



Inteligência Artificial em Medicina Reprodutiva

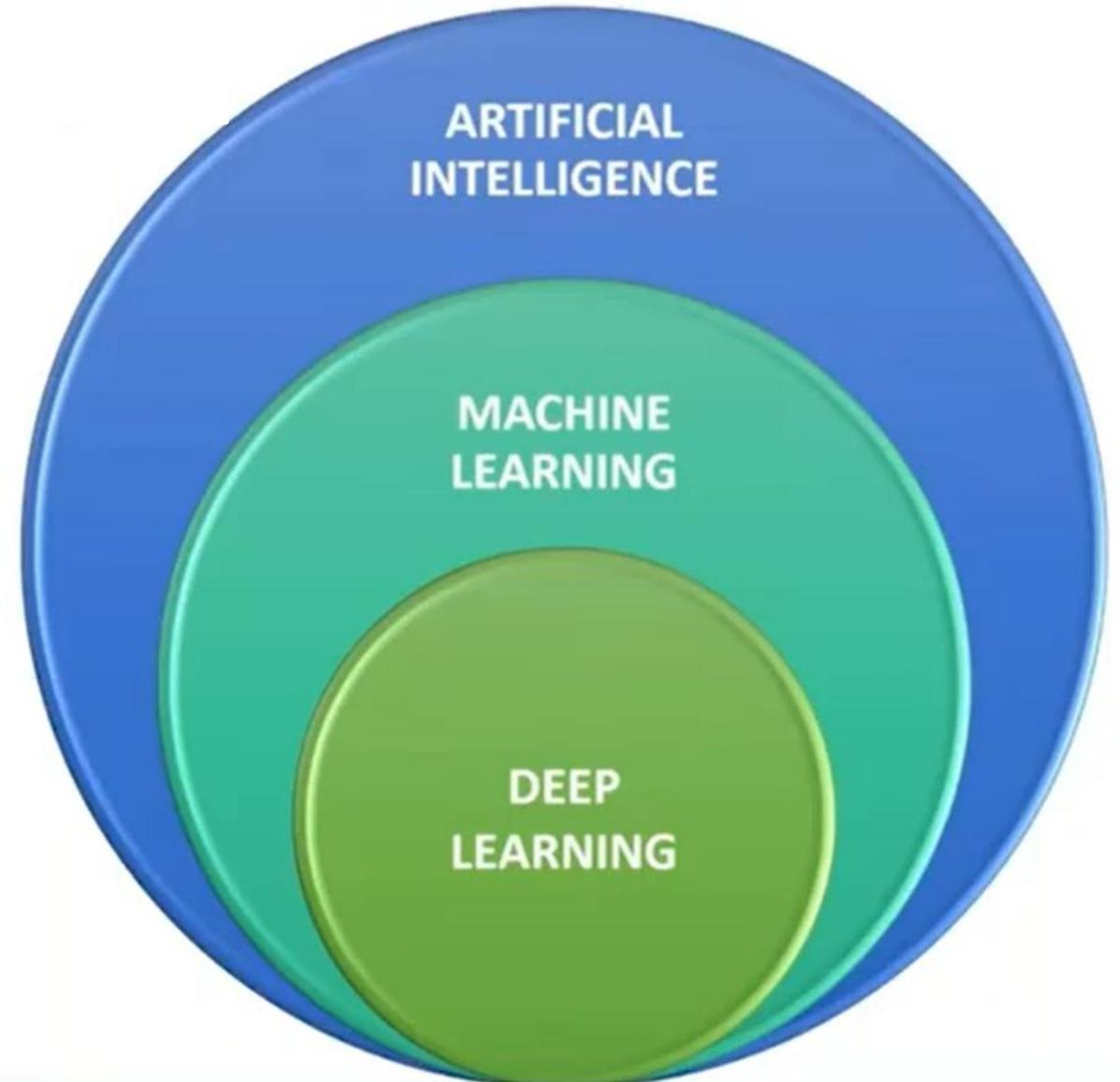
Edson Borges Jr.

The evolution of AI

1950s - Artificial Intelligence

1980s - Machine Learning

2010s - Deep Learning



Embryo through the lens: from time-lapse cinematography to artificial intelligence



Elnur Babayev, M.D. and Eve C. Feinberg, M.D.

Northwestern University Feinberg School of Medicine, Chicago, Illinois

<https://doi.org/10.1016/j.fertnstert.2019.12.001>

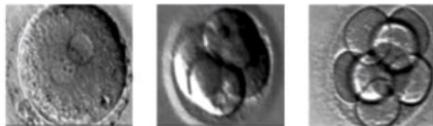
The February 1970 issue of Fertility and Sterility contains the article, **“In Vitro Fertilization of Rabbit Ova: Time Sequence of Events”** by Brackett. Phasecontrast microscopy and time-lapse micro-cinematography were used to observe rabbit oocyte fertilization and embryo development. The author provided detailed documentation on the timing of oocyte penetration by spermatozoa, polar body extrusion, formation of pronuclei, and cell divisions in early embryos.

Brackett BG. In vitro fertilization of rabbit ova: time sequence of events. Fertil Steril 1970;21:169–76.

History of « modern » TLT



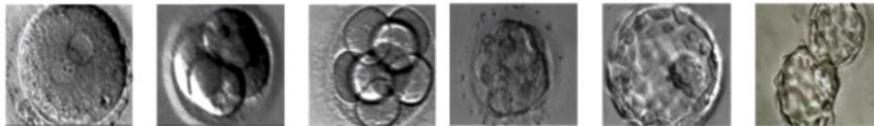
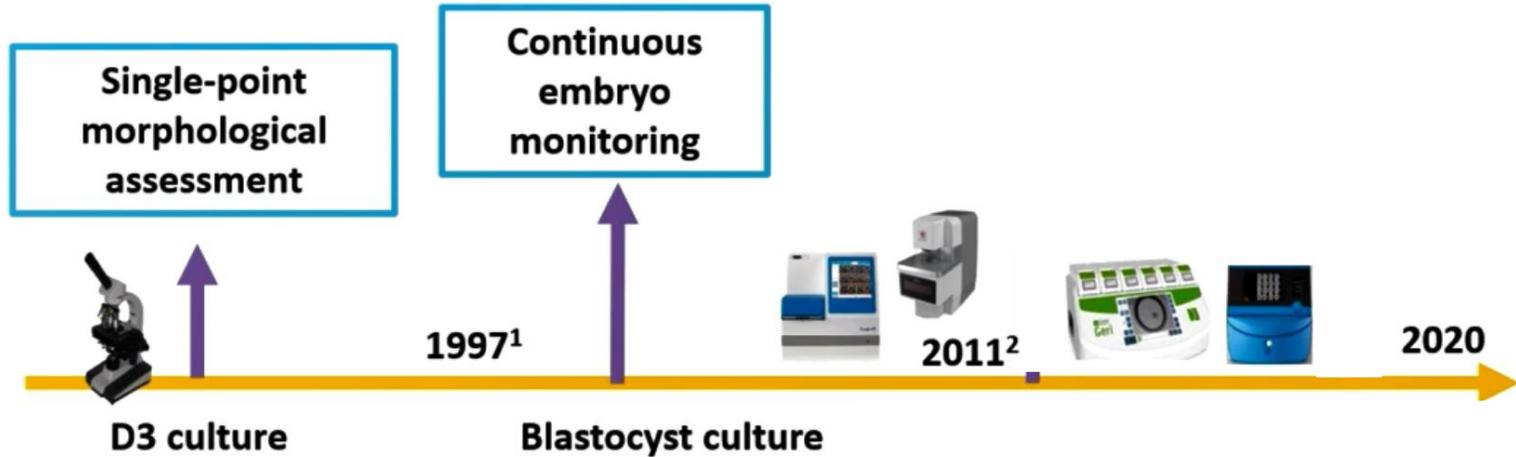
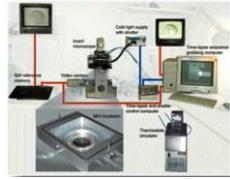
Single-point morphological assessment



¹Payne et al. *Hum Reprod.* 1997;**12**:532–541.

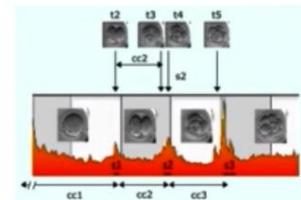
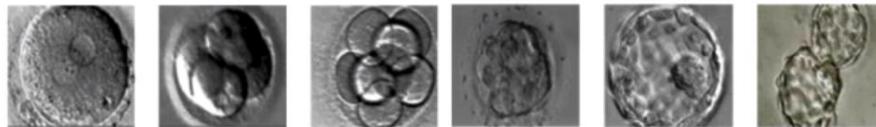
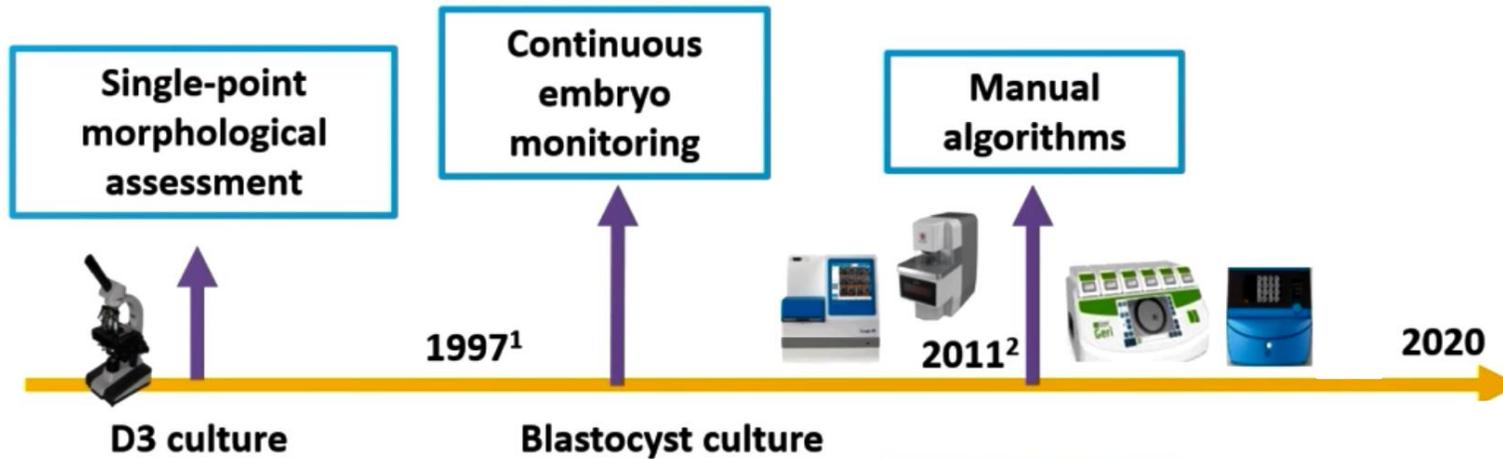
²Meseguer et al. *Hum Reprod.* 2011;**26**:2658–2671.

History of « modern » TLT



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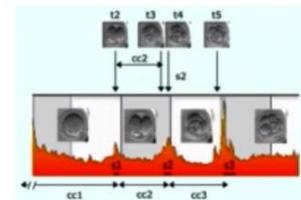
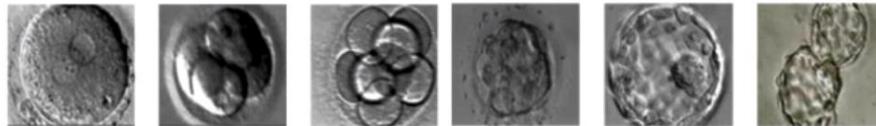
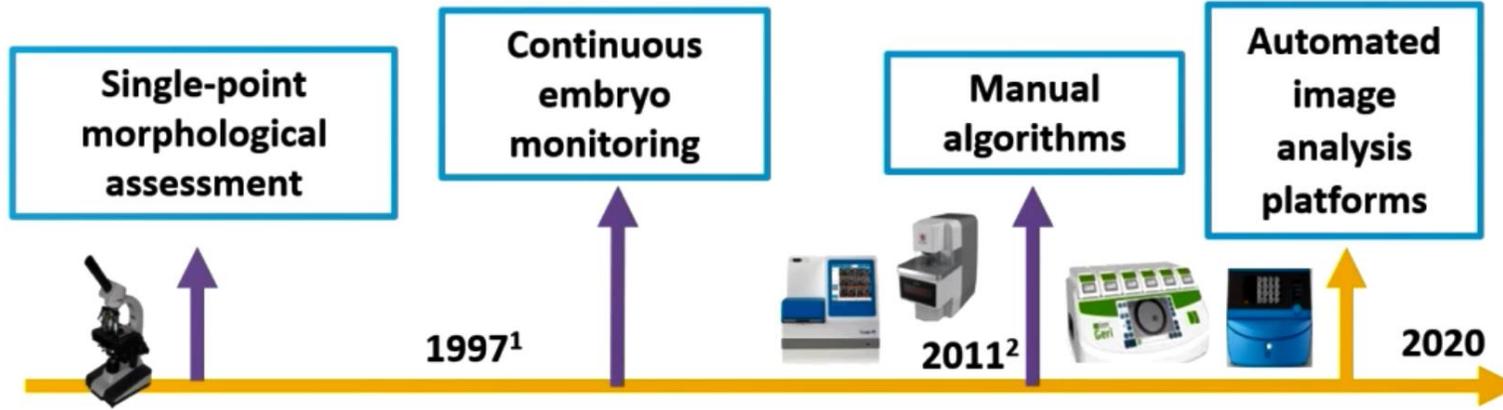
History of « modern » TLT



¹Payne et al. *Hum Reprod.* 1997;**12**:532–541.

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History of « modern » TLT



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²Meseguer et al. *Hum Reprod.* 2011;**26**:2658–2671.

Morphokinetics and what we do not see!

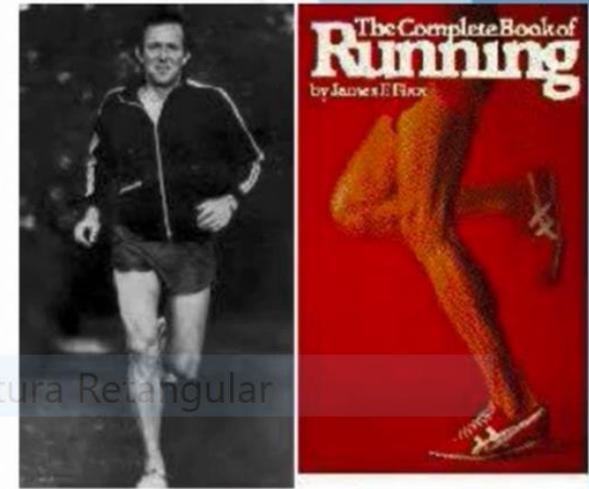
- ▶ Winston Churchill
- ▶ Drank
- ▶ Smoked Cigars
- ▶ Overweight



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



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



● Captura Retangular



Morphokinetics and what we do not see!

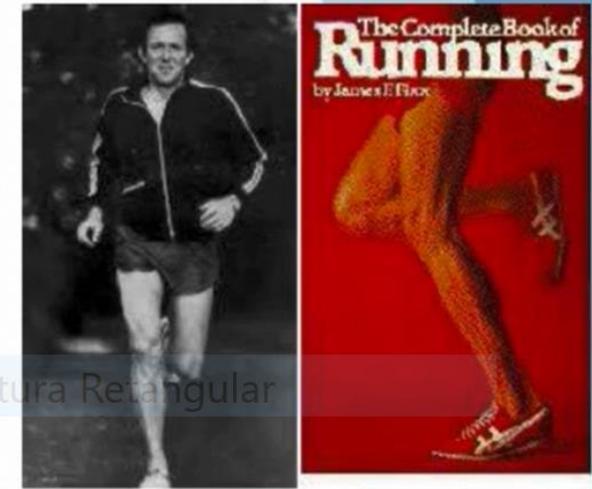
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● Captura Retangular

Who lived the longest?



Morphokinetics and what we do not see!

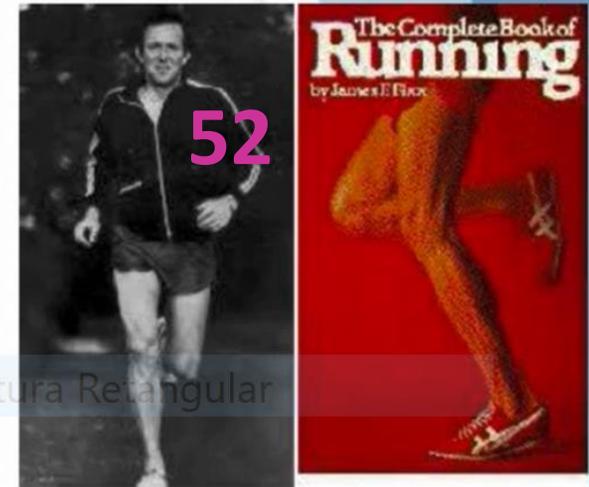
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Who lived the longest?



