TLM & ART

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- **Embryo Selection**

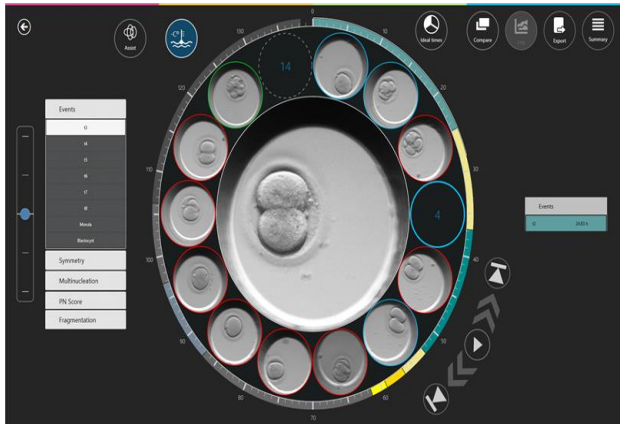
- **TLM**

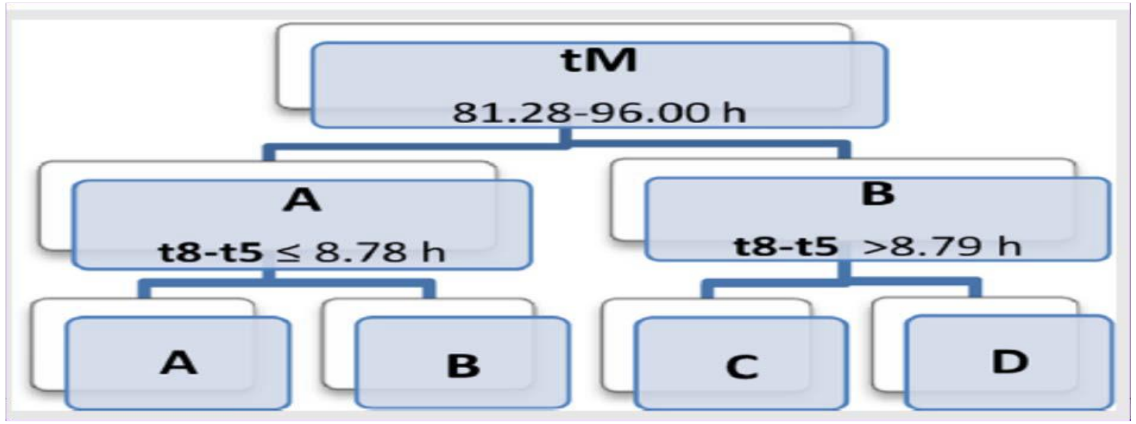
Traditional Embryo Morphology Evaluation

