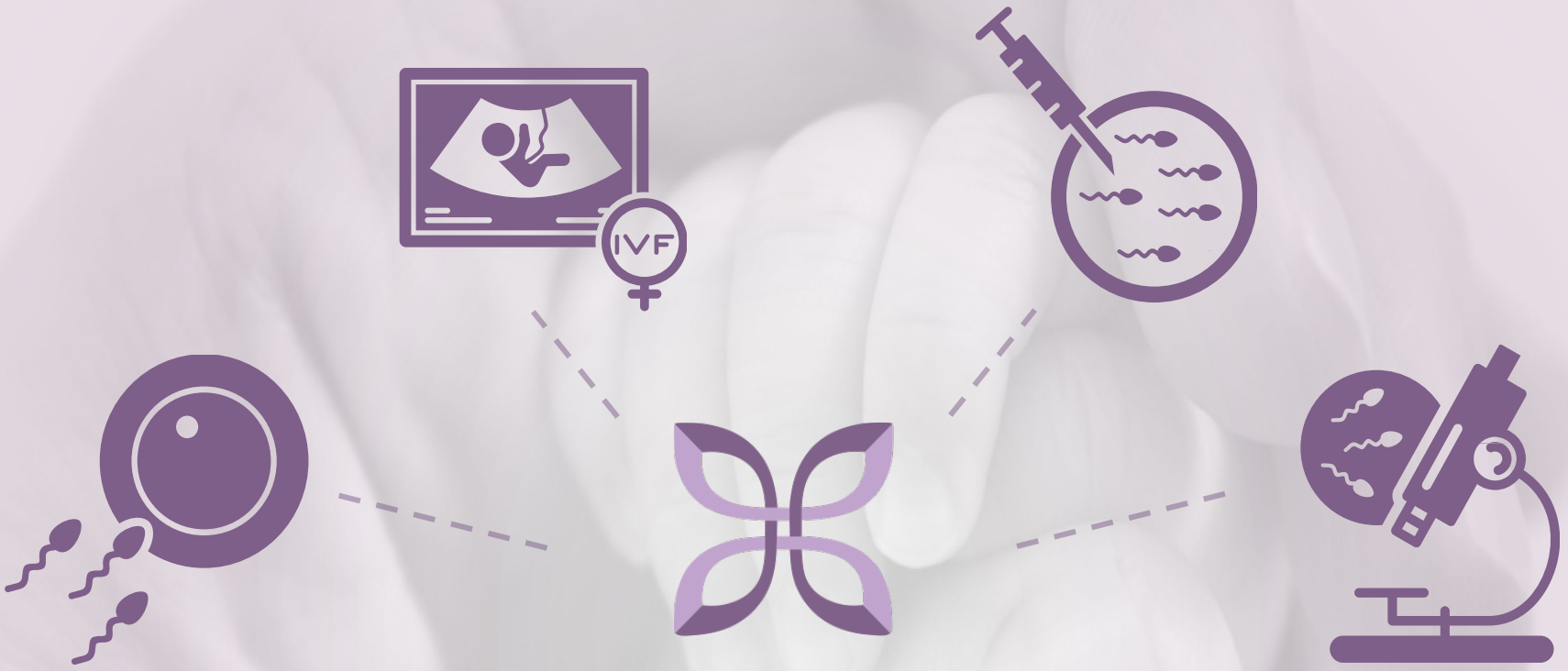

Embryo Sex Identification Through Non-Invasive Artificial Intelligence (AI) Algorithm

