1		28.8		**0.045**
Taxa de aborto (%)	31.3		32.0		0.915

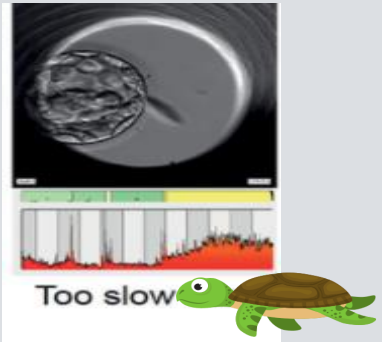
FERTILITY

EmbryoScope FERTILITY

KIDscore D5	≤ 2,5	2,6 – 5,0	5,1 – 7,5	> 7,5
Taxa de Implantação (%)	24,0[a]	27,3[b]	31,4[c]	37,2[d]

a ≠ b ≠ c ≠ d, p < 0,001
General linear model, função Log linear, distribuição Poison

FERTILITY



A fragmentação do DNA pode interferir na velocidade e no padrão das divisões celulares

FERTILITY

Morphokinetic parameter comparison between embryos from couples with high or low sperm DNA fragmentation index

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F&S Science (2021), doi: https://doi.org/10.1016/j.xfss.2021.10.001

- 118 patientes, 978 zigotos, ciclos de ICSI, fator masculino idiopático
- Marcadores morfocinéticos: tempo para pronúcleo, aparecimento e desapareciemnto (tPNa and tPNf), tempo para duas (t2), três (t3), quatro (t4), cinco (t5), seis (t6), sete (t7), e oito células (t8), e tempo de início (tSB) e de blastulação (tB).
- Baixo (<30%) ou alto (≥30%) DFI (índice de fragmentação do DNA do espermatozoide
- Modelos lineares generalizados mistos ajustados para potenciais confundidores, seguidos pelo teste de Bonferroni *post hoc*

FERTILITY

Table 2. Results from multivariate linear regression analysis followed by Bonferroni post hoc for the comparison of embryo morphokinetics between DFI groups (n=978)

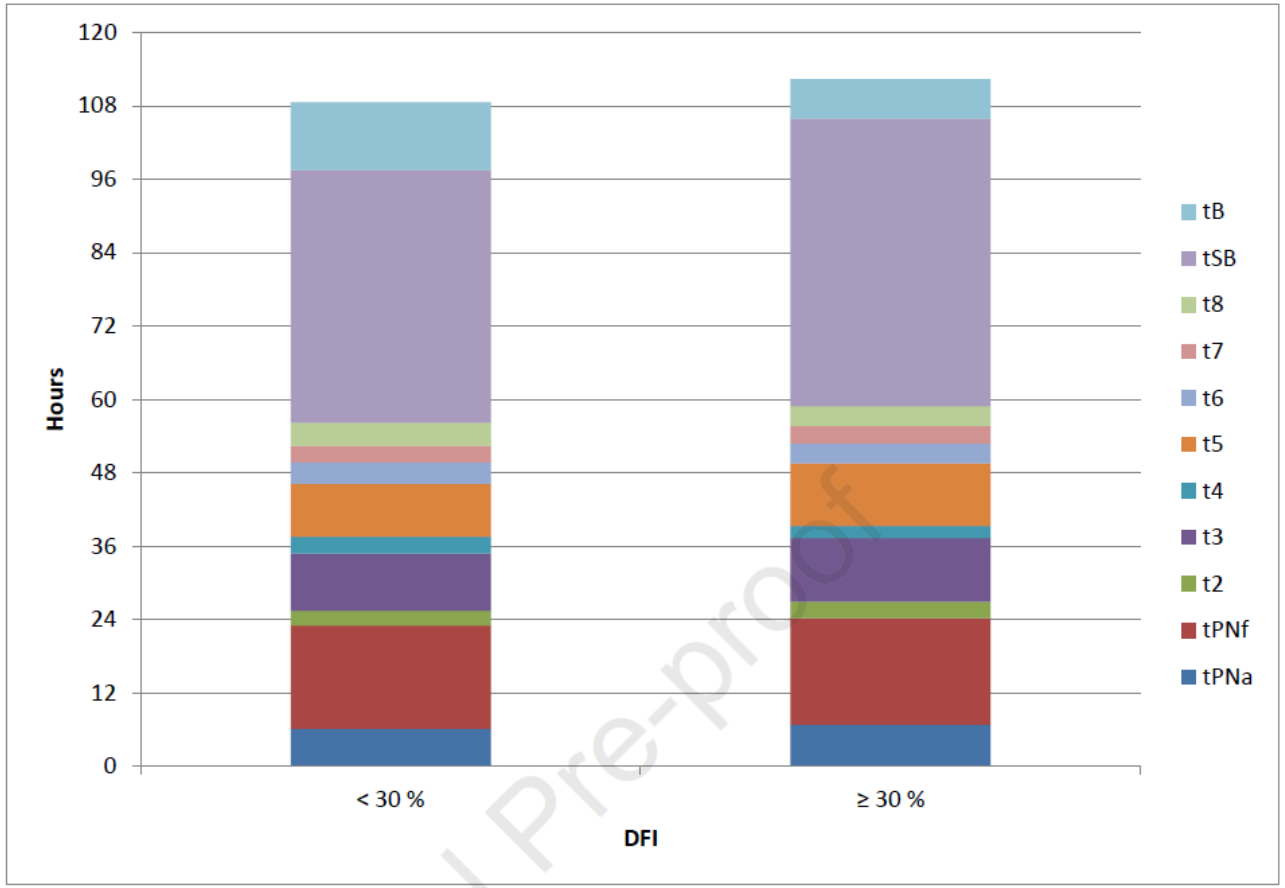
Morphokinetic data (hours)	<30% DFI (n=592)	≥30% DFI (n=386)	p-value
tPNa	6.1 ± 0.2	6.8 ± 0.2	0.030
tPNf	23.0 ± 0.3	24.2 ± 0.3	0.009
t2	25.4 ± 0.3	26.9 ± 0.3	0.002
t3	34.8 ± 0.3	37.3 ± 0.4	<0.001
t4	37.5 ± 0.4	39.3 ± 0.4	0.003
t5	46.2 ± 0.5	49.5 ± 0.6	<0.001
t6	49.7 ± 0.5	52.8 ± 0.6	0.001
t7	52.4 ± 0.6	55.6 ± 0.7	0.001
t8	56.2 ± 0.7	58.9 ± 0.8	0.017
tSB	97.5 ± 1.5	105.9 ± 1.7	0.002
tB	108.6 ± 0.8	112.4 ± 1.2	0.016

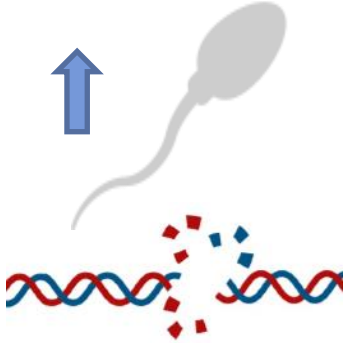
Note: Values are means ± standard deviation, unless otherwise noted. tPNa – timing to pronuclei appearance, tPNf – timing to pronuclei fading, t2 – timing to two cells, t3 – timing to three cells, t4 – timing to four cells, t5 – timing to five cells, t6 – timing to six cells, t7 – timing to seven cells, t8 – timing to eight cells, tSB – timing to start blastulation, tB – timing to blastulation (tB).

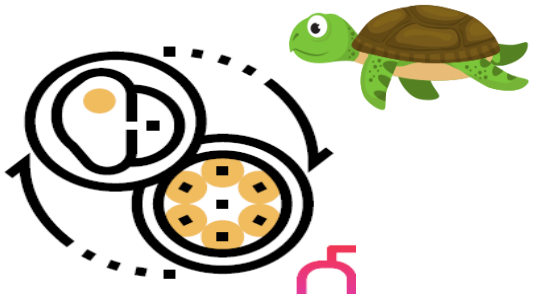
Proof

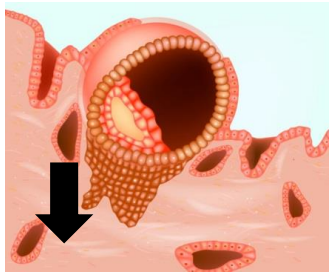
F&S Science (2021), doi: https://doi.org/10.1016/j.xfss.2021.10.001

Marcadores morfocinéticos









al Pre-proof

FERTILITY

F&S Science (2021), doi: https://doi.org/10.1016/j.xfss.2021.10.001

Origem do espermatozoide, resultados clínicos, a morfocinética embrionária e as incidências de padrões anormais de clivagem e multinucleação.

FERTILITY

Coorte → Janeiro /2019– Dezembro/2020 → Embriões cultivados em STL até D5

96 ciclos de ICSI

806 embriões

Pareamento por idades materna e paterna, número de óvulos recuperados e protocolo de EOC

PESA
32 ciclos
276 embriões

FMI
32 ciclos
284 embriões

CONTROLE
32 ciclos
246 embriões

FERTILITY

Resultados da comparação de dados morfocinéticos iniciais de embriões dos grupos PESA, FMI e Controle

Variáveis	PESA (n= 32)	FMI (n=32)	Controle (n=32)	Valor de p
tPNa (hrs.)	6,7 ± 0,1 [a]	6,1 ± 0,1 [b]	5,9 ± 0,1 [b]	<0,001
tPNf (hrs.)	24,0 ± 0,1 [a]	23,9 ± 0,2 [a,b]	22,0 ± 0,5 [b]	<0,001
t2 (hrs.)	27,0 ± 0,2 [a]	25,1 ± 0,2 [b]	24,2 ± 0,2 [c]	<0,001
t3 (hrs.)	36,7 ± 0,3 [a]	35,5 ± 0,3 [b]	34,4 ± 0,3 [c]	<0,001
t4 (hrs.)	39,2 ± 0,3 [a]	39,3 ± 0,2 [a]	36,7 ± 0,8 [b]	<0,001
t5 (hrs.)	47,4 ± 0,5 [a]	48,1 ± 0,5 [a]	44,6 ± 0,6 [b]	<0,001
t6 (hrs.)	52,1 ± 0,3	51,7± 0,4	50,0 ± 1,1	0,180
t7 (hrs.)	54,8 ± 0,3	54,7 ± 0,5	53,2 ± 1,2	0,439
t8 (hrs.)	60,7 ± 0,7 [a]	57,0 ± 0,7 [b]	54,7 ± 0,8 [b]	<0,001

tPNa – tempo para aparecimento do PN. tPNf – tempo para desaparecimento do PN. t2, t3, t4, t5, t6, t7 e t8 – tempo para a formação de 2, 3, 4, 5, 6, 7 e 8 células

Resultados da comparação de dados morfocinéticos iniciais de embriões dos grupos PESA, FMI e Controle

Variáveis	PESA (n= 32)	FMI (n=32)	Controle (n=32)	Valor de p
tPNa (hrs.)	6,7 ± 0,1 [a]	6,1 ± 0,1 [b]	5,9 ± 0,1 [b]	<0,001
tPNf (hrs.)	24,0 ± 0,1 [a]	23,9 ± 0,2 [a,b]	22,0 ± 0,5 [b]	<0,001
t2 (hrs.)	27,0 ± 0,2 [a]	25,1 ± 0,2 [b]	24,2 ± 0,2 [c]	<0,001
t3 (hrs.)	36,7 ± 0,3 [a]	35,5 ± 0,3 [b]	34,4 ± 0,3 [c]	<0,001
t4 (hrs.)	39,2 ± 0,3 [a]	39,3 ± 0,2 [a]	36,7 ± 0,8 [b]	<0,001
t5 (hrs.)	47,4 ± 0,5 [a]	48,1 ± 0,5 [a]	44,6 ± 0,6 [b]	<0,001
t6 (hrs.)	52,1 ± 0,3	51,7± 0,4	50,0 ± 1,1	0,180
t7 (hrs.)	54,8 ± 0,3	54,7 ± 0,5	53,2 ± 1,2	0,439
t8 (hrs.)	60,7 ± 0,7 [a]	57,0 ± 0,7 [b]	54,7 ± 0,8 [b]	<0,001

tPNa – tempo para aparecimento do PN. tPNf – tempo para desaparecimento do PN. t2, t3, t4, t5, t6, t7 e t8 – tempo para a formação de 2, 3, 4, 5, 6, 7 e 8 células

Resultados da comparação de dados morfocinéticos tardios de embriões dos grupos PESA, FMI e Controle

Variáveis	PESA (n= 32)	FMI (n=32)	Controle (n=32)	Valor de p
tM (hrs.)	95,0 ± 0,9 [a]	86,7 ± 0,9 [b]	83,3 ± 1,1 [c]	<0,001
tsB (hrs.)	99,5 ± 1,5	98,3 ± 0,8	97,8 ± 2,2	0,739
tB (hrs.)	109,3 ± 0,7	108,3 ± 0,5	106,3 ± 1,6	0,222

tM – tempo para morulação. tsB – tempo para início da blastulação. tB – tempo para blastulação completa.

FERTILITY

Resultados da comparação de dados morfocinéticos tardios de embriões dos grupos PESA, FMI e Controle

Variáveis	PESA (n= 32)	FMI (n=32)	Controle (n=32)	Valor de p
tM (hrs.)	95,0 ± 0,9 [a]	86,7 ± 0,9 [b]	83,3 ± 1,1 [c]	<0,001
tsB (hrs.)	99,5 ± 1,5	98,3 ± 0,8	97,8 ± 2,2	0,739
tB (hrs.)	109,3 ± 0,7	108,3 ± 0,5	106,3 ± 1,6	0,222

tM – tempo para morulação. tsB – tempo para início da blastulação. tB – tempo para blastulação completa.

FERTILITY

Resultados da comparação das incidências de multinucleação e clivagem anormal, resultado do KIDScore D-5 em embriões dos grupos PESA, FMI e Controle

Variávies	PESA (n= 32)	FMI (n=32)	Controle (n=32)	Valor de p
Multinucleação (%)	23,2 [a]	2,8 [b]	3,7 [b]	<0,001
Clivagem anormal (%)	11,1 [a]	11,3 [a]	4,3 [b]	0,001
KIDScore D-5	3,1 [a]	5,4 [b]	5,6 [b]	<0,001

KIDScore D-5 - nota atribuida a partir de dados de implantação conhecida para embriões transferidos no quinto dia.

FERTILITY

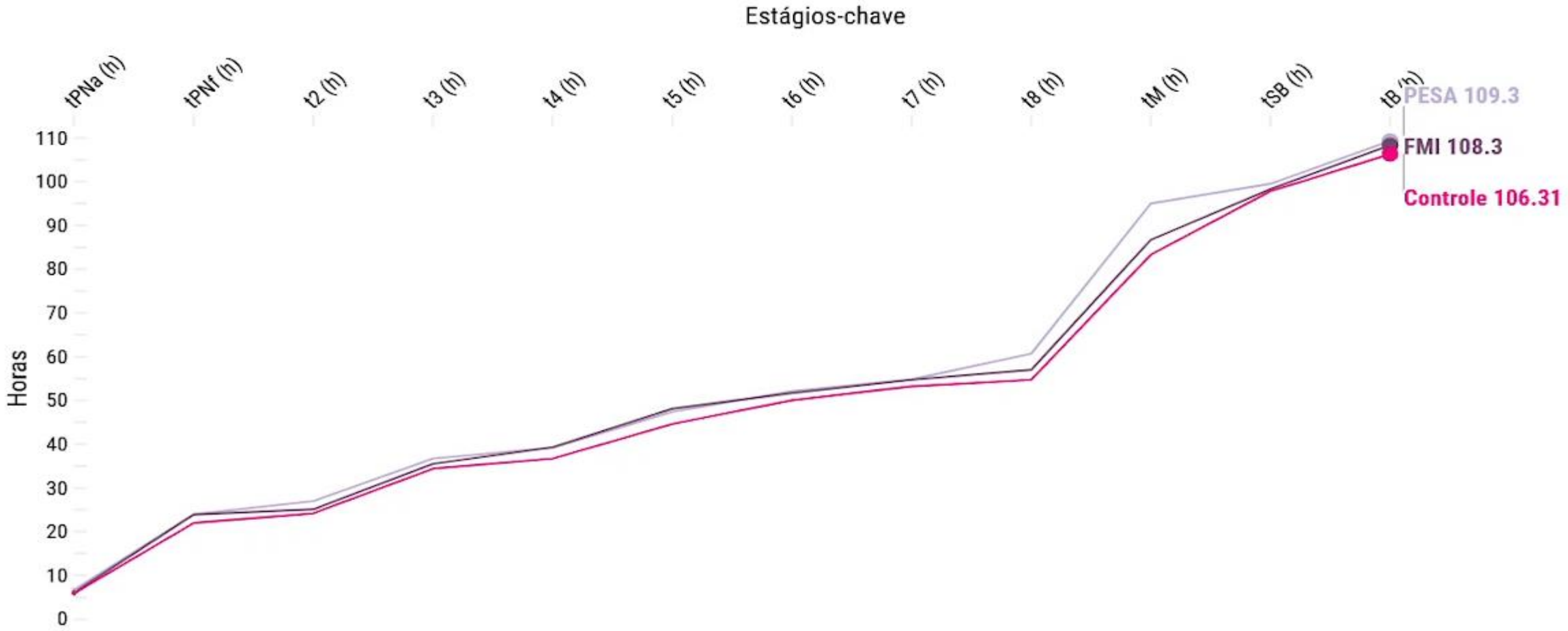
Resultados da comparação das incidências de multinucleação e clivagem anormal, resultado do KIDScore D-5 em embriões dos grupos PESA, FMI e Controle

Variávies	PESA (n= 32)	FMI (n=32)	Controle (n=32)	Valor de p
Multinucleação (%)	23,2 [a]	2,8 [b]	3,7 [b]	<0,001
Clivagem anormal (%)	11,1 [a]	11,3 [a]	4,3 [b]	0,001
KIDScore D-5	3,1 [a]	5,4 [b]	5,6 [b]	<0,001

KIDScore D-5 - nota atribuida a partir de dados de implantação conhecida para embriões transferidos no quinto dia.

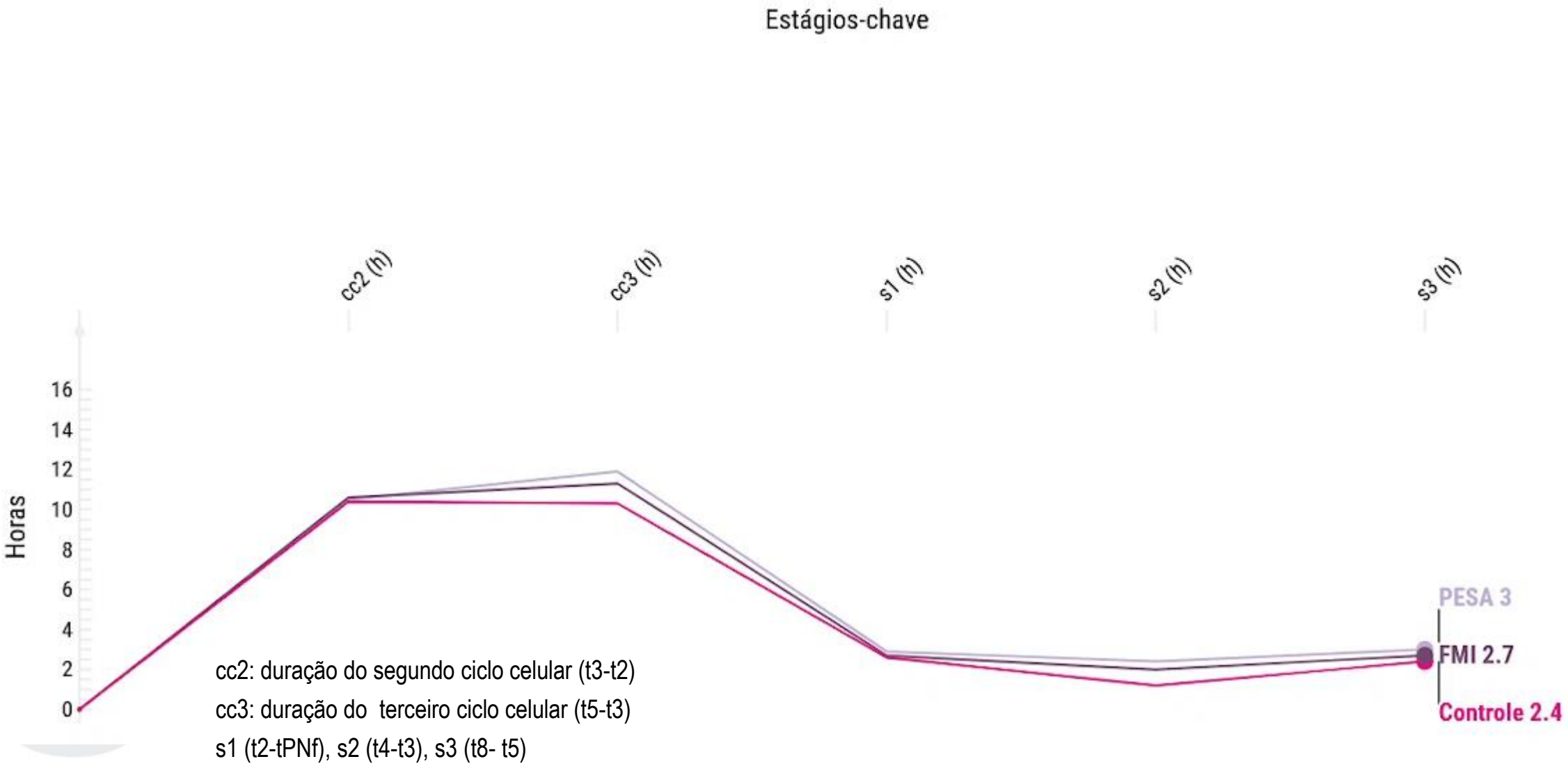
FERTILITY

Comportamento dos embriões dos grupos PESA, FMI e Controle em relação a eventos morfocinéticos iniciais e tardios



FERTILITY

Comportamento dos embriões dos grupos PESA, FMI e Controle em relação a ciclos celulares e divisões sincrônicas



cc2: duração do segundo ciclo celular (t3-t2)

cc3: duração do terceiro ciclo celular (t5-t3)

s1 (t2-tPNf), s2 (t4-t3), s3 (t8- t5)

Received: 31 March 2021 | Revised: 29 July 2021 | Accepted: 30 July 2021

DOI: 10.1111/and.14211

ORIGINAL ARTICLE

andrologia WILEY

Early and late paternal contribution to cell division of embryos in a time-lapse imaging incubation system

Amanda Souza Setti[1,2] | Daniela Paes de Almeida Ferreira Braga[1,2] | Livia Vingris[3] | Assumpto Iaconelli Jr.[2,4] | Edson Borges Jr.[2,4]

FERTILITY

RESULTS

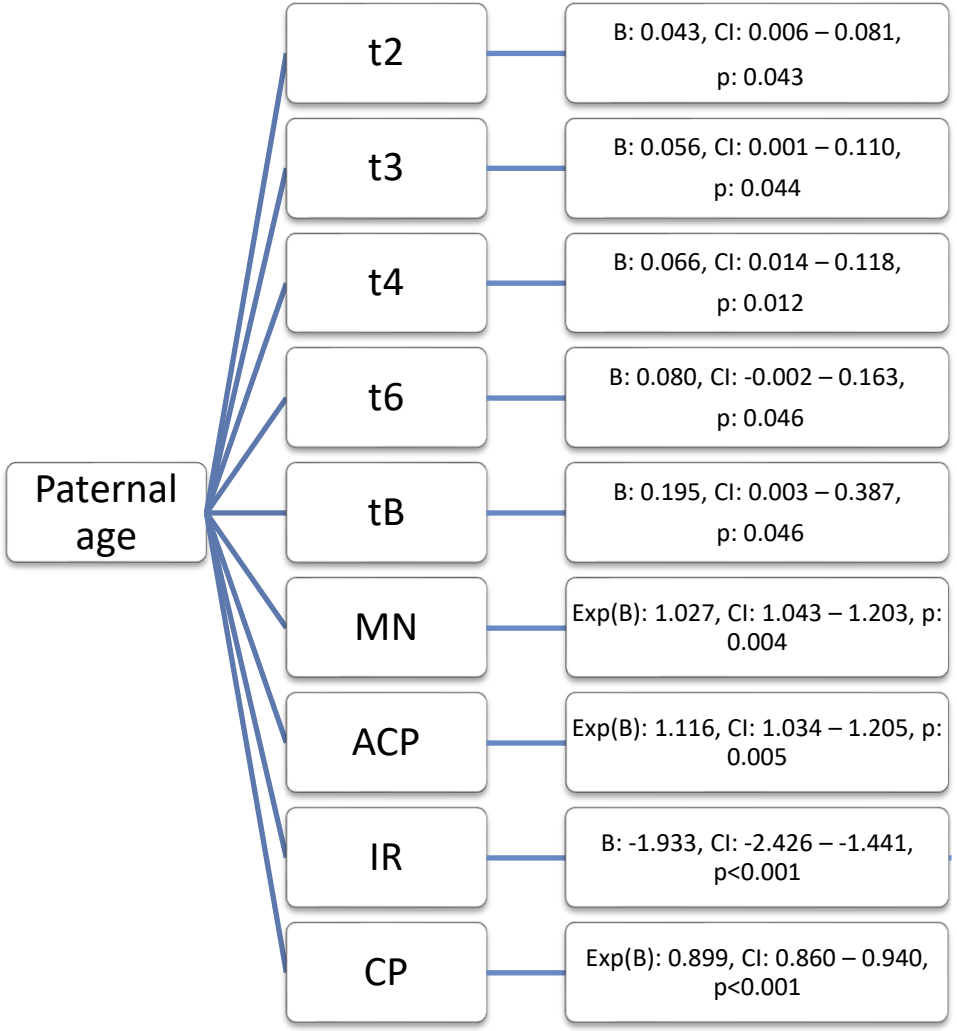
First International Journal of Andrology
ANDROLOGIA

Early and late paternal contribution to cell division of embryos in a time-lapse imaging incubation system

Variable	Mean ± SD
Semen analysis	
Male age (years)	41.3 ± 6.8
Ejaculatory abstinence length (days)	3.2 ± 2.5

FERTILITY

RESULTS


Paternal age
t2
B: 0.043, CI: 0.006 – 0.081, p: 0.043
t3
B: 0.056, CI: 0.001 – 0.110, p: 0.044
t4
B: 0.066, CI: 0.014 – 0.118, p: 0.012
t6
B: 0.080, CI: -0.002 – 0.163, p: 0.046
tB
B: 0.195, CI: 0.003 – 0.387, p: 0.046
MN
Exp(B): 1.027, CI: 1.043 – 1.203, p: 0.004
ACP
Exp(B): 1.116, CI: 1.034 – 1.205, p: 0.005
IR
B: -1.933, CI: -2.426 – -1.441, p<0.001
CP
Exp(B): 0.899, CI: 0.860 – 0.940, p<0.001

High oocyte immaturity rates impact embryomorphokinetics: Lessons of time-lapse imaging system

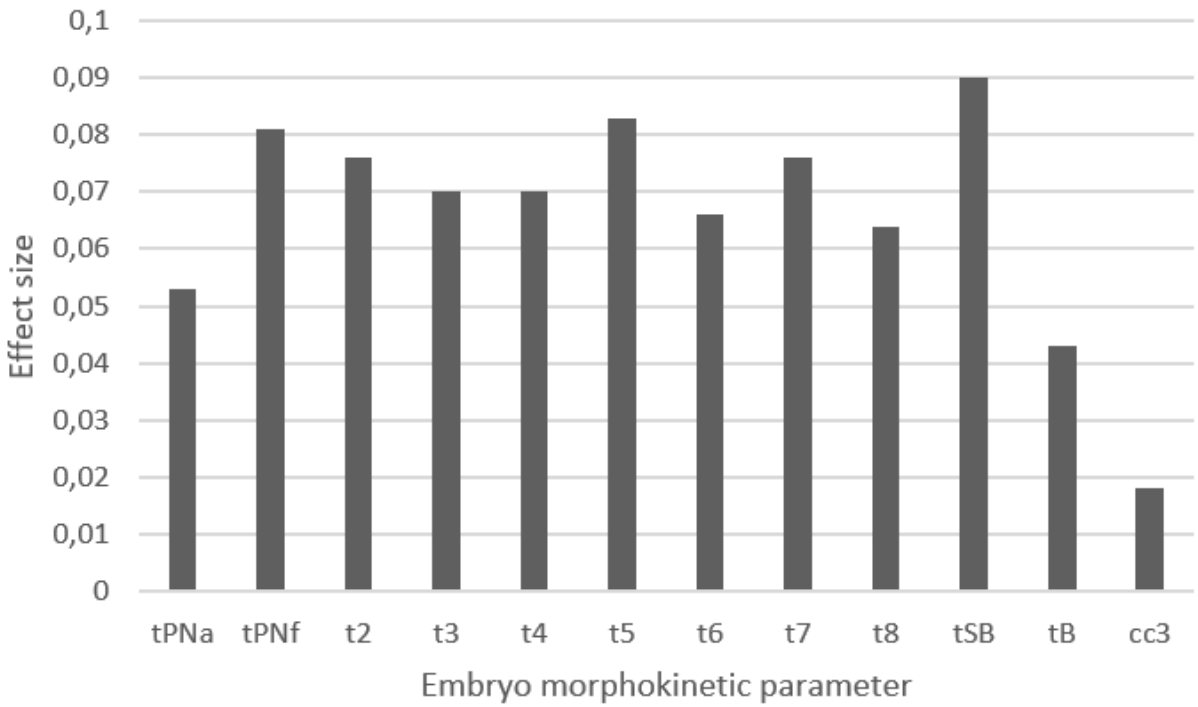
Table 3. Results from regression analysis for the influence of oocyte maturity rate on embryo morphokinetics (n=3368 embryos)

Morphokinetic parameters (h)	B	95% CI	p-value
tPNa	0.053	0.045 – 0.061	<0.001
tPNf	0.081	0.070 – 0.093	<0.001
t2	0.076	0.064 – 0.087	<0.001
t3	0.070	0.056 – 0.084	<0.001
t4	0.070	0.055 – 0.084	<0.001
t5	0.083	0.063 – 0.102	<0.001
t6	0.066	0.047 – 0.086	<0.001
t7	0.076	0.055 – 0.098	<0.001
t8	0.064	0.040 – 0.087	<0.001
tSB	0.090	0.014 – 0.165	0.020
tB	0.043	0.011 – 0.075	0.009
s1	-0.001	-0.004 – 0.003	0.725
s2	0.001	-0.008 – 0.009	0.887
s3	0.004	-0.015 – 0.0240	0.649
cc2	-0.003	-0.013 – 0.007	0.510
cc3	0.018	0.005 – 0.031	0.007

Note: Values are means ± standard deviation, unless otherwise noted. h – hours, B – Beta coefficient, CI – confidence interval, tPNa – timing to pronuclei appearance, tPNf – timing to pronuclei fading, t2 – timing to two cells, t3 – timing to three cells, t4 – timing to four cells, t5 – timing to five cells, t6 – timing to six cells, t7 – timing to seven cells, t8 – timing to eight cells, tSB – timing to start blastulation, tB – timing to blastulation, s1 – timing to complete t2-tPNf synchronous divisions, s2 – timing to complete t4-t3 synchronous divisions, s3 – timing to complete t8-t5 synchronous divisions, cc2 – duration of the second cell cycle (t3-t2), cc3 – duration of third cell cycle (t5-t3).

Borges E. *et al*

High oocyte immaturity rates impact embryomorphokinetics: Lessons of time-lapse imaging system



Borges E. *et al*

Figure 2. Illustration of cumulative delayed morphokinetic development in MII inseminated oocytes derived from cohorts with high proportion of immature sibling oocytes.

Table 3. Results from regression analysis for the influence of serum AMH concentration levels on embryo morphokinetics (n=114 cycles and 902 embryos)

Morphokinetic parameters (h)	B	95% CI	p-value
tPNa	0.251	-0.315 – 0.816	0.385
tPNf	-0.047	-0.071 – -0.024	<0.001
t2	-0.028	-0.056 – 0.001	0.057
t3	-0.070	-0.102 – -0.039	<0.001
t4	-0.080	-0.114 – -0.046	<0.001
t5	-0.075	-0.123 – -0.028	0.002
t6	-0.105	-0.147 – -0.064	<0.001
t7	-0.120	-0.165 – -0.075	<0.001
t8	-0.170	-0.220 – -0.119	<0.001
tSB	-4.898	-12.208 – 2.412	0.189
tB	-0.153	-0.224 – -0.082	<0.001
s1	-0.274	-0.686 – 0.137	0.191
s2	-0.009	-0.027 – 0.009	0.344
s3	-0.086	-0.129 - -0.044	<0.001
cc2	-0.041	-0.062 – -0.019	<0.001
cc3	-0.005	-0.036 – 0.025	0.739

Borges E. *et al*
(accepted)

FERTILITY

Figure 1. Illustration of faster embryo morphokinetic development according to increased serum AMH concentration levels

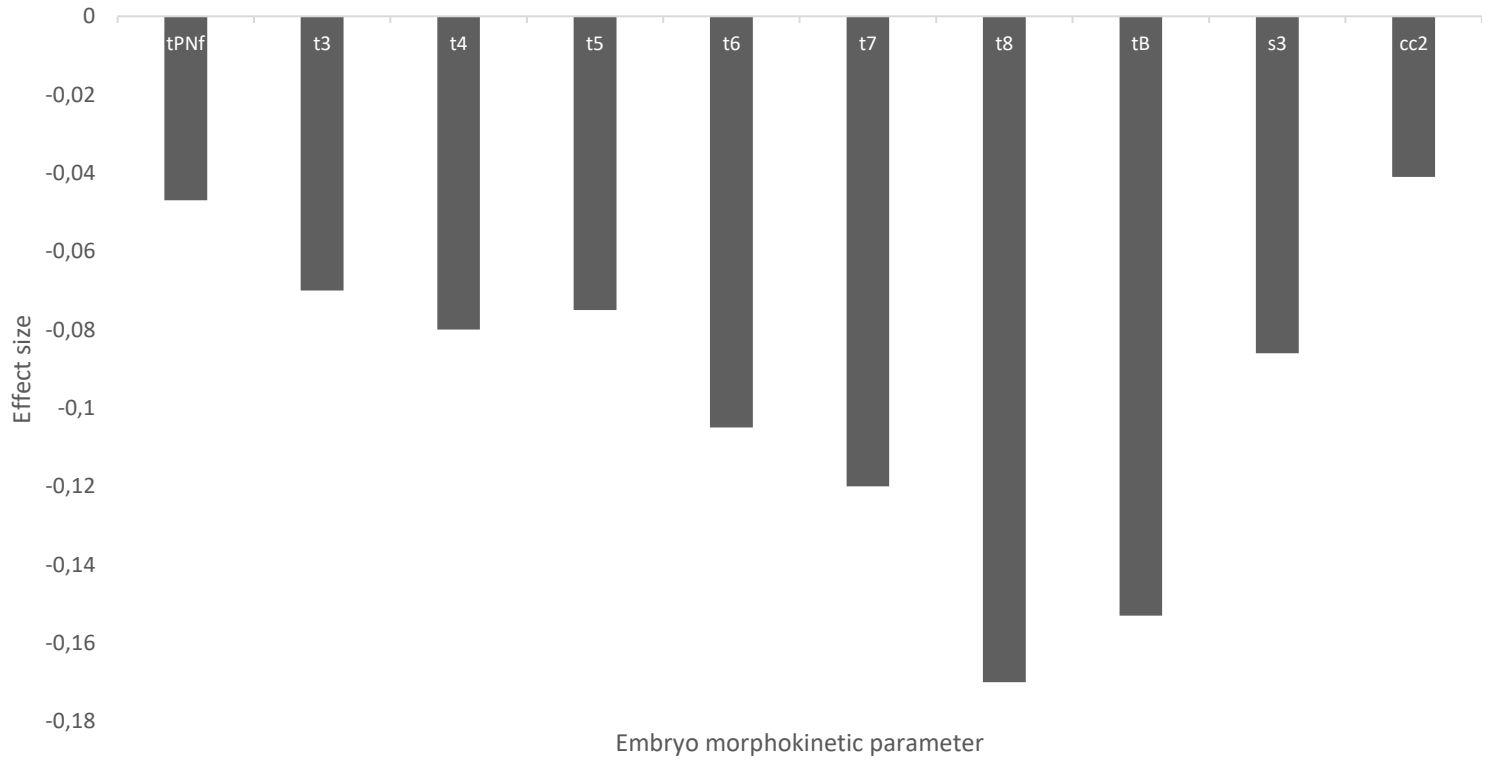
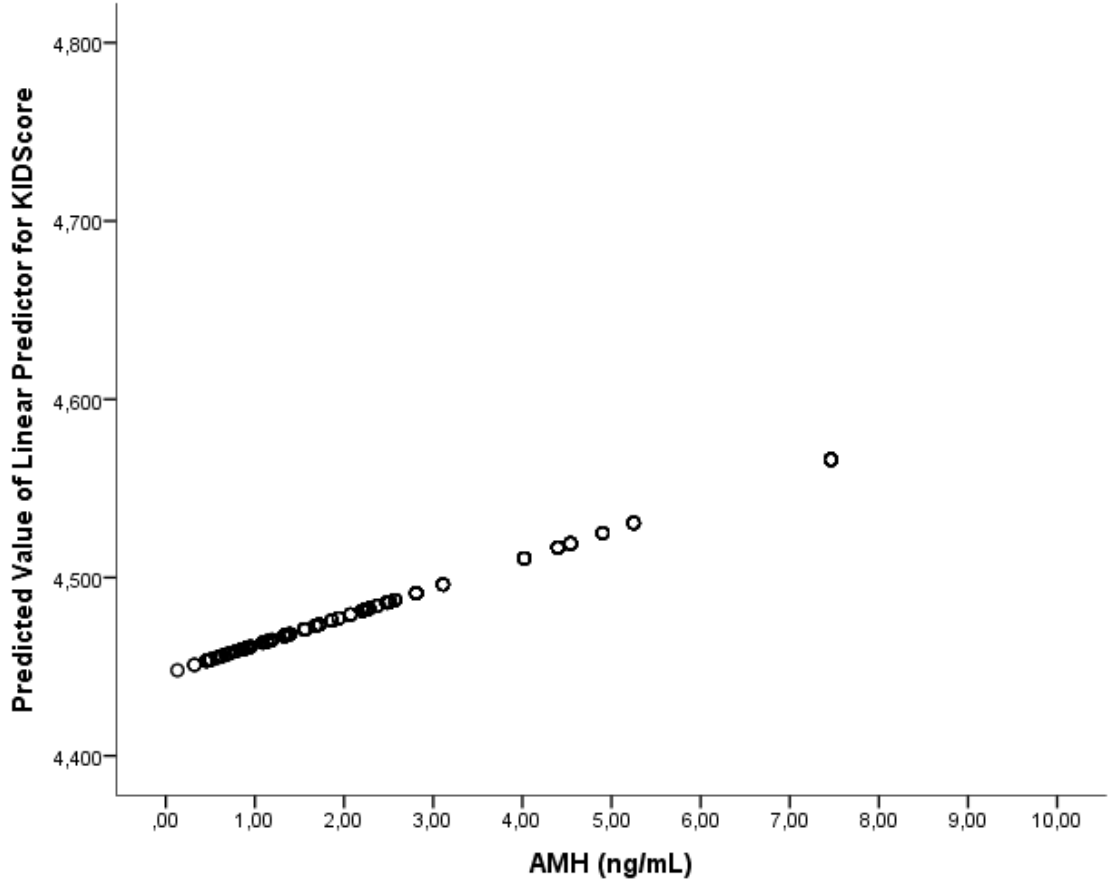
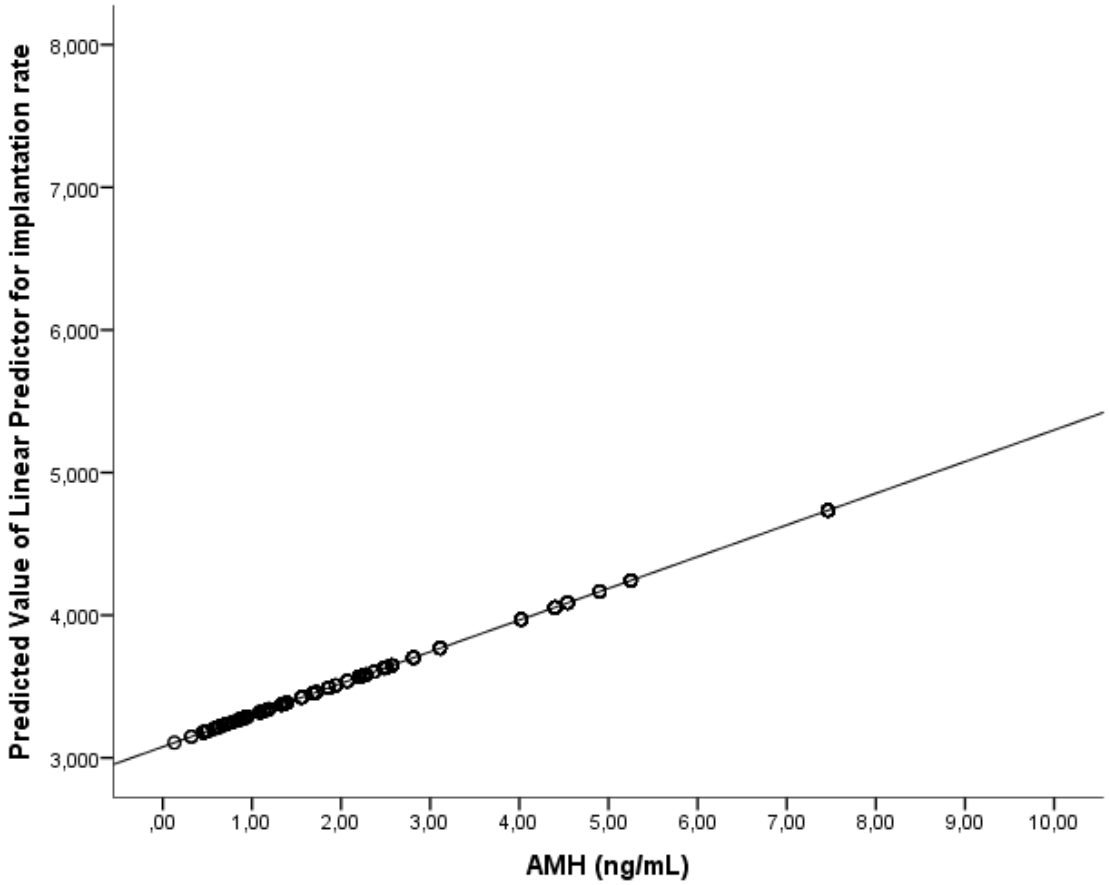


Figure 2. Illustration of the predictive value of AMH on embryos' KIDScore ranking (p=0.023)



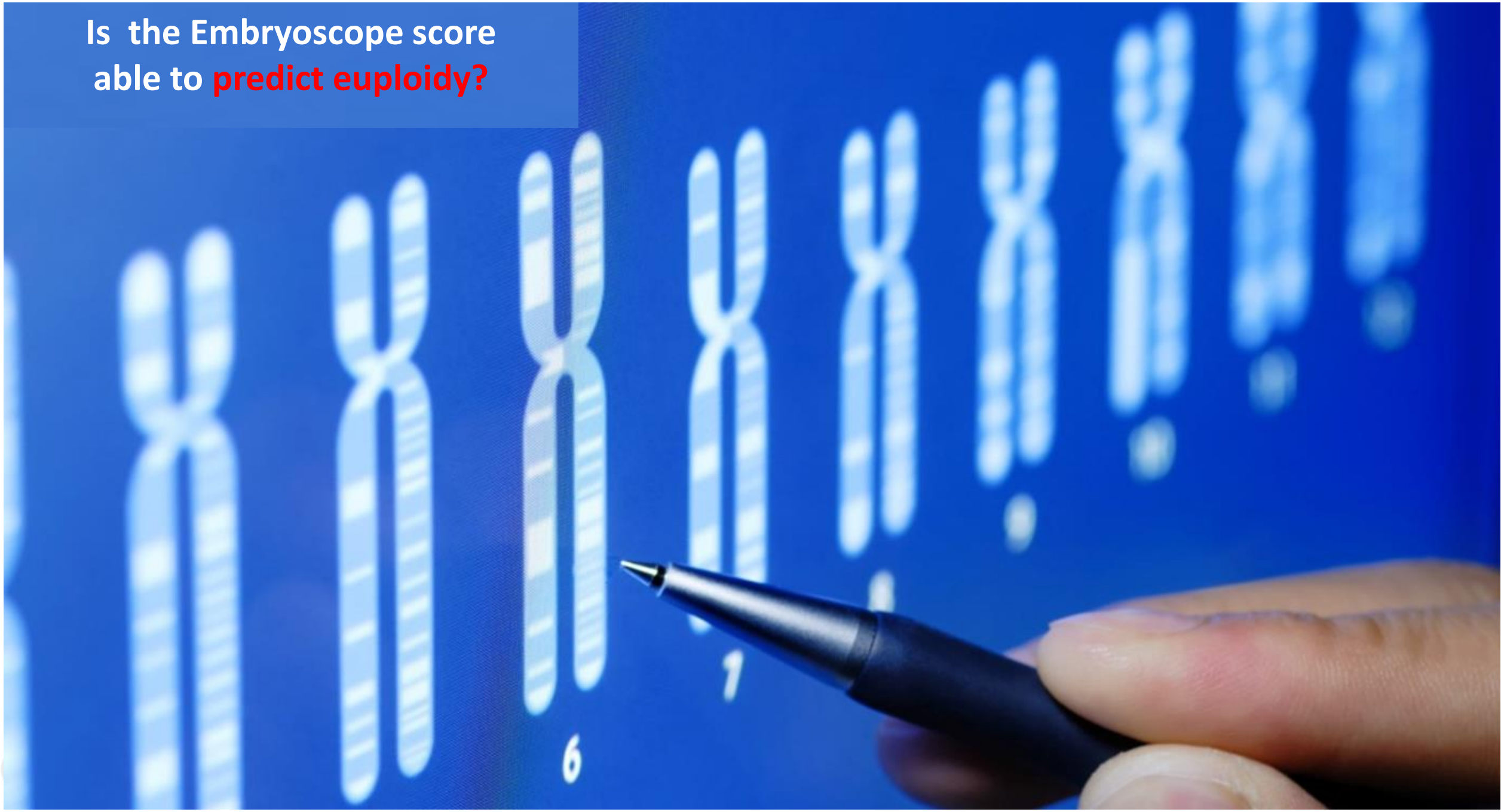
FERTILITY

Figure 3. Illustration of the predictive value of AMH on embryos' implantation rate (p<0.001)



FERTILITY

Is the Embryoscope score able to predict euploidy?



Time-lapse monitoring: an adjunct tool to select embryos for preimplantation genetic testing

Borges E. *et al*
(submitted)

Table 1: General characteristics of patients and laboratory ICSI cycle outcomes (n=316)

		Mean	Std. Deviation
Female age (years)		38.3	3.4
Male age (years)		40.2	5.5
Total dose of FSH	Follitropin alfa (IU)	2615.7	799.2
	Follitropin delta (µg)	152.8	34.7
Oestradiol level on hCG trigger (pg/mL)		2127.9	2104.2
Follicles (n)		13.1	8.6
Retrieved oocytes (n)		10.0	7.1
Oocyte yield (%)		76.8	17.0
Mature oocytes (n)		7.7	5.9
Mature oocyte rate (%)		77.4	19.2
Fertilization rate (%)		77.7	19.0
Blastocyst development (%)		53.6	31.4

Note: ICSI – intracytoplasmic sperm injection; FSH– follicle stimulating hormone; hCG – human chorionic gonadotropin

FERTILITY

Morphokinetic data	Euploid embryos (n=352)	Aneuploid embryos (n=593)			Mosaic embryos (n=22)			p-value
tPNa (hrs.)	6.15±0.16	6.55±0.12	0.394	0.001-0.787	6.75±0.63	0.595	-0.685-1.876	0.126
tPNf (hrs.)	22.50±0.157[a]	24.01±0.16[b]	0.997	0.48-1.51	24.81±0.79[a.b]	1.867	0.251-3.482	**< 0.001**
t2 (hrs.)	24.99±0.0[a]	26.8±0.172[b]	1.2	0.69-1.80	27.23±0.86[a.b]	1.68	-0.70-3.41	**< 0.001**
t3 (hrs.)	36.14±0.0[a]	38.08±0.20[b]	1.14	0.47-1.80	39.42±1.02[a.b]	2.47	0.40-4.54	**< 0.001**
t4 (hrs.)	37.25±0.22[a]	39.52±0.21[b]	1.55	0.85-2.24	39.75±1.07[a.b]	1.78	-0.39-3.9	**< 0.001**
t5 (hrs.)	49.86±0.41	50.53±0.31	0.76	-0.25-1.79	51.07±1.58	1.30	-1.90-4.51	**0.981**
t6 (hrs.)	50.78±000[a]	53.20±0.29[b]	1.42	0.450-2.39	55.26±1.49[a.b]	3.48	0.45-6.51	**< 0.001**
t7 (hrs.)	52.56±0.35[a]	53.65±0.42[b]	1.65	0.616-2.68	57.00±1.59[a.b]	1.65	0.11-6.58	**< 0.001**
t8 (hrs.)	55.43±0.51[a]	58.87±0.39[b]	2.22	0.95-3.49	60.4±1.94[a.b]	3.78	-0.17-7.73	**< 0.001**
tM (hrs.)	88.05±0.63[a]	88.0±0.48[b]	1.03	0.534-2.596	90.6±2.5[a.b]	5.56	0.50-10.62	**0.024**
tsB (hrs.)	96.68±0.69[a]	91.34±3.32[b]	2.23	0.53-3.92	98.90±0.52[a b]	-5.33	-11.98-1.30	**0.03**
tB (hrs.)	105.31±0.00[a]	109.64±0.477[b]	3.54	2.00-5.07	110.59±2.44[a.b]	4.49	0.45-9.44	**<0.001**
cc2 (hrs.)	11.3±0.13	11.28±0.10	-0.10	-0.46-0.24	12.19±0.54	0.79	-0.30-1.89	0.809
cc3 (hrs.)	12.7±0.25	12.44±0.20	-0.43	-1.09-0.22	11.65±1.00	-1.23	-3.27-0.81	0.327
s1 (hrs.)	2.5±0.04	2.64±0.03	0.10	-0.02-0.23	2.34±0.19	-0.186	-0.57-0.20	**0.108**
s2 (hrs.)	1.0±0.12[a]	1.3±0.09[b]	0.40	0.07-0.73	1.43±0.10[a,b]	-0.69	-1.71-0.33	**0.022**
s3 (hrs.)	7.0±0.38[a]	8.37±0.30[b]	1.28	0.30-2.26	9.35±1.50[a,b]	2.26	-0.79-5.32	**0.006**
MN (2 cell stage) %	32.0±2.8	36.0±2.3	0.20	-0.11-0.52	56.0±0.11	1.00	0.03-1.96	0.275
MN (4 cell stage) %	7.5±1.5	7.9±1.2	0.19	-0.37-0.76	11.0±7.4	0.52	-1.01-2.06	0.845

FERTILITY

Morphokinetic data	Euploid embryos (n=352)	Aneuploid embryos (n=593)			Mosaic embryos (n=22)			p-value
tPNa (hrs.)	6.15±0.16	6.55±0.12	0.394	0.001-0.787	6.75±0.63	0.595	-0.685-1.876	0.126
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t6 (hrs.)	50.78±000[a]	53.20±0.29[b]	1.42	0.450-2.39	55.26±1.49[a.b]	3.48	0.45-6.51	**< 0.001**
t7 (hrs.)	52.56±0.35[a]	53.65±0.42[b]	1.65	0.616-2.68	57.00±1.59[a.b]	1.65	0.11-6.58	**< 0.001**
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tM (hrs.)	88.05±0.63[a]	88.0±0.48[b]	1.03	0.534-2.596	90.6±2.5[a.b]	5.56	0.50-10.62	**0.024**
tsB (hrs.)	96.68±0.69[a]	91.34±3.32[b]	2.23	0.53-3.92	98.90±0.52[a b]	-5.33	-11.98-1.30	**0.03**
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cc2 (hrs.)	11.3±0.13	11.28±0.10	-0.10	-0.46-0.24	12.19±0.54	0.79	-0.30-1.89	0.809
cc3 (hrs.)	12.7±0.25	12.44±0.20	-0.43	-1.09-0.22	11.65±1.00	-1.23	-3.27-0.81	0.327
s1 (hrs.)	2.5±0.04	2.64±0.03	0.10	-0.02-0.23	2.34±0.19	-0.186	-0.57-0.20	**0.108**
s2 (hrs.)	1.0±0.12[a]	1.3±0.09[b]	0.40	0.07-0.73	1.43±0.10[a,b]	-0.69	-1.71-0.33	**0.022**
s3 (hrs.)	7.0±0.38[a]	8.37±0.30[b]	1.28	0.30-2.26	9.35±1.50[a,b]	2.26	-0.79-5.32	**0.006**
MN (2 cell stage) %	32.0±2.8	36.0±2.3	0.20	-0.11-0.52	56.0±0.11	1.00	0.03-1.96	0.275
MN (4 cell stage) %	7.5±1.5	7.9±1.2	0.19	-0.37-0.76	11.0±7.4	0.52	-1.01-2.06	0.845
KIDScore day 5	**6.52±0.13[a]**	**5.54±0.10[b]**	**-0.97**	**-1.30 - -0.64**	**4.62±0.49[a.b]**	**-1.89**	**-2.89 - -0.88**	**< 0.001**

FERTILITY

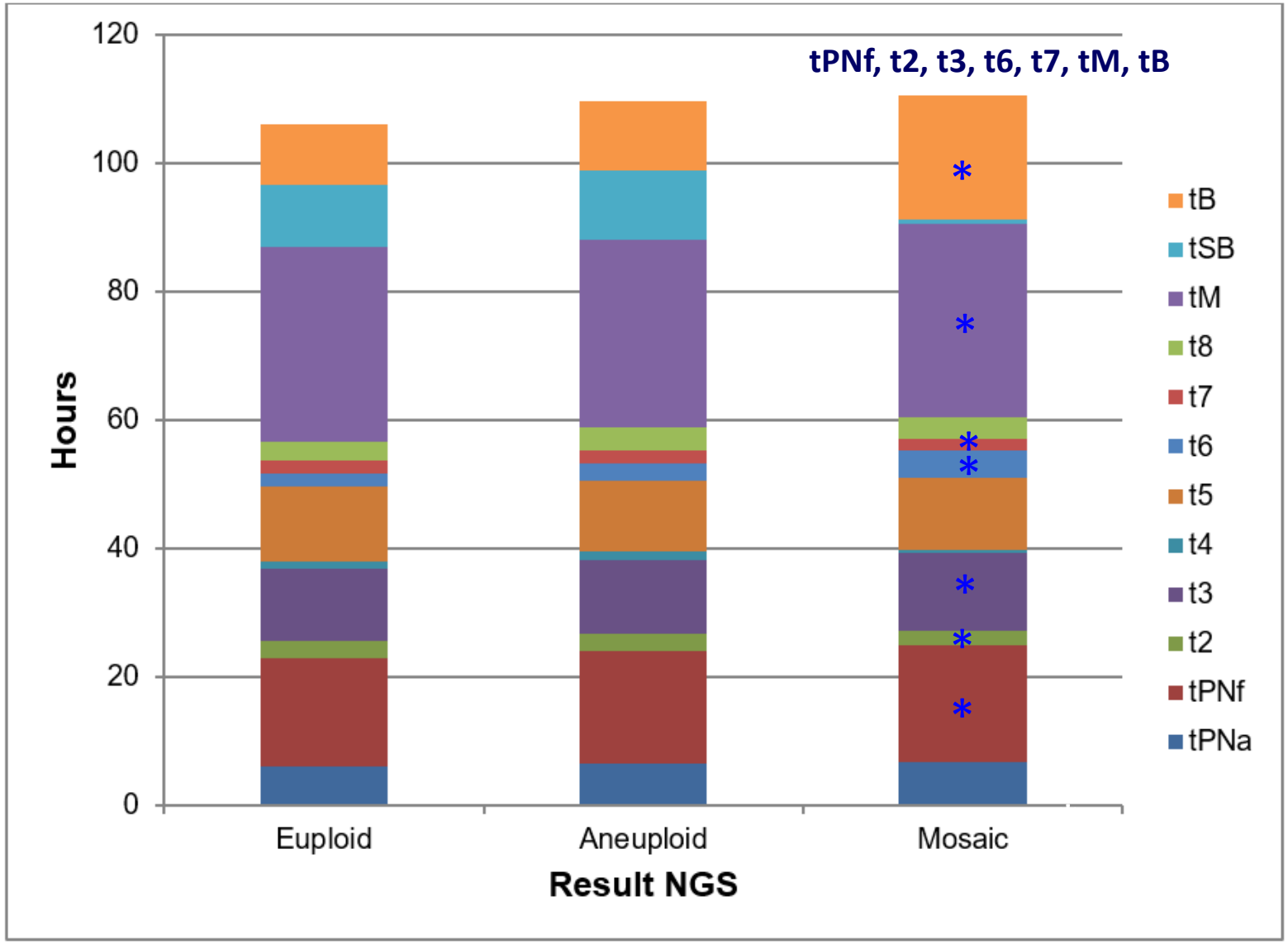


Figure 1: A comparison of the cumulative morphokinetic development of euploid, aneuploidy and mosaic embryos.

FERT

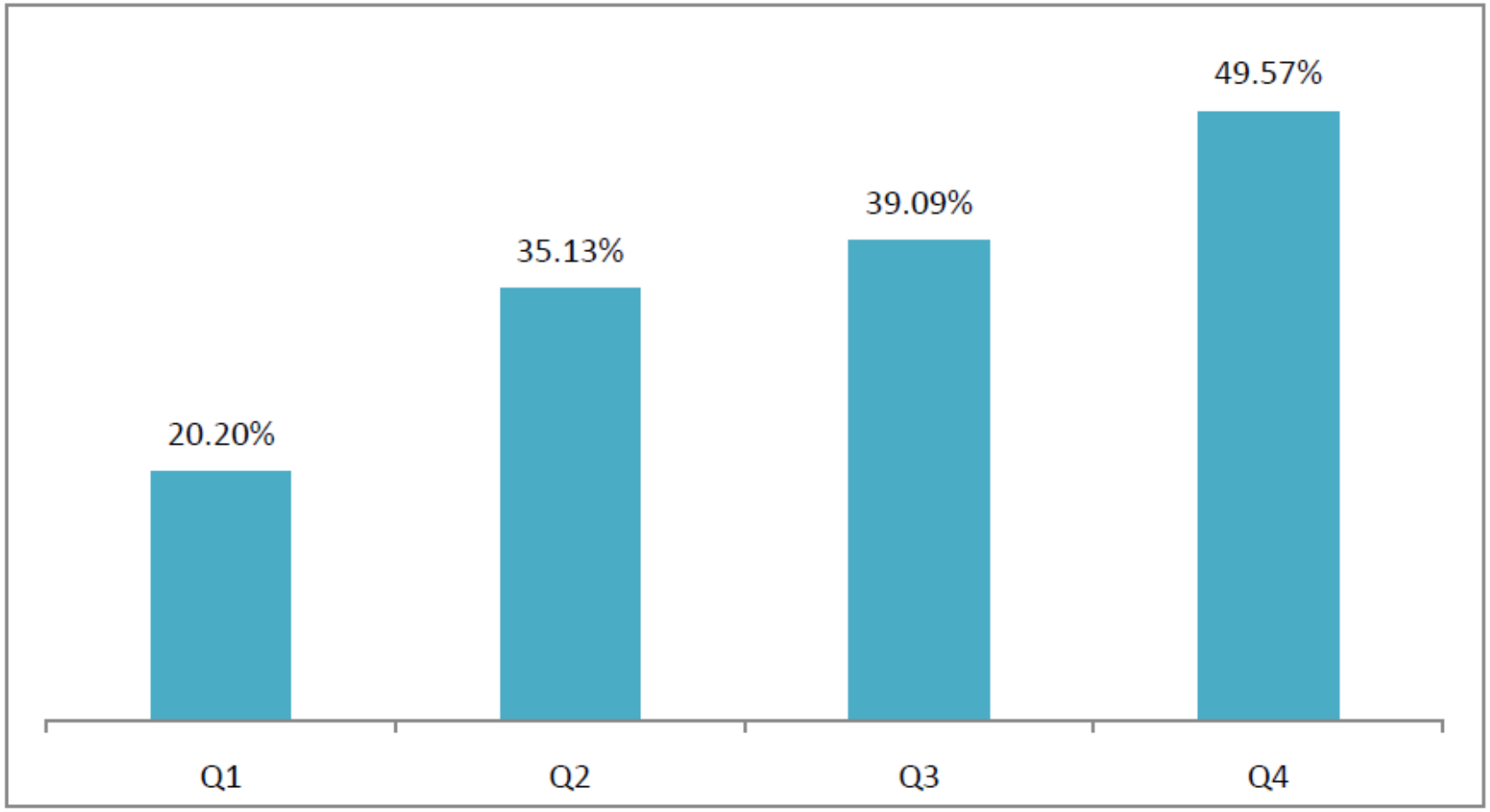


Figure 2: Distribution of the percentage of euploid embryos into the KIDScore D 5 categories, Q1 ≤3.9, Q2, between 4 and 5.6, Q3 between 5.7 and 7.5, and Q4 ≥7.6

FERTILITY

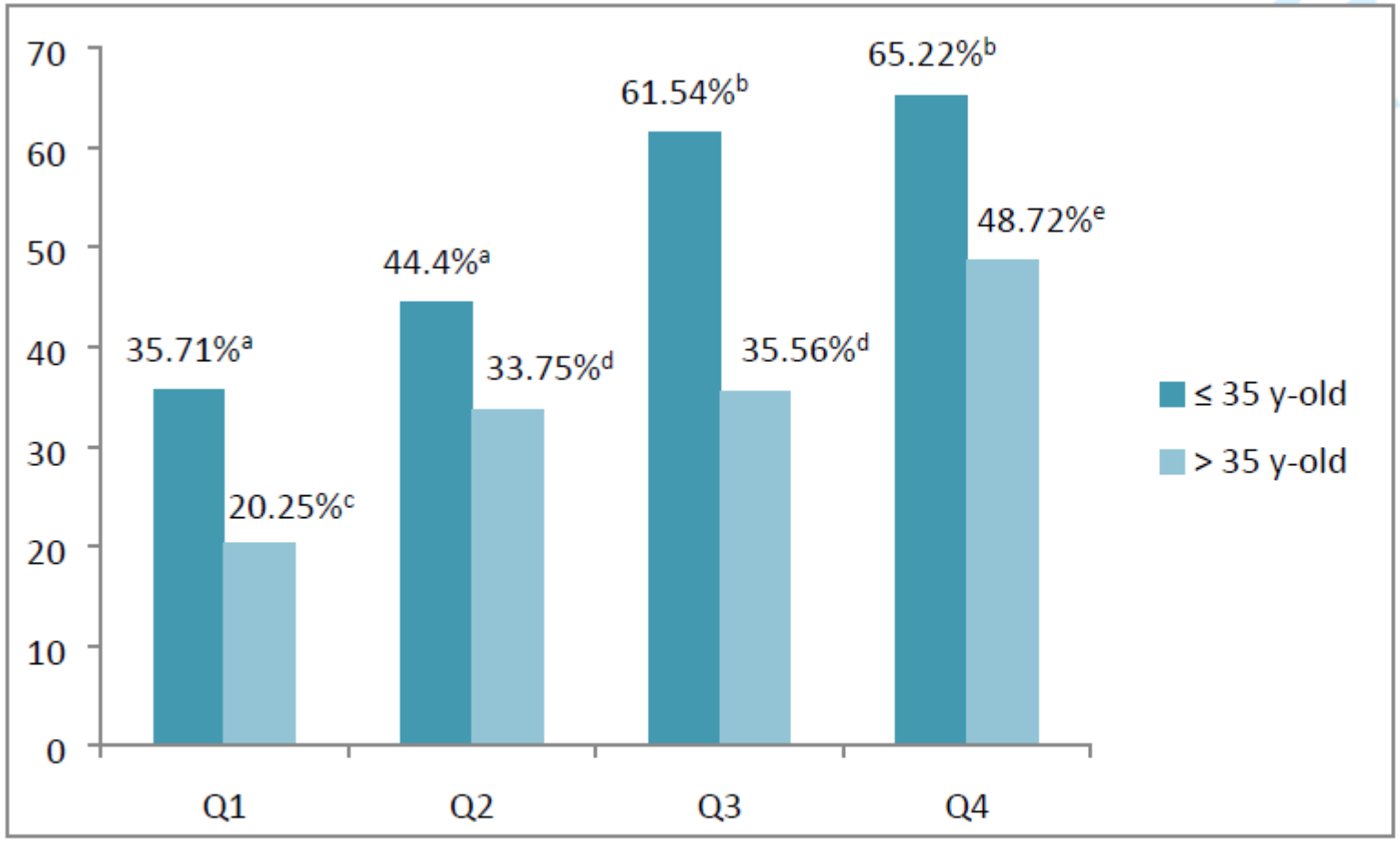
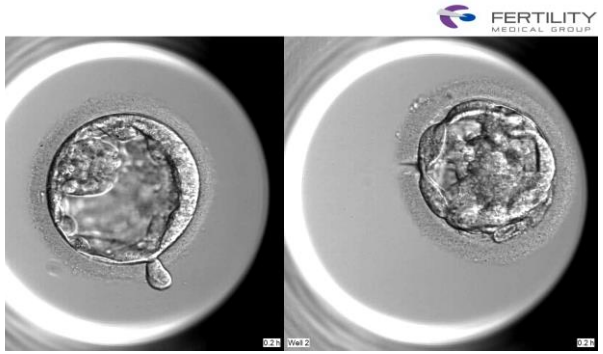


Figure 3: The distribution of the chance of being euploid according with the KIDScore D 5 category: Q1 ≤3.9, Q2 between 4 and 5.6, Q3 between 5.7 and 7.5, and Q4 ≥7.6. a≠b≠c≠d≠e.

