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ABSTRACT BOOK

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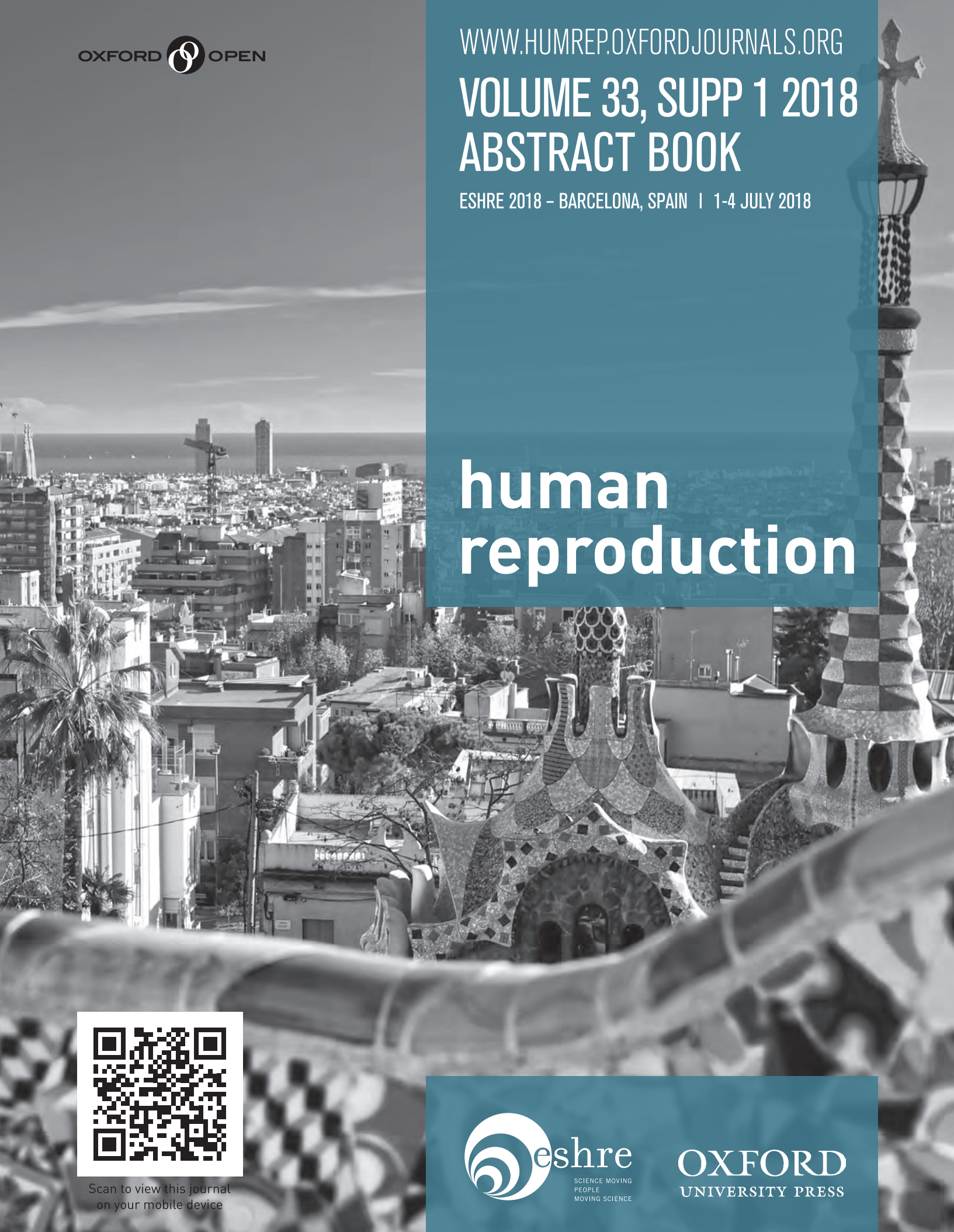
human reproduction



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may have an effect on the development of aneuploidy among human embryos. However, it is unclear what kinds of factors have an impact on the development of MNB. We aimed to investigate whether clinical and laboratory factors may affect the occurrence of MNB embryos.

Study design, size, duration: This is a retrospective observational study conducted at Kyono ART clinic Takanawa in Japan from January 2015 to April 2017. A total of 1509 embryos from 302 cycles of 189 patients were included in this study. All embryos were monitored by time-lapse cinematography.