Artificial intelligence for embryo assessment

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. Cooke², P.J. Illingworth², and D.K. Gardner¹



ARTICLE OPEN  Digital Medicine

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

Pegah Khosravi^{1,2}, Ehsan Kazemi³, Qiansheng Zhan⁴, Jonas E. Malmsten⁵, Marco Toschi⁴, Pantelis Zisimopoulos^{1,2}, Alexandros Sigaras^{1,2}, Stuart Lavery⁵, Lee A. D. Cooper⁶, Cristina Hickman⁵, Marcos Meseguer⁷, Zev Rosenwaks⁴, Olivier Elemento^{1,2,8}, Nikica Zaninovic⁴ and Iman Hailirasouliha^{1,2}

SCIENTIFIC
REPORTS
nature research

Reproductive BioMedicine Online (2013) 26, 42–49

Artificial intelligence techniques for embryo and oocyte classification

Claudio Manna^{a,b}, Loris Nanni^c, Alessandra Lumini^{d,*},
Sebastiana Pappalardo^a

Predicting pregnancy test results after embryo transfer by image feature extraction and analysis using machine learning

Alejandro Chavez-Badiola^{1*}, Adolfo Flores-Saifue Farias¹, Gerardo Mendizabal-Ruiz², Rodolfo Garcia-Sanchez¹, Andrew J. Drakeley³ & Juan Paulo Garcia-Sandoval⁴

Video Article

A Neural Network-Based Identification of Developmentally Competent or Incompetent Mouse Fully-Grown Oocytes

Federica Cavallera¹, Mario Zanoni¹, Valeria Merico¹, Thi Thu Hien Bui^{1,2}, Martina Belli^{1,3}, Lorenzo Fassina⁴, Silvia Garagna¹, Maurizio Zuccotti¹

Computers in Biology and Medicine 115 (2019) 103494

Automatic grading of human blastocysts from time-lapse imaging

Mikkel F. Kragh^{a,b,*}, Jens Rimestad^b, Jørgen Berntsen^b, Henrik Karstoft^a

human
reproduction

ORIGINAL ARTICLE *Embryology*

Development of an artificial intelligence-based assessment model for prediction of embryo viability using static images captured by optical light microscopy during IVF

M. VerMilyea^{1,2,†}, J.M.M. Hall^{3,4,†}, S.M. Diakiw³, A. Johnston^{3,5},
T. Nguyen³, D. Perugini³, A. Miller¹, A. Picou¹, A.P. Murphy³, and
M. Perugini^{3,6,*}

- Different images
- Different software
- Different culture conditions



FERTILITY

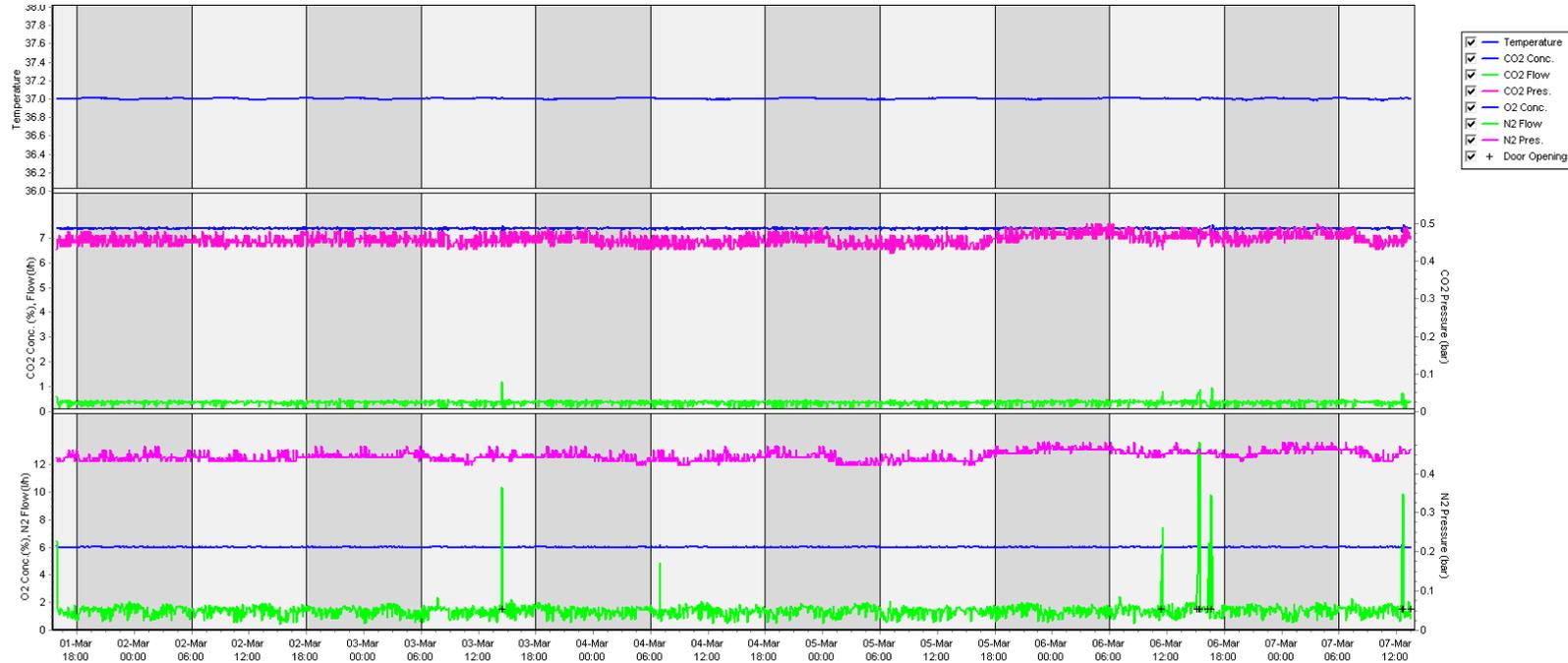
EMBRYOSCOPE *plus*

- 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



EMBRYOSCOPE *plus*

SAFE CULTIVE ENVIRONMENT FOR EMBRYOS



- Temperature
- CO₂ / O₂
- 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

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

Groups of similar interval length

Quartiles of similar sample size

$p < .05$

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

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

$p < .05$

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

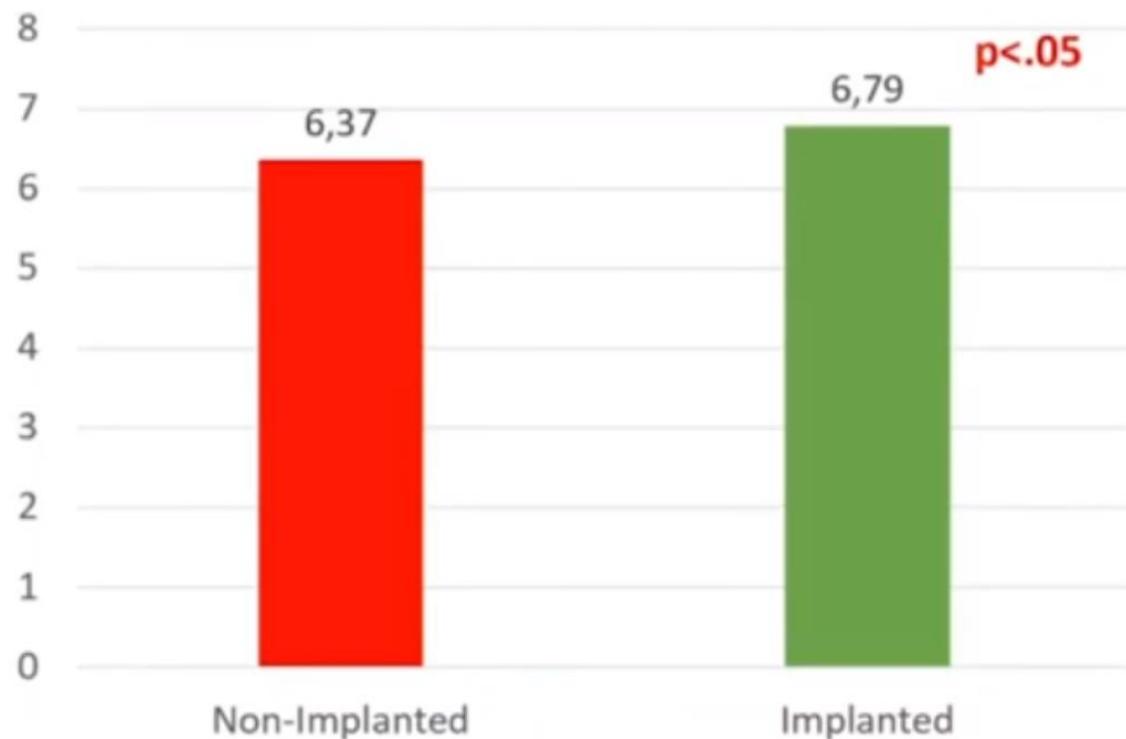
KIDScore Day 5 v3	≤ 5.3	5.4 - 6.4	6.5 - 7.4	≥ 7.5
Implantation Rate	41.0%	54.2%	59.3%	67.9%
N	215/524	274/506	270/455	317/467



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



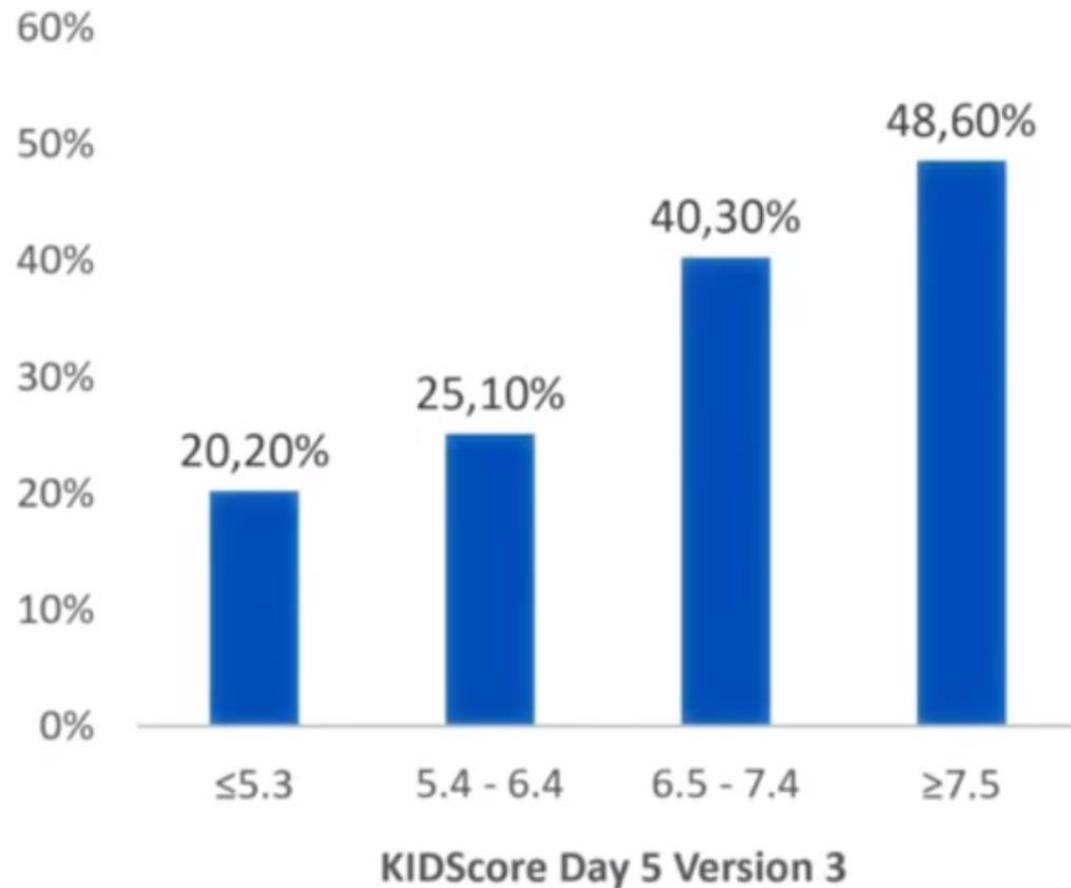
Relationship between Live Birth Rate and the KID Score Day 5

p<.05

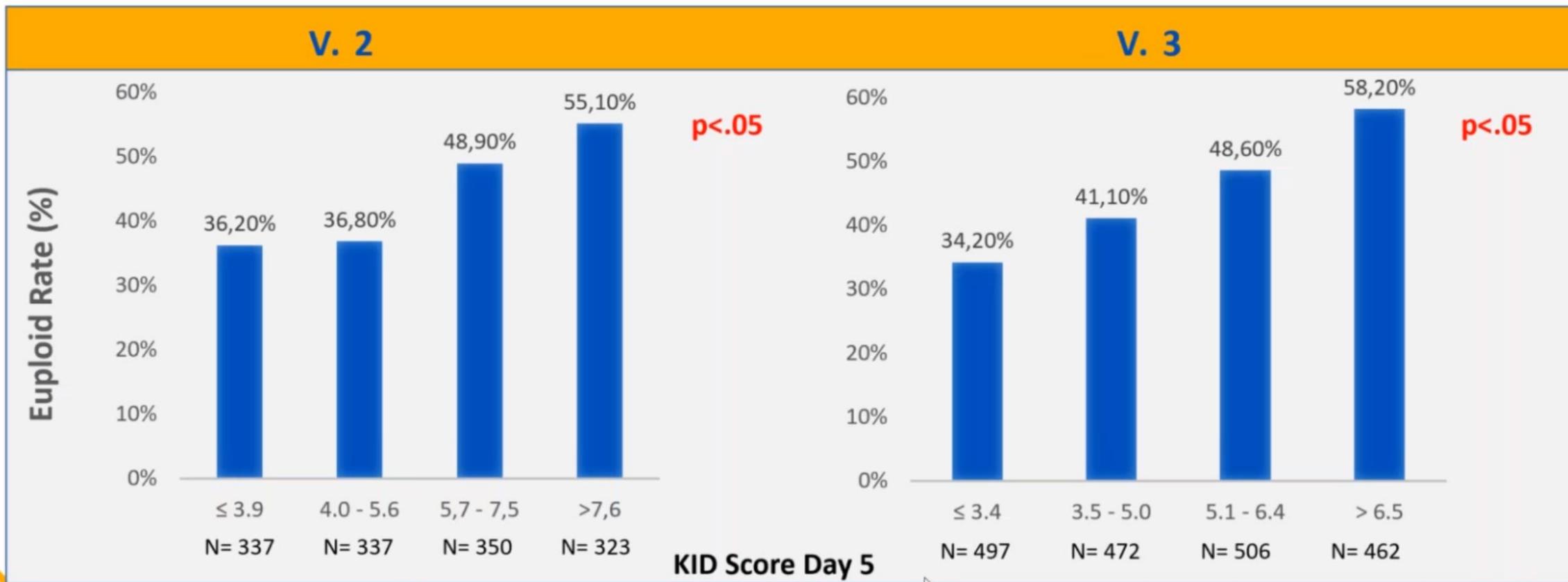
V2 1280 embryos	KIDScore Day 5 v2	≤ 5.3	5.4 - 7.1	7.2 - 7.9	≥8.0
	Live Birth Rate	24.8%	35.2%	44.8%	41.9%
N		79/318	121/344	141/315	127/303

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



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



Relationship between Chromosomal Content and the KID Score Day 5



V2
1347
embryos

V3
1937
embryos

KID Score Day 5 VERSION 2

p<.05

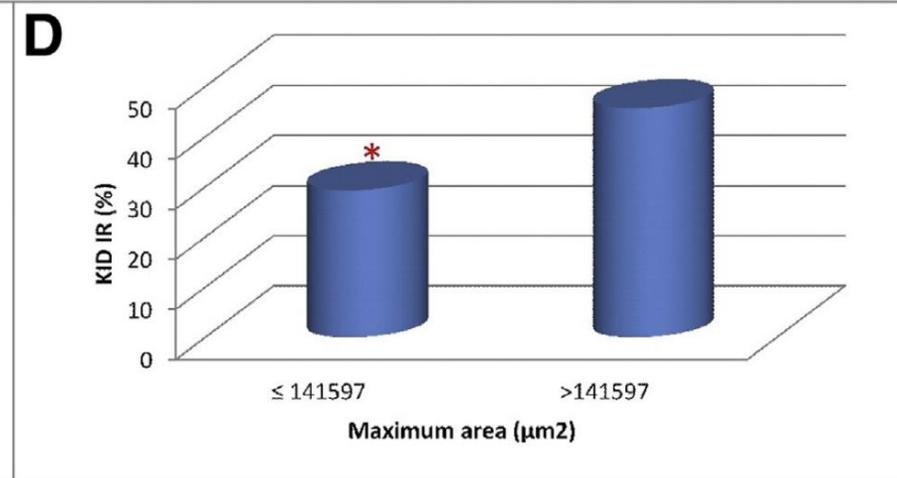
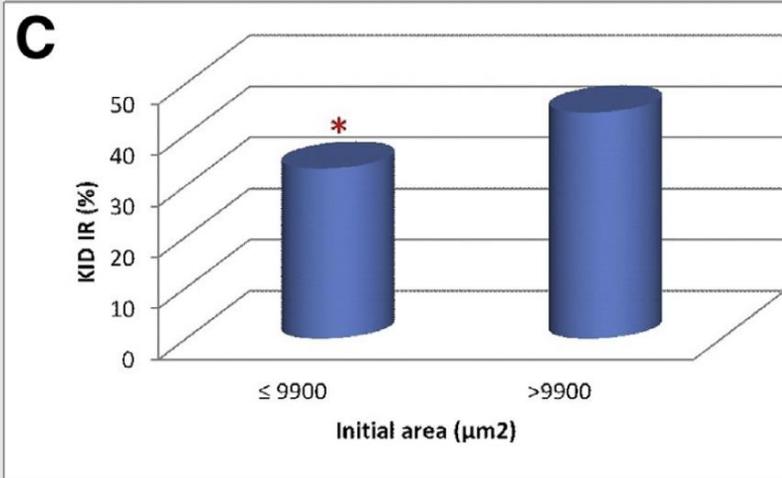
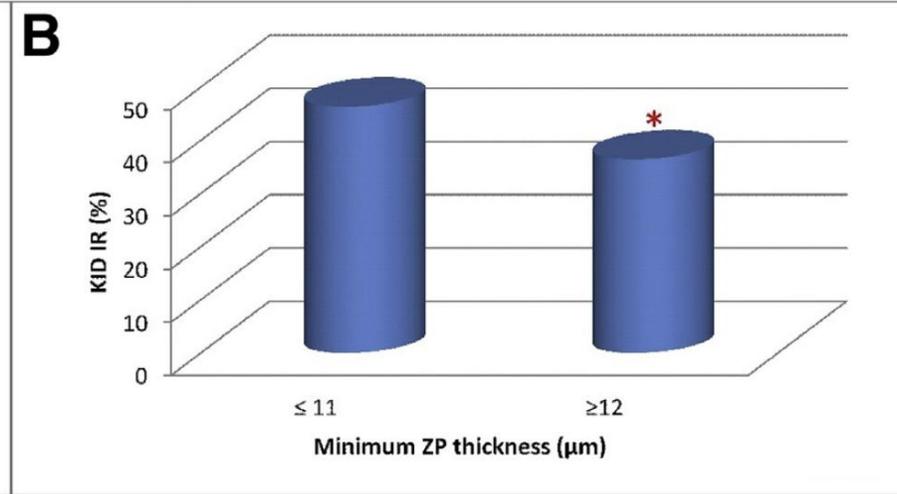
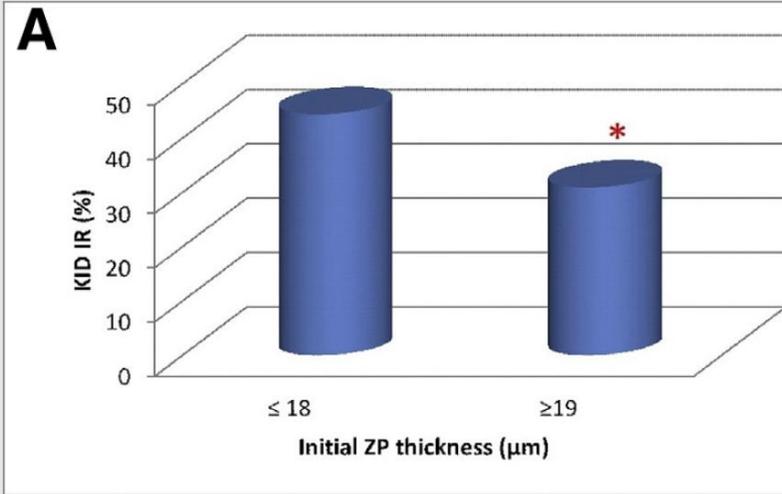
Ploidy	Mean	Standard Deviation	N
Euploid embryos	5.96	2.14	595
Aneuploid embryos	5.31	2.19	752

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





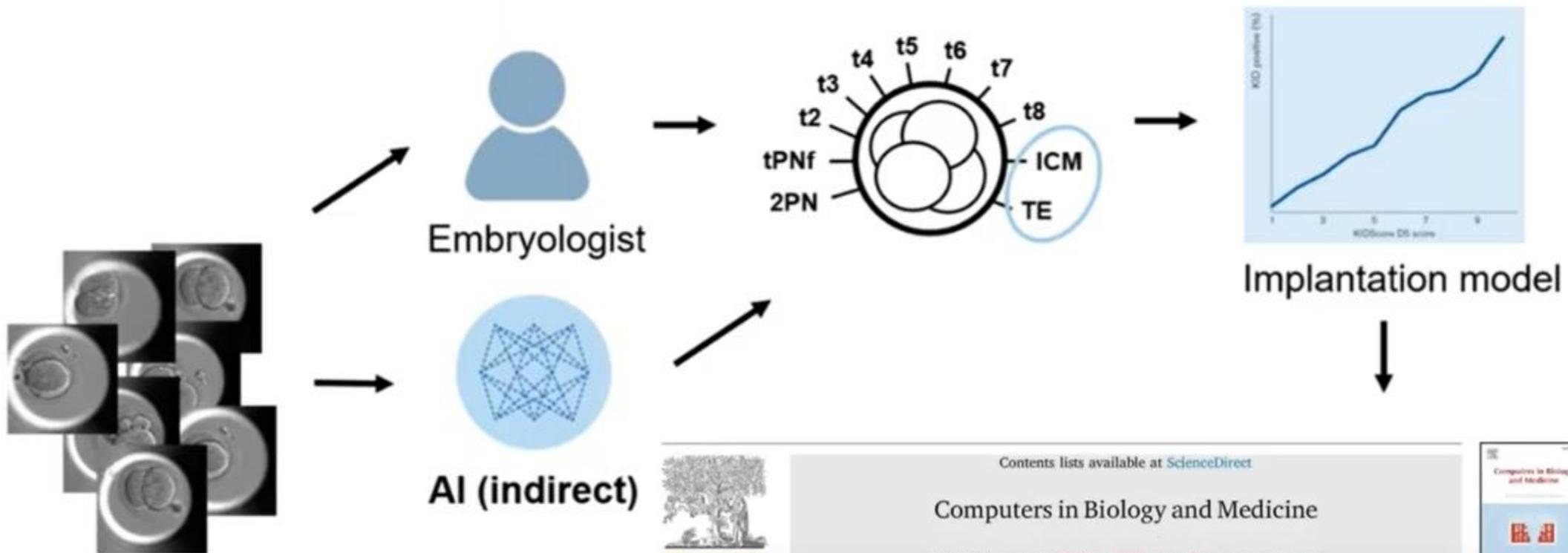
Percentage of implanting blastocysts with morphological dynamics variables within or beyond the ranges defined by the quartile limits for the total data set. The four panels show ranges and implantation for (A) initial ZP thickness, $*P=.02$; (B) minimum ZP thickness, $*P=.03$; (C) initial blastocyst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