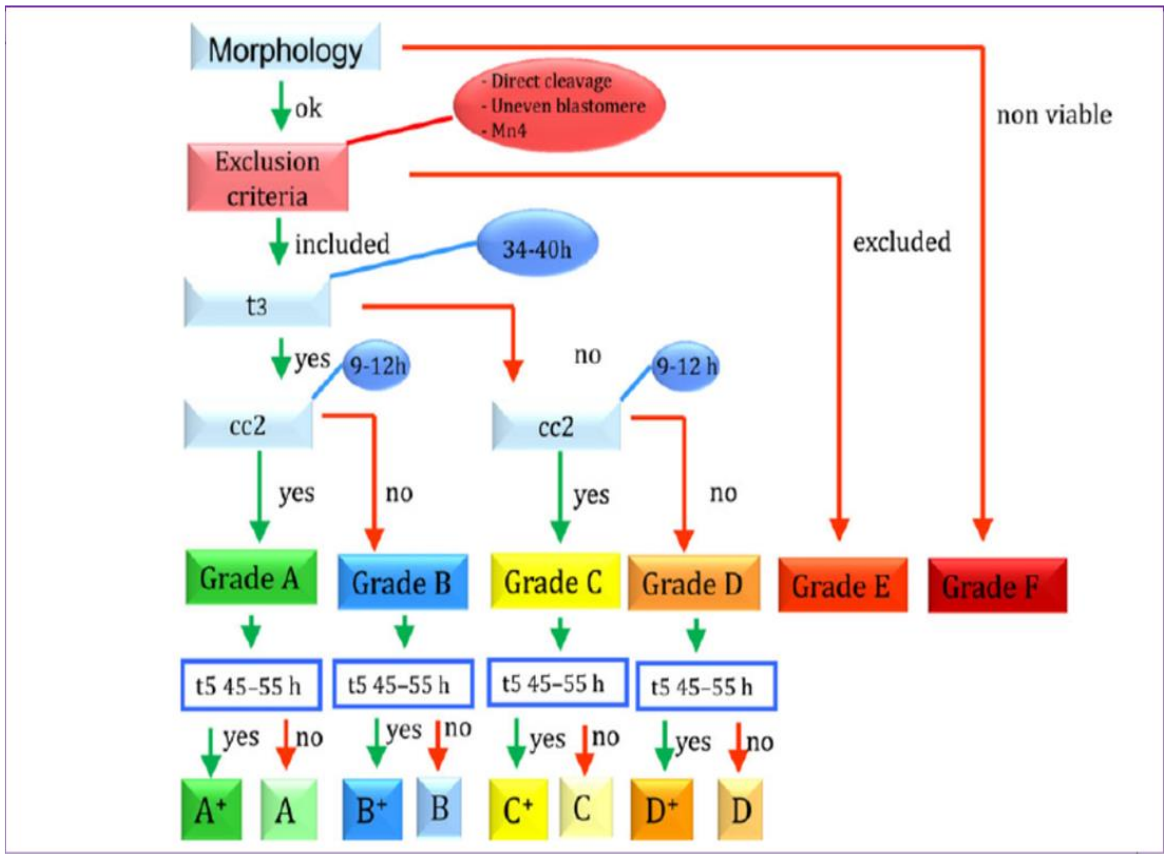
✓Static information
✓Significant fluctuations in culture conditions
✓Subjective