Participants/materials, setting, methods: We compared the backgrounds of the embryos which had at least one MNB between day 1 to day 3 embryo culture for age factor, fertilization method (c-IVF or ICSI), ovarian stimulation protocol (GnRH antagonist, agonist long, agonist short and others) and culture media (two different single culture media). Chi-squared and Fisher's test were used for statistical analysis. A P value of less than 0.05 was considered statistically significant.

Main results and the role of chance: The overall incidence of MNB was 33.7% (509 / 1509). MNB embryos showed lower blastulation rates (50.7%) compared to non-MNB embryos (55.9%), although this was not statistically significant ($P = 0.055$). The good morphology blastocyst (Gardner's grade 3BB or more) formation rate in the MNB embryos was significantly lower (18.3%) than that of the non-MNB embryos (25.1%) ($P = 0.003$). There was no significant difference in the MNB occurrence rate in terms of age factor (patients aged under 40 y.o. vs over 40 y.o.; 35.5% vs. 31.2%), and fertilization method (c-IVF vs ICSI; 33.6% vs. 33.8%). Also, there was no significant difference in MNB rate in terms of ovarian stimulation protocols. Culture media tended to have an impact on MNB incidence rate (media A vs B; 16.2% vs. 27.5%, $P = 0.067$) although this was not statistically significant.

Limitations, reasons for caution: The small sample size may have influenced these results. The details of culture media which have affected MNB is unclear.

Wider implications of the findings: MNB affects subsequent developmental potential of embryos, and these events may be affected by laboratory factors such as culture media. MNB formation may be related to an increase in aneuploidy rate and mosaic formation rate by using different culture media.

Trial registration number: not applicable.

P-127 Blastocyst development rates of embryos with morphokinetic variables and the effect of morphokinetic variables on clinical pregnancy rates in vitrified-warmed single blastocyst transfers

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Study question: How many embryos exhibiting morphokinetics variables could develop up to blastocyst stage? And how much the blastocysts were affected by morphokinetics variables on pregnancy?

Summary answer: The blastocyst development rates of embryos with morphokinetic variables were more than 40% and the clinical pregnancy rates of the blastocysts vitrified-warmed were adversely affected.

What is known already: In time-lapse cultures, morphokinetic variables are used to refer to two concepts; morphological assessment parameters and morphokinetic assessment parameters. Morphological assessment parameters include uneven pronuclei, blastomere, and multinucleation etc. Morphokinetic assessment parameters include direct division, reverse division, and rapid division etc. Morphokinetic variables generally have a fatal influence on the embryo development, implantation and pregnancy rates in fresh cycles. There are a few reports on the impact of various morphokinetic variables on blastocysts developments; and, there are a few reports on the effect of morphokinetic variables on vitrified-warmed blastocyst transfer cycles.

Study design, size, duration: Morphokinetic variables include uneven pronuclei, blastomere, multinucleation, and direct division, rapid and irregular division. Regularly developed embryos which are not observed in any kind of morphokinetic variables were compared with the embryos observed in morphokinetic variables. We conducted a review between January 2014 and November 2017. During the same period, the clinical pregnancy rates of the single blastocysts vitrified-warmed were determined and the effects of each type of morphokinetic variables on pregnancy rates were observed.

Participants/materials, setting, methods: Embryos were monitored in a time-lapse incubation system (embryoscope). Embryos were selected for transfers on day 3 or day 5, and surplus embryos were cultured for blastocyst development. The blastocysts were evaluated according to the blastocyst scoring system, and blastocysts graded 3BB or higher were cryopreserved. Vitrification and thawing processes were performed as lab protocols. In thawed blastocysts, they were graded CC or higher and were used for embryo transfers.

Main results and the role of chance: The blastocyst development rate and freezing rate of regularly developed embryos were 56.6% (2116/3739) and 45.1% (1687/3739) respectively. Uneven pronuclei were 43.4% (189/435) and 31.7% (138/435) respectively. Uneven blastomere were 55.9% (137/245) and 42.4% (104/245) respectively. Multinucleation were 53.5% (423/790) and 40.1% (317/790) respectively. Direct division were 40.2% (146/363) and 27.0% (98/363) respectively. Rapid division were 56.8% (162/285) and 39.3% (112/285) respectively. And, irregular division were 43.9% (94/214) and 24.3% (52/214) respectively. The blastocyst development rates of embryos with morphokinetic variables were lower than regularly developed embryos, but the blastocyst development rates of embryos with morphokinetis variables were more than 40%. The clinical pregnancy rate of regularly developed single blastocyst that vitrified-warmed was 37.7% (60/159). Uneven pronuclei were 20.0% (2/10). Uneven blastomeres were 10% (1/10). Multinucleation were 18.8% (6/32). Direct division was 6.3% (1/16). Rapid division was 0.0% (0/9). And, irregular division was 0.0% (0/5). The clinical pregnancy rates of single blastocyst with uneven pronuclei, blastomere and multinucleation were lower than a regularly developed single blastocyst. The clinical pregnancy rates of single blastocyst with direct, rapid and irregular divisions were much lower than a regularly developed single blastocyst.