Utilização do EMBRYOSCOPE no Descongelamento de embriões

FERTILITY MEDICAL GROUP

Data: **21/02/2022**



Dinâmica Morfológica Embrionária pós aquecimento

First Embryo for Transfer

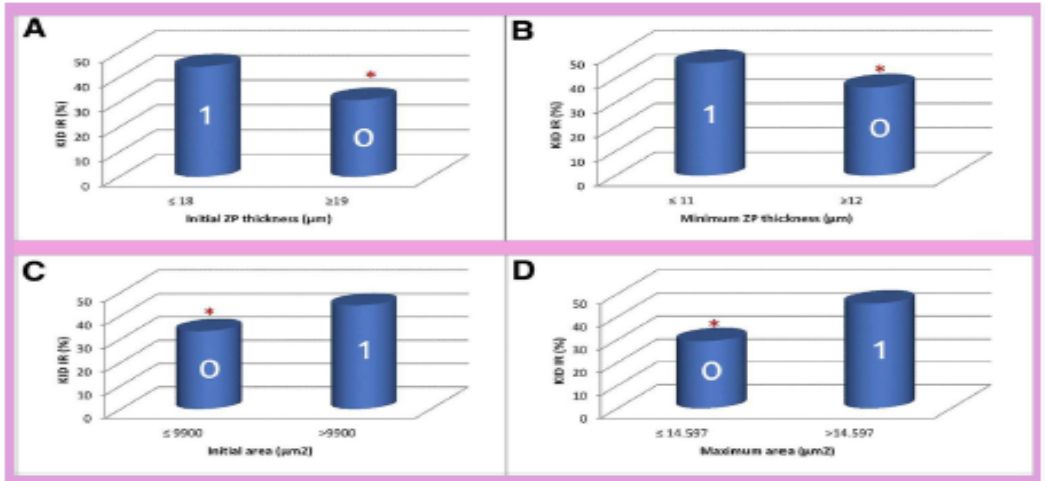
Número Embrião	Espessura ZP Inicial (A)	Pontuação ZP Inicial (A)	Espessura ZP Final (B)	Pontuação ZP Final (B)	Área BL Inicial (C)	Pontuação BL Inicial (C)	Área BL Final (D)	Pontuação BL Final (D)	Total	Expansão (E)
1	14 µ	1	10 µ	1	13782 µ²	1	20367 µ²	1	4	SIM

Second Embryo for Transfer

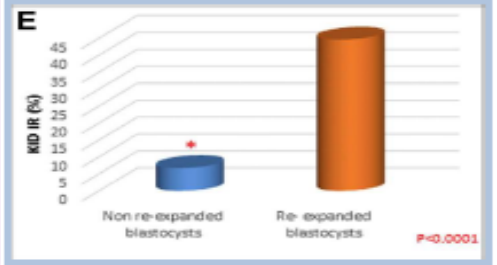
Número Embrião	Espessura ZP Inicial (A)	Pontuação ZP Inicial (A)	Espessura ZP Final (B)	Pontuação ZP Final (B)	Área BL Inicial (C)	Pontuação BL Inicial (C)	Área BL Final (D)	Pontuação BL Final (D)	Total	Expansão (E)
2	16 µ	1	14 µ	0	10973 µ²	1	19477 µ²	1	3	SIM

Pontuação: 0 = < taxa de implantação | 4 = > taxa de implantação

Valores de referência:



Percentual de blastocistos implantados com variáveis dinâmicas morfológicas dentro ou além das faixas definidas pelos limites do quartil para o total conjunto de dados. Os quatro painéis mostram faixas e implantação para (A) espessura inicial de zona pelúcida, * P=.02; (B) espessura mínima zona pelúcida, * P=.03; (C) área do blastocisto inicial * P=.04; e (D) área máxima do blastocisto, * P=.004



(E) Taxa de implantação dos blastocistos de acordo com a expansão da blastocele

Valores de referência segundo *Coello. Analysis of the morphological dynamics of blastocysts after vitrification/warming: defining new predictive variables of implantation. Fertil Steril. 2017.*

Em embriões com o *Assisted Hatching* realizado previamente a espessura da zona pelúcida pode não sofrer alterações na medida.

Utilização do EMBRYOSCOPE no Descongelamento de embriões

30 ciclos, 44 embriões transferidos

Taxa de gestação:

- **Espessura inicial zona pelúcida OR: 0.712, CI: 0.530 – 0.955, p: 0.023**
- **Espessura final zona pelúcida OR: 0.647, CI: 0.468 – 0.894, p: 0.008**
- **Taxa de gestação de acordo com a pontuação final total do blastocisto:**

  0: 0.0% vs 1: 42.9% vs 2: 77.8% vs 3: 41.7% vs 4: 77.8%, $p<0.001$

  0≠1 ($p=0.022$), 0≠2 ($p<0.001$), 0≠3 ($p=0.003$), 0≠4 ($p<0.001$)

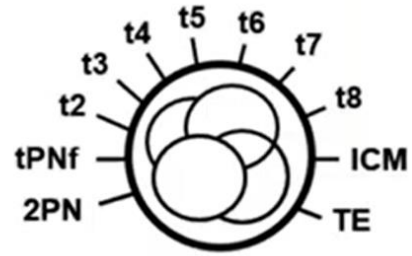
FERTILITY

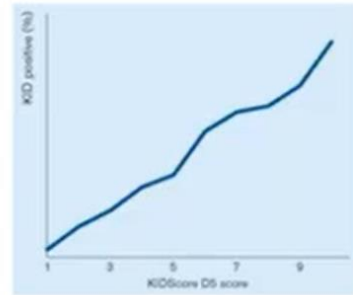
EMBRYO ANNOTATION AND SELECTION

Embryologist

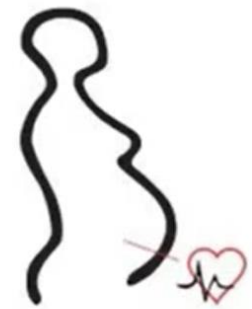
AI (indirect)

AI (direct)



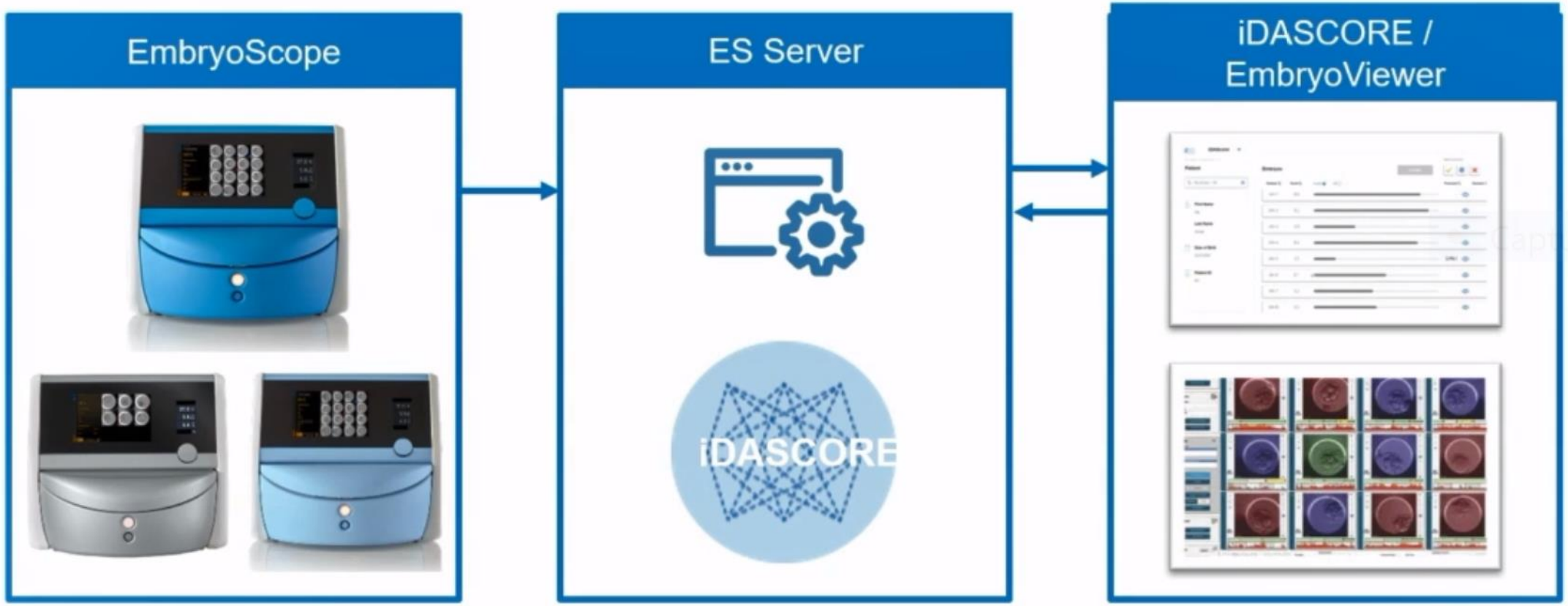


Implantation model



Ongoing pregnancy

FERTILITY

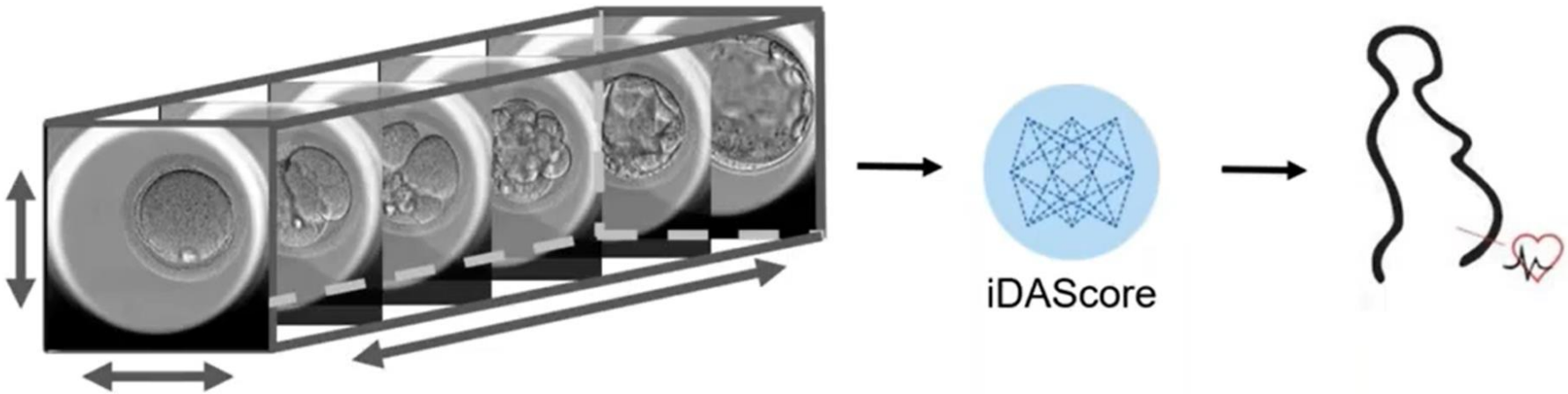


FERTILITY

IDASCORE

- Full time-lapse sequences
- 18 clinics
- Linked to fetal heartbeat (FH)

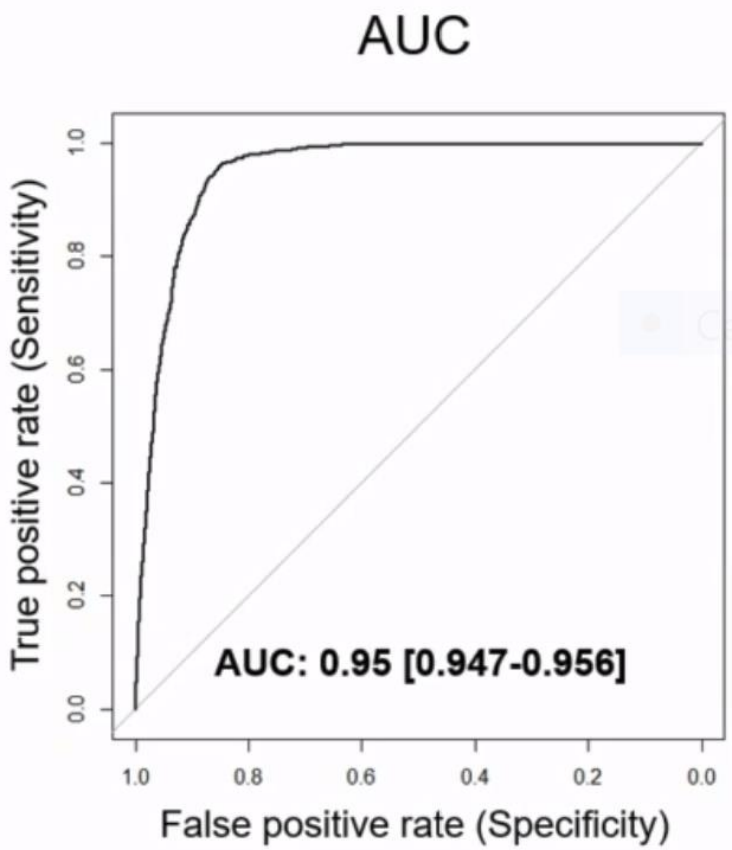
	IVY	iDAScore
FH+	694	4,337
FH-	1,079	10,307
Discards	7,063	101,188
Total	**8,836**	**115,832**



FERTILITY

EVALUATING iDASCORE

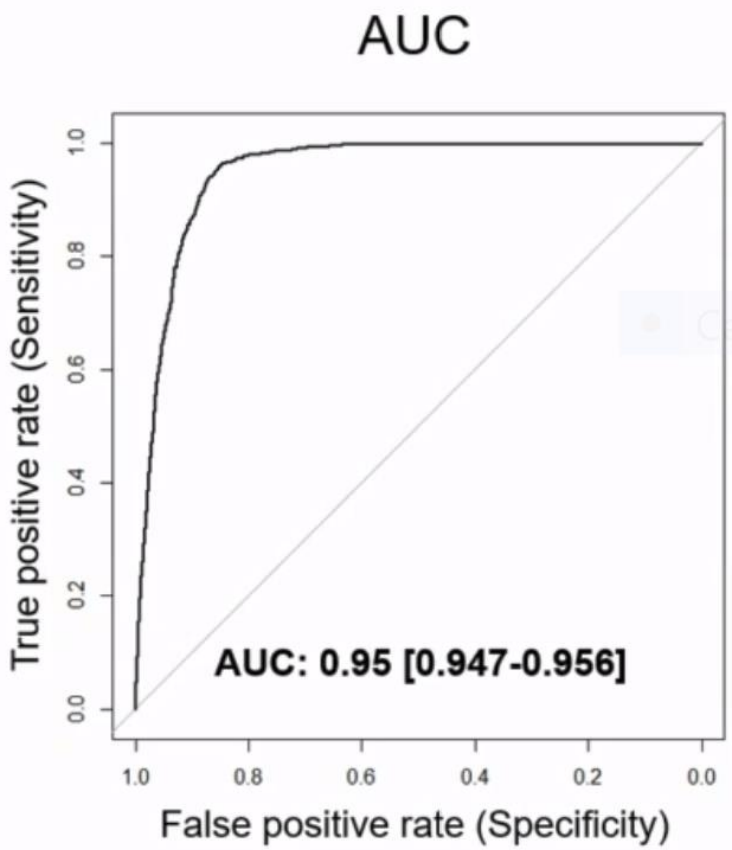
iDASCORE	Test
Clinics	18
Embryos	17.249
Positive fetal heartbeat	661
Negative fetal heartbeat	1.551
Discards	15.037



FERTILITY

EVALUATING iDASCORE

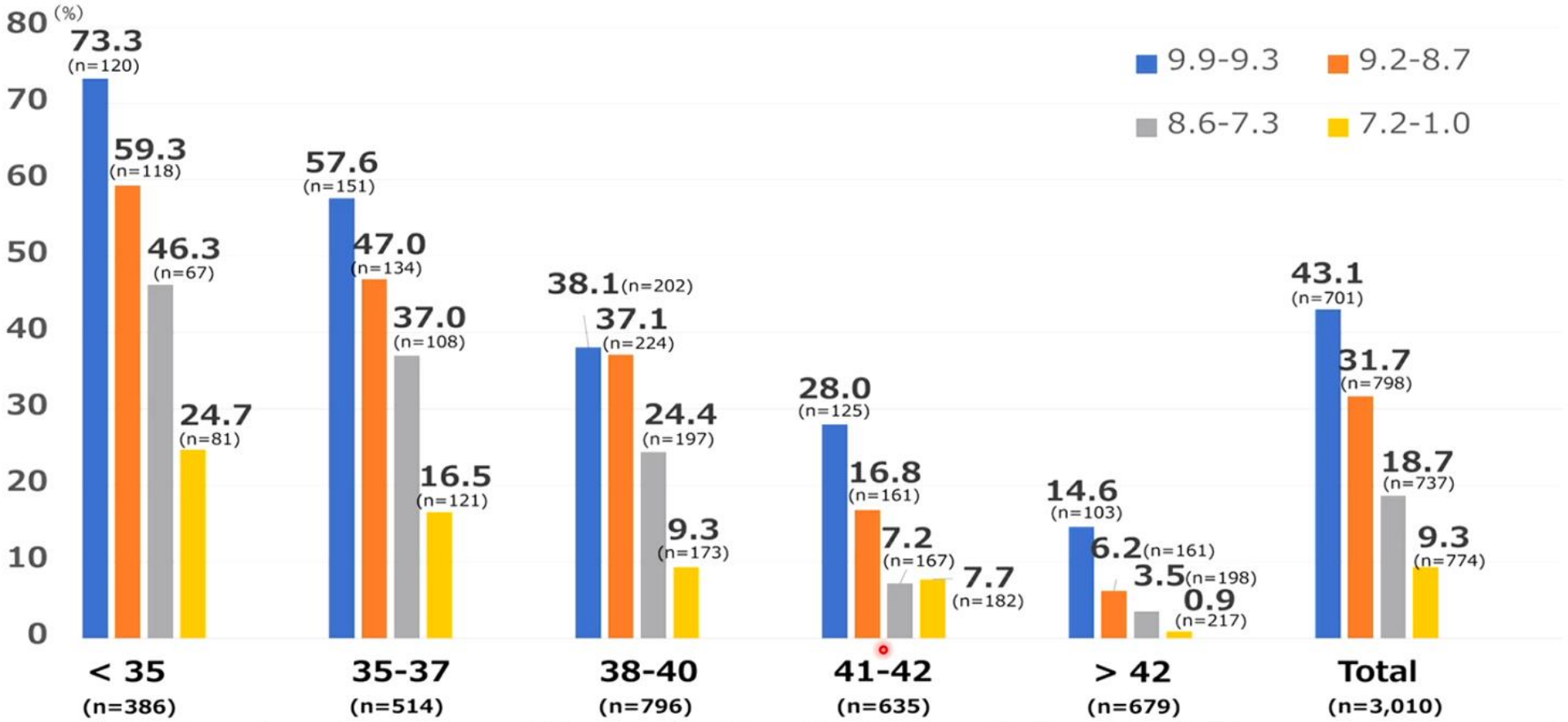
Area Under the Curve (AUC)	Diagnostic Test Quality
1.0-0.9	Excellent
0.9-0.8	Very Good
0.7-0.8	Good
0.6-0.7	Sufficient
0.5-0.6	Poor
<0.5	Test not usefull
Source: Šimundić, A.M., 2009. Measures of diagnostic accuracy: basic definitions. Ejifcc, 19(4), p.203.	



FERTILITY

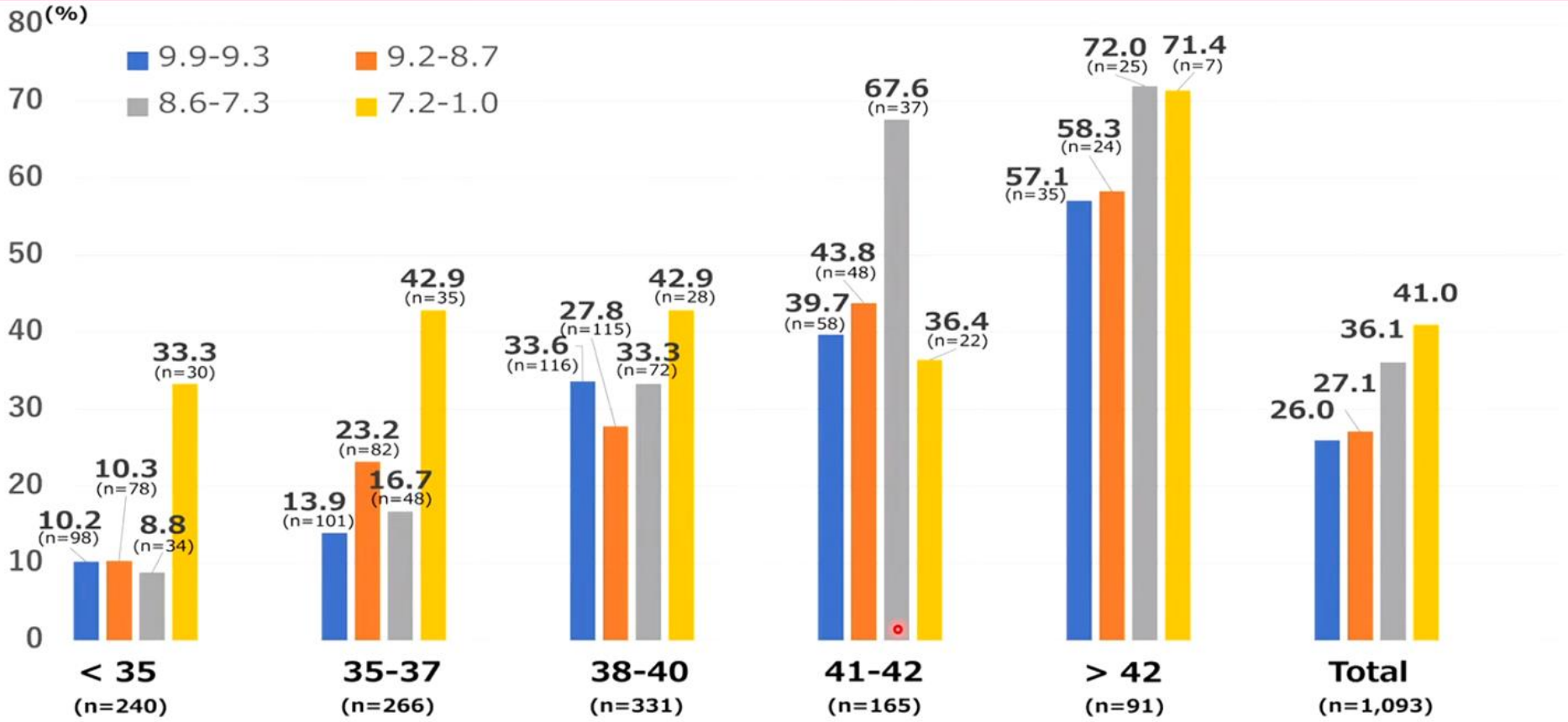
European Society of Human Reproduction and Embryology

The correlation between LB rates and each iDAScore group stratified by SART maternal age groups.



In each maternal age group, LB rates significantly decreased when the iDAScore group decreased ($P<0.05$)

The correlation between miscarriage rates and each iDAScore group stratified by maternal age



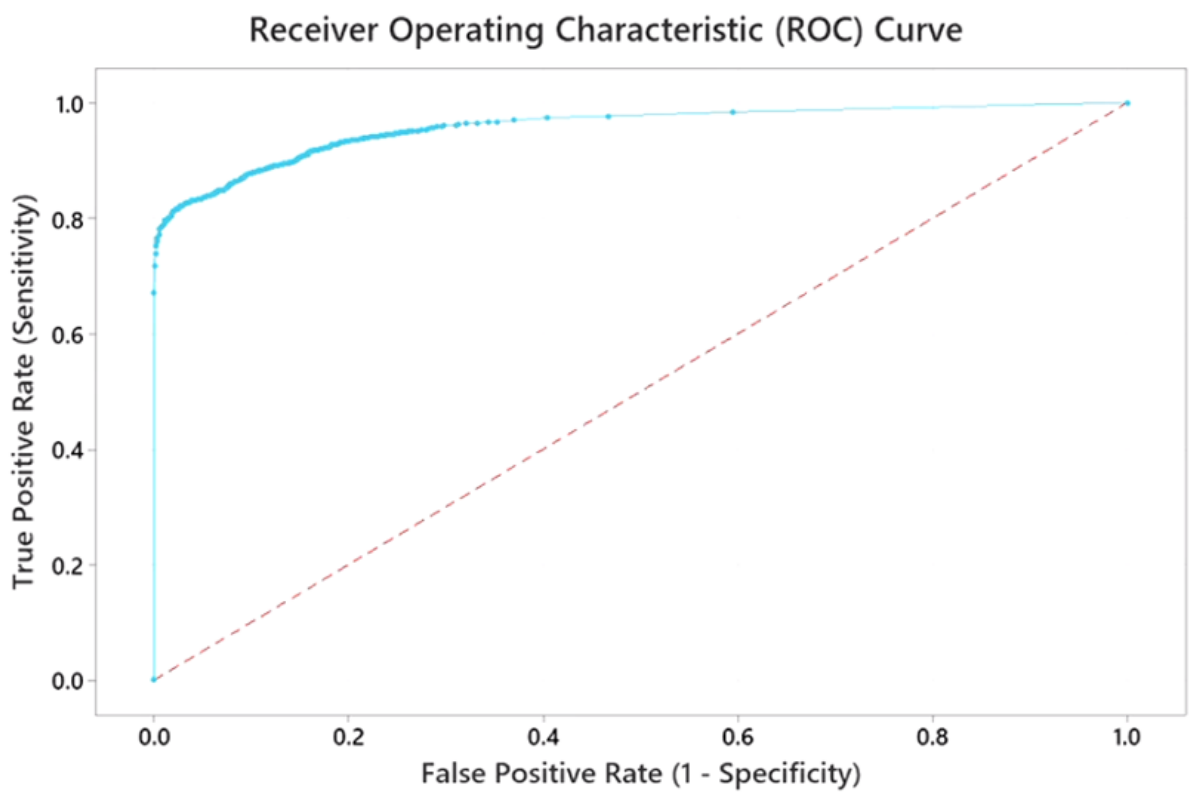
TM rates significantly increased progressively with decreasing iDAScores, except in the 38–40 year-old group and >42 years-old group ($P<0.05$).

Automatic morphokinetic assessment

Meet CHLOE.

Fairtility

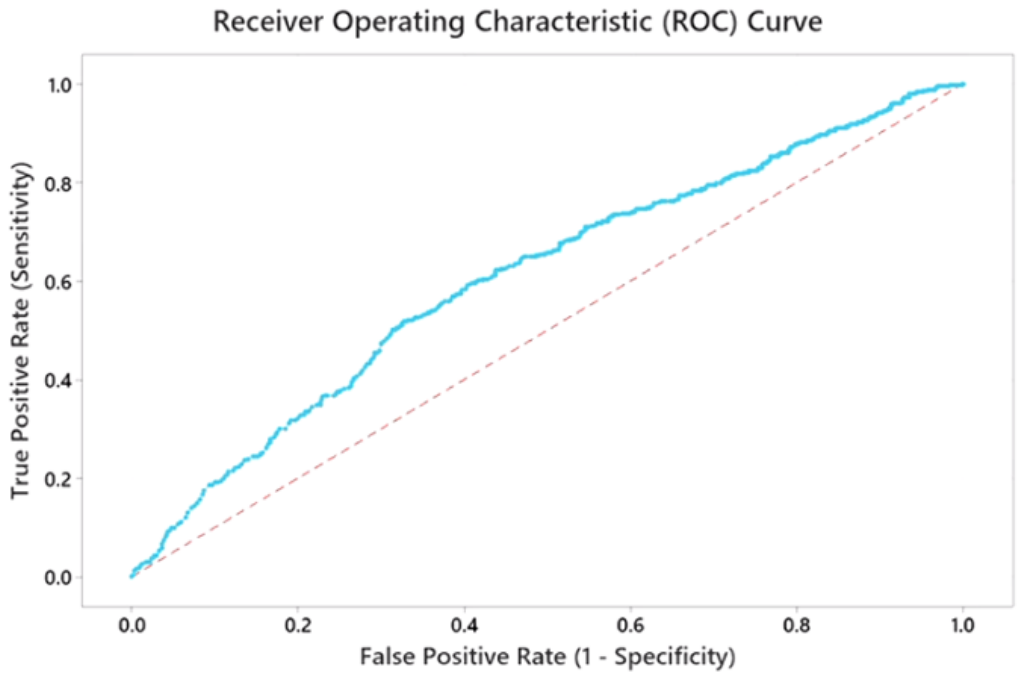
FERTILITY



Area Under Curve = 0.9578

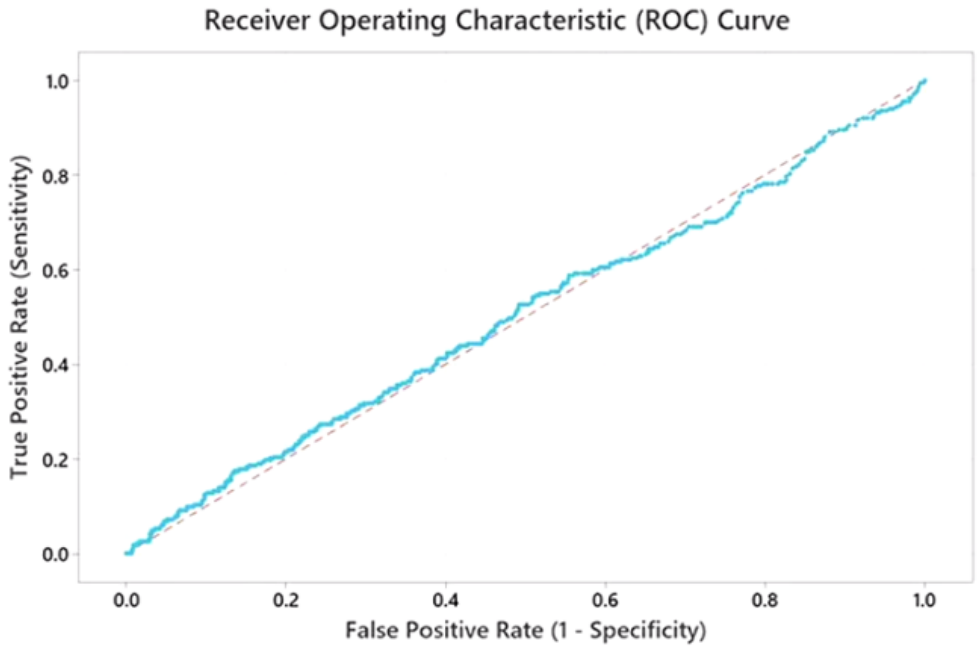
FERTILITY

CHLOE-EQ score for euploidy
(AUC=0.61, baseline=34% (501/1456), p<0.001)



Area Under Curve = 0.6077

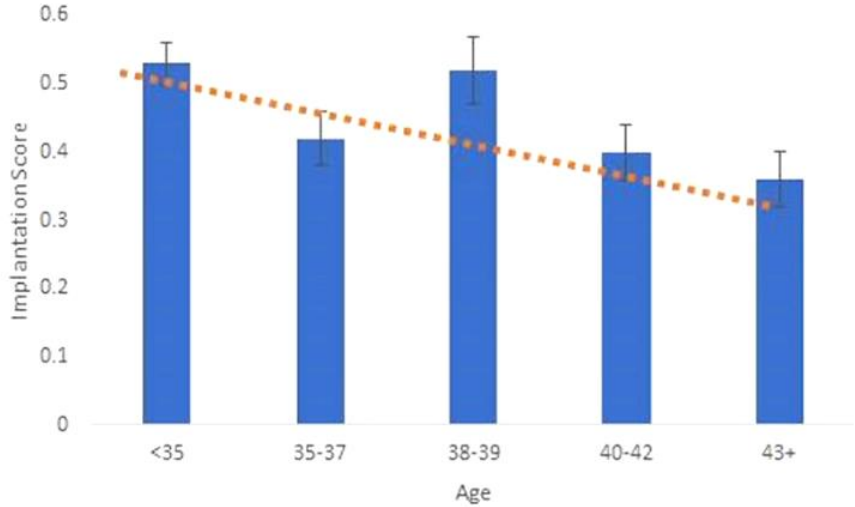
CHLOE-EQ score for mosaicism (AUC=0.5, baseline=19% (276/1456), p>0.05)



Area Under Curve = 0.5044

FERTILITY

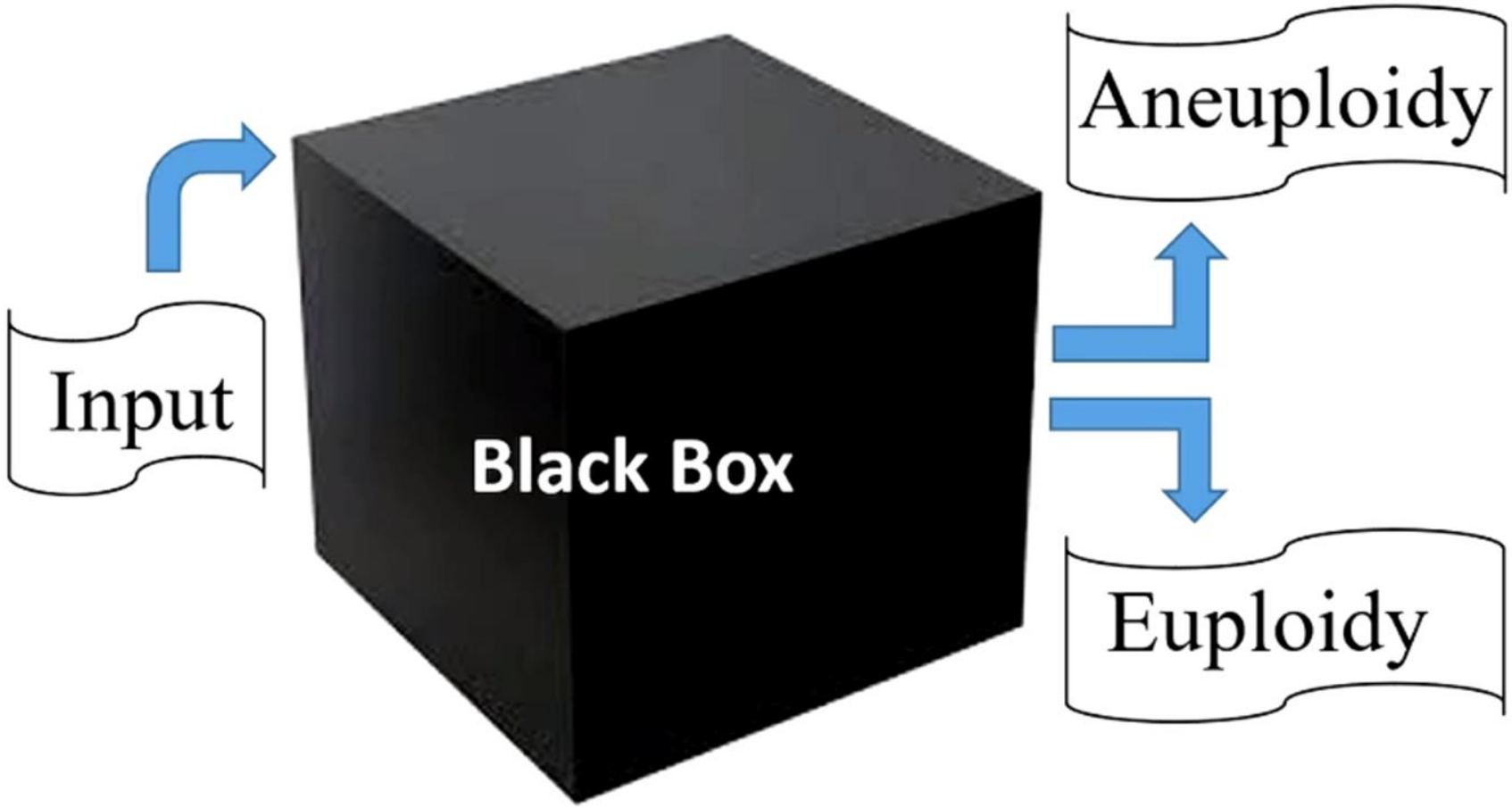
- Following SET of non-PGT-A embryos, CHLOE-EQ score decreased with increasing age ($p<0.001$).



- The type of aneuploidy (such as monosomy, trisomy, segmental) did not affect CHLOE-EQ score or CHLOE BLAST score ($p>0.05$).

FERTILITY

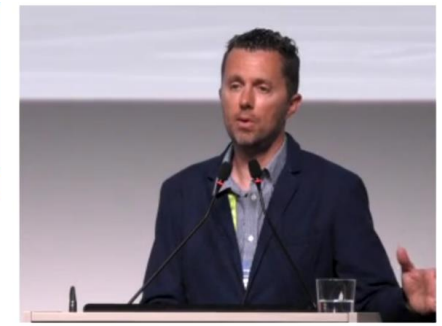
- Noninvasive PGT: Current Status

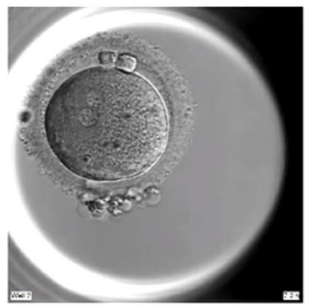
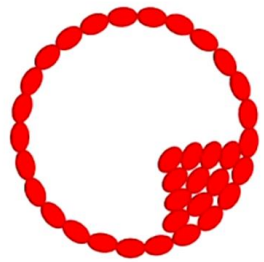
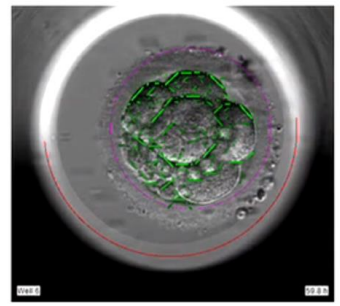
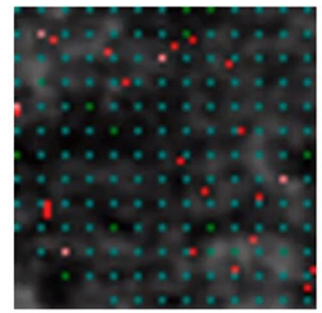
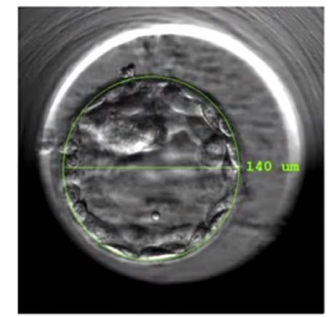


FERTILITY

IVIRMA Global Valencia | AIVF Israel

Results



Morphokinetics	Morphology	Cell división activity	Mitochondrias	Pumping events
				
52% accuracy ($p<0.05$)	68% accuracy ($p<0.05$)	73% accuracy ($p<0.05$)	77% accuracy ($p<0.05$)	56% accuracy ($p<0.05$)

Integrating all five features into a non-invasive AI model

While all 5 biological features are biologically distinct, they are not allways statistically independent from each other.

-The model was calculated with a 2/3 overlap between five features.

- Accuracy was calculated in the midpoint between the one in which the features were statistically independent and the accuracy for the worst-case scenario with 2/3 statistically dependent.

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Results

Validation

375 embryos(148 euploid, 227 aneuploid)

Output Class \ Target Class	Aneuploid	Euploid	
Aneuploid	208 (55.5%)	32 (8.5%)	86.7% 13.3%
Euploid	19 (5.1%)	116 (30.9%)	85.9% 14.1%
	91.6% 8.4%	78.4% 21.6%	86.4% 13.6%

Test

375 embryos (151 euploid, 224 aneuploid)

Output Class \ Target Class	Aneuploid	Euploid	
Aneuploid	210 (56%)	21 (5.6%)	90.9% 9.1%
Euploid	14 (3.7%)	130 (34.7%)	90.3% 9.7%
	93.8% 6.2%	86.1% 13.9%	90.7% 9.3%

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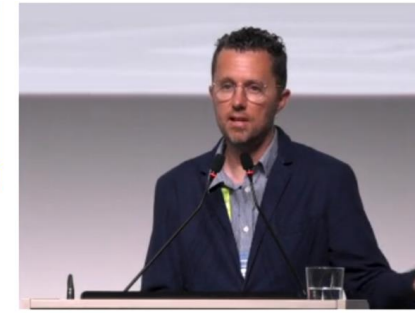

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93,8% sensibility

86,1% specificity

90,7% precision

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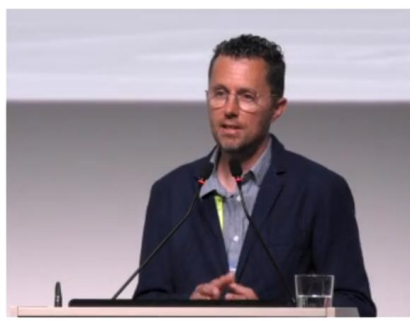
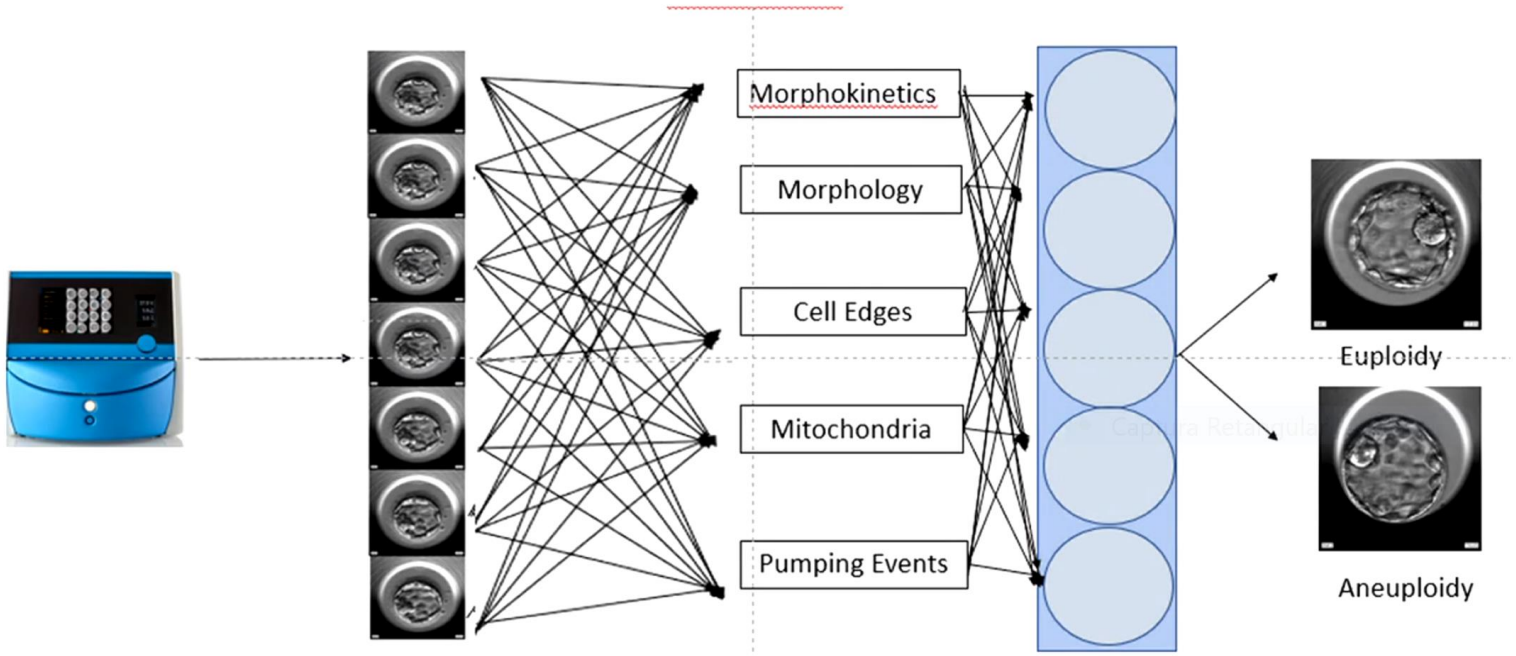
Results



2nd phase: from conception to product



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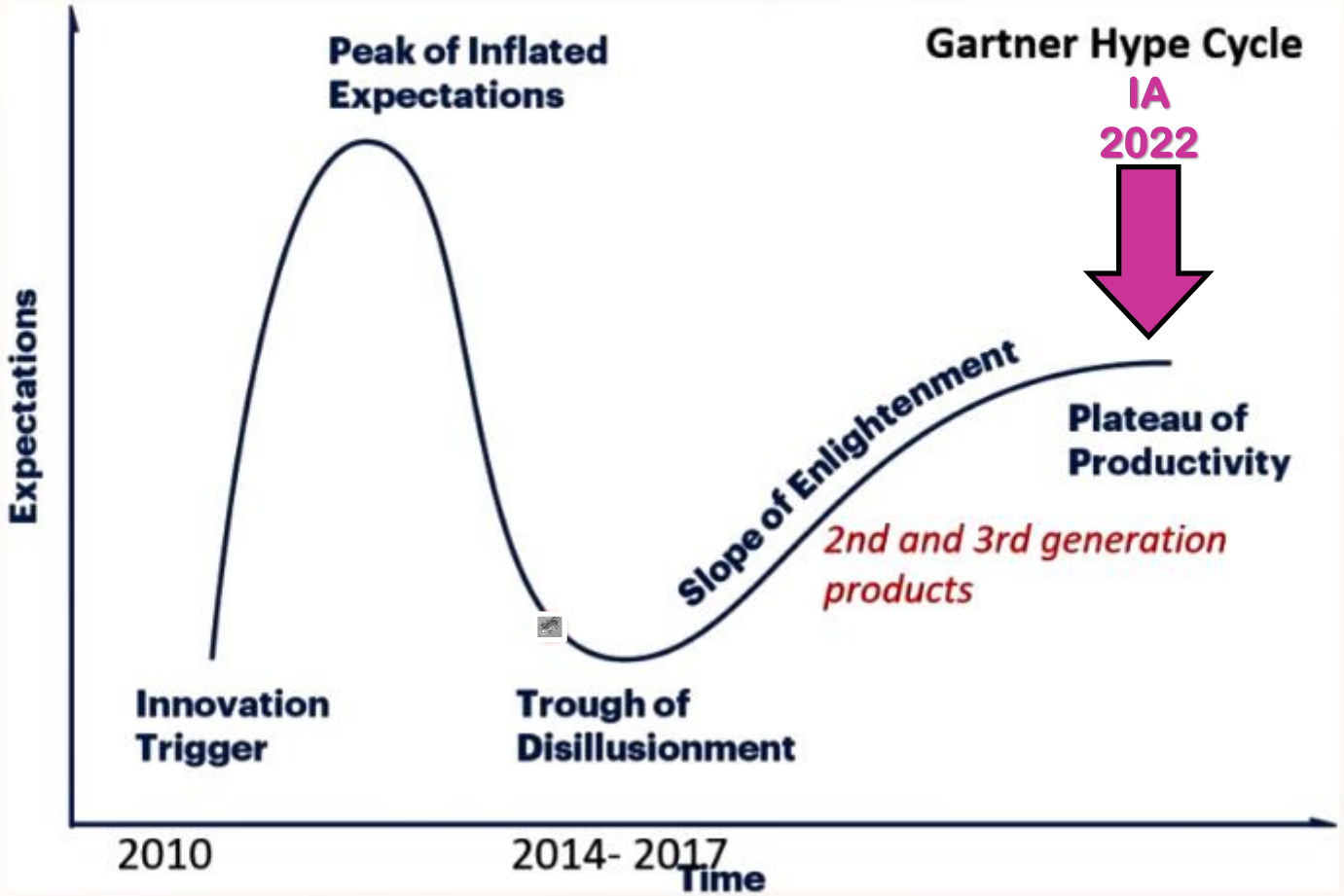
Gartner Hype cycle

Five key phases of a technology's life cycle



Take home message

- Ambiente de cultivo mais estável e seguro
- Disponibilização para o casal/paciente as imagens e vídeos dos embriões
- Maior precisão para a seleção e definição sobre a transferência embrionária
- Maior clareza do prognóstico - informação para casal/paciente

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Take home message

- Melhor entendimento das diversas situações clínicas que podem interferer no desenvolvimento embrionário
- Melhores taxas de implantação e gestação
- Predizer EUPLOIDIA ??

FERTILITY

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Margaret Meira
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FERTILITY

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ENQUETES
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INSTITUTO SAPIENTIAE
AULAS MINISTRADAS
VÍDEOS TÉCNICOS

AULAS MINISTRADAS

2022 2021 2020 2019 2018 2017 2016 2015

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Obrigado!

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FERTILITY
MEDICAL GROUP

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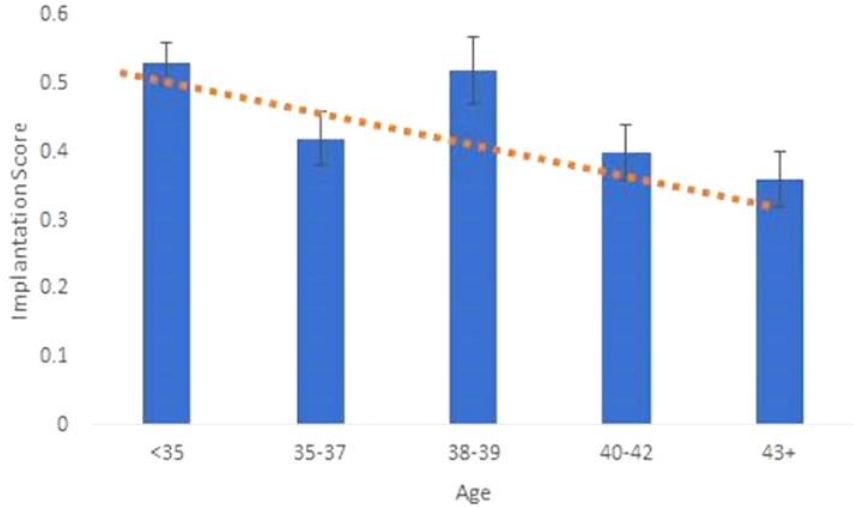
FERTILITY

- Following SET of non-PGT-A embryos, CHLOE-EQ score decreased with increasing age ($p<0.001$).



- The type of aneuploidy (such as monosomy, trisomy, segmental) did not affect CHLOE-EQ score or CHLOE BLAST score ($p>0.05$).

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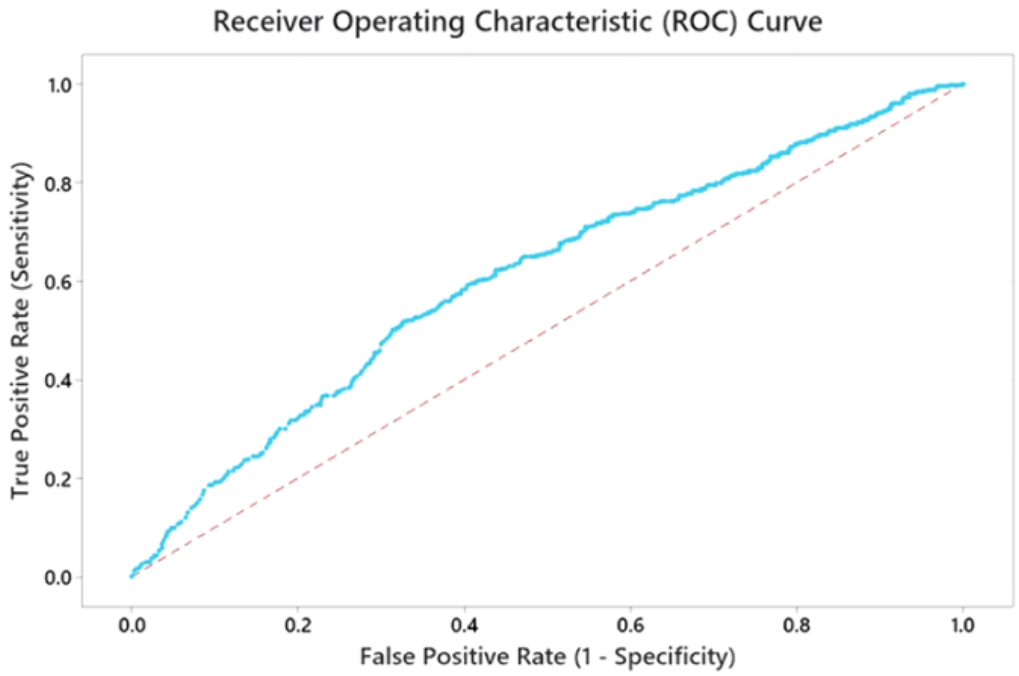
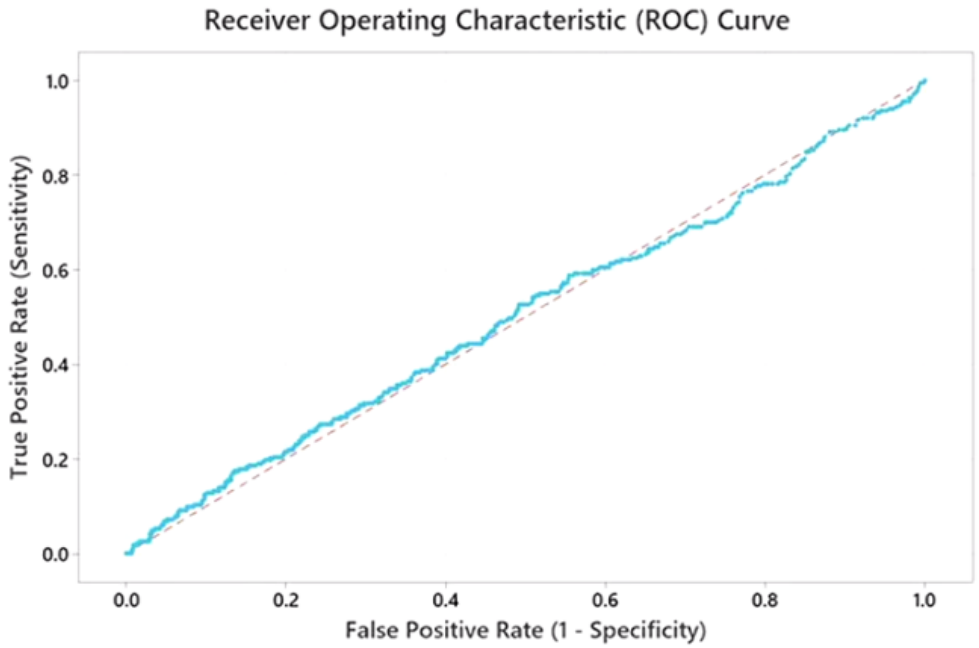
CHLOE-EQ score for euploidy
(AUC=0.61, baseline=34% (501/1456), p<0.001)



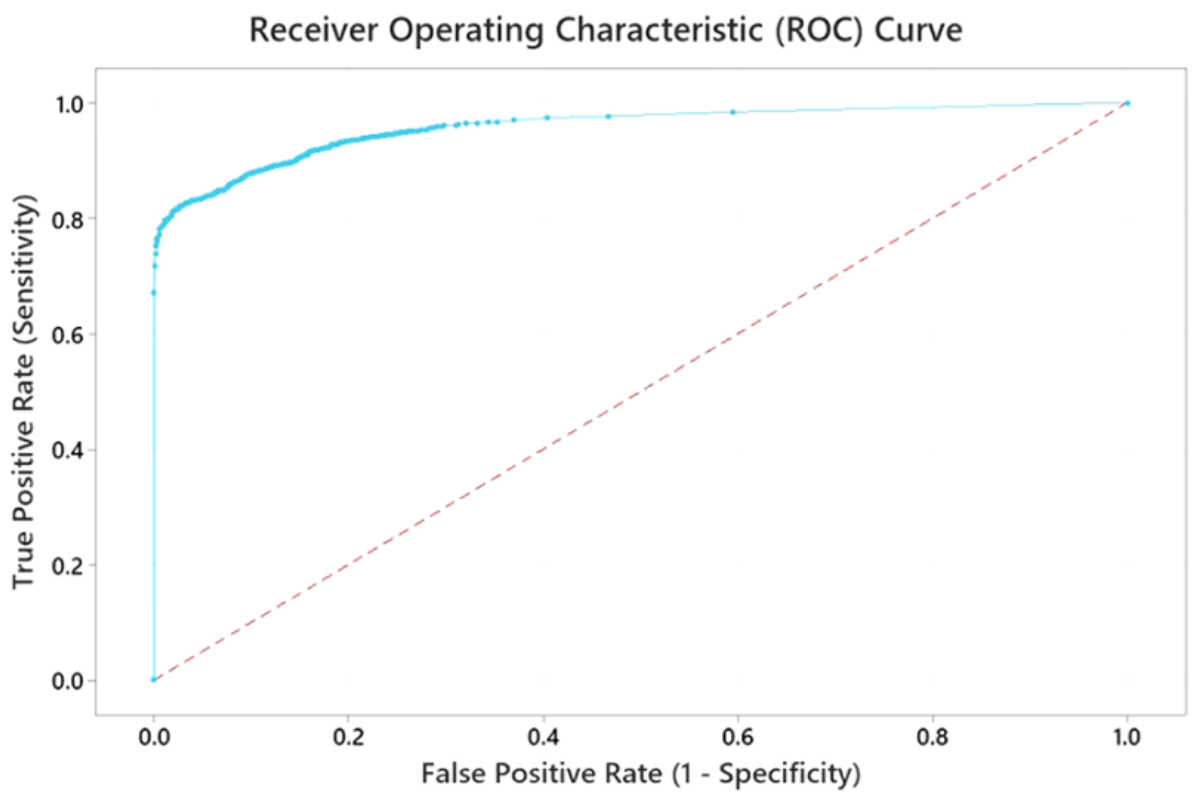
Area Under Curve = 0.6077

CHLOE-EQ score for mosaicism (AUC=0.5, baseline=19% (276/1456), p>0.05)



Area Under Curve = 0.5044

FERTILITY



Area Under Curve = 0.9578

FERTILITY

Automatic morphokinetic assessment

FERTILITY

Events	n	AI		Embryologist		ICC	CCC
		Mean	SD	Mean	SD		
tPNa	3415	8.44	3.69	8.69	3.26	0.78	0.78
tPNf	3467	24.57	5.32	24.79	5.02	0.89	0.89
t2	3486	27.57	5.89	27.64	5.62	0.91	0.91
t3	3458	36.85	7.29	37.33	6.9	0.89	0.89
t4	3397	41.36	9.39	39.77	7.6	0.73	0.73
t5	3333	49.38	9.62	48.84	9.49	0.83	0.83
t6	3257	53.24	9.54	53.06	9.52	0.86	0.86
t7	3123	58.42	12.13	55.92	9.91	0.63	0.63
t8	2993	62.89	12.91	59.65	10.99	0.68	0.68
t9	2932	71.80	11.23	68.34	11.85	0.66	0.66
tM	2553	84.66	9.67	89.81	9.75	0.71	0.71
tSB	2278	98.65	8.36	99.24	8.62	0.92	0.92
tB	1899	105.47	7.94	105.52	7.85	0.91	0.91
tEB	647	110.45	7.94	110.54	7.78	0.79	0.79

FERTILITY

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Very strong agreement

Strong agreement

N:number, AI: Artificial Intelligence, SD: Standard Deviation, ICC: Intraclass Correlation Coefficient, CCC: Concordance Correlation Coefficient

According to Bland-Altman (BA) analysis method; very weak (0-0.2), weak (0.21-0.4), moderate (0.41-0.6), strong (0.61-0.8), very strong (0.81-1.00)

WHAT IS KNOWN ABOUT AI IN IVF

- Tran et al.2018;
  Fetal hearth pregnancy →AUC 0.90
- Friedenthal et al.2021;
  Implantation rate (AI vs Embriologist) →65.3% vs 57.8%, p<0.0001
  Ongoing pregnancy/live birth rate →54.7% vs 48.1%, p=0.0001
- Zhan et al.2020;
  Prediction of Blastocyst Score for implantation →AUC= 0.606 (95% CI 0.581, 0.631)
  Euploidy prediction →AUC = 0.698 (95% CI 0.681, 0.715)
- Chavez-Badiola et al.2020;
  Euploidy prediction (ERICA) → AUC 0.79 (accuracy of 0.70)
- Huang et al. 2021;
  Euploidy predicition (EPA)→ AUC 0.8
- Bori et al. 2021;
  AI combined with proteomic (MMP-1 and IL-6) →euploidy prediction→ AUC of 1.0

Results: Unadjusted and adjusted odds ratio in iDAScore for neonatal characteristics in singletons following SVBT

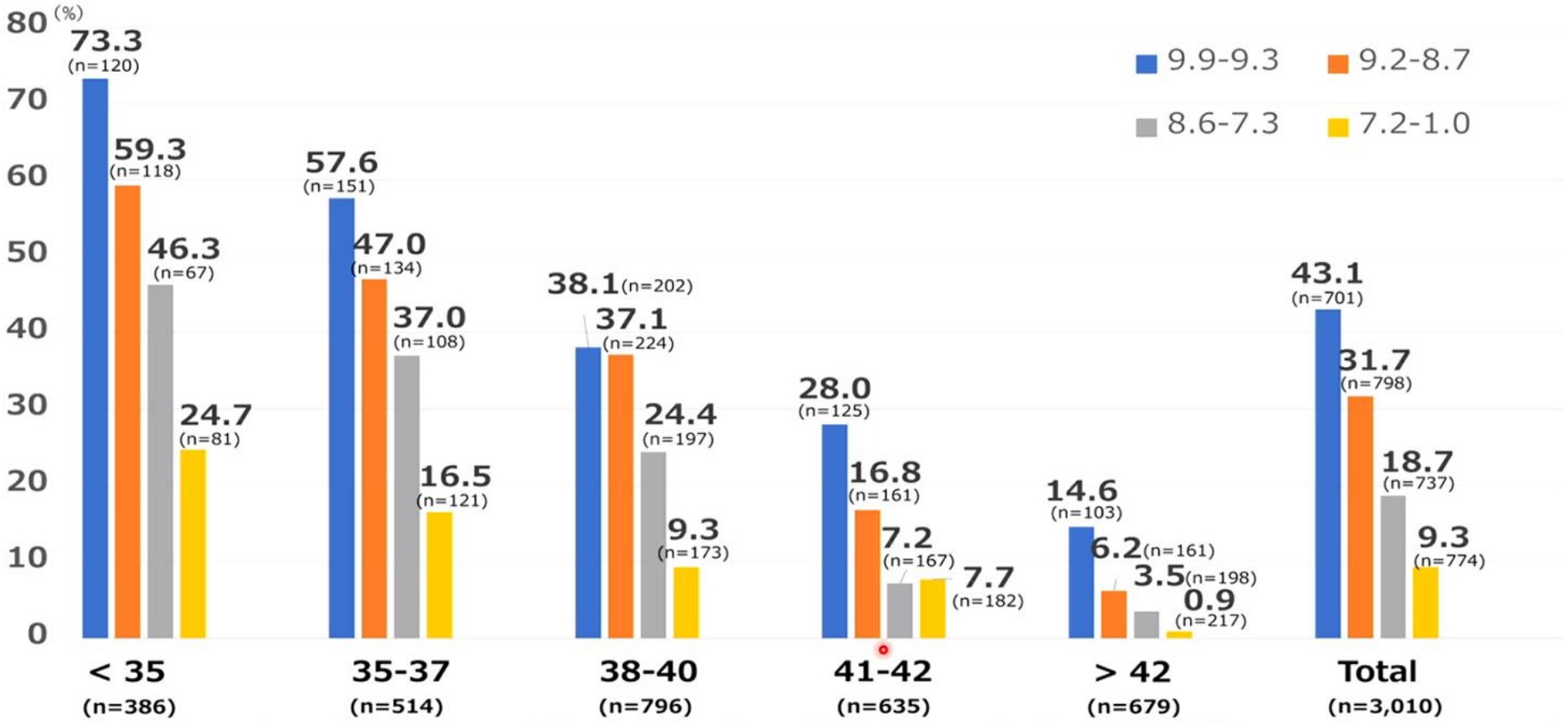
	Unadjusted			Adjusted		
	Odds	95%CI	p value	aOdds	95%CI	p value
Low birth weight	0.889	0.701-1.166	0.374	1.235	0.691-2.749	0.516
Small for gestation	0.789	0.477-1.631	0.462	2.608	0.361-281.1	0.426
Large for gestation	1.275	0.800-2.446	0.346	0.848	0.454-1.982	0.647
Preterm birth	0.893	0.669-1.264	0.495	0.897	0.420-2.681	0.806
Gender male	1.110	0.961-1.284	0.156	1.166	0.892-1.536	0.267
Major congenital malformation	0.921	0.690-1.305	0.617	0.905	0.487-2.110	0.781

Confounding factors: Maternal age, male age, BMI, Parity, Smoking, previous C/S

FERTILITY

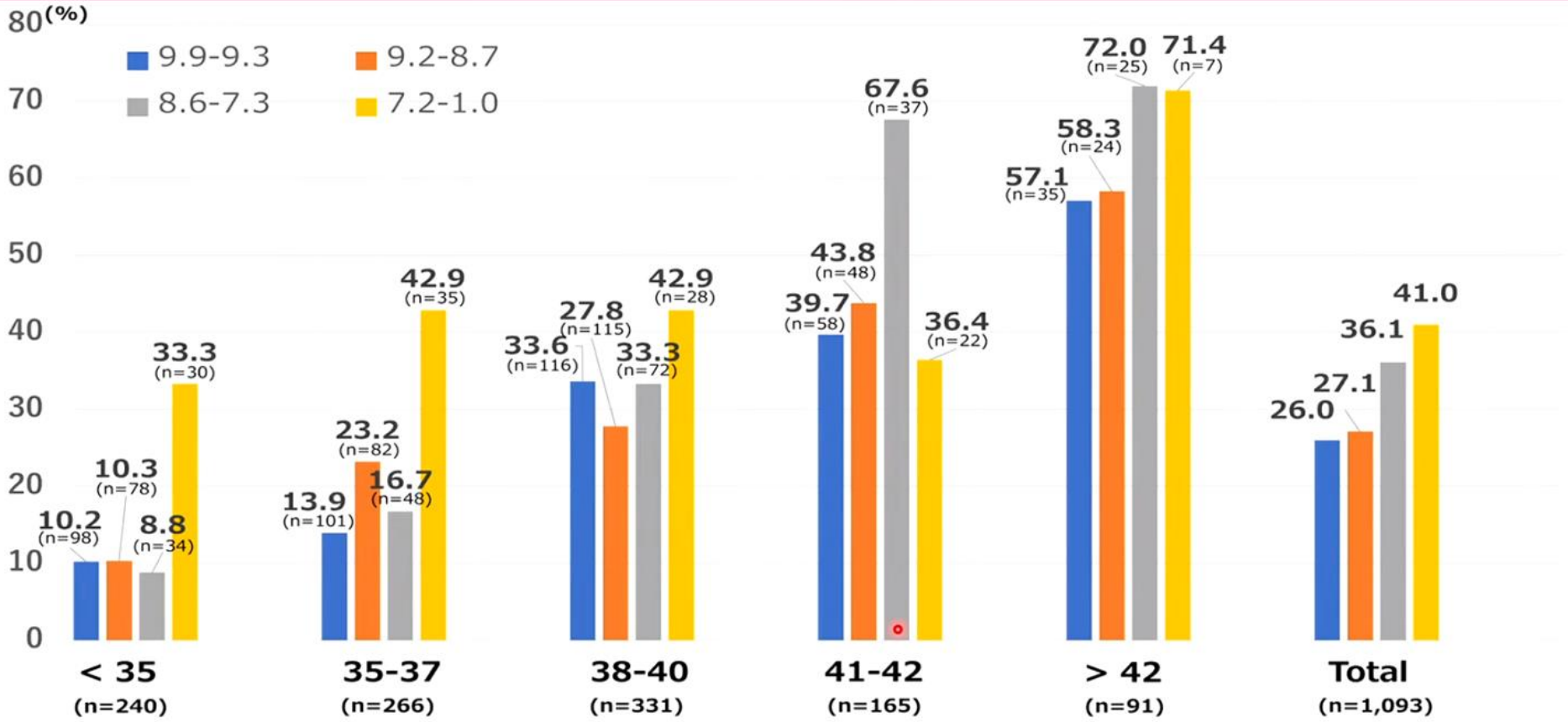
European Society of Human Reproduction and Embryology

The correlation between LB rates and each iDAScore group stratified by SART maternal age groups.