IA and deep learning – embryo evaluation



EMBRYO ANNOTATION AND SELECTION



Contents lists available at ScienceDirect

Computers in Biology and Medicine

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



Automatic grading of human blastocysts from time-lapse imaging

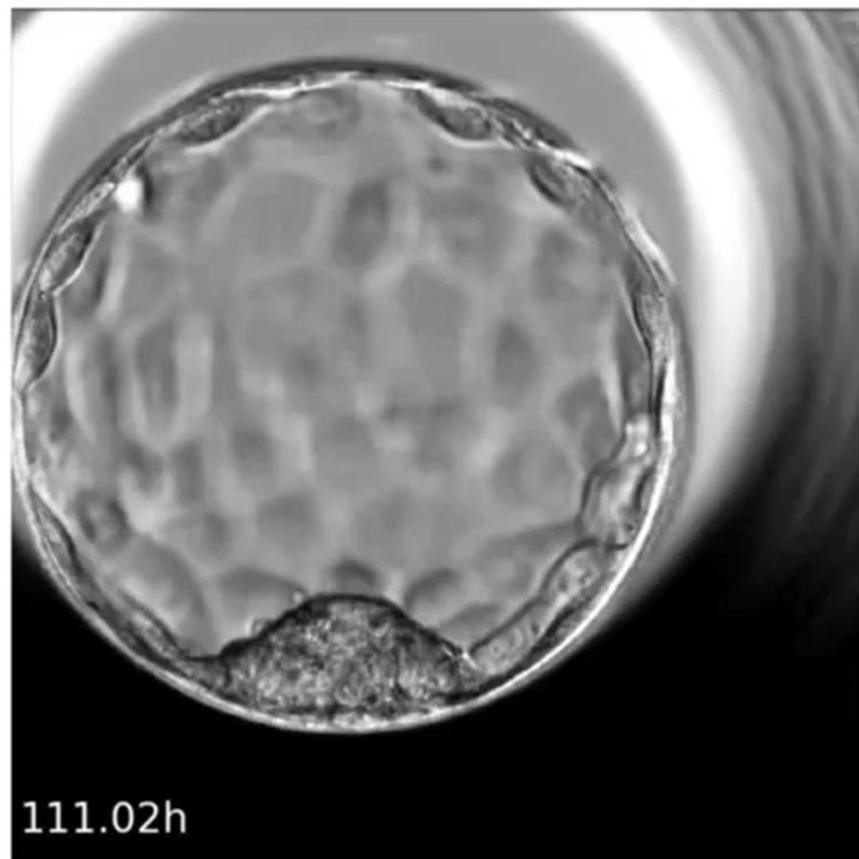
Mikkel F. Kragh ^{a,b,c}, Jens Rimestad ^b, Jørgen Berntsen ^b, Henrik Karstoft ^a

^a Department of Engineering, Aarhus University, Denmark

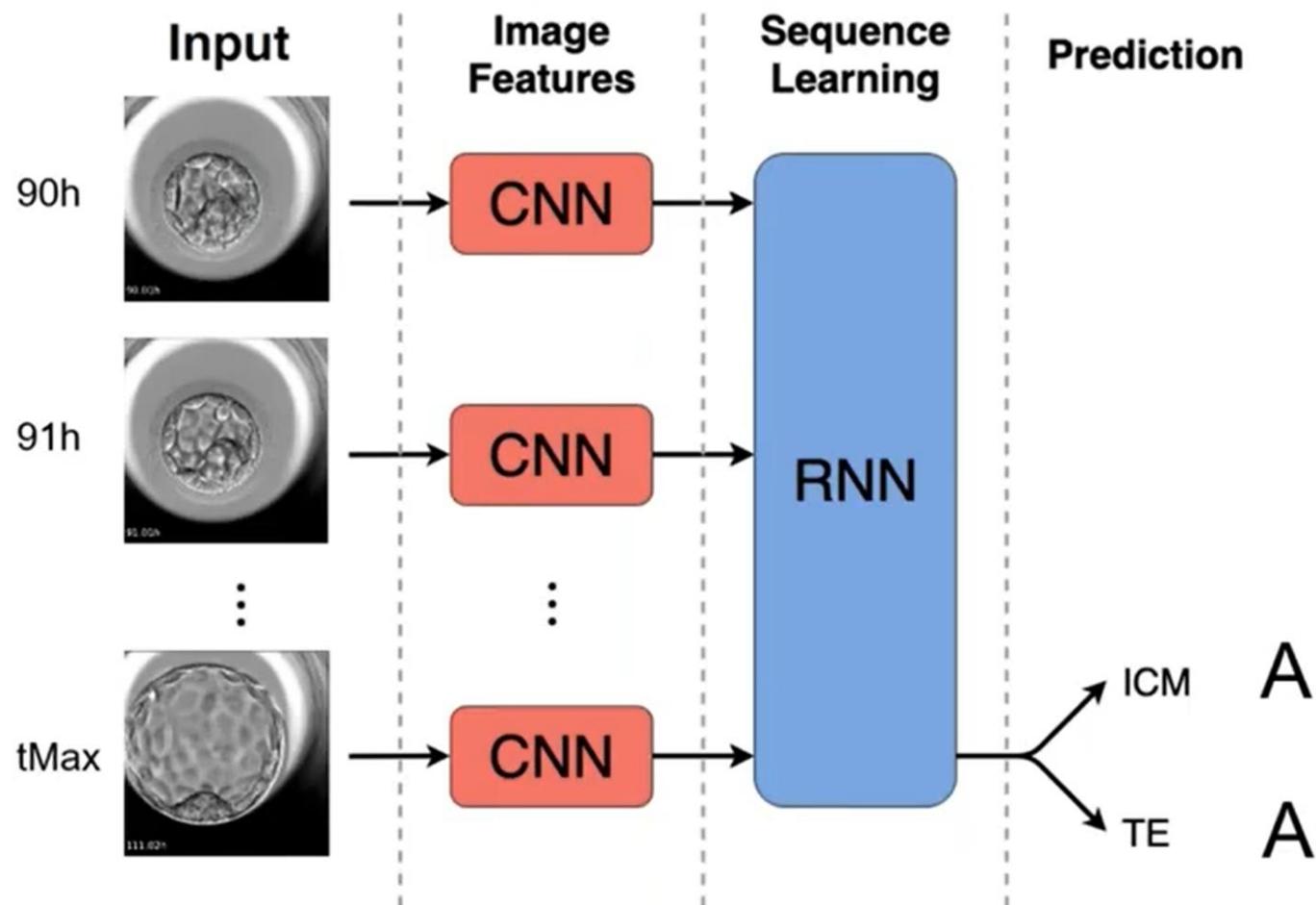
^b Vitrolife A/S, Denmark



BLASTOCYST GRADING WITH TIME-LAPSE VIDEOS

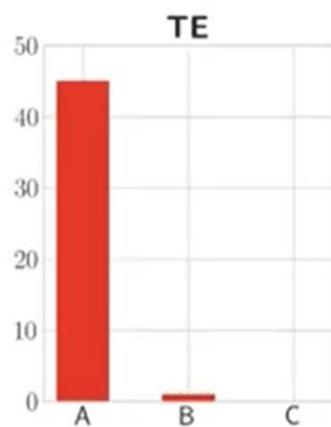
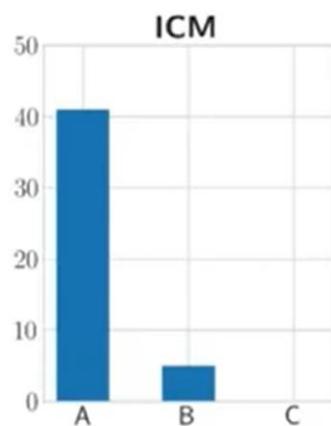
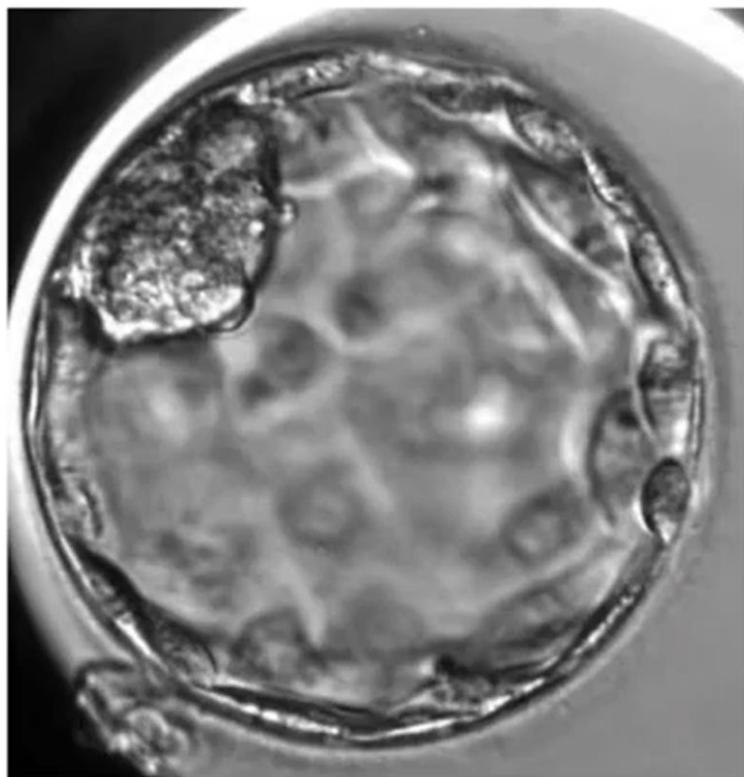


8664 day 5 blastocysts



CNN: Convolutional Neural Network
RNN: Recurrent Neural Network

INTER- AND INTRA-OBSERVER VARIATION

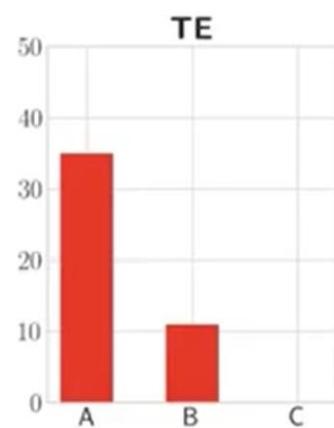
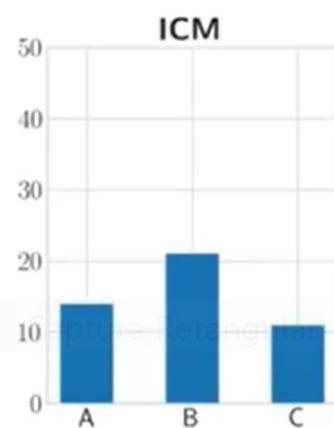
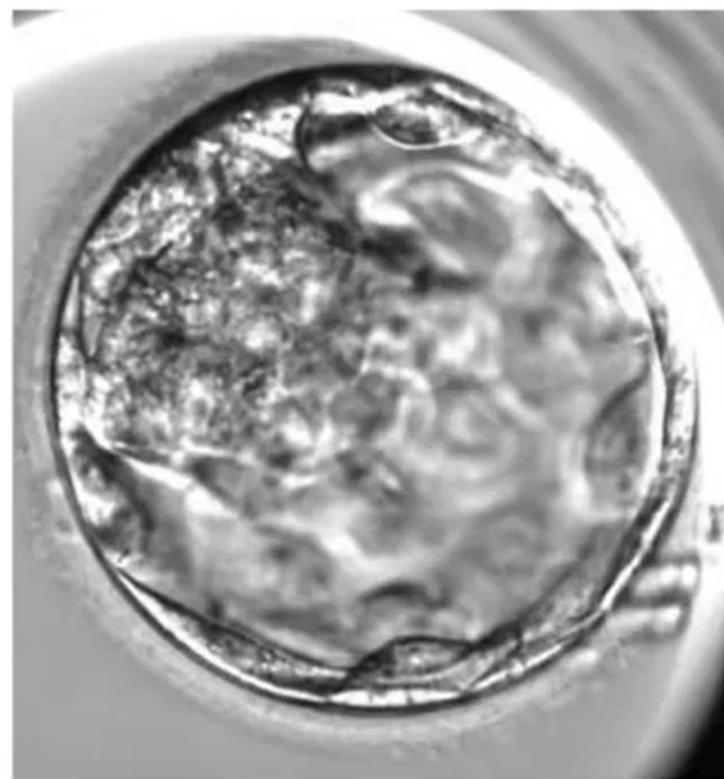
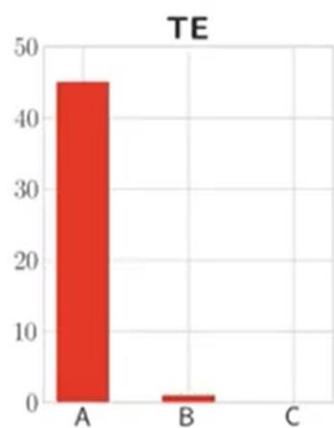
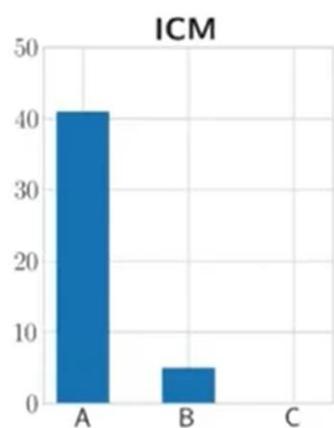
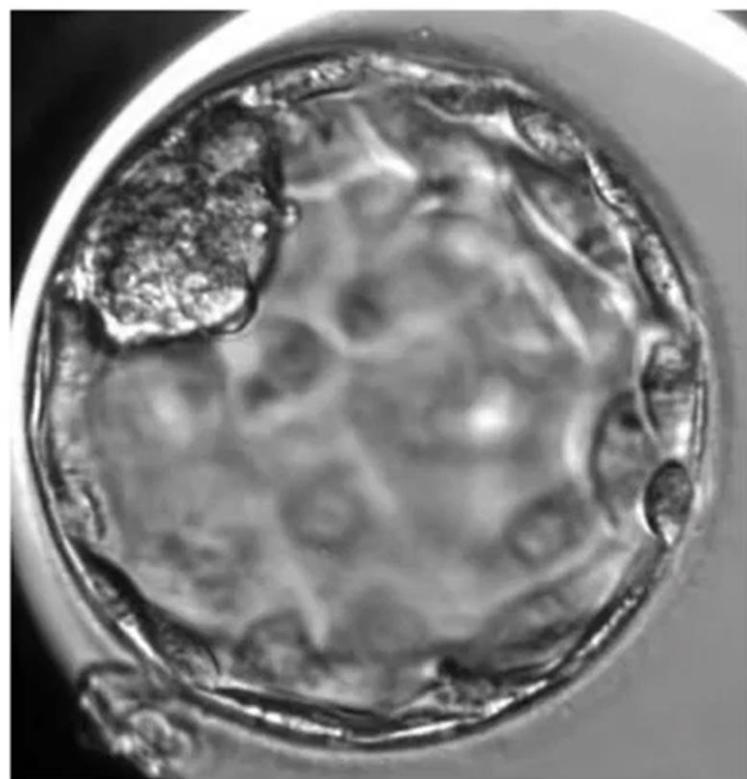


Similar studies: Richardson et al. (2015), Adolfsson et al. (2018)



FERTILITY

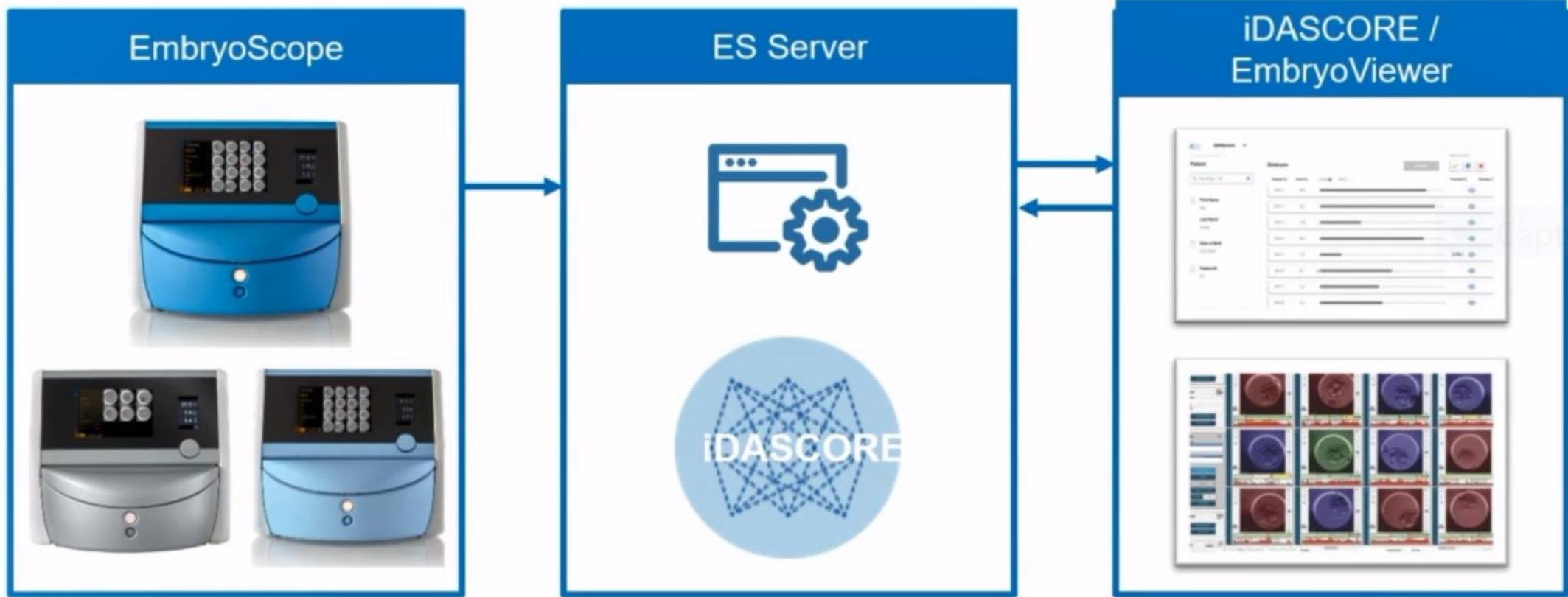
INTER- AND INTRA-OBSERVER VARIATION



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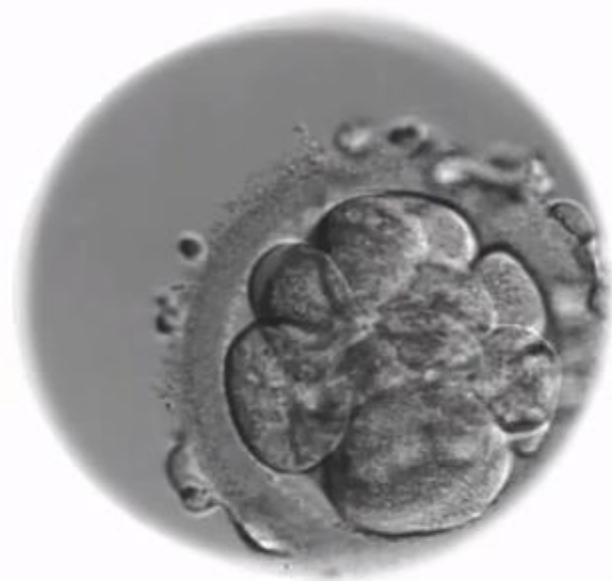
FERTILITY



