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performing the TE biopsies on D5-D6. After biopsy, embryo were transferred to an additional dish, until vitrification. The SCm of the original dish was transferred to PCR tubes containing 5 μl of lysis buffer (Yikon Genomics). The samples were stored at -80 °C until processing. Whole-genome amplification (WGA) and subsequent library preparation for TE samples were performed following the Verisec protocol (Illumina, San Diego, CA, USA), while for medium samples, the NICSInst protocol (Yikon Genomics) was used. All samples (from TE and SCM) were sequenced using the Illumina MiSeq platform according to the recommendations detailed in the mentioned protocols. About 1 million reads were obtained per sample, allowing a resolution of ~10 Mph. For the subsequent analysis, the BlueFuse Multi (Illumina) and ChromGO (Yikon) software were used for the TE and medium samples, respectively.

RESULTS: WGA was 100% effective for all the samples (TE and SCM). A total of 17 true-positives, 9 true-negatives, 0 false-negative, and 4 false-positives were obtained after comparisons. These values correspond to 87% concordance, 81% sensitivity, 100% specificity, 100% positive predictive values (PPV), and 69% negative predictive values (NPV). False-negative results correspond to two cases of full autosomal aneuploidies, and two cases of low-level mosaicism detected through the TE biopsy. In the four cases, the culture media showed euploid results.

CONCLUSIONS: niPGT-A starting from cfDNA showed excellent results in comparison to the current gold standard method (TE biopsy). Discordances correspond to four false-negatives, where the non-invasive method showed euploid results while TE biopsy showed aneuploidies. If niPGT-A is a more reliable representation of the whole embryo than TE biopsy, this 13% of discordance, is the kind of result that points out that the non-invasive method is a valuable alternative tool for PGT-A.

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LIVE BIRTH RATE FOLLOWING PGT RESULTS IN LOWER LIVE BIRTH RATE COMPARED TO UNTESTED EMBRYOS TRANSFERRED AT DAY 5/6. Kevin J. Doody, M.D., Kathleen M. Doody, MD CARE Fertility, Bedford, TX.

OBJECTIVE: Embryos progressing through day 5/6 can be transferred fresh or following thaw without biopsy for genetic testing. Alternatively, these embryos may be biopsied, cryopreserved and subsequently thawed and transferred using information obtained from aneuploidy screening. The outcomes of treatments employing these two distinct strategies were compared.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Analysis of publicly available ART outcomes using the 2018 SART National Summary Report was performed. Filters were applied to view the outcomes of the two groups: 1) Autologous IVF cycles without PGT with day 5/6 embryos transferred, and 2) Autologous IVF cycles with PGT. Both groups were compared with respect to their first embryo transfer only.

RESULTS: PGT resulted in a lower chance of live birth in all age groups compared to transfer of day 5/6 embryos without PGT (Table). Although PGT results in higher pregnancy rates following transfer, the majority of PGT procedures done in women over age 38 did not ultimately result in an embryo transfer. Although the rate of miscarriage increased with age in both treatment groups, PGT resulted in a markedly lower risk of pregnancy loss.

CONCLUSIONS: Previous studies have concluded that PGT for aneuploidy improves the success rate for embryo transfers. These studies have generally failed to do appropriately corrected comparisons. Success rates calculated “per transfer” do not reliably approximate “intent to treat”. Success rates should be calculated “per PGT cycle”. Women in all age groups very frequently will not have euploid embryos available for transfer following biopsy and genetic testing. When the success rate “per PGT cycle” is compared to a similar cohort possessing developing embryos suitable for transfer on day 5/6, the apparent improved success rate obtained by performing PGT is erased. The increased implantation rate following transfer of tested euploid embryos is more than counter-balanced by decreased ET procedures following biopsy and testing. PGT is best viewed as a strategy to decrease the risk of pregnancy loss and does not improve chance of live birth.

SUPPORT: None

THE EFFECT OF MATERNAL AGE ON CHROMOSOMAL MOSAICISM: AN ANALYSIS BY CHROMOSOME TYPE AND MOSAIC RESULT. Jenna Reich, BS, Jennifer K. Blakemore, MD, Andria G. Besser, MS, CCC; Brooke Hodes-Weritz, MD, MPH, James A. Grifo, MD, PhD; NYU School of Medicine, New York, NY; NYU Langone Prelute Fertility Center, New York, NY; New York University Langone Fertility Center, New York, NY; NYU Langone Prelute Fertility Center, New York, NJ.