In each maternal age group, LB rates significantly decreased when the iDAScore group decreased ($P<0.05$)

The correlation between miscarriage rates and each iDAScore group stratified by maternal age



TM rates significantly increased progressively with decreasing iDAScores, except in the 38–40 year-old group and >42 years-old group ($P<0.05$).

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https://fertility.com.br/aulas-ministradas/

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Obrigado !

Edson Borges Jr.

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O objetivo do presente estudo foi determinar se a origem do espermatozoide impacta os resultados clínicos, a morfocinética embrionária e as incidências de padrões anormais de clivagem e multinucleação.

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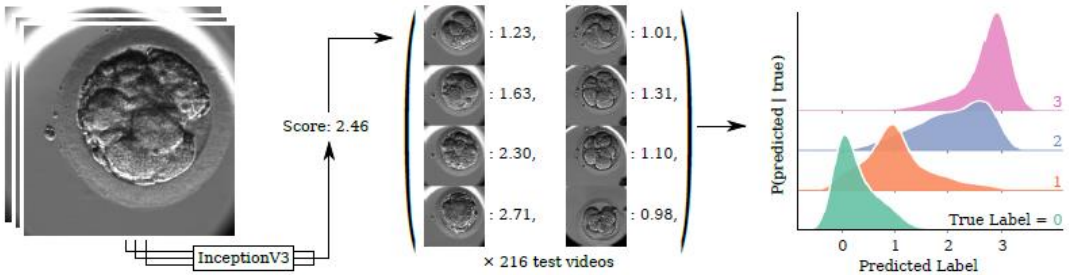
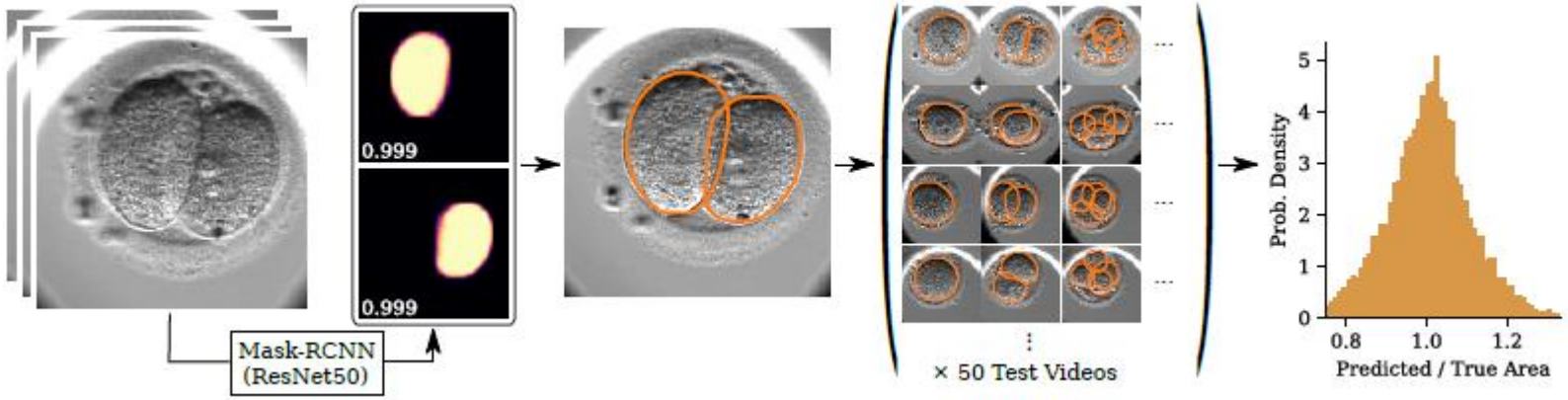
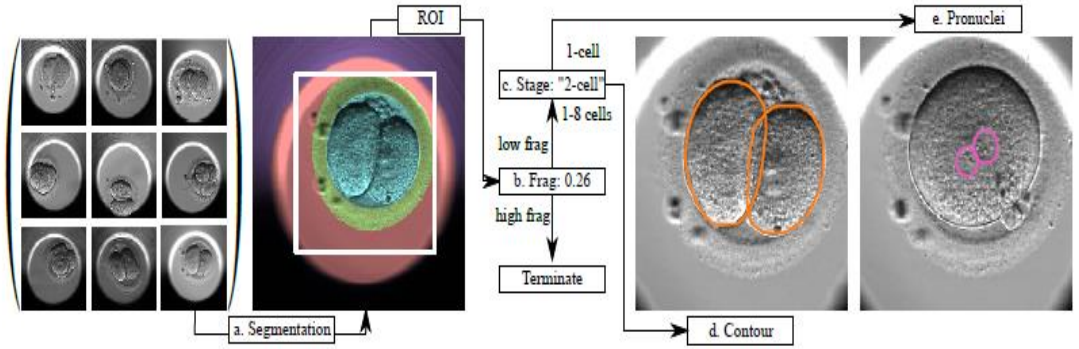


Fragmentation Scoring: score the embryo's degree of fragmentation using a regression CNN.The network takes a single-focus image as input and predicts a fragmentation score of 0 (0% fragments), 1 (<10%), 2 (10-20%), or 3 (20%), following clinical practice.



Stage Classication



FERTILITY

Embryoscope FERTILITY

ICSI e OVODON

Variáveis	Convencional (n=764)		Embryoscope (n=119)		p
	Média	DP	Média	DP	
IdadePaciente	37,8	3,8	38,7	4,5	**0,004**
IMC	24,6	4,3	24,7	4,1	0,914
FSH (UI)	2658,3	671,6	2751,5	676,9	0,131
E2 (pg/mL)	2057,3	1936,0	1777,4	1863,3	0,219
Folículos puncionados (n)	13,5	13,2	14,1	15,8	0,645
Oócitos obtidos (n)	9,8	9,5	10,4	10,8	0,469
yield (%)	69,9	24,0	73,2	23,5	0,099
MII (n)	7,3	7,2	7,4	7,8	0,861
Taxa de MII (%)	71,3	23,9	73,2	22,7	0,356
Taxa de fertilização (%)	76,5	25,0	74,4	26,5	0,255
Taxa de blastocisto (%)	59,2	25,0	66,0	25,4	**0,003**
Embriões transferidos (n)	2,0	0,6	1,2	0,9	**<0,001**
Taxa de implantação (%)*	24,5	37,3	36,4	42,2	**0,006**
Taxa de gestação (%)*	34,6		55,7		**<0,001**
Taxa de aborto (%)*	11,5		2,3		**0,001**

*ajustado para idade materna

FERTILITY

Embryoscope FERTILITY

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*ajustado para idade materna

FERTILITY

ASRM 2019 – Time Lapse

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P-109 Odds of euploidy are significantly associated with not only age but blastocyst morphokinetic parameters and ICM/trophectoderm characteristics

Nina Desai, Ph.D., HCLD,[a] Jeffrey M. Goldberg, M.D.,[b] Rebecca Flyckt, MD,[a] Marjan Attaran, M.D.,[a] Julie Tantibhedhyangkul, M.D.,[a] Cynthia M. Austin, M.D.[a]

[a]Cleveland Clinic, Beachwood, OH; [b]Cleveland Clinic, Cleveland, OH

- **Objetivo**: Avaliar o valor preditivo de parâmetros morfocinéticos e morfologia do TE e MCI para euploidia

2 493 zigotos cultivados em incubadoras com STL

- t2, t3, t4, t5, t8, tM, tSB, tBL, tEBL, tHB foram anotados
- Presença de dismorfismos anotada
- Grau de maturidade do blastocisto, qualidade de TE e MCI avaliadas
- Atribuido score ao blastocsito de 1 a 6

FERTILITY

Biopsia de TE para PGT-A

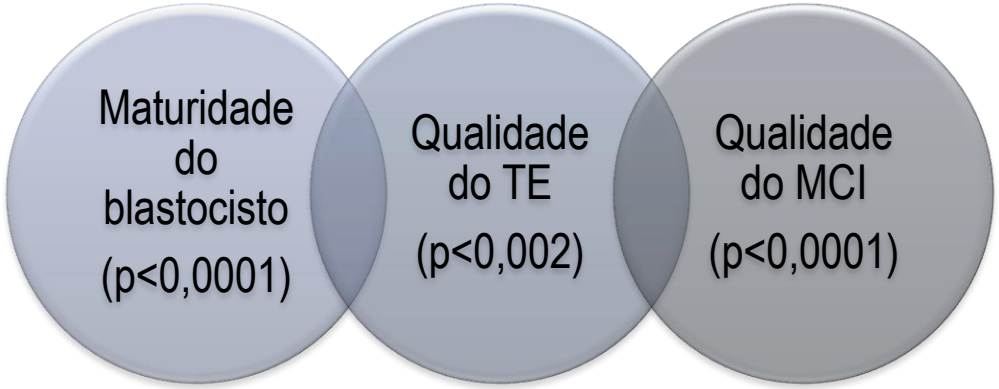
- **Resultados**

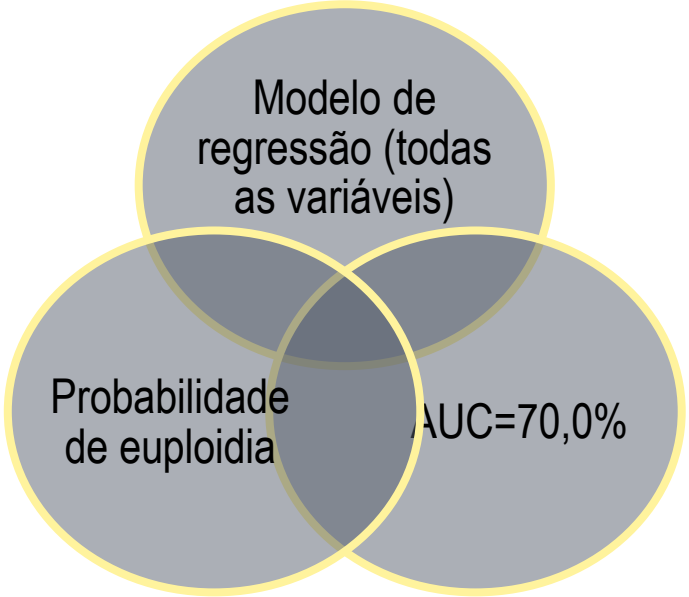
1258 blastocistos biopsiados → 465 (37%) euplóides

Presença de mais de um dismorfismo durante o estágio de clivagem → Diminuição de 49% na chance de euploidia

Para cada hora a mais no tempo entre início de blastulação e eclosão

Diminuição na chance de euploida em 4,1%





FERTILITY

P-310 Impact of different degrees of genetic mosaicism in the kinetic profile of the human embryo

Angel M. Bastida, MSc,[a] Carmen Vidal, M.D., Ph.D.,[a] Lorena Rodrigo, PhD,[b] Amparo Mercader, PhD,[a] Carmen Rubio, PhD,[b] Juan Giles, M.D., Ph.D.,[a] Jose Alejandro Remohi, MD, PhD,[c] Ma Jose de los Santos, PhD[a]

[a] IVIRMA Valencia, Valencia, Spain; bIgenomix Spain, Paterna (Valencia), Spain; cIVIRMA Valencia, Valencia, Spain.

- **Objetivo**: correlacionar os diferentes graus de mosaicismo com o perfil morfocinétco de embriões cultivados no STL

688 embriões de 172 pacientes

Parâmetros Morfocinéticos

tPB2, tPNa, tPNf, t2, t3, t4, t5, t8 and t9, tSC, tM, tSB, tB, tEB tHB

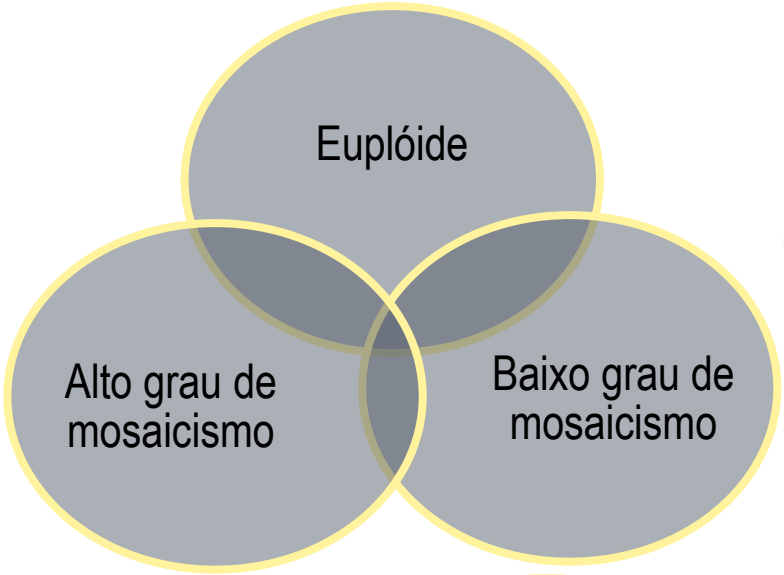
Conteúdo de células aneuplóides por NGS: euplóide (<30%), baixo grau de mosaicismo (30-50%) e alto grau de mosaicismo (50-70%)

ANOVA e postroc de bonferroni

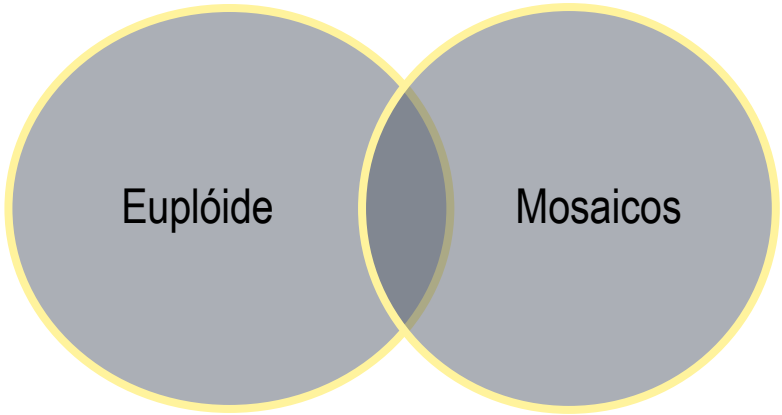
FERTILITY

- **Resultados**

382 (55,5%) aneuplóides



Sem diferença quando os três grupos foram comparados em relação aos fatores morfocinéticos



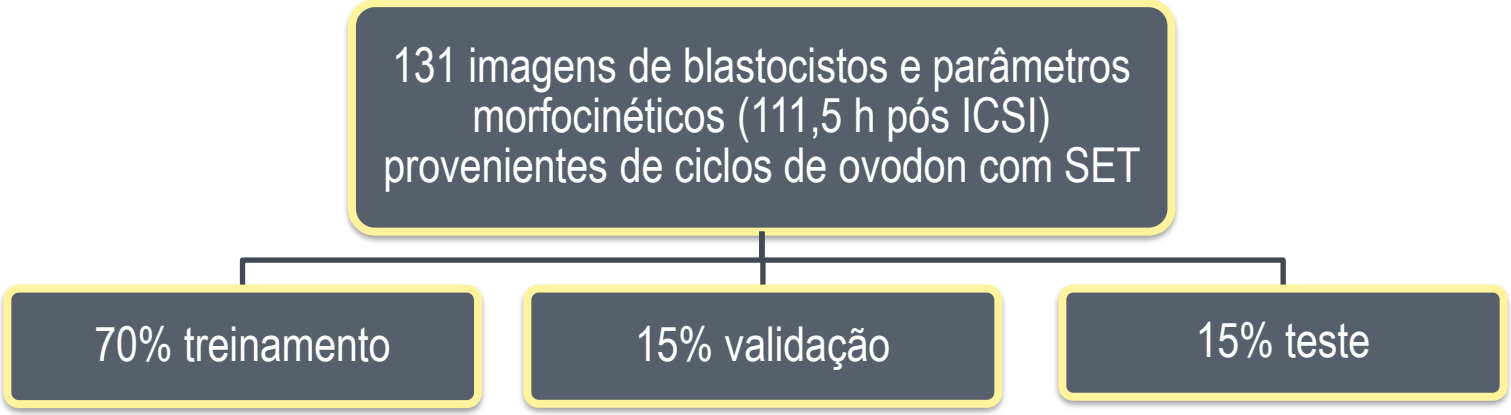
tPNf, t2, t3, t4, tSB

FERTILITY

O-184 Is there any room to improve embryo selection? Artificial Intelligence technology applied for live birth prediction on blastocysts

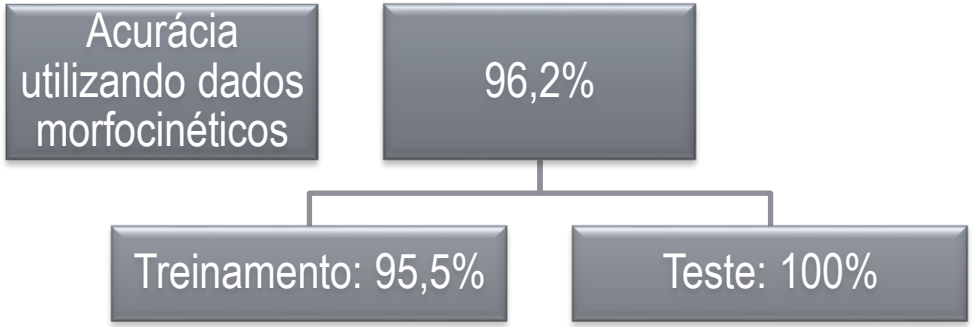
Marcos Meseguer, PhD,[a] Cristina Hickman, PhD,[b] Lorena Bori Arnal, PhD,[c] Lucia Alegre, PhD,[c] Marco Toschi, MS, [c,d] Raquel Del Gallego, PhD,[c] Jose Celso Rocha,PhD[e]
[a]IVIRMA Global, Valencia, Spain, Tel Aviv, Israel; [b]Imperial College London, London, United Kingdom; [c]IVIRMA Global, Valencia, Spain; [d]IVIRMA, Rome, Italy; [e]State University of São Paulo Júlio de Mesquita Filho, Assis, Brazil.

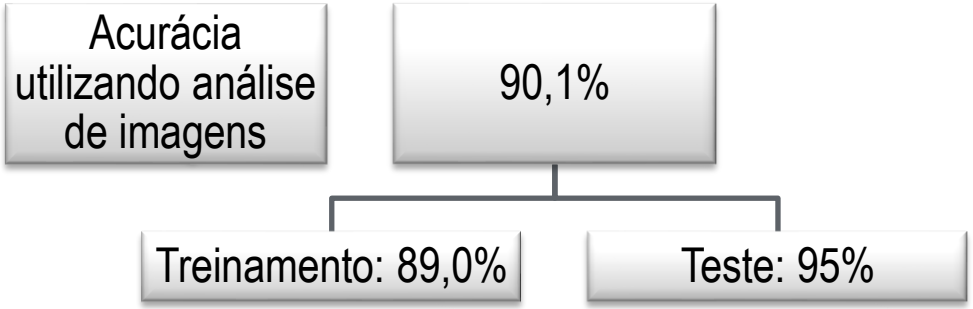
- **Objetivo**: aplicar a tecnologia de AI ao STL e parâmetros morfocinéticos para predizer nascidos vivos.

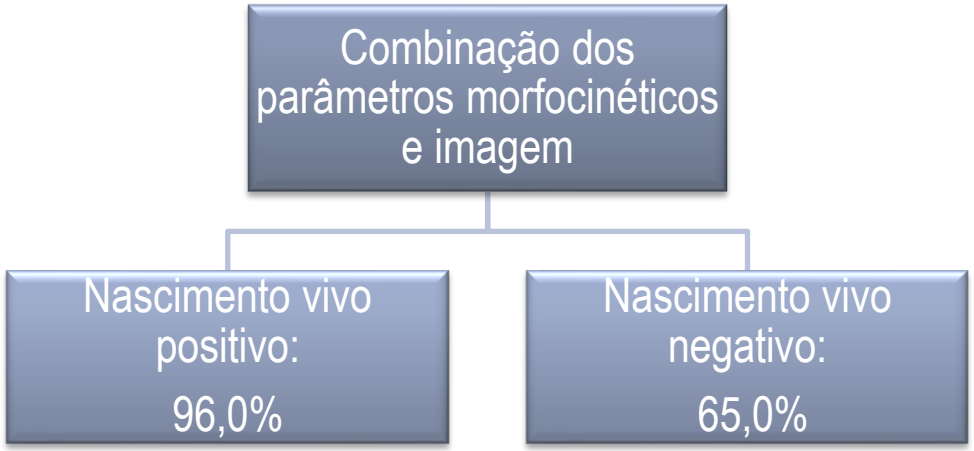


FERTILITY

- **Resultados**







FERTILITY

O-91 Artificial intelligence assessment of time-lapse images can predict with 77% accuracy whether a human embryo capable of achieving a pregnancy will miscarry

Rishabh Hariharan, BSc,[a] Peter He,[a] Marcos Meseguer, PhD,[b] Marco Toschi, MSc,[c] Jose Celso Rocha, PhD,[d] Nikica Zaninovic, Ph.D.,[e] Jonas Malmsten, MSc,[e] Qiansheng Zhan, MSc,[e] Cristina Hickman, PhD[a]

[a]Imperial College London, London, United Kingdom; [b]IVIRMA Global, Valencia, Spain; [c]IVIRMA, Rome, Italy; [d]State University of São Paulo Júlio de Mesquita Filho, Assis, Brazil; [e]Ronald O. Perlman and Claudia Cohen Center for Reproductive Medicine, New York, NY.

- **Objetivo**: Avaliar a IA como uma ferramenta capaz de predizer a chance de abortamento
- **Métodos**

Imagens obtidas pelo STL a 111,5 horas após inseminação

3 412 imagens de blastocistos provenientes de ciclos de SET

1756 nascidos vivos (51%)

1656 culminaram com aborto (49%)

FERTILITY

- **Métodos**

Fase 1: treinamento — 2 140 Imagens de blastocistos e correlação com abortamento

Fase 2: validação — 536 Predição de gestação pelo modelo

Fase 3: teste — 736 Teste do modelo prospectivamente

- **Resultados**

Validação: AUC: 85,0%

Teste: AUC: 79,0%

Acurácia do teste: 77,0%

Especificidade: 58%

Sensibilidade : 95%

Embriões classificados com alto risco de aborto

Taxa de aborto: 92,0%

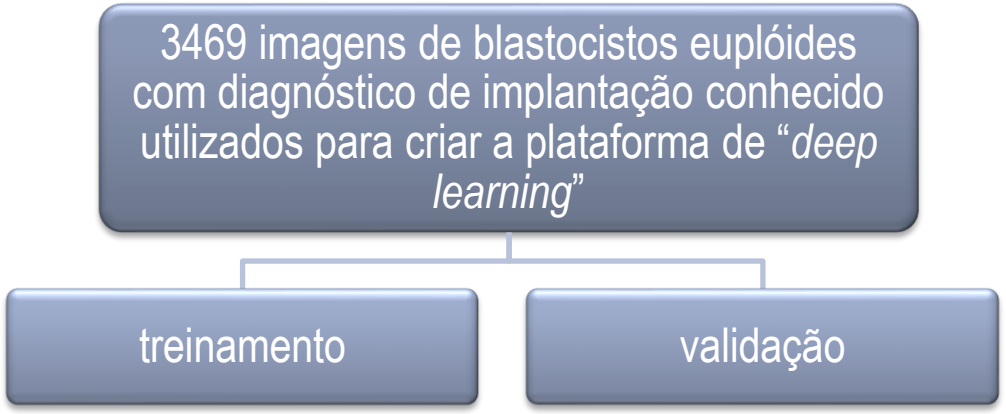
FERTILITY

O-185 A deep learning framework outperforms embryologists in selecting day 5 euploid blastocysts with the highest implantation potential

Eduardo Hariton, MD, MBA,[a] Irene Dimitriadis, MD,[a] Manoj Kumar Kanakasabapathy, MS,[b] Prudhvi Thirumalaraju, BS,[b] Raghav Gupta, BTech,[b] Rohan Pooniwala, BTech,[a] Irene Souter, MD,[a] Sarah T. Rice, MS,[a] Pragati Bhowmick, MD,[a] Leslie B. Ramirez, PhD,[c] Carol Lynn Curchoe, PhD, TS (ABB),[d] Jason E. Swain, PhD,[e] Lynn M. Boehnlein, BS,[f] Charles L. Bormann, PhD,[a] Hadi Shafiee, PhD.[b]

[a]Massachusetts General Hospital, Harvard Medical School, Boston, MA; [b]Brigham and Women's Hospital, Harvard Medical School, Boston, MA; [c]Extend Fertility, New York, NY; [d]San Diego Fertility Center, San Diego, CA; eCCRM Fertility Network, Lone Tree, CO; [f]Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of Wisconsin, Madison, WI

- **Objetivo**: Avaliar o desempenho de um sistema de IA combinado a um algoritmo genético, para a seleção de blastocistos euplóides para a transferência



FERTILITY

Fase de teste

97 embriões euplóides

Sistema de IA

15 embriologistas bem treinados

- **Resultados**

IA	• Acurácia: 73,3%
Embriologistas	• Acurácia: 67,4%

IA

Sensibilidade: 84,2%

Especificidade: 64,5%

Teste t

IA superior aos embriologistas bem treinados ao identificar embriões euploides com maior potencial de implantação (p<0,001)

FERTILITY

P-411 Predicting blastocyst formation of day 3 embryos using a convolutional neural network (CNN): a machine learning approach

Pietro Bortoletto, MD,[a] Manoj Kumar Kanakasabapathy, MS,[b] Prudhvi Thirumalaraju, BS,[c] Raghav Gupta, BTech,[b] Rohan Pooniwala, BTech,[d] Irene Souter, MD,[d] Irene Dimitriadis, MD,[e] Kristy Dickinson, BS, TS,[a] Eduardo Hariton, MD, MBA,[a] Charles L. Bormann, PhD,[e] Hadi Shafiee, PhD.[c]

[a]Division of Reproductive Endocrinology and Infertility, Boston, MA; [b]Brigham and Women's Hospital, Harvard Medical School, Boston, MA; [c]Division of Engineering in Medicine, Cambridge, MA; [d]Massachusetts General Hospital, Harvard Medical School, Boston, MA; [e]Massachusetts General Hospital, Boston, MA.

P-414 Artificial neural-network analysis combined with time-lapse imaging predicts embryo ability to develop to the blastocyst stage

Giovanni Coticchio, Ph.D.,[a] Raffaella Sciajno, B.Sc.,[a] Giulia Fiorentino, B.Sc.,[b] Federica Cavalera, Ph.D.,[b] Giovanna Nicora, B.Sc.,[c] Riccardo Bellazzi, Ph.D.,[c] Andrea Borini, M.D.,[a] Silvia Garagna, Ph.D.,[b] MaurizioZuccotti, Ph.D.[b]

- **Objetivo**: avaliar o potencial da IA para análise de imagens de embriões em estágio de clivagem, para prever quais embriões atingem o estagio de blastocisto
- **Conclusão**: IA tem uma acurácia de 70 - 73% para prever quais embriões que atingem o estagio de blastocisto

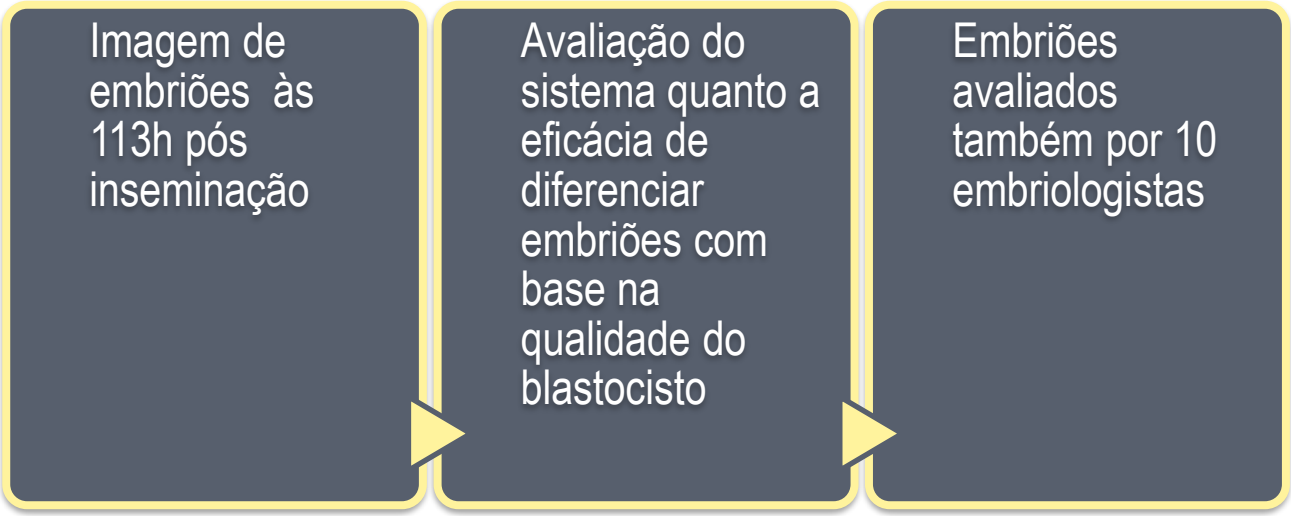
FERTILITY

P-444 Deep learning-enabled smartphone-based system for automated embryo assessments and evaluation

Manoj Kumar Kanakasabapathy, MS,[a] Prudhvi Thirumalaraju, BS,[a] Charles L. Bormann, PhD,[b] Hemanth Kandula, BS,[a] Sandeep Kota Sai Pavan, BS,[a] Divyank Yarravarapu, BS,[a] Hadi Shafiee, PhD.[a]

[a]Brigham and Women's Hospital, Harvard Medical School, Boston, MA; [b] Massachusetts General Hospital, Harvard Medical School, Boston, MA.

- **Objetivo**: avaliar a eficiência de um aplicativo para smartphone (<$5) para a classificação de imagens de embriões produzidos in vitro



FERTILITY

- **Resultados**

smartphone system

- Acurácia: 96,0%

smartphone system

Sensibilidade: 93,5%

Especificidade: 100%

Chi square → Embryoscope-based deep-learning vs smartphone system → Sem diferença signifcativa P>0.05

FERTILITY

ESHRE 2020 – Time Lapse / IA

FERTILITY

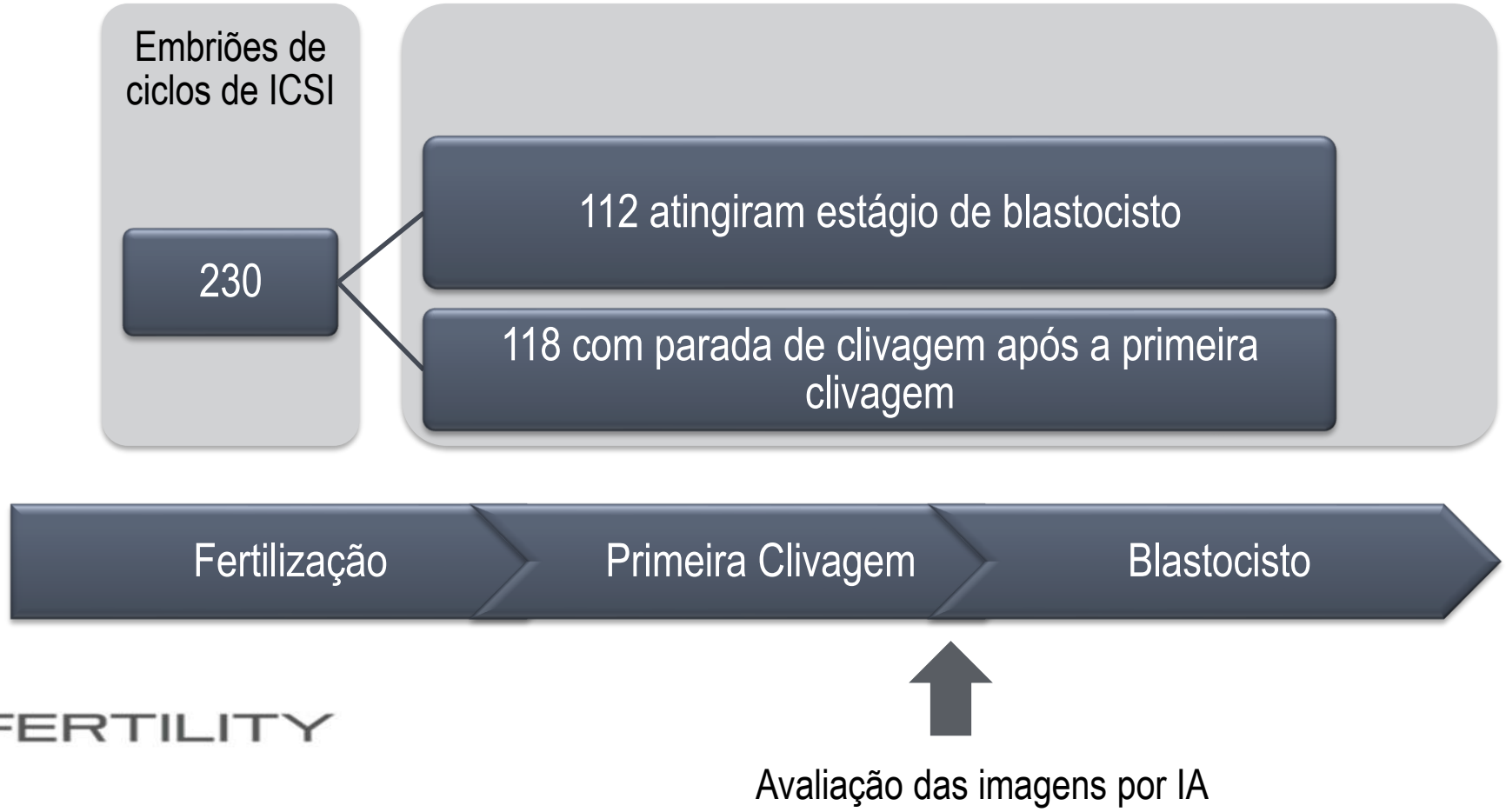
O-043 Prediction of oocyte and embryo competence by advanced image analysis and AI

M. Zuccotti, G. Fiorentino , G. Nicora , R. Sciajno , F. Cavalera , R. Bellazzi , A. Borini , S. Garagna , G. Coticchio

Itália

Objetivo: Verificar se a avaliação de imagens por IA das duas primeiras divisões celulares é capaz de predizer o potencial de desenvolvimento embrionário até a fase de blastocisto

Métodos

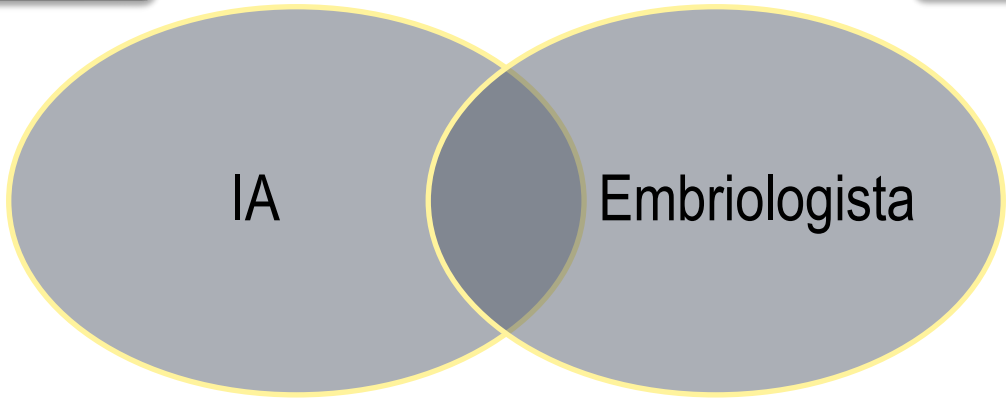


FERTILITY

- **Resultados**

Acurácia

Embriologista	IA
75,4%	75,4%



82,6%

- **Conclusão**: esses dados indicam a possibilidade de prever o desenvolvimento de blastocistos já no estágio de 4 células. Além disso, os resultados destacam a força de combinar a avaliação de um embriologista experiente com as ferramentas de IA

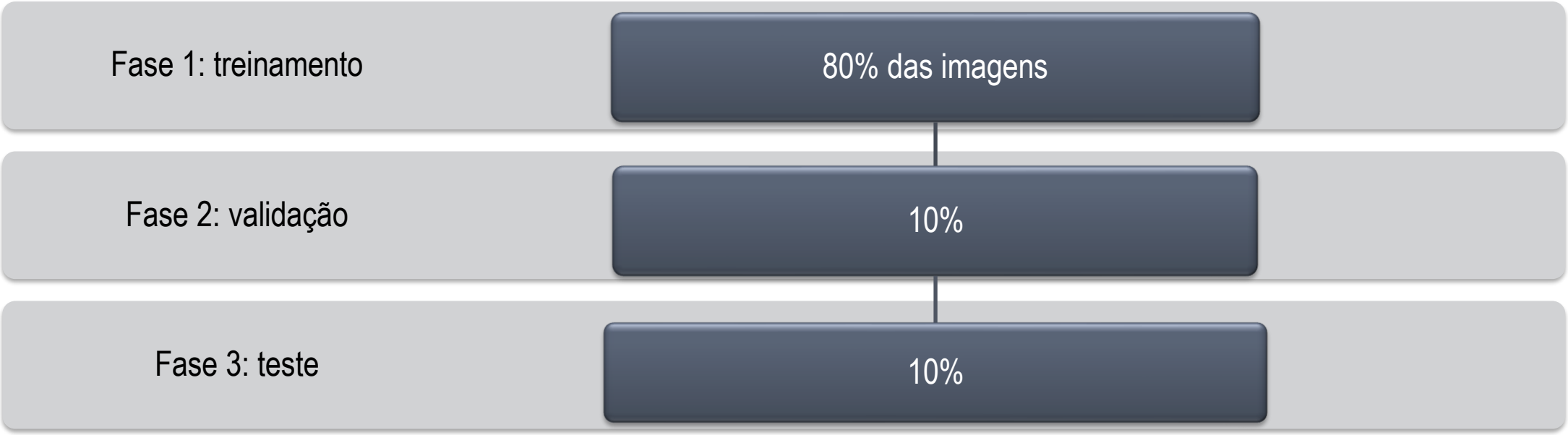
FERTILITY

O-117 Automated evaluation system based on artificial intelligence and visualization technology can effectively improve the accuracy of blastocyst evaluation

S. Wang, L. Chen , C. Zhou , D. Zhang , H. Sun
China

Objetivo: Verificar quais são os principais fatores para a classificação de imagem de blastocisto baseada em IA

- **Métodos:** 1 025 blatocistos divididos em alta e baixa qualidade (10 957 imagens)



FERTILITY

Avaliação das imagens por IA

- **Resultados**

Acurácia : 91.74% → Modelo considerando TE, ICM, and ZP. AUC: 0.970

- **Conclusão**: Na classificação de imagens de blastocistos humanos baseados em IA, os fatores essenciais são trofectoderma (TE), massa celular interna (ICM) e zona pelúcida (ZP).

FERTILITY

O-207 Patient-oriented counselling: predicting live birth probability (LBP) at each step of the In Vitro Fertilization (IVF) process via machine learning.

V. Grzegorczyk Martin, T. Fréour , C. Avril , A. de Bantel - Finet , P. Barrière , J.L. Pouly , M. Grynberg , I. Parneix , J. Roset , T. Grzegorczyk

França

Objetivo: Avaliar o peso de um modelo preditivo de nascimento vivo durante diferentes fases do tratamento de FIV

Métodos

Modelo de regressão logistica uni- e multivariada

Variável reposta

Nascido vivo

Variáveis preditoras

- Idade materna
- IMC
- Causa de infertilidade
- AMH
- CFA
- Dose de gonadotrofinas
- Espessura endometrial

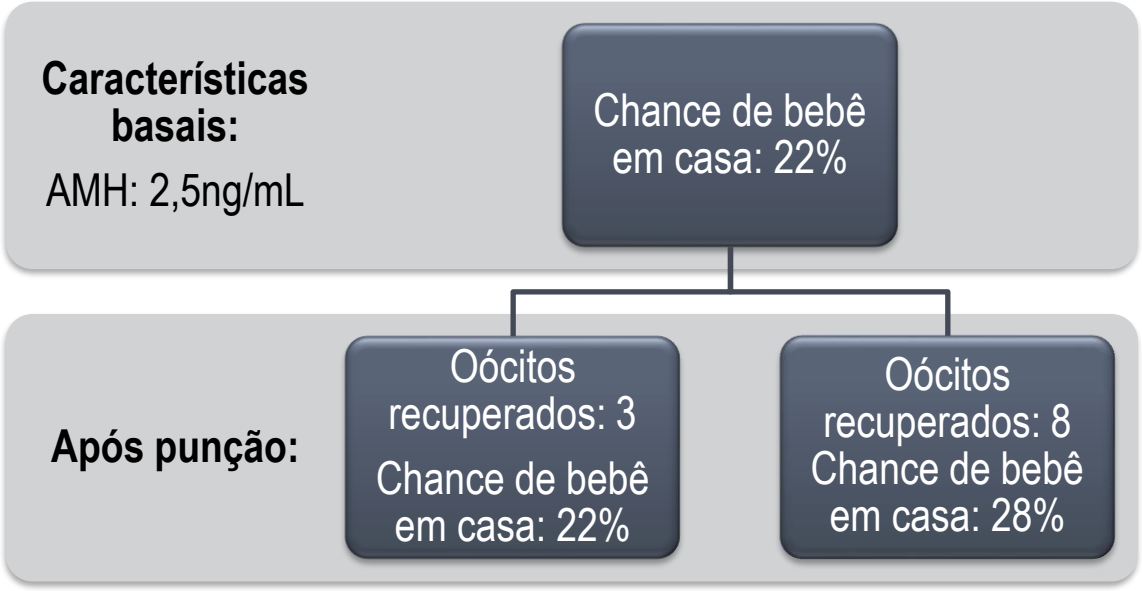
Diferentes fases do ciclo

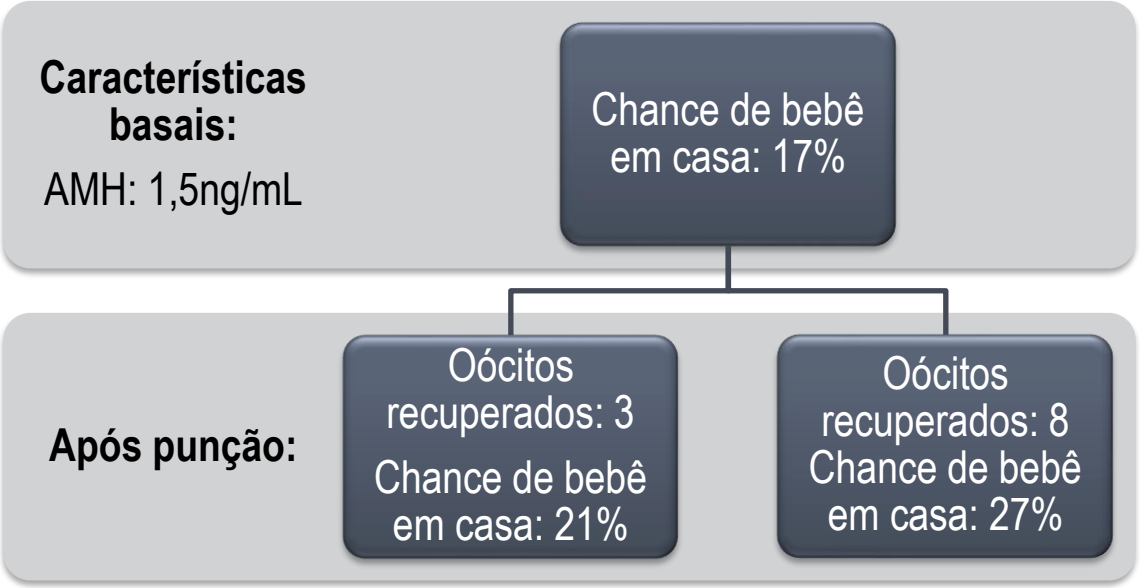
FERTILITY

- **Resultados**

A acurácia do modelo aumenta progressivamente de 0,64 para 0,72 conforme fatores do EOC e laboratoriais vão sendo adicionados

Exemplo: paciente de 38 anos





FERTILITY

- **Conclusão**: O modelo proposto é uma ferramenta prática e evolutiva para ajudar os médicos a acompanhar seus pacientes e fornecer estimativas personalizadas e recentes de chance de bebê em casa

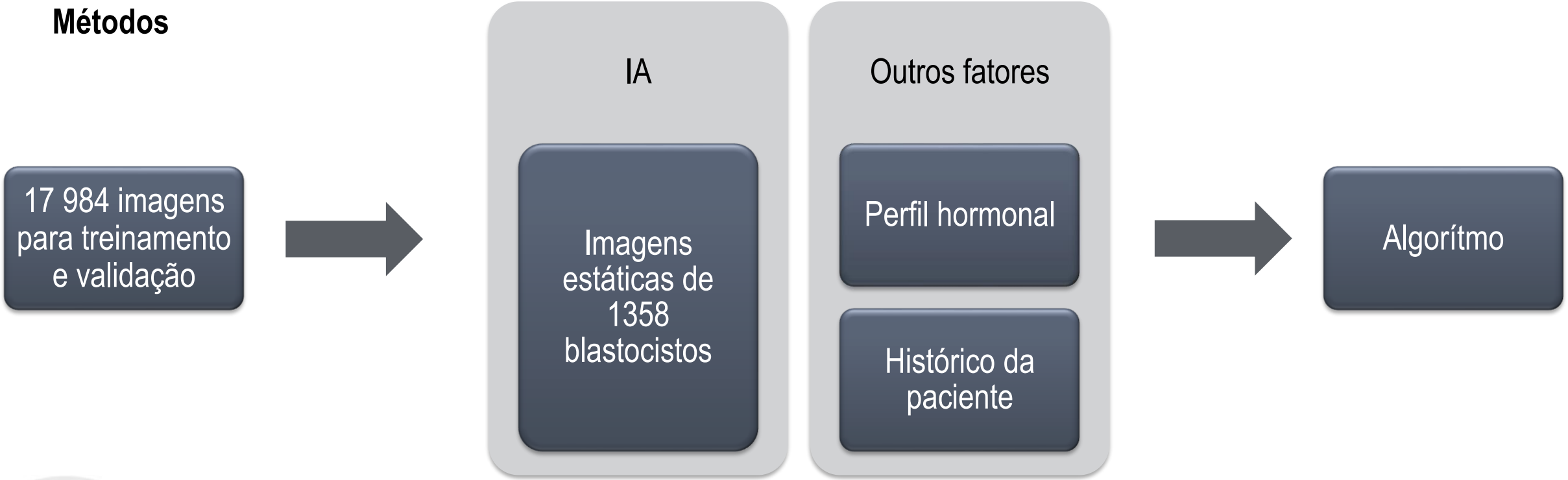
O-115 Artificial Intelligence (AI) system combining both images and non-image inputs can improve the accuracy of human embryo viability prediction

Miyatsuka, K. Shimizu , T. trisitichoke , A. My Le , N. Enatsu , M. Inubushi

Japão

Objetivo: Verificar se um sistema de IA que combina recursos de imagem e não imagem pode melhorar a previsão de viabilidade de embriões

Métodos



FERTILITY

- **Resultados**

Acurácia

Embriologistas	Modelo
49,8% (Blastocistos graus 3-6/ batimento fetal)	62,7%

- **Conclusão**: Comparado às avaliações morfológicas convencionais, algoritmos de IA baseados em imagem, em conjunto com outros fatores melhora a precisão em prever a viabilidade embrionária em 4%

FERTILITY

O-114 A universal algorithm is available in last generation time-lapse incubators: embryo score provided by the KIDScoreD5 is strongly correlated with chromosomal status and clinical outcomes.

L. Bori, F. Meseguer , M.A. Valera Cerdá , L. Alegre , A. Tejera , J. Remohí , M. Meseguer

IVI - Espanha

Objetivo: Avaliar a eficácio do EmbryoScope e EmbryoScopePlus em identificar embriões euploides

Métodos

FERTILITY

- **Resultados**

		Kid Score	p
Status cromossômico	Euploide	5,3 ± 1,9	<,05
	Aneuploide	4,6 ± 1,8	

Kid Score	Implantação Positiva	p
5,3	54,2	<,05
5,4 – 6,4	59,3	
>7.5	67,9	
Kid Score	**Nascimento vivo**	
5,3	20,2	<,05
5,4 – 6,4	25,1	
>7.5	40,3	

FERTILITY

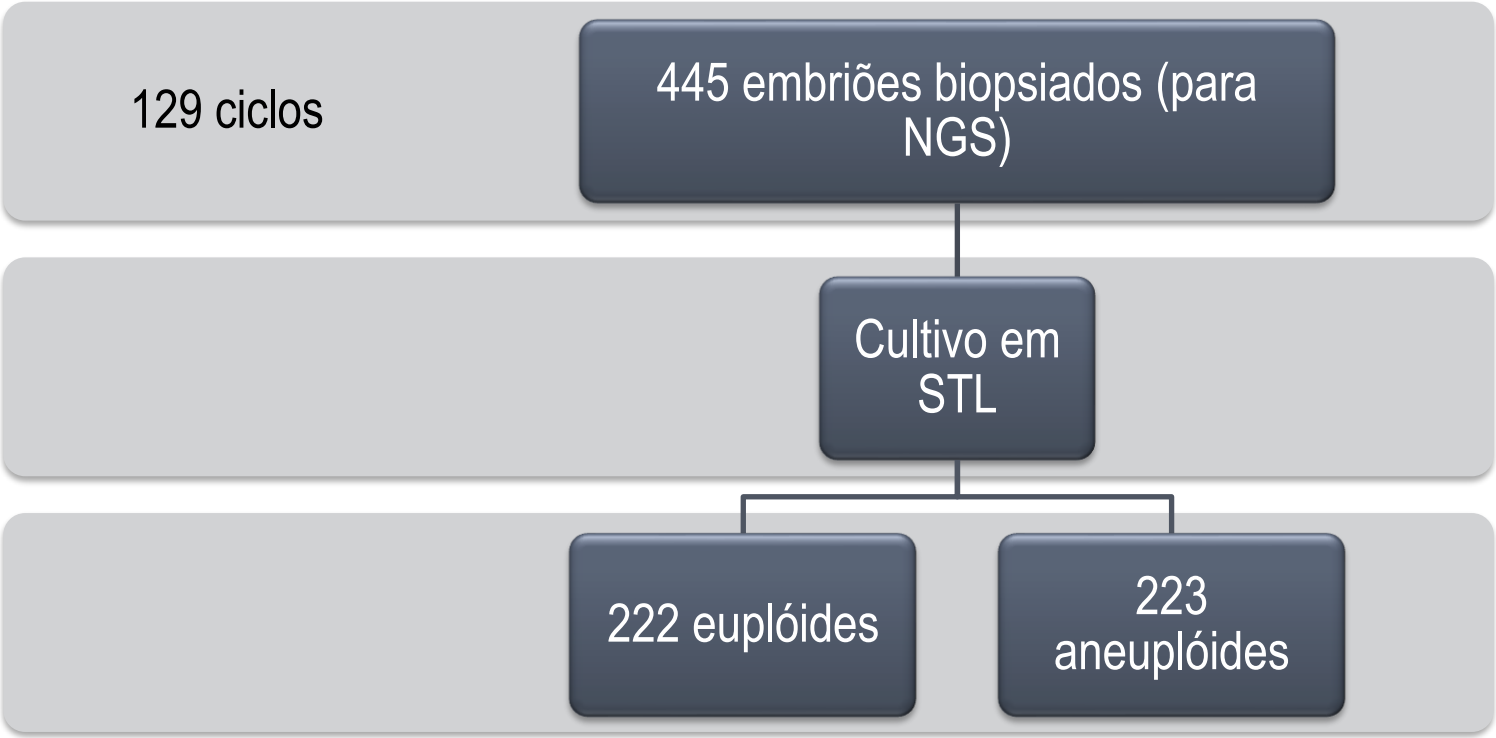
O-113 Compared to traditional statistics, using machine learning algorithms increases prediction of euploidy in human embryos from weak (61%) to acceptable (72%)

S. De Gheselle, J. Chambost , K. Declerck , C. Jacques , I. De Croo , C. Hickman , K. Tilleman

Bélgica
França

Objetivo: Comparar o potencial de predição de aneuploidia por meio de estatísticas tradicionais versus IA

Métodos



FERTILITY

Métodos e Resultados

Modelo estatístico tradicional (regressão logística múltipla)

- Dados morfocinéticos
- Dados da pacientes (como idade)
- Dados do ciclo
- AUC de 61% (IC: 56%-67%).

Modelo de IA

- Modelo aleatório
- AUC de 72% (CI: 68%-77%)

- **Conclusão**: A IA aumentou a precisão de 61% (fraca) para 72% (aceitável). Considerando a grande quantidade de variáveis que afetam os resultados da TRA, os métodos estatísticos tradicionais devem ser substituídos pelo modelo de IA

FERTILITY

FERTILITY

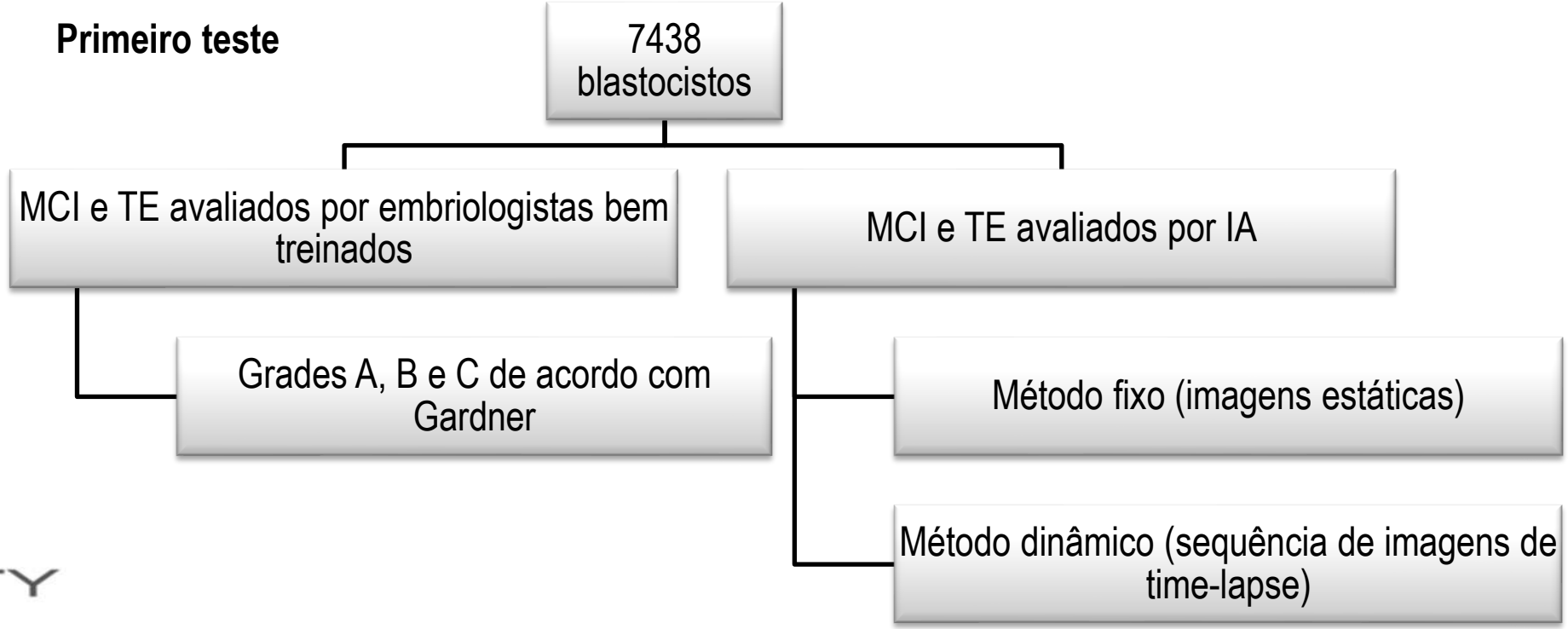
O-168 Automatic morphological grading of human blastocysts with time-lapse imaging and artificial intelligence

M.F. Kragh[1], J. Rimestad[2], J. Berntsen[2],H.Karstoft[3]
[1]Vitrolife A/S & Aarhus University, Research & development, Aarhus S, Denmark, [2] Vitrolife A/S, Research & development, Aarhus S, Denmark, 3. Aarhus University, Department of Engineering, Aarhus N, Denmark

- **Objetivo**: Verificar se a avaliação de blastocistos humanos pode ser totalmente automatizada com imagens de STL e IA para fornecer informações semelhantes ou superiores aquelas obtidas por embriologistas experientes.