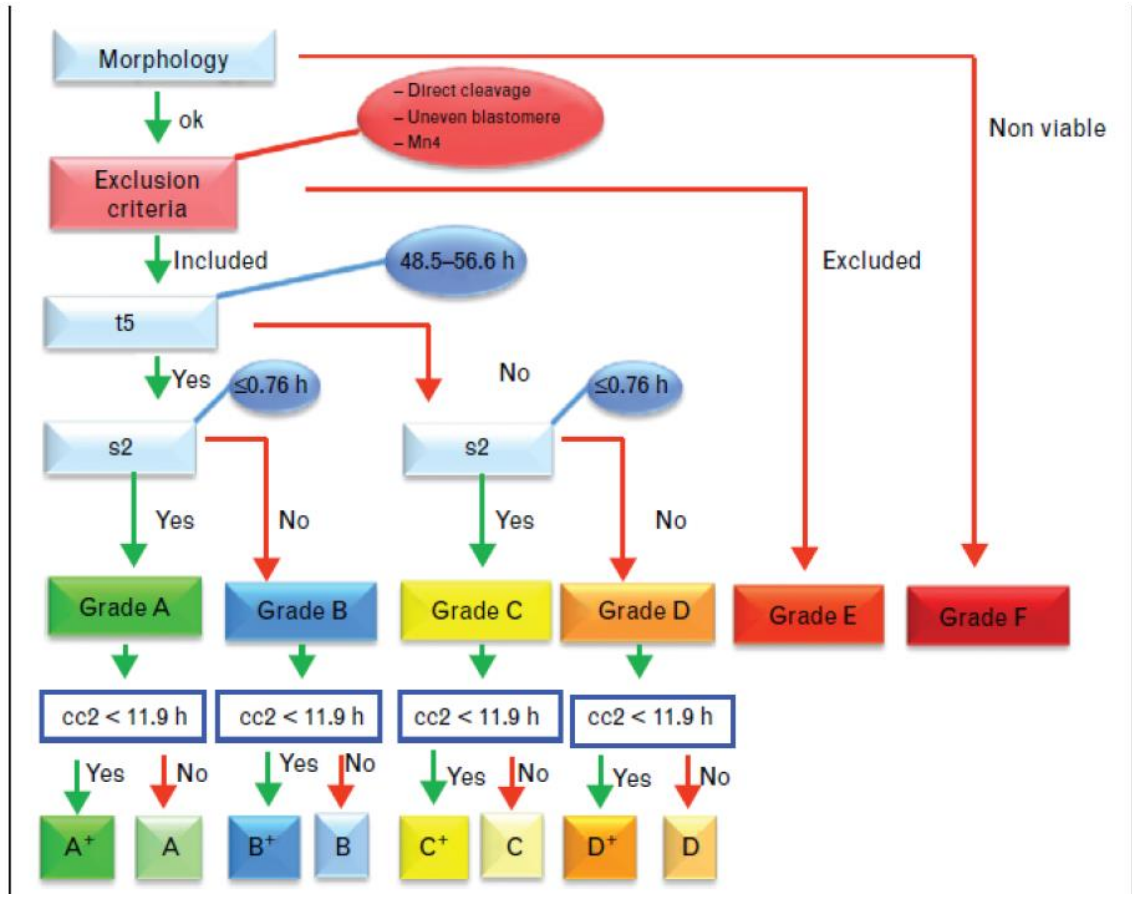
Time Lapse Monitoring

✓Stable culture condition
✓Continuous assessment
✓Dynamic evaluations




tM
81.28–96.00 h
A
t8-t5 ≤ 8.78 h
B
t8-t5 >8.79 h
A
B
C
D


Morphology
ok
- Direct cleavage
- Uneven blastomere
- Mn4
non viable
Exclusion criteria
excluded
included
34-40h
t3
yes
9-12h
no
9-12 h
cc2
cc2
yes
no
yes
no
Grade A
Grade B
Grade C
Grade D
Grade E
Grade F
t5 45–55 h
t5 45–55 h
t5 45–55 h
t5 45–55 h
yes
no
yes
no
yes
no
yes
no
A+
A
B+
B
C+
C
D+
D


Morphology
ok
– Direct cleavage
– Uneven blastomere
– Mn4
Non viable
Exclusion criteria
Excluded
Included
48.5–56.6 h
t5
Yes
≤0.76 h
No
≤0.76 h
s2
s2
Yes
No
Yes
No
Grade A
Grade B
Grade C
Grade D
Grade E
Grade F
cc2 < 11.9 h
cc2 < 11.9 h
cc2 < 11.9 h
cc2 < 11.9 h
Yes
No
Yes
No
Yes
No
Yes
No
A+
A
B+
B
C+
C
D+
D

An investigation into the effect of potential confounding patient and treatment parameters on human embryo morphokinetics

Amy Barrie, Ph.D.,[a] Garry McDowell, Ph.D.,[b] and Stephen Troup, Ph.D.[c]

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TABLE 1

Multiple regression analysis results for the effect of maternal age, maternal body mass index (BMI), suppression protocol, infertility diagnosis, and treatment type on absolute morphokinetic parameters.