OBJECTIVE: Previous work by our group (1) showed that the rate of chromosomal mosaic decreases with maternal age. However, the types of chromosomes involved, as well as the types of chromosomal mosaicism in individual embryos, have not yet been examined. Our objective was to determine whether maternal age was associated with the rate of sex and autosomal chromosome mosaicism and the rates of various types of mosaicism.

DESIGN: Retrospective cohort study of all blastocysts that underwent trophectoderm biopsy for preimplantation genetic testing for aneuploidy (PGT-A) from 1/2015 to 12/2018 at our center.

MATERIALS AND METHODS: All patients with blastocysts that underwent trophectoderm biopsy for PGT-A via Next Generation Sequencing with ≥1 chromosome in the mosaic range (20-80%) were included. The primary outcomes were: 1) the rate of sex and autosomal chromosome mosaicism and 2) rates of segmental mosaicism, full chromosome mosaicism and complex (≥3 mosaic chromosomes) stratified by maternal age. Statistical analyses included Kruskal-Wallis (KW) and linear regression (LR) to control for paternal age, with p<0.05 considered significant.

RESULTS: 1,670 patients with 10,545 embryos biopsied overall and 3,611 embryos with ≥1 mosaic chromosome met inclusion criteria. The number of embryos biopsied decreased with maternal age (p<0.01) as expected. 3,366 (93.2%) embryos had only autosomal chromosome mosaics, which was independent of maternal age (p=0.50). Alternatively, the percent of embryos with ≥1 sex chromosome mosaic (6.8% n=245) was significantly associated with maternal age without clear trend by age group (p<0.01). Table 1 shows PGT-A results by type of mosaicism stratified by maternal age. Segmental mosaicism peaked at maternal age 35-37, while complex mosaicism increased
with maternal age. Full chromosome mosaicism was similar across age groups.

CONCLUSIONS: Among our embryo cohort, rates of segmental mosaicism and complex mosaicism increased with maternal age. These results remained significant when controlling for paternal age. The rate of sex chromosome mosaicism was associated with maternal age but may not be sufficiently powered given the low number of chromosomes. Our results provide further data for counseling patients about mosaic embryo results.

References: 1. A. An Analysis Of The Effect Of Maternal And Paternal Age On Chromosomal Mosaicism, Pacific Coast Reproductive Society Annual Conference – Cancelled by COVID-19

P-769 4:30 PM Tuesday, October 20, 2020
PRENATAL AND POSTNATAL GENETIC TESTING AFTER PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) FOR A NON-SELECTION CLINICAL TRIAL. Xin Tao, Ph.D.; Li Ma, BS; Yiping Zhan, Ph.D.; Ashley W. Tiegts, MD; Christine V. Whitehead, BSN, RN; Richard Thomas Scott, Jr., MD; Chaim Jalas, N/A; Foundation for Embryonic Competence, Basking Ridge, NJ; 2The Foundation for Embryonic Competence, Basking Ridge, NJ; 3IVI RMA New Jersey, Basking Ridge, NJ; 4IVI-RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: PGT-A detects whole chromosome aneuploidy before transfer and thus increases live birth rates and decrease early pregnancy failure rates. A prospective and blinded non-selection study using Next Generation Sequencing (NGS) based PGT-A (PGTseq-A) validated the ability of an ‘aneuploidy’ analytical result to predict the failure to deliver. This study was aimed to further validate the accuracy of PGTseq-A. Prenatal genetic testing (through CVS or amniocentesis) or postnatal genetic testing (through newborn buccal DNA) was performed after the non-selected transfer cycles, then karyotypes were compared to the unblinded PGTseq-A results. Products of conception (POC) were tested when the miscarriage happened.

DESIGN: Retrospective
MATERIALS AND METHODS: Sixty-eight human embryos diagnosed clinically as mosaicism were rebiopsed and dissected into three parts: TE, ICM and the remaining parts of embryos (a combination of TE and ICM). All the samples were examined and compared with original clinical diagnosis. Whole genome amplification using the Malbac DNA amplification system followed by NGS via the ThermoFisher DA8600 platform was performed. Statistical analysis was performed using chi square.