Limitations, reasons for caution: In this study, it was possible to assess the effect of morphokinetic variables on pregnancy rates. However, further studies will be required to accumulate sufficient data to determine the effects of each type of morphokinetic variables on pregnancy, delivery, and congenital anomaly rates.

Wider implications of the findings: More than 40 percent of embryos exhibiting morphokinetic variables could develop up to blastocyst stages in the time-lapse system. Therefore, it was important that freezing the embryos were to be done carefully, because the embryos with morphokinetic variables were not easy to implant, even if morphology was good after thawing.

Trial registration number: not applicable.

P-128 A prediction model powered by a Group Method of Data Handling (GMDH) algorithm for selecting patients of a single frozen embryo

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Study question: As frozen embryo transfer (FET) cycles become more common, policies regarding the number of embryos to transfer need to be formulated for individual patients.

Summary answer: Using the most relevant factors relating to patients, embryos and fresh cycle outcomes, this GMDH predictive model can reasonably predict the occurrence of implantation.

What is known already: The introduction of vitrification has improved both embryo survival and FET success and has led to a large increase in routine embryo freezing. The improvement of embryo cryopreservation significantly increases the overall success for superovulation cycle. But a high proportion of twins results after transfer of 2 frozen embryos. Studies from fresh cycles suggested that acceptable pregnancy rates could be

achieved after transfer of a single frozen embryo in selected groups of patients.

Study design, size, duration: A retrospective analysis of all FET cycles carried out at Waterstone clinic between Feb 2012 and Dec 2017 was conducted.

Participants/materials, setting, methods: All embryos in the study had been vitrified on day 5 or day 6. Success rates were compared after transfer of either one or two embryos. SET cycle outcomes were also analysed with the factors which most strongly predicted success after FET. Two statistical models were used: the logistic regression and the GMDH algorithm.

Main results and the role of chance: From Feb 2012 to Dec 2017, a total of 1535 out of 1601 vitrified embryos survived after warming 95.9% and were transferred in 1205 cycles. Two embryos were transferred in 327 FET cycles and one embryo was transferred in 878 cycles. The clinical pregnancy (fetal heart activity at 8/40) rates were 41.9%/ transfer and 33.3%/ transfer for 2-ET vs. 1-ET cycles. The overall implantation rate was 31.4%. The proportion of pregnancies which were twins in the 2-ET group was 37.2%.

A logistic analysis was performed based on SET events to investigate the relationship between the implantation of embryos and different prognostic factors. We identified three prognostic factors that made the most significant contributions to the success of implantation: the woman's age, the quality of the inner cell mass (ICM) and the success or failure of the fresh cycle from which the frozen embryos derived. The predictive ability of the model measured by the area under the receiver operating characteristic (ROC) curve was 0.61 when using logistic analysis. Prediction ability was significantly improved by application of a GMHD algorithm which increased the ROC to 0.67 with the negative and positive predictive value of 70.5% and 76.9%.

Limitations, reasons for caution: This prediction model may be benefited by including uterine factors. Prospective studies are now required to confirm the clinical validity of the model.

Wider implications of the findings: Application of this GMHD algorithm may help in the decision making by accurately predicting success. It should identify patients for whom single embryo transfer is indicated and a smaller number of patients for whom a 2-embryo transfer would be wiser.

Trial registration number: na.

P-129 Polar body transfer in a mouse model to overcome transmission of mitochondrial diseases

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Study question: Can polar body transfer (PBT) serve as an efficient type of germline nuclear transfer (NT), to overcome mitochondrial diseases?

Summary answer: This mouse model study supports the efficient use of first (PB1) polar body transfer for overcoming mitochondrial DNA (mtDNA) disorders.

What is known already: Since mtDNA diseases are difficult to treat and manifest with life-threatening consequences, their prevention is a priority. Different germline NT have recently been proposed as novel technologies for preventing mtDNA mutations transmission, including germinal vesicle transfer (GVT), spindle transfer (ST), pronuclear transfer (PNT) and even PBT. Previous mouse studies have revealed full potential of PB1/2 genomes for embryonic development, by replacing female genome of oocytes/zygotes with PB1/2. However, PB2T requires female PN identification in zygotes, which is arduous in human. Therefore, we tested if MII oocytes can be used for both PB1/2T and compared its efficiency with ST and PNT.