	t2		t3		t4		t5		t6		t7		t8		t9		tM		tSB		tB	
	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B
Maternal age	.007[a]	−.006	.050	−.013	.007[a]	−.029	.791	−.004	.809	.004	.464	−.020	.152	−.052	.964	.001	.404	−.029	.058	.063	.043[a]	.078
Maternal BMI	.001[a]	−.009	.295	−.008	.362	−.012	.622	−.010	.093	−.037	.302	−.033	.267	−0.49	.330	−.036	.305	−.043	.133	−.060	.272	−.052
Suppression	.573	−.012	.613	−.030	.251	−.113	.754	0.47	.971	−.006	.558	−.144	.552	−.199	.625	.136	.577	.179	.843	.060	.229	.429
Infertility diagnosis																						
Ovarian	.913	−.004	.261	−.111	.866	−.028	.877	−.038	.326	−.269	.352	−.378	.928	.050	.472	.331	.863	−.091	.437	.390	.977	−.017
Uterine	.223	.045	.262	−.119	.958	−.009	.958	.014	.716	−.108	.662	.192	.173	.809	.593	.266	.494	.391	.156	.768	.204	.806
Donor	.027[a]	−.310	.019[a]	−.945	.044[a]	−1.340	.168	−1.388	.161	−1.572	.036[a]	−3.478	.230	−2.698	.021[a]	−4.343	.327	−2.121	.238	−2.419	.014[a]	−5.894
Unexplained	.571	−.019	.968	.004	.432	.123	.230	.285	.558	.155	.705	.148	.564	.306	.485	.310	.375	.454	.157	.685	.254	.647
Endocrine	.103	−.178	.802	.078	.403	.432	.385	.678	.216	1.077	.315	1.293	.220	2.140	.713	.536	.568	.960	.108	2.559	.404	1.557
Secondary	.002[a]	−.329	.418	−.250	.263	−.572	.746	−.250	.184	−1.143	.156	−1.806	.313	−1.741	.668	−.619	.013[a]	−4.137	.051	−3.069	.021[a]	−4.256
Treatment type																						
ICSI	.001[a]	−.098	.281	.087	.114	.211	.539	.124	.245	.262	.516	.216	.618	.255	.990	.005	.232	.520	.005[a]	1.157	.002[a]	1.510
IMSI	.306	−.074	.377	.184	.421	.277	.830	−.112	.512	−.381	.427	−.682	.501	−.783	.683	.397	.009[a]	2.938	.073	1.905	.210	1.560
TESE ICSI	.435	−.076	.462	.203	.811	.110	.337	.664	.275	.841	.455	.851	.373	1.378	.726	.453	.576	.831	.050	2.769	.272	1.817
D-IVF	.084	.183	.164	.422	.245	.583	.107	1.222	.514	.552	.090	2.121	.152	2.424	.024[a]	3.199	.407	1.353	.101	2.535	.007[a]	4.882
D-ICSI	.014[a]	.341	.001[a]	1.304	.084	1.137	.008[a]	2.650	.033[a]	2.367	.107	2.642	.248	2.571	.030[a]	4.036	.941	.160	.206	2.568	.099	3.930

Note: Time to two-cell (t2), three-cell (t3), four-cell (t4), five-cell (t5), six-cell (t6), seven-cell (t7), eight-cell (t8), nine-cell (t9), start of compaction (tM), blastulation (tSB), and time to full blastocyst (tB) are included. *P* values and beta coefficients (*B*) are shown for each parameter. A negative *B* indicates a decrease in the parameter in hours for every unit increase in the independent variable. ICSI = intracytoplasmic sperm injection; IMSI = intracytoplasmic morphologically selected sperm injection; TESE = testicular sperm extraction; D-IVF = donor in vitro fertilization; D-ICSI = donor ICSI.

[a] Statistically significant.

Barrie. Confounders of an embryo's morphokinetic profile. Fertil Steril 2020.

TABLE 2

Multiple regression analysis results for the effect of maternal age, maternal body mass index (BMI), suppression protocol, infertility diagnosis, and treatment type on interval morphokinetic parameters.