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RSI REPRODUCTIVE SOLUTIONS

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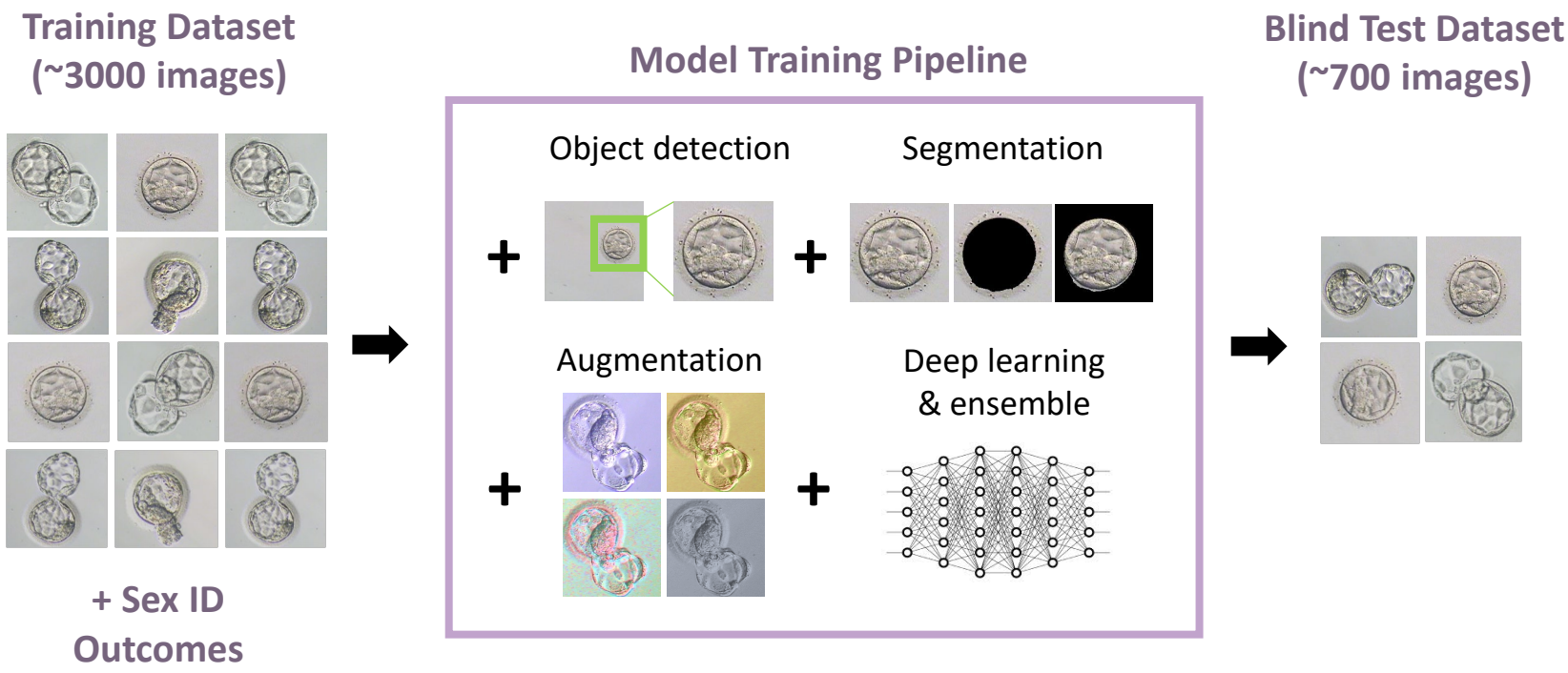
Background

- **Research question:** Is it possible to identify the sex of the embryo via AI-based analysis of morphology at day 5?
- Traditionally, sex selection in the USA is performed by PGT-A
  - 42% of IVF clinics that perform PGT-A use the results for non-medical sex selection (Baruch S, et al. Fertil Steril. 2008 May; 89(5):1053-1058)
- Is it theoretically possible that sex will be identifiable based on embryo morphology at day 5?
  - Evidence that X-chromosome inactivation occurs from 8-cell stage on Day 3 (X-chromosome inactivation: Petropoulos, et al. Cell. 2016 May 5; 165(4):1012-26.)
  - Evidence that Y-chromosome genes are expressed from Day 4 (mRNA) (Y-chromosome genes: Moreira de Mello, et al. Sci Rep. 2017 Sep 7; 7(1):10794)

