O-084

Computer vision can distinguish between euploid and aneuploid embryos. A novel artificial intelligence (AI) approach to measure cell division activity associated with chromosomal status.

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Study question:
Can we distinguish between top-grade euploid and aneuploid embryos by AI measurement of cell edges in time-lapse videos?

Summary answer:
Aneuploid embryos can be distinguished from euploid embryos by AI determination of a longer time to blastulation and higher cell activity.

What is known already:
Continuous monitoring of the embryo development has brought out morphokinetic parameters that are used to predict pre-implantation genetic testing (PGT) results. Previous publications showed that euploid embryos reach blastulation earlier than non-euploid embryos. However, time-lapse data are currently under-utilized in making predictions about embryo chromosomal content. AI and computer vision could take advantage of the massive amount of data embedded in the images of embryo development. This is the first attempt to distinguish between euploid and aneuploid embryos by computer vision in an objective and indirect way based on the measurement of cell edges as a proxy for cell activity.

Study design, size, duration:
We performed a retrospective analysis of 1,314 time-lapse videos from embryos cultured to the blastocyst stage with PGT results. This single-center study involved two phases; a comparison of the start time of blastulation between euploid (n=544) and aneuploid embryos (n=797). In phase two, we designed a novel methodology to examine whether precise measurement of cell edges over time could reflect cell activity differences in blastulation.

Participants/materials, setting, methods:
We assumed that the delay in blastulation is reflected by higher cell activity that could be determined accurately for the first time using computer vision and machine learning to measure the length of the edges (from t2 to t8). We compared computer vision based measurements of cell edges, reflecting cell number and size, in videos of 231 top-grade euploid (n=111) and aneuploid (n=120) embryos.

Main results and the role of chance:
The mean and standard deviation of blastulation start time was 100.1±6.8 h for euploid embryos and 101.8±8.2 h for aneuploid embryos ($p<0.001$). Regarding the measurement of cell activity, a computer vision algorithm identified the edges and provided a certainty score for each edge, higher when the algorithm is more certain that this is a cell edge (as opposed to noise in the images). A threshold was set to distinguish cell edges from noise using this score. The following results for top-grade embryos are shown as the sum of the edge lengths (μm) average of 160 pictures per embryo (frames between t2 and t8). The total length of the cell edges increased from two cells (420±85 μm) to eight cells (861±237 μm), in line with the mitosis events. Both the average total edge measured (450±162 μm for euploid embryos and 489±215 μm for aneuploid embryos, $p<0.01$) and the average total of the difference between consecutive frames (135±47 μm for euploid embryos and 153±64 μm for aneuploid embryos, $p<0.01$) were higher for aneuploid embryos than for euploid embryos. A regression model to differentiate between the two classes achieved 73% sensitivity and 73% specificity on this dataset.

Limitations, reasons for caution:
The main limitation of this study is the difficulty to correlate our findings to other measure of cell activity. A more robust AI function (using not only cell edges lengths) would be required for future analysis to measure the cell activity in cell division up to the blastocyst stage.

Wider implications of the findings:
Our results show for the first time that an AI based system can precisely measure microscopic cell edges in the dividing embryo. Using this novel method, we could distinguish between euploid and aneuploid embryos. This non-invasive method could further enhance our knowledge of the developing embryo.

Trial registration number: -

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