Capura Retan

SCORE

Score: 2.0



Score: 6.3

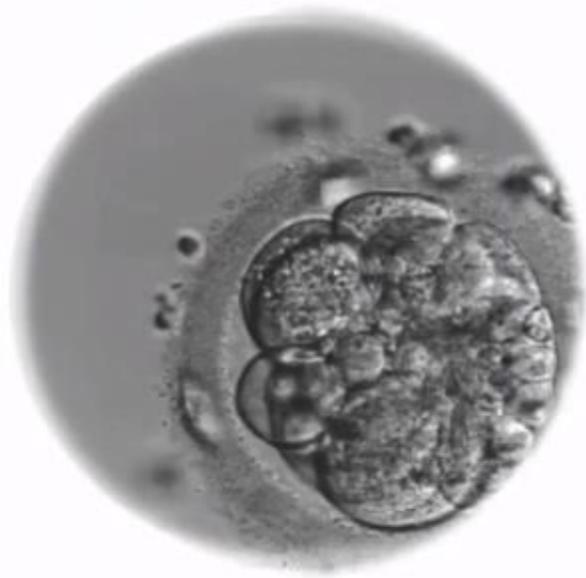


Score: 9.5



SCORE

Score: 2.0



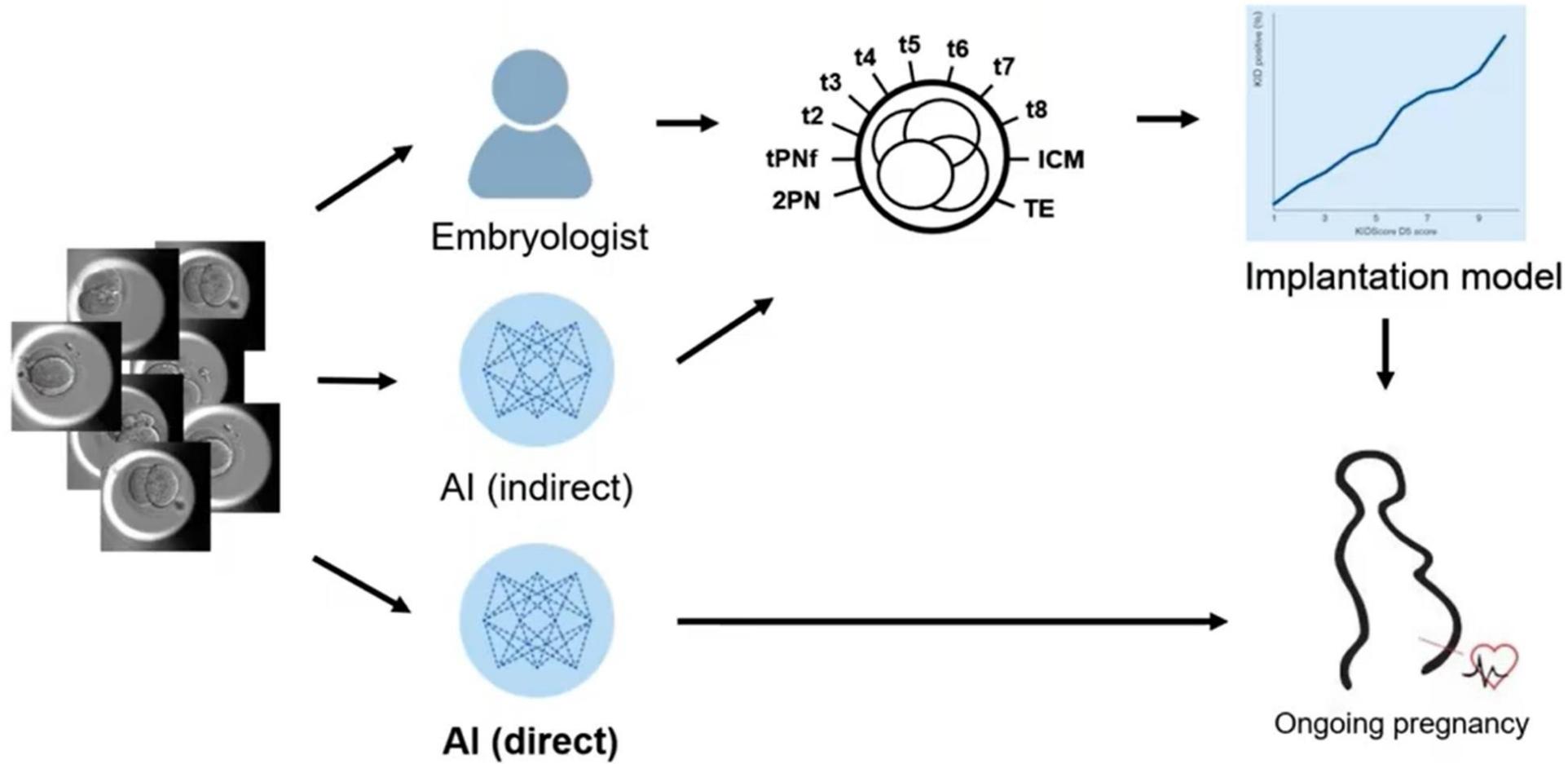
Score: 6.3



Score: 9.5



EMBRYO ANNOTATION AND SELECTION

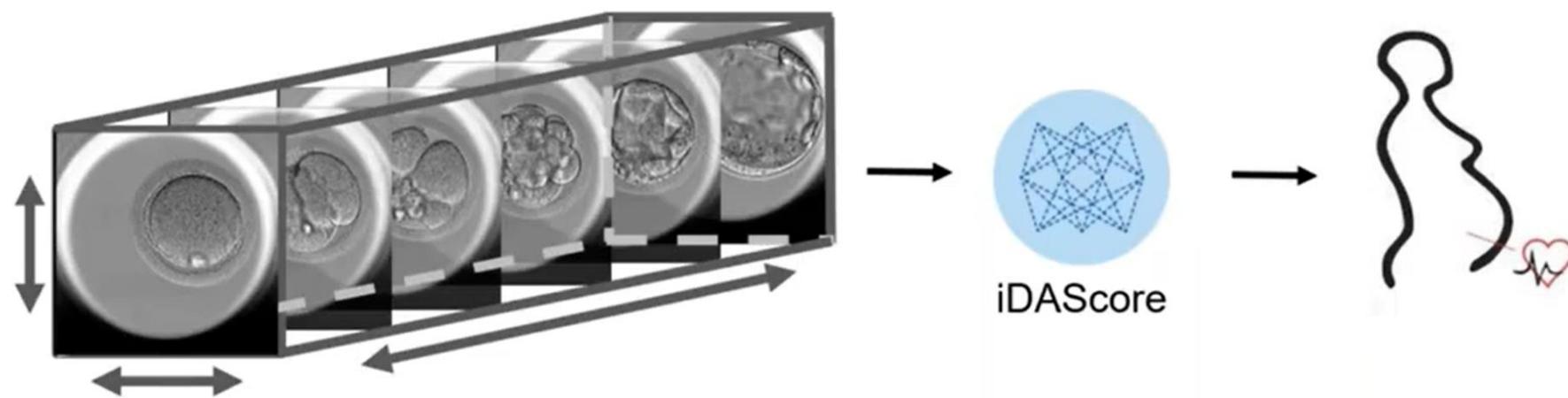


Captura Retangulo

IDAScore

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

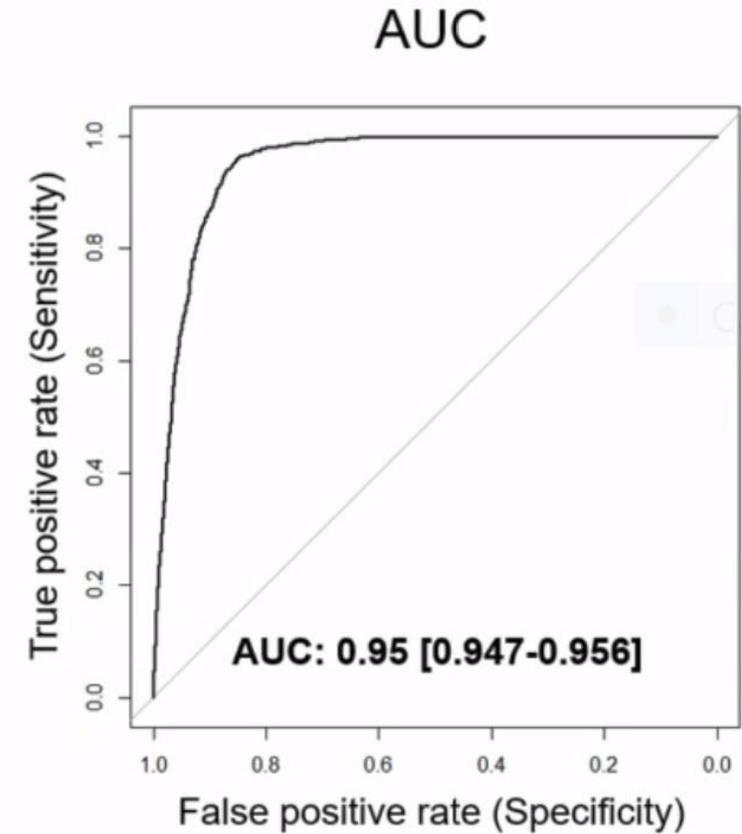
	IVY	iDAScore
FH+	694	4,337
FH-	1,079	10,307
Discards	7,063	101,188
Total	8,836	115,832



Captura Retangi

EVALUATING iDAScore

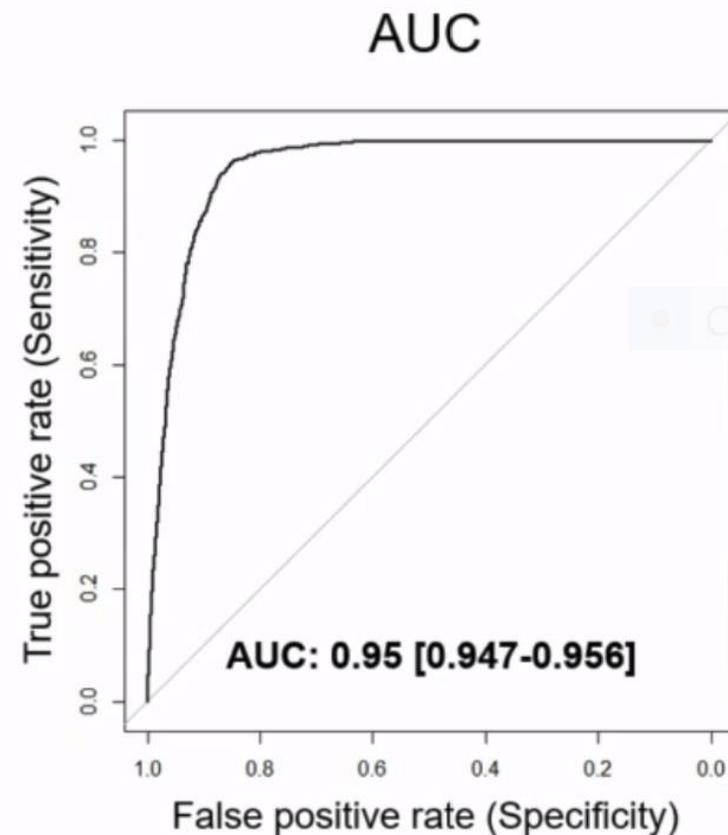
iDAScore	Test
Clinics	18
Embryos	17.249
Positive fetal heartbeat	661
Negative fetal heartbeat	1.551
Discards	15.037



EVALUATING iDAScore

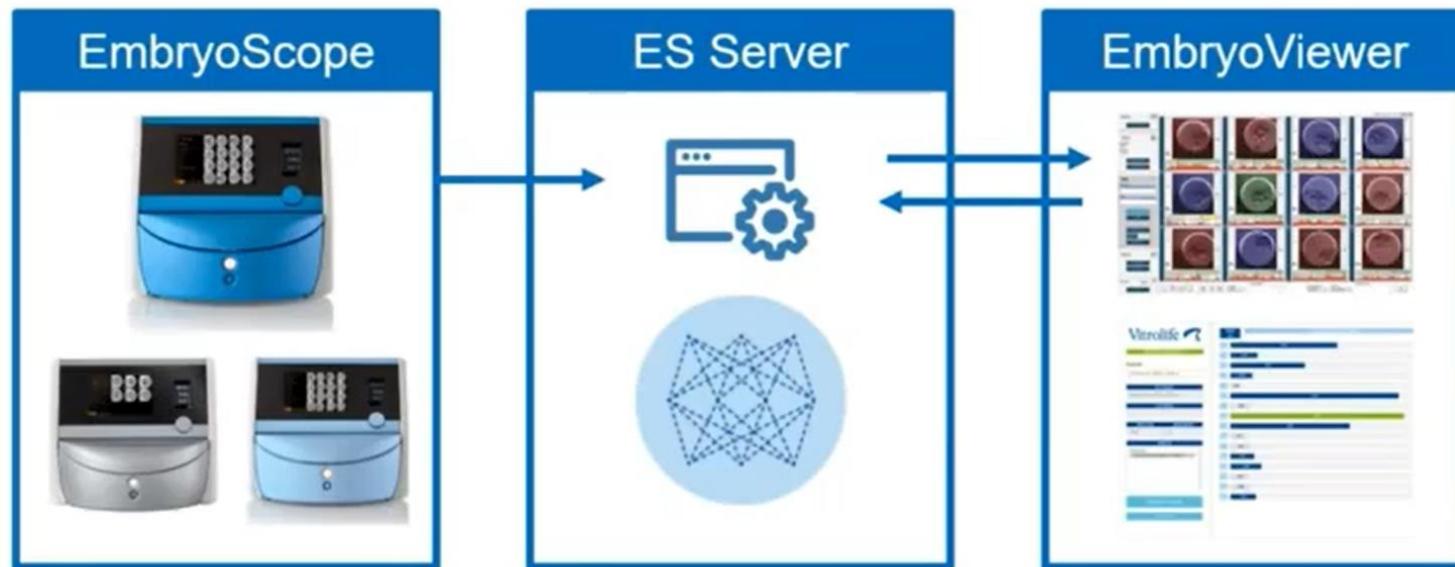
Area Under the Curve (AUC)	Diagnostic Test Quality
1.0-0.9	Excellent
0.9-0.8	Very Good
0.7-0.8	Good
0.6-0.7	Sufficient
0.5-0.6	Poor
<0.5	Test not usefull

Source: Šimundić, A.M., 2009. Measures of diagnostic accuracy: basic definitions. Ejifcc, 19(4), p.203.



INSIDE THE CLINIC

- Integrates with existing system
- Instant evaluation
- Consistent and accurate
- Fully automatic
 - No manual annotations
 - Independent of embryologist experience



