Talk/Debate -

AI use in ART: Is it Artificial or Intelligent?

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Disclosures

- Ravi Gada
 - O Owner/Co-Owner Founder/Co-Founder: ReUnite Rx
- Ilan Tur-Kaspa
 - Consulting Fee (e.g., Advisory Board): Ferring Pharmaceutical
 - Stock Option Holder (Individual stocks/Stock options; diversified mutual funds do not need to be disclosed): Embryonics Ltd, Israel
- Charlie Bormann
 - \odot $\,$ Nothing to Disclose

Learning Objectives

- 1) Demonstrate knowledge of AI potential use in Reproductive Medicine.
- 2) Use AI assisted decision making tools.
- 3) Integrate AI tools in clinic and and IVF Lab specific practices to improve ART outcome.

Repro-Al to optimize ART outcome

Repro-AI is defined as the interdisciplinary technology between reproductive medicine and mathematical sciences to advance the applications of AI in the diagnosis and treatment of infertility.

Debate - AI Use in ART: Is It Artificial or Intelligent? Pros and Cons

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Should humans improve their intelligence instead of AI ?

Repro-Al to optimize ART outcome

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PCRS 2024

Al to optimize IVF outcome

Disclosures – no financial conflict of interests

- Past Head, Medical Advisory Board, 2/2021-9/2023, for Embryonics, Ltd, an AI startup developing and applying AI data-driven solutions to improve IVF outcome.
- Pinnacle fertility, USA PI, Pinnacle AI Study Group
- Ferring Advisory Boards, 2022-2023



Needs Assessment and Expected Learning Outcomes

1. The participant should be able to describe AI potential use in Reproductive Medicine.

2. The participant should be able to to experiment the management of ART patients with AI assisted decision making tools.

3. The participant should be able to objectively select AI tools for clinical and Lab setup to improve ART outcome.

Artificial Intelligent (AI) is everywhere

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"Classical" Al Machine Learning



A Human defines how to identify a BRAD

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Model "training"-Feature Engineering:

An Expert defines what are the important features and a BRAD "map" is extracted from previous examples. <70% accuracy

AI Deep learning - How is it different than classical models?

Hint: no feature engineering

BRAD or Not BRAD?





Model "training" -The model "sees" samples of BRAD and Not BRAD and learns it's own important feature for identification >99.9% accuracy

Published medical AI studies grew by 2,400% in last decade

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Meskó, B., Görög, M, npj Digit. Med 2022. Attia Z. et al., The Lancet, 2019. Elul Y. et al., PNAS, 2021. Shamai G. et al, JAMA Network 2021. Choi S. Y. et. al. Medicine (Baltimore), 2021

Daniel Kahneman. Nobel Prize in Economics in 2002

How human judgment may take heuristic shortcuts that systematically depart from basic principles of probability



The Knowledge Funnel



"Whenever there is judgment, there is noise"

Why AI in ART?

- Simultaneous objective, accurate, and rapid assessment of relevant variables
- Precision, standardization, and automation
- Minimal training needed
- May provide guidance in clinical decisions
- Al for image analysis: embryos, sperm, oocytes, and ultrasound pictures.
- Key for success: combining knowledge of Fertility Experts with AI scientists [Repro-AI]

Clinical	Lab
Diagnosis	Sperm - diagnosis and treatment
Treatment plan – protocol, dosage	Oocyte – prognosis
Cycle monitoring, trigger, ai ER test	Embryo – selection, aiPGT, prediction

Canis et al, Fert Steril, Adenomyosis, 2018; Liao S et al, JAMA Netw Open. 2020; Letterie G 2021; Tur-Kaspa et al, 2022

AI to assist in individualized FSH starting dose for IVF AI for the optimal day of trigger during COS for IVF



Dose response curve generated for each participant using 100 nearest neighbors matched by age, BMI, AMH and AFC. **Dose-responsive group (1/3):** With optimal FSH starting dose, patients had 1.5 more MII oocytes, and 0.6 more ALIFE Stim Assist **Cycle Clarity** Fanton et al, F&S 2022

Fanton et al, RBMO 2022

- Retrospective multicenter of 30,278 IVF cycles (2014-2020).
- Patients with early or late triggers compared with matched patients with on-time triggers, had on average 2.5 fewer MII oocytes and 0.9 fewer usable blastocysts



Stim Day

-1000

AI, Deep neural network with Geometric Layers, to Optimize Ovarian Stimulation for IVF: From Stimulation Protocols to Mature Oocyte Yield

- Study Question: Can AI, using patient demographics, routine preliminary blood tests and AFC assist in choosing the optimal controlled ovarian stimulation (COS) to maximize mature oocyte yield and enhance IVF success?
- Used IHR.