	cc2		cc3		cc4		s2		s3		t9-tM		tM-tSB		tSB-tB	
	P	B	P	B	P	B	P	B	P	B	P	B	P	B	P	B
Patient age	.285	−.007	.094	.025	.082	.053	.081	−.016	.141	−.048	.348	−.031	< .001[a]	.092	.454	.016
BMI	.940	.001	.904	.002	.726	.013	.759	−.003	.319	−.039	.847	−.008	.584	−.017	.736	.009
Suppression	.749	−.018	.240	.160	.236	.335	.331	−.083	.410	−.245	.886	.043	.610	−.119	.055	.369
Infertility diagnosis																
Ovarian	.260	−.107	.962	−.011	.546	.381	.556	.083	.858	.088	.392	−.422	.211	.481	.200	−.407
Uterine	.108	−.164	.924	.023	.279	−.543	.470	.110	.134	.795	.814	.125	.363	.377	.912	.038
Unexplained	.805	.023	.456	.162	.993	.004	.380	.120	.964	.021	.763	.143	.534	.231	.902	−.038
Donor[a]	.102	−.635	.958	−.048	.387	−1.645	.494	−.394	.514	−1.309	.271	2.222	.850	−.298	.007[a]	−3.475
Endocrine[a]	.394	.256	.730	.246	.277	−1.604	.430	.354	.348	1.462	.787	.424	.190	1.599	.319	−1.002
Secondary[a]	.052	−.579	.648	.322	.441	1.122	.467	−.322	.333	−1.491	.023[a]	−3.518	.375	1.068	.232	−1.188
Treatment type																
ICSI	.018[a]	.185	.636	−.087	.564	−.220	.283	.124	.802	.101	.203	.515	.044[a]	.637	.175	.353
IMSI[b]	.198	.258	.413	−.389	.230	1.180	.755	.093	.518	−.671	.015[a]	2.541	.204	−1.033	.606	−.346
TESE ICSI[b]	.296	.279	.380	.555	.479	−.924	.813	−.094	.605	.714	.785	.377	.073	1.938	.285	−.952
D-IVF[b]	.414	.239	.355	.639	.588	.776	.711	.161	.427	1.201	.224	−1.846	.318	1.182	.016[a]	2.348
D-ICSI[b]	.012[a]	.963	.096	1.513	.436	1.465	.770	−.167	.968	−.079	.052	−3.876	.121	2.408	.288	1.362

Note: Duration of second cell cycle (cc2; t3-t2), third cell cycle (cc3; t5-t4), fourth cell cycle (cc4; t9-t8), synchrony of the second cell cycle (s2; t3-t4), synchrony of the third cell cycle (s3; t8-t5), time between t9 and tM, time between tM and tSB, and time between tSB and tB are included. *P* values and beta coefficients (*B*) are shown for each parameter. A negative *B* indicates a decrease in the parameter in hours for every unit increase in the independent variable. ICSI = intracytoplasmic sperm injection; IMSI = intracytoplasmic morphologically selected sperm injection; TESE = testicular sperm extraction; D-IVF = donor in vitro fertilization; D-ICSI = donor ICSI.

[a] Statistically significant.

[b] Reduced sample size (<20 patients included).

Barrie. Confounders of an embryo's morphokinetic profile. Fertil Steril 2020.

TABLE 1 ATYPICAL PHENOTYPES OBSERVED WITH TIME-LAPSE MONITORING

Parameters	Description	References
Pronuclei formation at syngamy	Incorrect pronuclei movement in the cytoplasm.	*Coticchio et al. (2018)*
Appearance of two pronuclei Pronuclei reappearance	Asynchronous appearance and disappearance of pronuclei. Pronuclei fading and reappearance.	*Coticchio et al. (2018)* *Coticchio et al. (2019)*
Pronuclei size	Difference in pronuclear areas before pronuclear fading.	*Otsuki et al. (2017)*
Pronuclei fragmentation Pronuclei fusion	Formation of micronuclei. A pronucleus formed by the fusion of two pre-existing pronuclei.	*Mio and Maeda (2008)* *Coticchio et al. (2018)*
Unipolar cleavage furrow Tripolar cleavage furrow Pseudofurrows	Appearance of cleavage furrow on one side of the zygote. Appearance of three cleavage furrows. Zygote presenting oolemma ruffling before cytokinesis.	*Wong et al. (2010)* *Athayde Wirka et al. (2014)*
Absent cleavage Reverse cleavage	Arrest at zygote stage. Fusion of two cells into one blastomere.	*Barrie et al. (2017)* *Desai et al. (2014)*
Direct cleavage	Cleavage of zygote to three cells or one blastomere divides to three cells.	AthaydeWirka *et al.* (2014) *Barrie et al. (2017)* *Meseguer et al. (2011)*
Blastomere movement	Blastomere and cytoplasm movement before division.	*Ezoe et al. (2019)* *Coticchio et al. (2019)*
Multinucleation	Blastomere with more than one nucleus.	*Desai et al. (2014)* *Hashimoto et al. (2016)*
Internalization of cellular fragments	Fragments reabsorbed into one blastomere.	*Mio and Maeda (2008)*
Irregular chaotic division	Disordered cleavage behaviour with uneven cleavages and fragmentation.	*Athayde Wirka et al. (2014)* *Barrie et al. (2017)* *Meseguer et al. (2011)*
Early compaction	Formation of tight junctions between blastomeres in day-3 embryos.	*Iwata et al. (2014)*
Cell exclusion	Exclusion of one or more blastomeres from the morula formation.	*Coticchio et al. (2019)* Coticchio *et al.* (2021)
Spontaneous blastocyst collapse	Collapse of blastocyst with complete disappearance of blastocoel cavity.	*Marcos et al. (2015)* *Sciorio et al. (2020a)* *Sciorio et al. (2020b)*