Study design, size, duration: In a first set, PB1/2T were carried out in B6D2F1 mice, by introducing PB1/2 into enucleated oocytes (spindle removal, PB1T/novel PB2T) or zygote (female pronucleus removal, PB2T). For controls, ST, PNT and ICSI groups were implemented. In a second set, ST, PNT and routine PB2T were performed between NZB/OlaHsd and B6D2F1 mice for evaluating effect of heterologous NT on embryonic developmental potential. Oocytes/zygotes from B6D2F1 mice served as recipients, while karyoplasts originated from NZB/OlaHsd mice.

Participants/materials, setting, methods: Oocytes/zygotes were from superovulated B6D2F1 and NZB/OlaHsd female mice (6-8 weeks). NT was performed in KSOM-HEPES (2 µg/ml cytochalasin D, 1 µg/ml nocodazole). Karyoplasts were exposed to Sendai virus for fusion with enucleated oocytes/zygotes. One part of ST-, PB1T- and novel PB2T-oocytes were fertilized (ICSI) and exposed to cytochalasin D (only for novel PB2T) to prevent PB2 extrusion. Another part were examined for *de novo* spindle formation through polarized microscopy, and spindle morphology assessment via confocal analysis.

Main results and the role of chance: For homologous NT between B6D2F1 mice, after ICSI, novel PB2T-oocytes showed significantly lower two-cell formation rates compared to ST and PB1T groups (50.0%, 83.8% and 90.0%), but not different with ICSI control (70.6%). For routine PB2T, blastocyst rates (52.2%) were comparable with PB1T group and ICSI control (77.8% and 75.0%, respectively), but these were significant lower than ST- and PNT-embryos (80.6% and 100%, $p<0.05$ and $p<0.005$ respectively). Remarkably, no blastocyst formation could be achieved in the novel PB2T group. Polarized microscopy showed most reconstructed oocytes after novel PB2T contained a visible spindle (22/27, 81.5%) similar to PB1T-reconstructed oocytes (12/17, 70.6%). Confocal analysis, however, revealed that 61.5% of novel PB2T-oocytes displayed an abnormal spindle-chromosome-complex compared to 33.3% in PB1T-oocytes showing aberrant spindles. After heterologous NT from NZB/OlaHsd to B6D2F1 mice, following fertilization, 38.5% of ST-oocytes developed to blastocysts, significantly lower than ICSI control (B6D2F1-oocytes) (72.7%, $p<0.05$) and the homologous ST group (80.6%, $p<0.05$). In heterologous routine PB2T and PNT groups, two-cell rates were similar (69.2% and 83.3%, respectively), whereas PNT-embryos yielded higher blastocyst rates (27.8% vs 100%, $p<0.001$).

Limitations, reasons for caution: Further investigation is currently ongoing to determine whether these NT techniques would alter the genetic and transcriptomic landscape of resulting blastocysts and to assess the mitochondrial carry over level.

Wider implications of the findings: Intra-strain NT in B6D2F1 mice, routine PB1/2T, ST and PNT, did not compromise embryonic development. Novel PB2T could not support blastocyst formation, probably owing to embryonic aneuploidy. Inter-strain NT between NZB/OlaHsd and B6D2F1 mice resulted in declined development in routine PB2T and ST groups contrast with PNT and ICSI controls.

Trial registration number: Not applicable.

P-130 Predictive value of total number of normal morphology and progressively motile sperm on the fertilization failure of short-term insemination in in vitro fertilization

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Study question: To investigate the predictive value of total number of normal morphology and progressively motile sperm (TNNPS) on the fertilization failure of short-term insemination.

Summary answer: TNNPS may be considered as a potential parameter for predicting the failure of short-term insemination.

What is known already: Short-term insemination combined with early-rescued ICSI has some advantages in decreasing the incidence rate of fertilization failure. However, some studies suggested that short-term insemination can lead to increase the abnormal fertilization. For the patients treated by short-term insemination and early rescue ICSI, they had to withstand greater economic and mental stress. Therefore, it is necessary to predict the rate of fertilization failure of short-term insemination. TNNPS contains numerous information of semen and has shown to closely related with fertilization failure in IVF and IUI. Therefore, it is potential to be a parameter to predict the failure of short-term insemination.