Mean average error (MAE) for the AI was 3.5, far superior to classical models

Mean Absolute Error for Al Model Compared to Random



Mean Absolute Error (MAE), representing average expected deviation from the true value of three models: a random model where actual mature oocyte yields from the data set were randomly ascribed to a patient; a linear prediction model; and the deep learning network model, which was significantly more accurate.

Tur-Kaspa et al, ESHRE, July 2022

Personalized Fertility Calculator (PFC)

- Fertility preservation is on the rise.
- Young healthy women are turning to online resources to educate themselves and planning for the future.
- Better prediction means better planning.
- Data driven literature integration is a way to gap between outcomes of infertility treatments and fertility preservation cycles.

Aviram T, Silver DH, Rosentraub S, Fordham D, **Tur-Kaspa I.** An AI based Personalized Fertility Calculator (PFC) to Assist Decision-making Before Oocyte Cryopreservation. ISFP 2022

"I would've given anything if someone had said to me, 'Freeze your eggs. Do yourself a favor."

 Do yourself a favor."

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Jennifer Aniston Has Nothing to Hide

JENNIFER ANISTON HAS SPENT MOST OF HER ADULT LIFE IN THE SPOTLIGHT, WITH ALL ITS GLARE. AT 53, SHE OPENS UP ABOUT HER PATH TO LEAVING REGRETS AND SOME DEEPLY PERSONAL PAIN BEHIND.

BY: **DANIELLE PERGAMENT** PHOTOGRAPHED BY: **ZOEY GROSSMAN**

Personalized Fertility Calculator (PFC)

- Evidence based patient education resources
- Oocyte yield per cycle
- Pprobability of live birth per number of mature cryopreserved oocytes.

Aviram T, Silver DH, Rosentraub S, Fordham D, **Tur-Kaspa I**. An AI based Personalized Fertility Calculator (PFC) to Assist Decision-making Before Oocyte Cryopreservation. ISFP 2022.





Ultrasound and Endometrial Receptivity

AI and Endometrial Receptivity = aiER

Tur-Kaspa et al, in preparation

Objective: To compare Al interpretation of US images with ER test results and with ET/FET outcomes

- The ability of Ultrasound to determine Endometrial Receptivity is poor. (Human Repro Update 2019)
- There is a drive to incorporate AI techniques used in other areas of radiology to improve the efficacy of US in this area.



Endometrial receptivity

Ethical & Patients' privacy considerations

Al in IVF an assistive technology



• Al to assist or taking control in the decision making:

what if the AI and the clinician disagree?

• Liability: no change

1. when medical/lab decision is based on an AI product

2. when AI is NOT used to assist in medical/lab decision

• HIPAA and data privacy of large datasets -Secure large data-sharing by blockchain ?

Vayena et al, 2018; Char et al, 2018; Price et al, 2019; You et al, 2021; Duffourc et al. JAMA 2024

The Future of IVF



Carol Lynn Curchoe, Ph.D., Jonas Malmsten, M.S., D.P.S., Charles Bormann, Ph.D., Hadi Shafiee, Ph.D., Adolfo Flores-Saiffe Farias, M.Sc., Ph.D.,eGerardo Mendizabal, Ph.D.,Alejandro Chavez-Badiola, M.D., Alexandros Sigaras, M.S.,h Hoor Alshubbar, M.Sc.,i,j Jerome Chambost, M.Sc.,i Celine Jacques, Ph.D.,i Chris-Alexandre Pena, M.Sc.,i Andrew Drakeley, M.B.Ch.B., M.D.,k Thomas Freour, Pharm.D., Ph.D., Iman Hajirasouliha, Ph.D.,h Cristina Fontes Lindemann Hickman, Ph.D., Olivier Elemento, Ph.D.,h Nikica Zaninovic, Ph.D., and Zev Rosenwaks, M.D., Predictive modeling in reproductive medicine: Where will the future of artificial intelligence research take us? Fertil Steril, 2020

Please show me that your AI is better than my HI ..!

Pinnacle AI Study Group



Thank you

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