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

D. Tran^{1,*}, S. Cooke², P.J. Illingworth², and D.K. Gardner³

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

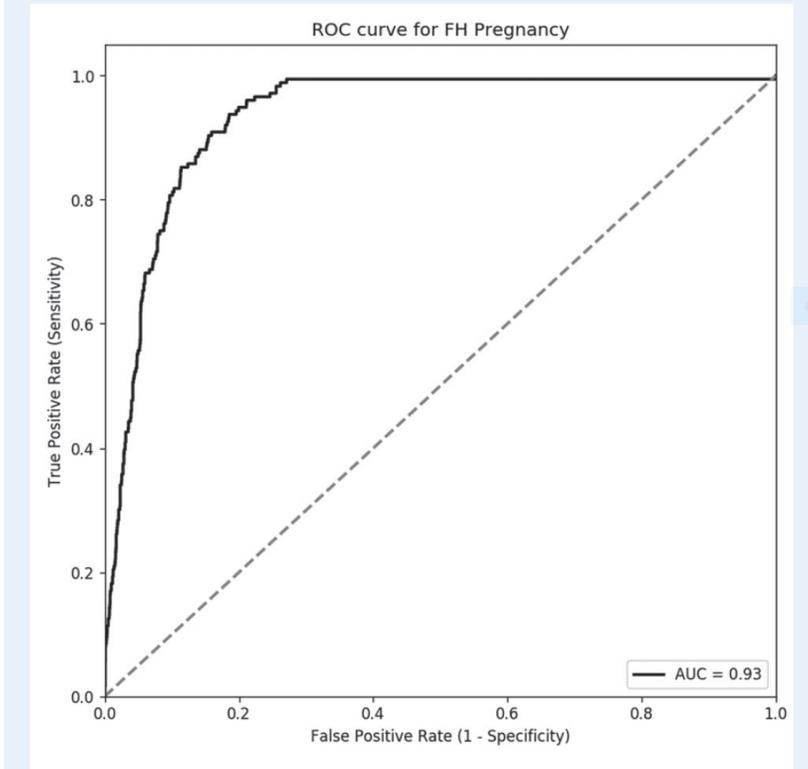
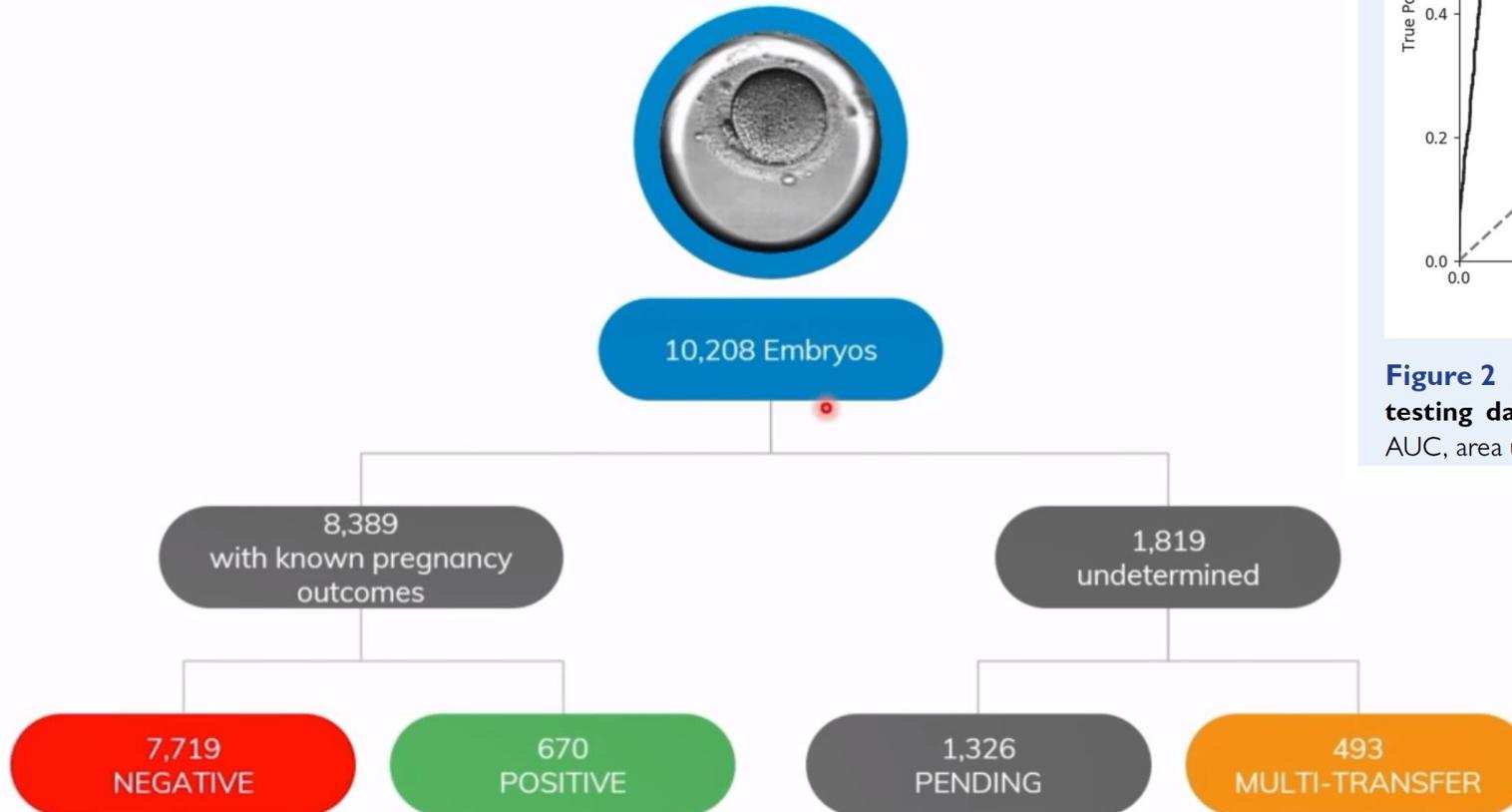
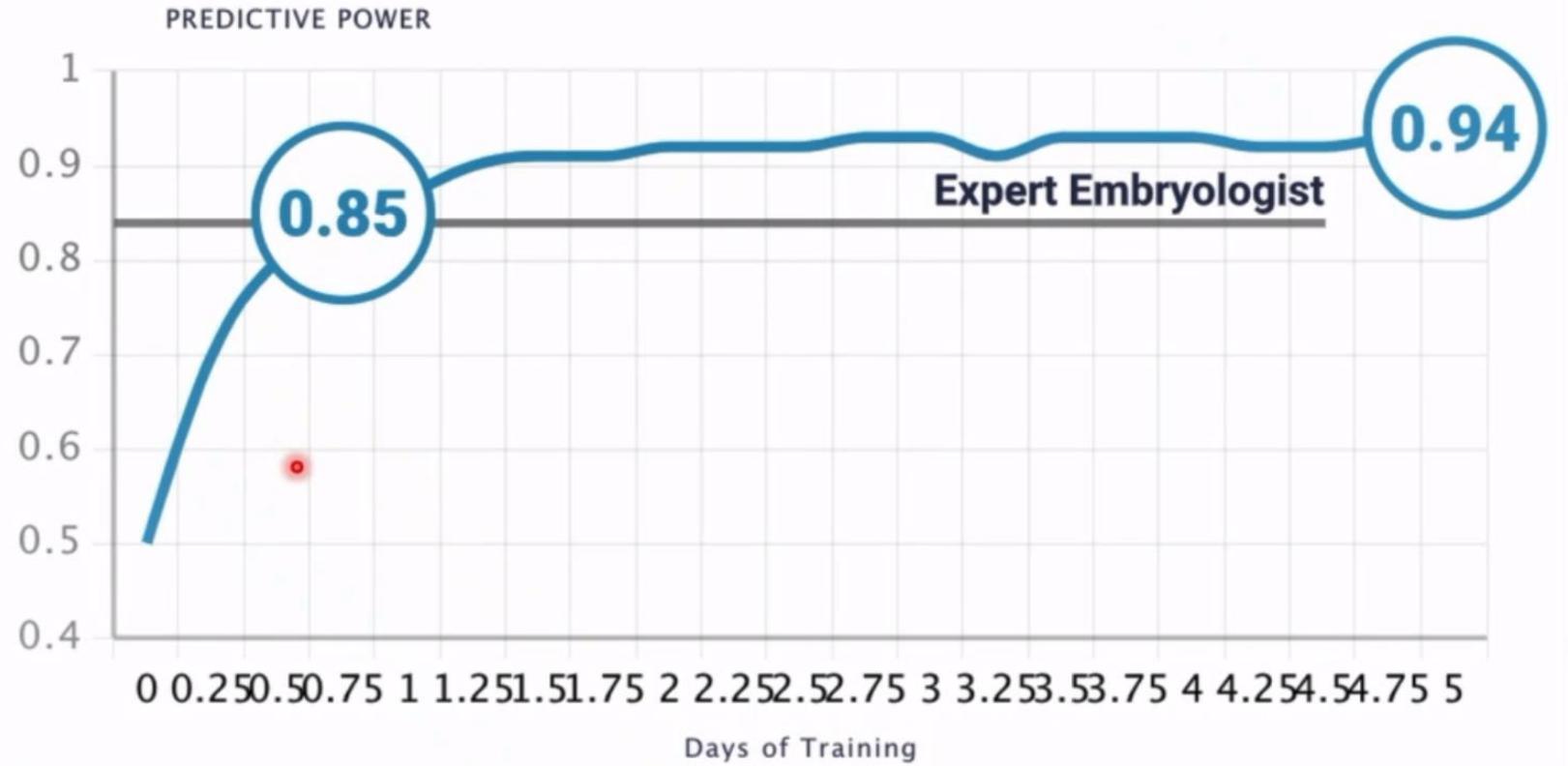


Figure 2 ROC curve for prediction of FH pregnancy on the testing dataset by IVY. ROC, Receiver operating characteristic; AUC, area under the curve.

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

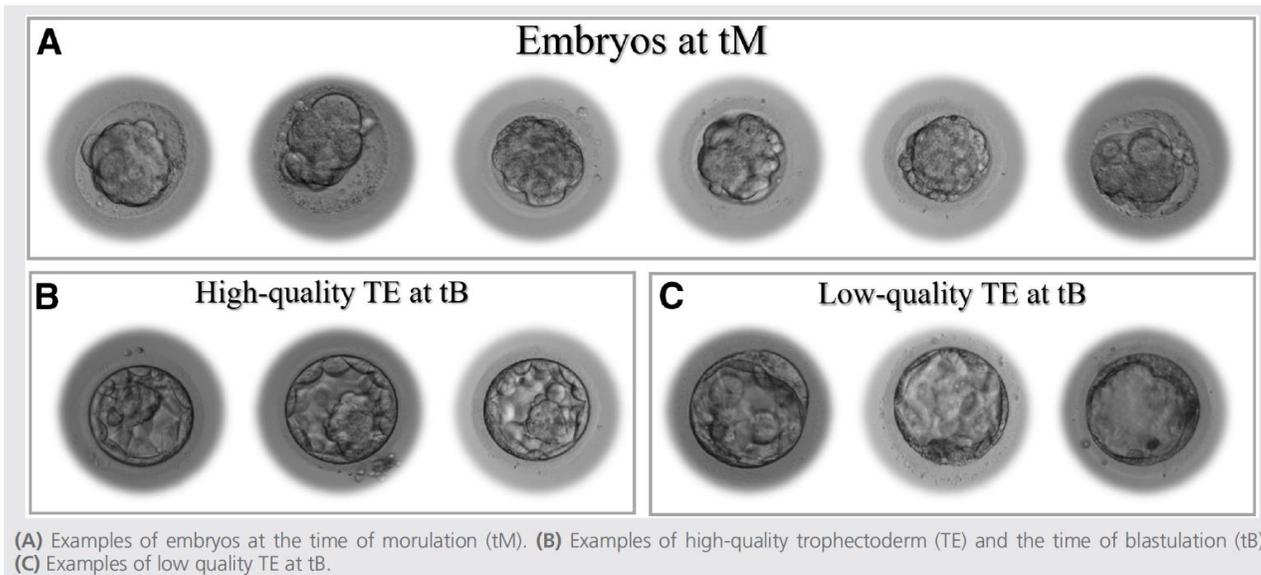


FERTILITY

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 Remohí, 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

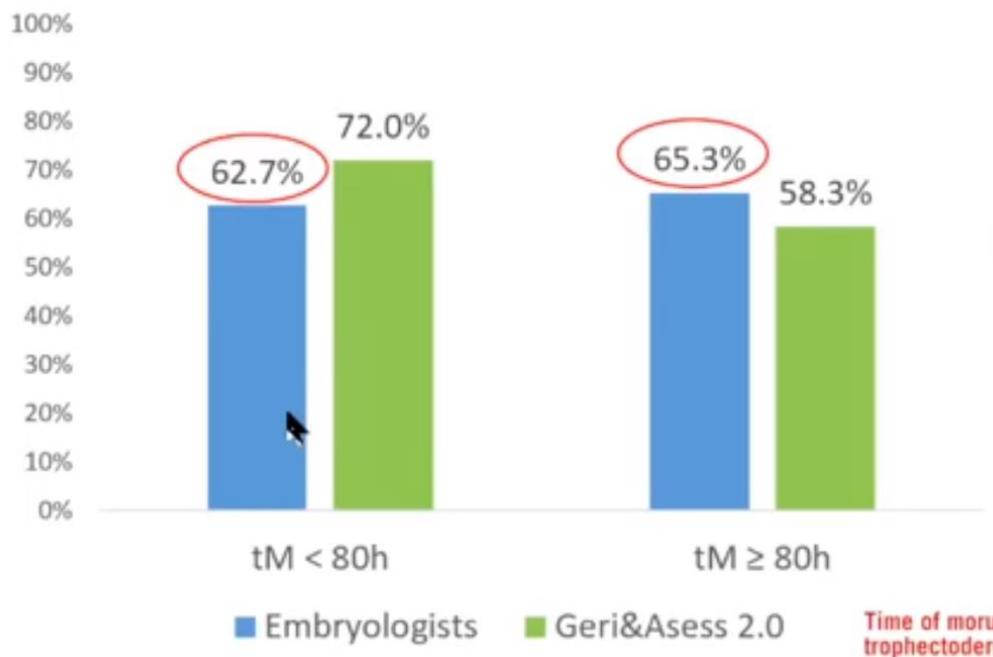


- Only *time of morulation (tM)* and *trophectoderm quality* were outlined as *putative predictors of live birth at two IVF centers*.
- In the validation set, the euploid blastocysts characterized by *tM <80 hours and high-quality trophectoderm* resulted in a LBR of *55.2% (n = 37/67)*, while those with *tM >80 hours and a low quality trophectoderm* resulted in a LBR of *25.5% (N = 13/51)*.

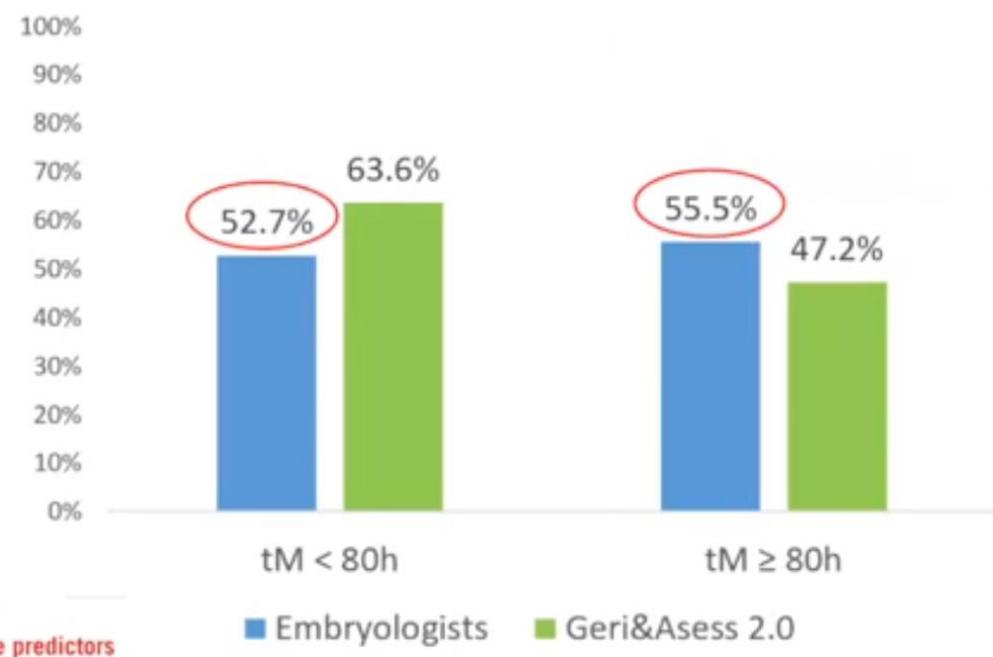
Clinical Result Prediction

tM < 80 h
n = 510 embryos

Implantation Rate



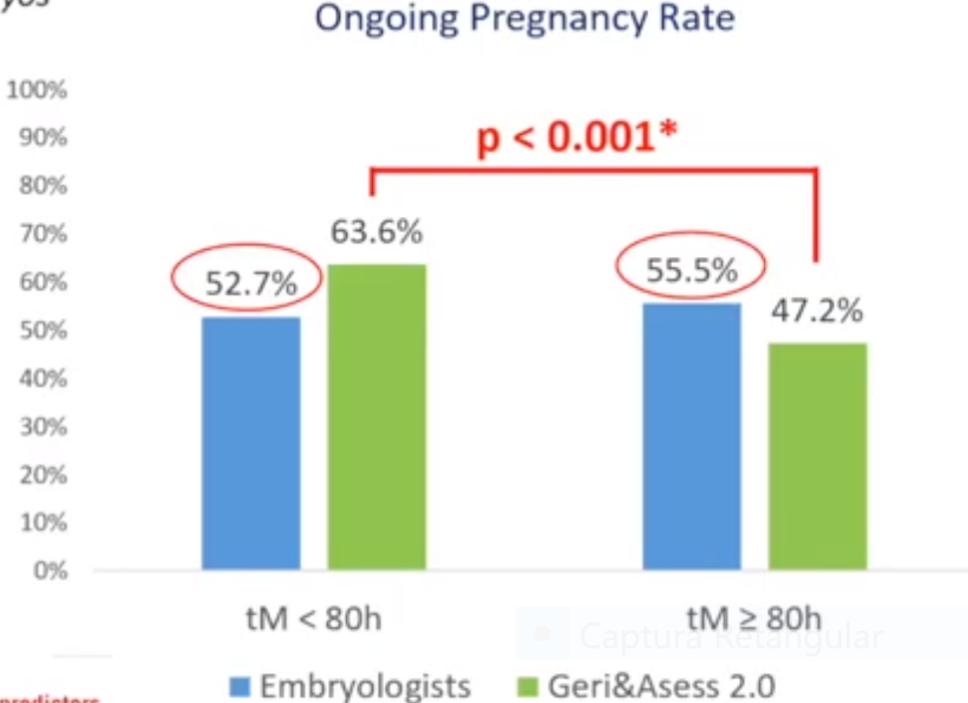
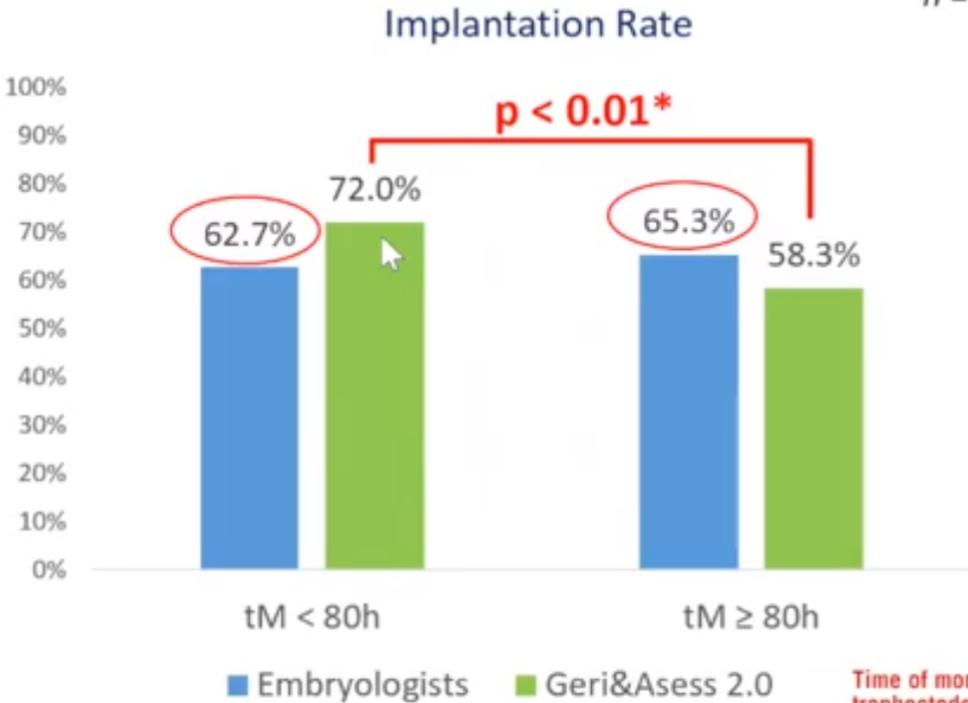
Ongoing Pregnancy Rate



Time of morulation and trophoctoderm quality are predictors

Clinical Result Prediction

tM < 80 h
n = 510 embryos



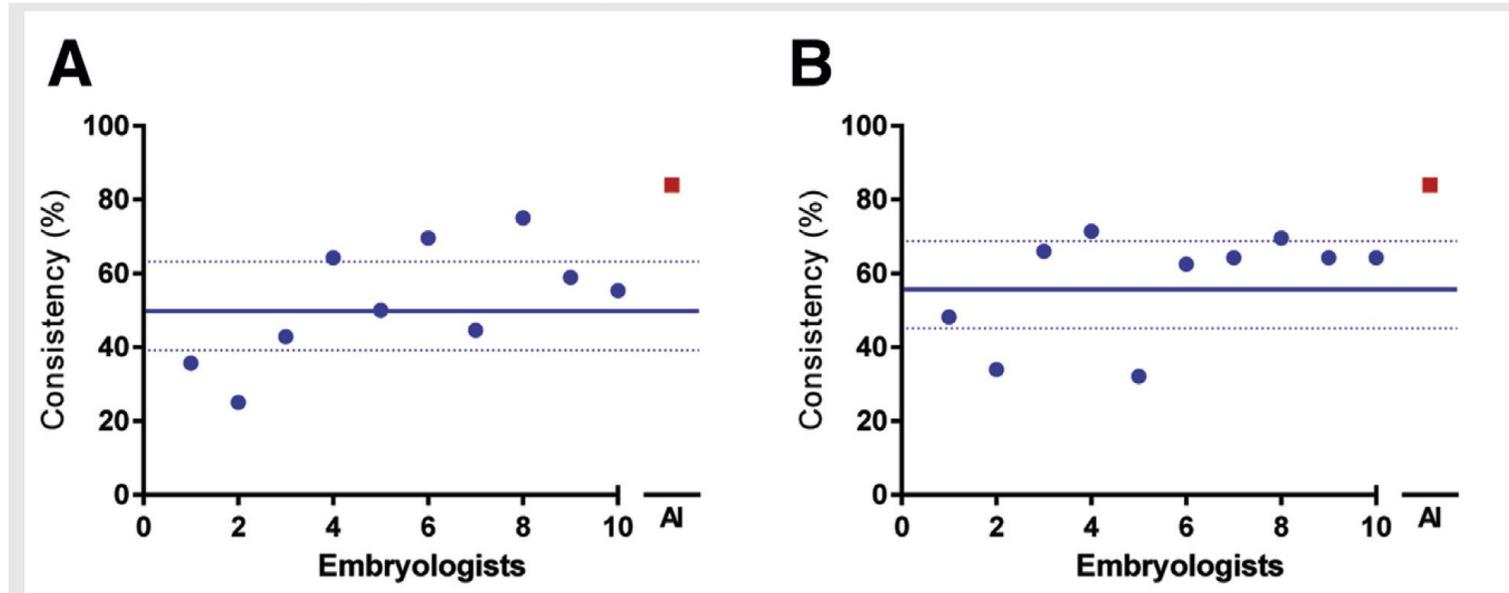
Time of morulation and trophectoderm quality are predictors

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%

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

Does a universal TLT algorithm exist?

