

Disclosure

- Scientific advisor for Vitrolife and Alife
- Travel/lecture fee Ferring, IBSA, Gedeon Richter, Organon
- Associate editor Human reproduction update

Intro: *why* do we evaluate embryos?

- Because we are paid for it !?!
- To rank and prioritize embryos within a cohort
- To discard non viable embryos



Intro: *how* do we evaluate embryos?

- Static morphology
- Dynamic morphology - morphokinetics
- PGT-A
- AI
- others



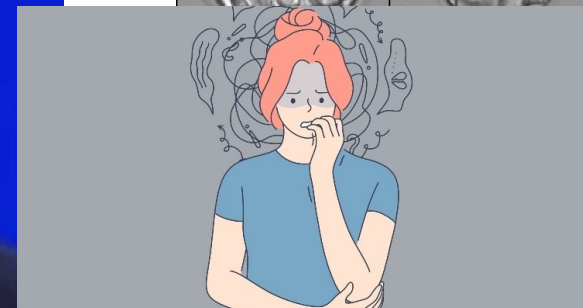
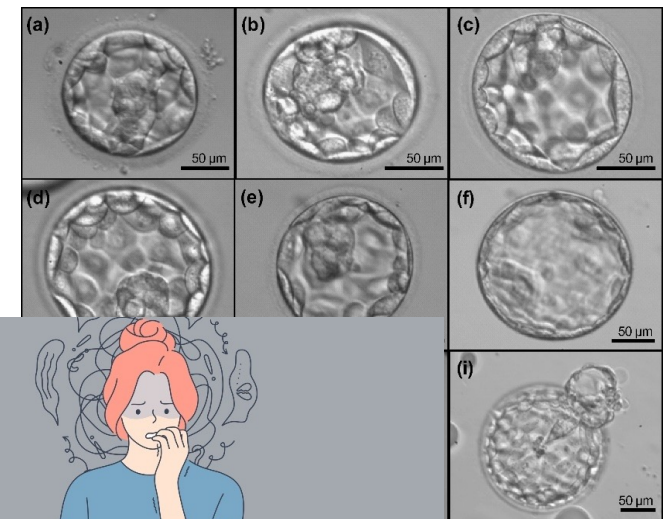
What is the ultimate goal of embryo quality assessment?



- Inform and counsel patients / doctors
- And tend towards the best outcomes :
 - shorten time-to-pregnancy
 - and increase cumulative live birth rate
 - with the lowest risk
 - avoiding drop-out

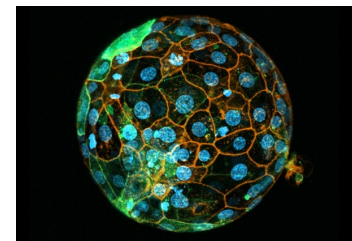
Extended culture up to the blastocyst stage is the gold standard in clinical practice

- But what about co-culture blastocysts?
- And what about patients' information and counselling throughout embryo culture?



The current limitations of embryo morphology, and other conventional quality assessment methods

- They could mostly be used as ranking tools, not as deterministic indicators of viability
- Their respective predictive power is at best correct, except in rare cases (complete aneuploidy, developmental arrest)
- The biological mechanisms underlying embryo development are still poorly understood (cell fate, mosaicism, metabolism etc...)



Question?

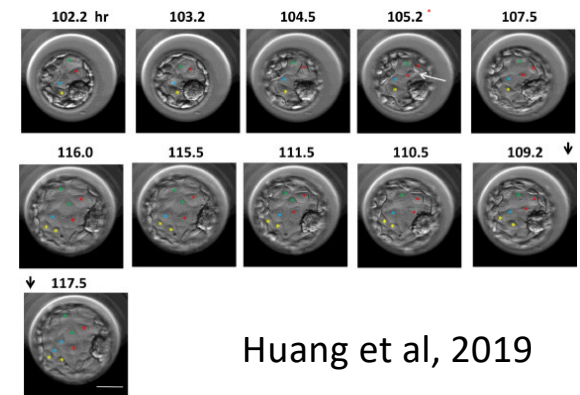
Should we go deeper into embryo characteristics and maximize information, or step back and use a minimalist approach to avoid any disturbance of the embryo?