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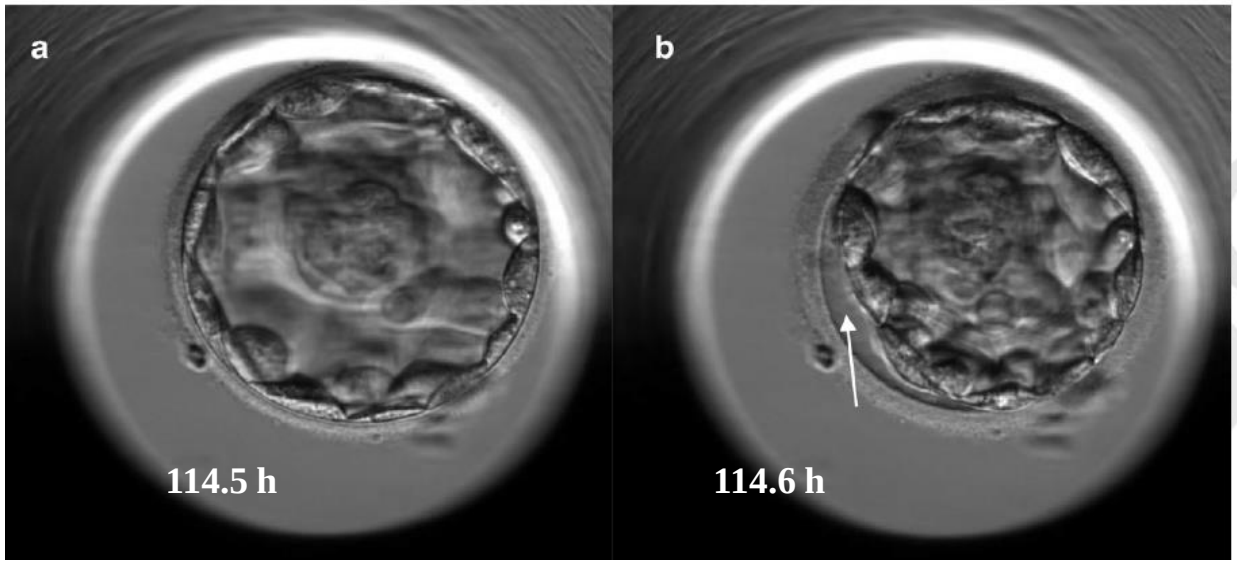
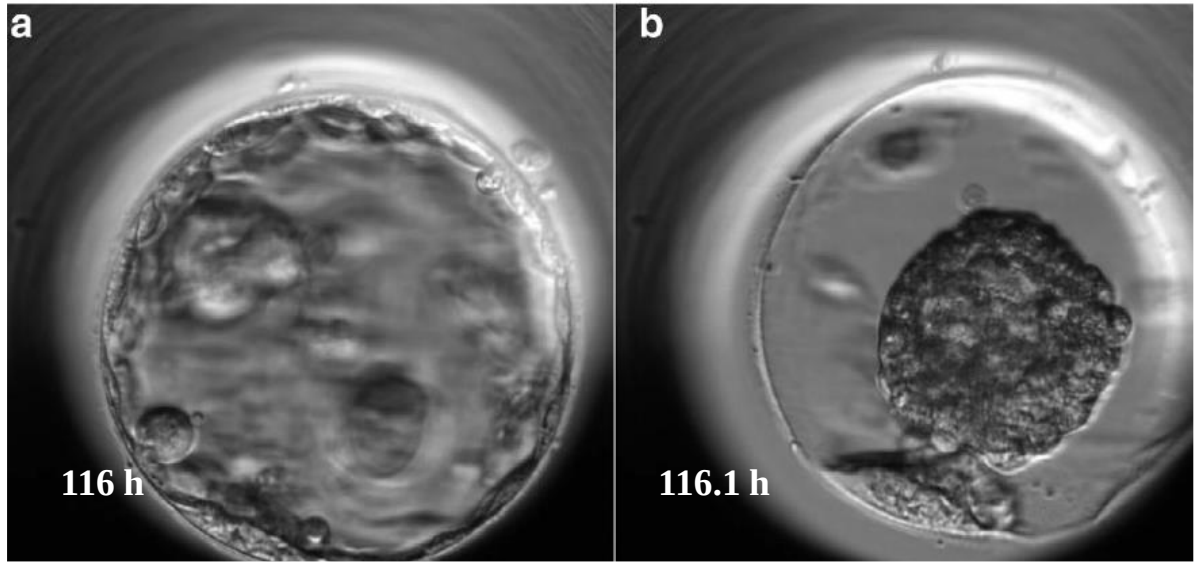
ARTICLE