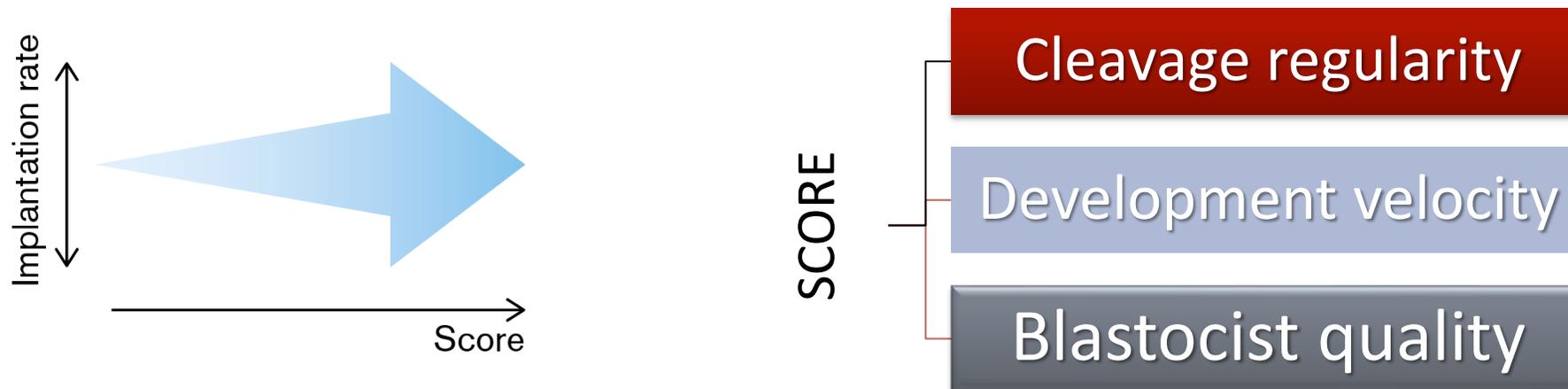
- Probably not.
- Each laboratory should perform a proper validation, certifying the value of each variable introduced and the corrections for putative confounders that could influence the algorithms

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)



FERTscore FERTILITY

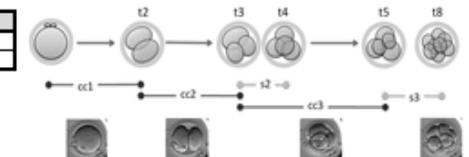
- PN
- pronuclei appearance (tPNa)
- timing to pronuclei fading (tPNf)
- timing to two (t2), three (t3), four (t4), five, (t5), six (t6), seven (t7), and eight cells (t8)
- timing to blastulation (tB)
- duration of the second cycle (t3-t2) - cc2
- duration of the third cycle (t5-t3) - cc3
- (t2-tPNf)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

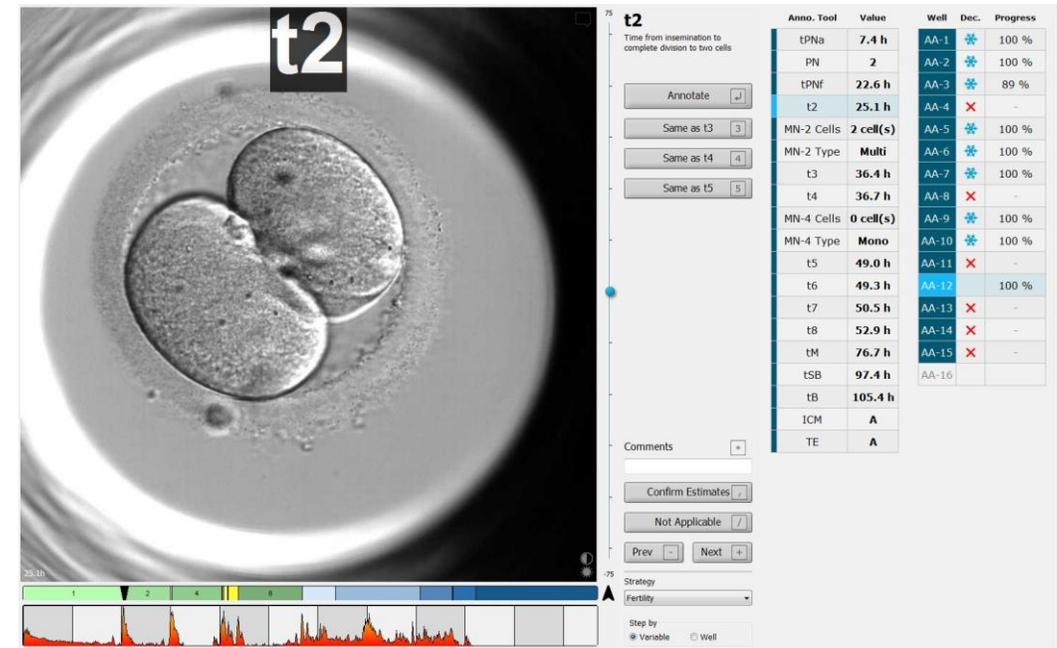
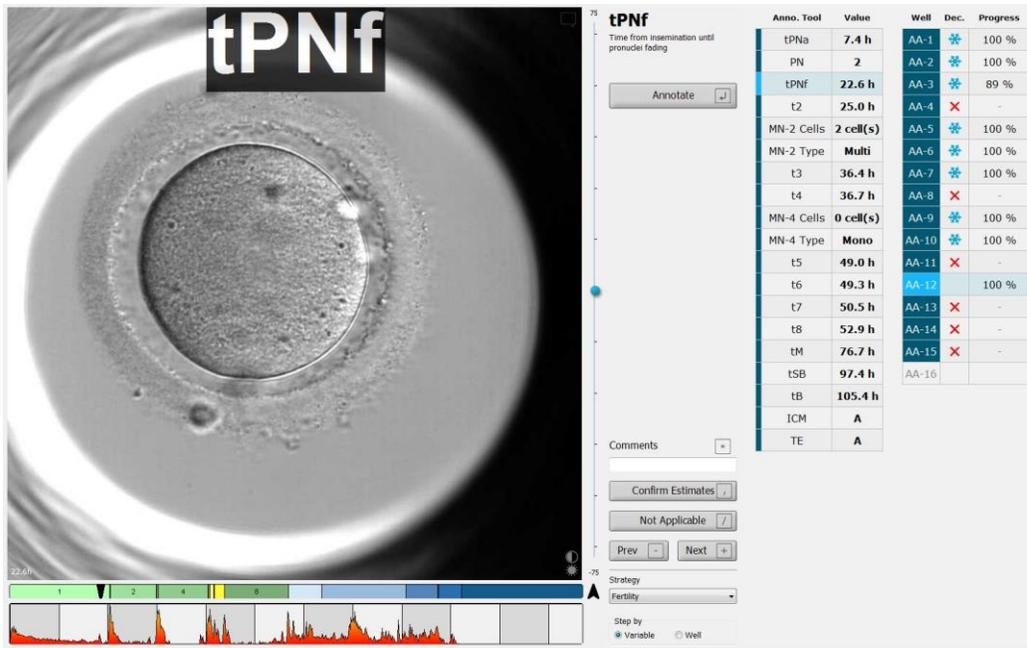
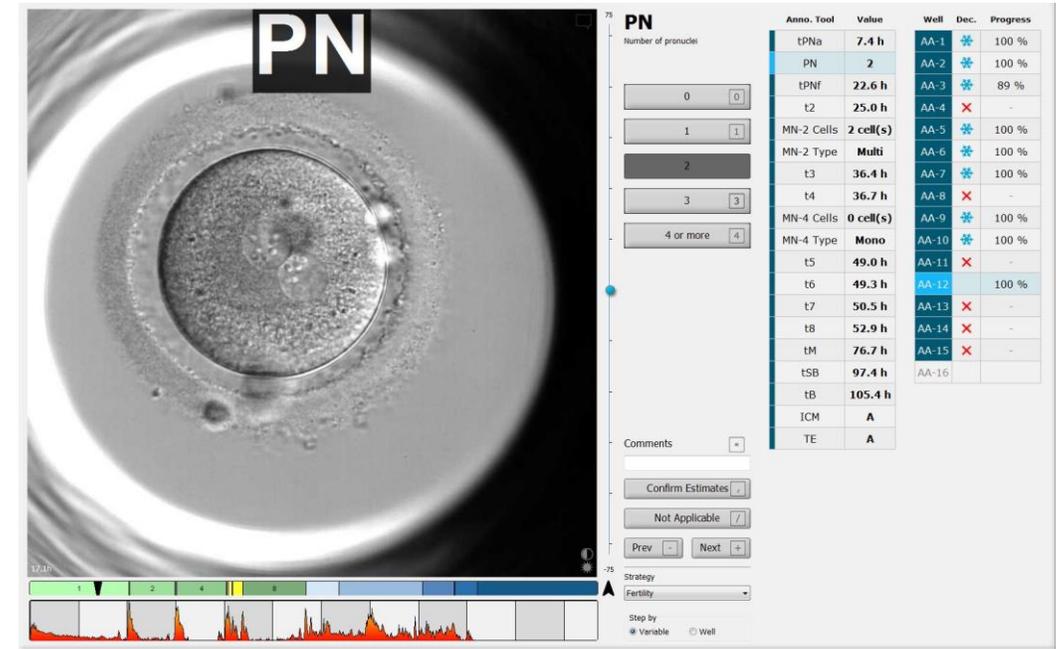
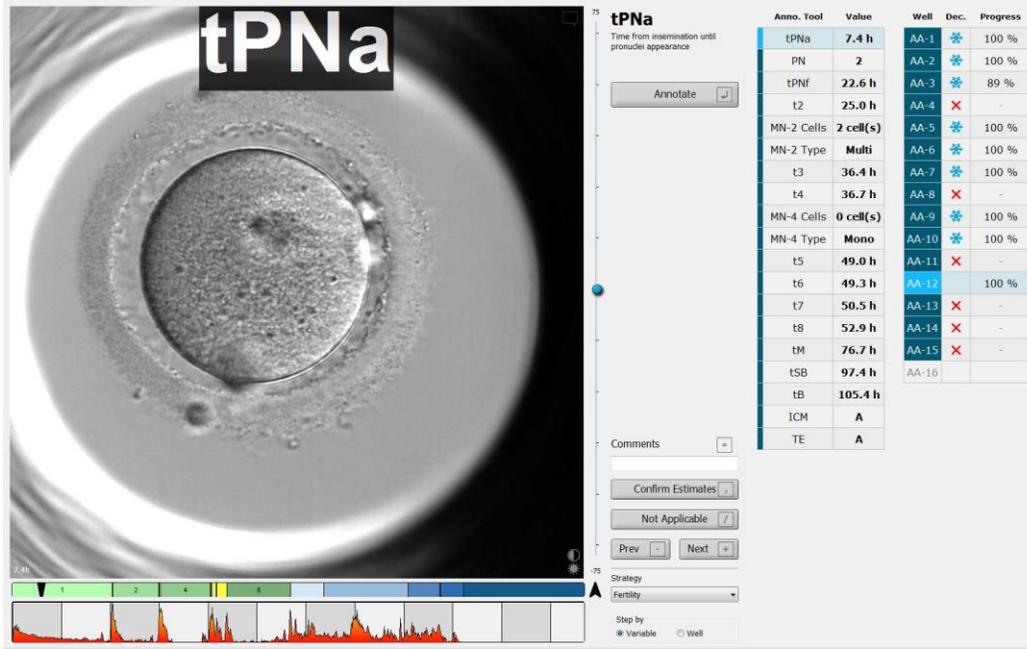
Parâmetros de Avaliação Embryoscope - Fertility

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 - 41.1h	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 Trofotoderma	A, B, C	classificar entre 115-120h (verificar ficha classificação D5)	-	-



Legenda	
	Parâmetros que geram o algoritmo
	Parâmetros que não geram o algoritmo





MN-2 Cells

Assessment of the number of blastomeres with multinucleation at 2-cell stage

0

1

2

Anno.	Tool	Value	Well	Dec.	Progress
tPNa		7.4 h	AA-1	✳	100 %
PN		2	AA-2	✳	100 %
tPNf		22.6 h	AA-3	✳	89 %
t2		25.1 h	AA-4	✗	-
MN-2 Cells		2 cell(s)	AA-5	✳	100 %
MN-2 Type		Multi	AA-6	✳	100 %
t3		36.4 h	AA-7	✳	100 %
t4		36.7 h	AA-8	✗	-
MN-4 Cells		0 cell(s)	AA-9	✳	100 %
MN-4 Type		Mono	AA-10	✳	100 %
t5		49.0 h	AA-11	✗	-
t6		49.3 h	AA-12	✳	100 %
t7		50.5 h	AA-13	✗	-
t8		52.9 h	AA-14	✗	-
tM		76.7 h	AA-15	✗	-
tSB		97.4 h			
tB		105.4 h			
ICM		A			
TE		A			

Comments

Confirm Estimates

Not Applicable

Prev Next

Strategy: Fertility

Step by: Variable Well

MN-2 Type

Nuclear morphology at 2-cell stage

Mono

Bi

Multi

Micro

Cluster

Unknown

Anno.	Tool	Value	Well	Dec.	Progress
tPNa		7.4 h	AA-1	✳	100 %
PN		2	AA-2	✳	100 %
tPNf		22.6 h	AA-3	✳	89 %
t2		25.1 h	AA-4	✗	-
MN-2 Cells		2 cell(s)	AA-5	✳	100 %
MN-2 Type		Multi	AA-6	✳	100 %
t3		36.4 h	AA-7	✳	100 %
t4		36.7 h	AA-8	✗	-
MN-4 Cells		0 cell(s)	AA-9	✳	100 %
MN-4 Type		Mono	AA-10	✳	100 %
t5		49.0 h	AA-11	✗	-
t6		49.3 h	AA-12	✳	100 %
t7		50.5 h	AA-13	✗	-
t8		52.9 h	AA-14	✗	-
tM		76.7 h	AA-15	✗	-
tSB		97.4 h			
tB		105.4 h			
ICM		A			
TE		A			

Comments

Confirm Estimates

Not Applicable

Prev Next

Strategy: Fertility

Step by: Variable Well

t3

Time from insemination to complete division to three cells

Annotate

Same as t4

Same as t5

Same as t6

Anno.	Tool	Value	Well	Dec.	Progress
tPNa		7.4 h	AA-1	✳	100 %
PN		2	AA-2	✳	100 %
tPNf		22.6 h	AA-3	✳	89 %
t2		25.1 h	AA-4	✗	-
MN-2 Cells		2 cell(s)	AA-5	✳	100 %
MN-2 Type		Multi	AA-6	✳	100 %
t3		36.4 h	AA-7	✳	100 %
t4		36.7 h	AA-8	✗	-
MN-4 Cells		0 cell(s)	AA-9	✳	100 %
MN-4 Type		Mono	AA-10	✳	100 %
t5		49.0 h	AA-11	✗	-
t6		49.3 h	AA-12	✳	100 %
t7		50.5 h	AA-13	✗	-
t8		52.9 h	AA-14	✗	-
tM		76.7 h	AA-15	✗	-
tSB		97.4 h			
tB		105.4 h			
ICM		A			
TE		A			

Comments

Confirm Estimates

Not Applicable

Prev Next

Strategy: Fertility

Step by: Variable Well

t4

Time from insemination to complete division to four cells

Annotate

Same as t5

Same as t6

Same as t7

Anno.	Tool	Value	Well	Dec.	Progress
tPNa		7.4 h	AA-1	✳	100 %
PN		2	AA-2	✳	100 %
tPNf		22.6 h	AA-3	✳	89 %
t2		25.1 h	AA-4	✗	-
MN-2 Cells		2 cell(s)	AA-5	✳	100 %
MN-2 Type		Multi	AA-6	✳	100 %
t3		36.4 h	AA-7	✳	100 %
t4		37.4 h	AA-8	✗	-
MN-4 Cells		0 cell(s)	AA-9	✳	100 %
MN-4 Type		Mono	AA-10	✳	100 %
t5		49.0 h	AA-11	✗	-
t6		49.3 h	AA-12	✳	100 %
t7		50.5 h	AA-13	✗	-
t8		52.9 h	AA-14	✗	-
tM		76.7 h	AA-15	✗	-
tSB		97.4 h			
tB		105.4 h			
ICM		A			
TE		A			

Comments

Confirm Estimates

Not Applicable

Prev Next

Strategy: Fertility

Step by: Variable Well



MN-4 Cells

Assessment of the number of blastomeres with multinucleation at 4-cell stage

0
1
2
3
4

Anno. Tool	Value	Well	Dec.	Progress
tPNa	7.4 h	AA-1	✳	100 %
PN	2	AA-2	✳	100 %
tPNf	22.6 h	AA-3	✳	89 %
t2	25.1 h	AA-4	✗	-
MN-2 Cells	2 cell(s)	AA-5	✳	100 %
MN-2 Type	Multi	AA-6	✳	100 %
t3	36.4 h	AA-7	✳	100 %
t4	37.4 h	AA-8	✗	-
MN-4 Cells	0 cell(s)	AA-9	✳	100 %
MN-4 Type	Mono	AA-10	✳	100 %
t5	49.0 h	AA-11	✗	-
t6	49.3 h	AA-12	✳	100 %
t7	50.5 h	AA-13	✗	-
t8	52.9 h	AA-14	✗	-
tM	76.7 h	AA-15	✗	-
tSB	97.4 h	AA-16		
tB	105.4 h			
ICM	A			
TE	A			

Comments

Confirm Estimates

Not Applicable

Prev Next

Strategy
Fertility

Step by
Variable Well

MN-4 Type

Nuclear morphology at 4-cell stage

Mono
Bi
Multi
Micro
Cluster
Unknown

Anno. Tool	Value	Well	Dec.	Progress
tPNa	7.4 h	AA-1	✳	100 %
PN	2	AA-2	✳	100 %
tPNf	22.6 h	AA-3	✳	89 %
t2	25.1 h	AA-4	✗	-
MN-2 Cells	2 cell(s)	AA-5	✳	100 %
MN-2 Type	Multi	AA-6	✳	100 %
t3	36.4 h	AA-7	✳	100 %
t4	37.4 h	AA-8	✗	-
MN-4 Cells	0 cell(s)	AA-9	✳	100 %
MN-4 Type	Mono	AA-10	✳	100 %
t5	49.0 h	AA-11	✗	-
t6	49.3 h	AA-12	✳	100 %
t7	50.5 h	AA-13	✗	-
t8	52.9 h	AA-14	✗	-
tM	76.7 h	AA-15	✗	-
tSB	97.4 h	AA-16		
tB	105.4 h			
ICM	A			
TE	A			