Computer vision-based artificial intelligence model (deep learning) for identifying sex from single, 2D images of blastocysts at day 5 post-insemination

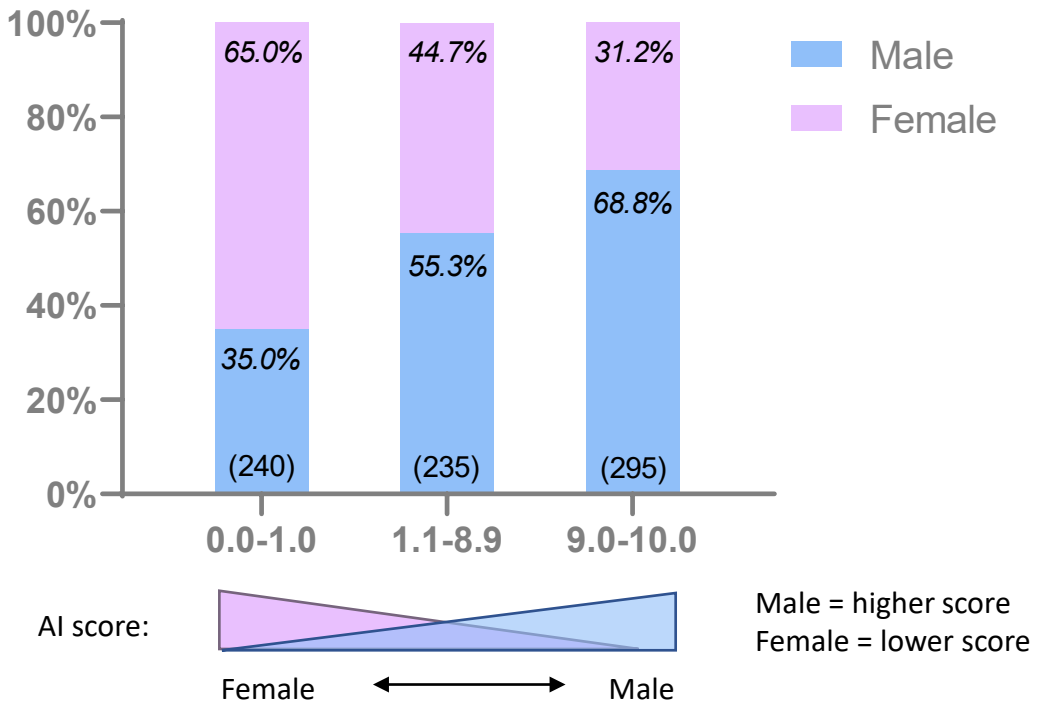
Development of an AI for sex identification