RESULTS: Among the 68 blastocysts, the original mosaicism diagnosis was confirmed in at least one additional biopsy in 14 (20.6%) blastocysts; 12 (17.6%) displayed de novo abnormalities; and 42 (61.8%) were euploid. Stratification analysis showed that the type of mosaicism within the original biopsy diagnosis was associated with the concordance across the embryos. The concordance rate with the ICM results was highest for whole-chromosome mosaicism (41.2%), followed by complex mosaicism (20.0%), while that for segmental and mixed mosaicism was lowest (3.3% and 0%, respectively). However, it was not associated with the gain or loss of chromosomes (P=0.138). Close examination of the level of mosaicism within the original biopsy diagnoses revealed that the concordance rate increased with increasing levels of mosaicism (P<0.001). In addition, the second TE biopsy for mosaicism showed a sensitivity of 68.8% and specificity of 92.9% for predicting abnormalities in the ICM portions.

CONCLUSIONS: This novel study exposes false-positive errors in NGS-based PGT and the limitations of a single TE biopsy for predicting the cytogenetic constitution of the ICM and whole embryos. It also provides suggestions for the transfer of mosaic embryos, indicating that those with segmental mosaicism and a low rate of aneuploidy should be prioritized and that a second TE biopsy is an option for doctors and patients facing a dilemma.

SUPPORT: This study was supported by grants from the National Key R&D Program of China (No. 2016YFC1000206-5)

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RELIABILITY OF THE NEXT-GENERATION SEQUENCING (NGS) DIAGNOSIS OF MOSAICISM TO PREDICT THE CHROMOSOMAL CONSTITUTION OF THE INNER CELL MASS. Hui He, Msc, Bo Huang, PHD, Li Wu, Msc Huazhong University of Science and Technology, WUHAN, China.

OBJECTIVE: To investigate the reliability of next-generation sequencing (NGS) for diagnosing mosaicism and the predictive diagnostic value of trophoderm (TE) biopsy for assessing the genetic status of the inner cell mass (ICM) in mosaicism.

DESIGN: Prospective study.
MATERIALS AND METHODS: Sixty-eight human embryos diagnosed clinically as mosaicism were rebiopsed and dissected into three parts: TE, ICM and the remaining parts of embryos (a combination of TE and ICM). All the samples were examined and compared with original clinical diagnosis. Whole genome amplification using the Malbac DNA amplification system followed by NGS via the ThermoFisher DA8600 platform was performed. Statistical analysis was performed using chi square.

RESULTS: Among the 68 blastocysts, the original mosaicism diagnosis was confirmed in at least one additional biopsy in 14 (20.6%) blastocysts; 12 (17.6%) displayed de novo abnormalities; and 42 (61.8%) were euploid. Stratification analysis showed that the type of mosaicism within the original biopsy diagnosis was associated with the concordance across the embryos. The concordance rate with the ICM results was highest for whole-chromosome mosaicism (41.2%), followed by complex mosaicism (20.0%), while that for segmental and mixed mosaicism was lowest (3.3% and 0%, respectively). However, it was not associated with the gain or loss of chromosomes (P=0.138). Close examination of the level of mosaicism within the original biopsy diagnoses revealed that the concordance rate increased with increasing levels of mosaicism (P<0.001). In addition, the second TE biopsy for mosaicism showed a sensitivity of 68.8% and specificity of 92.9% for predicting abnormalities in the ICM portions.

CONCLUSIONS: This novel study exposes false-positive errors in NGS-based PGT and the limitations of a single TE biopsy for predicting the cytogenetic constitution of the ICM and whole embryos. It also provides suggestions for the transfer of mosaic embryos, indicating that those with segmental mosaicism and a low rate of aneuploidy should be prioritized and that a second TE biopsy is an option for doctors and patients facing a dilemma.

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P-771 4:30 PM Tuesday, October 20, 2020
VALIDATION OF PREIMPLANTATION GENETIC TESTS FOR ANEUPLOIDY WITH CELL-FREE DNA FROM SPENT CULTURE MEDIA (SCM): CONCORDANCE ASSESSMENT AND IMPLICATION. Li Meng, Ph.D; HCLD, Baoli Yin, PHD, Cuilian Zhang, MD; Ph.D Henan Provincial People’s Hospital, Zhengzhou, CA, China.

OBJECTIVE: Preclinical validation of cell-free DNA in SCM represents ploidy status of the chromosomal constitution of a blastocyst.

DESIGN: Validation study