- **Métodos**

Primeiro teste



FERTILITY

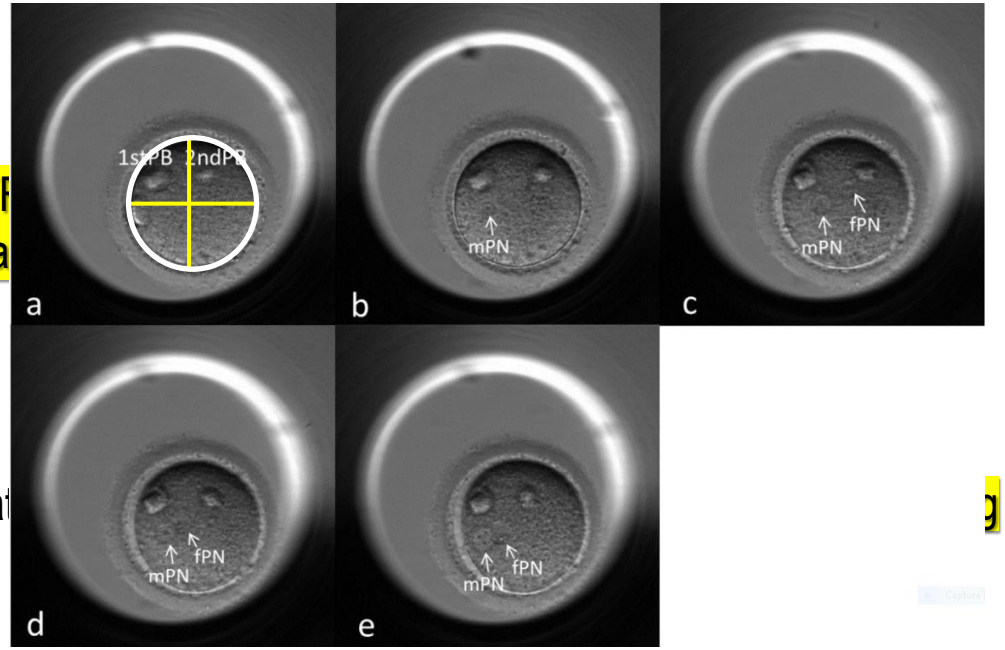
O-116 Non-invasive embryo selection: Live birth can be predicted by means of the kinetic analysis of female and male pronuclei formations

J. Otsuki[1,2], T. Iwasaki[2], N. Enatsu[2], Y. Katada[2], K. Furuhashi[2], M. Shiotani[2]

[1]Okayama University, ART Center, Okayama, Japan, [2]Hanabusa Women's Clinic, Reproductive Medicine, Kobe- Hyogo, Japan

- ✓ Time-lapse recordings were performed and the areas of male and female pronuclei were retrospectively analyzed by measuring their vertical and horizontal diameters. These measurements were taken 4 and 8 hours before the pronuclear membrane breakdown (PNMBD), and immediately before the PNMBD.

- ✓ When normal embryos were defined as A∪C∩B, the birth rates for IVF respectively. For the remaining embryos, defined as abnormal, birth ra



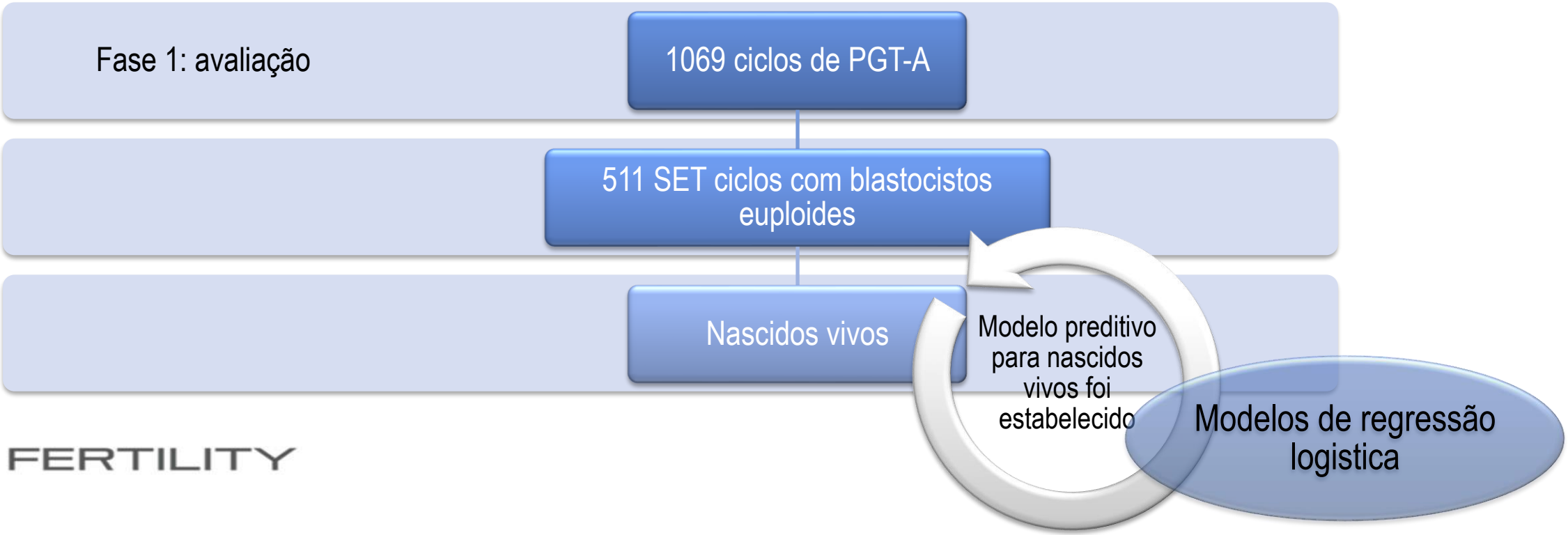
- ✓ **Wider implications of the findings:**
  In this study, we established a method of non-invasive embryo evaluat g
  trophectoderm cells.

FERTILITY

O-006 Time of morulation and trophectoderm quality are associated with live birth after euploid blastocyst transfer: a multicenter study

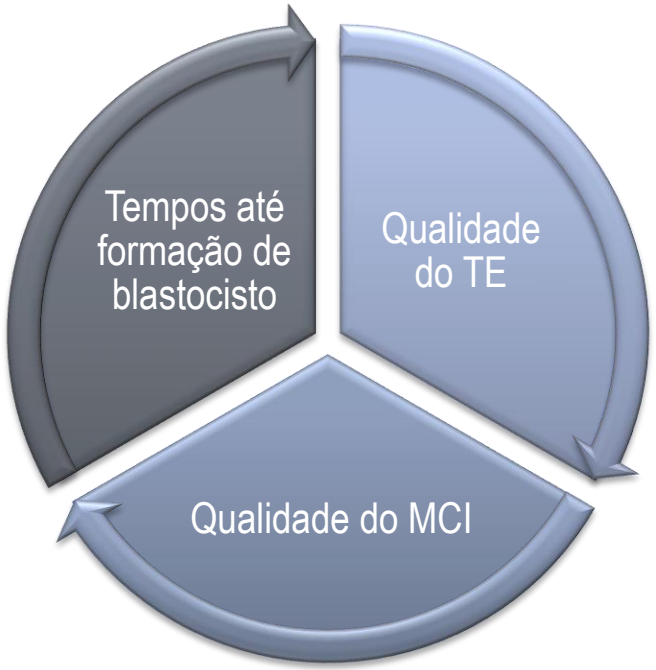
L.F. Rienzi[1], D. Cimadomo[1], A. Delgado[2], M.G. Minasi[3], G. Fabozzi[1], R. Del Gallego[2], M. Stoppa1, J. Bellver[2], A. Giancani[1], M. Esbert[4], A. Capalbo[5], J. Remohì[2], E.Greco[3], F.M.Ubaldi[1], M.Meseguer[2]
1. Clinica Valle Giulia, G.EN.E.R.A. Center for Reproductive Medicine, Roma, Italy, 2. IVI-RMA, IVI-Valencia, Valencia, Spain, 3. European Hospital, Center for reproductive medicine, Rome, Italy, 4. IVI-RMA, IVI-Barcelona, Barcelona, Spain, 5. Igenomix, Igenomix Italia, Marostica, Italy

- **Objetivo**: Avaliar se a caracterização morfodinâmica de blastocistos euploides tem valor prognóstico para o resultado de gestação.



FERTILITY

- **Métodos**



Fase 2: Validação

546 ciclos de PGT-A

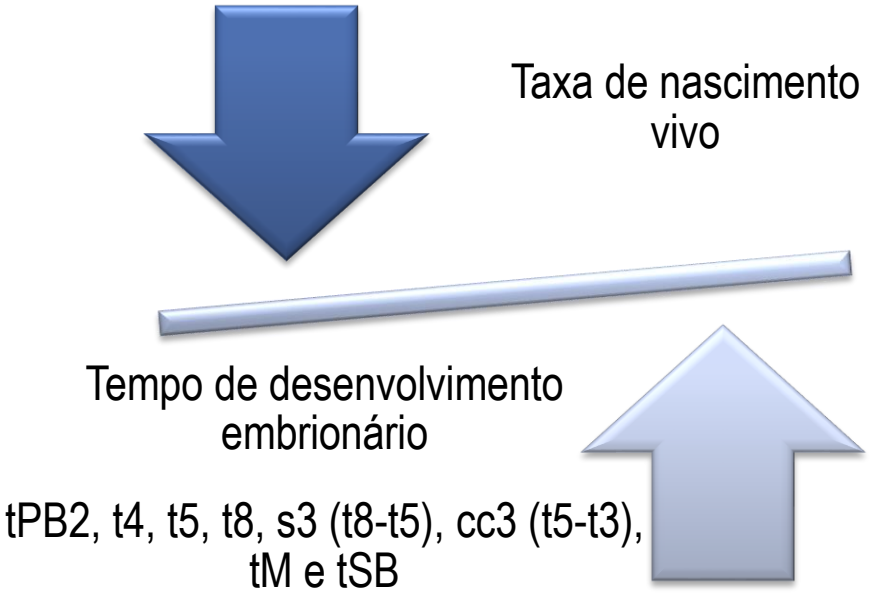
319 SET ciclos com blastocistos euploides

Gestação continuada

FERTILITY

Resultados

- Taxa de nascidos vivos nos três centros com SET de blastocistos euploides: 40%

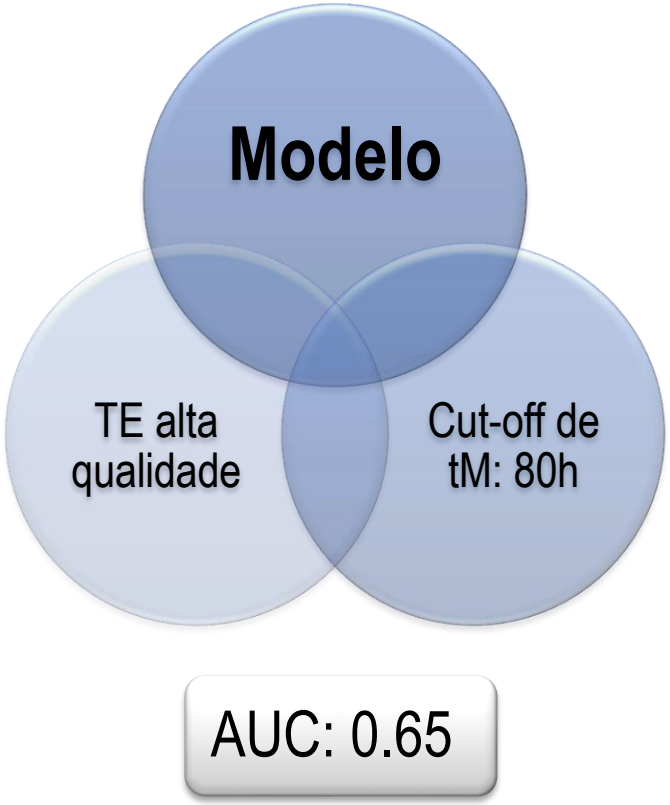


Qualidade do MCI e TE correlacionaram-se positivamente com chance de nascidos vivos

Apenas tM e qualidade de TE foram variáveis independentes correlacionadas com taxa de nascidos vivos (análise multivariada)

FERTILITY

- **Resultados**



O modelo validado em 319 embriões transferidos (em SET) em 3 centros diferentes

Modelo (n=117)	Gestação continuada
TE alta qualidade e tM< 80h	61,2% (41/67)
TE baixa qualidade e tM>80h	30,0% (15/50)
p	>0,001

- **Conclusão**: O tempo de morulação e a qualidade do trofectoderma são fatores preditivos para nascimento vivo.

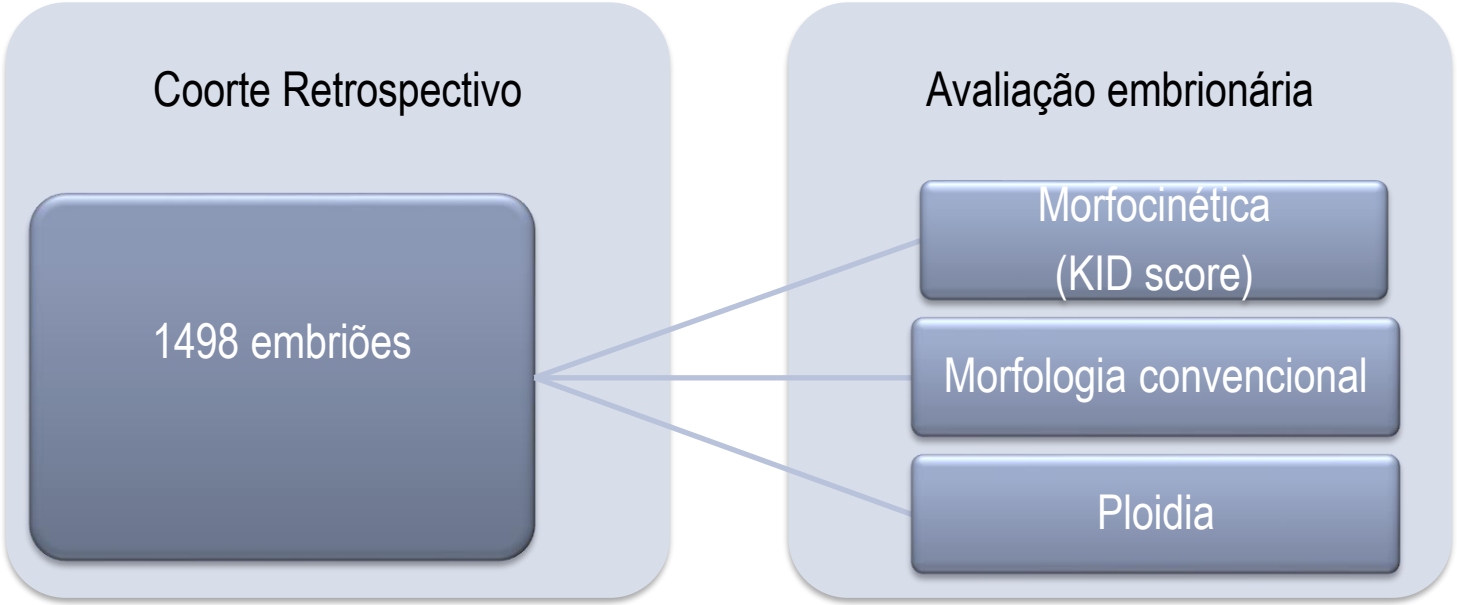
FERTILITY

O-199 Morphokinetics may provide a useful adjunct for selecting Euploid embryos with a high chance of implantation

Y.Y. Lim[1], M.S.R. Lim[1], J.J. Chen[1], P.S.Wong[2]
[1]Sunfert International Fertility Centre - Bangsar South, PGT Department, Bangsar South- Kuala Lumpur, Malaysia, [2]Sunfert International Fertility Centre - Bangsar South, Clinical, Bangsar South- Kuala Lumpur, Malaysia

- **Objetivo**: Avaliar se o modelo morfocinético universal baseado em dados conhecidos de implantação (KID) aumentam a chance de selecionar embriões euplóides com maior potencial de implantação

- **Métodos**



FERTILITY

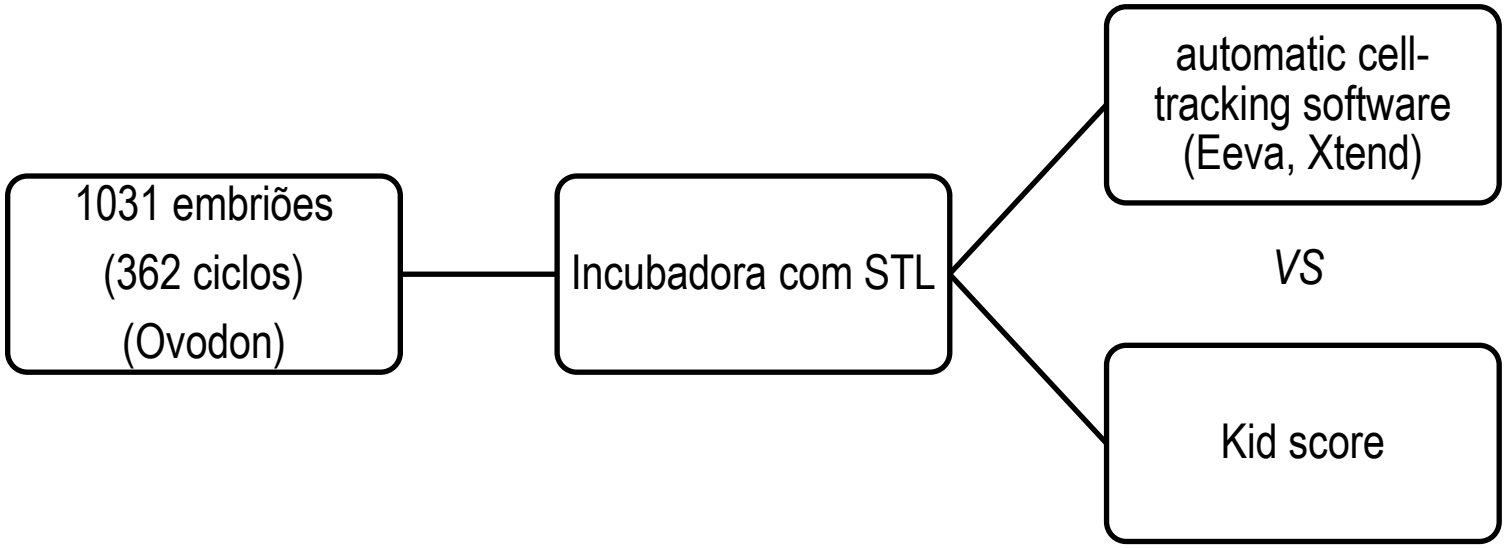
O-170 Clinical validation of an automatic time-lapse algorithm classification system for blastocyst selection

B. Aparicio-Ruiz[1], S. Perez[1], L. Romany[1], T. Viloria[1], L. Alegre[1], J. Remohi[2], M.Meseguer[1]

[1]IVIRMA Global, IVF Laboratory, Valencia, Spain, [2] IVIRMA Global, Gynecologist Department. IVI President, Valencia, Spain

- **Objetivo**: Avaliar a correlação entre uma classificação automática de algoritmos de STL (Xtend) com potencial de implantação de blastocistos e verificar se avaliação da morfologia padrão é compatível ou combinável com o Xtend

- **Métodos**



FERTILITY

- **Resultados**

	Taxa de implantação / categoria de blasto				
	1	2	3	4	5
KID score	53,91%	52,63%	45,68%	39,02%	24%
Xtend	56,7%	55,9%	51,6%	39,35%	27,8%

	Implantação/Qualidade do blastocisto	
	(1-3) A/B	4-8 (Não A/B)
Xtend	53,91%	52,63%
ASEBIR	56,7%	55,9%

		Classificação ASEBIR	
		A/B	Não A/B
Categorias Xtend	1-3	83,9%	54,4%
	4-5	16,10%	49,5%

- **Resultados**

	Chance de gestação (regressão logística)
	(1-3 vs 4-5)
Xtend	OR: 1,9 (IC 95%: 1,40-3,77)
ASEBIR	(A/B vs não A/B)
	OR: 2,3 (IC 95%: 1,11-3,30)

- **Conclusão**: Existe uma correlação direta entre as categorias Xtend e o potencial de implantação dos blastocistos. Essa relação é ainda mais evidente para embrtiões de boa qualidade de acordo com a classificação morfológica padrão.

- **Implicações**:
  - ✓ Esse é o maior conjunto de dados usando o algoritmo Xtend.
  - ✓ Os resultados confirmam que a classificação morfológica convencional e as classificações pelo STL/Xtende são independentes e combináveis, mostrando que nem todos os embriões classificados morfologicamente como A / B correspondem a melhor classificação Xtend

FERTILITY

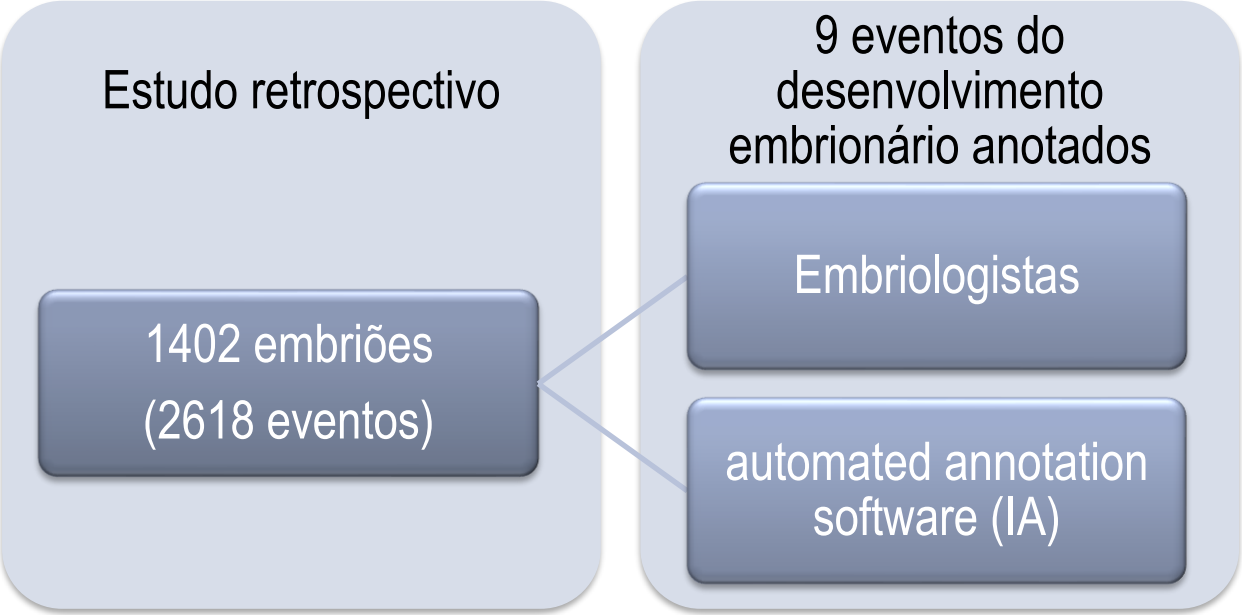
O-171 Embryo development detection by automated software vs. embryologist team

R. Del Gallego Bonilla[1], L. Alegre[1], L. Bori[2], T. Peura[3], S. Azaña[2], M. Meseguer[1]

[1]IVI Valencia- SL, IVF Laboratory, Valencia, Spain, [2] IVI Valencia- SL, Research, Valencia, Spain, [3] Genea, Research, Sydney, Australia

- **Objetivo**: Comparar os resultados e a precisão das anotações de eventos morfocinéticos do embrião realizado em uma prática clínica de rotina àquelas realizadas por um software de avaliação automática de embriões

- **Métodos**



- Aparecimento de PN
- Desaparecimento de PN
- T2, T3, T4, T5 e T6
- Formação de mórula
- Início de blastulação

FERTILITY

- **Resultados**

- As menores taxas de concordância na detecção de eventos morfocinéticos foram encontradas naqueles mais subjetivos: desaparecimento dos PNs, formação de mórula e expansão do balstocisto

- Diferenças nos tempos variaram de acordo com o evento, as maiores diferenças detectadas nos eventos tardios. Entretanto, na grande maioria dos eventos, principalmente as primeiras clivagens, a taxa de correspondência foi muito alta

- **Conclusão**: Foi observada alta concordância na classificação embrionária entre os embriologistas e software. Esta nova tecnologia é uma ferramenta útil sob um supervisão embriologista qualificada.

- **Implicações**:
  - ✓ As anotações automatizadas facilitam a carga de trabalho dos embriologistas e, especialmente, os primeiros eventos podem ser anotados com alta precisão.

  - ✓ A automatização das anotações da morcinética embrionária é a progressão natural para uma clínica que utiliza sistemas de timelapse.

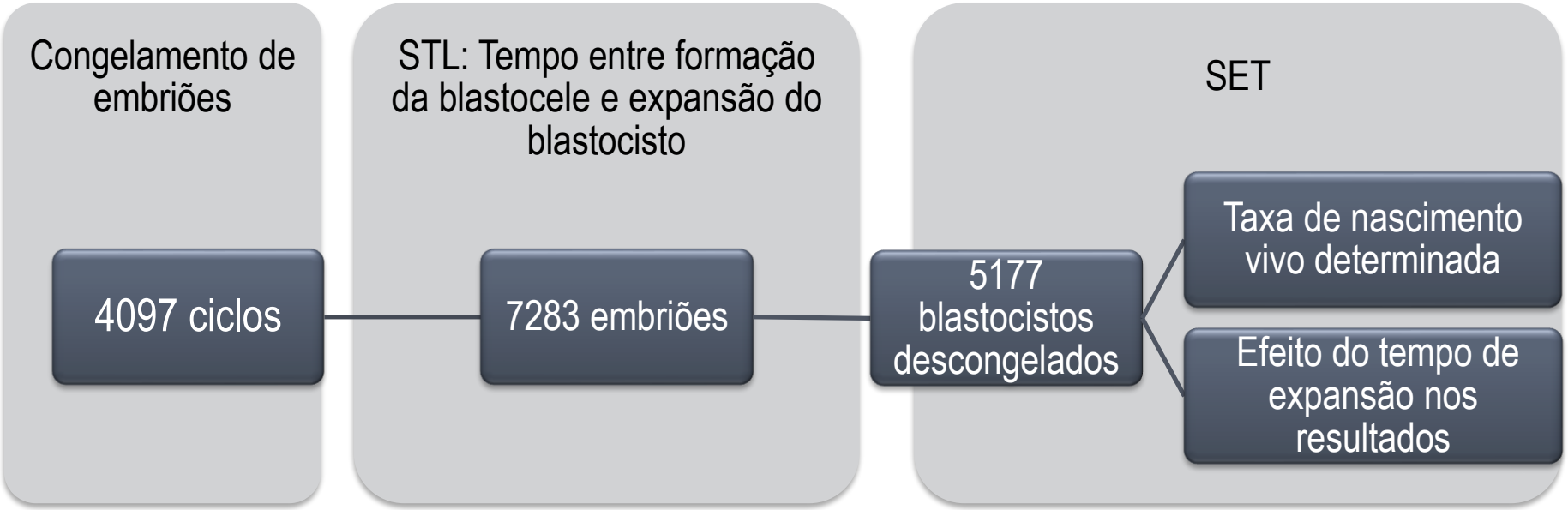
FERTILITY

P-24 Embryos frozen within a short time of reaching the expanded blastocysts from the early blastocysts have high viability: time-lapse investigation of 5177 blastocysts

Yuki Kobayashi, B.A., Rie Matsunaga, M.A., Hiromi Morita, M.A., Rui Hasegawa, B.A., Kana Isobe, B.A., Megumi Miura, M.A, Minako Kamihata, B.A., Shinichi Watanabe, DVM, Tomoko Maeda, Ph.D., Hiroshi Makino, Ph.D., Masanori Ochi, Ph.D., Toshitaka Horiuchi, Ph.D.

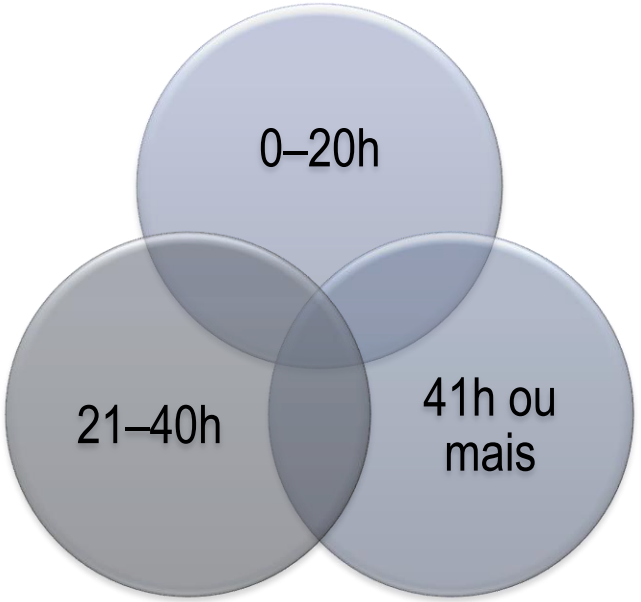
OCHI YUME CLINIC NAGOYA, Nagoya, Japan.

- **Objetivo**: Avaliar se o intervalo entre a blastulação inicial e a expansão do blastocisto afeta a viabilidade embrionária



FERTILITY

- **Resultados**



0–20h

Maiores taxas de gestação e nascimento vivo

FERTILITY

- **Resultados**

Acurácia	
84,6% para identificação de embriões viáveis	**Cross validation: 71,6%.**
57,7% para identificação de embriões não viáveis	**Melhoria de 32% quando comparado aos embriologistas**

- **Conclusão**: O desenvolvimento de um modelo geral de IA produziu uma melhoria na precisão da viabilidade embrionária em comparação com avaliação morfológica tradicional do embriologista.

- **Implicações**:

  - ✓ A seleção de embriões é fortemente baseada na avaliação morfológica e outras tecnologias invasivas incluindo biópsia embrionária para classificação da ploidia
  - ✓ Os dados aqui apresentados, mostram , pela primeira vez, como um modelo de IA pode ser aplicado em um ambiente misto e multicêntrico (diferentes centros em diferente países), resultando em uma precisão de 70% para a identificação de embriões viáveis e não viáveis.

FERTILITY

O-118 Time-lapse imaging acquired nucleation status of 2-cell pre-implantation embryos is predictive of implantation and live births following IVF

S. Sayed[1], M. Myhre Reigstad[2], B. Molt Petersen[3], A. Schwennicke[1], J.Wegner Hausken[1], R. Storeng[2]
[1]Klinikk Hausken, IVF and Gynecology, Haugesund, Norway, [2]Norwegian National Advisory Unit on Women's Health, Oslo University Hospital, Oslo, Norway 3BMP Analytics, Consultancy, Viby J, Denmark

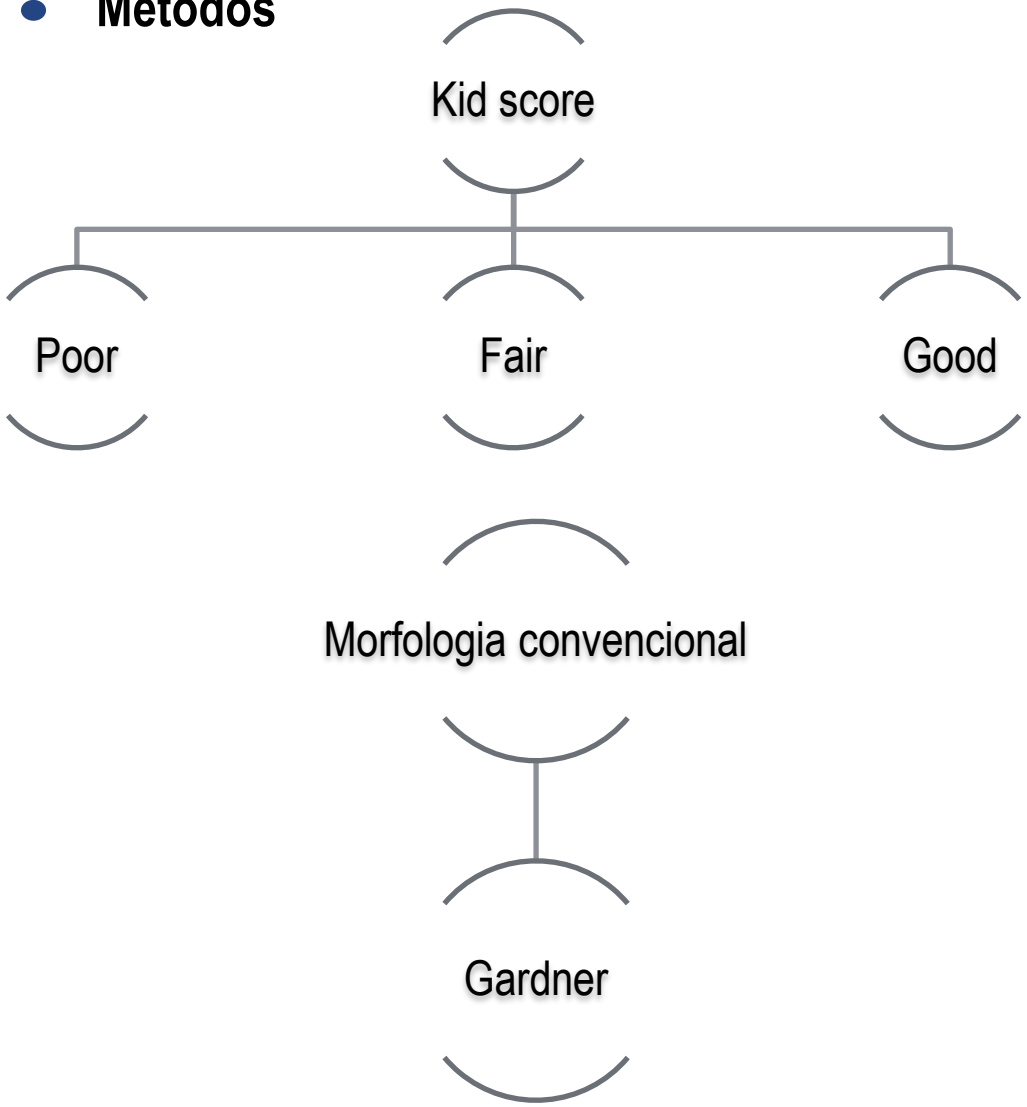
- ✓ Nucleation errors such as micronucleation, binucleation, multinucleation and other minor error groups, were annotated in the time-lapse images which were taken every 10 or 20 minutes for a minimum of 44 hours post insemination.

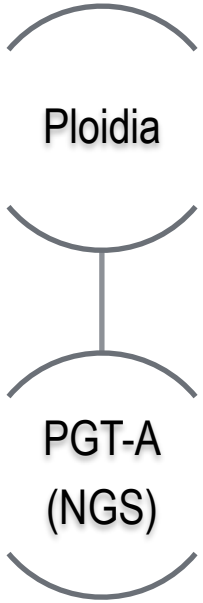
- ✓ Nucleation error phenotypes (NEP) data was collected from TLI for 2959 transferred embryos. A total of 2082 treatment cycles with exact traceability of transferred embryos were included in the analysis.

- ✓ Statistically significant lower implantation and live birth rates for embryos with all types of nucleation errors at **the 2-cell stage** (22.9% of the transferred embryos), compared to embryos not presenting nucleation errors; 14.2% vs. 23,9% for implantation and 11.8% vs. 21.0% for live birth respectively, $P<0.001$.

FERTILITY

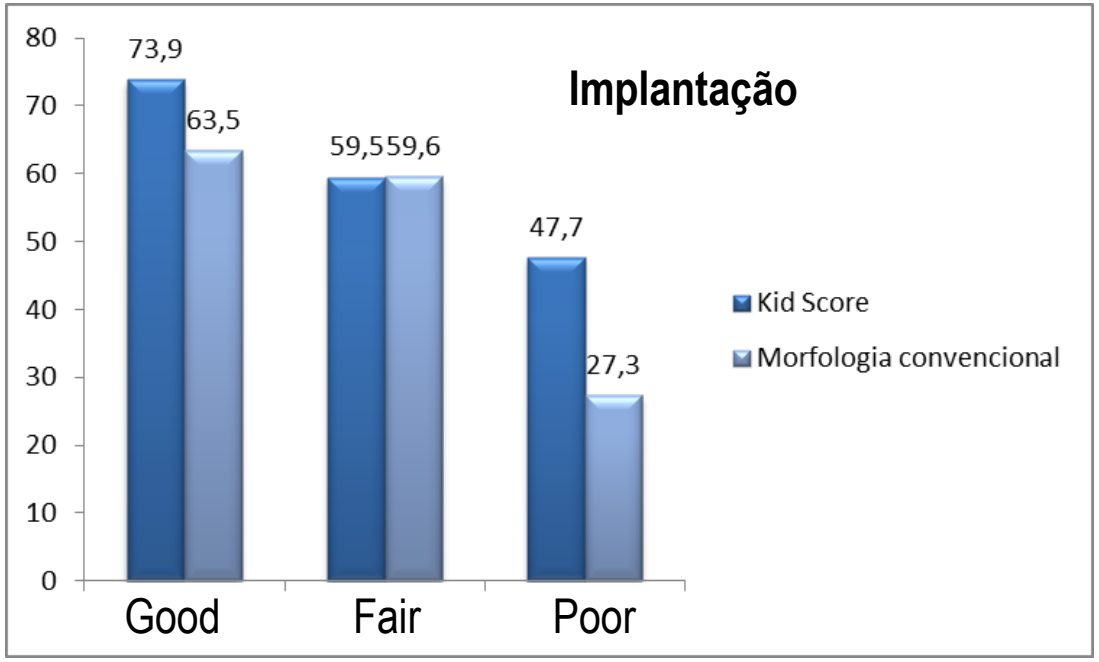
- **Métodos**





FERTILITY

- **Resultados**



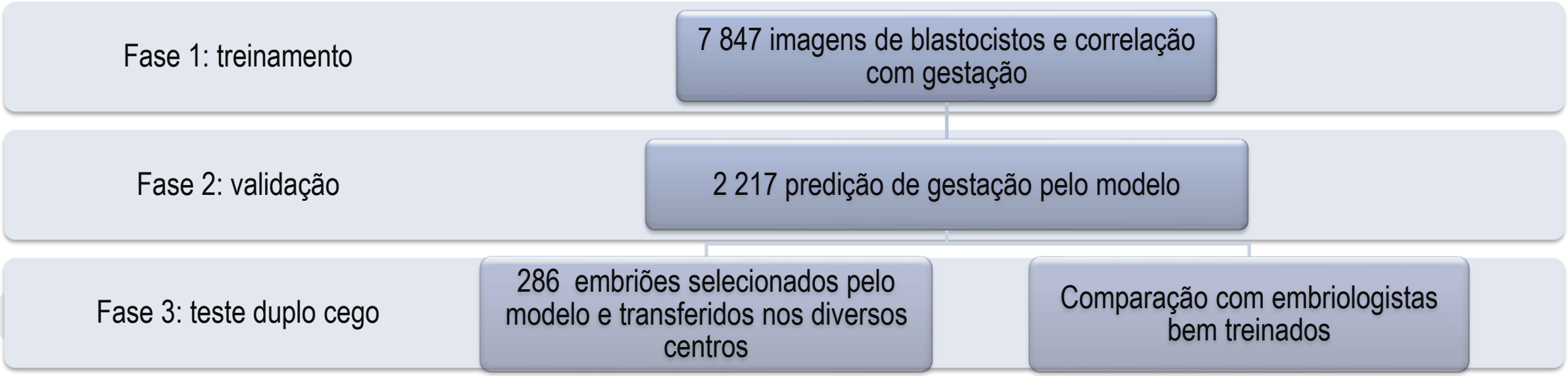
FERTILITY

O-004 Artificial intelligence (AI) technology can predict human embryo viability across multiple laboratories with varying demographics with high accuracy and reproducibility

M.VerMilyea[1,2],A.Miller[1],A.Picou[1],M.Lane[3,4],G.Adaniya[5],B.Bopp[6], D. Morbeck[7], E. Behnke[8], L. Click[8], R. Matthews[9], A. Lim[10], J. Hall[11], A. Murphy[11],D. Perugini[11],M. Perugini[11]

1. Ovation Fertility, Laboratory, Austin, U.S.A.; 2. Texas Fertility Center, Clinic, Austin, U.S.A. ; 3. Monash IVF Group, Laboratory, Richmond, Australia ; 4. Repromed, Laboratory, Adelaide, Australia ; 5. Ovation Fertility, Laboratory, Indianapolis, U.S.A.; 6. Midwest Fertility Specialists, Clinic, Carmel, U.S.A. ; 7. Fertility Associates, Laboratory, Auckland, New Zealand ; 8. Ovation Fertility, Laboratory, Cincinnati, U.S.A.; 9. Oregon Reproductive Medicine, Laboratory, Portland, U.S.A. ; 10. Alpha Fertility Centre, Laboratory, Petaling Jaya, Malaysia ; 11. Life Whisperer, Company, Adelaide, Australia

- **Objetivo**: Verificar se a avaliação de imagens de embriões por IA podem predizer a viabilidade embrionária
- **Métodos**



- **Resultados**

84,6% para identificação de embriões viáveis

57,7% para identificação de embriões não viáveis

Cross validation: 71,6%.

Melhoria de 32% quando comparado aos embriologistas

- **Implicações**: Os dados aqui apresentados, mostram , pela primeira vez, como um modelo de IA pode ser aplicado em um ambiente misto e multicêntrico (diferentes centros em diferente países), resultando em uma precisão de 70% para a identificação de embriões viáveis e não viáveis.

FERTILITY

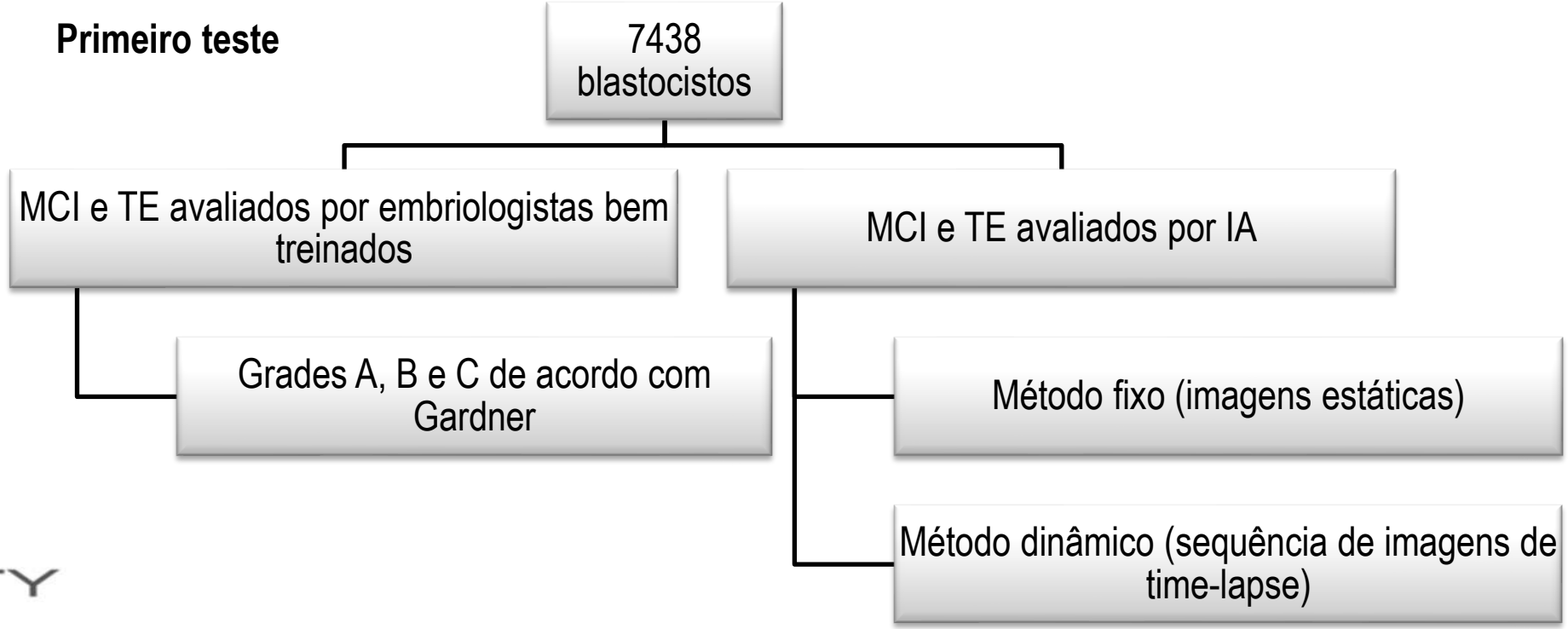
O-168 Automatic morphological grading of human blastocysts with time-lapse imaging and artificial intelligence

M.F. Kragh[1], J. Rimestad[2], J. Berntsen[2],H.Karstoft[3]
[1]Vitrolife A/S & Aarhus University, Research & development, Aarhus S, Denmark, [2] Vitrolife A/S, Research & development, Aarhus S, Denmark, 3. Aarhus University, Department of Engineering, Aarhus N, Denmark

- **Objetivo**: Verificar se a avaliação de blastocistos humanos pode ser totalmente automatizada com imagens de STL e IA para fornecer informações semelhantes ou superiores aquelas obtidas por embriologistas experientes.

- **Métodos**

Primeiro teste



FERTILITY

- **Métodos**

INTELIGÊNCIA ARTIFICIAL

Treinamento (imagens estáticas)

Validação

Teste

Segundo teste

55 embriões transferidos foram avaliados por um grupo de embriologistas e maioria dos votos comparado com IA

FERTILITY

- **Teste 1**

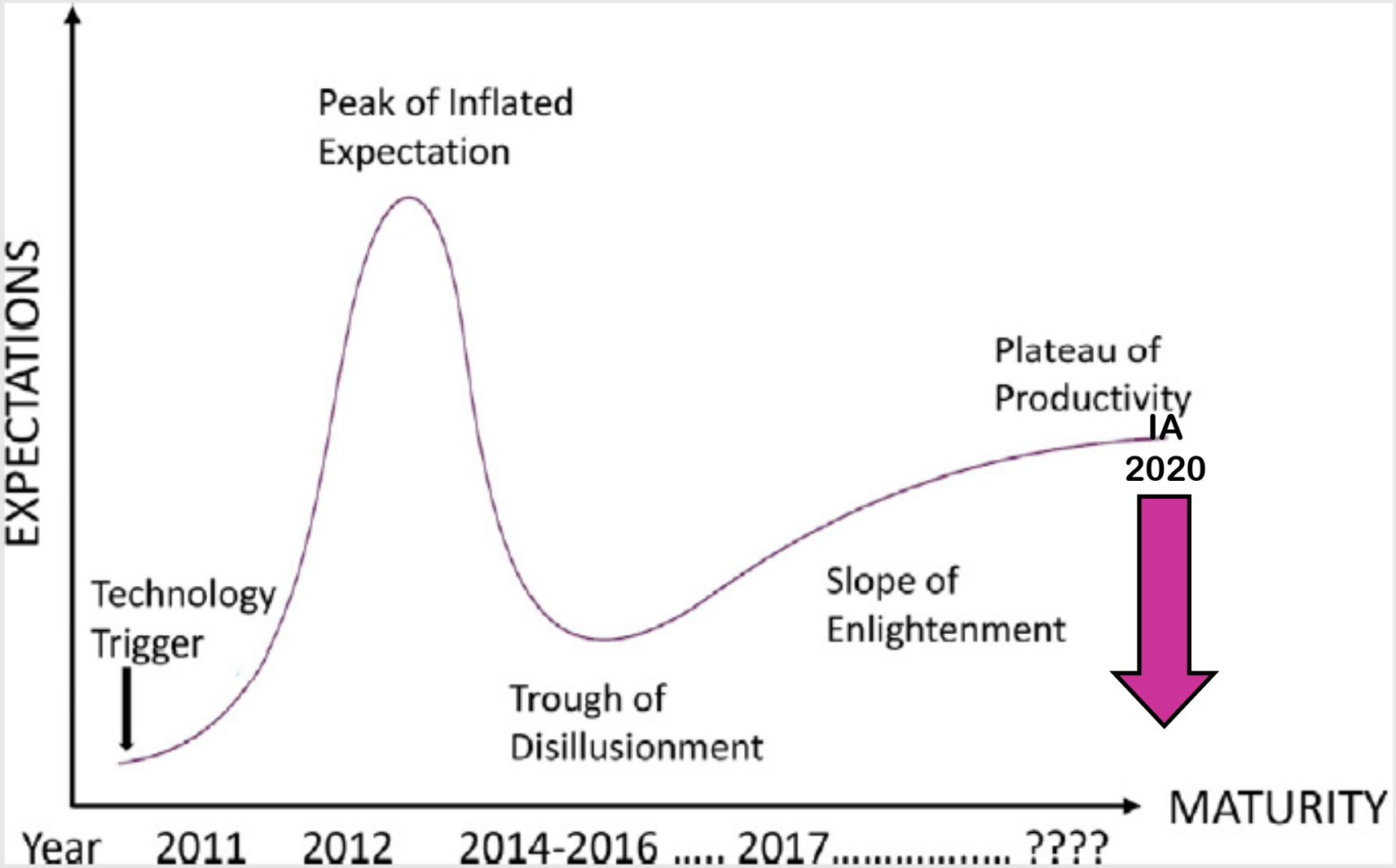
		Acurácia
Embriologistas	MCI	65,1
	TE	73,8
IA	MCI	72,7
	TE	77,6

- **Teste 2**

		Implantação
Embriologistas	Top quality	44,6
	Good quality	30,7
IA	Top quality	46,0
	Good quality	34,4

- **Conclusão**: A IA teve um desempenho melhor que os embriologistas para avaliação do MCI e TE e a seleção dos embriões por meio da IA levou a melhores taxas de implantação para o grupo de embriões com melhores classificações

FERTILITY



The Gartner hype cycle of innovation for time-lapse imaging.

FERTILITY

Embryoscope FERTILITY

ICSI					
Variáveis	Convencional (n=728)		Embryoscope (n=89)		p
	Média	DP	Média	DP	
IdadePaciente	37,4	3,4	37,4	4,1	0,774
IMC	24,6	4,3	24,7	4,1	0,914
FSH (UI)	2658,3	671,6	2751,5	676,9	0,131
E2 (pg/mL)	2057,3	1936,0	1777,4	1863,3	0,219
Folículos puncionados (n)	13,5	13,2	14,1	15,8	0,645
Oócitos obtidos (n)	9,8	9,5	10,4	10,8	0,469
yield (%)	69,9	24,0	73,2	23,5	0,099
MII (n)	7,3	7,2	7,4	7,8	0,861
Taxa de MII (%)	71,3	23,9	73,2	22,7	0,356
Taxa de fertilização (%)	76,3	25,1	72,3	27,8	0,054
Taxa de blastocisto (%)	58,0	24,9	67,4	22,7	**<0,001**
Embriões transferidos (n)	2,0	0,7	1,0	1,0	**<0,001**
Taxa de implantação (%)	22,8	35,9	20,7	36,6	0,668
Taxa de gestação (%)	34,5		40,0		0,360
Taxa de aborto (%)	11,9		0,0		**0,050**

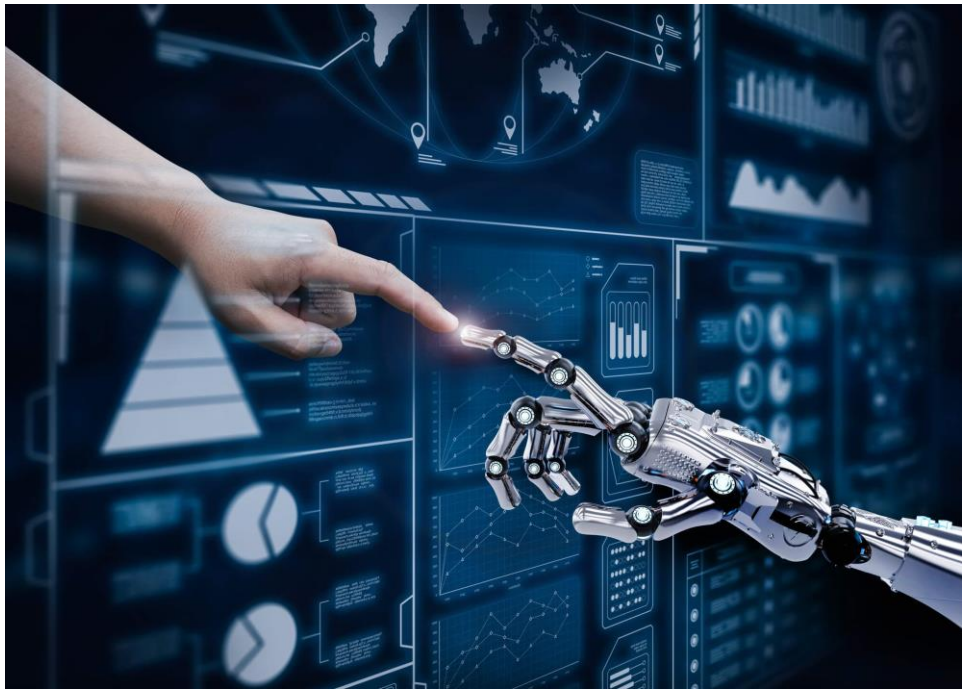
FERTILITY

Embryoscope FERTILITY

OVODON

Variáveis	Convencional (n=36)		Embryoscope (n=30)		p
	Média	DP	Média	DP	
IdadePaciente	44,4	5,0	42,5	3,4	**0,009**
Oócitos injetados (n)	5,9	1,5	6,1	1,6	0,504
Taxa de fertilização (%)	78,4	24,1	80,4	21,8	0,608
Taxa de blastocisto (%)	70,1	23,6	63,1	30,8	0,386
Embriões transferidos (n)	1,9	0,5	1,7	0,5	0,202
Taxa de implantação (%)*	38,3	44,5	44,2	35,6	0,195
Taxa de gestação (%)*	46,7		68,8		**0,021**
Taxa de aborto (%)*	15,4		5,6		0,222

FERTILITY



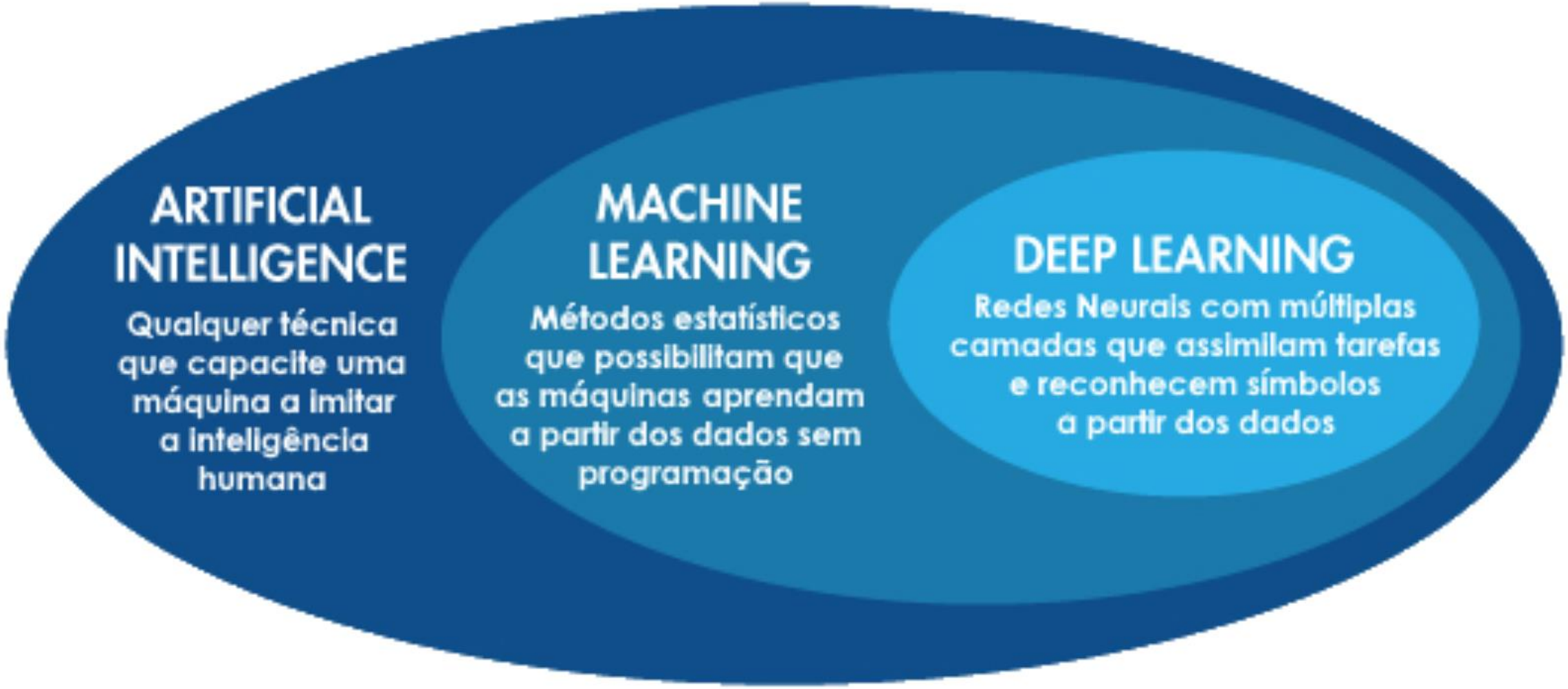
FERTILITY

Machine Learning vs Artificial Intelligence

Machine Learning vs Artificial Intelligence

Machine learning is statistical models used for prediction of an outcome or event.

It provides tools for AI.


ARTIFICIAL INTELLIGENCE
Qualquer técnica que capacite uma máquina a imitar a inteligência humana
MACHINE LEARNING
Métodos estatísticos que possibilitam que as máquinas aprendam a partir dos dados sem programação
DEEP LEARNING
Redes Neurais com múltiplas camadas que assimilam tarefas e reconhecem símbolos a partir dos dados

FERTILITY

What is a success in IVF?

- A pregnancy
- A live birth
- A healthy live birth
- A healthy offspring
- A healthy adult
- Future Generations

- 1970s
- 1980s
- 1990s
- 2000s
- 2010s
- Next

Selecting the best embryo will be more than picking a viable embryo

Captura Retan

EMBRYOSCOPE – CLASSIFICAÇÃO D5

GRAU DE EXPANSÃO	
KIDSCORE D5	Laboratório

MASSA CELULAR INTERNA (grau 3 – 6)		
KIDSCORE D5		Laboratório
A	Muitas células bem compactadas. Os limites das células não são	

TROFECTODERMA (grau 3 – 6)		
KIDSCORE D5		Laboratório
A	Muitas células achatadas (geralmente> 40) formam uma camada coesiva que reveste a cavidade da blastocele. As células geralmente contêm núcleos claramente visíveis e o citoplasma é homogêneo.	Ok
B	Várias (geralmente> 20) células. A camada não é completamente coesa e a forma das células varia na camada. O citoplasma celular pode parecer não homogêneo e pode ser difícil distinguir núcleos	Irregular
C	Muito poucas células que são geralmente grandes e esticadas em uma área grande. O citoplasma frequentemente parece não homogêneo e vacúolos podem estar presentes.	Poucas células e irregular
		Granular
		Com células degeneradas
		Com células excluídas na cavidade

FERTILITY

10,208 Embryos

8 Labs from
Australia, Ireland, Denmark and United Kingdom
2014 to 2018

IVFAustralia
Leading minds dedicated to your success

MelbourneIVF
Leading minds dedicated to your success

QueenslandFertilityGroup
Leading minds dedicated to your success

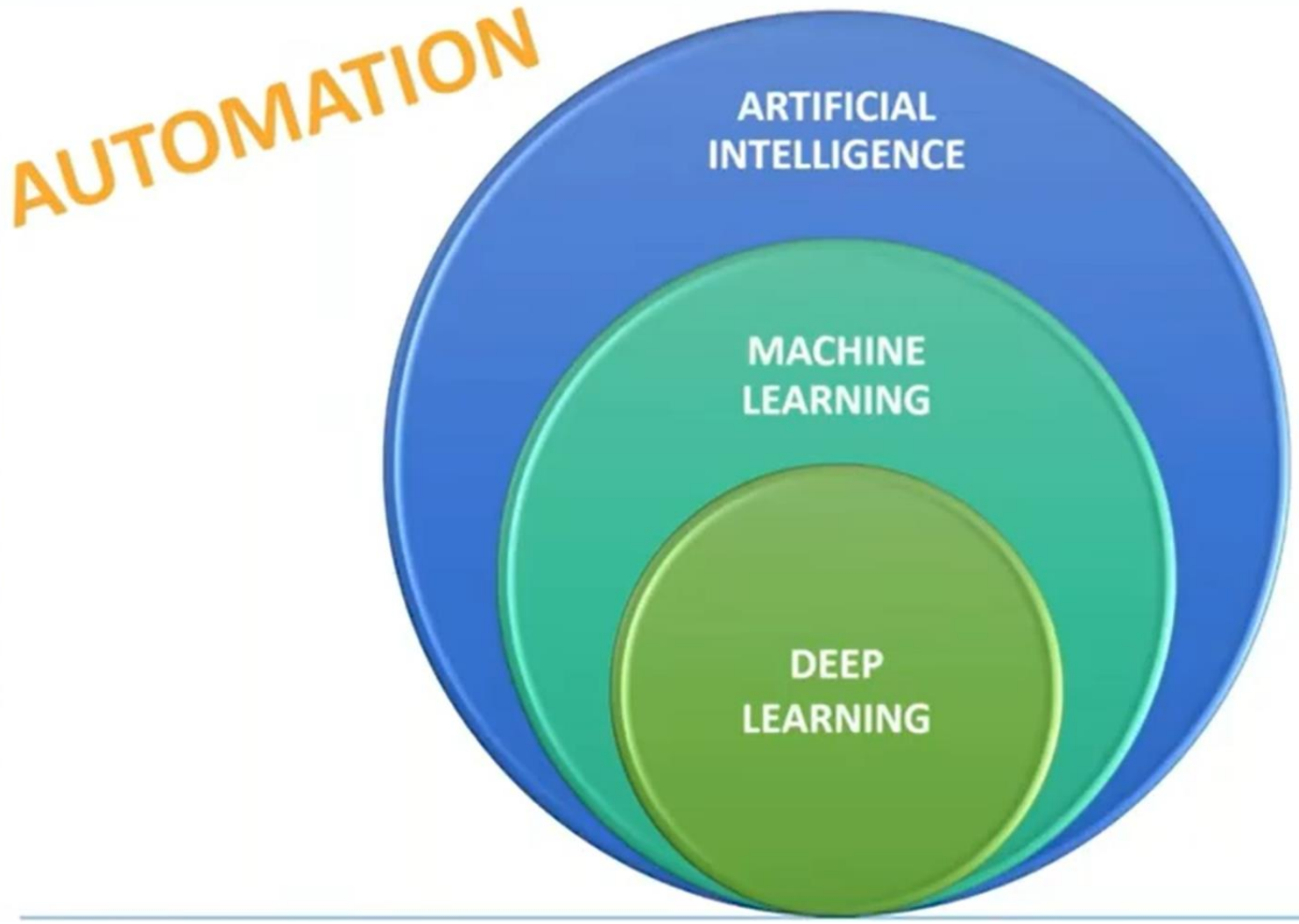
sims IVF

complete™
FERTILITY CENTRE
SOUTHAMPTON

aagaard

FERTILITY

FERTILITY

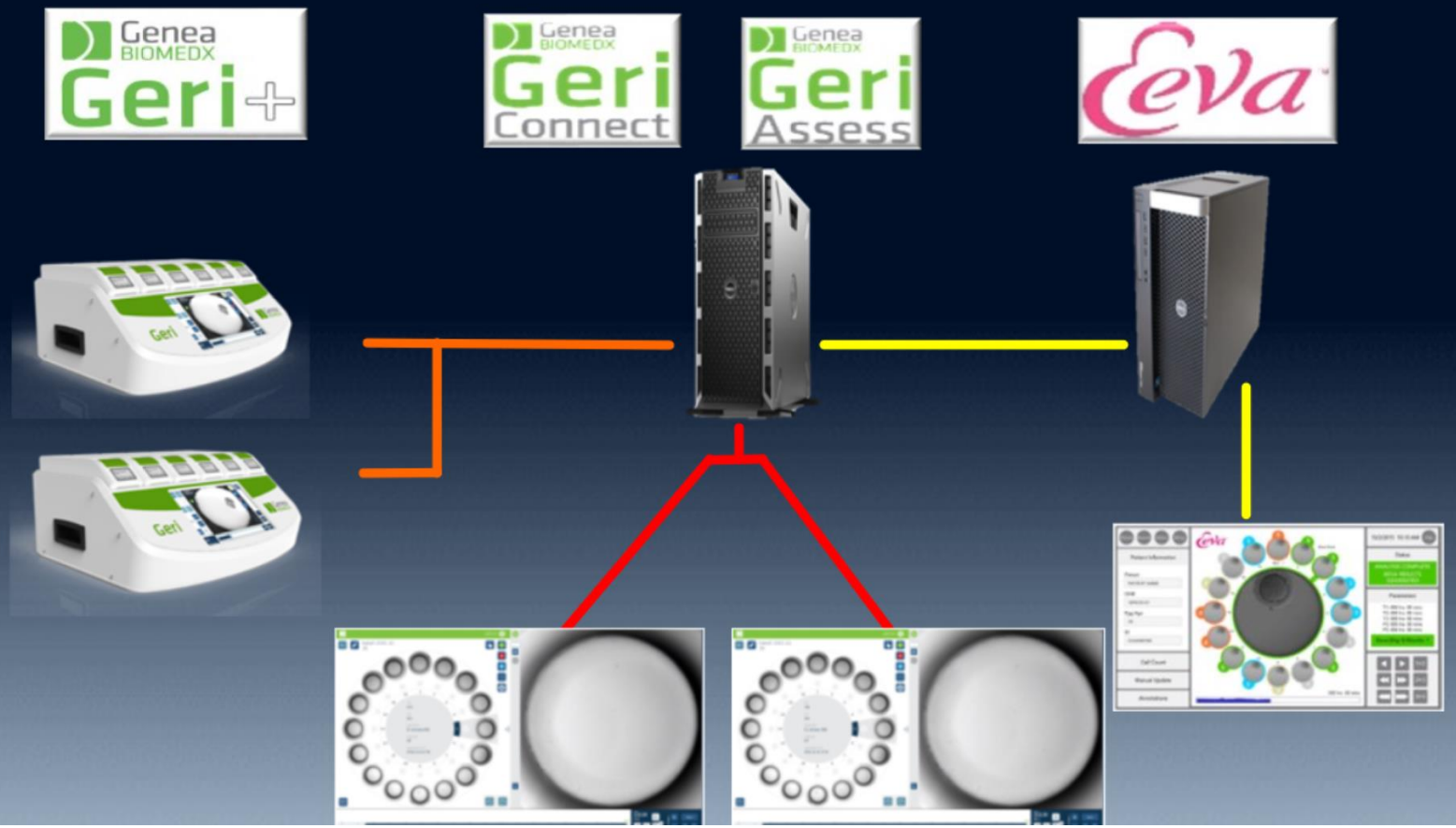


Is the theory and development of computer systems capable of performing tasks normally requiring human intelligence.