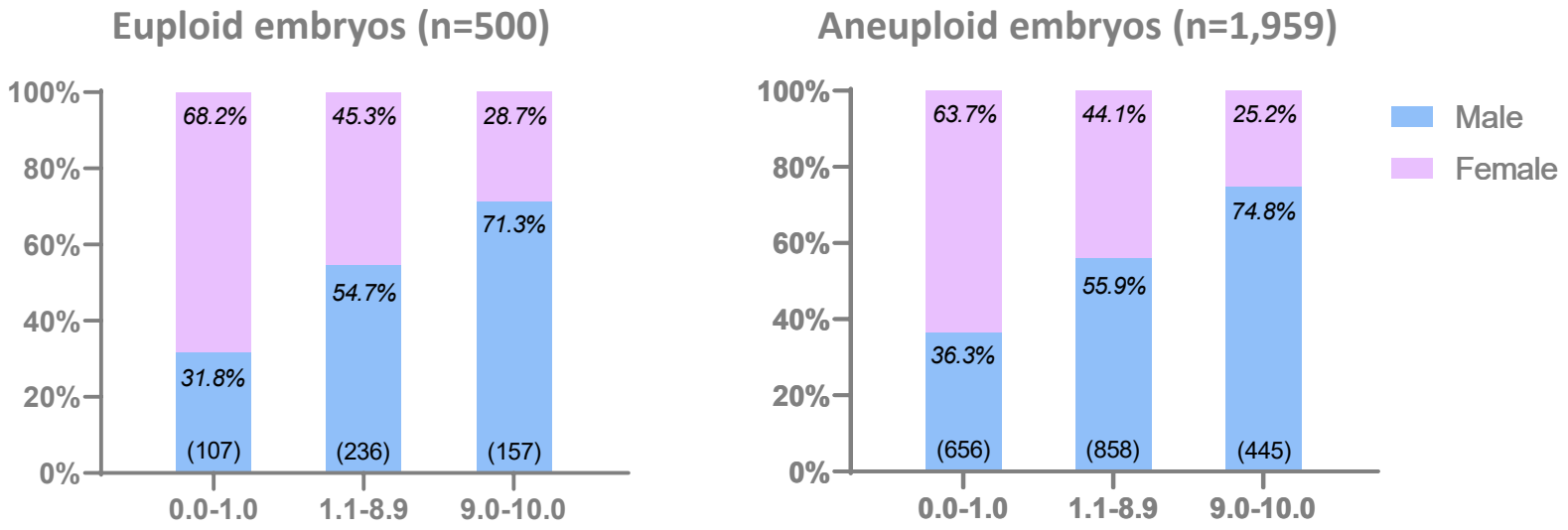
- AI development methods:
  - VerMilyea M, et al. *Hum Reprod*. **2020** Apr 28;35(4):770-784. doi: 10.1093/humrep/deaa013.
  - Diakiw SM, et al. *Hum Reprod*. **2022** Jul 30;37(8):1746-1759. doi: 10.1093/humrep/deac131.

AI score correlates with the probability of sex ID

- AI score from 0.0 (female) to 10.0 (male)
- Images divided by score: ~1/3 embryos in each group
- 65.8% of embryos were FEMALE when scored 0-1 by the AI
- 68.1% of embryos were MALE when scored 9-10 by the AI
- Chi-square p<0.0001