Comments

Confirm Estimates

Not Applicable

Prev Next

Strategy
Fertility

Step by
Variable Well

t5

Time from insemination to complete division to five cells

Annotate
Same as t6
Same as t7
Same as t8

Anno. Tool	Value	Well	Dec.	Progress
tPNa	7.4 h	AA-1	✳	100 %
PN	2	AA-2	✳	100 %
tPNf	22.6 h	AA-3	✳	89 %
t2	25.1 h	AA-4	✗	-
MN-2 Cells	2 cell(s)	AA-5	✳	100 %
MN-2 Type	Multi	AA-6	✳	100 %
t3	36.4 h	AA-7	✳	100 %
t4	37.4 h	AA-8	✗	-
MN-4 Cells	0 cell(s)	AA-9	✳	100 %
MN-4 Type	Mono	AA-10	✳	100 %
t5	49.0 h	AA-11	✗	-
t6	49.3 h	AA-12	✳	100 %
t7	50.5 h	AA-13	✗	-
t8	52.9 h	AA-14	✗	-
tM	76.7 h	AA-15	✗	-
tSB	97.4 h	AA-16		
tB	105.4 h			
ICM	A			
TE	A			

Comments

Confirm Estimates

Not Applicable

Prev Next

Strategy
Fertility

Step by
Variable Well

t6

Time from insemination to complete division to six cells

Annotate
Same as t7
Same as t8

Anno. Tool	Value	Well	Dec.	Progress
tPNa	7.4 h	AA-1	✳	100 %
PN	2	AA-2	✳	100 %
tPNf	22.6 h	AA-3	✳	89 %
t2	25.1 h	AA-4	✗	-
MN-2 Cells	2 cell(s)	AA-5	✳	100 %
MN-2 Type	Multi	AA-6	✳	100 %
t3	36.4 h	AA-7	✳	100 %
t4	37.4 h	AA-8	✗	-
MN-4 Cells	0 cell(s)	AA-9	✳	100 %
MN-4 Type	Mono	AA-10	✳	100 %
t5	49.0 h	AA-11	✗	-
t6	49.3 h	AA-12	✳	100 %
t7	50.5 h	AA-13	✗	-
t8	52.9 h	AA-14	✗	-
tM	76.7 h	AA-15	✗	-
tSB	97.4 h	AA-16		
tB	105.4 h			
ICM	A			
TE	A			

Comments

Confirm Estimates

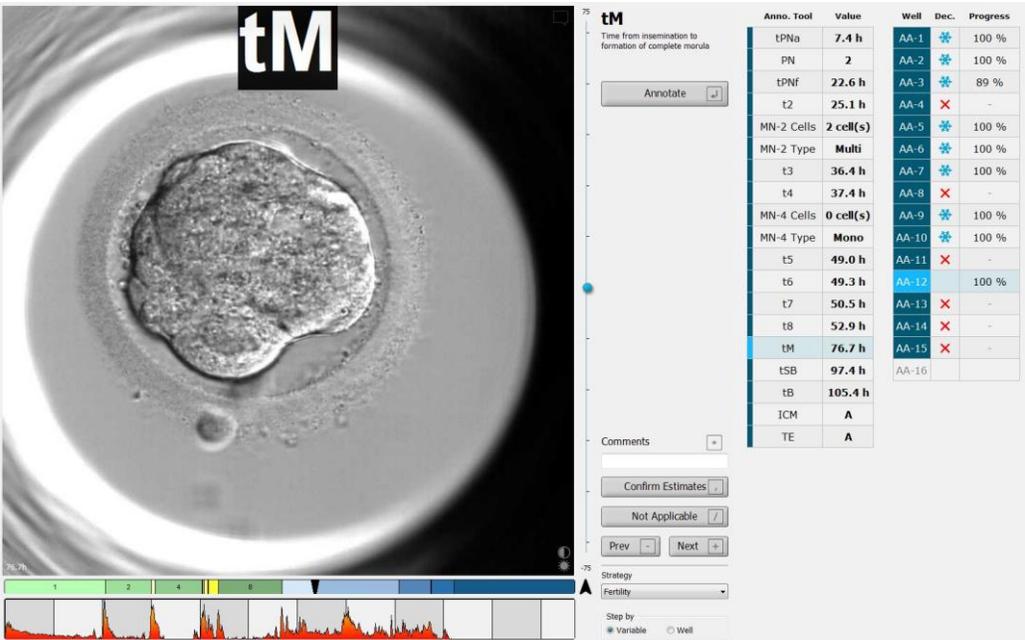
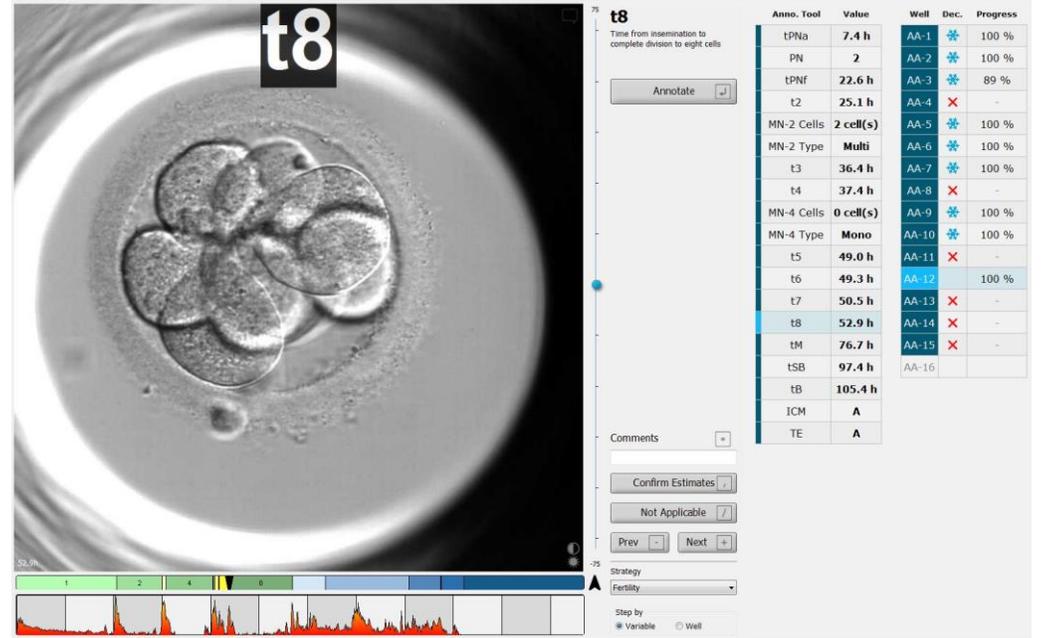
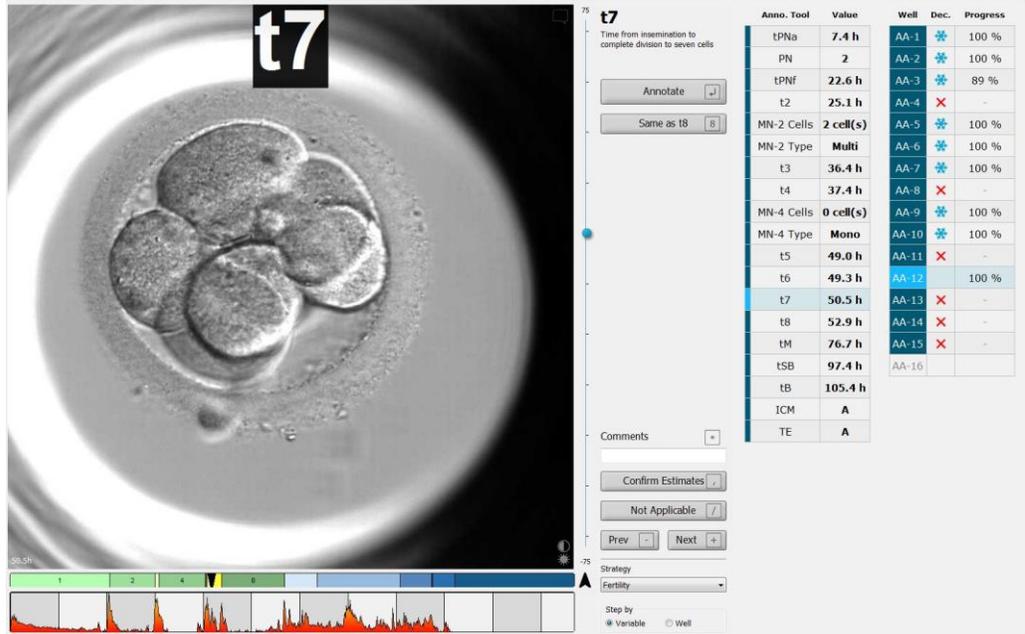
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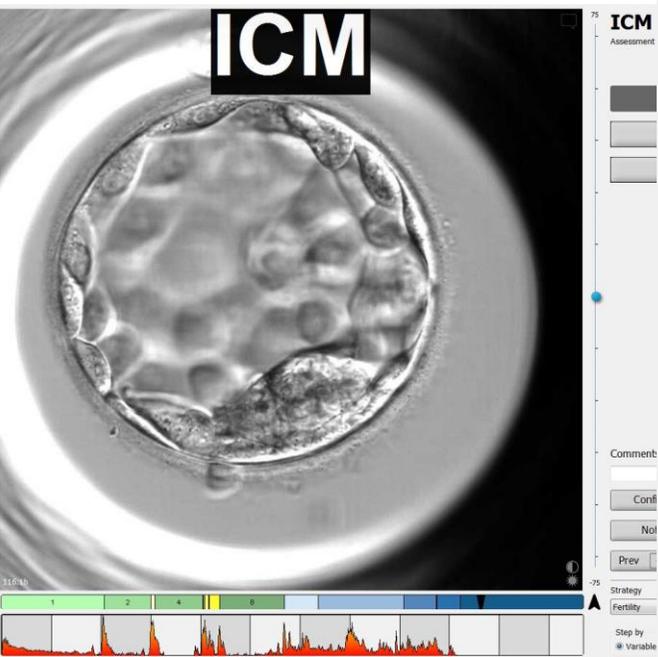
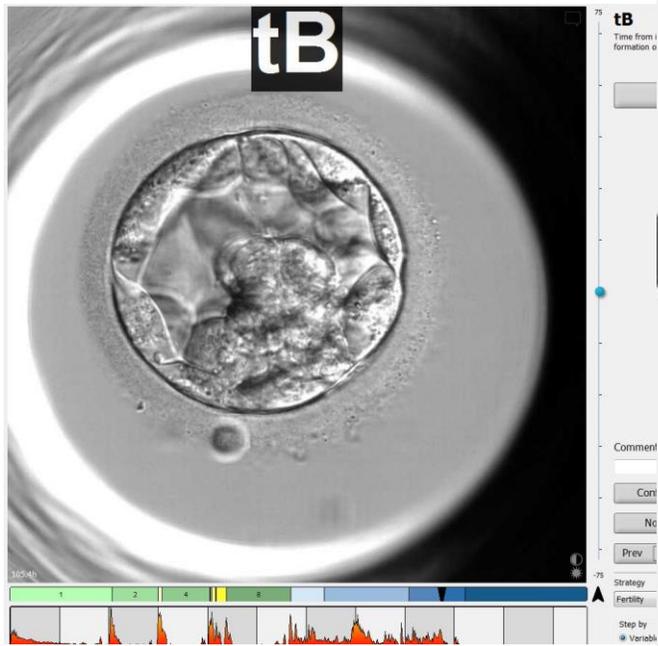
Prev Next

Strategy
Fertility

Step by
Variable Well







Anno. Tool	Value	Well	Dec.	Progress
tPNa	7.4 h	AA-1	❄️	100 %
PN	2	AA-2	❄️	100 %
tPNf	22.6 h	AA-3	❄️	89 %
t2	25.0 h	AA-4	❌	-
MN-2 Cells	2 cell(s)	AA-5	❄️	100 %
MN-2 Type	Multi	AA-6	❄️	100 %
t3	36.4 h	AA-7	❄️	100 %
t4	36.7 h	AA-8	❌	-
MN-4 Cells	0 cell(s)	AA-9	❄️	100 %
MN-4 Type	Mono	AA-10	❄️	100 %
t5	49.0 h	AA-11	❌	-
t6	49.3 h	AA-12	❄️	100 %
t7	50.5 h	AA-13	❌	-
t8	52.9 h	AA-14	❌	-
tM	76.7 h	AA-15	❌	-
tSB	97.4 h	AA-16		
tB	105.4 h			
ICM	A			
TE	A			

TE
Assessment of Trophoblast

Panel A

Anno. Tool	Value	Well	Dec.	Progress
tPNa	7.4 h	AA-1	❄️	100 %
PN	2	AA-2	❄️	100 %
tPNf	22.6 h	AA-3	❄️	89 %
t2	25.1 h	AA-4	❌	-
MN-2 Cells	2 cell(s)	AA-5	❄️	100 %
MN-2 Type	Multi	AA-6	❄️	100 %
t3	36.4 h	AA-7	❄️	100 %
t4	37.4 h	AA-8	❌	-
MN-4 Cells	0 cell(s)	AA-9	❄️	100 %
MN-4 Type	Mono	AA-10	❄️	100 %
t5	49.0 h	AA-11	❌	-
t6	49.3 h	AA-12	❄️	100 %
t7	50.5 h	AA-13	❌	-
t8	52.9 h	AA-14	❌	-
tM	76.7 h	AA-15	❌	-
tSB	97.4 h	AA-16		
tB	105.4 h			
ICM	A			
TE	A			

Comments

Confirm Estimates

Not Applicable

Prev Next

Strategy: Fertility

Step by: Variable Well



Running

View Running

Patients

Patient Name: ANDREIA DE FREITAS MARTINS PEREIRA
 Patient ID: 036560

View All Patients
 Patient Details

Slides

Treatment ID: FIV 11/03/2020
 Slide ID: AA-D2020.03.11_S00497_I3167_P

View Slide
 Timeline

Time (h)	Well: 1 Morphological Grade 5AA D5	Well: 2 Morphological Grade NF	Well: 3 Morphological Grade 5AA D5	Well: 4 Morphological Grade 5CB D6	Well: 5 Morphological Grade 5BA D5
17					
26					
44					
68					



Running

View Running

Patients

Patient Name: ANDREIA DE FREITAS MARTINS PEREIRA
 Patient ID: 036560

View All Patients
 Patient Details

Slides

Treatment ID: FIV 11/03/2020
 Slide ID: AA-D2020.03.11_S00497_I3167_P

Well	Dec.	Current score	NOT2PN	t2	t3	t4	t5	tB	ICM	TE	Last stage	Morph. grade	Last image	Saved score
AA-1	❄️	8.5	●	24.1	34.9	35.8	47.9	100.9	A	A	B	5AA D5		8.5
AA-2	❌	0	△	?	?	?	?	?	?	?	-	NF		0
AA-3	❄️	8.8	●	26.6	38.5	38.5	51.7	99.8	A	A	B	5AA D5		8.8
AA-4	❄️	4.7	●	24.3	34.1	35.4	46.9	101.1	C	B	B	5CB D6		4.7
AA-5	❄️	7.3	●	24.0	35.0	35.2	35.2	105.3	B	A	B	5BA D5		7.3
AA-6	❌	NA	?	?	?	?	?	?	?	?	-			NA

