AI and computer vision remove the need for cell biopsy in testing embryos

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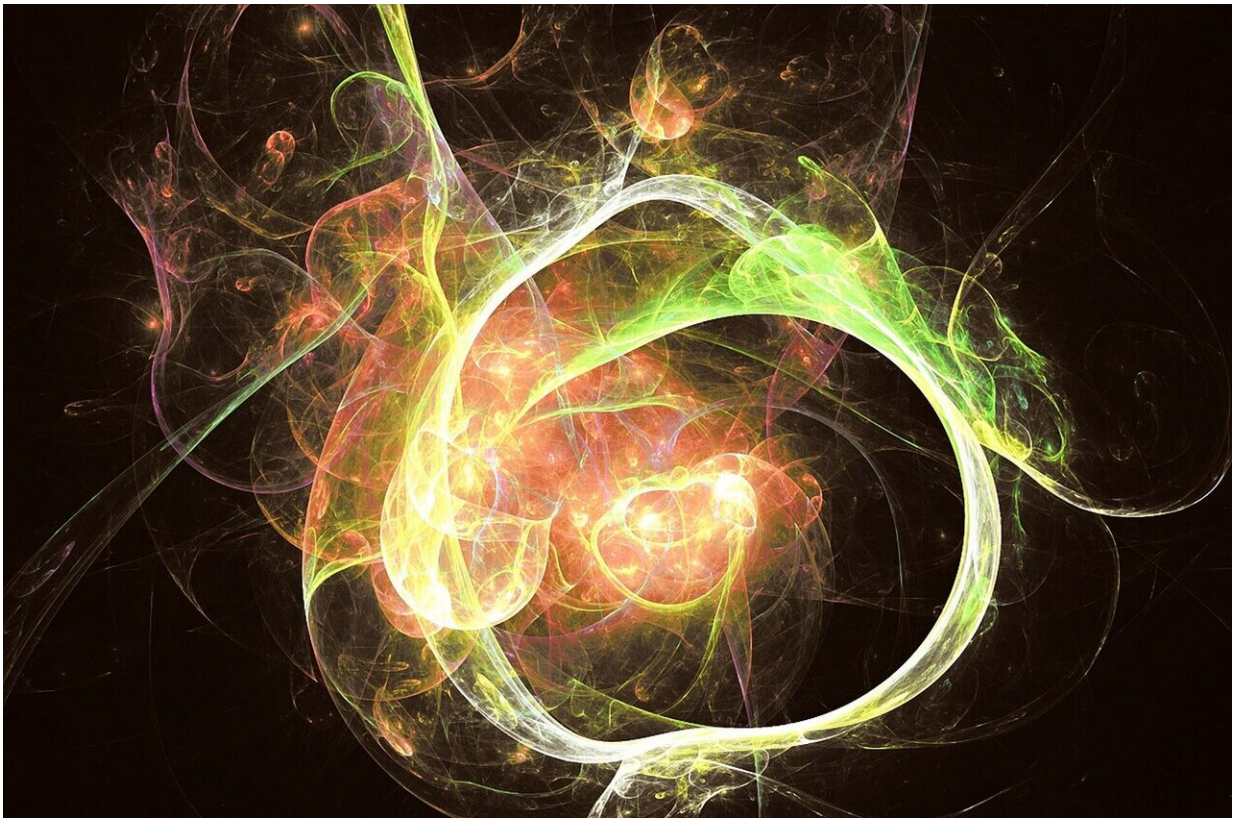

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Despite continuing controversies over its value in improving birth rates in IVF, testing embryos for their chromosomal content has become routine in many fertility clinics. Embryos with a normal complement of

chromosomes (known as "euploid") are known to have a good chance of implanting in the uterus to become a pregnancy, while abnormal embryos (aneuploid) have no chance. Testing embryos for aneuploidy (known as PGT-A) has so far required a sample single cell or several cells taken from the embryo by biopsy, and this too has raised fears over safety such that a search for non-invasive methods has arisen in recent years.

Now, a new study suggests that euploid embryos can be visually distinguished from aneuploid according to artificial intelligence references of cell activity as seen by time-lapse imaging—and thus without the need for cell biopsy. The results of the study will be presented today at the online annual meeting of ESHRE by Ms Lorena Bori from IVIRMA in Valencia, Spain, on behalf a joint research team from IVIRMA Valencia and AIVF, Israel, co-directed by Dr. Marcos Meseguer from Valencia and Dr. Daniella Gilboa from Tel-Aviv.

The visualisation of embryo growth has been revolutionised in the past decade by time-lapse technology, which provides an image of each moment of an embryo's development until as a blastocyst it is ready for transfer to the uterus. However, so far information from time lapse imaging has not been able to offer an accurate assessment of an embryo's chromosomal status. Now, however, computer vision with AI may provide an objective and reliable prediction.

Behind the study lay the finding that chromosomally normal embryos begin their development as blastocysts at a slightly earlier time than aneuploid embryos, and this can be identified in computer vision by microscopic measurement of the cells' edges. This is known to be a precise method of quantifying the number of cells and cell cycle of the blastomeres (the cells which form the embryo). Applying this finding, the study thus retrospectively compared computer vision-based measurements of cell edges in the time-lapse videos of 111 euploid and

120 aneuploid embryos.

Results showed that the aneuploid embryos achieve their growth to the blastocyst stage faster than the euploid embryos, said the authors, because of their higher level of cell activity.

"Our results show for the first time," they added, "that an AI based system can precisely measure microscopic cell edges in the dividing embryo, which allowed us to distinguish between euploid and aneuploid embryos."

"Our early results had shown that euploid and aneuploid embryos are visually distinct," explained study director Marcos Meseguer, "significantly enough to merit further computer vision investigation and to test if a non-invasive PGT-A test could conceivably match the results of current invasive methods—without the cost and damage to the embryo that the invasive methods might cause. We used the measurement of cell edges as a proxy for cell activity (which include DNA replication and cell division) and achieved 73% sensitivity and specificity in our results."

While Meseguer described the results and future research as "one of the milestones" of AI in reproductive medicine, he said further studies are still needed to test and validate the algorithms in larger datasets. For example, the model so far classifies mosaic embryos (with a combination of euploid and aneuploid) as abnormal, even though some studies have shown their viability in pregnancy.

Nevertheless, Meseguer acknowledged that all methods so far explored for testing embryos without the need for biopsy have not proved as accurate as the traditional biopsy methods. "Our present algorithm faces the same situation," said Meseguer. "Our prediction capability is still limited, in which case our models could only be applied in those patients

who do not require genetic testing according to a pre-defined medical indication. So our test so far could only be used to reduce the risk of selecting a chromosomally abnormal embryo for transfer."

However, results from this time-lapse visualisation approach show it to be fast and economical, particularly when compared with the non-invasive methods so far explored (which rely on analysing the culture media in which the embryo develops). "These [other non-invasive] results," said Meseguer, "take several days to produce because of the genetic analysis, which forces patients to freeze all their embryos and delay their infertility treatment." While the AI method described in this study needs further validation, it is simple in its concept, can be home-built, and may yet provide the most efficient means of testing embryos for aneuploidy and their selection for transfer.

More information: Presentation O-084, Monday 28 June 2021: 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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