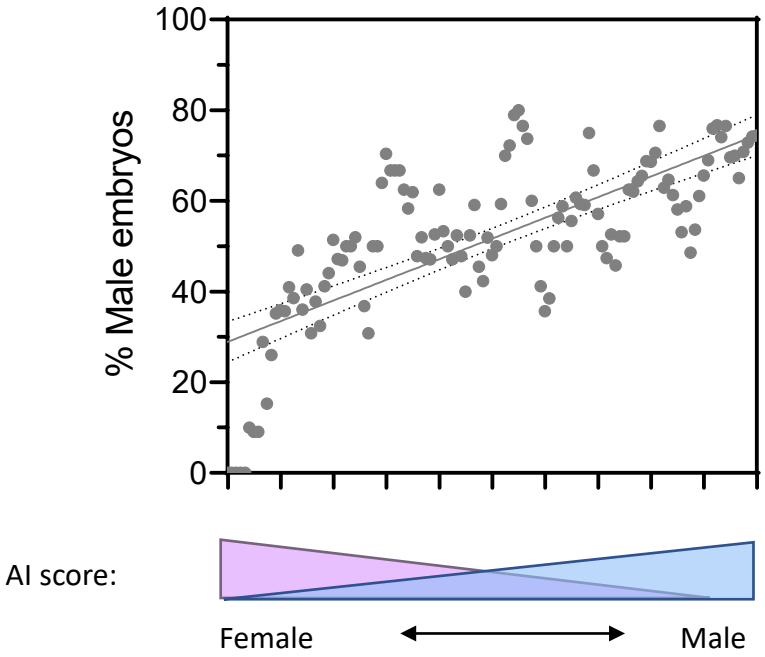


Sex ID AI works on euploid and aneuploid embryos



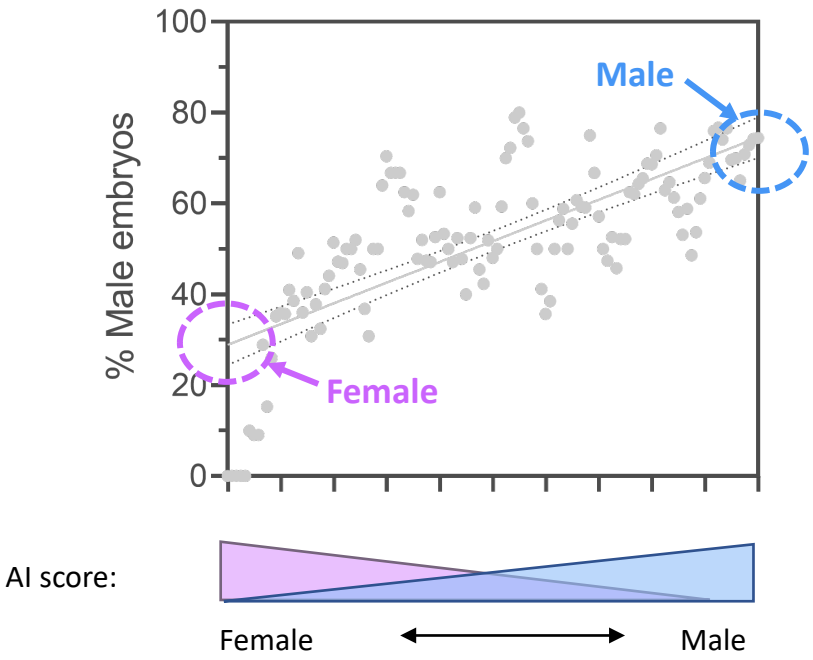
- Significant correlation between score and sex ID on euploid and aneuploid embryos
- Most likely to be applicable when sex isn't known through PGT-A

Linear correlation of AI score with sex ID



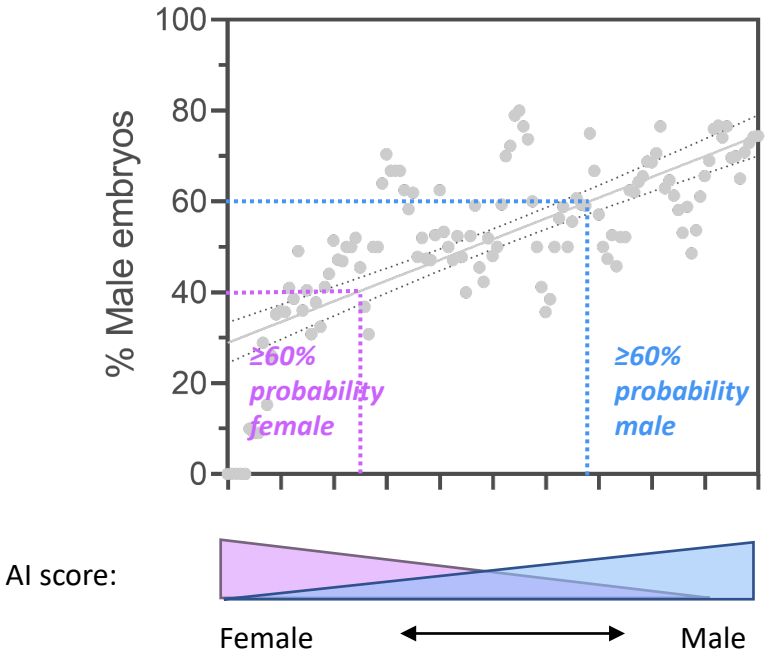
- Significant linear correlation between AI score and sex ID
- Slope = +3.840, R^2 = 0.5330

