Manuscript Number: XAGR-D-22-00492

Manuscript Title: Embryo Ploidy Status Classification Through Computer-Assisted

Morphology Assessment Journal: AJOG Global Reports

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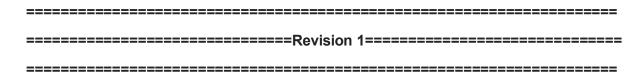
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Manuscript Number: XAGR-D-22-00492

Entitled; Embryo Ploidy Status Classification Through Computer-Assisted Morphology Assessment

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Reviewer #1: This study developed a machine learning model for a non-invasive ploidy status prediction and the model has the ability to predict aneuploid embryo with high confidence level.

- 1. The sample size of this study was relatively small, especially in euploid group.
- 2.Lack of baseline for inclusion population.
- 3. The inclusion and exclusion criteria for images should be described in detail.

Reviewer #2: The study aimed to develop an artificial intelligence model to predict ploidy status in human embryos. This is a topic of interest, and I appreciate that results of two case study comparisons were presented. However I do have some concerns

please see as the following:

- 1. As the authors mentioned, an optimal model should be able to classify different classes with similar accuracy, precision and recall. While the most robust prediction model, using Gradient Boosting algorithm, yielded good precision and recall in predicting auploidy, it has very poor precision and recall in predicting euploidy (0.35 and 0.33 respectively). It seems the model has little value in predicting euploidy, this is confusing.
- 2. I think the proportion of mosaic embryos in the study was relatively high (416/1123=37%). Please describe what method was used for PGT-A (NGS? SNP array? etc.); and how euploid, aneuploid, and mosaic was defined. Please also provide more information on the study population.
- 3. For the binary classification of the embryos, I have some concerns with putting mosaic embryos and aneuploid embryos into one classification. Recent studies have shown that mosaic embryos could result in normal live births, especially low-level mosaic embryos. As over one third of the embryos included in the model was designated as mosaic, this could have a great impact on the model.
- 4. To help evaluate performance of the model, please add the receiver-operating characteristic curve and precision-recall curve (with AUC value).

Editor: 1. Please address the points raised by the Reviewers, such as inclusion criteria and mosaic embryo classification, etc.

- 2. Could you please discuss more about the unique of your AI model compared with those preciously developed models?
- 3. Is it possible to test the performance of the AI model in another separate embryo database?.

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Manuscript Number; XAGR-D-22-00492R1

Entitled; Embryo Ploidy Status Classification Through Computer-Assisted Morphology Assessment

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REVIEWER 1, POINT 2 (follow same A, B, C, D format)

REVIEWER 2, POINT 1 (follow same A, B, C, D format)

EDITOR COMMENT, POINT 1 (follow same A, B, C, D format)

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EDITOR/REVIEWER COMMENTS:

Editor Comment(s):

Reviewer #2: Please consider adding method of PGT-A and threshold for euploid, aneuploid and mosaic in the method section.

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Dear Mr. Danardono:
We are pleased to inform you that your submission number XAGR-D-22-00492R2 entitled, "Embryo Ploidy Status Classification Through Computer-Assisted Morphology Assessment," is accepted for publication in AJOG Global Reports.
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