Is a field of artificial intelligence that uses statistical techniques to give computer systems the ability to "learn" from data, without being explicitly programmed.

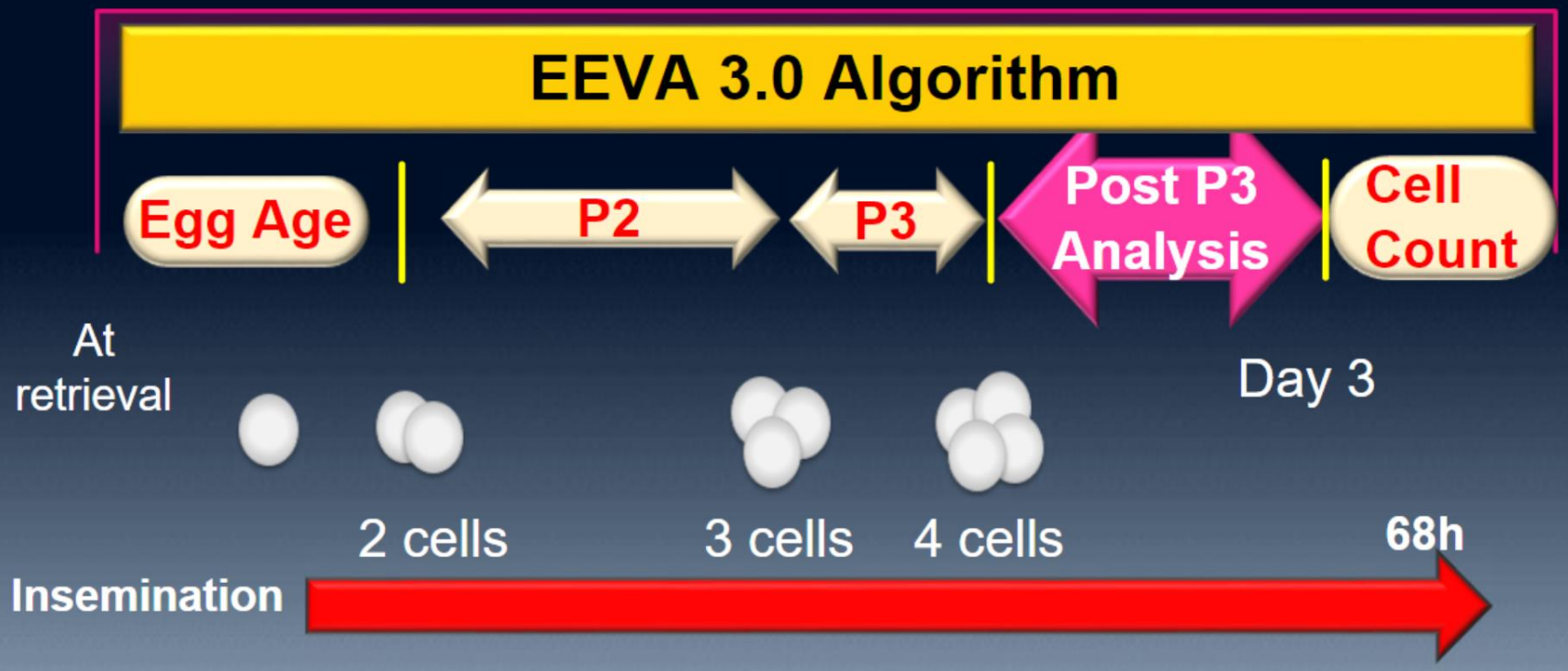
Is a subset of machine learning that has networks capable of learning unsupervised from data that is unstructured or unlabeled.

Geri+ Ver.6.0.1 + Geri Connect & Assess 2.0 + EEVA System



FERTILITY

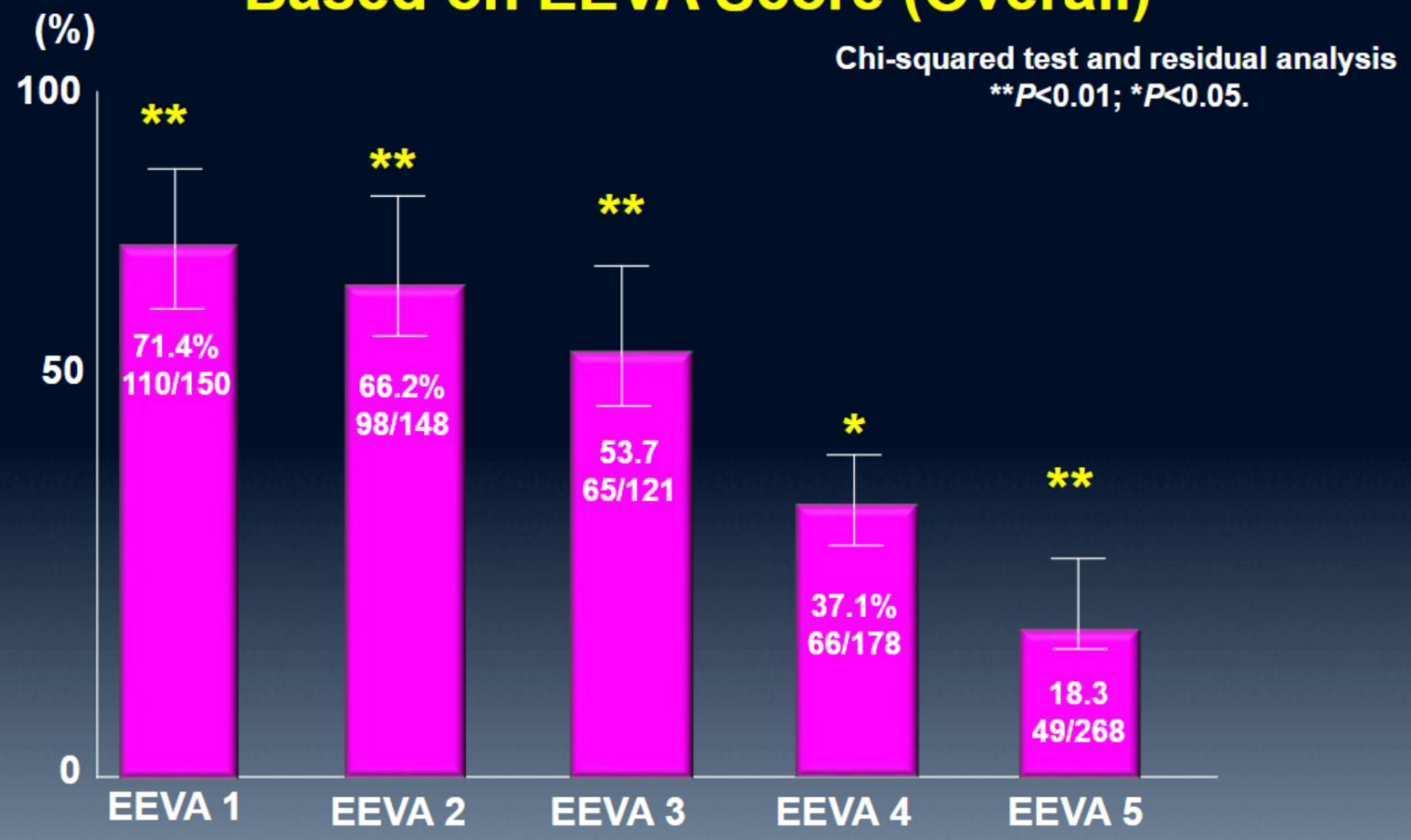
Five Parameters
Defining EEVA 3.0 Xtend Algorithm



FERTILITY

Is the EEVA score a predictive factor for the blastocyst development rate?

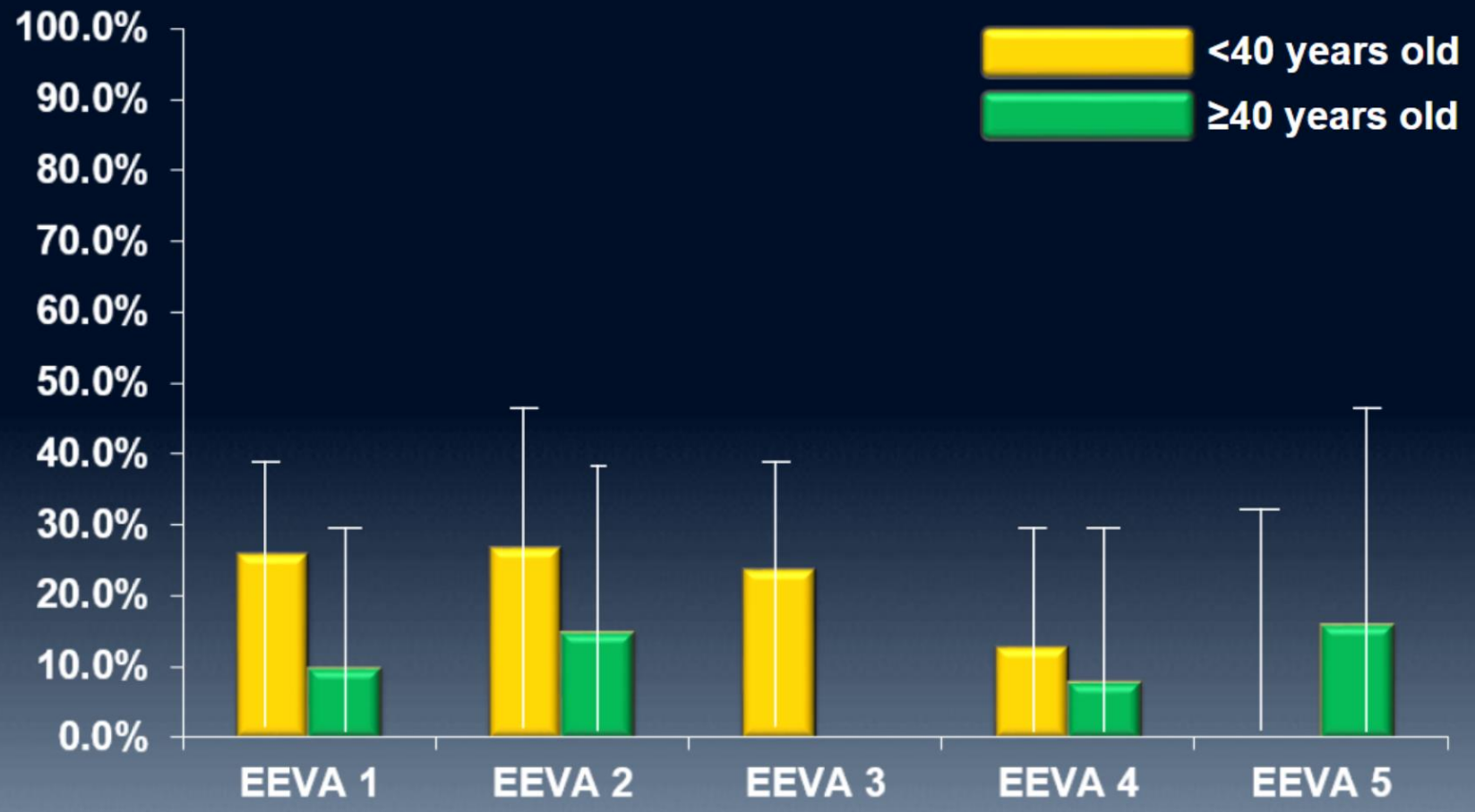
Blastocyst Development Rate Based on EEVA Score (Overall)



FERTILITY

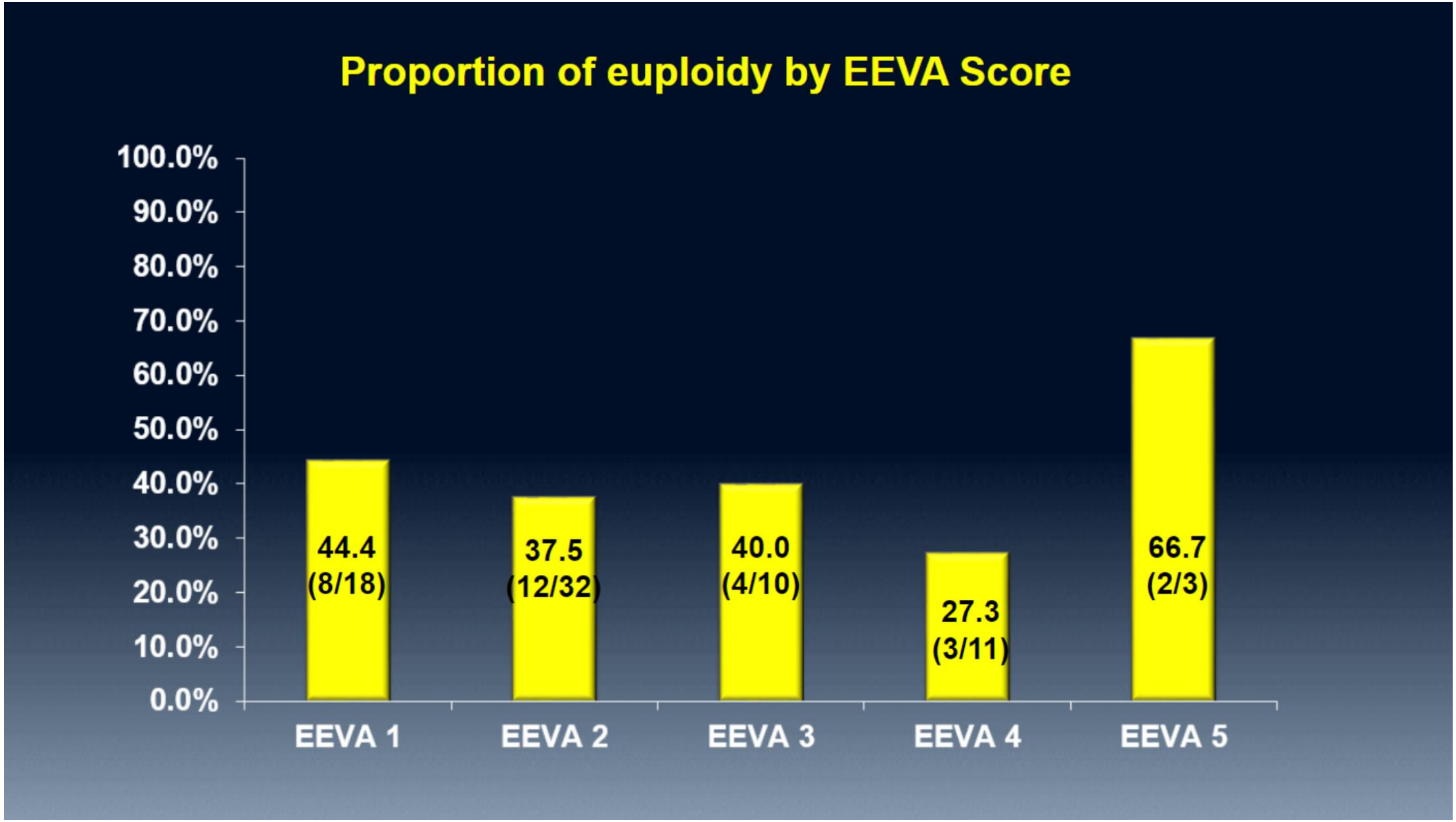
Is the EEVA score
correlated with
the pregnancy rate?

Pregnancy Rate after Single Blastocyst Transfer by EEVA Score



FERTILITY

Is the EEVA score able to predict euploidy?


Proportion of euploidy by EEVA Score
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
44.4 (8/18)
37.5 (12/32)
40.0 (4/10)
27.3 (3/11)
66.7 (2/3)
EEVA 1
EEVA 2
EEVA 3
EEVA 4
EEVA 5

FERTILITY

Machine learning and ART

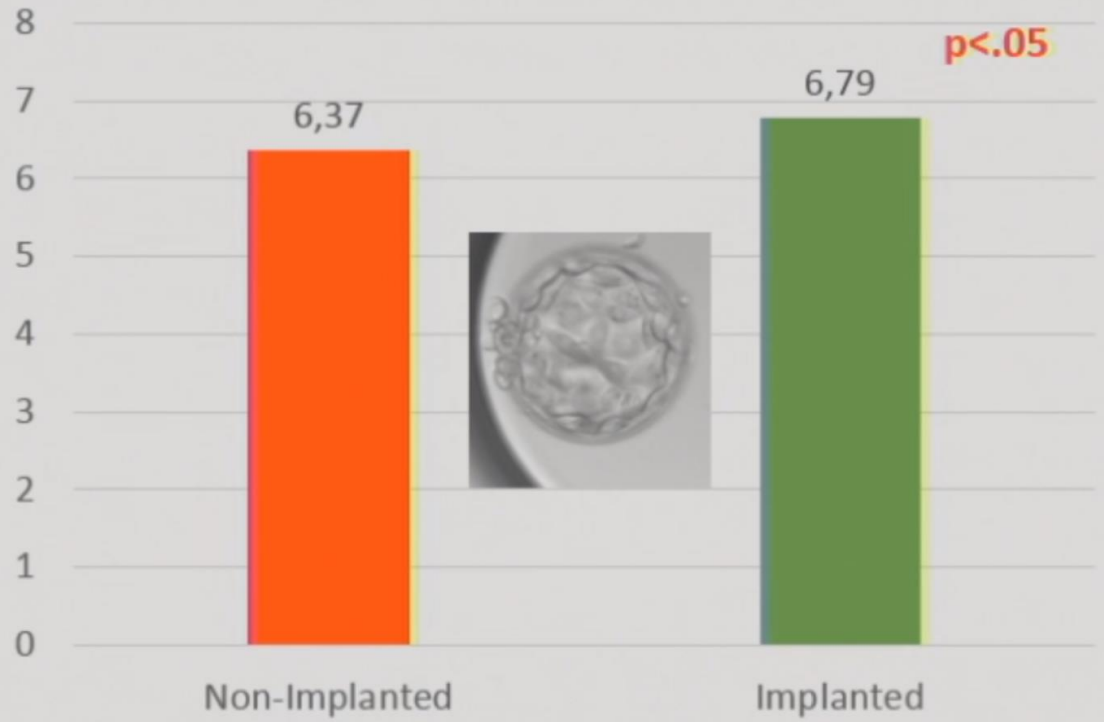
Outcome to Predict	Inputs	Status
Chance of success with IVF	Age, AMH, duration of infertility, BMI	Available
Oocyte • Cryocompetence • Developmental competence	Patient factors Stimulation characteristics Timing	In development
Embryo viability	Patient factors Morphokinetics Metabolomics Image analysis PGT-A	Available
Laboratory Performance	Embryo images, KPIs Daily QC	In development

FERTILITY

Relationship between **Implantation Rate** and the KID Score Day 5 in **good quality embryos (A+B,** *ASEBIR Criteria 2015***)**

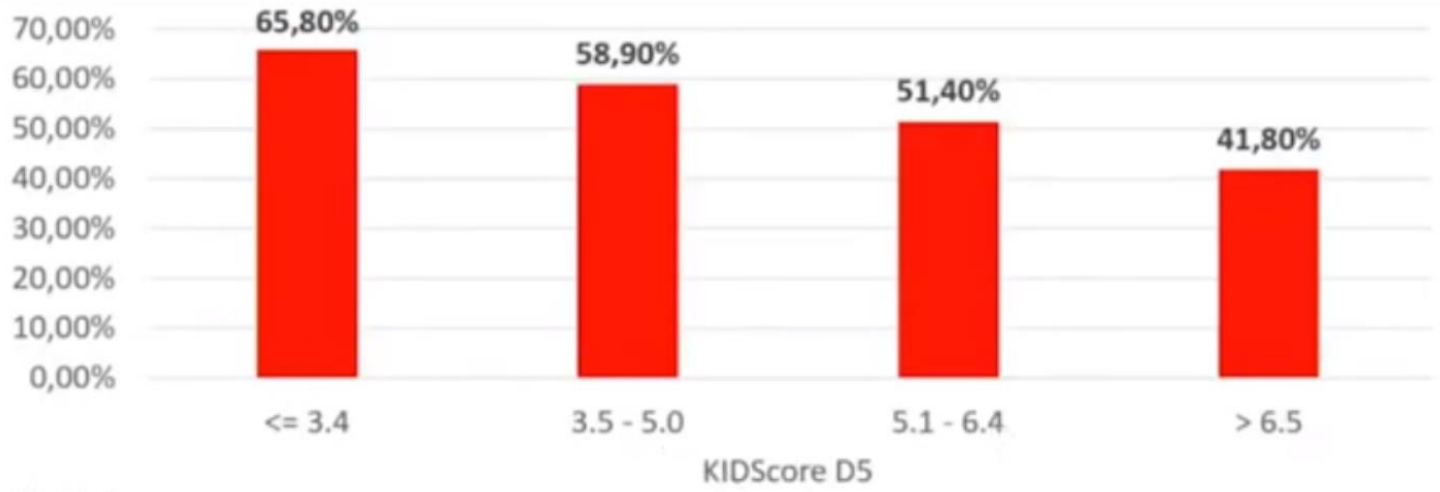
KID Score Day 5 VERSION 3

Implatation	Mean	Standard Deviation	N
Implanted	6.790	1.5420	972
Non-implanted	6.368	1.5502	696

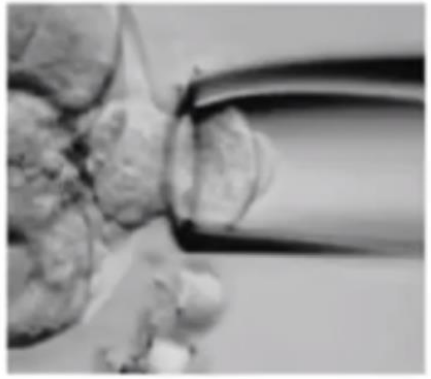


FERTILITY

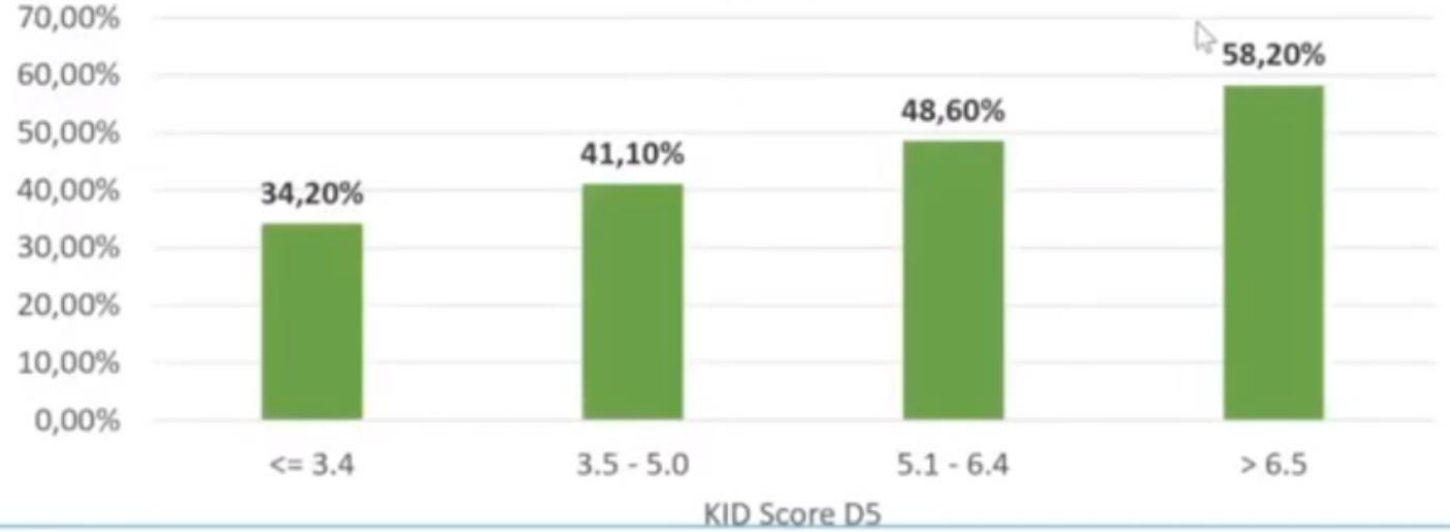
ANEUPLOIDES



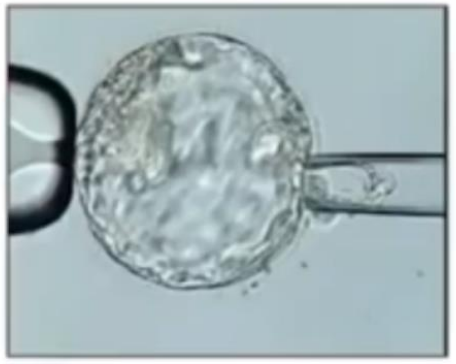
p<.05



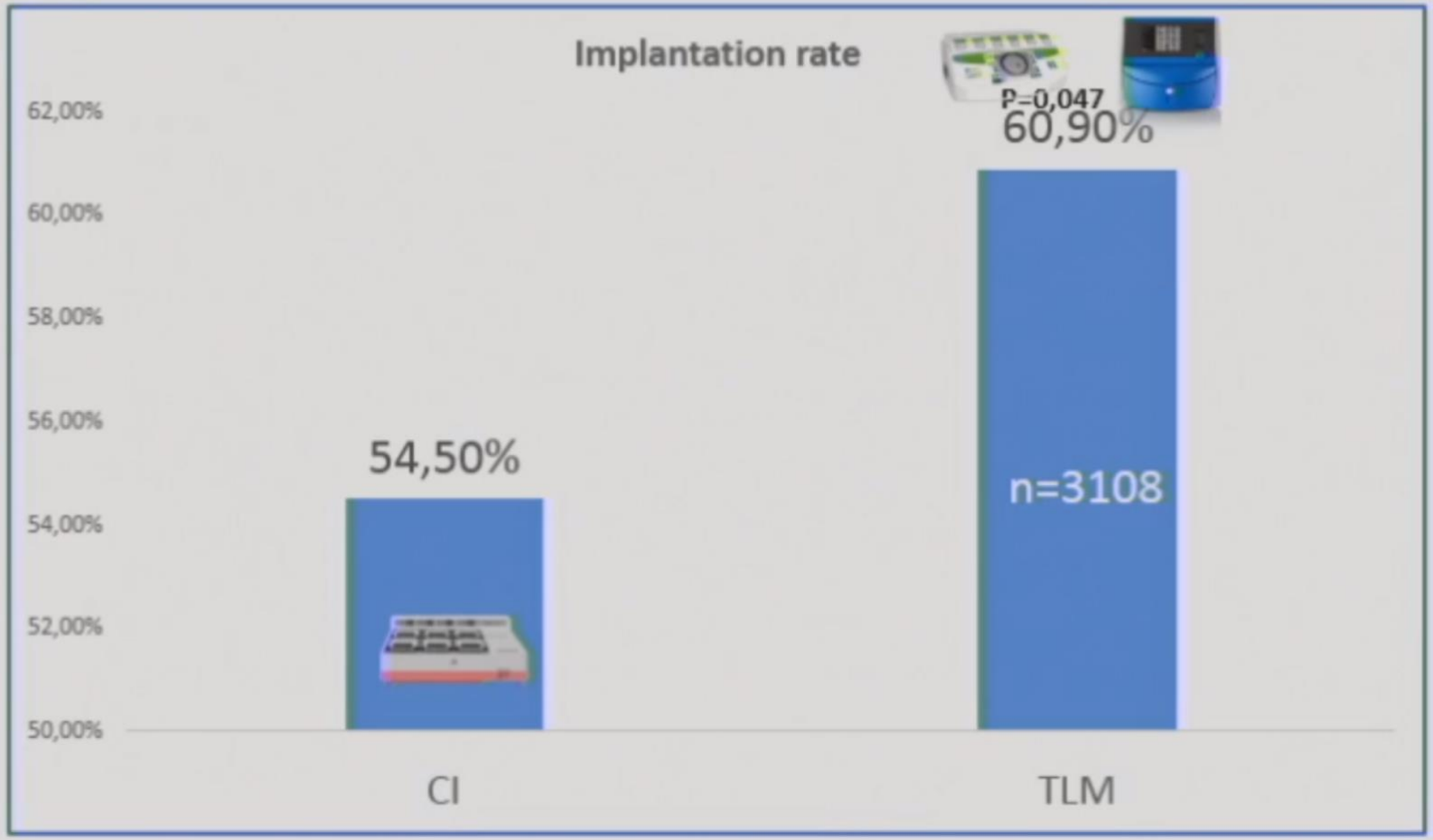
EUPLOIDES



p<.05



FERTILITY


Implantation rate
P=0,047
60,90%
62,00%
60,00%
58,00%
56,00%
54,00%
52,00%
50,00%
54,50%
n=3108
CI
TLM

FERTILITY

Cochrane Library

Cochrane Database of Systematic Reviews

Time-lapse systems for embryo incubation and assessment in assisted reproduction (Review)

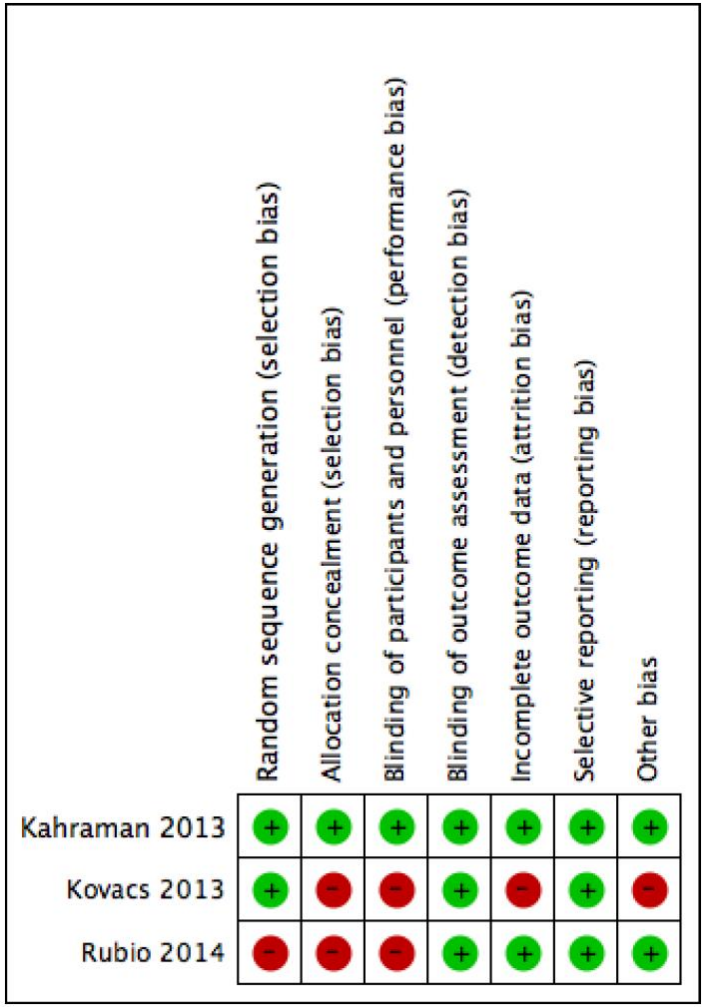
Copyright © 2015 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Time-lapse systems for embryo incubation and assessment in assisted reproduction (Review)

Armstrong S, Arroll N, Cree LM, Jordan V, Farquhar C

Authors' conclusions

There is insufficient evidence of differences in live birth, miscarriage, stillbirth or clinical pregnancy to choose between TLS and conventional incubation. Further data explicitly comparing the incubation environment, the algorithm for embryo selection, or both, are required before recommendations for a change of routine practice can be justified.



FERTILITY

PLOS ONE | https://doi.org/10.1371/journal.pone.0178720 June 1, 2017

RESEARCH ARTICLE

Does time-lapse imaging have favorable results for embryo incubation and selection compared with conventional methods in clinical in vitro fertilization? A meta-analysis and systematic review of randomized controlled trials

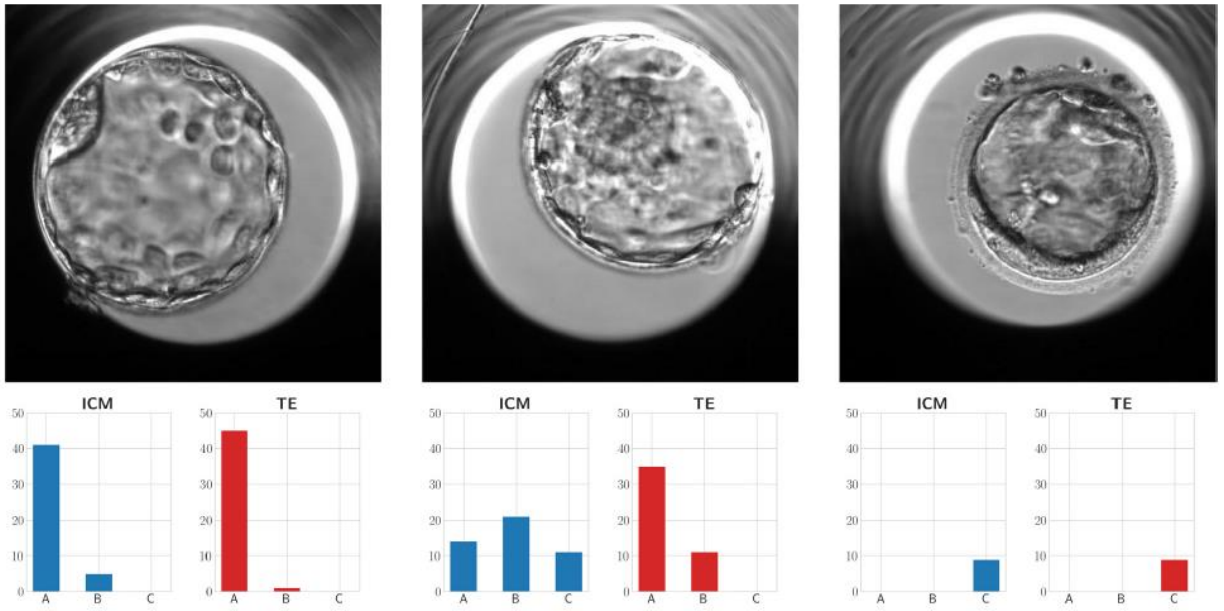
Minghao Chen[1], Shiyou Wei[2], Junyan Hu[3], Jing Yuan[4], Fenghua Liu[1]*

1 Reproductive Center, Guangdong Women and Children Hospital, Guangzhou, China, 2 Department of Thoracic Surgery, West China Hospital, Sichuan University, Chengdu, China, 3 Department of Emergency, The Third Affiliated Hospital of Guangzhou Medical University, Guangzhou, China, 4 School of Traditional Chinese Medicine, Jinan University, Guangzhou, China

Conclusions

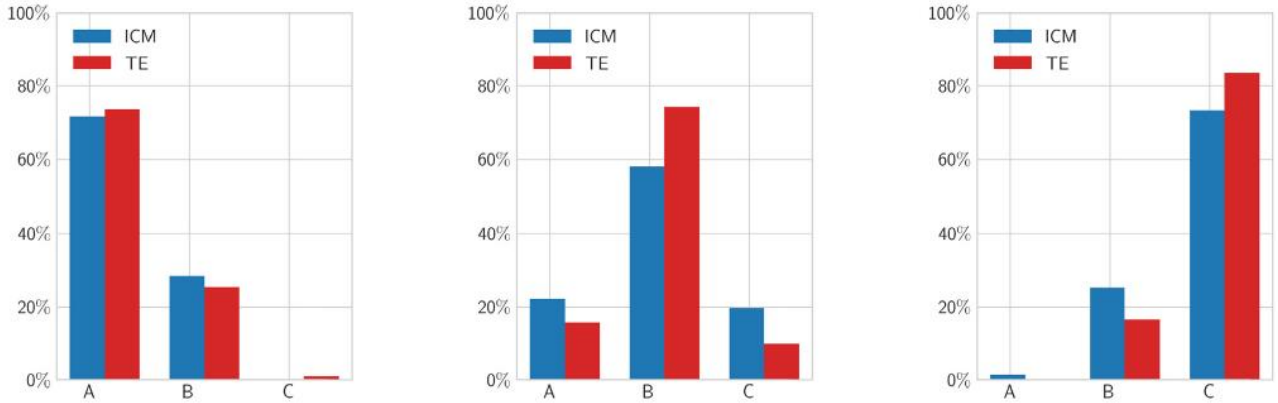
Currently there is insufficient evidence to support that TLI is superior to conventional methods for human embryo incubation and selection. In consideration of the limitations and flaws of included studies, more well designed RCTs are still in need to comprehensively evaluate the effectiveness of clinical TLI use.

FERTILITY



(a) ICM: A, TE: A (b) ICM: B, TE: A (c) ICM: C, TE: C

Fig. 3. Example blastocysts from dataset 2 with different ICM and TE ratings. The upper row shows the center focal planes at 115 hpi, while the lower row shows histograms the embryologists' annotations.

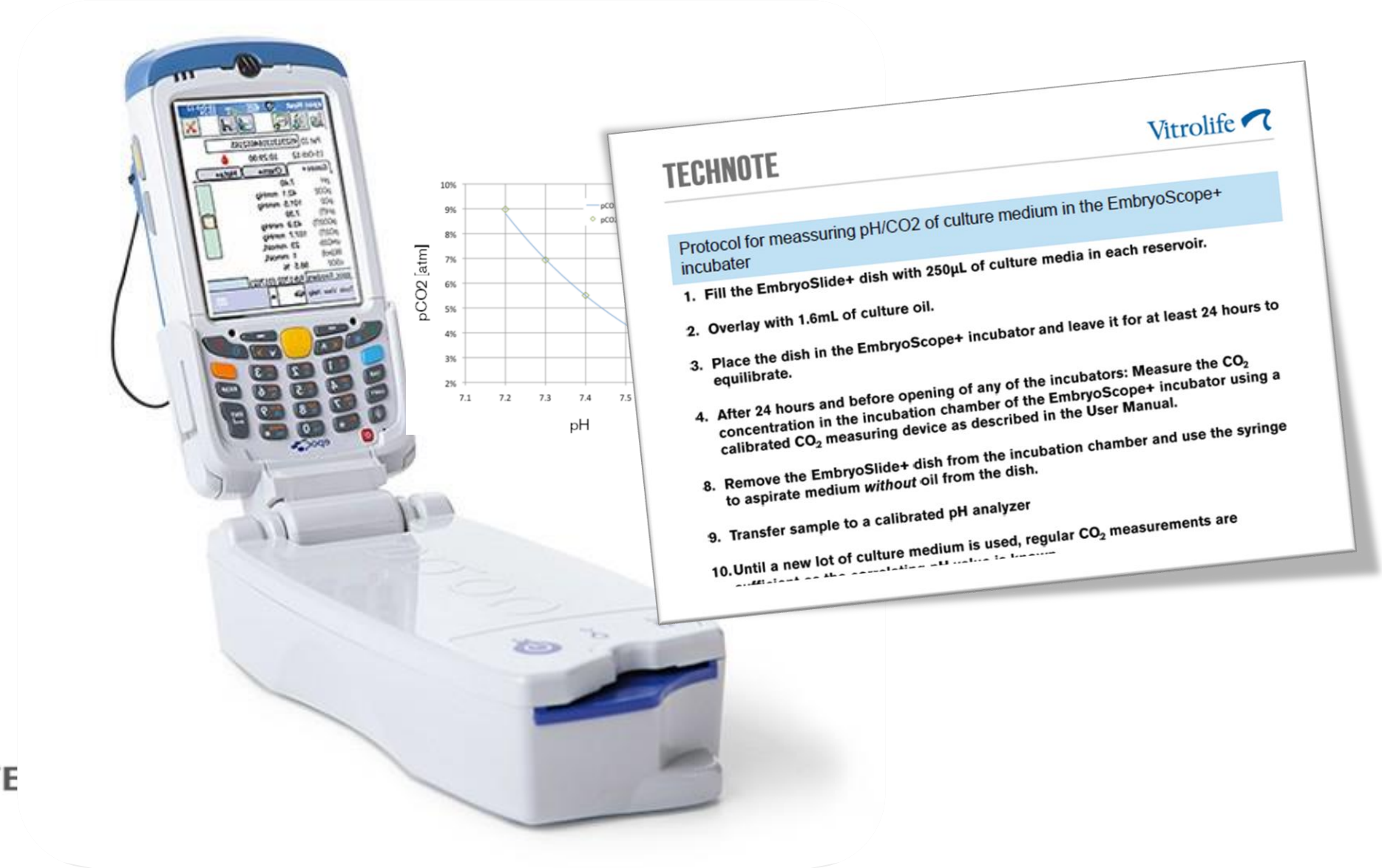


(a) Majority vote: A (b) Majority vote: B (c) Majority vote: C

FERTILITY

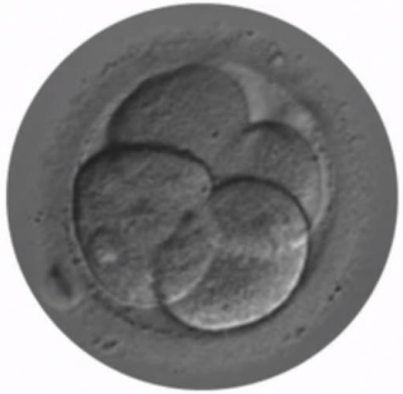
EMBRYOSCOPE - pH

AMBIENTE DE CULTIVO SEGURO PARA OS EMBRIÕES

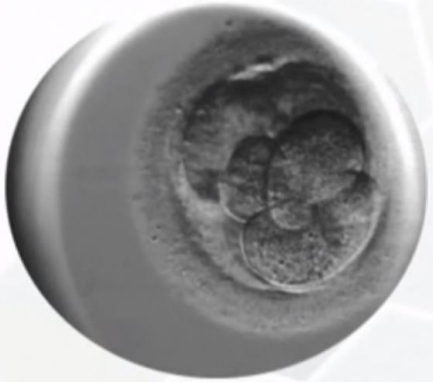


POOR PROGNOSIS EVENTS DURING IN-VITRO EMBRYO DEVELOPMENT

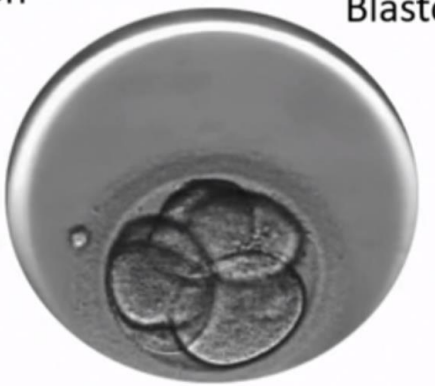
Fragmentation



Blastomere Asymmetry

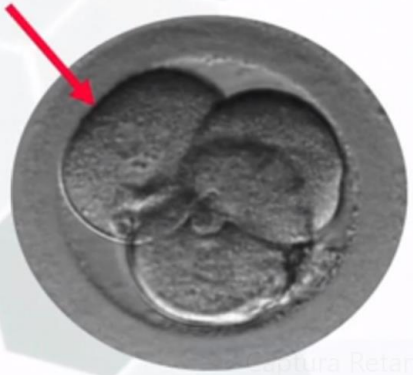


Reverse Cleavage



Direct Cleavage

Blastocyst Collapse



Multinucleation

FERTILITY

MULTINUCLEATION

Impact of the presence of one or more multinucleated blastomeres on the developmental potential of the embryo to the blastocyst stage

YAKIN, K., BALABAN, B., & URMAN, B. (2005)

The impact of multinucleated blastomeres on embryo developmental competence, morphokinetics, and aneuploidy

Hanna Balakier, Ph.D.,[a] Agata Sojecki, M.Sc.,[a] Gelareh Motamedi, M.Sc.,[a] and Clifford Librach, M.D.[a,b,c,d]

[a] Create Fertility Centre, [b] Department of Obstetrics and Gynecology, and [c] Department of Physiology, University of Toronto; and [d] Department of Gynecology, Women's College Hospital, Toronto, Ontario, Canada

Blastomere multinucleation: Contributing factors and effects on embryo development and clinical outcome

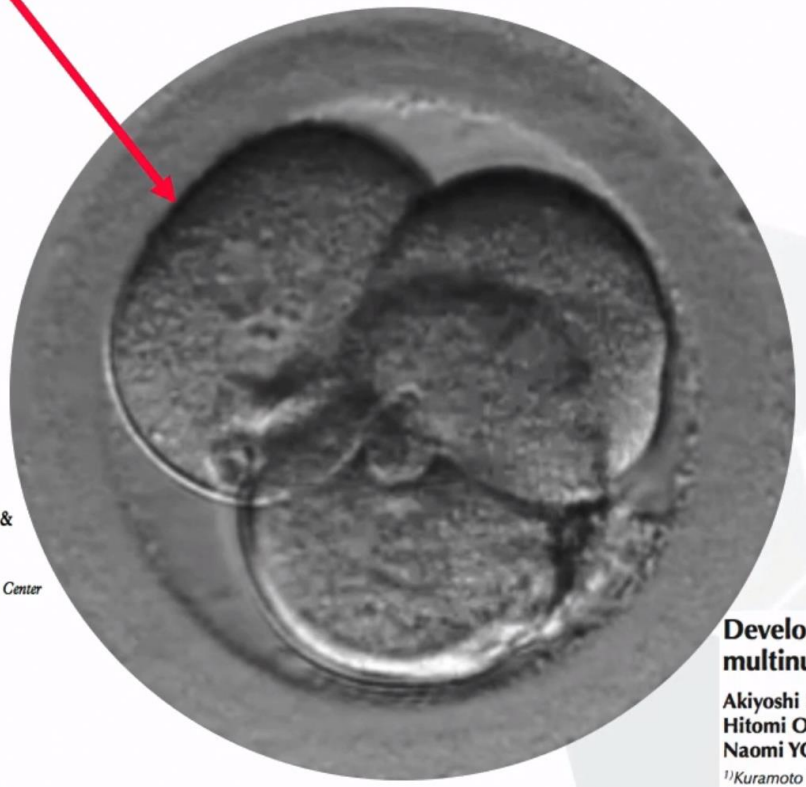
RITA DE CÁSSIA SAVIO FIGUEIRA[1,2], AMANDA SOUZA SETTI[2], DANIELA PAES DE ALMEIDA FERREIRA BRAGA[1,2], ASSUMPTO IACONELLI JR.[1], & EDSON BORGES JR.[1,2]

[1]*Fertility – Assisted Fertilization Center, São Paulo, SP, Brazil, and* [2]*Sapientiae Institute – Educational and Research Center in Assisted Reproduction, São Paulo, SP, Brazil*

Frequency of embryo multinucleation detected by time-lapse system and its impact on pregnancy outcome

Elif G. Ergin, M.D., Eray Çalişkan, M.D., Ender Yalçinkaya, M.Sc., Zeynep Öztel, B.Sc., Kevser Çökelez, B.Sc., Alev Özay, M.D., and Hakan M. Özörnek, M.D.

Eurofertil IVF Center, Istanbul, Turkey



Study of nucleation status in the second cell cycle of human embryo and its impact on implantation rate

Jesus Aguilar, Ph.D.,[a] Irene Rubio, Ph.D.,[b] Elkin Muñoz, M.D., Ph.D.,[a] Antonio Pellicer, M.D., Ph.D.,[b] and Marcos Meseguer, Ph.D.[b]

[a] IVI Vigo, Vigo; and [b] Instituto Valenciano de Infertilidad, Universidad de Valencia, Valencia, Spain

Is the nuclear status of an embryo an independent factor to predict its ability to develop to term?

Patricia Fauque, M.D., Ph.D.,[a] Etienne Audureau, M.D., Ph.D.,[b] Roger Leandri, M.D., Ph.D.,[c] Lucie Delaroche, M.D.,[d] Stéphanie Assouline, M.D.,[f] Sylvie Epelboin, M.D.,[e] Pierre Jouannet, M.D.,[f] and Catherine Patrat, M.D., Ph.D.[d]

[a] Laboratoire de Biologie de la Reproduction, Hôpital de Dijon, Université de Bourgogne, Dijon; [b] Unité de Biostatistique et Epidémiologie, Hôtel Dieu, Assistance Publique des Hôpitaux de Paris, Université Paris Descartes, Paris; [c] Laboratoire de Biologie de la Reproduction, Hôpital Paule de Viguier, Toulouse; and [d] Laboratoire de Biologie de la Reproduction and [e] Service de Gynécologie-Obstétrique, Hôpital Bichat-Claude Bernard, Assistance Publique des Hôpitaux de Paris, Université Paris Diderot, Paris; and [f] Centre de Recherche Sens, Éthique, Société (Unité Mixte de Recherche 8137/Centre National de la Recherche Scientifique), Université Paris Descartes, Paris, France

Developmental capacity and implantation potential of the embryos with multinucleated blastomeres

Akiyoshi EGASHIRA[1)], Nobuhiko YAMAUCHI[2)], Keiko TANAKA[1)], Chihiro MINE[1)], Hitomi OTSUBO[1)], Masao MURAKAMI[1)], Md. Rashedul ISLAM[2, 3)], Misako OHTSUKA[1)], Naomi YOSHIOKA[1)] and Takashi KURAMOTO[1)]

[1)]*Kuramoto Women's Clinic, Fukuoka 812-0013, Japan*
[2)]*Department of Animal and Marine Bioresource Sciences, Graduate School Kyushu University, Fukuoka 812-8581, Japan*
[3)]*Department of Genetics and Animal Breeding, Hajee Mohammad Danesh Science and Technology University, Dinajpur-5200, Bangladesh*

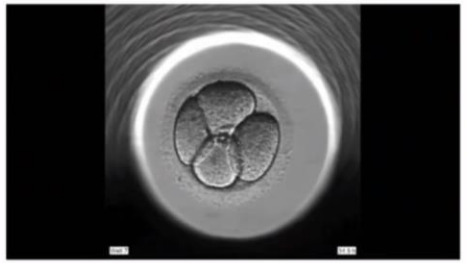
Incidence : 11-34%; 15-20%; 17-69%

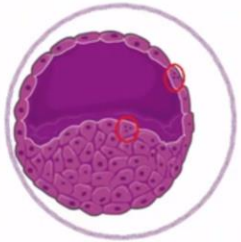
FERTILITY

261 Analyzed

MNC Blastocysts Transferred

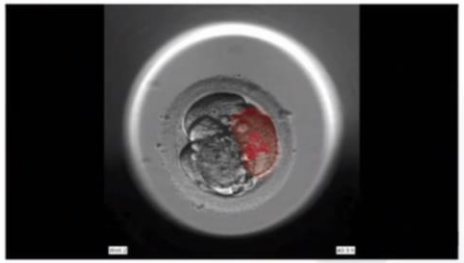
MNC-1

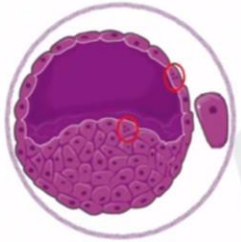




⊖ Exclussion
⊕ MNC Blastocyst

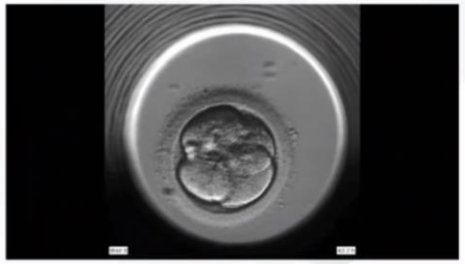
MNC-2

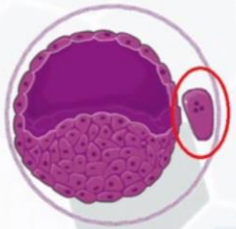




⊕ Exclussion
⊕ MNC Blastocyst

MNC-3





⊕ Exclussion
⊖ MNC Blastocyst

FERTILITY MEDICAL GROUP

FERTILITY

Using AI for Embryo Selection

AI to Identify Which Embryos are Most Likely to Lead to a Pregnancy

AI to predict implantation success and assist in embryo selection

IVF Process

Fertilize eggs/oocytes with sperm

Embryos form after 5 days

Assess embryos & decide which to transfer to the patient

Transfer the Embryo to the patient

Pregnancy after 6 weeks (fetal heartbeat)

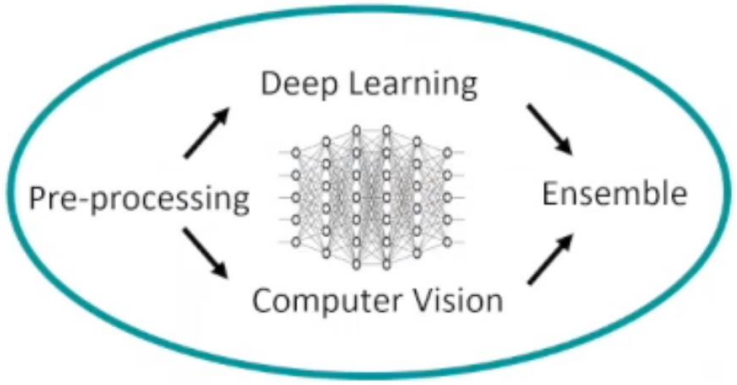
AI Model Development

AI Training Dataset

+

Pregnancy Outcome

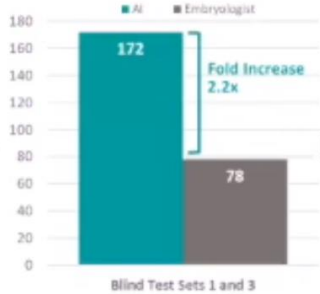
AI Training



AI Validation
& Model Selection

AI Model

AI Blind
Testing: Accuracy



AI
Accuracy

FERTILITY

Automation is already here

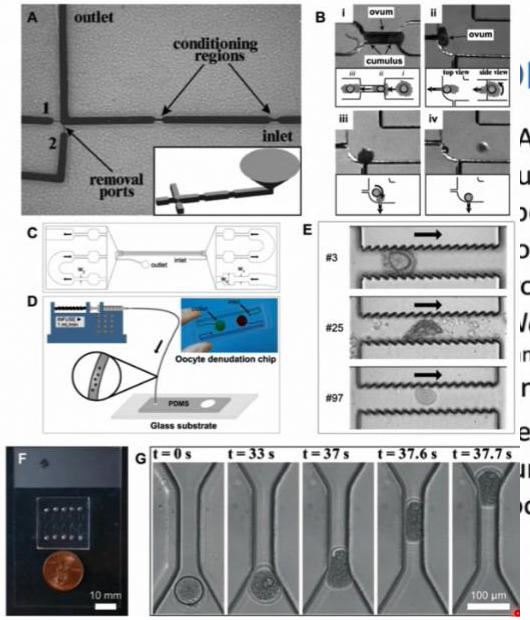
- Sperm selection
- Oocyte denudation
- Robotic ICSI
- Microfluidics – embryo culture
- Vitrification
- e-Witnessing
- Robotic cryo storage
- Time lapse technology

FERTILITY

Oocyte denudation using microfluidics

- Mouse oocytes denuded by MF had similar fertilization and developmental competence compared with traditional mechanical pipetting
- On-chip denudation generates a smaller shear than manual denudation and thus impose less mechanical stress on the cells
- shear stress generated in microfluidic channels must be controlled carefully by optimizing the geometry and flow rate to preserve the structure and functionality of oocytes

Weng 2019



mputer-aided sperm analysis (CASA)

ASA-Conc, -Mot, -Morph

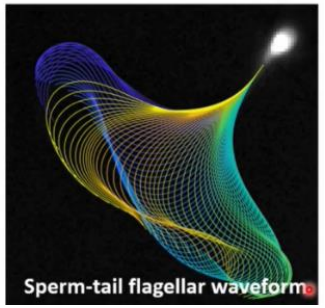
urrent CASA systems focus almost exclusively on analysing and tracking the perm head

ome newer systems check for the presence of a tail to help exclude debris om analyses

Vo [CASA] is alternative to skilled and experienced andrology staff' (ABA UK, nders et al. 2017 Br. J. Biomed. Sci)

mited use.

evelopment and inclusion of flagellar tracking into urrent CASA-Mot systems may improve its use as a ool for clinical diagnostics



er et al 2018, Reprod Fertil Devel

Robotic ICSI

First report Lu et al 2011.

- visual tracking of single sperm
- robotic immobilization of sperm
- aspiration of sperm
- insertion of sperm into an oocyte
- hamster oocyte-human sperm model

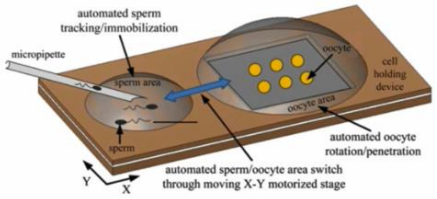


Fig. 3. Robotic ICSI consists of automated sperm manipulation and oocyte injection.

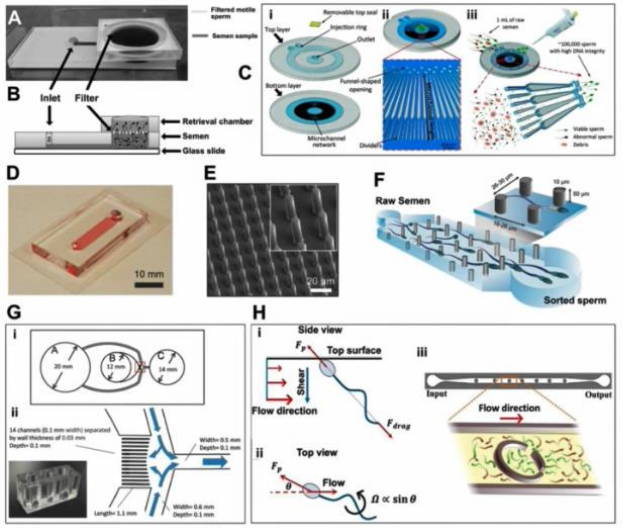
Challenge of robotic ICSI: confirmation of oolemma penetration before sperm injection

Mor et al 2020

- Video paper in FS
- Electrical resistance increase ΔR reliable tool to confirm oocyte penetration and viability, independent of optical visualization

FERTILITY

Microfluidic systems for sperm sorting

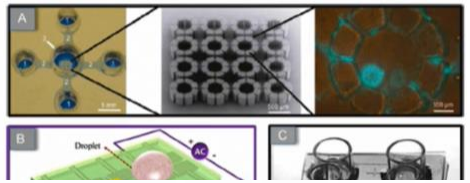


Molecular Human Reproduction, Vol.23, No.4 pp. 213–226, 2017
Advanced Access publication on October 4, 2016 doi:10.1093/molehr/gaw061

molecular human reproduction NEW RESEARCH HORIZON *Review*

Microfluidics for mammalian embryo culture and selection: where do we stand now?

Séverine Le Gac[1,*] and Verena Nordhoff[2]



Various microfluidic platforms proposed

- microwell arrays, whose ancestor is the well-of-the-well (Fig.A)
- microliter-sized droplets
- EWOD (electrowetting-on-a-dielectric) platform (Fig.B)
- fully microfuidic devices with microchannels or microcha (Fig.C-E).

The future: IVF lab on a chip

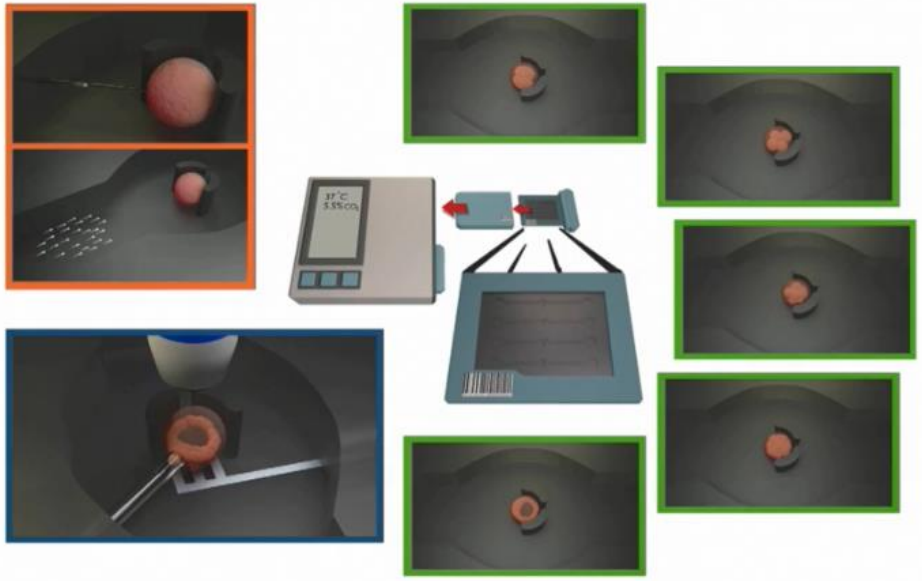


Figure from:
Le Gac & Nordhoff, 2017

To integrate all steps of IVF in a single platform (sperm selection, fertilisation, culture, invasive/non-invasive assessment)

FERTILITY

Robotic cryostorage

- Robotic platform for automated cryostorage
- Vapour-phase LN freezing
- sample management through robotic handling, digital inventory control, continuous remote reporting of tank parameters such as temperature, LN2 level and LN2 consumption rate predictive analytics that can help avoid system failure.
- System suggests increased security, stability and efficiency compared to conventional methods of cryostorage.