Linear correlation of AI score with sex ID



- Significant linear correlation between AI score and sex ID
- Slope = +3.840, R^2 = 0.5330
- Minimum score = 71% female (29% male)
- Maximum score = 75% male

Linear correlation of AI score with sex ID



- ¾ of embryo images have ≥ 60% probability of being either male or female
- ¼ images the AI is less certain

- Significant linear correlation between AI score and sex ID
- Slope = +3.840, R^2 = 0.5330
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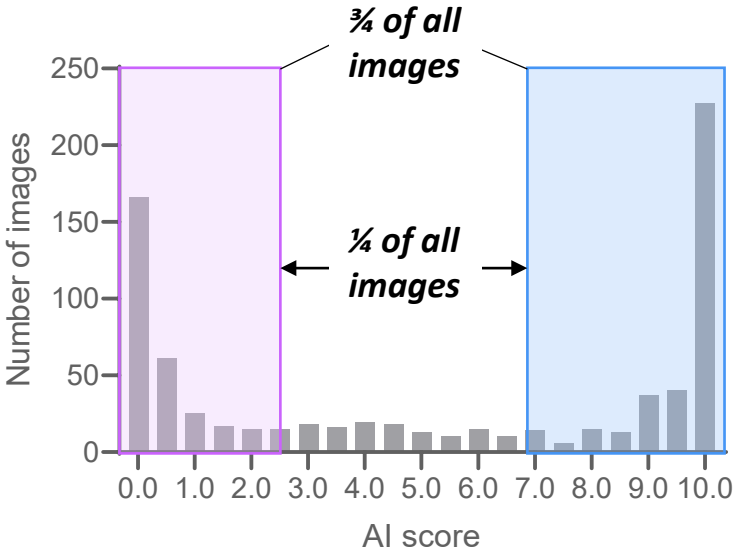
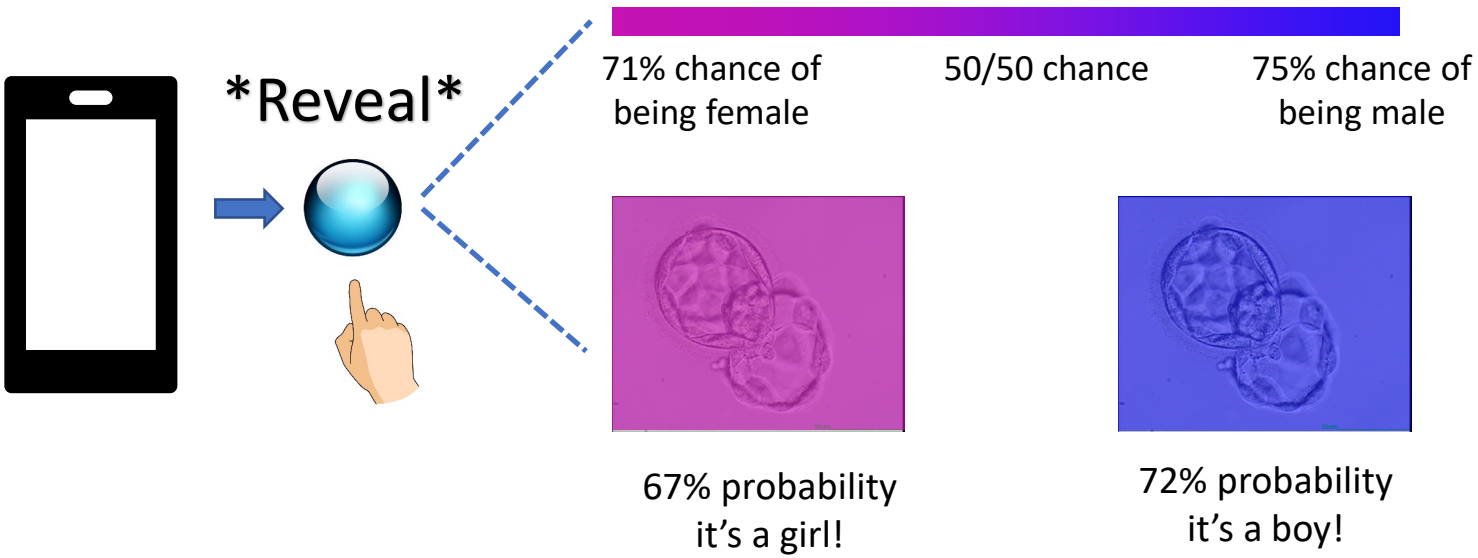


