# A NON-INVASIVE ARTIFICIAL INTELLIGENCE (AI) ALGORITHM FOR ASSESSING EUPLOIDY OF BLASTOCYSTS CAN BE USED TO PREDICT LIVE BIRTH REGARDLESS OF WHETHER PGT-A WAS PERFORMED

**Authors:** VerMilyea, MD (1,2), Diakiw, SM (2), Hall, JMM (3,4,5), Nguyen, TV (3), Storr, A (6), Giménez (7), Meseguer M (8), Perugini, D (3), Perugini, M (3,9)

**Affiliations:** (1) Ovation Fertility, Austin TX 78731, USA; (2) Texas Fertility Center, Austin TX 78731, USA (3) Life Whisperer Diagnostics (a subsidiary of Presagen), San Francisco CA 94404, USA, and Adelaide SA 5000, Australia; (4) Australian Research Council Centre of Excellence for Nanoscale BioPhotonics, Adelaide SA 5005, Australia; (5) School of Physical Sciences, The University of Adelaide, Adelaide SA 5005 Australia; (6) Flinders Fertility, Glenelg SA 5045, Australia; (7) IVI Foundation - La Fe Health Research Institute - IVIRMA Valencia, IVIRMA Valencia, Research and Innovation, València 46004, Spain; (8) IVIRMA Valencia, IVF Laboratory, València 46004, Spain; (9) Adelaide Medical School, The University of Adelaide, Adelaide SA 5000, Australia

**Background:**

Development of non-invasive technologies for evaluating the ploidy status of embryos during IVF is of great importance in the field to help improve live birth outcomes. Currently, the gold standard for assessing ploidy is invasive pre-implantation genetic testing for aneuploidies (PGT-A), which relies on the skill of the embryologist to perform biopsies, and advanced genome sequencing technologies to identify chromosomal copy numbers.

**Objective:**

To investigate whether a non-invasive, image-based AI algorithm for evaluating embryo euploidy[1] is predictive of live birth for embryos of unknown ploidy status (did not undergo PGT-A), as well as those known to be euploid according to PGT-A results.

**Materials and Methods:**

A total of 1898 2-d Day 5 embryo images with known live birth outcomes were collected from patients treated between 2015 and 2023 at 4 IVF clinics in the USA, Spain, and Australia. A dataset of 1472 images was initially collected where PGT-A status was not known for all embryos (live birth rate 40%). Additional data was collected to form an expanded dataset of 1649 images of embryos where PGT-A was not performed (live birth rate 30%), and a dataset of 122 images of embryos where PGT-A was performed (live birth rate 50%). The AI model for evaluating euploidy was applied to all 3 datasets.

**Results:**

On the initial dataset, the AI significantly predicted live birth with a ROC-AUC value of 0.609. On the expanded dataset where PGT-A had not been performed, ROC-AUC was slightly improved to 0.615. Interestingly, predictivity was maintained to a similar level on the dataset of known euploid embryos, with a ROC-AUC of 0.608. In each case the ROC-AUC for the AI was higher than that of two Gardner-based prediction methods (a 3BB threshold and 4-group system[2]). On the dataset of known euploid embryos, the ROC-AUC of Gardner methods was not significant (p=0.46-0.69), demonstrating no predictive power for manual morphological methods after PGT-A.

Additionally, the AI was able to reduce the number of transfers needed for live birth by up to 14% compared to the 3BB Gardner threshold, using a simulated cohort analysis method[2]. First-transfer live birth rate was also improved by 7-10%. This was true of all datasets, regardless of whether the embryos were known to be euploid, or if PGT-A had not been performed.

**Conclusions:**

An AI for evaluating euploidy from blastocyst images showed significant predictive ability for live birth on images of embryos of unknown ploidy status. Surprisingly, the AI maintained similar predictivity even on images of embryos that had undergone PGT-A and were known to be euploid. This translated to an improved first-transfer live birth rate and reduced time to live birth compared to morphological methods, regardless of whether PGT-A was performed. While embryo genetics is known to correlate with the likelihood of live birth, the ability of the AI to maintain predictivity even after removal of aneuploid embryos identified via PGT-A suggests that the AI can identify additional morphological characteristics associated with genetic integrity beyond the ability of PGT-A, indicating the potential for complementary usage.

| Dataset: | Initial (combined) | No PGT-A | PGT-A (known euploid) |
|---|---|---|---|
| ROC-AUC analyses: Raw AUC values | | | |
| AI | 0.609 | 0.615 | 0.608 |
| Gardner 3BB | 0.566 | 0.578 | 0.460 (NS) |
| Gardner 4-group | 0.608 | 0.611 | 0.465 (NS) |
| Simulated cohort analyses: AI improvement over Gardner 3BB | | | |
| Time to live birth (number of transfers) | 12.8% | 12.6% | 13.6% |
| Live birth rate (first transfer) | 9.9% | 9.8% | 7.0% |

NS = not significant

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**References:**

1. Diakiw, S. M., et al. Development of an artificial intelligence model for predicting the likelihood of human embryo euploidy based on blastocyst images from multiple imaging systems during IVF, Hum. Reprod., 37(8), 1746–1759 (2022).

2. Diakiw, S. M., et al. An artificial intelligence model correlated with morphological and genetic features of blastocyst quality improves ranking of viable embryos. Reprod. Biomed. Online, 45(6), 1105–1117 (2022).