Sharp et al 2019

- Initial validation using mouse embryos.
- Post-thaw survival and blastocyst formation similar to manual method

Electronic witnessing

- Barcode identification
  - Limitations: Errors while printing barcode labels, circumvention by staff)
- Radiofrequency identification
  - More accurate tha barcode. information on the safety of radiowaves for oocytes and embryos is lacking
- Embryo direct tagging
  - attachment of biofunctionalized polysilicon barcodes to the outer surface of the zona pellucida of fresh and frozen embryos
- RFID tagging for cryopreserved samples (cryo carriers)

De los Santos and Ruiz 2013
Rienzi et al 2015
Cimadomo et al 2016
Novo et al 2013

FERTILITY

Human Reproduction, Vol.34, No.6, pp. 1011–1018, 2018
Advance Access Publication on May 21, 2019 doi:10.1093/humrep/dez064

human reproduction ORIGINAL ARTICLE *Embryology*

Deep learning as a predictive tool for fetal heart pregnancy following time-lapse incubation and blastocyst transfer

D. Tran[1,*], S. Cooke[2], P.J. Illingworth[2], and D.K. Gardner[3]

[1]Medical AI, Harrison AI, Barangaroo, NSW, Australia [2]Embryology, IVF Australia, Greenwich, NSW, Australia [3]Embryology, Melbourne IVF, East Melbourne, Victoria, Australia

*Correspondence address. Harrison AI, Barangaroo, New South Wales, Australia. E-mail: Aengus@harrison.ai

Table I Number of embryos, patient ages and culture media used in each laboratory.

Laboratory number	Laboratory	Number of embryos studied	Mean age	Age range	Media used in the laboratory
1	IVFAustralia (Sydney, Australia)	1264	36.8	23–46	Vitrolife, Sequential; Vitrolife, Single Stage (G-TL™)
2	IVFAustralia (Canberra, Australia)	150	34.2	24–44	Sage, Sequential
3	Hunter IVF (Newcastle, Australia)	632	34.8	25–43	Vitrolife, Single Stage (G-TL™)
4	Melbourne IVF (Melbourne, Australia)	758	36.6	30–45	Vitrolife, Single Stage (G-TL™)
5	Queensland Fertility Group (Brisbane, Australia)	3827	35.6	22–50	Sage, Sequential; COOK, Sequential; Vitrolife, Single Stage (G-TL™)
6	SIMS IVF (Dublin, Ireland)	1454	35.9	25–46	Vitrolife, Single Stage (G-TL™)
7	Complete Fertility Centre (Southampton, UK)	915	34.7	24–44	Vitrolife, Sequential; Vitrolife, Single Stage (G-TL™)
8	Aagard Fertility (Aarhus, Denmark)	1683	34.2	24–44	Sage 1-step
		n=10683			

FERT

Human Reproduction, Vol.34, No.6, pp. 1011–1018, 2018
Advance Access Publication on May 21, 2019 doi:10.1093/humrep/dea064

human reproduction ORIGINAL ARTICLE *Embryology*

Deep learning as a predictive tool for fetal heart pregnancy following time-lapse incubation and blastocyst transfer

D. Tran[1,*], S. Cooke[2], P.J. Illingworth[2], and D.K. Gardner[3]

[1]Medical AI, Harrison AI, Barangaroo, NSW, Australia [2]Embryology, IVF Australia, Greenwich, NSW, Australia [3]Embryology, Melbourne IVF, East Melbourne, Victoria, Australia

*Correspondence address. Harrison AI, Barangaroo, New South Wales, Australia. E-mail: Aengus@harrison.ai

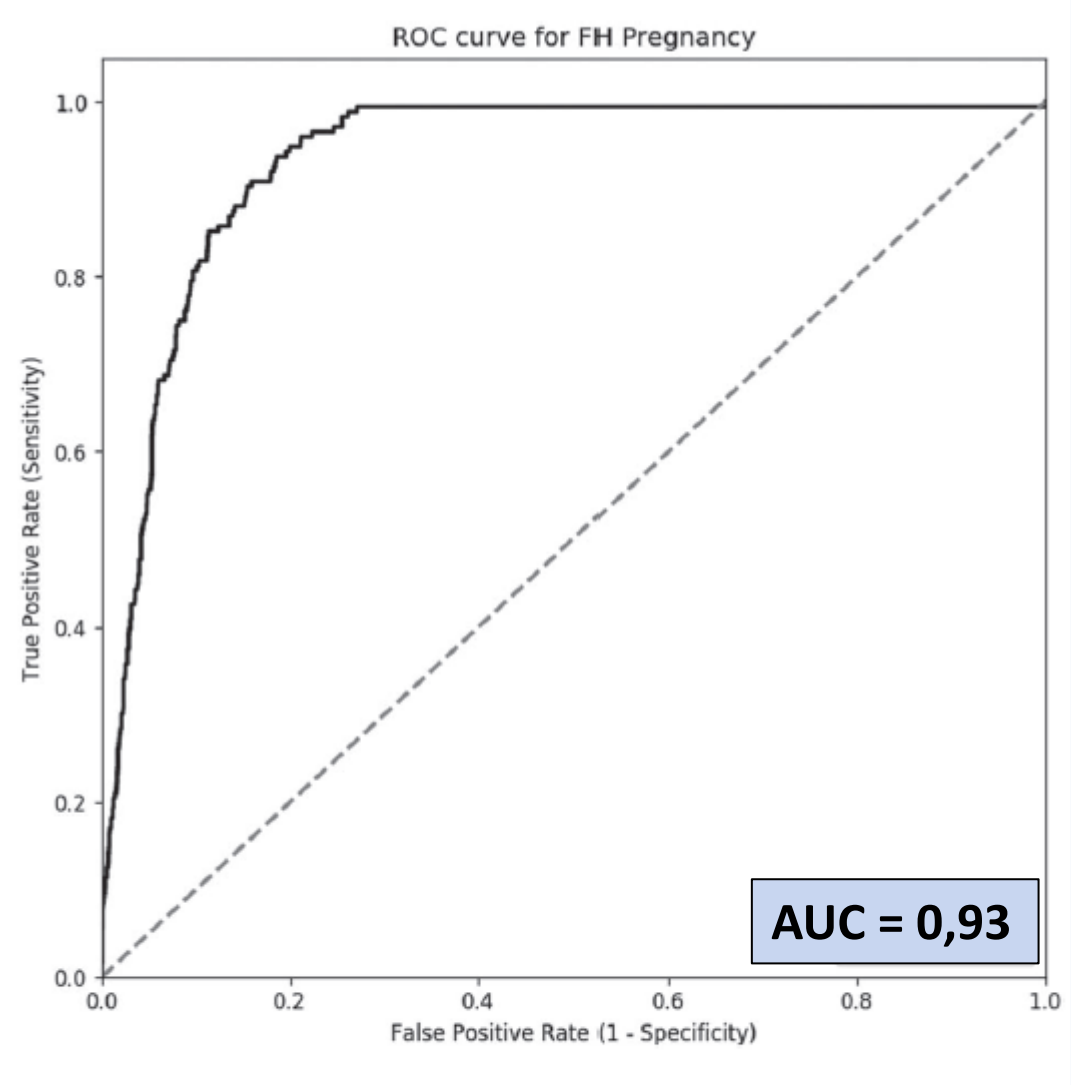
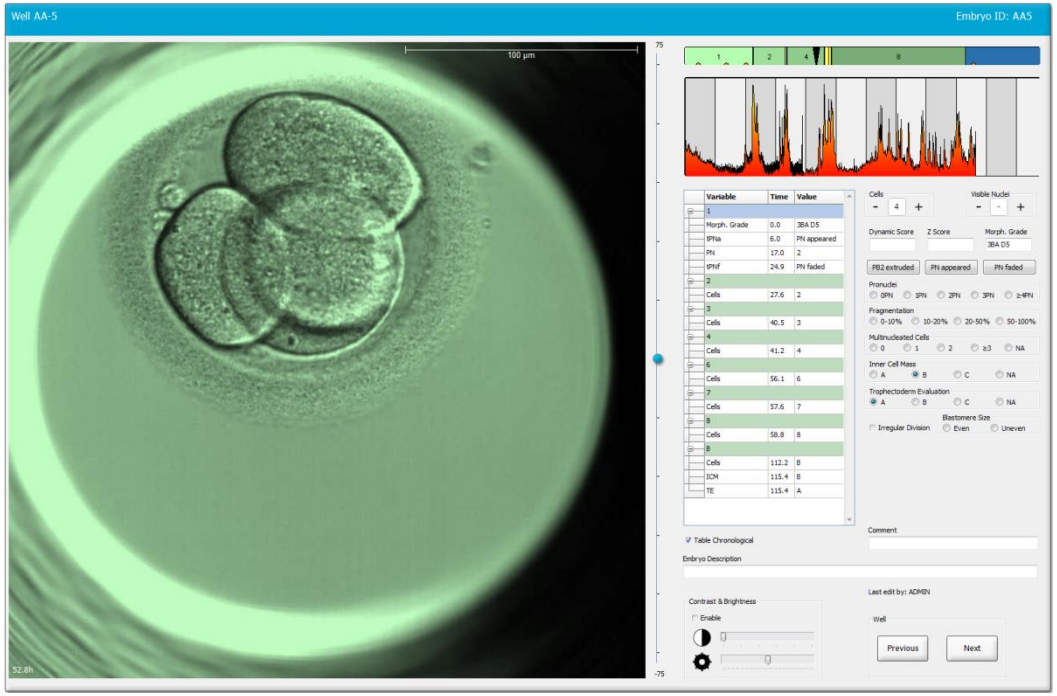


Figure 2 ROC curve for prediction of FH pregnancy on the testing dataset by IVY. ROC, Receiver operating characteristic; AUC, area under the curve.

FERTILITY

EMBRYOSCOPE - ANOTAÇÕES



FERTILITY

FERTscore FERTILITY

GRAU DE EXPANSÃO	
KIDSCORE D5	Laboratório

MASSA CELULAR INTERNA (grau 3 – 6)	
KIDSCORE D5	Laboratório
Muitas células bem compactadas. Os limites das células não são	

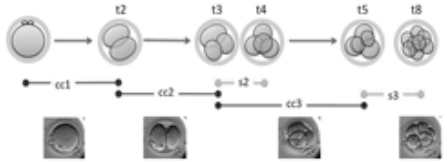
TROFECTODERMA (grau 3 – 6)		
	KIDSCORE D5	Laboratório
A	Muitas células achatadas (geralmente> 40) formam uma camada coesiva que reveste a cavidade da blastocele. As células geralmente contêm núcleos claramente visíveis e o citoplasma é homogêneo.	Ok
B	Várias (geralmente> 20) células. A camada não é completamente coesa e a forma das células varia na camada. O citoplasma celular pode parecer não homogêneo e pode ser difícil distinguir núcleos	Irregular
C	Muito poucas células que são geralmente grandes e esticadas em uma área grande. O citoplasma frequentemente parece não homogêneo e vacúolos podem estar presentes.	Poucas células e irregular
		Granular
		Com células degeneradas
		Com células excluídas na cavidade

FERTILITY

Parâmetros de Avaliação Embryoscope - Fertility

Variável	Descrição	Valores	Avaliação	Intervalo	Referência
PN	Quantidade de pronúcleos	Selecionar	Entre 16 - 18h após ICSI	-	-
tPNa	Tempo da inseminação até o aparecimento dos pronúcleos.	Horas	Anotar primeira imagem que **todos** os PNs podem ser observados.	9.16–9.64h	Aguilar 2014
tPNf	Tempo da inseminação até os pronúcleos desaparecerem	Horas	Anotar primeira imagem que todos os PNs desaparecem	>20h45m / 23.42–24.12h / 24.3 - 25.3h	Azarello 2012 / Aguilar 2014 / Desai 2014
t2	Tempo da inseminação até a completa divisão em 2 cel	Horas	No momento de divisão em 2cel	26.5 - 27.8 h	Desai 2014
t3	Tempo da inseminação até a completa divisão em 3 cel	Horas	No momento de divisão em 3cel	34-40h / 36.5 - 38.7 h	Basile 2015 / Desai 2014
t4	Tempo da inseminação até a completa divisão em 4 cel	Horas	No momento de divisão em 4cel	39.0 - 41.1 h	Desai 2014
t5	Tempo da inseminação até a completa divisão em 5 cel	Horas	No momento de divisão em 5cel	48.8 - 56.6 h / 50.8 - 53.2 h	Cruz 2012 / Desai 2014
t6	Tempo da inseminação até a completa divisão em 6 cel	Horas	No momento de divisão em 6cel	-	-
t7	Tempo da inseminação até a completa divisão em 7 cel	Horas	No momento de divisão em 7cel	-	-
t8	Tempo da inseminação até a completa divisão em 8 cel	Horas	No momento de divisão em 8cel	54.9 ± 5.2 h / 60.2 - 64.0 h	Dal Canto 2012 / Desai 2014
tB	Tempo da inseminação até a formação do blastocito	Horas	A última imagem antes do início da expansão (blastocito empurra a ZP)	120h / 103.8 - 106.6 h	Rubio 2014 / Desai 2014
ICM	Avaliação da Massa Celular Interna	A, B,C	classificar entre 115-120h (verificar ficha classificação D5)	-	-
TE	Avaliação do Trofectoderma	A, B,C	classificar entre 115-120h (verificar ficha classificação D5)	-	-

Legenda	
	Parâmetrar que geram o algoritmo
	Parâmetrar que não geram o algoritmo



FERTscore FERTILITY

- pronuclei appearance (tPNa)
- timing to pronuclei fading (tPNf)
- timing to two (t2), three (t3), four (t4), five, (t5), six (t6), seven (t7), and eight cells (t8)
- timing to blastulation (tB)
- duration of the second cycle (t3-t2) - cc2
- duration of the third cycle (t5-t3) - cc3
- (t2-tPNf) - s1
- (t4-t3) - s2,
- (t8-t5) - s3

FERTILITY

Consistency and objectivity of automated embryo assessments using deep neural networks

Charles L. Bormann, Ph.D.,[a,b] Prudhvi Thirumalaraju, B. Tech,[c] Manoj Kumar Kanakasabapathy, M. Tech,[c] Hemanth Kandula, B. Tech,[c] Irene Souter, M.D.,[a] Irene Dimitriadis, M.D., Ph.D.,[a,b] Raghav Gupta, B. Tech,[c] Rohan Pooniwala, B. Tech,[c] and Hadi Shafiee, Ph.D.[a,b]

Fertility and Sterility® Vol. 113, No. 4, April 2020

Results:

- Embryologists exhibited a high degree of variability *(%CV averages: 82.84% for 70 hpi and 44.98% for 113 hpi)* in grading embryo.
- When selecting blastocysts for biopsy or cryopreservation, embryologists had an average consistency of 52.14% and 57.68%, respectively.
- The neural network outperformed the embryologists in selecting blastocysts for biopsy and cryopreservation with a *consistency of 83.92%.*

Conclusions:

The results of our study show a high degree of interembryologist and intraembryologist variability in scoring embryos, likely due to the subjective nature of traditional morphology grading. *This may ultimately lead to less precise disposition decisions and discarding of viable embryos.*

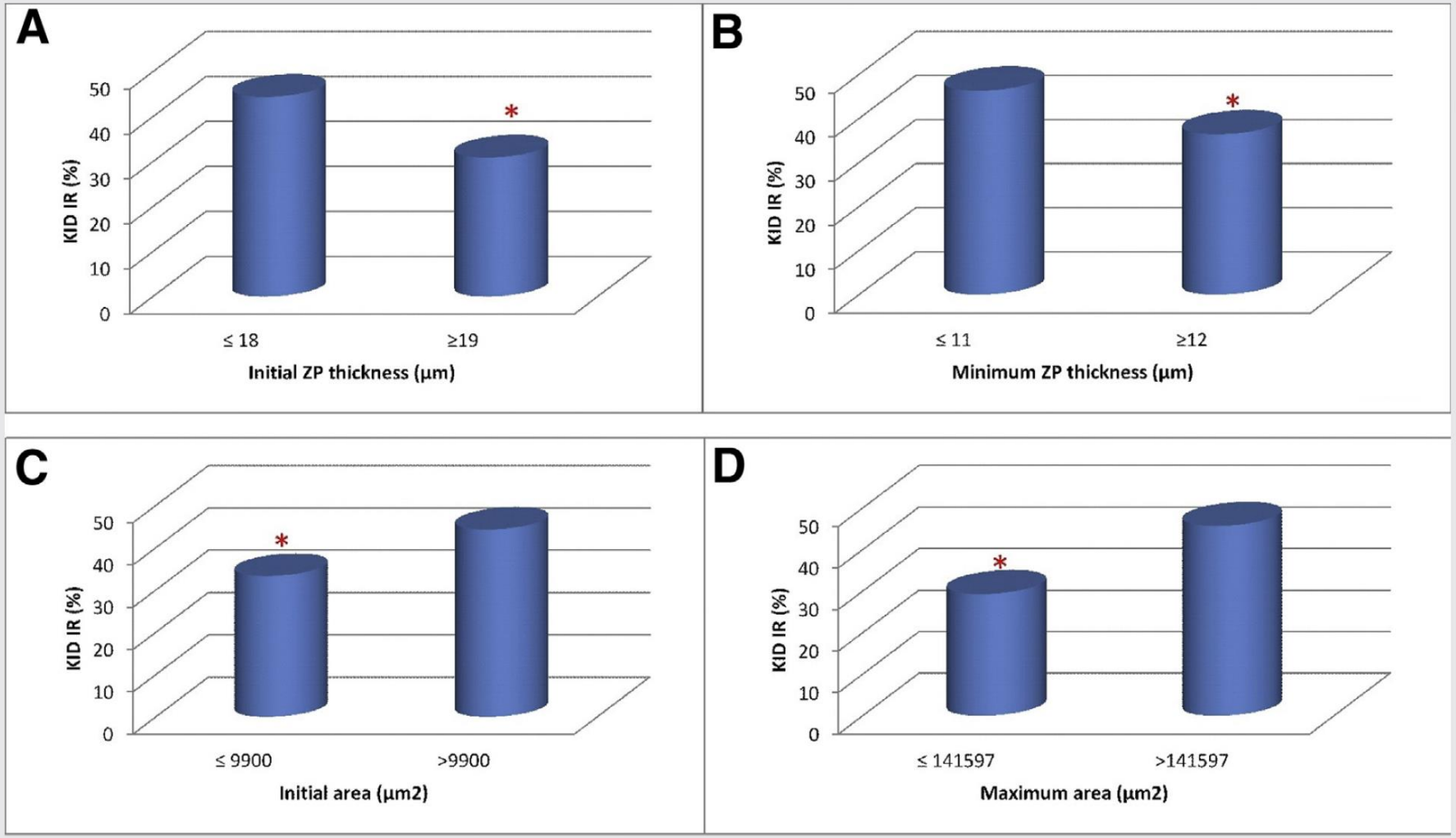
FERTILITY

Analysis of the morphological dynamics of blastocysts after vitrification/warming: defining new predictive variables of implantation

Aila Coello, Ph.D., Marcos Meseguer, Ph.D., Arancha Galán, Ph.D., Lucia Alegre, Ph.D., José Remohí, M.D., and Ana Cobo, Ph.D.

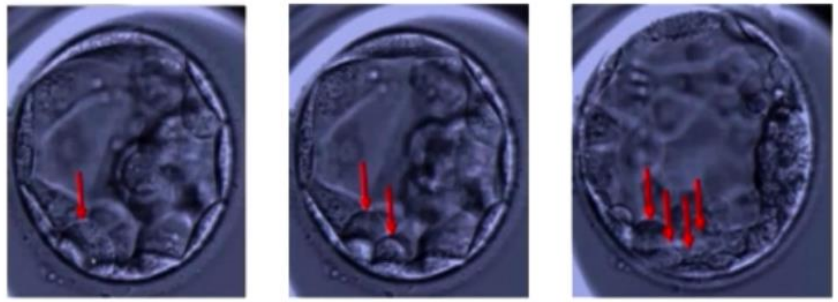
Instituto Valenciano de Infertilidad, INCLIVA-Universidad de Valencia, Valencia, Spain

Fertility and Sterility® Vol. 108, No. 4, October 2017

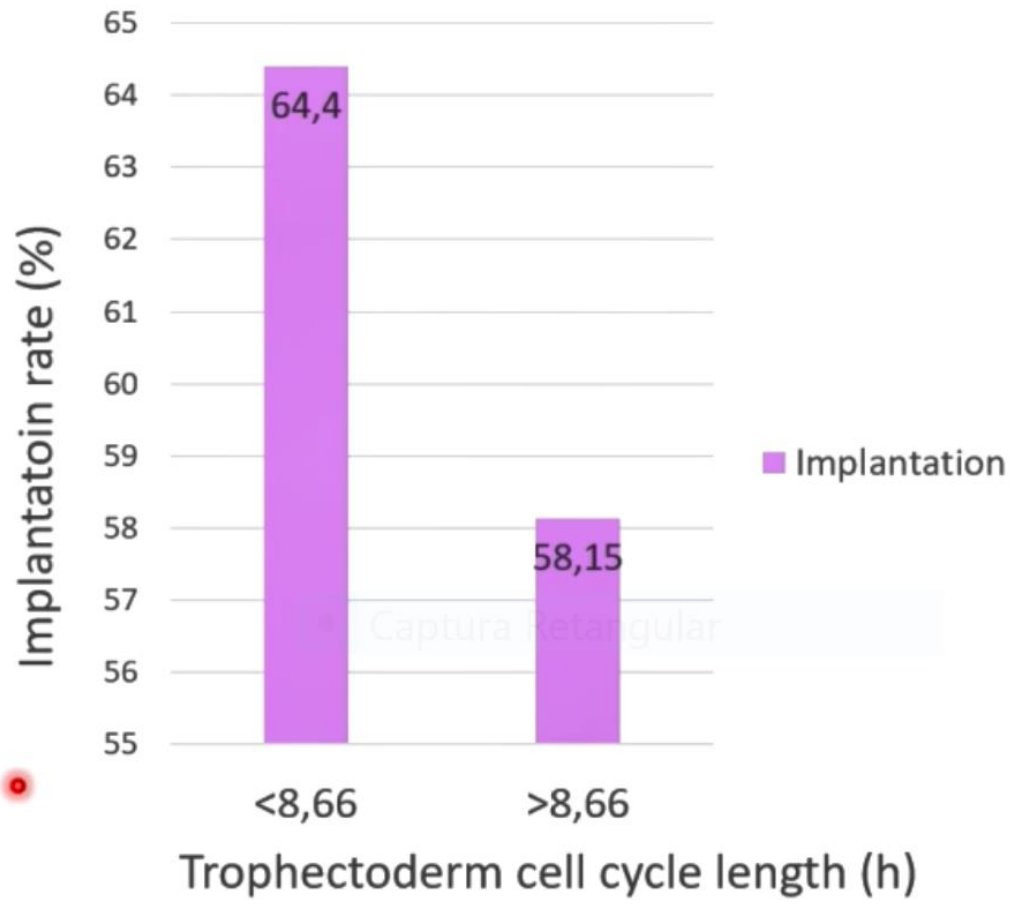


Percentage of implanting blastocysts with morphological dynamics variables within or beyond the ranges defined by the quartile limits for the tota data set. The four panels show ranges and implantation for (**A**) initial ZP thickness, *P=.02; (**B**) minimum ZP thickness, *P=.03; (**C**) initial blastocyst area, *P=.04; and (**D**) maximum blastocyst area, *P=.004.

FERTIL

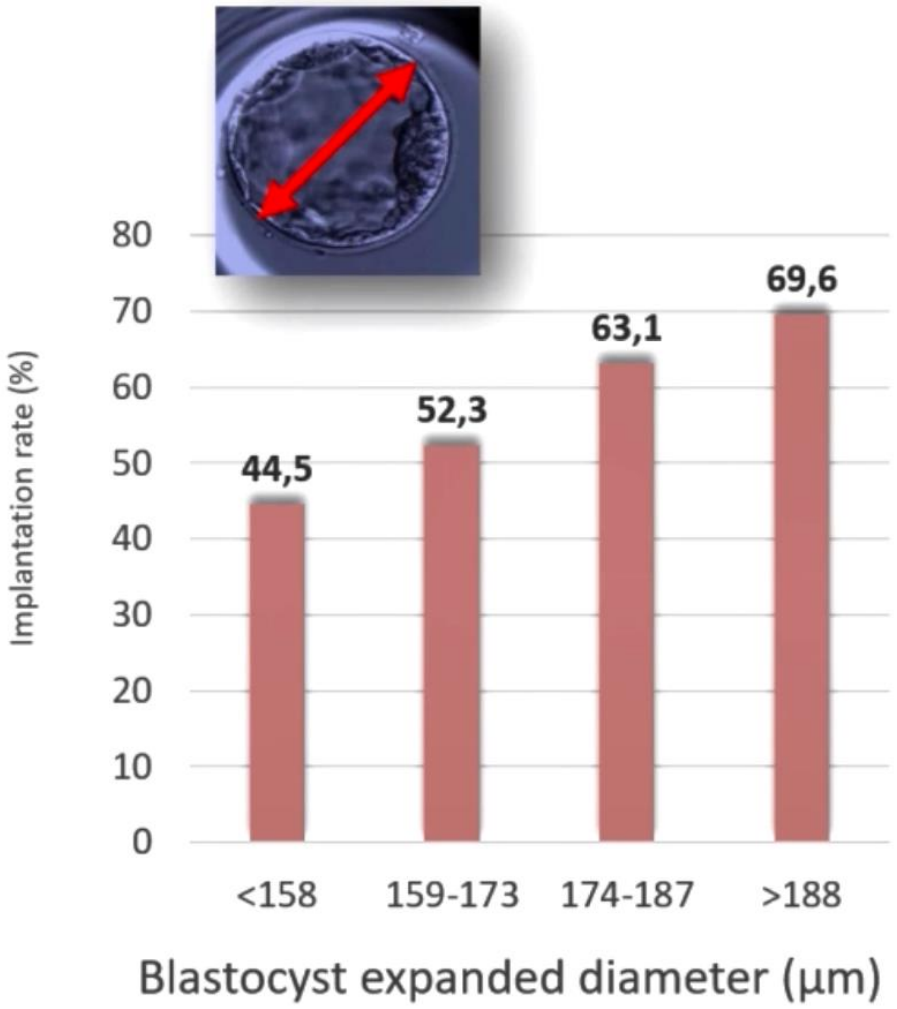


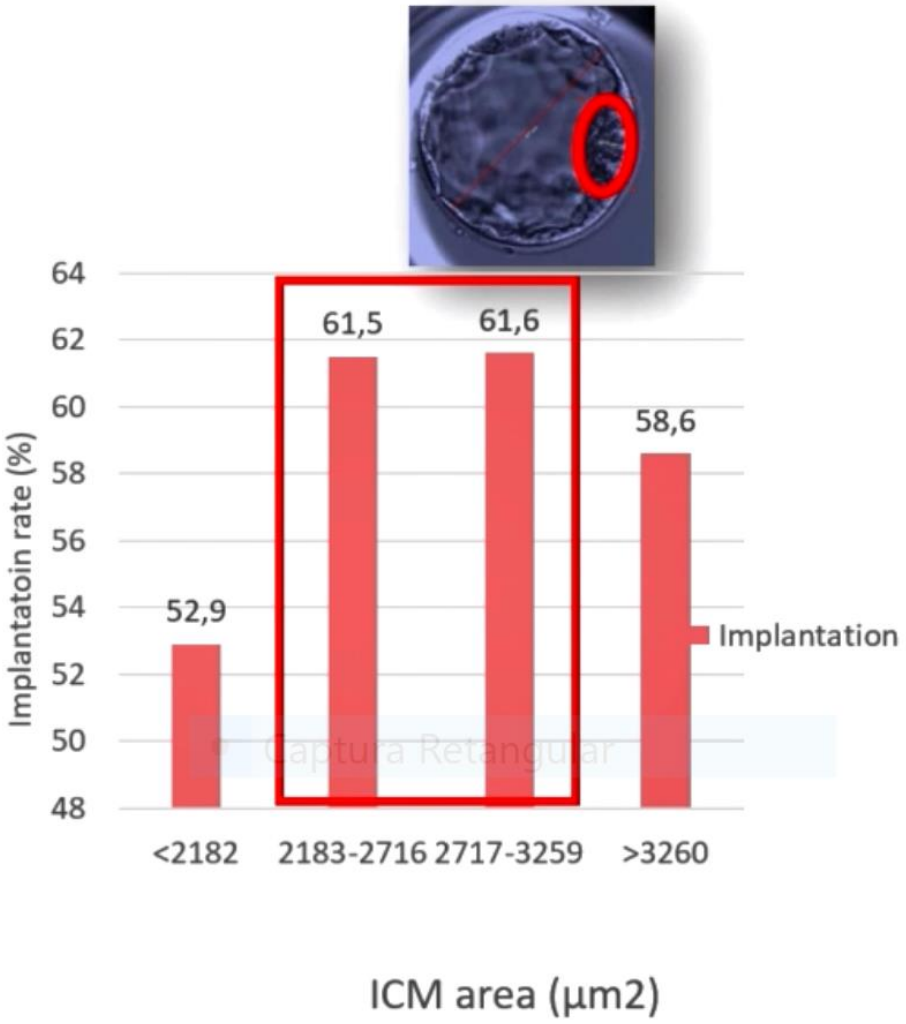
Trophectoderm cell cycle length (h)	Total embryos	Implantation rate (%)
<8,66	90	64,4
8,67-9,79	90	54,4
9,80-9,79	91	61,5
>11,21	89	58,4



Bori L and Meseguer ASRM (2018)

FERTILITY





Bori L and Meseguer ASRM (2018)

FERTILITY

Human Reproduction, Vol.34, No.8, pp. 1439–1449, 2019
Advance Access Publication on July 9, 2019 doi:10.1093/humrep/dez085

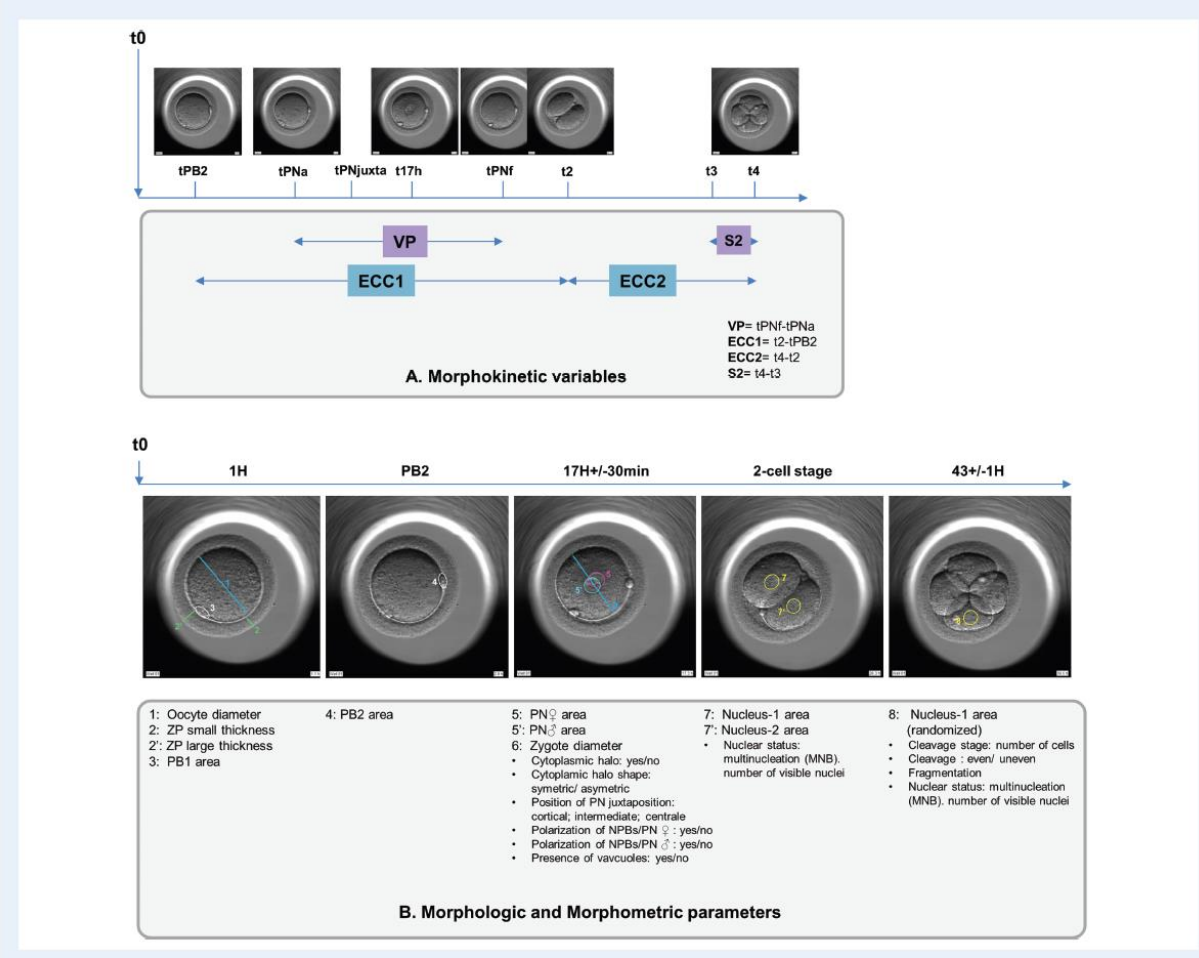
human reproduction **ORIGINAL ARTICLE** ***Embryology***

Can novel early non-invasive biomarkers of embryo quality be identified with time-lapse imaging to predict live birth?

J. Barberet[1,2,†], C. Bruno[1,2,†], E. Valot[1], C. Antunes-Nunes[1], L. Jonval[3], J. Chammas[1], C. Choux[4], P. Ginod[4], P. Sagot[4], A. Soudry-Faure[3], and P. Fauque[1,2,*]

- **Central PN juxtaposition** was associated with a 2-fold increase in the odds of live birth (OR=2.20; 95% CI, [1.26–3.89]; *P*=0.006), while **the presence of MNB$_{2cell}$** was associated with half the odds of live birth (OR=0.51; 95% CI, [0.27–0.95]; *P*=0.035). These two parameters were independent of embryo kinetics.

- The 33 remaining parameters had no significant association with the capacity of transferred embryos to develop to term.



FERTILITY

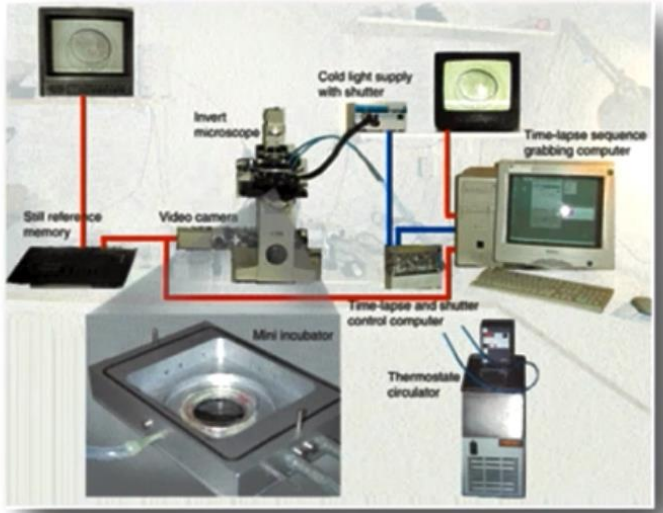
History: early days of TLT

- Vol 17 No 3. 2008 385-391 Reproductive BioMedicine Online; www.rbmonline.com/Article/3327 on web 30 July 2008

Article

Kinetic markers of human embryo quality using time-lapse recordings of IVF/ICSI-fertilized oocytes

Lemmen et al, 2008



Internalization of cellular fragments in a human embryo: time-lapse recordings

Hardarson et al, 2002

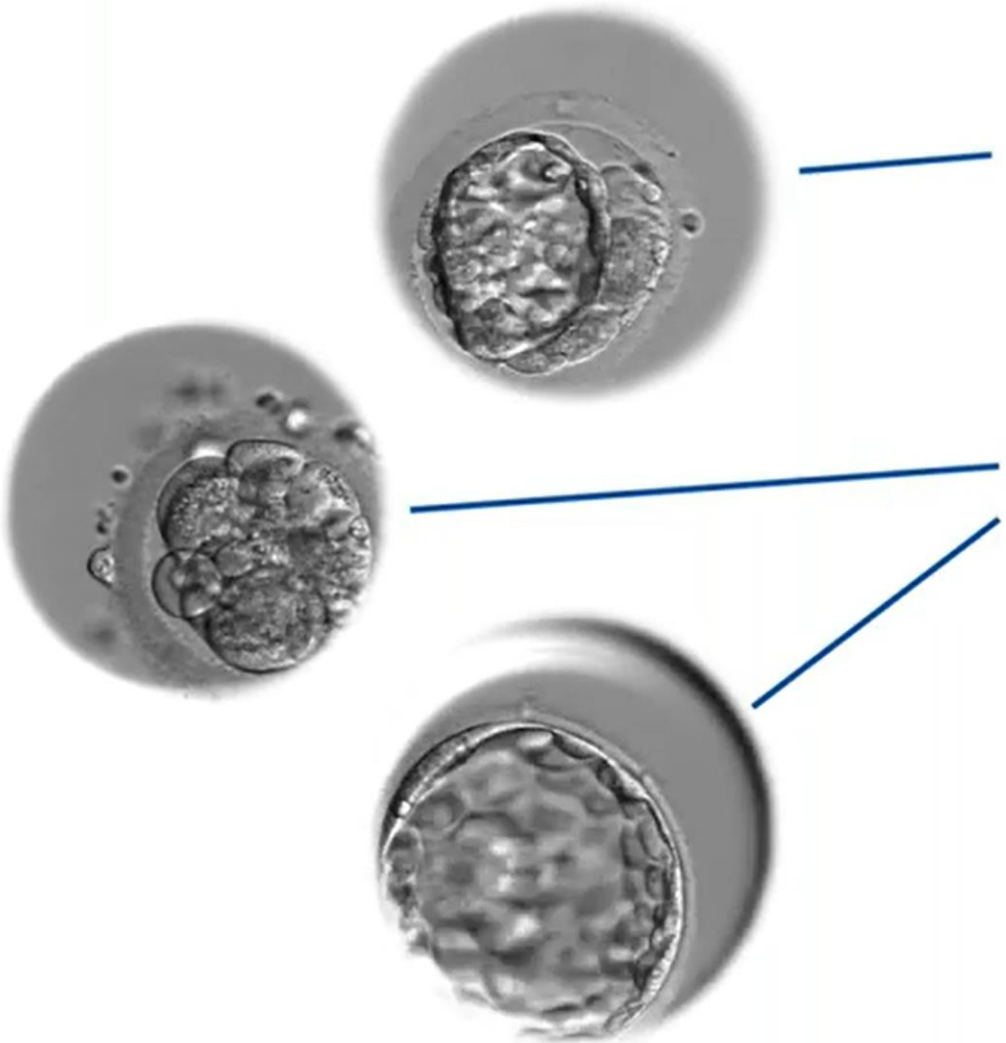
Human Reproduction vol.12 no.3 pp.532–541, 1997

Preliminary observations on polar body extrusion and pronuclear formation in human oocytes using time-lapse video cinematography

Payne et al, Hum Reprod, 1997

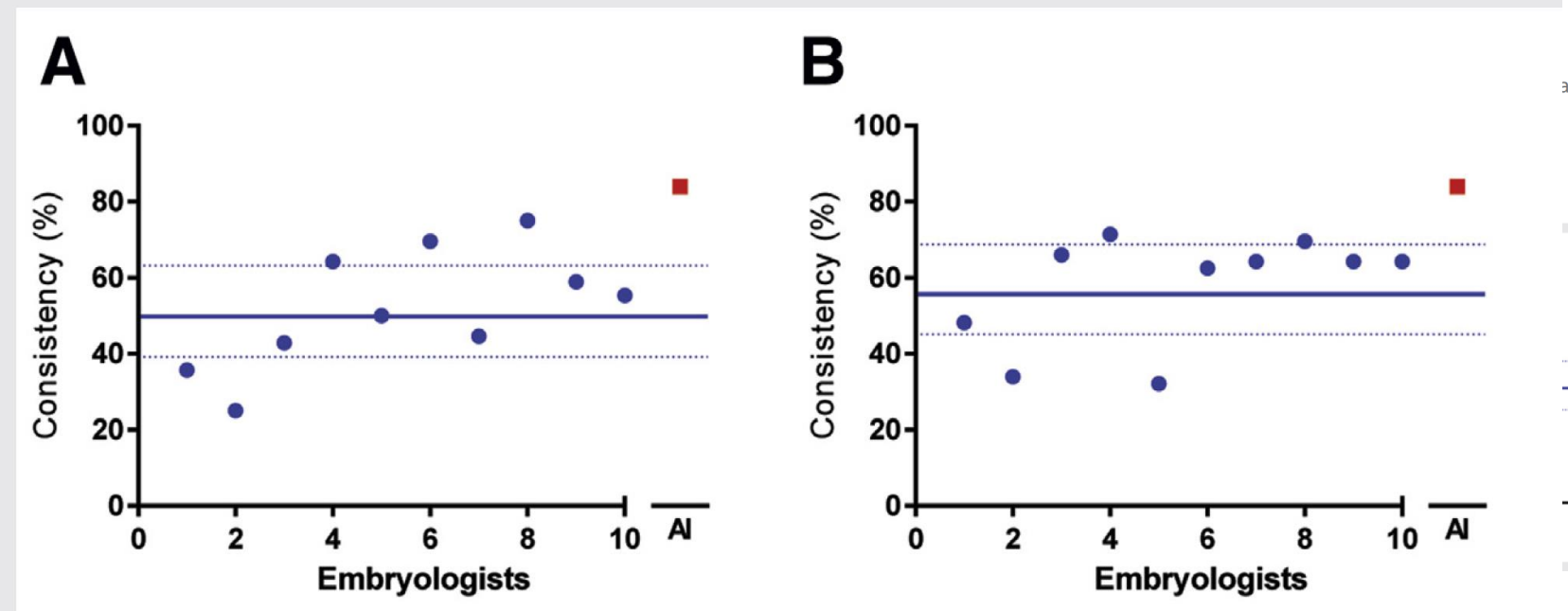
FERTILITY

SCORING AND SELECTION

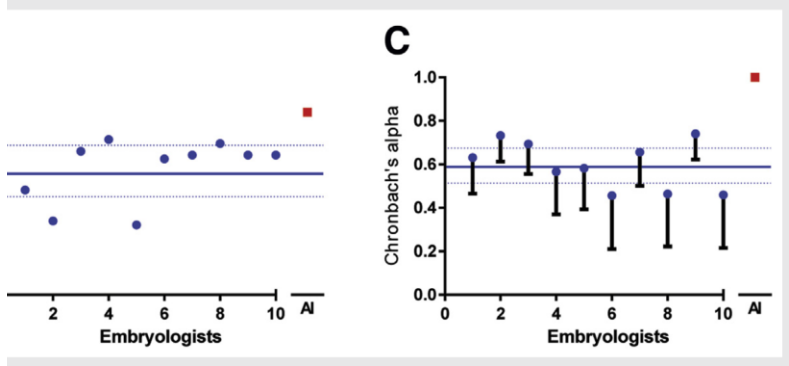


FERTILITY

Consistency and objectivity of automated embryo assessments using deep neural networks



apathy, M. Tech,[c]



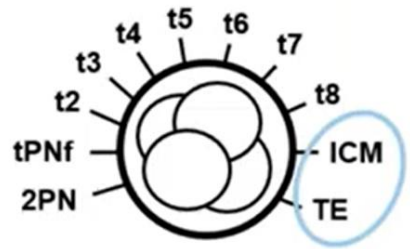
respectively.

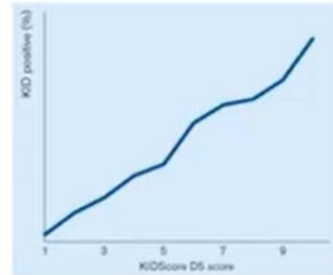
- The neural network outperformed the embryologists in selecting blastocysts for biopsy and cryopreservation with a *consistency of 83.92%*.

FERTILITY

EMBRYO ANNOTATION AND SELECTION

Embryologist





Implantation model

AI (indirect)

AI (direct)

Contents lists available at ScienceDirect

Computers in Biology and Medicine

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

ELSEVIER

Automatic grading of human blastocysts from time-lapse imaging

Mikkel F. Kragh [a,b,*], Jens Rimestad [b], Jørgen Berntsen [b], Henrik Karstoft [a]

[a] Deparment of Engineering, Aarhus University, Denmark

[b] Vitrolife A/S, Denmark

FERTILITY

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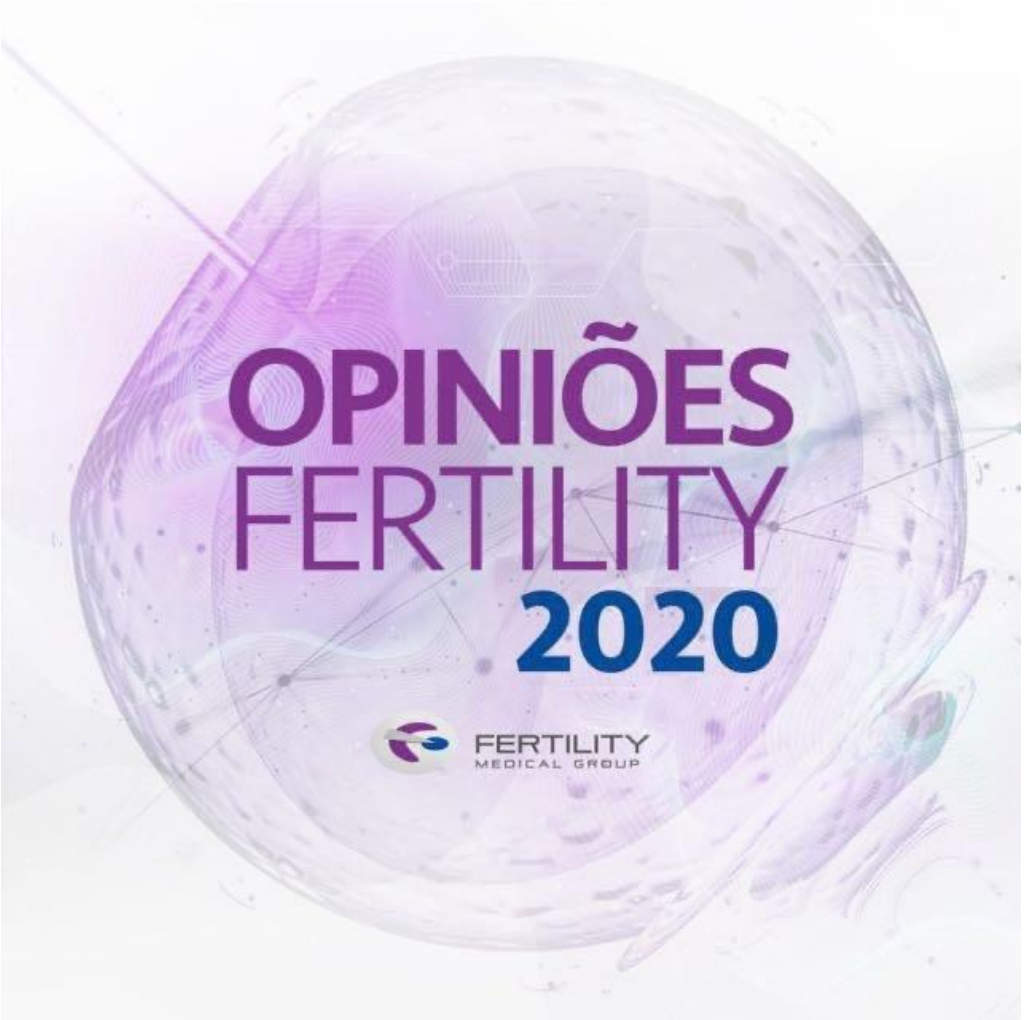
Time Lapse e a Inteligência Artificial

2° MEETING VIRTUAL DE GENÉTICA REPRODUTIVA

Resultados recentes no uso do Time Lapse e IA como avaliação embrionária

Edson Borges Jr.

FERTILITY



Inteligência Artificial em Medicina Reprodutiva

Edson Borges Jr.

FERTILITY

Abstract title:

Paternal contribution to embryo morphokinetics in a time-lapse incubator system

Session title: Session 04: Male fertility related predictors and their use

Session type: Selected oral communications

Presentation number: O-015

A. Setti[12], D. Braga[12], R. Provenza[3], A. Iaconelli Jr.[4], E. Borges Jr.[24].
[1]Fertility Medical Group, Scientific research, São Paulo, Brazil.
[2]Instituto Sapientiae- Centro de Estudos e Pesquisa em Reprodução Assistida, Scientific research, São Paulo, Brazil.
[3]Fertility Medical Group, Andrology laboratory, São Paulo, Brazil.
[4]Fertility Medical Group, Clinical department, São Paulo, Brazil.

1220 embryos, 139 ICSI cycles
male factor infertility

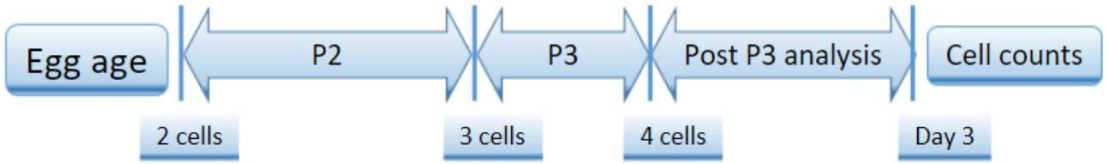
FERTILITY

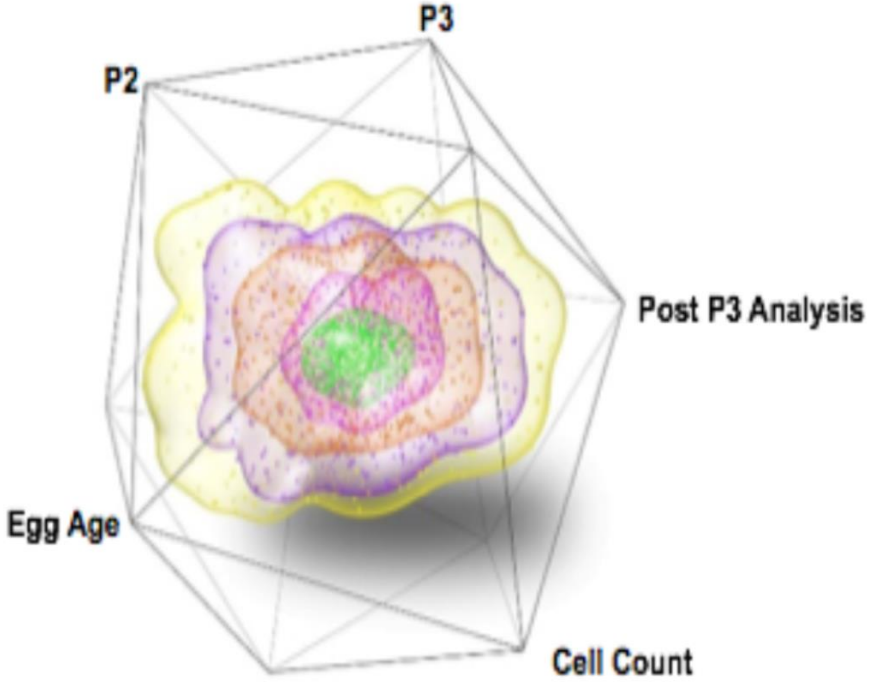
AI systems for embryo selection

- IVY
- Life Whisperer
- ERICA
- STORK
- IVFvision.ai

FERTILITY

XTEND ALGORITHM

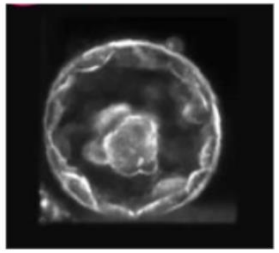




FERTILITY

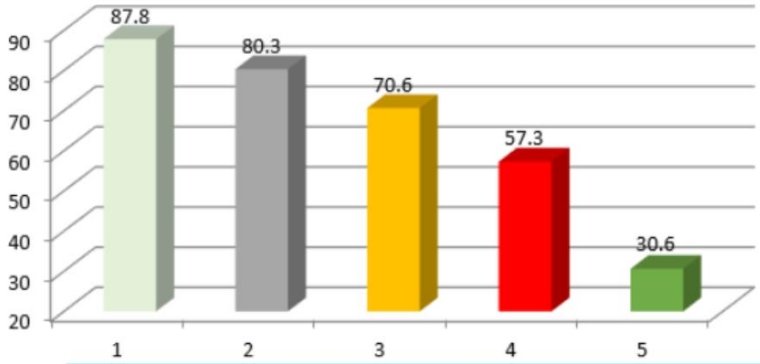
Xtend categories (1-5) embryo analysis

Automation

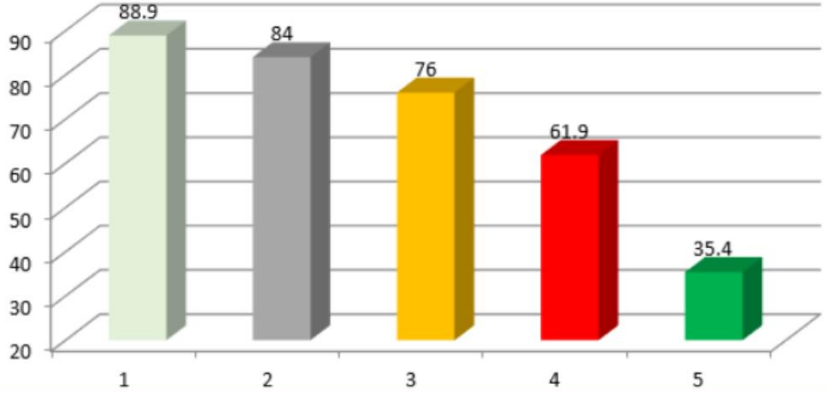


Xtend	Category
1	1303
2	1049
3	813
4	895
5	961
Total	5021

BLASTULATION D5 p<0.001



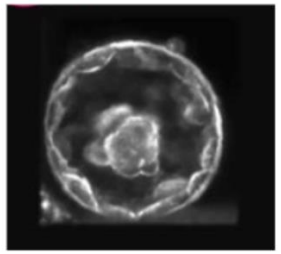
BLASTULATION D5+D6 p<0.001



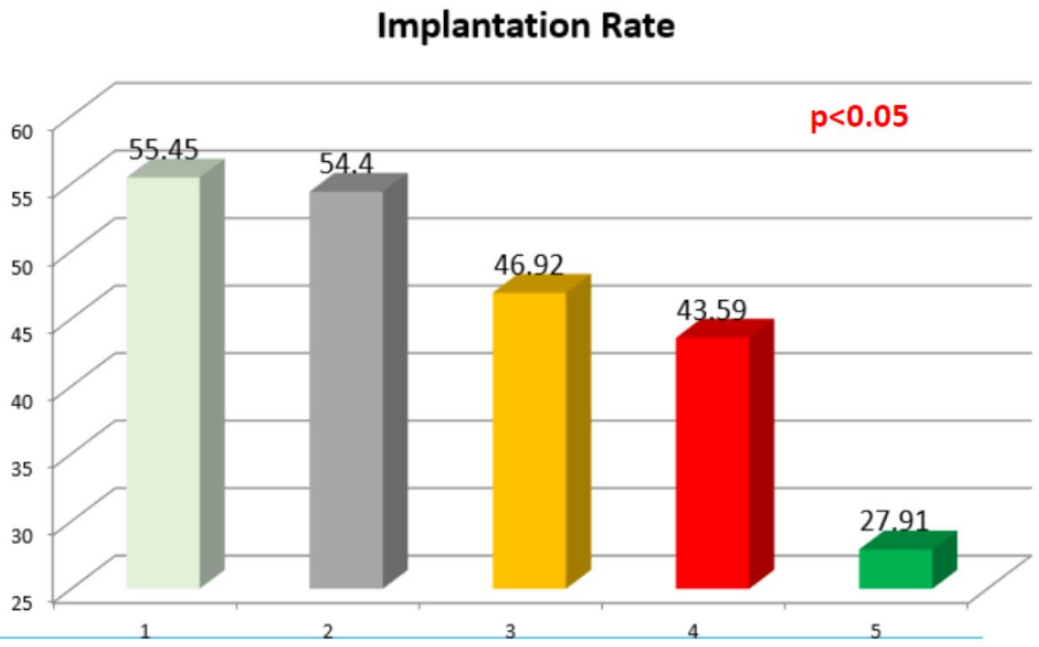
FERTILITY

Xtend categories (1-5) embryo analysis

Automation

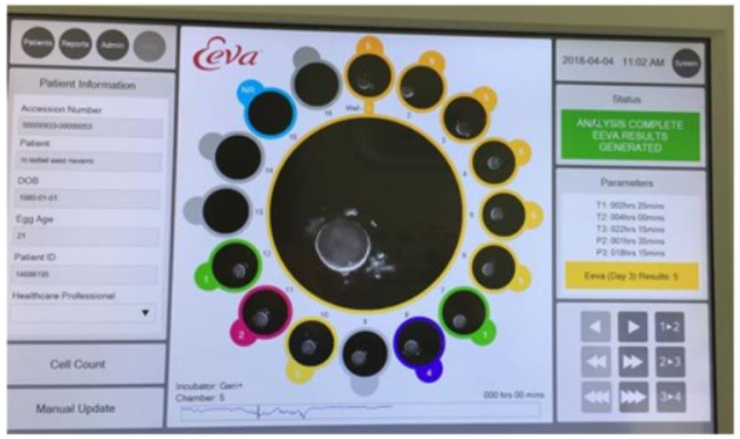


Xtend	Category
1	306
2	220
3	130
4	78
5	43
Total	777



FERTILITY

Technology solutions; Xtend categories-PGT Program n=310 biopsied blastocyst

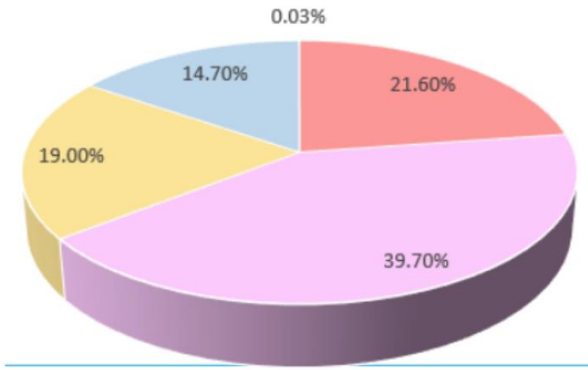


Automation

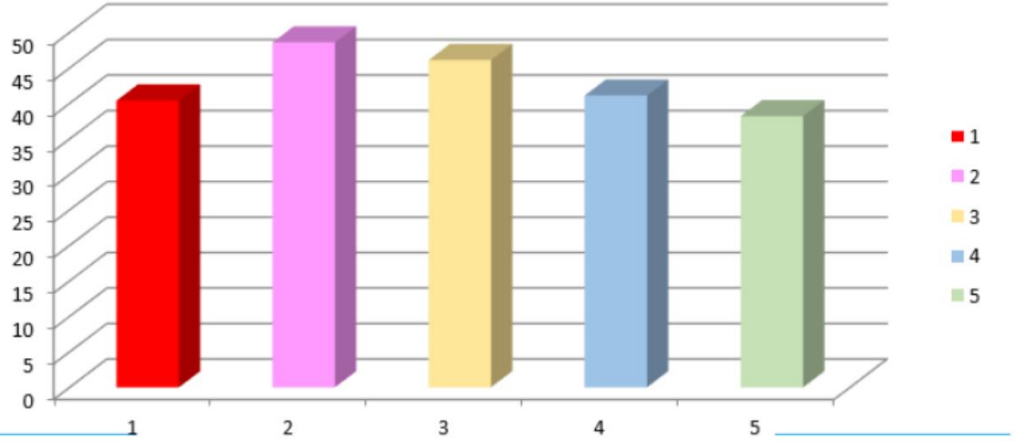
692 blastocyst Biopsied (42.4%)

42,9% euploid (n=297)

EUPLOID AND XTEND CATEGORIES



%Euploid by Xtend



FERTILITY

Human Reproduction Open, pp. 1–26, 2020
doi:10.1093/hropen/hoaa008

human reproduction open

ESHRE PAGES

Good practice recommendations for the use of time-lapse technology†

ESHRE Working group on Time-lapse technology, Susanna Apter[1], Thomas Ebner[2], Thomas Freour[3], Yves Guns[4], Borut Kovacic[5], Nathalie Le Clef[6], Monica Marques[7], Marcos Meseguer[8], Debbie Montjean[9], Ioannis Sfontouris[10], Roger Sturmey[11], and Giovanni Coticchio[12,*]

STUDY QUESTION: What recommendations can be provided on the approach to and use of time-lapse technology (TLT) in an IVF laboratory?

SUMMARY ANSWER: The present ESHRE document provides 11 recommendations on how to introduce TLT in the IVF laboratory.

WHAT IS KNOWN ALREADY: Studies have been published on the use of TLT in clinical embryology. However, a systematic assessment of how to approach and introduce this technology is currently missing.

STUDY DESIGN, SIZE, DURATION: A working group of members of the Steering Committee of the ESHRE Special Interest Group in Embryology and selected ESHRE members was formed in order to write recommendations on the practical aspects of TLT for the IVF laboratory.