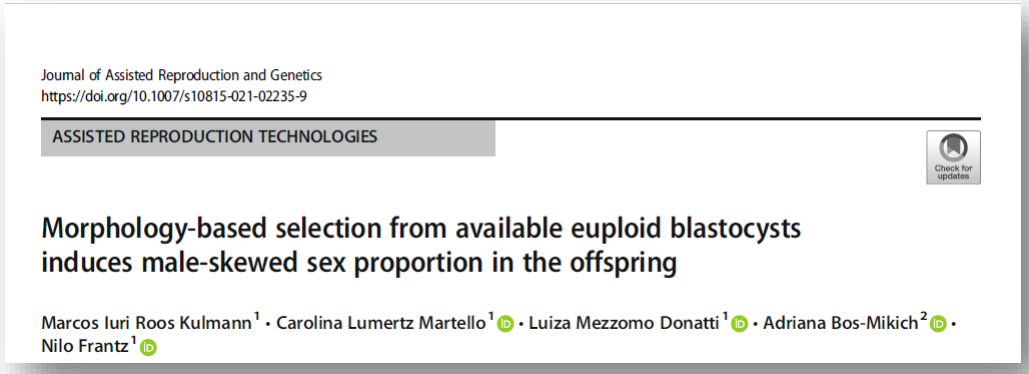
Clinical applicability?

- Sex selection
  - Even at the extreme ends of the AI score scale, there is still a ~25-30% chance that the AI is incorrect
  - Use in countries where genetic testing for sex selection is prohibited?
- Gender reveal
  - Probability of sex ID revealed after embryo transferred (patient app)



Clinical applicability?

- Bias mitigation
  - Male embryos develop faster than female embryos (cavitate earlier, reach blastocyst stage earlier, have a higher number of trophectoderm cells)
  - Is IVF biased towards a higher proportion of males being born? Yes → approximately 55% male to 45% female live births (Dean JH, et al. BJOG. 2010 Dec; 117(13):1628-34)
  - Could an AI for sex ID redress this imbalance?



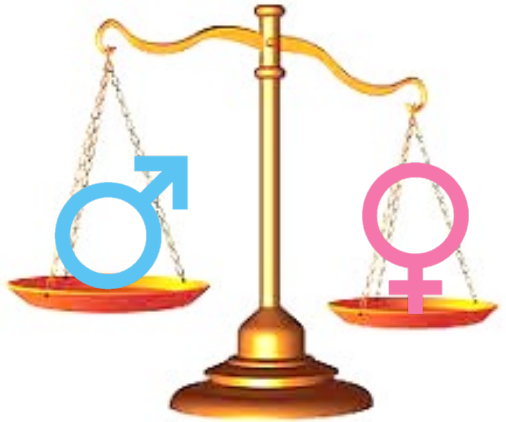
Journal of Assisted Reproduction and Genetics
https://doi.org/10.1007/s10815-021-02235-9

ASSISTED REPRODUCTION TECHNOLOGIES

Check for updates

Morphology-based selection from available euploid blastocysts induces male-skewed sex proportion in the offspring

Marcos Iuri Roos Kulmann[1] · Carolina Lumertz Martello[1] · Luiza Mezzomo Donatti[1] · Adriana Bos-Mikich[2] · Nilo Frantz[1]



Future Embryologist…