I am an advocate for the maximalist approach in order to improve our ability to inform patients and provide the best outcomes

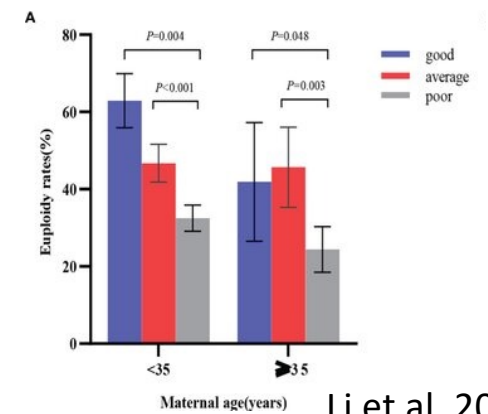
Why we need more information than just fertilization check and blastocyst morphology?

- Static morphology is poorly representative of developmental events and dynamics
 - Time lapse helps decoding the time frame of embryo development



Huang et al, 2019

- Morphology is poorly predictive of euploidy status
 - PGT-A might bring additional insights



Beyond static morphology: the devil is in the details






- Fertilization
- Abnormal cleavage
- Developmental dynamics

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human
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MINI-REVIEW *Developments in reproductive biology and medicine*

Fertilization signatures as biomarkers of embryo quality




Giovanni Coticchio ¹, Andrea Borini ¹, Carlotta Zacà ¹, Evangelos Makrakis ², and Ioannis Sfontouris ²

Journal of
Clinical Medicine



Article

Cleavage Patterns of 9600 Embryos: The Importance of Irregular Cleavage

Maya Shavit ^{1,2,*}, Daniel Gonen ², Yuval Atzmon ^{1,2}, Nardin Aslih ^{1,2}, Asaf Bilgory ^{1,2} , Yasmin Shibli Abu-Raya ^{1,2}, Moamina Sharqawi ^{1,2}, Daniela Estrada Garcia ¹ , Mediea Michaeli ¹, Diana Polotov ¹ and Einat Shalom-Paz ^{1,2} 








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<https://doi.org/10.1093/humrep/deae239>
Advance Access Publication Date: October 25, 2024
Original Article

Embryology

Time will tell: time-lapse technology and artificial intelligence to set time cut-offs indicating embryo incompetence

Giovanni Coticchio ^{1,*}, Alessandro Bartolacci^{2,9}, Valentino Cimadomo³, Samuele Trio⁴, Federica Innocenti ⁵, Andrea Borini ⁶, Alberto Vaiarelli ⁷, Laura Rienzi ^{5,7}, Aisling Ahlström ⁸, and Danilo Cimadomo ⁵

The need to shorten time-to-pregnancy (and maintain CLBR)

- ‘The main goal of an IVF treatment is for patients to bring home a healthy baby in the shortest period of time with the lowest number of embryo transfers performed.’
- Patients want to know their real chances to conceive a baby at the first attempt.
- This goal is relevant for specific interventions that will improve the success rate in terms of live birth at the first attempt, even if there will be no change in the CLBR.