Focus on time-lapse analysis: blastocyst collapse and morphometric assessment as new features of embryo viability





Faster fertilization and cleavage kinetics reflect competence to achieve a live birth after intracytoplasmic sperm injection, but this association fades with maternal age

Mariabeatrice Dal Canto, Ph.D.,[a] Alessandro Bartolacci, B.S.,[a] Diana Turchi, B.S.,[a] Daniela Pignataro, Ph.D.,[a] Monia Lain, B.S.,[a] Elena De Ponti, B.S.,[b] Claudio Brigante, M.D.,[a] Mario Mignini Renzini, M.D.,[a] and Jose Buratini, Ph.D.[a,c]

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Journal of Assisted Reproduction and Genetics
https://doi.org/10.1007/s10815-021-02172-7

EMBRYO BIOLOGY

Check for updates

Migration speed of nucleolus precursor bodies in human male pronuclei: a novel parameter for predicting live birth

Taketo Inoue[1,2] · Sayumi Taguchi[1] · Mikiko Uemura[3] · Yoshiko Tsujimoto[1] · Kazunori Miyazaki[1] · Yoshiki Yamashita[1]

Received: 12 November 2020 / Accepted: 22 March 2021

Artificial intelligence & Time Lapse

Journal of Assisted Reproduction and Genetics
https://doi.org/10.1007/s10815-020-01881-9

REVIEW

Artificial intelligence in the IVF laboratory: overview through the application of different types of algorithms for the classification of reproductive data

Eleonora Inácio Fernandez[1] · André Satoshi Ferreira[1] · Matheus Henrique Miquelão Cecílio[1] · Dóris Spinosa Chéles[1,2] · Rebeca Colauto Milanezi de Souza[1] · Marcelo Fábio Gouveia Nogueira[2] · José Celso Rocha[1,3]

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Deep learning neural network analysis of human blastocyst expansion from time-lapse image files

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Evaluation of artificial intelligence using time-lapse images of IVF embryos to predict live birth

TABLE 2 LIVE BIRTH RATES FOR THE COMBINATION OF CONVENTIONAL MORPHOLOGICAL EVALUATION AND THE ARTIFICIAL INTELLIGENCE SYSTEM

Embryo evaluation	Live birth rate % (*n*/*N*)
Embryos with good morphological quality and CS ≥0.341	41.1 (23/56)
Embryos with poor morphological quality and CS ≥0.341	23.3 (20/86)
Embryos with good morphological quality and CS <0.341	20.2 (21/104)
Embryos with poor morphological quality and CS <0.341	6.9 (9/130)

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REPRODUCTIVE BIOMEDICINE ONLINE