Current Model

KIDScoreD5 v3

Created 2018-11-01 by Vitrolife

Saved Model

Save Score KIDScoreD5 v3

Saved 2020-03-17 12:19:08 by ADMIN

Transfer Info

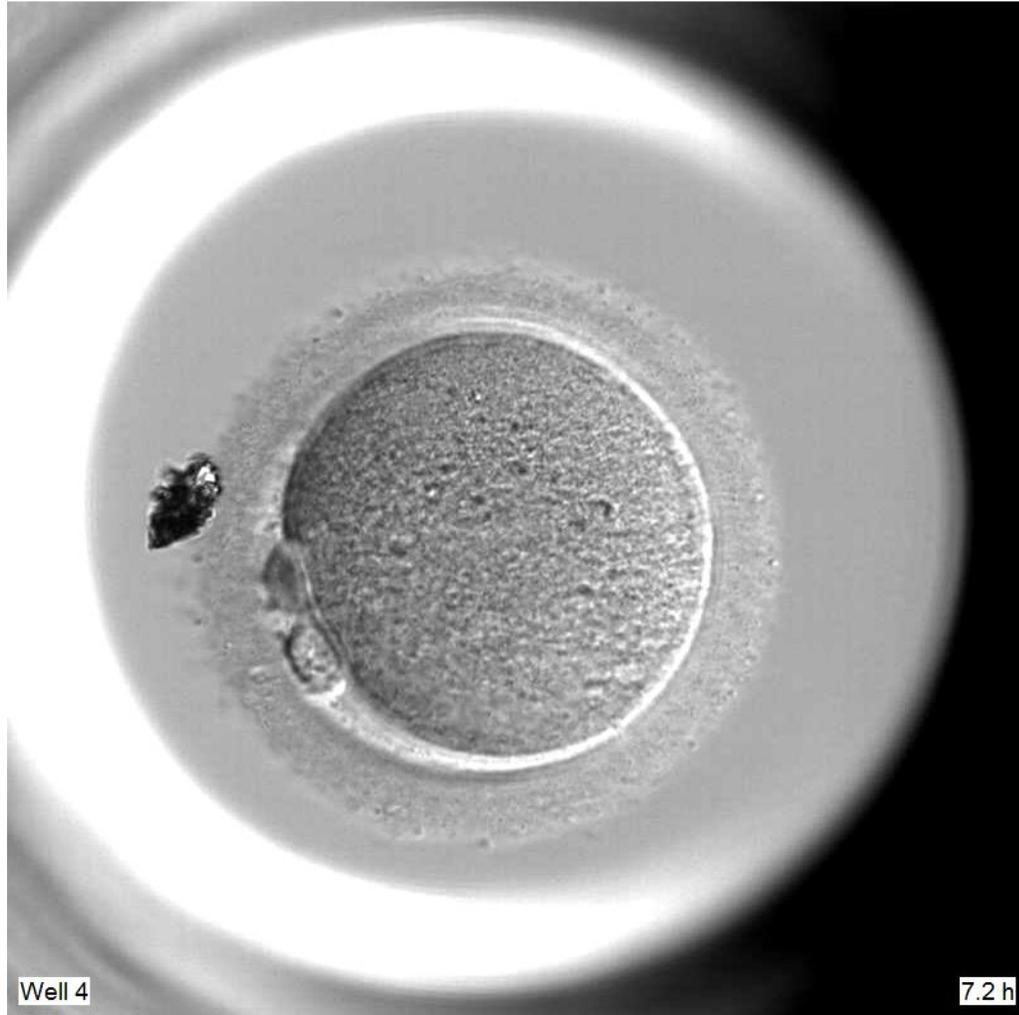
Save Info Transfer Date 2020-03-17

View All Patient Embryos

Assincronia PN



FERTILITY
MEDICAL GROUP

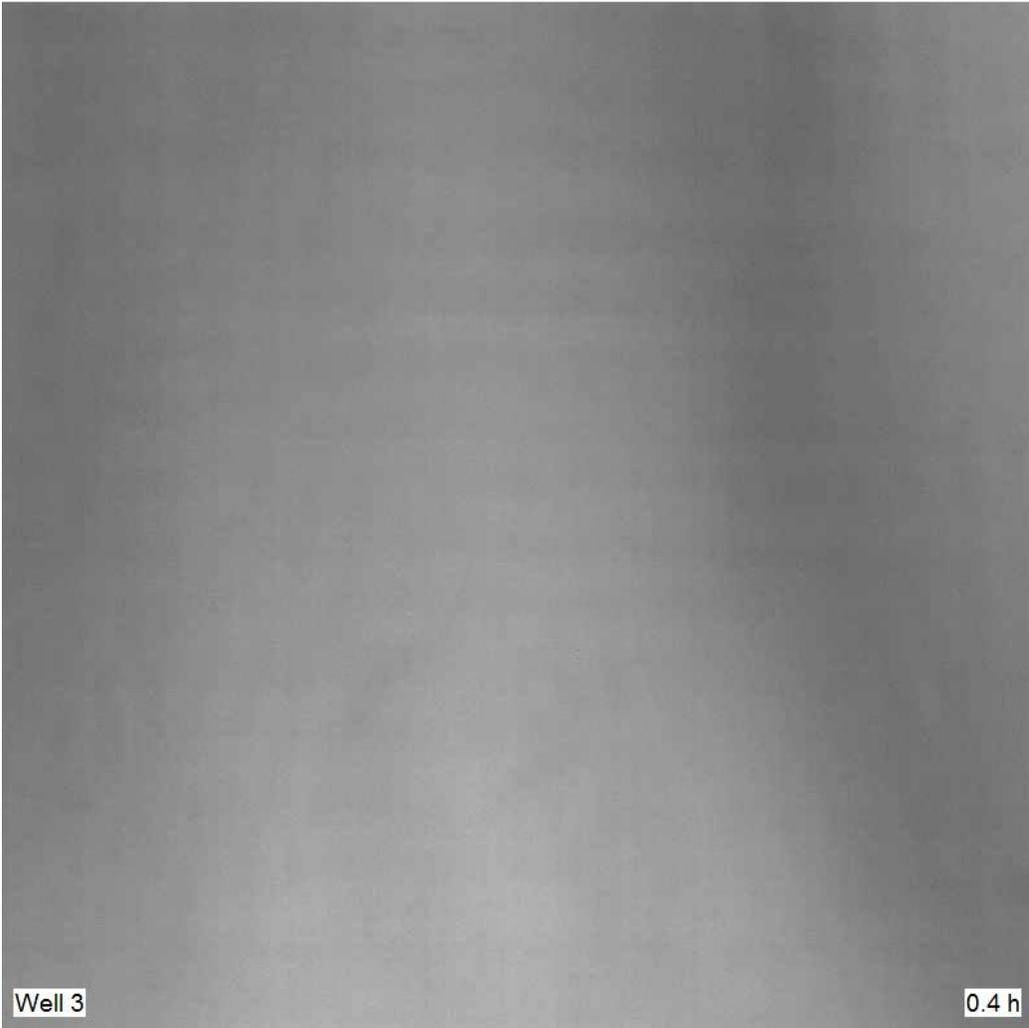


FERTILITY

Clivagem caótica



FERTILITY
MEDICAL GROUP



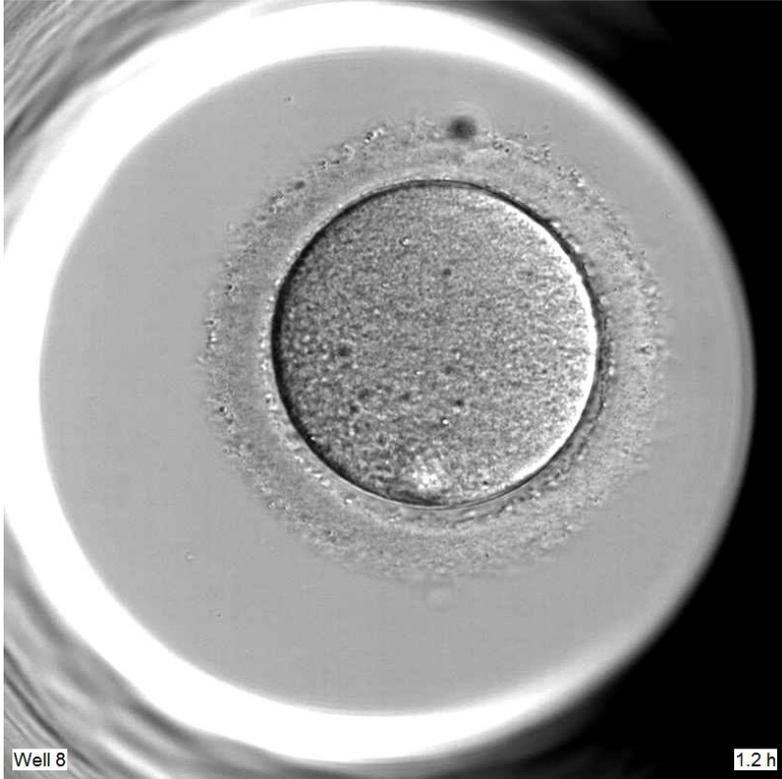
Well 3

0.4 h



FERTILITY

Clivagem direta 1-3



Clivagem direta 1-4



Clivagem direta 2-5



Clivagem reversa



Multinucleação



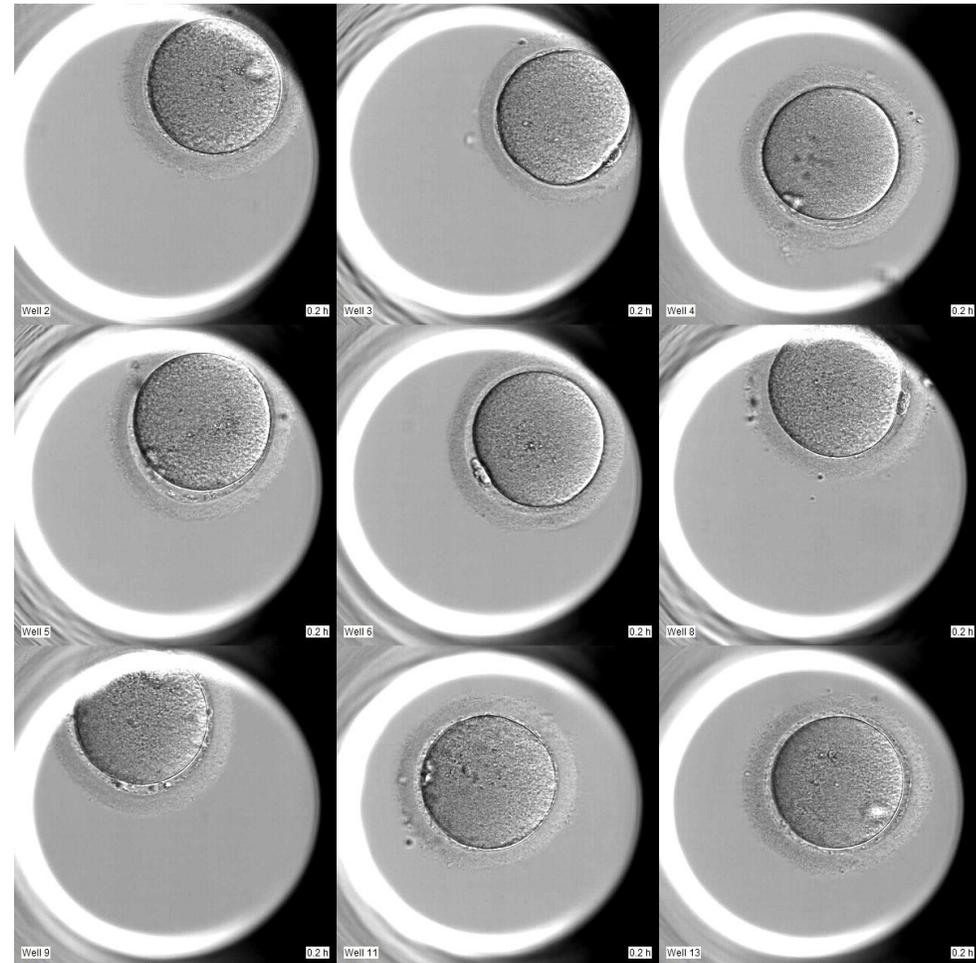
Embryoscope FERTILITY



- 427 ciclos
- 372 pacientes

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

- 2018: **49,9% 2PN**



Embryoscope FERTILITY



Cut-off	Variável	Não blastocisto (n=657)		Blastocisto (n=563)		p-value
		Média	DP	Média	DP	
	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

Embryoscope FERTILITY



Cut-off	Variável	Não blastocisto (n=657)		Blastocisto (n=563)		p-value
		Média	DP	Média	DP	
	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

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

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

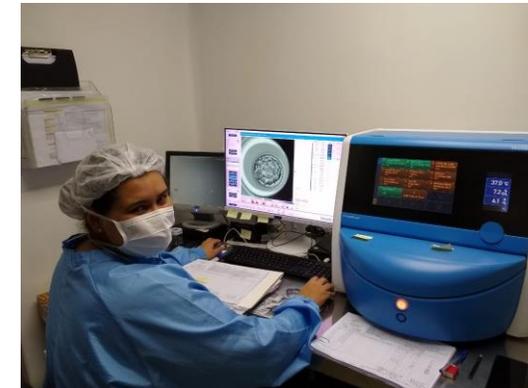


EmbryoScope FERTILITY

KIDscore D5	$\leq 2,5$	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

$a \neq b \neq c \neq d, p < 0,001$

General linear model, função Log linear, distribuição Poisson

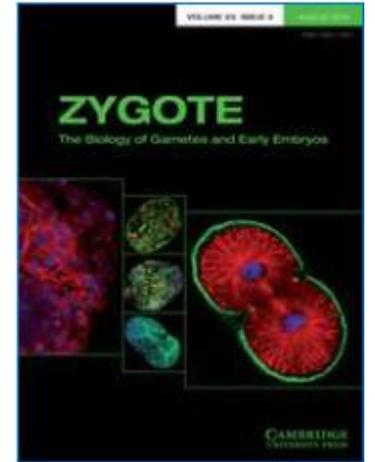


Improved embryonic development and utilization rates with EmbryoScope: A within-subject comparison versus a benchtop incubator

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.

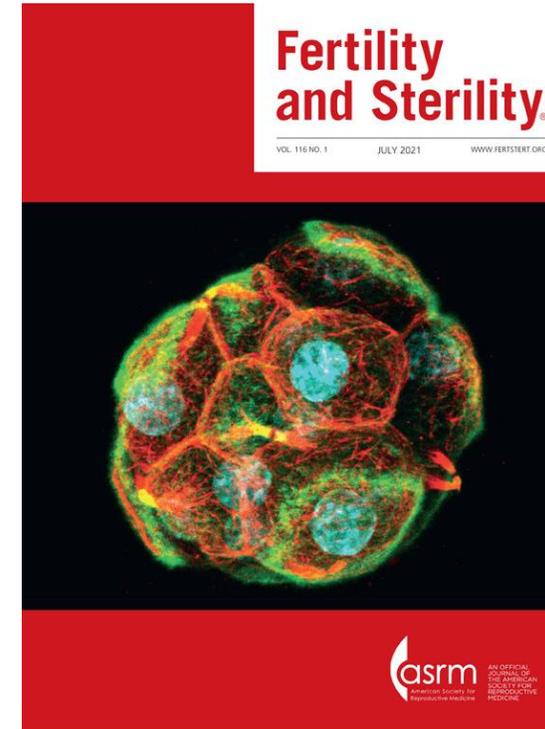


Time-lapse monitoring: an adjunct tool to select embryos for preimplantation genetic testing

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



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

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Manuscript Type:	Original Article
Date Submitted by the Author:	n/a
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Keywords:	male age, semen, morphokinetics, Time-lapse imaging



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 \pm SD
Female age (years)	37.7 \pm 3.8



FERTILITY

RESULTS

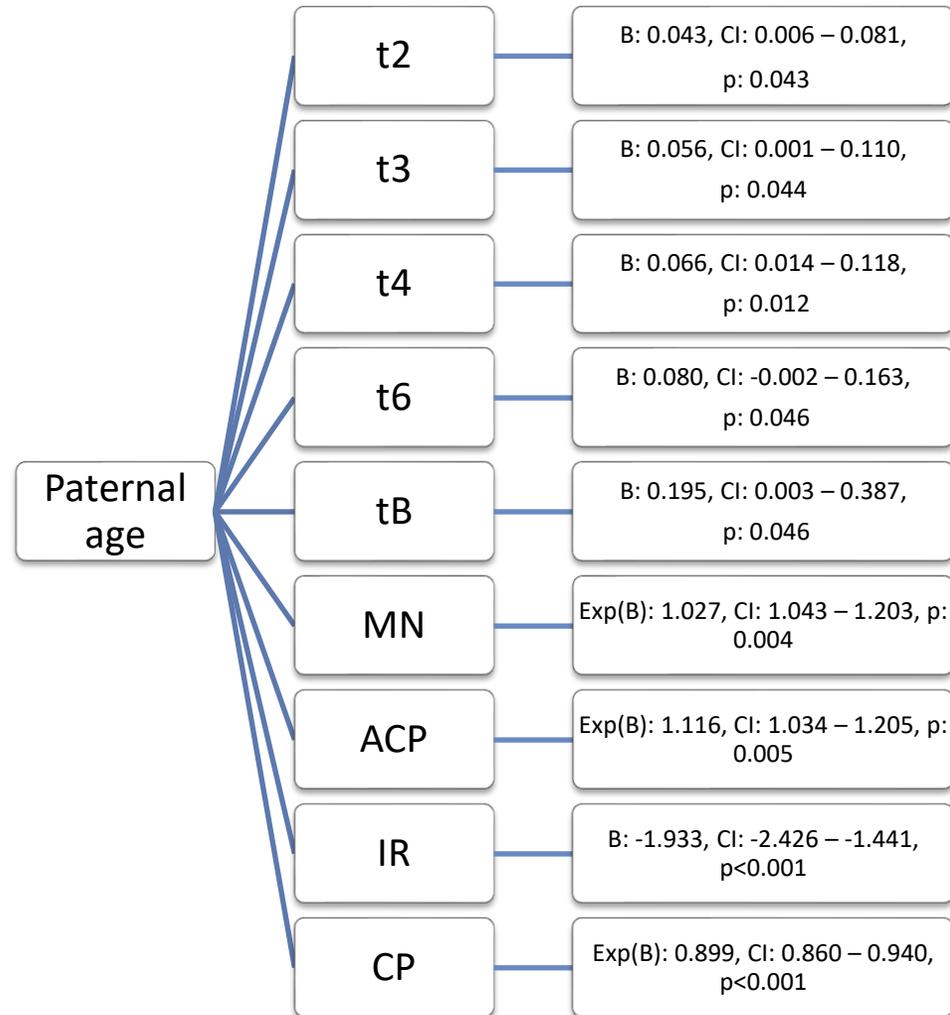
Variable	Mean \pm SD
Semen analysis	
Male age (years)	41.3 \pm 6.8
Ejaculatory abstinence length (days)	3.2 \pm 2.5



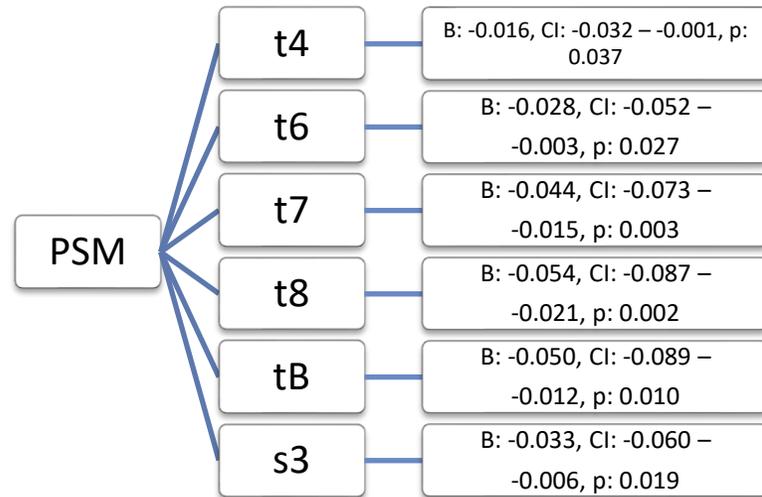
RESULTS

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

RESULTS

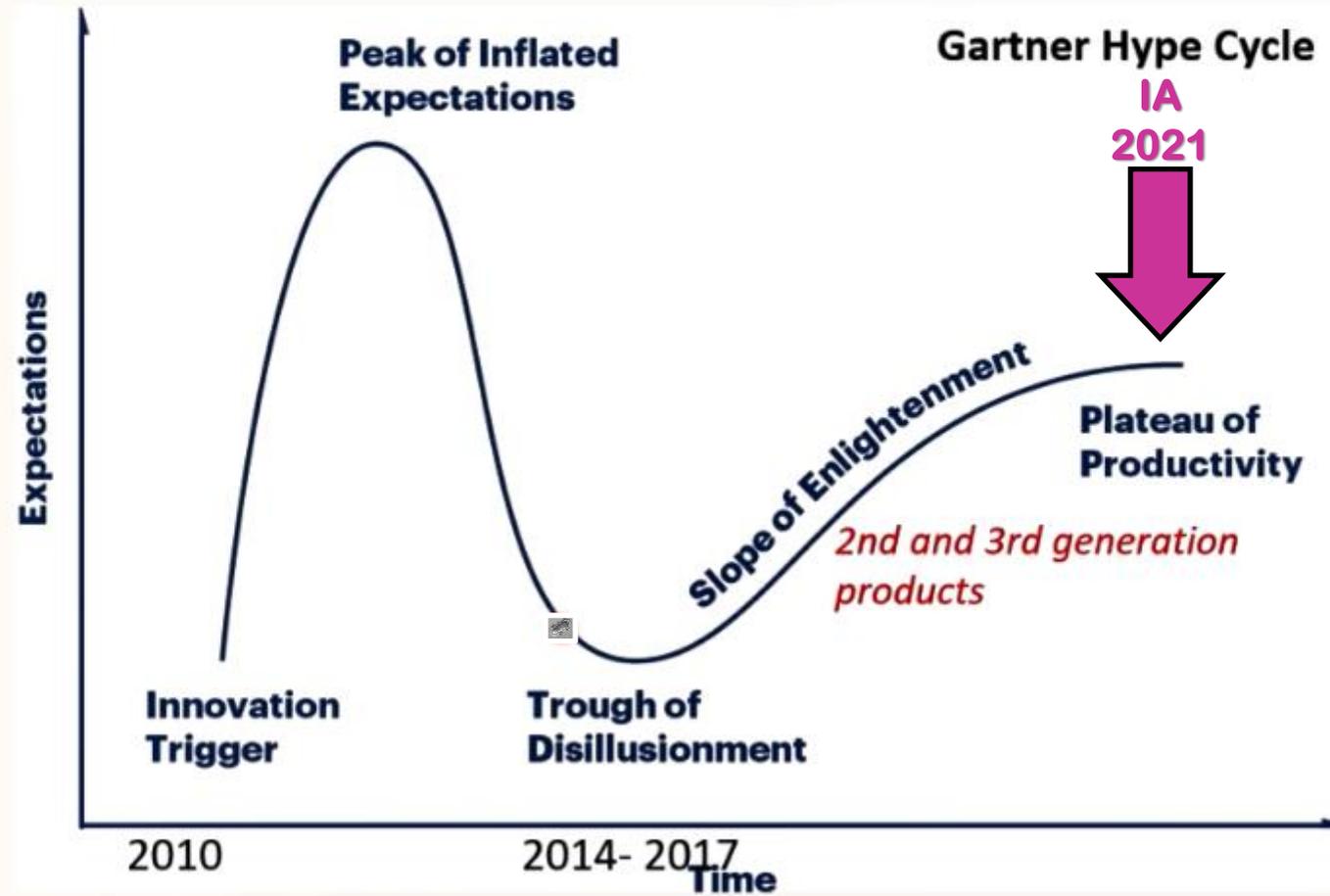


RESULTS



Gartner Hype cycle

Five key phases of a technology's life cycle





Time lapse technology (TLT) –
Ideal automation partner



From past to future...

Embryo through the lens: from time-lapse cinematography to artificial intelligence



Elnur Babayev, M.D. and Eve C. Feinberg, M.D.

Northwestern University Feinberg School of Medicine, Chicago, Illinois

<https://doi.org/10.1016/j.fertnstert.2019.12.001>

“Once a new technology rolls over you, if you’re not part of the steamroller, you’re part of the road.”

—Stewart Brand



Brackett BG. In vitro fertilization of rabbit ova: time sequence of events. Fertil Steril 1970;21:169–76.



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

AULAS MINISTRADAS

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2020

2019

2018

2017

2016

2015



Obrigado!

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FERTILITY
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FERTILITY