FERTILITY

Table V **Possible confounding factors with the use of TLT algorithms.**

	Parameters to consider	References
Patient-related factors	Age	(Akarsu *et al.*, 2017, Akhter and Shahab, 2017, Gryshchenko *et al.*, 2014, Kirkegaard *et al.*, 2016, Siristatidis *et al.*, 2015)
	Type of infertility	(Freis *et al.*, 2018, Sundvall *et al.*, 2015, Wissing *et al.*, 2014)
	Weight/BMI/obesity	(Bellver *et al.*, 2013, Kirkegaard *et al.*, 2016, Leary *et al.*, 2015)
	Ovarian stimulation protocol	(Gryshchenko *et al.*, 2014, Gurbuz *et al.*, 2016, Kirkegaard *et al.*, 2016, Munoz *et al.*, 2013, Wdowiak and Bojar, 2015)
	Type of responder/ovarian reserve	(Akarsu *et al.*, 2017, Bhide *et al.*, 2017, Hojnik *et al.*, 2016, Rienzi *et al.*, 2015)
	Smoking	(Freour *et al.*, 2013, Salvarci *et al.*, 2017, Siristatidis *et al.*, 2015)
Gamete, embryo or laboratory-related factors	Sperm factor	(Desai *et al.*, 2018a, Knez *et al.*, 2013, Lammers *et al.*, 2015, Mangoli *et al.*, 2018, Neyer *et al.*, 2015, Wdowiak *et al.*, 2015)
	Oocyte morphology	(Mizobe *et al.*, 2016b, Otsuki *et al.*, 2018, Van Blerkom, 1990)
	IVM	(Dal Canto *et al.*, 2016, Escrich *et al.*, 2012, Roesner *et al.*, 2017, Walls *et al.*, 2015, Wilken-Jensen *et al.*, 2014)
	Fertilisation technique	(Bodri *et al.*, 2015, Cruz *et al.*, 2013, Inoue *et al.*, 2019, Joergensen *et al.*, 2014, Kim *et al.*, 2017, Kirkegaard *et al.*, 2013b, Kirkegaard *et al.*, 2013c, Kirkegaard *et al.*, 2016, Liu *et al.*, 2015)
	Biopsy	(Bar-El *et al.*, 2016, Kalma *et al.*, 2018, Kirkegaard *et al.*, 2012b)
	Cryopreservation	(Chamayou *et al.*, 2015, Cobo *et al.*, 2017, Coello *et al.*, 2017, De Munck *et al.*, 2015, Eastick *et al.*, 2017, Ebner *et al.*, 2017, Kovacic *et al.*, 2018, Maezawa *et al.*, 2014)
	Sex of the embryo	(Bodri *et al.*, 2016a, Bronet *et al.*, 2015, Huang *et al.*, 2019, Serdarogullari *et al.*, 2014, Zeyad *et al.*, 2018)

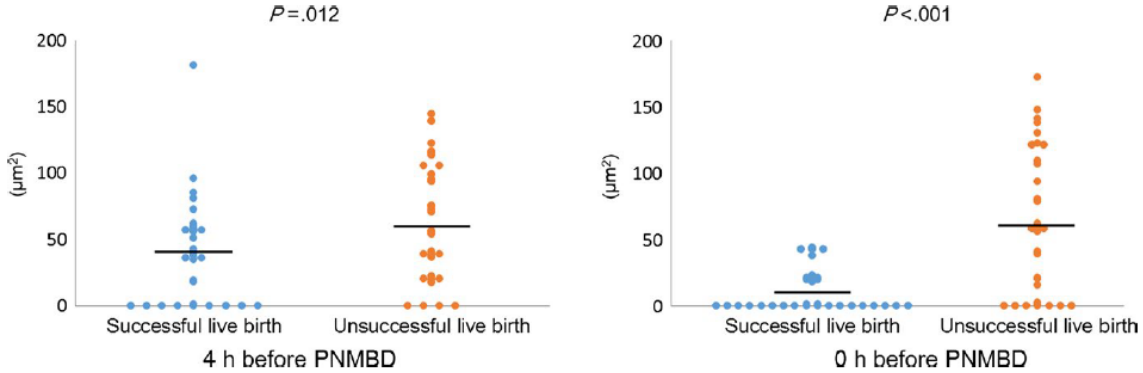
Received: 31 October 2016 | Accepted: 9 February 2017
DOI: 10.1002/rmb2.12032

ORIGINAL ARTICLE

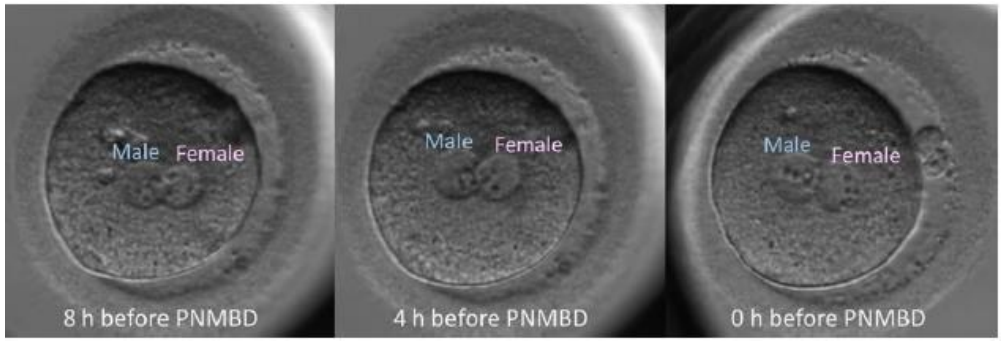
WILEY Reproductive Medicine and Biology

Potential of zygotes to produce live births can be identified by the size of the male and female pronuclei just before their membranes break down

Junko Otsuki | Toshiroh Iwasaki | Yuta Tsuji | Yuya Katada | Haruka Sato | Yukari Tsutsumi | Kanae Hatano | Kohyu Furuhashi | Yukiko Matsumoto | Shoji Kokeguchi | Masahide Shiotani



birth	No.	4 h before PNMBD	*P* birth	0 h before PNMBD	*P* birth
Successful live birth	34	39.9 μm^2 (±37.8)	a	11.6 μm^2 (±15.5)	c
Unsuccessful live birth	34	62.8 μm^2 (±43.0)	b	62.8 μm^2 (±53.3)	d



Conclusion:

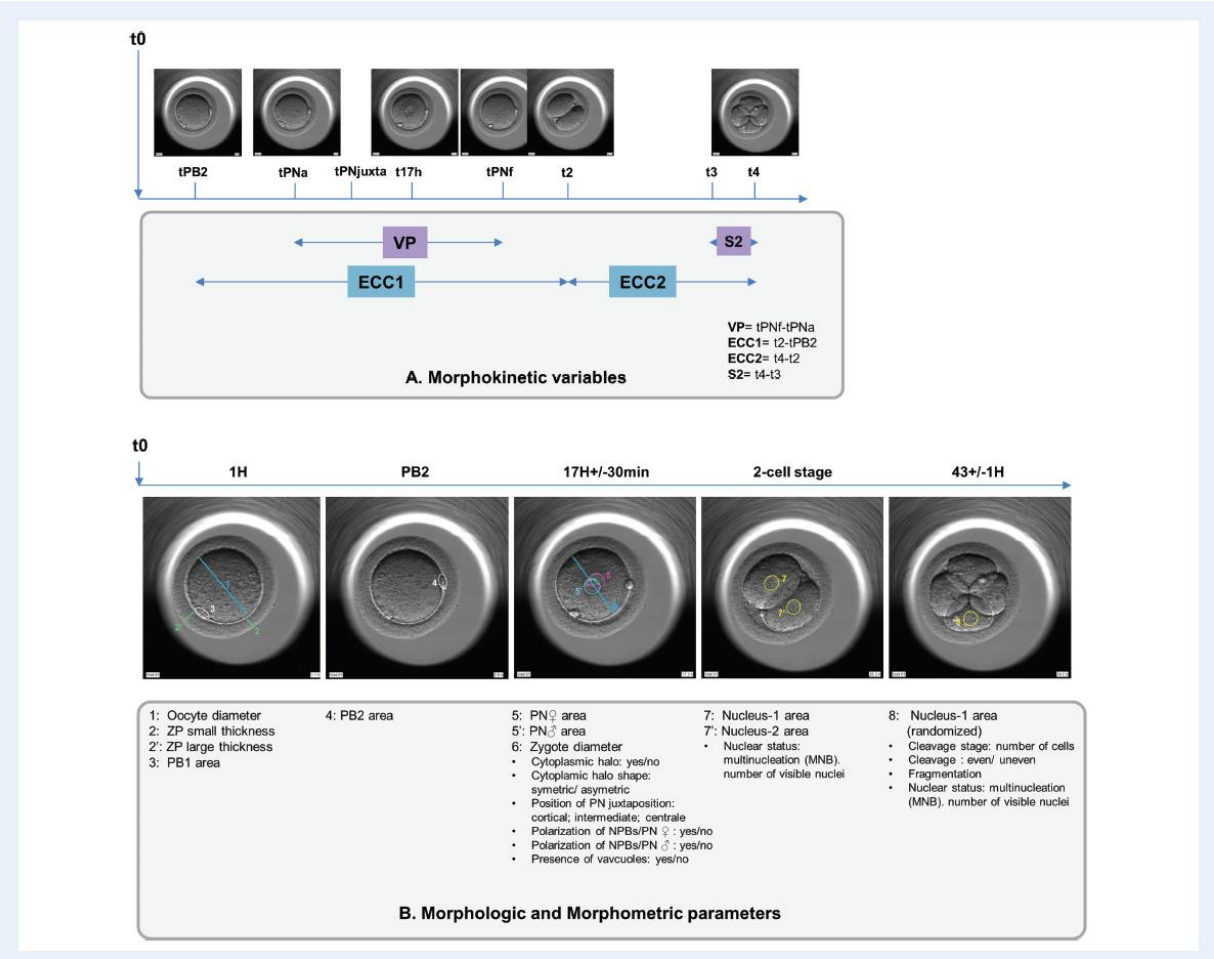
- The birth of healthy babies resulted from *zygotes that contained pronuclei of similar size when the measurements were made immediately before the PNMBD*.
- Evaluating the size of each pronucleus immediately before the PNMBD *provides an effective indicator of the embryo's potential at an early stage of development*.

Human Reproduction, Vol.34, No.8, pp. 1439–1449, 2019
Advance Access Publication on July 9, 2019 doi:10.1093/humrep/dez085

human reproduction **ORIGINAL ARTICLE** ***Embryology***

Can novel early non-invasive biomarkers of embryo quality be identified with time-lapse imaging to predict live birth?

J. Barberet[1,2,†], C. Bruno[1,2,†], E. Valot[1], C. Antunes-Nunes[1], L. Jonval[3], J. Chammas[1], C. Choux[4], P. Ginod[4], P. Sagot[4], A. Soudry-Faure[3], and P. Fauque[1,2,*]



- **Central PN juxtaposition** was associated with a 2-fold increase in the odds of live birth (OR=2.20; 95% CI, [1.26–3.89]; *P*=0.006),

- **Presence of MNB$_{2cell}$** was associated with half the odds of live birth (OR=0.51; 95% CI, [0.27–0.95]; *P*=0.035). These two parameters were independent of embryo kinetics.

FERTILITY

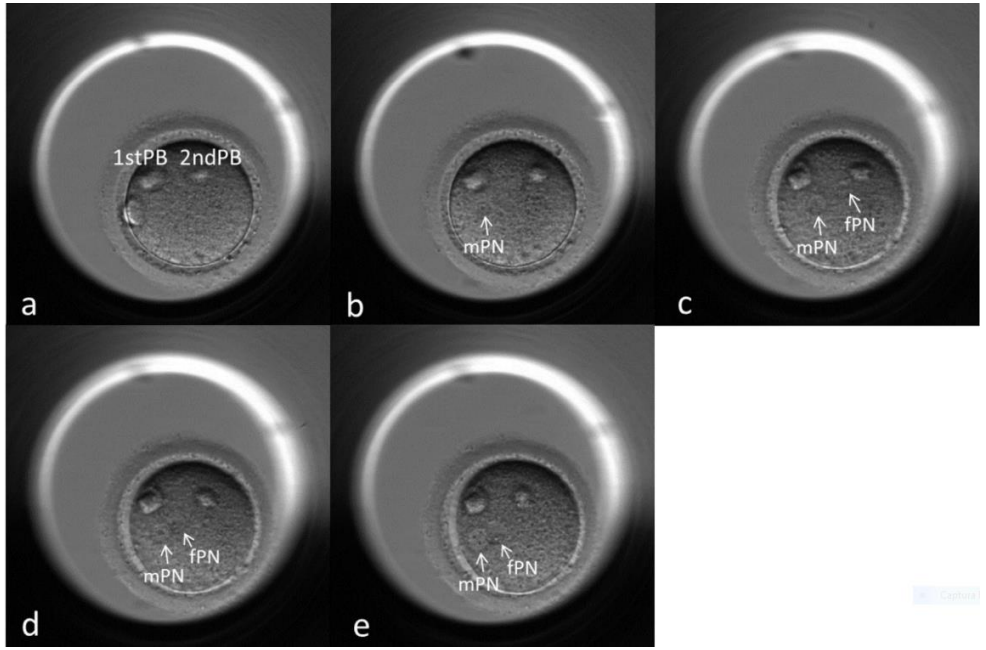
Noninvasive embryo selection: kinetic analysis of female and male pronuclear development to predict embryo quality and potential to produce live birth

Junko Otsuki, Ph.D.,[a,b] Toshiroh Iwasaki, D.V.M., Ph.D.,[a] Noritoshi Enatsu, M.D., Ph.D.,[a] Yuya Katada, B.S.,[a] Kohyu Furuhashi, B.S.,[a] and Masahide Shiotani, M.D., Ph.D.[a]

[a] Hanabusa Women's Clinic, Kobe; and [b] Okayama University Assisted Reproductive Technology Center, Okayama, Japan

Fertility and Sterility® Vol. 112, No. 5, November 2019

- Time-lapse recordings were performed and the areas of male and female pronuclei were retrospectively analyzed by measuring their vertical and horizontal diameters. These measurements were taken 4 and 8 hours before the pronuclear membrane breakdown (PNMBD), and immediately before the PNMBD.



FERTILITY

Noninvasive embryo selection: kinetic analysis of female and male pronuclear development to predict embryo quality and potential to produce live birth

Junko Otsuki, Ph.D.,[a,b] Toshiroh Iwasaki, D.V.M., Ph.D.,[a] Noritoshi Enatsu, M.D., Ph.D.,[a] Yuya Katada, B.S.,[a] Kohyu Furuhashi, B.S.,[a] and Masahide Shiotani, M.D., Ph.D.[a]

[a] Hanabusa Women's Clinic, Kobe; and [b] Okayama University Assisted Reproductive Technology Center, Okayama, Japan

Fertility and Sterility® Vol. 112, No. 5, November 2019

- When normal embryos were defined as A∪C∩B, the birth rates for IVF and ICSI were 68.1% (47/69) and 50.0% (32/64) respectively. For the remaining embryos, defined as abnormal, birth rates were 9.3% (3/32) for IVF and 4.2% (2/48) for ICSI.

- In this study, we established a method of non-invasive embryo evaluation which may exceed the success rates of PGT-A using trophectoderm cells.

FERTILITY

Human Reproduction, Vol.35, No.3, pp. 557–564, 2020
Advance Access Publication on March 12, 2020 doi:10.1093/humrep/deaa001

human reproduction ORIGINAL ARTICLE *Embryology*

Development of automated annotation software for human embryo morphokinetics

M. Feyeux[1,3,†], A. Reignier[1,2,†], M. Mocaer[1], J. Lammers[1,2], D. Meistermann[1], P. Barrière[1,2], P. Paul-Gilloteaux[3,§], L. David[1,3,§], and T. Fréour[1,2,*,§]

An automated morphokinetic annotation tool was developed based *on gray level coefficient of variation and detection of the thickness of the zona pellucida and human embryo development* from fertilization to expanded blastocyst stage (Kinetembryo)

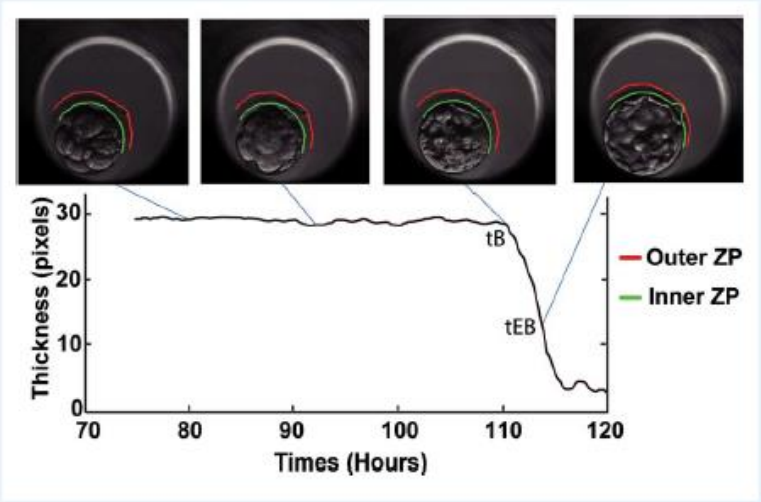


Figure 2 Representative illustration of measurement of human embryo ZP thickness (40× magnification).

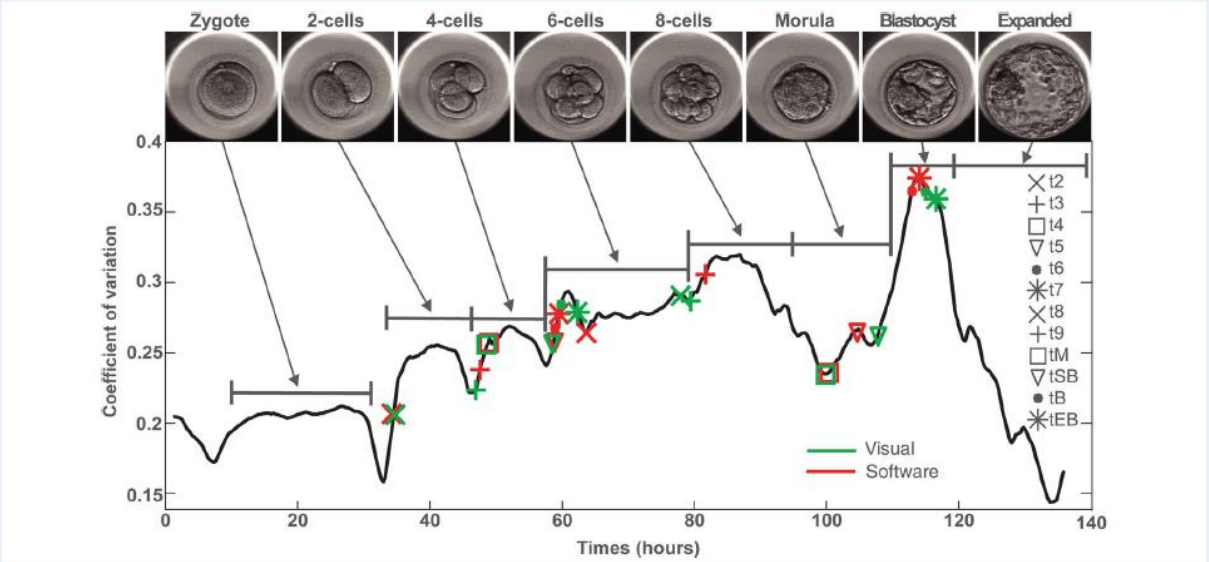


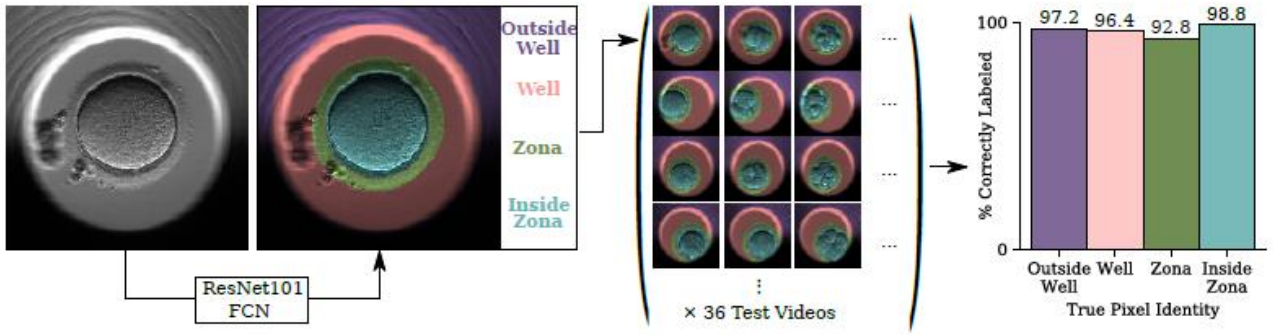
Figure 3 Representative illustration of the evolution of gray level coefficient of variation throughout human embryo development from fertilization to expanded blastocyst stage (40× magnification).

FERTILITY

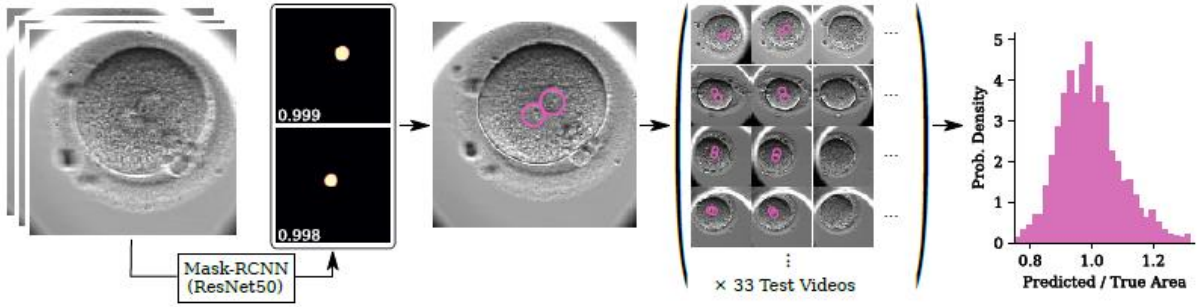
Automated Measurements of Key Morphological Features of Human Embryos for IVF

B. D. Leahy*[1,2], W.-D. Jang*[1], H. Y. Yang*[3], R. Struyven[1], D. Wei[1], Z. Sun[1], K. R. Lee[2], C. Royston[2], L. Cam[2], Y. Kalma[4], F. Azem[4], D. Ben-Yosef[4], H. Pfister[1], and D. Needleman[1,2]

[1] School of Engineering and Applied Sciences,
[2] Department of Molecular and Cellular Biology,
[3] Harvard Graduate Program in Biophysics,
Harvard University, Cambridge, MA USA
[4] Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
bleahy@seas.harvard.edu



Zona Pellucida Segmentation: semantic segmentation to identify regions of the embryo, segmenting the image into four regions: pixels outside the well, inside the well, the zona pellucida, and the space inside the zona pellucida (the perivitelline).



Pronucleus Object Instance Segmentation

Time-lapse imaging: clearly useful to both laboratory personnel and patient outcomes versus just because we can doesn't mean we should

Richard J. Paulson, M.D., M.S.,[a] David E. Reichman, M.D.,[b] Nikica Zaninovic, M.S., Ph.D., H.C.L.D., E.L.D.,[b] Linnea R. Goodman, M.D.,[c] and Catherine Racowsky, Ph.D.[d]

[a] Department of Obstetrics and Gynecology, University of Southern California, Keck School of Medicine, Los Angeles, California; [b] The Ronald O. Perelman Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medical College, New York, New York; [c] IVI/RMA New Jersey, Basking Ridge, New Jersey; and [d] Department of Obstetrics, Gynecology and Reproductive Biology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts

Disclaimer: Authors for "fertile battles" are chosen to represent the full breadth of opinions. Individual authors, even within one side of the debate, do not necessarily agree with all viewpoints expressed.

PRO: Time-lapse imaging: clearly useful to both laboratory personnel and patient outcome

David E. Reichman, M.D.

Nikica Zaninovic, M.S., Ph.D., H.C.L.D., E.L.D.

CON: Time-lapse imaging: just because we can, doesn't mean we should

Linnea R. Goodman, M.D.

Catherine Racowsky, Ph.D.

FERTILITY

Review REPRODUCTIVE BIOMEDICINE ONLINE 35 (2017) 511–520

Time-lapse culture with morphokinetic embryo selection improves pregnancy and live birth chances and reduces early pregnancy loss: a meta-analysis

Csaba Pribenszky [a,*], *Anna-Maria Nilselid* [b], *Markus Montag* [c]

[a] *University of Veterinary Science, Istvan u. 2., Budapest 1078, Hungary*
[b] *Vitrolife Sweden AB, Box 9080, Göteborg SE-400 92, Sweden*
[c] *ilabcomm GmbH, Eisenachstr. 34, Sankt Augustin 53757, Germany*

KEY MESSAGE

A meta-analysis was conducted on five studies with 1637 patients. The analysis showed that the application of time-lapse monitoring together with an embryo-evaluating algorithm was associated with a significantly higher ongoing pregnancy rate, a significantly lower early pregnancy loss and a significantly higher live birth rate.

Cochrane Library

Cochrane Database of Systematic Reviews

Time-lapse systems for embryo incubation and assessment in assisted reproduction.
Cochrane Database of Systematic Reviews 2019, Issue 5. Art. No.: CD011320.

Time-lapse systems for embryo incubation and assessment in assisted reproduction (Review)

Armstrong S, Bhide P, Jordan V, Pacey A, Marjoribanks J, Farquhar C

Main results

Nine RCTs (N = 2955 infertile couples). ***The quality of the evidence ranged from very low to low***. The main limitations were high risk of bias in the included studies, imprecision, indirectness, and inconsistency. **There were no data on cumulative live birth or ongoing pregnancy rate or cumulative clinical pregnancy rate.**

Overall conclusions

There is no good evidence showing that TLS is more or less effective than conventional methods of embryo incubation. Patients may wish to take part in randomized controlled trials on TLS in order to add to the existing evidence base and to help guide assisted reproductive technology patients in the future.

FERTILITY

npj Digital Medicine

www.nature.com/npjdigitalmed

ARTICLE OPEN

Deep learning enables robust assessment and selection of human blastocysts after in vitro fertilization

Pegah Khosravi[1,2], Ehsan Kazemi[3], Qiansheng Zhan[4], Jonas E. Malmsten[4], Marco Toschi[4], Pantelis Zisimopoulos[1,2], Alexandros Sigaras[1,2], Stuart Lavery[5], Lee A. D. Cooper[6], Cristina Hickman[5], Marcos Meseguer[7], Zev Rosenwaks[4], Olivier Elemento[1,2,8], Nikica Zaninovic[4] and Iman Hajirasouliha[1,2]

npj Digital Medicine (2019)2:21 ; https://doi.org/10.1038/s41746-019-0096-y

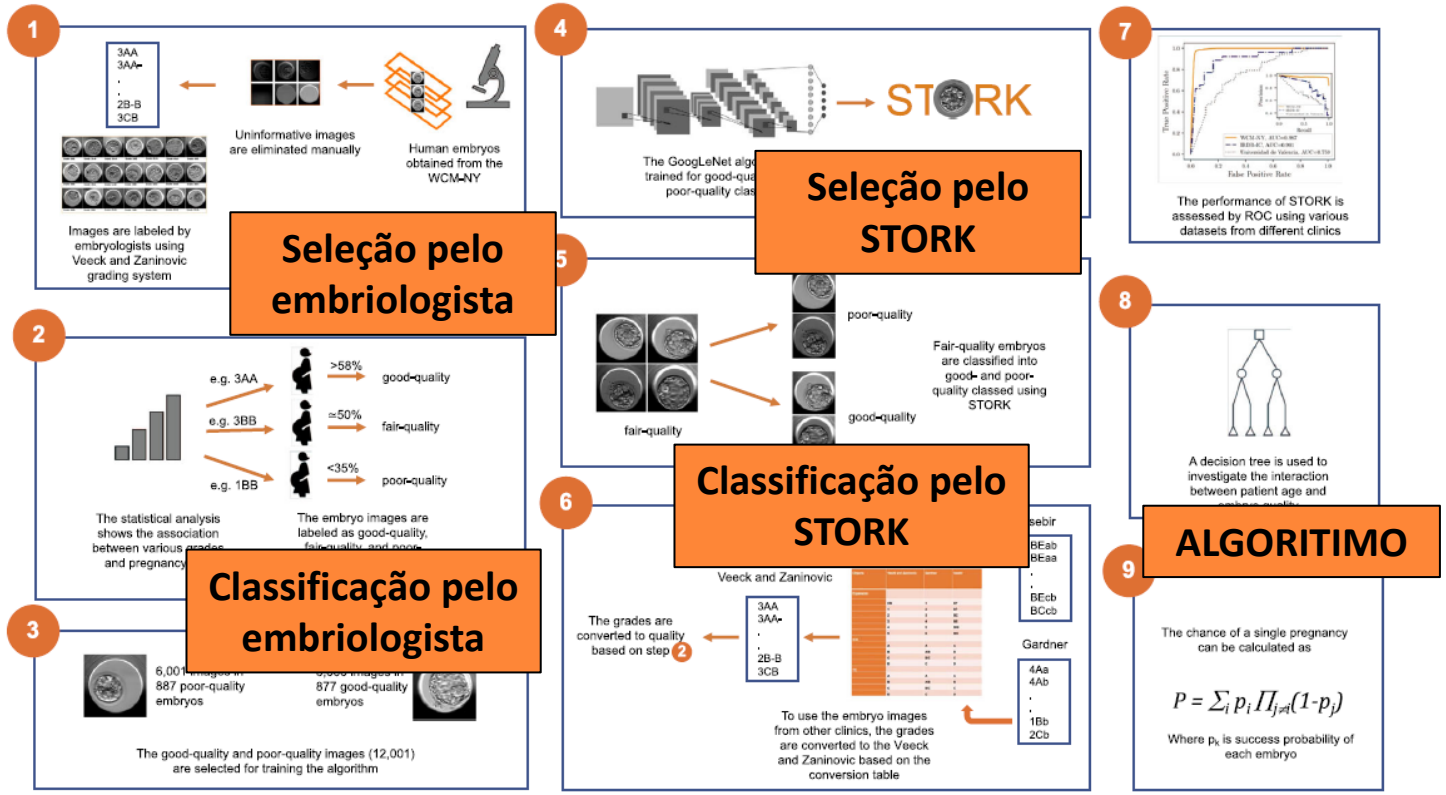


Fig. 1 The STORK flowchart: This flowchart illustrates the design and assessment of STORK. First, Human embryo images are provided from the embryology lab and labeled by embryologists as good-quality or poor-quality based on their pregnancy likelihood. Then, the labels and clinical information from the extracted images are integrated, and the Inception-V1 algorithm is trained for good-quality and poor-quality classes. Furthermore, STORK is evaluated by a blind test set to assess its performance in predicting embryo quality. Finally, the CHAID decision tree is used to investigate the interaction between patient age and embryo quality

FERTILITY

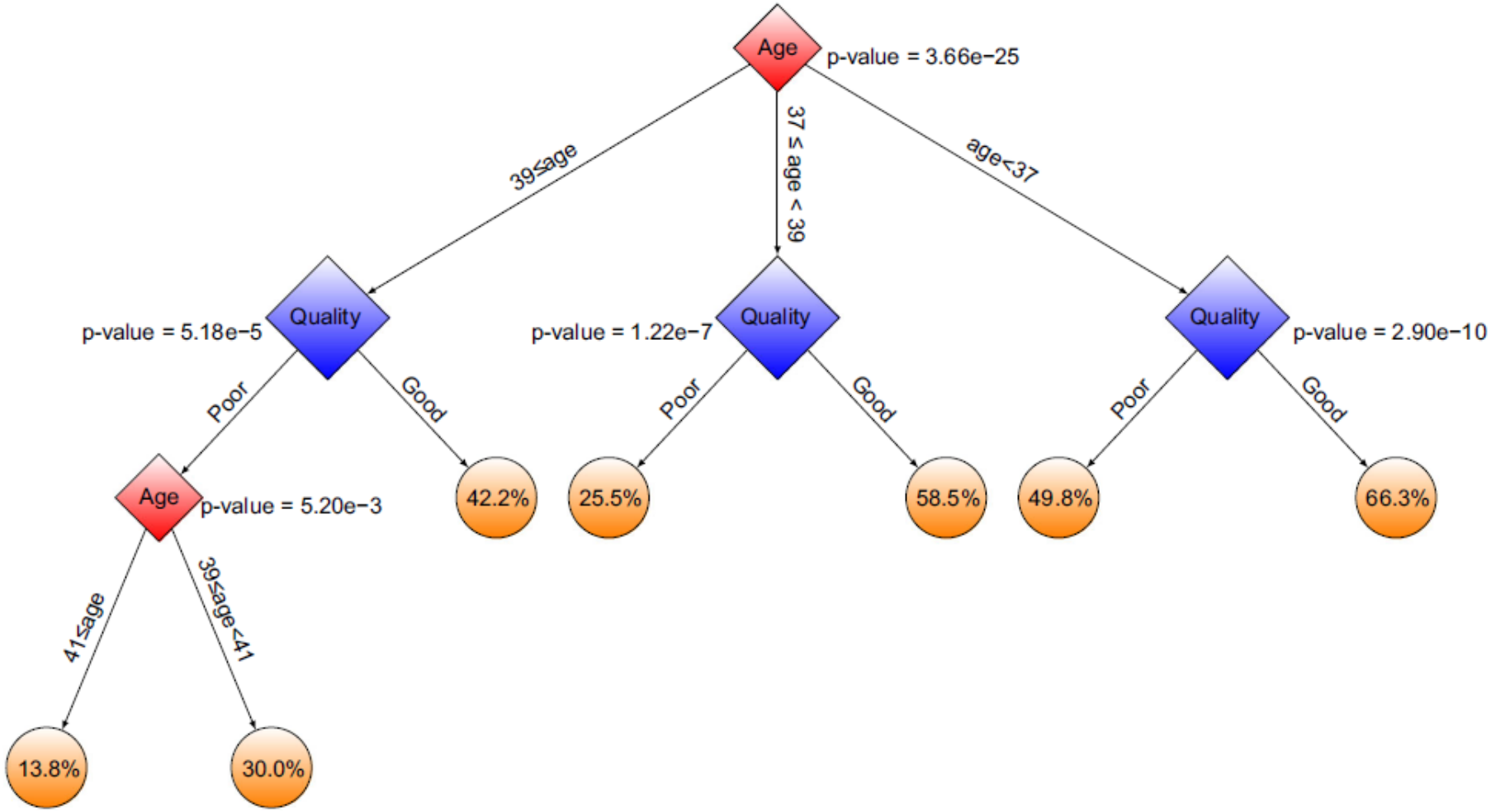


Fig. 6 Interactions between age and embryo quality: The decision tree shows the interactions between IVF patient age and embryo quality using CHAID

FERTILITY

Paternal fators and time-lapse imaging

Received: 22 February 2018 | Revised: 13 April 2018 | Accepted: 6 May 2018
DOI: 10.1111/and.13061

ORIGINAL ARTICLE

WILEY andrologia

Influence of human sperm origin, testicular or ejaculated, on

human reproduction

ORIGINAL ARTICLE *Embryology*

The impact of male factor infertility on early and late morphokinetic parameters: a retrospective analysis of

ORIGINAL ARTICLE

andrologia WILEY

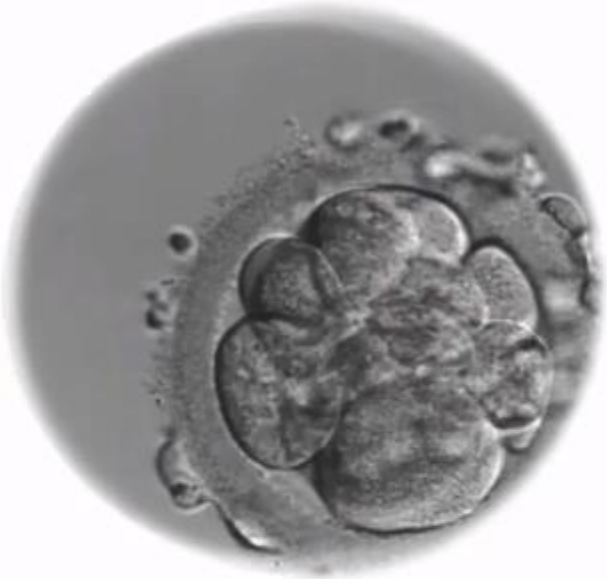
IMSI procedure improves clinical outcomes and embryo morphokinetics in patients with different aetiologies of male infertility

Esmat Mangoli[1] | Mohammad Ali Khalili[1] | Ali Reza Talebi[1] | Azam Agha-Rahimi[1] | Mehrdad Soleimani[1] | Azita Faramarzi[2] | Majid Pourentezari[3]

FERTIL

SCORE

Score: 2.0

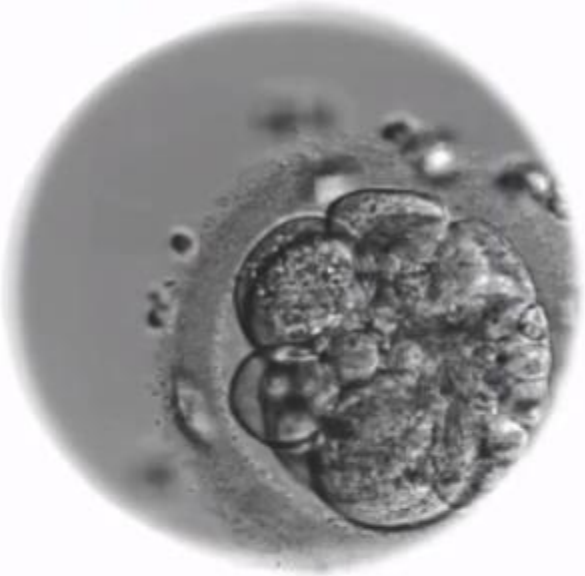


Score: 6.3

Score: 9.5

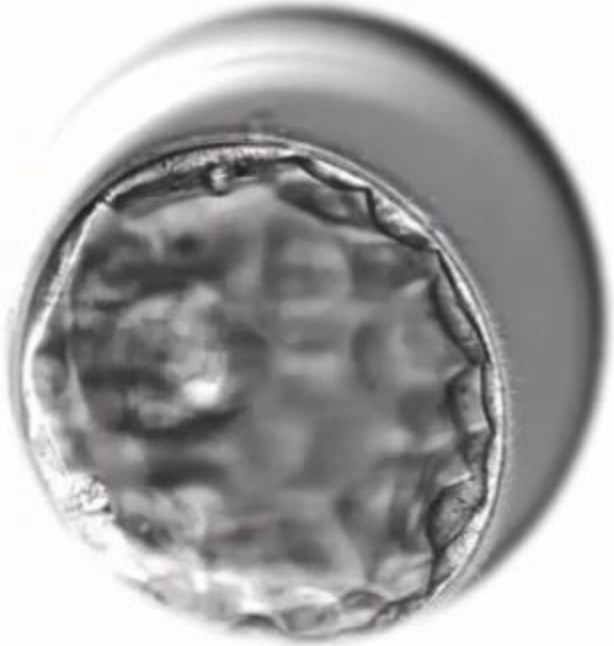
SCORE

Score: 2.0



Score: 6.3

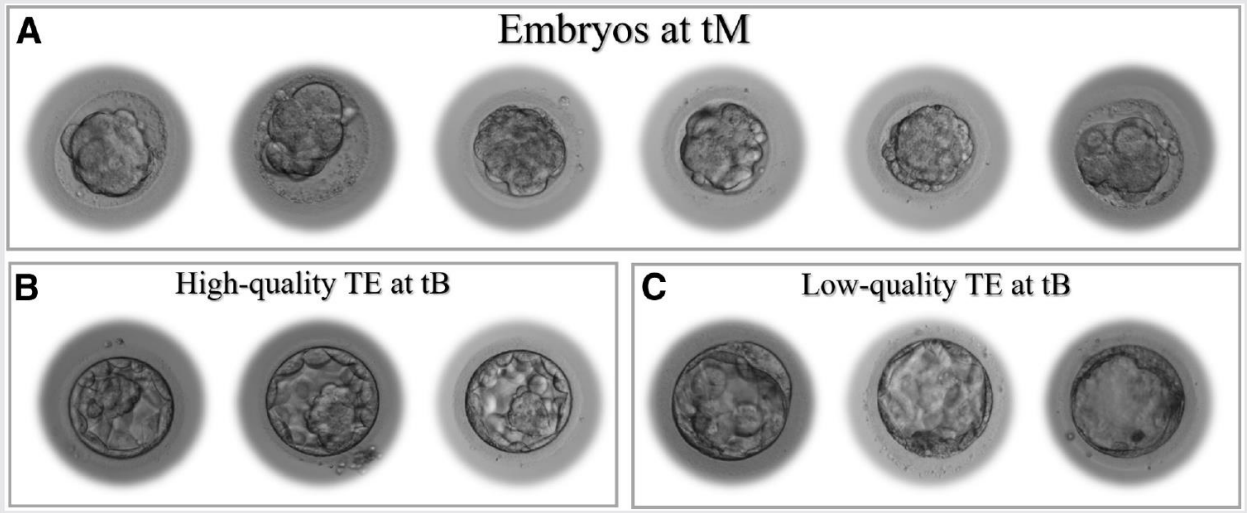
Score: 9.5



Time of morulation and trophectoderm quality are predictors of a live birth after euploid blastocyst transfer: a multicenter study

Laura Rienzi, M.Sc.,[a] Danilo Cimadomo, Ph.D.,[a] Arantxa Delgado, Ph.D.,[b] Maria Giulia Minasi, M.Sc.,[c] Gemma Fabozzi, M.Sc.,[a] Raquel del Gallego, M.Sc.,[b] Marta Stoppa, M.Sc.,[a] Jose Bellver, M.D.,[b] Adriano Giancani, M.Sc.,[a,d] Marga Esbert, Ph.D.,[e] Antonio Capalbo, M.Sc.,[d,f] Jose Remohì, M.D.,[b] Ermanno Greco, M.D.,[c] Filippo Maria Ubaldi, M.D., Ph.D.,[a] and Marcos Meseguer, Ph.D.[b]

Fertility and Sterility® Vol. 112, No. 6, December 2019



(A) Examples of embryos at the time of morulation (tM). **(B)** Examples of high-quality trophectoderm (TE) and the time of blastulation (tB). **(C)** Examples of low quality TE at tB.

- Only *time of morulation (tM) and trophectoderm quality were outlined as putative predictors of live birth at two IVF centers*.

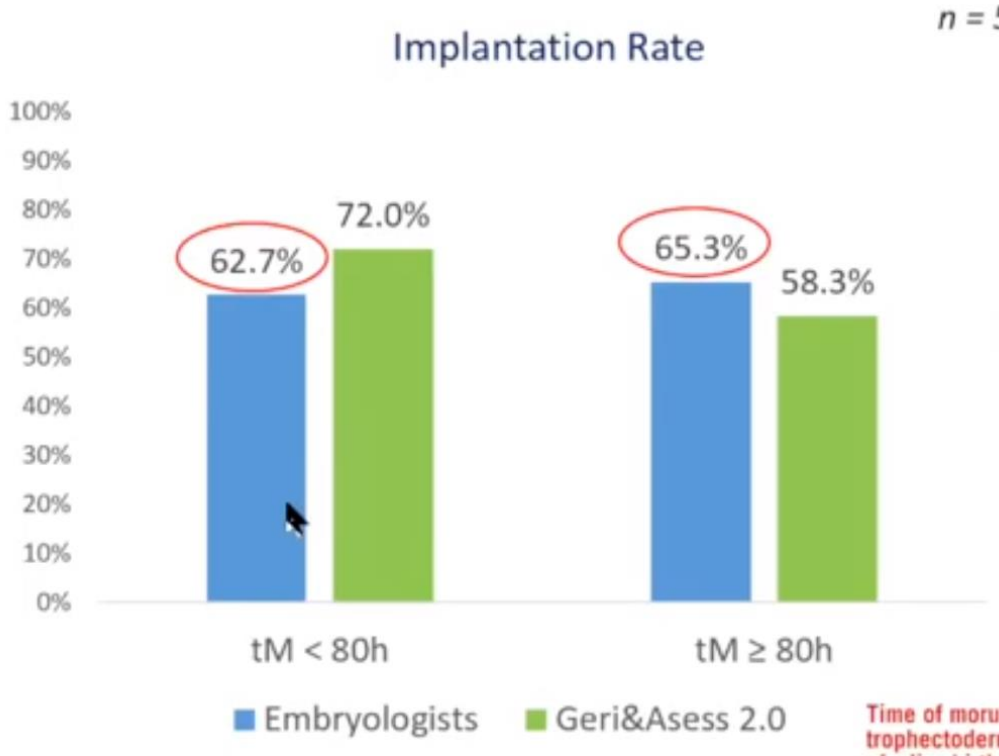
- In the validation set, the euploid blastocysts characterized by *tM <80 hours and high-quality trophectoderm resulted in a LBR of 55.2% (n = 37/67), while those with tM >80 hours and a low quality trophectoderm resulted in a LBR of 25.5% (N = 13/51).*

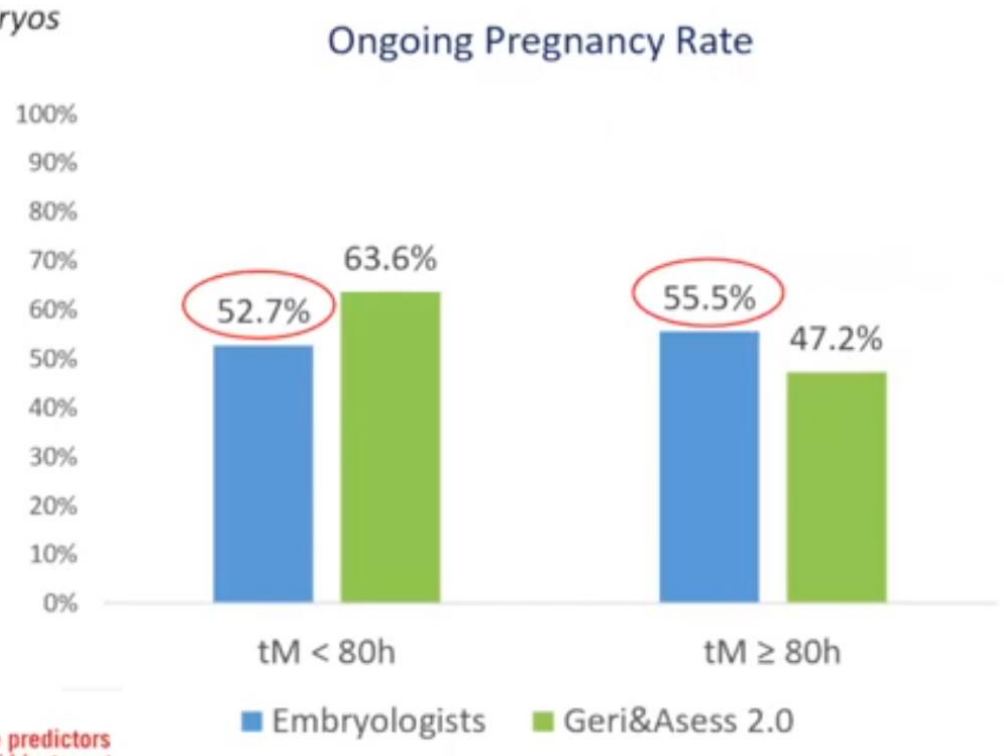
FERTILITY

Clinical Result Prediction

tM < 80 h

n = 510 embryos





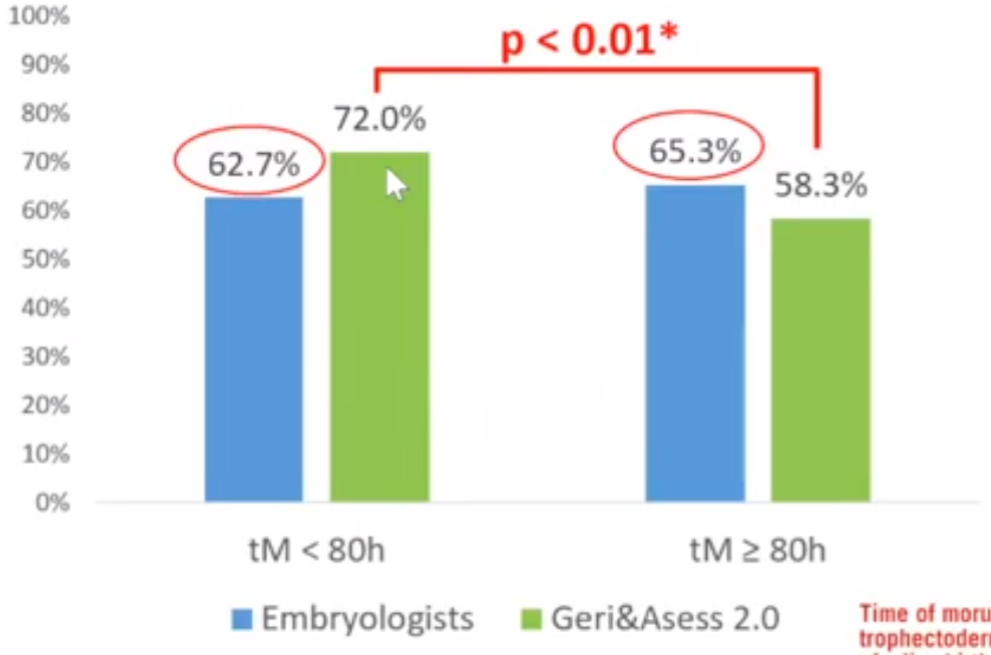
Time of morulation and trophectoderm quality are predictors

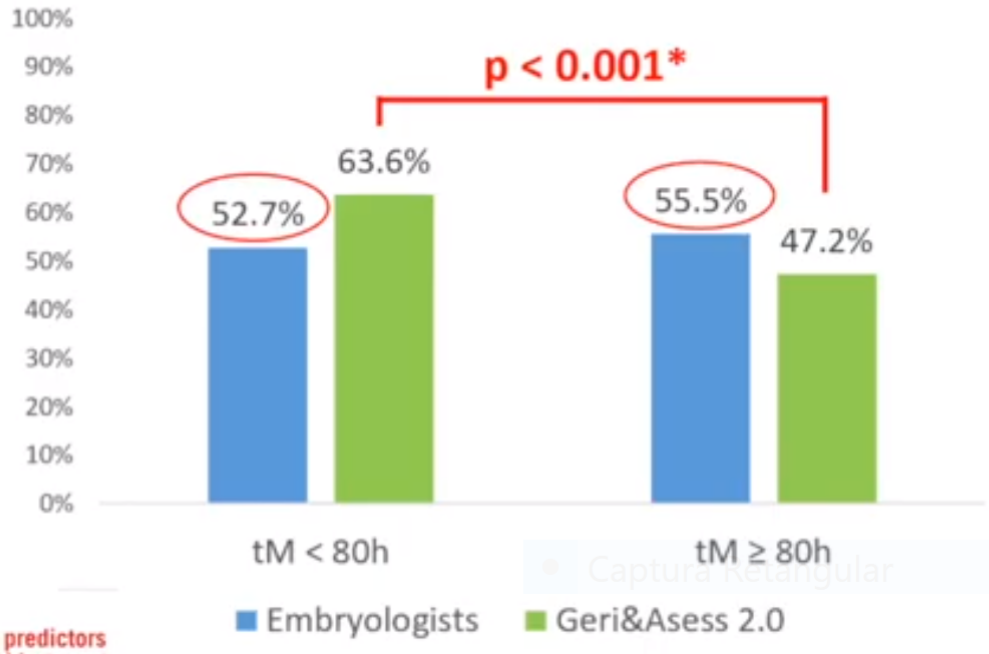
FERTILITY

Clinical Result Prediction

tM < 80 h

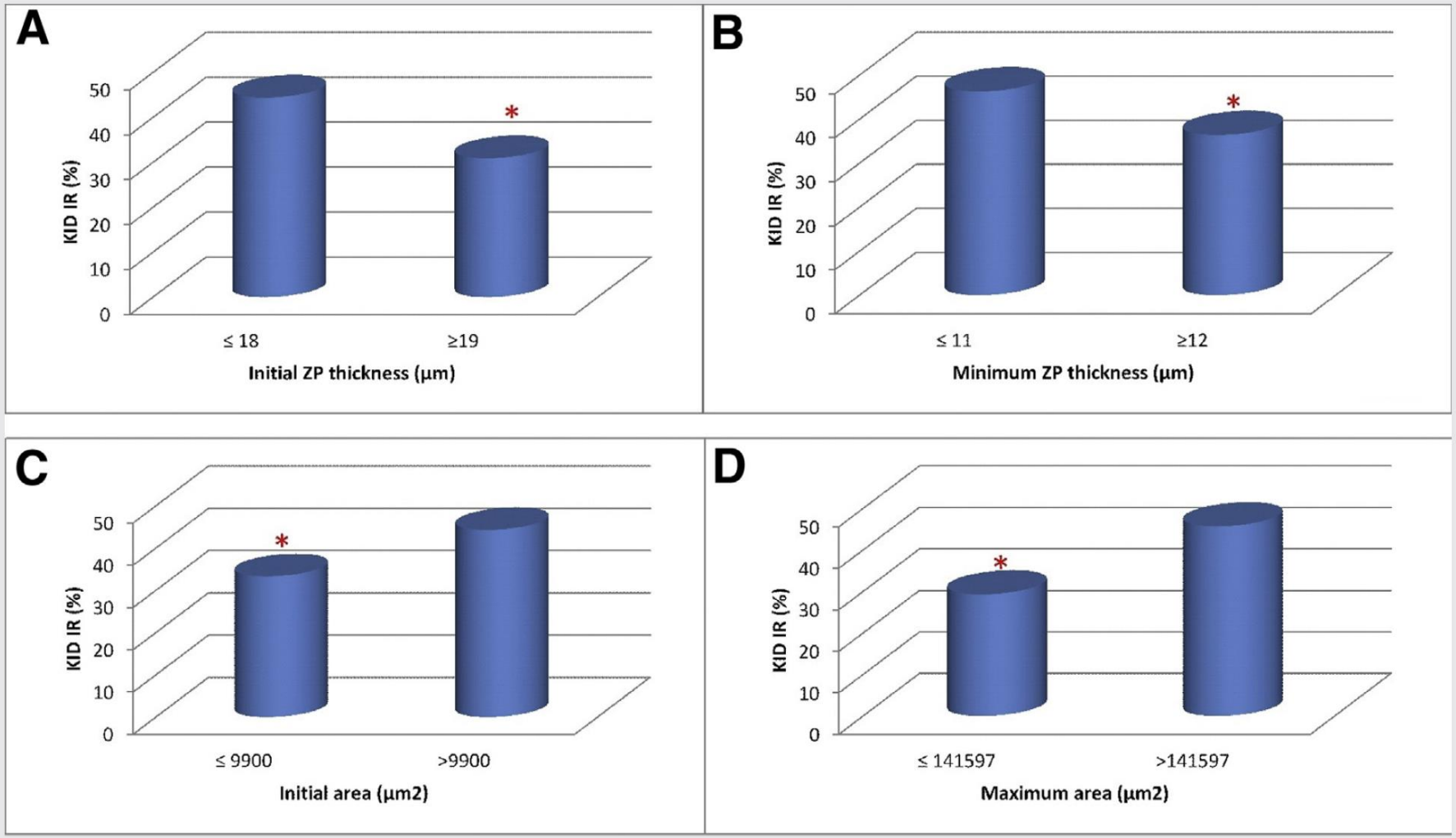
n = 510 embryos





Time of morulation and trophectoderm quality are predictors

FERTILITY



Percentage of implanting blastocysts with morphological dynamics variables within or beyond the ranges defined by the quartile limits for the total data set. The four panels show ranges and implantation for (**A**) initial ZP thickness, **P*=.02; (**B**) minimum ZP thickness, **P*=.03; (**C**) initial blastocyst area, **P*=.04; and (**D**) maximum blastocyst area, **P*=.004.

Obstetric and perinatal outcomes of pregnancies conceived with embryos cultured in a time-lapse monitoring system

Maria Fernanda Insua, Ph.D.,[a] Ana Cristina Cobo, Ph.D.,[a] Zaloa Larreategui, Ph.D.,[b] Marcos Ferrando, M.D.,[b] Vicente Serra, Ph.D.,[a] and Marcos Meseguer, Ph.D.[a]

[a] IVI Valencia, Valencia; and [b] IVI Bilbao, Bilbao, Spain

Fertility and Sterility® Vol. 108, No. 3, September 2017

Patient(s): Of 856 randomized patients, 378 gave birth to a live-born infant: 216 of the deliveries originated from embryos incubated in TLS, and 162 deliveries were from embryos cultured in SI.

Result(s): No significant differences were observed in the baseline characteristics of the study population. *The delivery rate was 49.3% (TLS) vs. 40.0% (SI), and multiple deliveries were higher in the TLS group: 31.0% (67 of 216) vs. 24.7% (40 of 162) in the SI group.*

Conclusion(s): *No detrimental effects were observed in obstetric and perinatal outcomes when a time-lapse incubator was used rather than a more widely used conventional incubator*.

FERTILITY

Relationship between **Implantation Rate** and the KID Score Day 5

Groups of similar interval length

p<.05

V2
1316
embryos

KIDScore Day 5 v2	≤ 2.5	2.6 - 5.0	5.1 - 7.5	> 7.5
Implantation Rate	38.6%	38.2%	52.5%	56.7%
N	34/88	83/217	277/528	274/483

p<.05

V3
1952
embryos

KIDScore Day 5 v3	≤ 2.5	2.6 - 5.0	5.1 - 7.5	> 7.5
Implantation Rate	35.44%	41.55%	55.77%	68.01%
N	28/79	145/349	609/1092	294/432

Quartiles of similar sample size

KIDScore Day 5 v2	≤ 5.3	5.4 - 7.1	7.2 - 7.9	≥8.0
Implantation Rate	39.3%	48.4%	59.2%	56.6%
N	129/328	168/347	190/321	181/320

KIDScore Day 5 v3	≤5.3	5.4 - 6.4	6.5 - 7.4	≥7.5
Implantation Rate	41.0%	54.2%	59.3%	67.9%
N	215/524	274/506	270/455	317/467

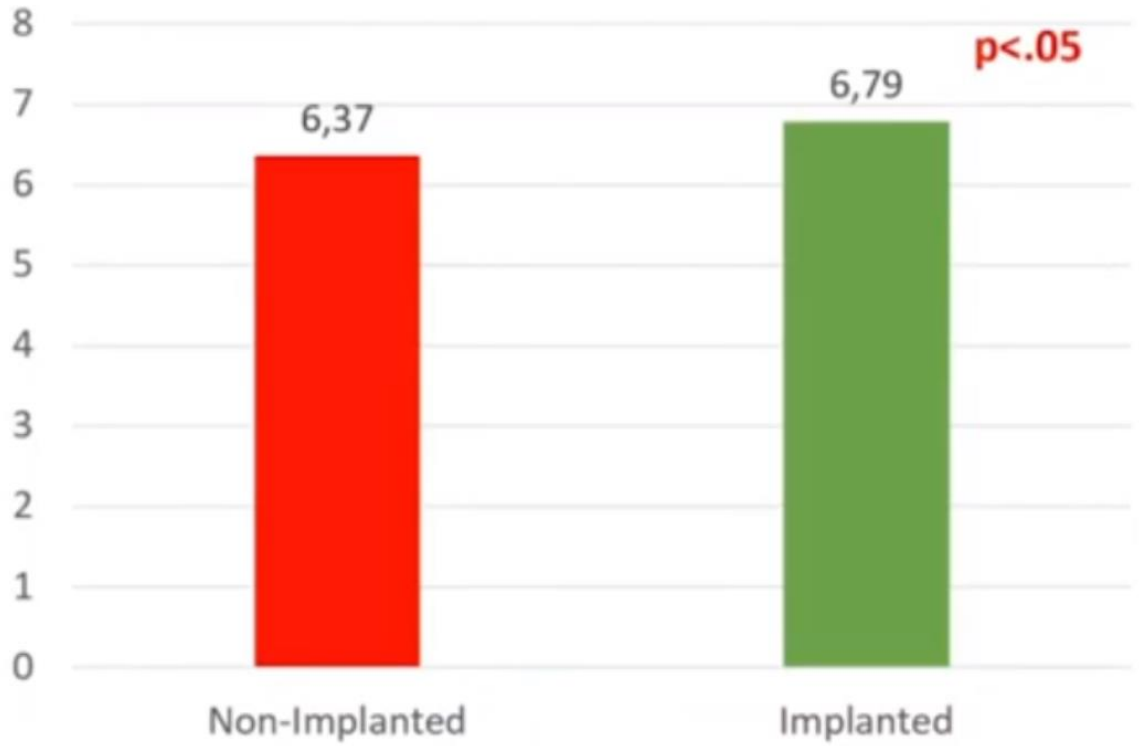
Innovation

FERTILITY

Relationship between **Implantation Rate** and the KID Score Day 5 in **good quality embryos (A+B,** *ASEBIR Criteria 2015***)**

KID Score Day 5 VERSION 3

Implatation	Mean	Standard Deviation	N
Implanted	6.790	1.5420	972
Non-implanted	6.368	1.5502	696



Innovation

FERTILITY

Relationship between **Live Birth Rate** and the KID Score Day 5

p<.05

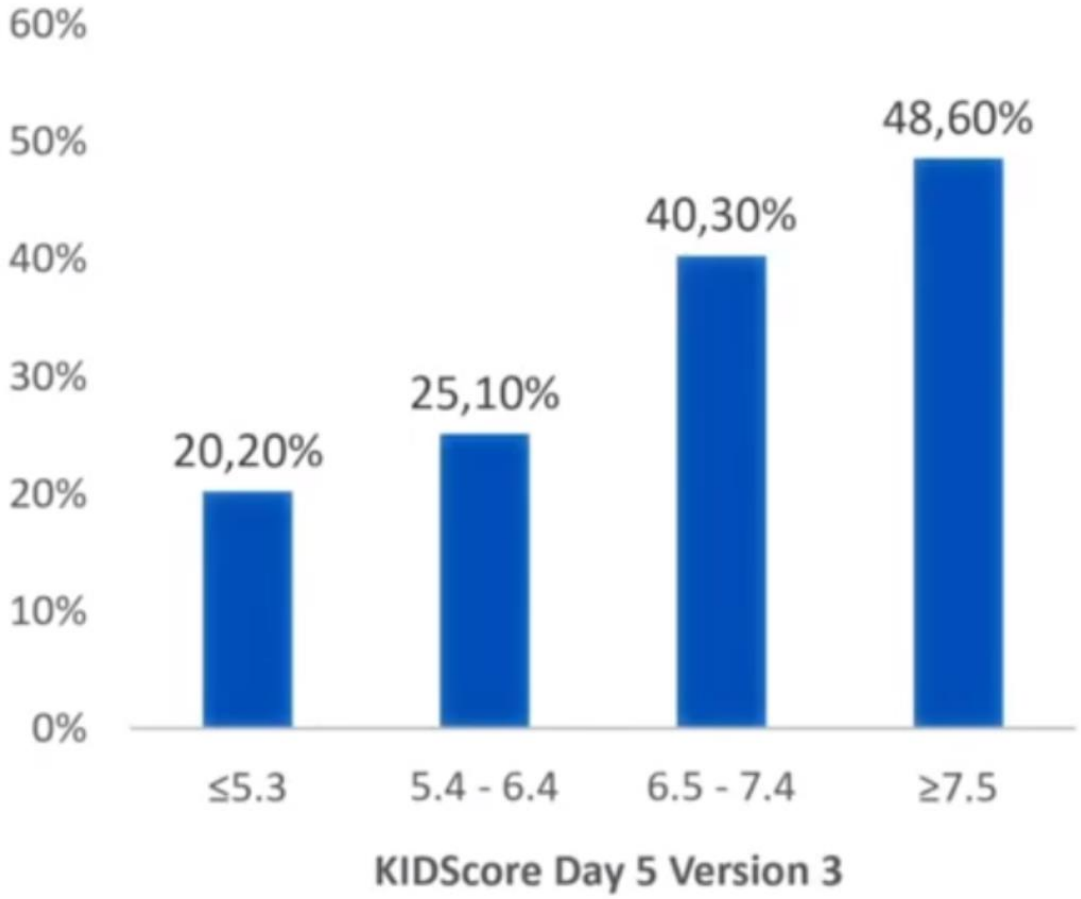
V2
1280
embryos

KIDScore Day 5 v2	≤ 5.3	5.4 - 7.1	7.2 - 7.9	≥8.0
Live Birth Rate	24.8%	35.2%	44.8%	41.9%
N	79/318	121/344	141/315	127/303

p<.05

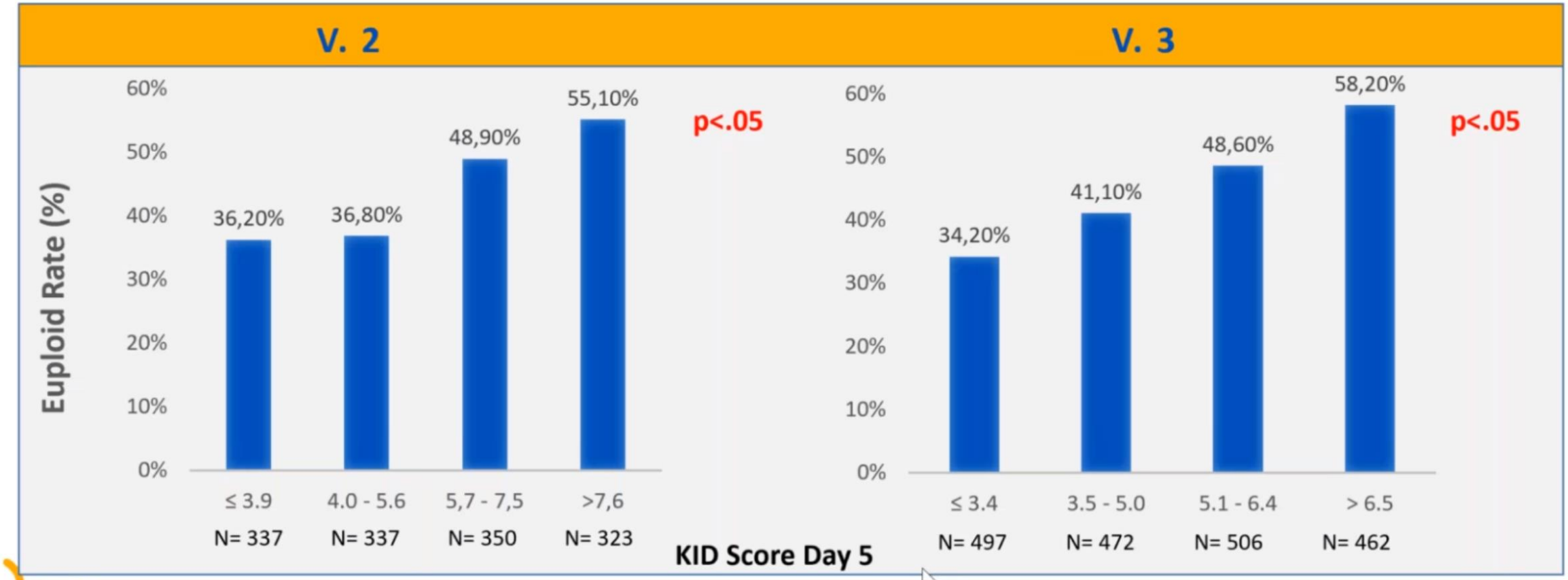
V3
867
embryos

KIDScore Day 5 v3	≤5.3	5.4 - 6.4	6.5 - 7.4	≥7.5
Live Birth Rate	20.20%	25.10%	40.30%	48.60%
N	49/242	55/219	79/196	102/210



FERTILITY

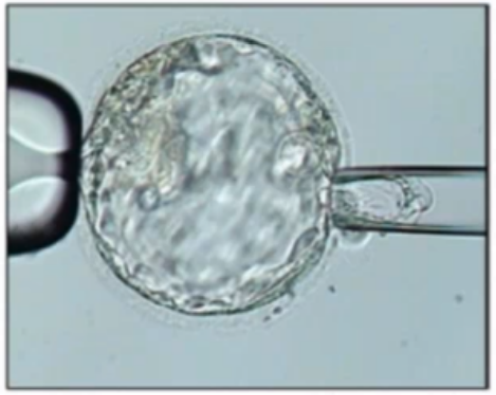
Relationship between **Euploid Rate** and the KID Score Day 5



Innovation

FERTILITY

Relationship between **Chromosomal Content** and the KID Score Day 5



V2
1347
embryos

KID Score Day 5 VERSION 2 — $p<.05$

Ploidy	Mean	Standard Deviation	N
Euploid embryos	5.96	2.14	595
Aneuploid embryos	5.31	2.19	752

V3
1937
embryos

KID Score Day 5 VERSION 3 — $p<.05$

Ploidy	Mean	Standard Deviation	N
Euploid embryos	5.25	1.87	879
Aneuploid embryos	4.59	1.80	1058

Innovation

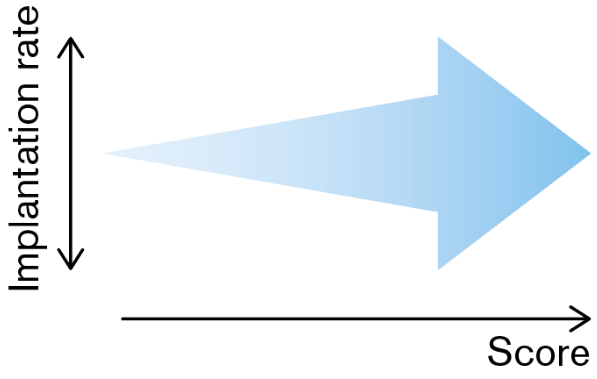
FERTILITY

EMBRYOSCOPE – KIDScore D5

KIDscore D5 is based on information on embryonic development up to the 5th of approximately 1100 embryos with known implantation status.