INKLINGS

Time to pregnancy: as important for patients as underestimated by doctors

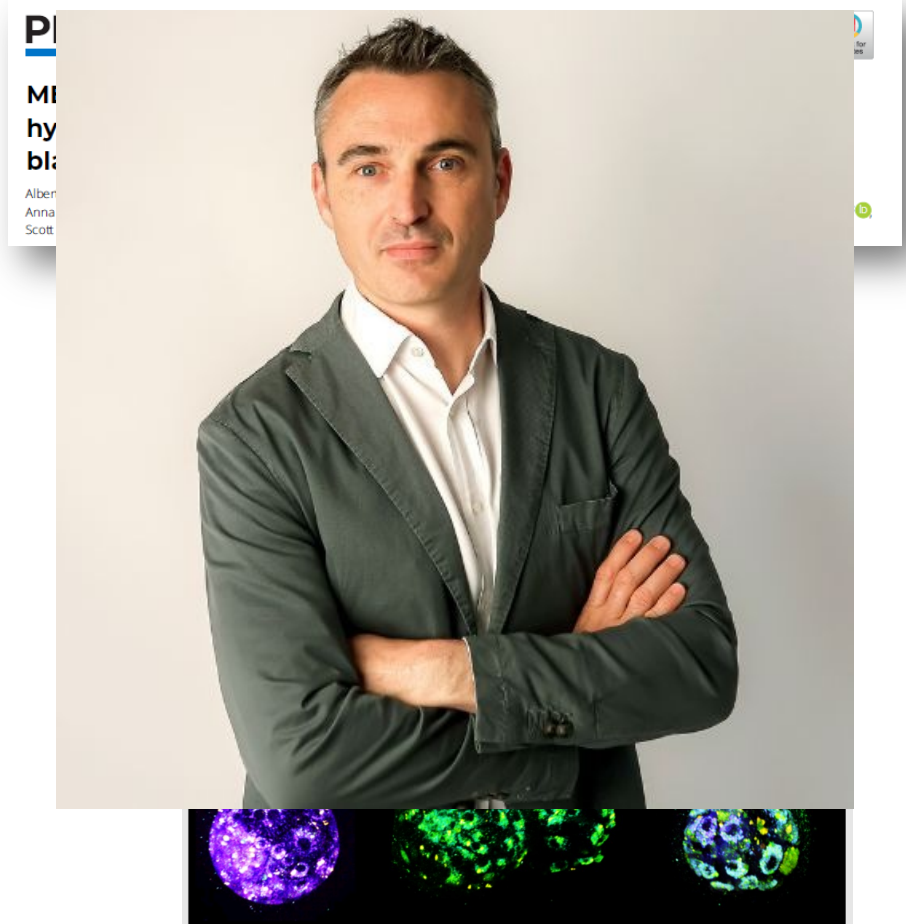
Roque & Simon, 2020

The next chapter: science to go further

The example of embryo metabolism

Recent development of label-free methods to evaluate directly human preimplantation embryo metabolism

- Variations in metabolic signatures between ICM and TE, association with embryo day and expansion
- substantial embryo-to-embryo variability but not associated with variations in morphology
- enhanced resolution for distinguishing morphologically similar embryos with varying physiological statuses, improving classification as compared to embryologists



Discussion

Should we implement *all* innovations?

- Not all add-ons are relevant clinically
- Beware of ‘fashion effect’
- Need for proper validation



Discussion

Is maximalist approach time-consuming?

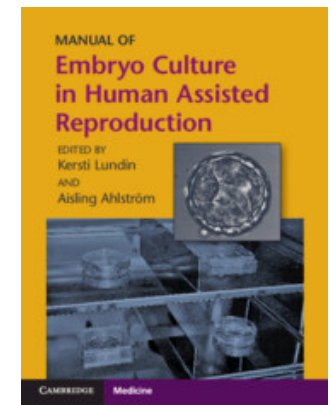
- All embryo quality assessment methods, including morphology assessment, take time
- But...
- Morphology assessment and morphokinetic annotation can be automated
- AI tools work in full autonomy



This debate needs to be transparent and honest

Do you know the author of these words?

- In the chapter “*From Identification to Witnessing: Traceability to Ensure the Safety of the Embryo during Culture*”, the authors describes embryo culture period (up to 6–7 days) with **repeated assessment and manipulation, highlighting the need for careful monitoring and tracking of embryos during development**
- “Het ivf-labo blijft continu investeren in nieuwe technologie. Een voorbeeld zijn de ‘**time lapse**’- incubatoren, die ons in staat stellen om de morfologische kwaliteit van de embryo’s te evalueren zonder dat we het schaalpje uit de incubator hoeven te halen.”



Conclusion & take-home message

- No embryo quality assessment methods will ever improve embryo quality intrinsically, and add-ons should be considered carefully
- But our duty is to inform patients transparently and tend towards the best outcome, i.e. shorten time-to-pregnancy and increase cumulative live birth rate with low risk
- In this respect, evaluating and ranking embryos with all the available and validated tools participates in the P4 medicine policy



'Minimalist approach' in UZ Gent in the afternoon