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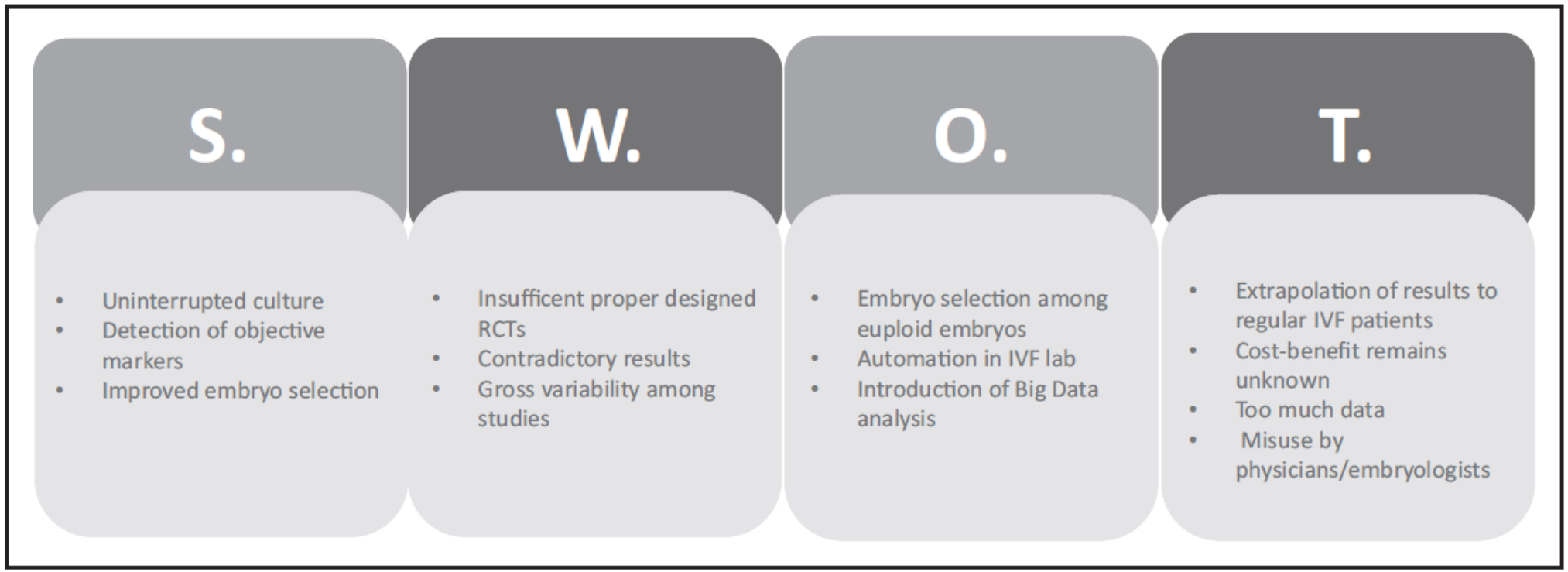
ARTICLE | VOLUME 42, ISSUE 2, P340-350, FEBRUARY 01, 2021

An artificial intelligence model based on the proteomic profile of euploid embryos and blastocyst morphology: a preliminary study

Lorena Bori • Francisco Dominguez • Eleonora Inacio Fernandez • ... Marcelo Fabio Gouveia Nogueira • Jose Celso Rocha • Marcos Meseguer • Show all authors

Published: October 07, 2020 • DOI: https://doi.org/10.1016/j.rbmo.2020.09.031 •



A summary of the Strength, Weaknesses, Opportunities and Threats of using a time-lapse system for embryo culture in the IVF laboratory.

Summary

✓Different algorithms have been developed correlating embryo kinetics to blastocyst formation, implantation potential, chromosomal content and live birth rate.

✓ We are still in the early stages of learning how to analyze time-lapse results to take proper advantage of this technology for the real benefit of the patients.

✓ Automation and the use of artificial intelligence have recently been introduced to improve this technology.

- Evidence on clinical benefit is still lacking
- Lack of prospective multicenter validation