.

Score: 1 - 9,9 (according to the chance of implantation)



FERTILITY

Utilização do EMBRYOSCOPE no Descongelamento de embriões

30 ciclos, 44 embriões transferidos

Taxa de gestação

- **Espessura inicial zona pelúcida OR: 0.712, CI: 0.530 – 0.955, p: 0.023**
- **Espessura final zona pelúcida OR: 0.647, CI: 0.468 – 0.894, p: 0.008**
- Taxa de gestação de acordo com a pontuação da zona pelúcida (0: 40.0% vs 1: 60.6%, p: 0.381).
- Area inicial do blastocisto OR: 1.000, CI: 1.000 – 1.000, p: 0.379
- Area final do blastocisto OR: 1.000, CI: 1.000 – 1.000, p: 0.168
- Taxa de gestação de acordo com a pontuação da área do blastocisto (0: 42.9% vs 1: 75.0% vs 2: 56.5% p: 0.388).
- **Taxa de gestação de acordo com a pontuação final total do blastocisto (0: 0.0% vs 1: 42.9% vs 2: 77.8% vs 3: 41.7% vs 4: 77.8%, p<0.001).**

  0≠1 (p:0.022), 0≠2 (p<0.001), 0≠3 (p: 0.003), 0≠4 (p<0.001)
- Taxa de gestação de acordo com a expansão do blastocisto (sim: 60.0% vs não: 50.0%, p: 0.614).

FERTILITY

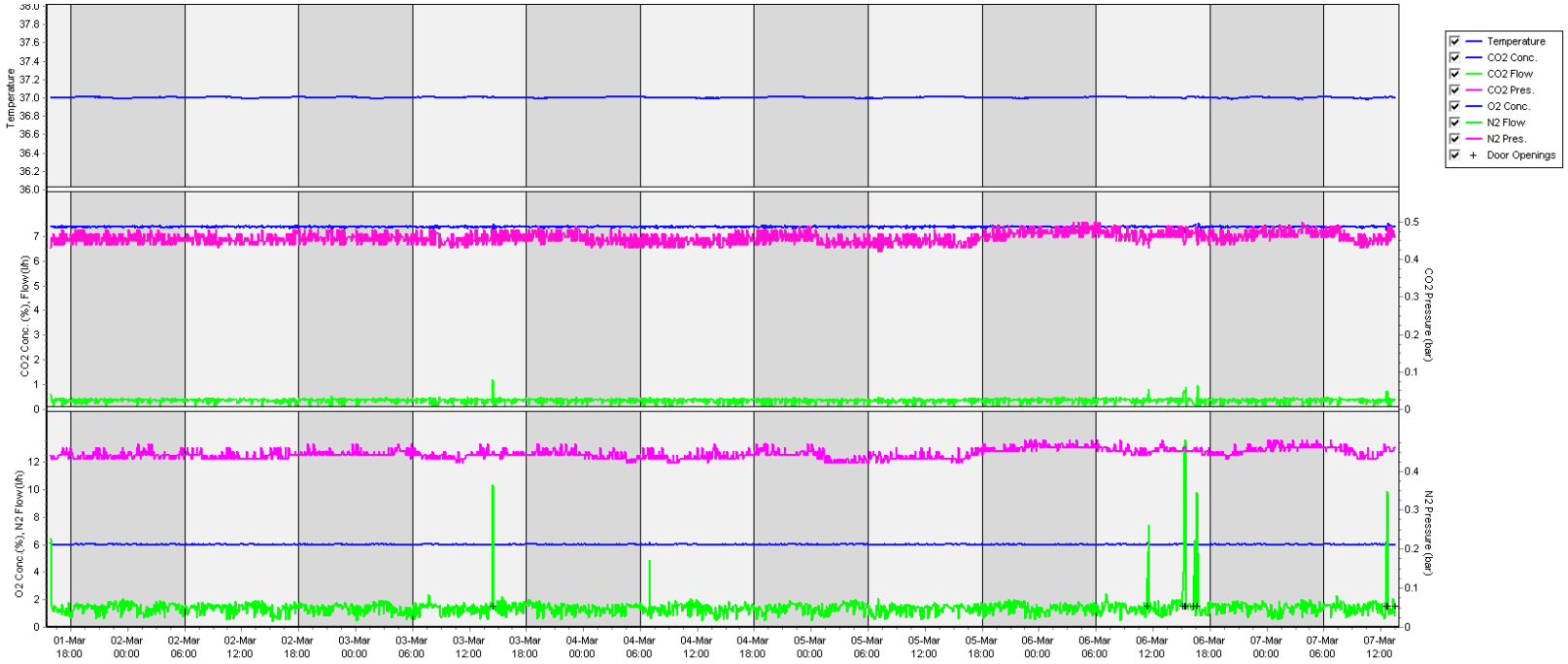
EMBRYOSCOPE *plus*

- ❑ CO2 / O2 incubator
- ❑ Capacity: 15 patients with 16 embryos (total 240 embryos)
- ❑ Air purified by activated carbon and HEPA filter
- ❑ Total time of exposure to light: <40 sec / day (per embryo)
- ❑ High-quality Hoffman modulation contrast optics
- ❑ Time between image acquisitions: 10 minutes
- ❑ Image acquisition in multiple focal planes
- ❑ Dry incubation

FERTILITY

EMBRYOSCOPE *plus*

SAFE CULTIVE ENVIRONMENT FOR EMBRYOS



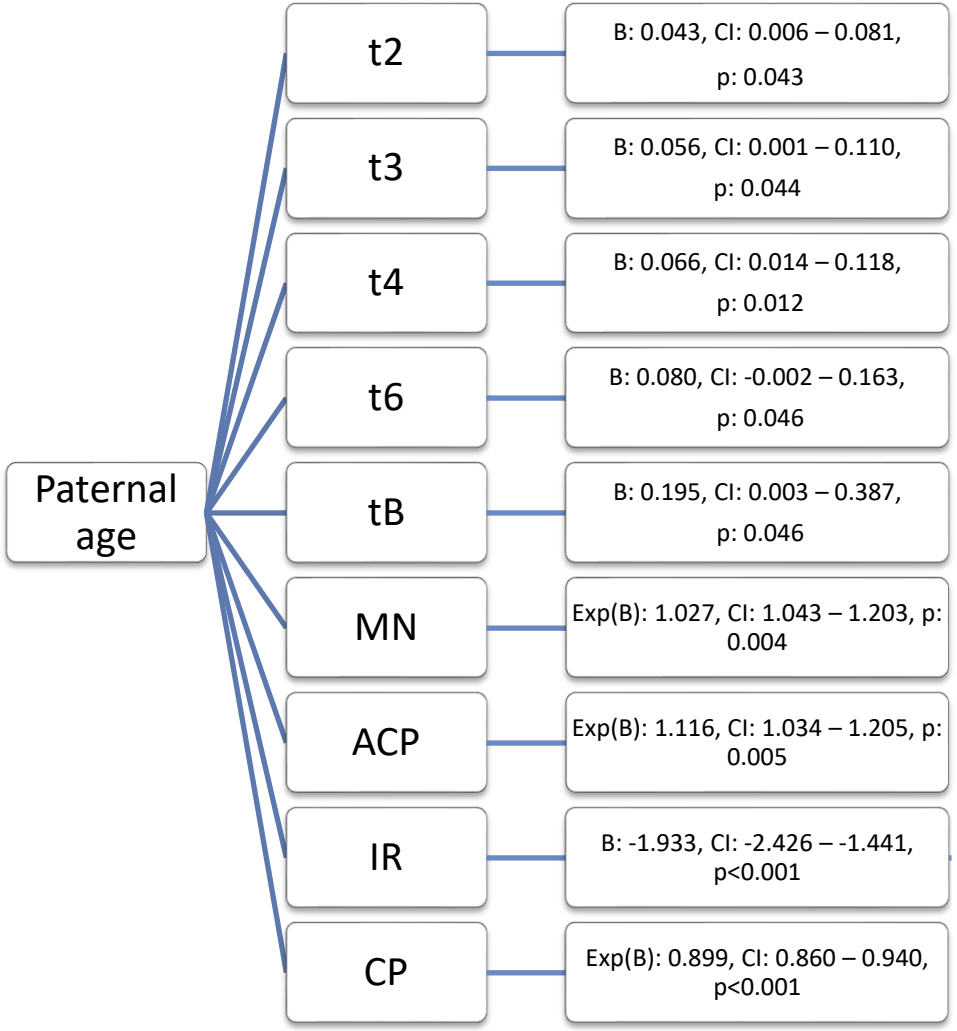
- Temperature
- CO_2 / O_2
- pH
- VOC
- Images
- Alarm

Summary | Alarms | Warnings | Log | Other

Variable	Unit	Average	Min	Max	StdDev	Set-Point
Temperature	C	37.00	36.98	37.02	0.007	37.0
CO2 Concentration	%	7.38	7.25	7.46	0.032	7.4
CO2 Flow	l/h	0.36	0.01	0.60	0.096	0.0
CO2 Pressure	bar	0.46	0.42	0.50	0.016	0.0
O2 Concentration	%	6.01	5.97	6.15	0.011	6.0
N2 Flow	l/h	1.38	0.45	6.45	0.361	0.0
N2 Pressure	bar	0.44	0.42	0.48	0.013	0.0

FERTILITY

RESULTS


Paternal age
t2
B: 0.043, CI: 0.006 – 0.081, p: 0.043
t3
B: 0.056, CI: 0.001 – 0.110, p: 0.044
t4
B: 0.066, CI: 0.014 – 0.118, p: 0.012
t6
B: 0.080, CI: -0.002 – 0.163, p: 0.046
tB
B: 0.195, CI: 0.003 – 0.387, p: 0.046
MN
Exp(B): 1.027, CI: 1.043 – 1.203, p: 0.004
ACP
Exp(B): 1.116, CI: 1.034 – 1.205, p: 0.005
IR
B: -1.933, CI: -2.426 – -1.441, p<0.001
CP
Exp(B): 0.899, CI: 0.860 – 0.940, p<0.001

Analysis of the morphological dynamics of blastocysts after vitrification/warming: defining new predictive variables of implantation

Aila Coello, Ph.D., Marcos Meseguer, Ph.D., Arancha Galán, Ph.D., Lucia Alegre, Ph.D., José Remohí, M.D., and Ana Cobo, Ph.D.

FERTILITY

FERTILITY
MEDICAL GROUP

Table 2. Embryonic morphokinetic parameters in study group (n= 114 cycles and 902 embryos)

Morphokinetic parameters (h)	Mean	SD
tPNa	6.2	2.9
tPNf	23.9	4.8
t2	26.8	5.7
t3	37.2	6.4
t4	39.0	6.8
t5	48.9	9.4
t6	51.2	8.2
t7	54.5	8.8
t8	57.8	9.9
tM	91.3	13.6
tSB	93.0	11.3
tB	108.2	11.4
s1	2.9	2.1
s2	1.9	3.6
s3	9.6	8.2
cc2	10.4	4.2
cc3	11.9	6.0

FERTILITY

Inteligência Artificial em Medicina Reprodutiva:

Aplicação clínica

Edson Borges Jr.

FERTILITY

- O uso de espermatozoides provenientes dos epidídimos está correlacionado com clivagens celulares mais lentas, as quais parecem se corrigir até o momento da formação do blastocisto.

- Os embriões apresentam maiores taxas de multinucleação e padrões anormais de clivagem, quando comparados àqueles derivados de amostras seminais de parceiros sem fator masculino de infertilidade.

FERTILITY

Time-lapse monitoring: an adjunct tool to select embryos for preimplantation genetic testing

(submitted)

Results from General Linear Models followed by Bonferroni Post Hoc for the comparison of embryo morphokinetics between aneuploidy and euploidy embryos.

Morphokinetic data	Euploid embryos (n=352)	Aneuploid embryos (n=605)	*p-value*
tPNa	6.220 ± 000	6,222±,057	0.974
tPNf	22.503 ± 0.157	24,063±0.000	**< 0.001**
t2	24,998±0.0	24,998±0.157	**< 0.001**
t3	36,141±,000	37,684±,152	**< 0.001**
t4	37,254±,227	39,259±,171	**< 0.001**
t5	49,868±,000	49,862±,239	0.981
t6	50,780±,000	53,026±,268	**< 0.001**
t7	52,561±,358	54,797±,269	**< 0.001**
t8	55,435±,431	58,653±,338	**< 0.001**
tM	85,845±,467	87,370±,366	**0.024**
tB	105,319±0.000	108,639±0,000	**<0.001**
cc2	11.3±0.13	11.3±0.10	0.809
cc3	12.7 ± 0.25	12.4 ± 0.19	0.327
s1	2.5 ± 0.04	2.6 ± 0.03	0.108
s2	1.0 ± 0.12	1.3 ± 0.09	**0.022**
s3	7.0 ± 0.38	8.37 ± 0.29	**0.006**
MN in two cell stage	0.32 ± 0.028	0.36 ± 0.022	0.275
MN in four cell stage	0.075 ± 0.015	0.079 ± 0.012	0.845
KidScore D5	6.6 ±0.0	5.7 ± 0.83	**< 0.001**

FERTILITY

Resultados da comparação dos tempos para se completar os ciclos celulares e as divisões síncronas em embriões dos grupos PESA, FMI e Controle

Variávies	PESA (n= 32)	FMI (n=32)	Controle (n=32)	Valor de p
cc2 (hrs.)	10,5 ± 0,2	10,6 ± 0.1	10,4 ± 0,5	0,634
cc3 (hrs.)	11,9 ± 0.4 [a]	11,3 ± 0,4 [a,b]	10,3 ± 0,4 [b]	0,013
s1 (hrs.)	2,9 ± 0,2 [a]	2,7 ± 0.0 [b]	2.6 ± 0.0 [b]	0,343
s2 (hrs.)	2,4 ± 0,21	2,0 ± 0,14	1,2 ± 0,52	0,05
s3 (hrs.)	3,0 ± 0,1 [a]	2,7 ± 0,1 [b]	2,4 ± 0,1 [b]	<0,001

cc2 – duração do segundo ciclo celular (t3-t2). cc3 – duração do terceiro ciclo celular (t3-t2). s1 – tempo para completer as divisões sincrônicas t2-tPNf. s2 – tempo para completer as divisões sincrônicas t4-t3. s3 - – tempo para completer as divisões sincrônicas t8-t5.

FERTILITY

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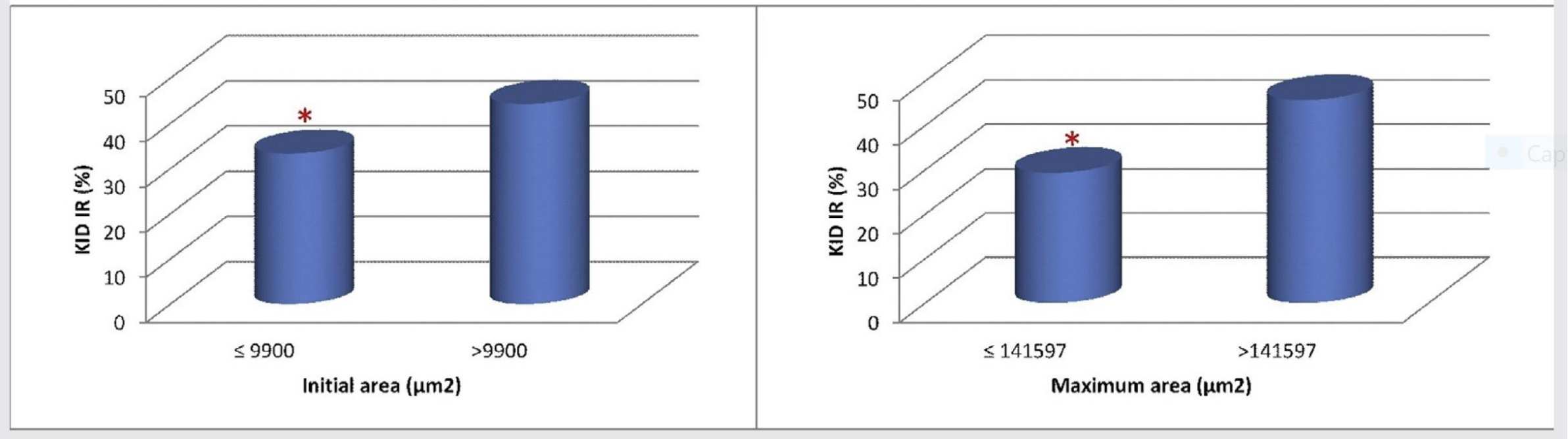
FERTILITY

Área da zona pelúcida



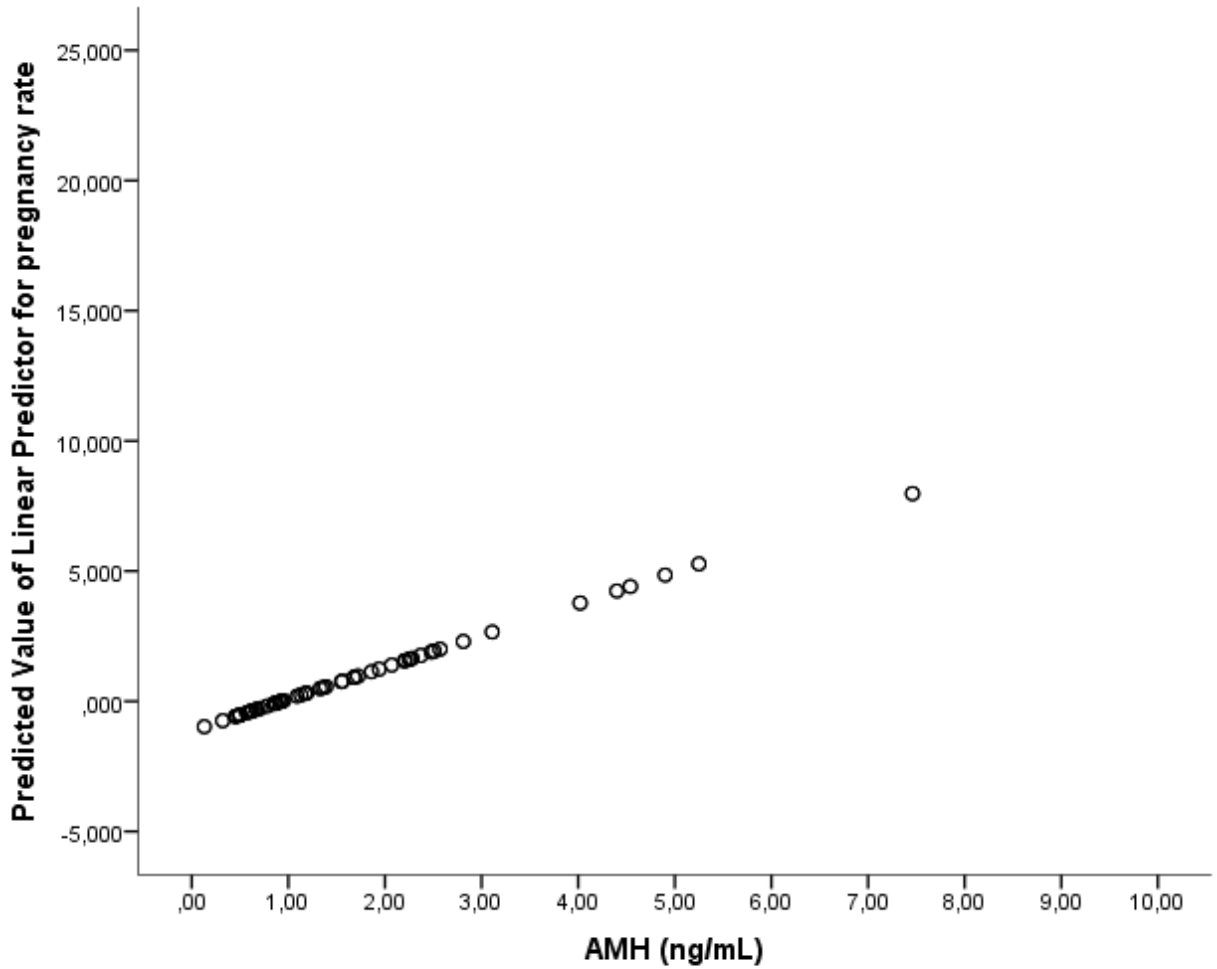
FERTILITY

- ✓ O uso de espermatozoides provenientes dos epidídimos está correlacionado com clivagens celulares mais lentas, as quais parecem se corrigir até o momento da formação do blastocisto.

- ✓ Entretanto, os embriões apresentam maiores taxas de multinucleação e padrões anormais de clivagem, quando comparados àqueles derivados de amostras seminais de parceiros sem fator masculino de infertilidade.

FERTILITY

Figure 4. Illustration of the predictive value of AMH on pregnancy rate (p=0.090)



FERTILITY

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FERTILITY

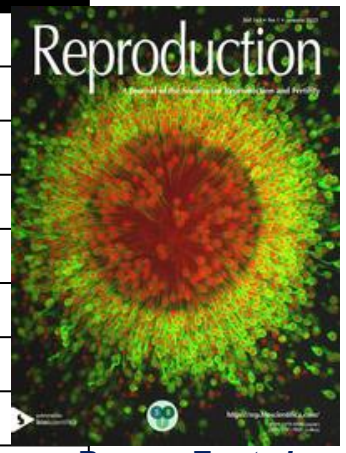
O objetivo do presente estudo foi determinar se a origem do espermatozoide impacta os resultados clínicos, a morfocinética embrionária e as incidências de padrões anormais de clivagem e multinucleação.

FERTILITY

Serum anti-müllerian hormone concentrations impact not only the quantity, but also the quality of the ovarian reserve: the importance of time-lapse imaging system

Table 1. Demographic characteristics and ICSI outcomes in study group (n= 114 cycles, 902 embryos)

Variable		Values
Female age (years)		37.2 ± 3.4
Male age (years)		39.9 ± 7.5
Female BMI		24.8 ± 5.4
Total dose of FSH	Folllitropin alpha (IU)	2169.0 ± 1039.6
	Follitropin delta (mcg)	151.0 ± 32.2
Estradiol level on hCG trigger (pg/mL)		2158.6 ± 2252.6
Follicles (n)		15.1 ± 12.1
Retrieved oocytes (n)		11.1 ± 9.0
Mature oocyte (n)		7.4 ± 6.3
Mature oocyte rate (%)		75.3 ± 21.3
Fertilization rate (%)		73.9 ± 26.5
Blastocyst development (%)		61.4 ± 26.8
High-quality blastocyst rate (%)		70.0
Transferred embryos (n)		1.7 ± 0.6
Implantation rate (%)		30.0 ± 36.2
Pregnancy rate (%)		20/36 (55.5)
Miscarriage rate (%)		6/20 (30.0)



Borges E. *et al*
(submitted)

FERTILITY

RESULTS

Variable	Mean ± SD
Female age (years)	37.7 ± 3.8

Correlation between continuous DFI and embryo morphokinetics (n = 978).

Morphokinetic data (h)	B (95% CI)	*P* value
tPNa	0.041 (0.020–0.062)	< .001
tPNf	0.068 (0.034–0.102)	< .001
t2	0.068 (0.036–0.100)	< .001
t3	0.085 (0.047–0.124)	< .001
t4	0.070 (0.029–0.110)	.001
t5	0.120 (0.062–0.179)	< .001
t6	0.117 (0.056–0.178)	< .001
t7	0.104 (0.040–0.167)	.001
t8	0.109 (0.037–0.181)	.003
tSB	0.402 (0.203–0.602)	< .001
tB	0.153 (0.038–0.268)	.009

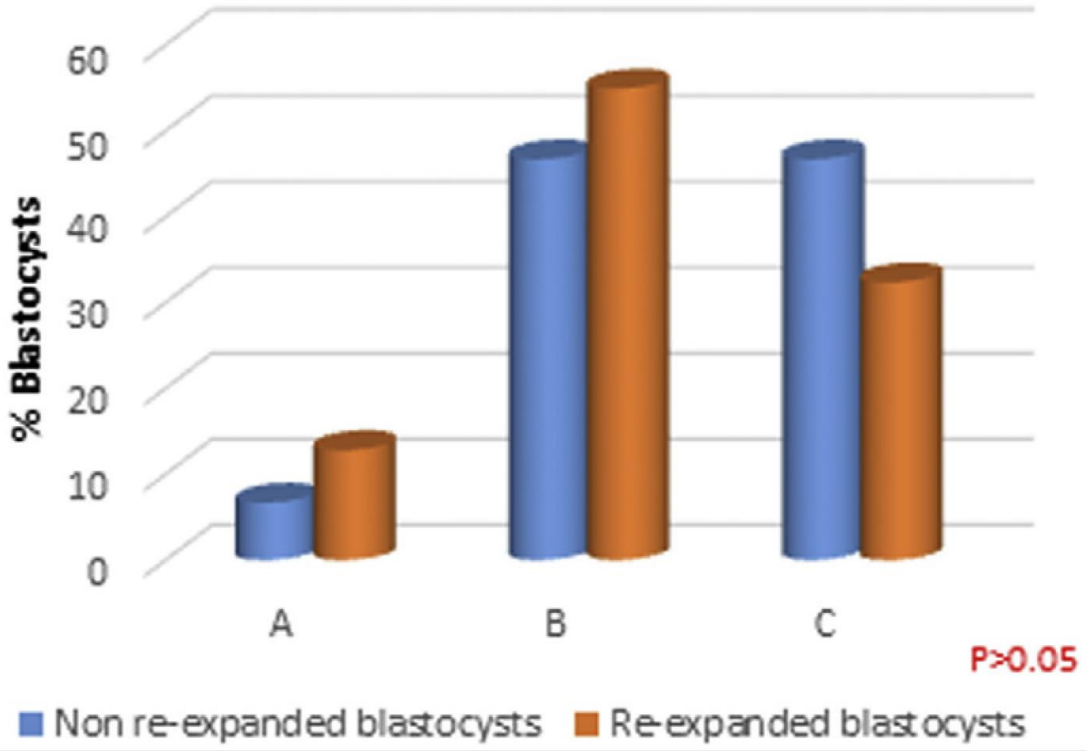
Note: B = beta coefficient; CI = confidence interval; DFI = sperm deoxyribonucleic acid fragmentation index; tB = timing to blastulation; tPNa = timing to pronuclei appearance; tPNf = timing to pronuclei fading; tSB = timing to start blastulation; t2 = timing to 2 cells; t3 = timing to 3 cells; t4 = timing to 4 cells; t5 = timing to 5 cells; t6 = timing to 6 cells; t7 = timing to 7 cells; t8 = timing to 8 cells.

Setti. Sperm DNA and embryo morphokinetics. Fertil Steril Sci 2021.

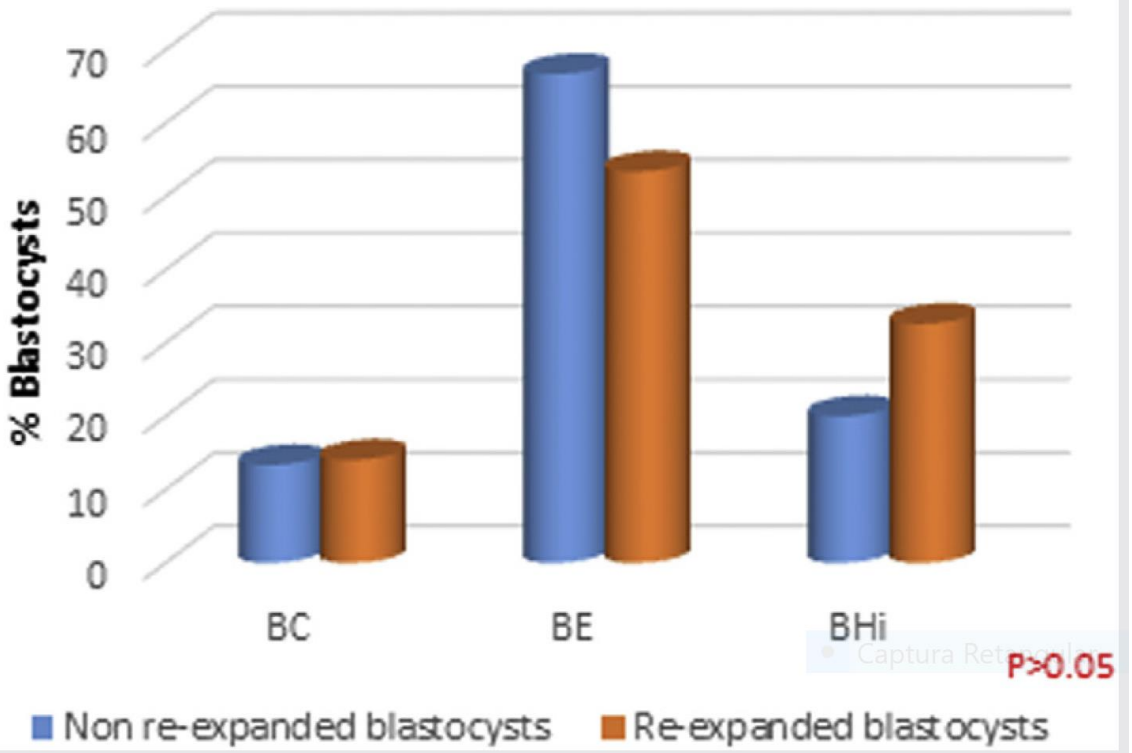
FERTILITY

F&S Science (2021), doi: https://doi.org/10.1016/j.xfss.2021.10.001

Rexpanção do Blastocisto



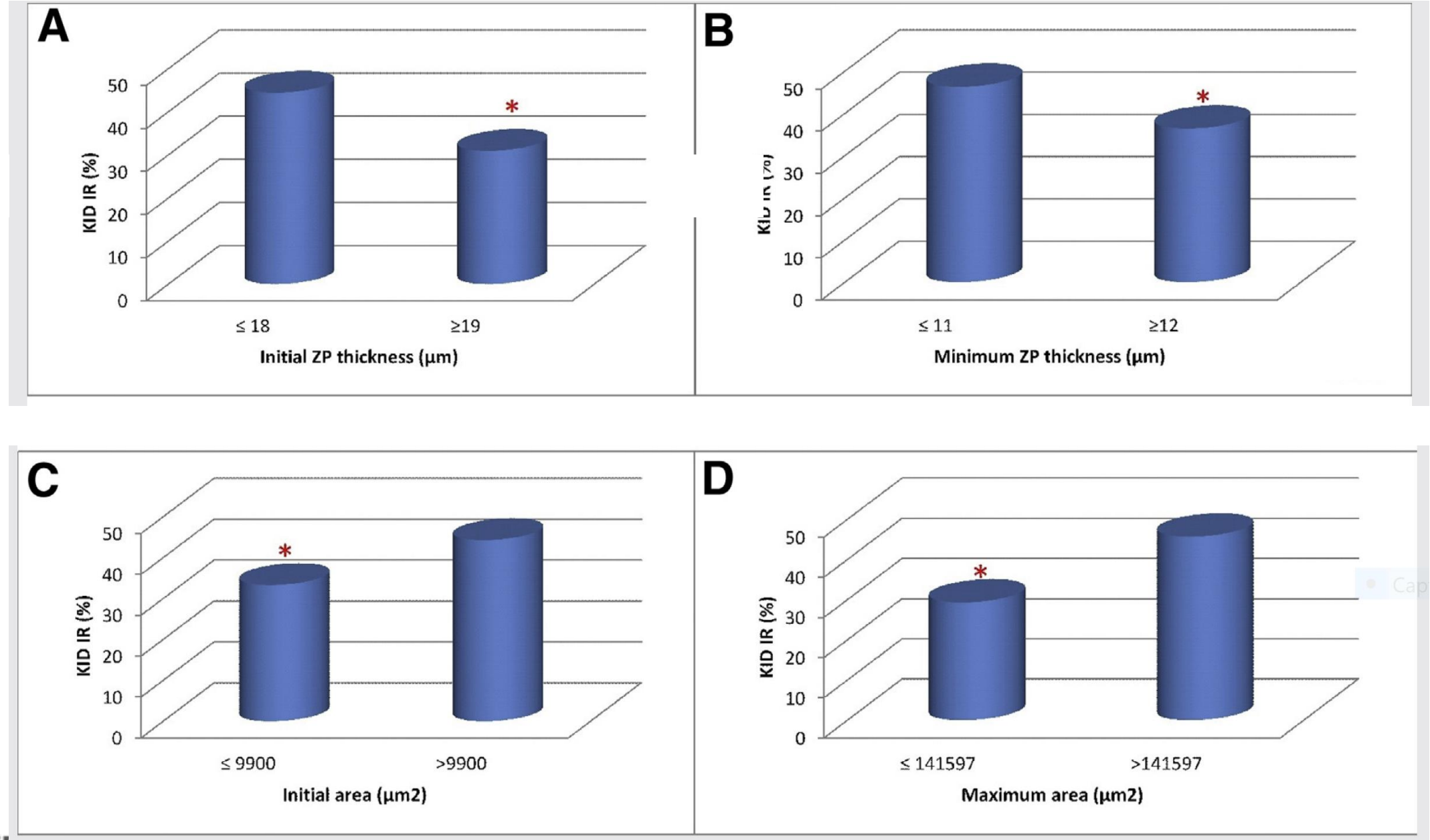
Proportion of blastocysts according to ASEBIR classification previtrification



Proportion of blastocysts according to degree of expansion previtrification.

FERTILITY

Espessura da zona pelúcida
Área do embrião



FERTILITY

Rexpanção do Blastocisto

Analysis of the morphological dynamics of blastocysts after vitrification/warming: defining new predictive variables of implantation

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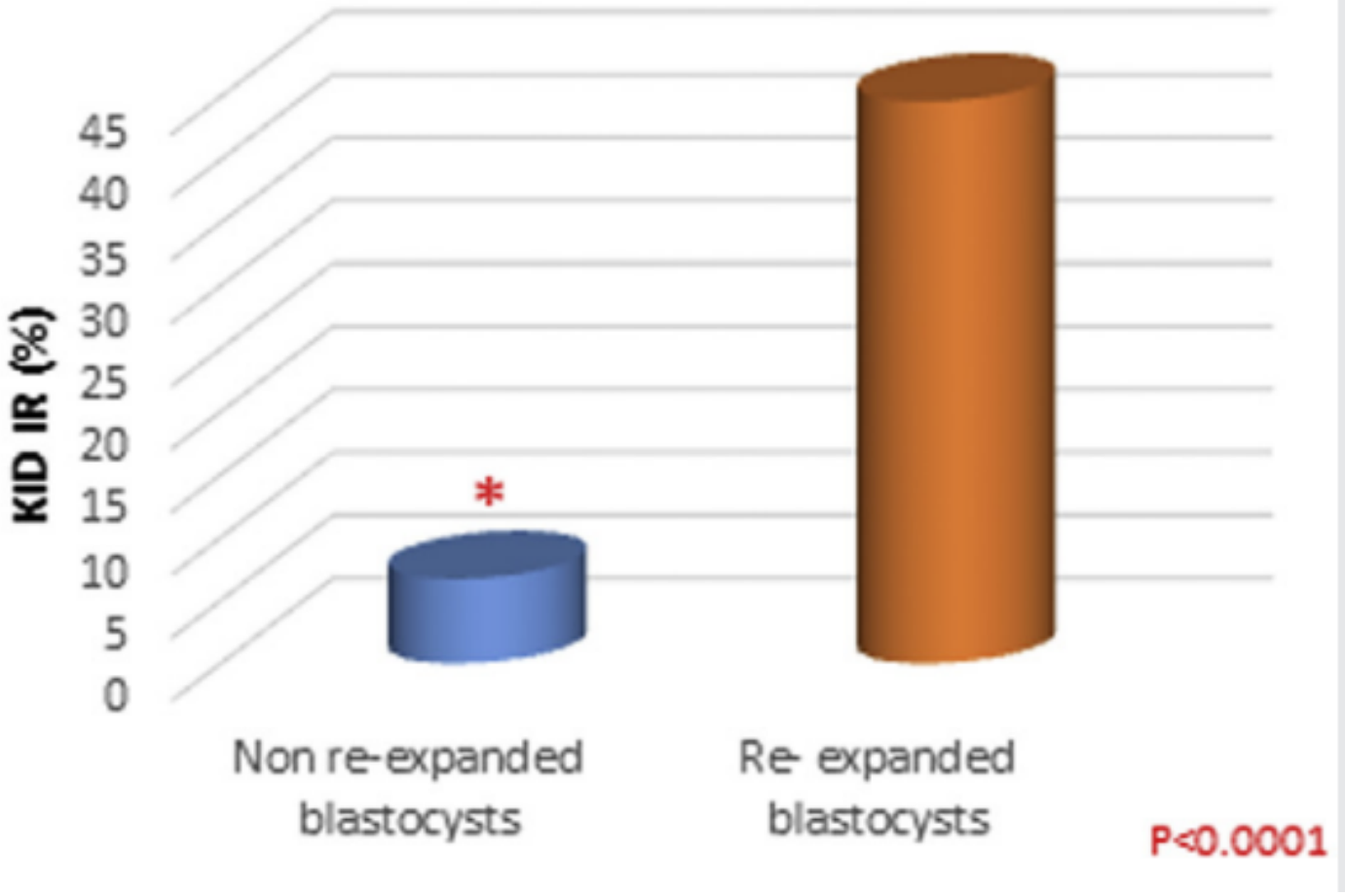


FERTILITY

RESULTS

First International Journal of Andrology
andrologia

Early and late paternal contribution to cell division of embryos in a time-lapse imaging incubation system

Variable	Mean ± SD
ICSI outcomes	
Fertilization rate (%)	75.8
Blastocyst development (%)	64.4
Transferred embryos (n)	1.3 ± 0.5
Endometrial thickness (mm)	8.3 ± 4.4
Implantation rate (%)	24.4 ± 56.0
Pregnancy rate (%)	24.0
Miscarriage rate (%)	0.0

FERTILITY

II SUMMIT MEETING IN ASSISTED REPRODUCTION – EMPOWERING TECHNOLOGIES: TIME LAPSE AND AI

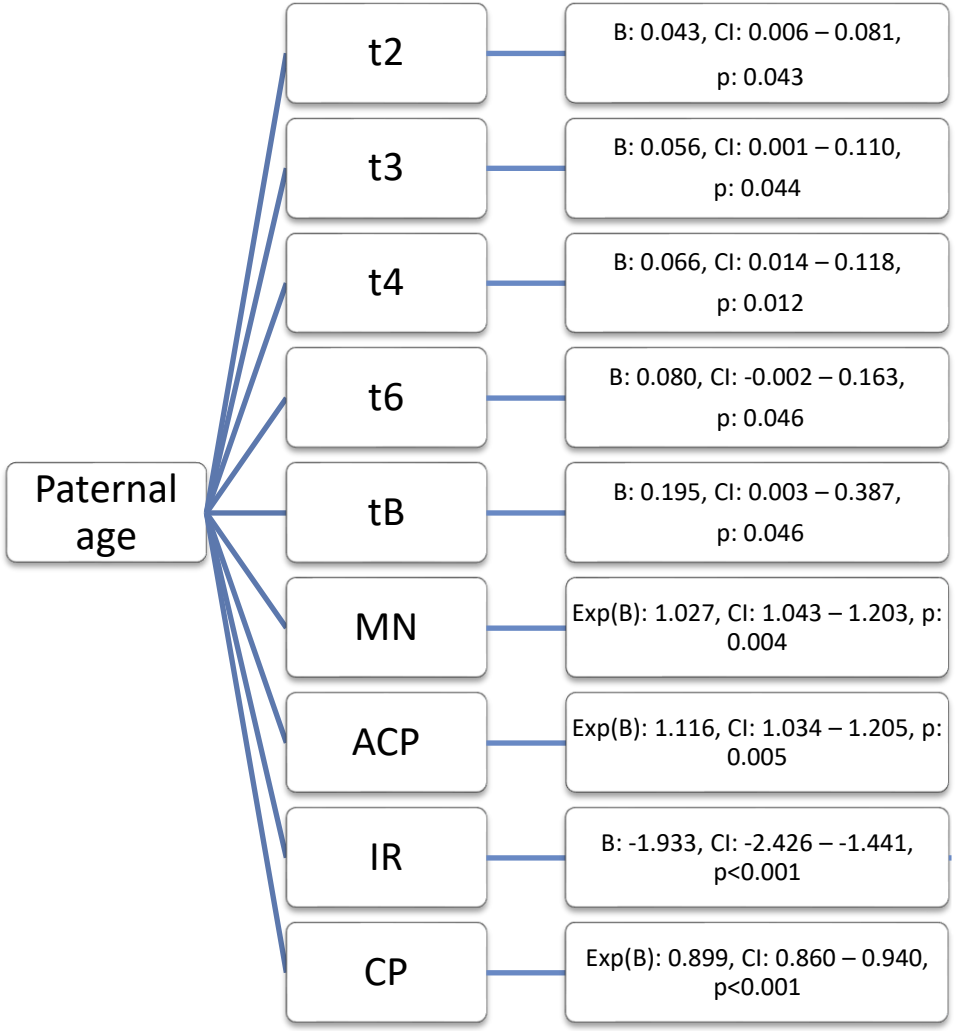
How Embryoscope has helped couples achieve a pregnancy

Edson Borges Jr.

Fertility Medical Group

FERTILITY

RESULTS


Paternal age
t2
B: 0.043, CI: 0.006 – 0.081, p: 0.043
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t4
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B: 0.080, CI: -0.002 – 0.163, p: 0.046
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B: -1.933, CI: -2.426 – -1.441, p<0.001
CP
Exp(B): 0.899, CI: 0.860 – 0.940, p<0.001

IVY TO iDASCORE

IVY	Total
Clinics	8
Embryos	8.836
Positive fetal heartbeat	694
Negative fetal heartbeat	1.079
Discards	7.063

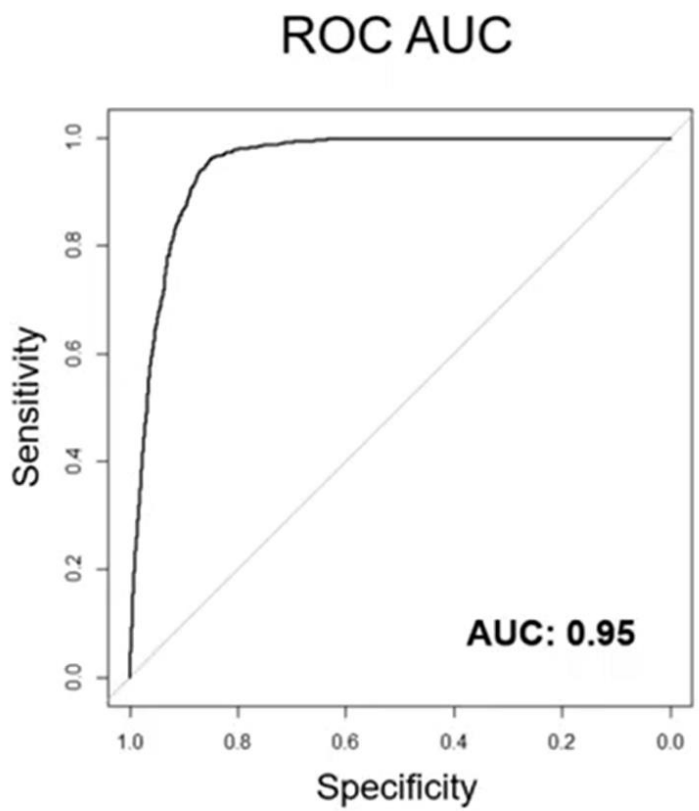
Captura Retang

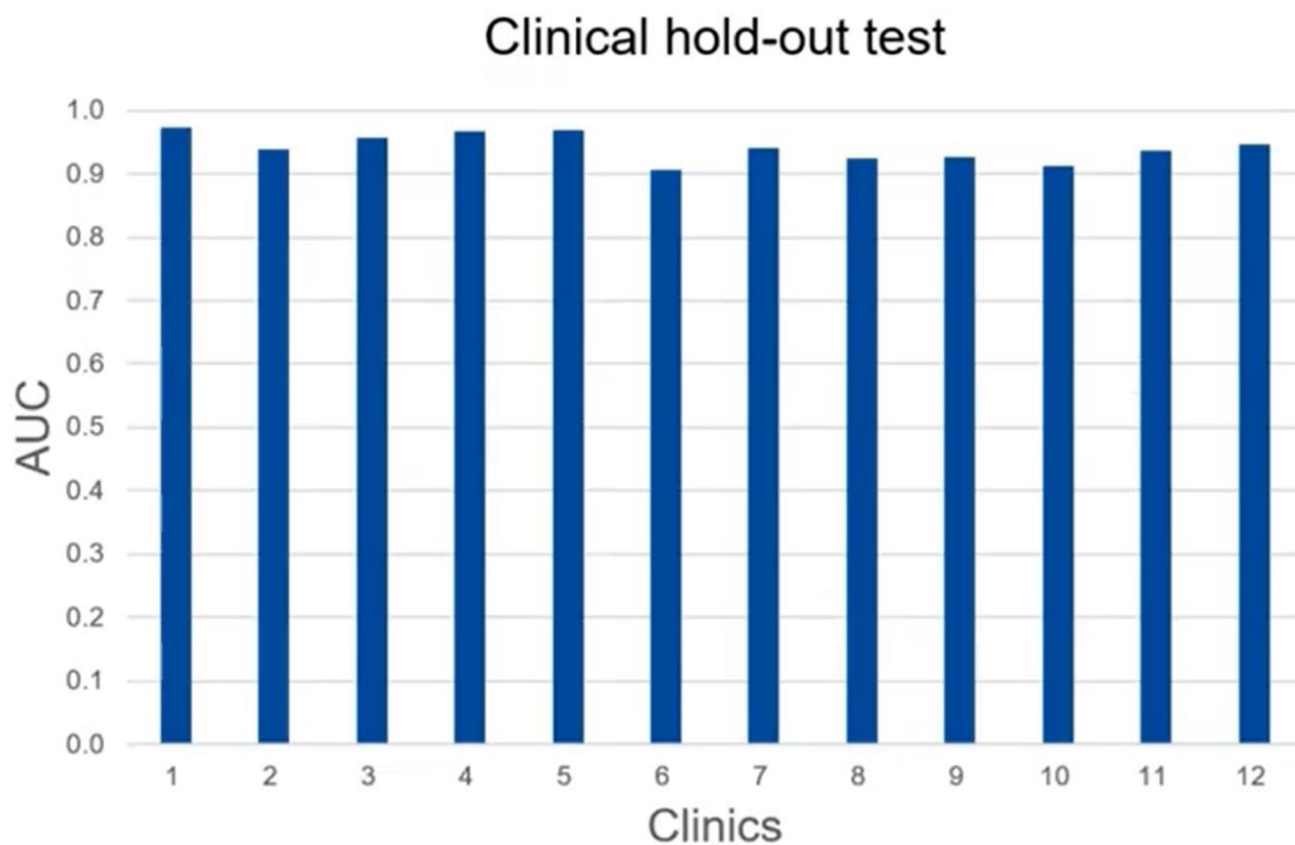
IVY TO iDASCORE

IVY	Total
Clinics	8
Embryos	8.836
Positive fetal heartbeat	694
Negative fetal heartbeat	1.079
Discards	7.063

iDASCORE	Total
Clinics	18
Embryos	115.832
Positive fetal heartbeat	4.337
Negative fetal heartbeat	10.307
Discards	101.188

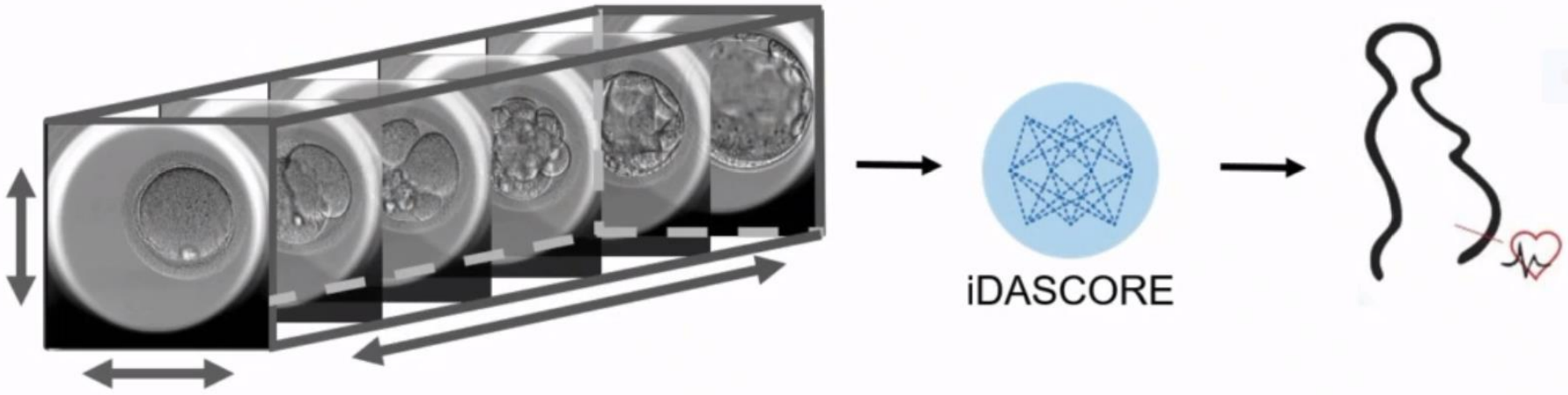
RESULTS





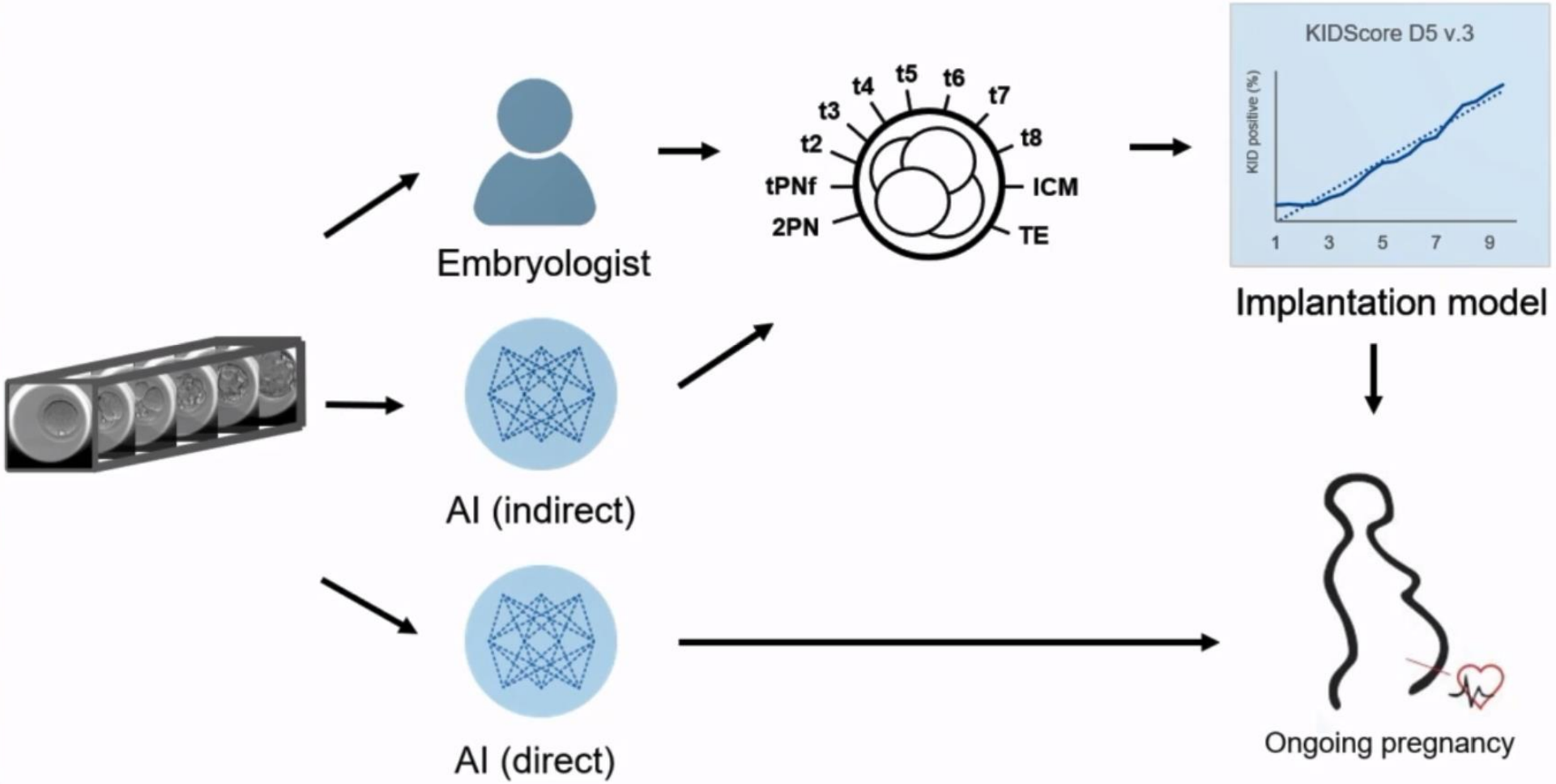
FERTILITY

iDASCORE



FERTILITY

EMBRYO ANNOTATION AND SELECTION

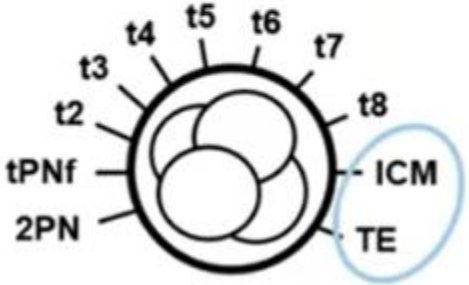


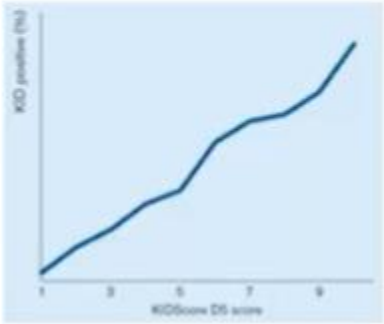
Vitrolife

EMBRYO ANNOTATION AND SELECTION

Embryologist

AI (indirect)





Implantation model

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Computers in Biology and Medicine

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

ELSEVIER

Automatic grading of human blastocysts from time-lapse imaging

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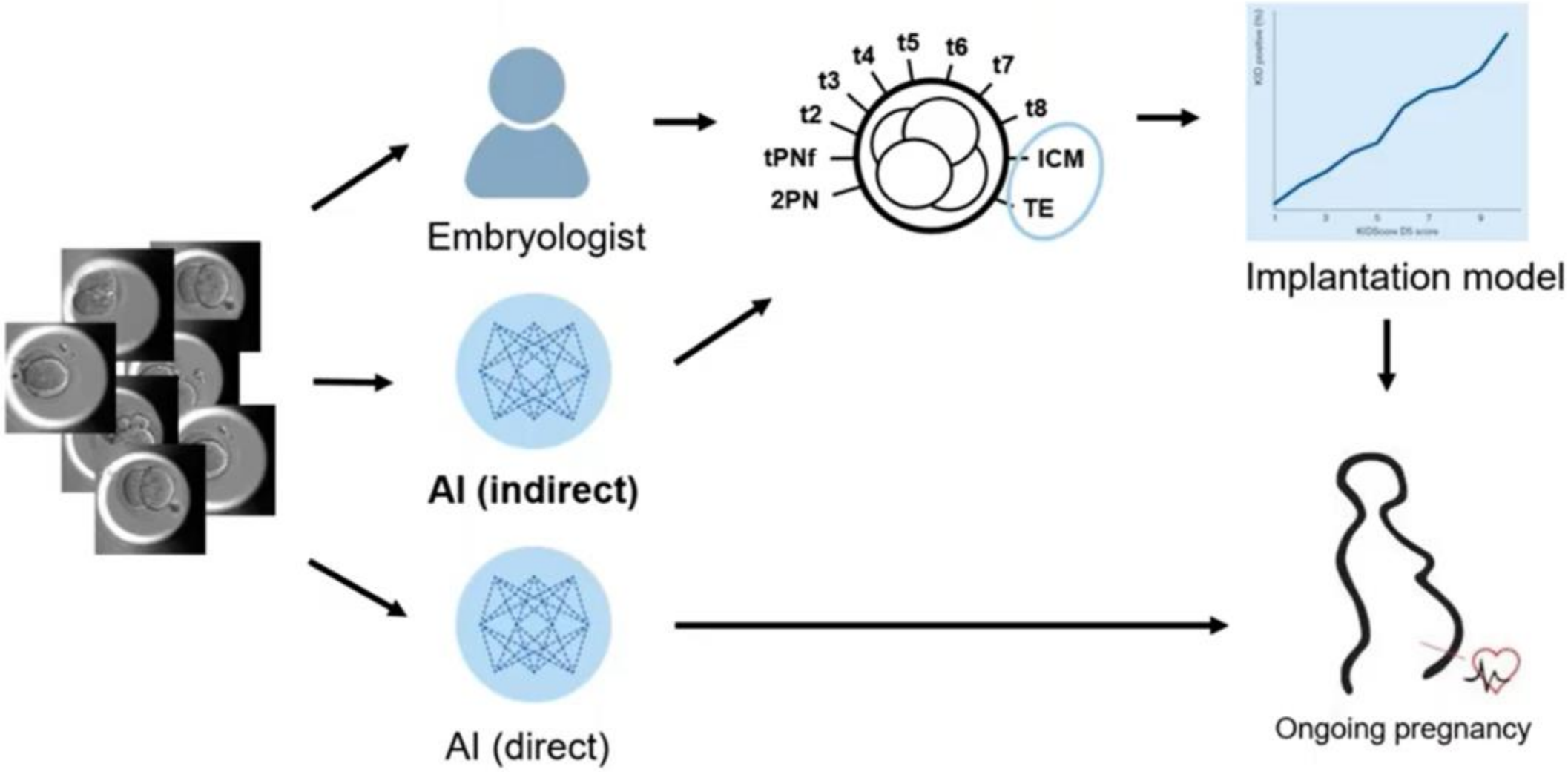
EMBRYO ANNOTATION AND SELECTION

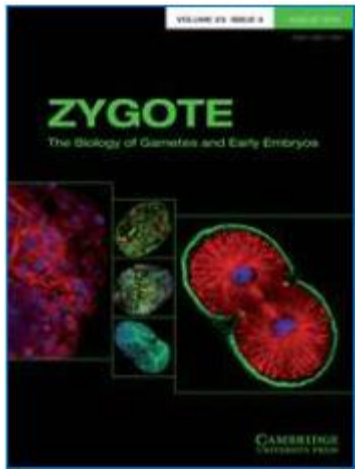


Improved embryonic development and utilization rates with EmbryoScope: A within-subject comparison versus a benchtop incubator

Table 2. Comparison of embryonic development between Control and TLI groups using GzLM followed by Bonferroni post hoc test

Variables	Control group (n=71)	TLI group (n=71)	p-value
Fertilization (%)	76.0 ± 1.3 (73.5 – 78.7)	80.0 ± 1.4 (77.2 – 82.6)	0.044
Non-fertilization (%)	14.8 ± 0.6 (13.7 – 15.9)	6.3 ± 0.4 (5.6 – 7.0)	<0.001
Day-2 non-cleavage (%)	3.8 ± 0.2 (3.3 – 4.3)	1.1 ± 0.1 (0.9 – 1.3)	<0.001
Cleavage (%)	85.3 ± 1.2 (83.0 – 87.7)	84.2 ± 1.3 (81.7 – 86.8)	0.521
Day-5 embryos (%)	62.4 ± 1.0 (60.5 – 64.3)	86.4 ± 1.1 (84.2 – 88.6)	<0.001
Blastocyst development (%)	40.9 ± 1.1 (38.8 – 43.1)	55.6 ± 1.3 (53.1 – 58.1)	<0.001
Frozen blastocyst (%)	31.8 ± 0.8 (30.3 – 33.3)	37.0 ± 0.9 (35.2 – 38.9)	<0.001
OUR	40.7 ± 1.0 (38.8 – 42.7)	50.2 ± 1.1 (48.0 – 52.4)	<0.001
EUR	52.4 ± 1.1 (50.3 – 54.7)	66.6 ± 1.2 (64.3 – 68.9)	<0.001

Note: Values are means ± standard error (95% confidence interval). TLI: timelapse imaging, GzLM: generalized linear models, OUR: oocyte utilization rate, EUR: embryo utilization rate.



Borges E. *et al*