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Morphokinetic parameters comparison between embryos from couples with high or low sperm DNA fragmentation index: what is the human eye missing during conventional morphological assessment?

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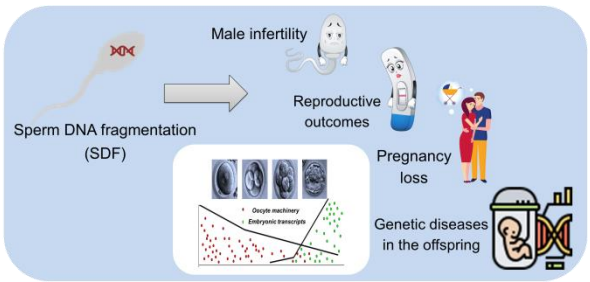
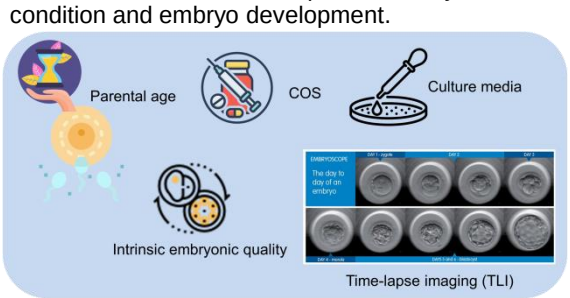
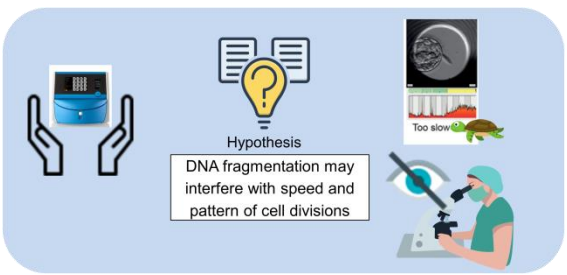
Introduction

As paternal genome activation occurs late in the embryo, the negative impact of sperm DNA fragmentation on embryo development is more often observed in the outcomes of pregnancy, than in the potential for embryonic development.



Embryo development is affected in subtle ways by a multitude of factors. The introduction of new technologies into the in vitro fertilization (IVF) laboratory, such as the time-lapse imaging (TLI), has demonstrated to improve embryo culture condition and embryo development.





The objective of this study was to investigate whether TLI can identify morphokinetic events impacted by high sperm DNA fragmentation index (DFI).

Methods

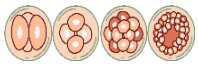
Historical cohort / Mar 2019 - Aug 2020
Private university-affiliated IVF center

118 ICSI cycles

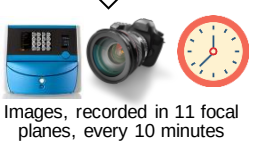
Idiopathic male infertility

< 30% SDF (n=84)

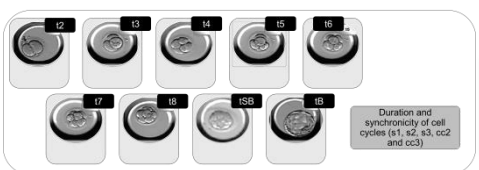
≥ 30% SDF (n=34)



n=978 embryos



Images, recorded in 11 focal planes, every 10 minutes



Generalized linear models – Bonferroni post hoc

Results

Embryos derived from sperm samples with ≥30% DFI showed significantly slower divisions compared to those from <30% DFI (Table 1 , Figures 1, 2 and 3).

Morphokinetic data (hours)	<30% DFI (n=592)	≥30% DFI (n=386)	p-value
tPNa	6.1 ± 0.2	6.8 ± 0.2	0.030
tPNf	23.0 ± 0.3	24.2 ± 0.3	0.009
t2	25.4 ± 0.3	26.9 ± 0.3	0.002
t3	34.8 ± 0.3	37.3 ± 0.4	<0.001
t4	37.5 ± 0.4	39.3 ± 0.4	0.003
t5	46.2 ± 0.5	49.5 ± 0.6	<0.001
t6	49.7 ± 0.5	52.8 ± 0.6	0.001
t7	52.4 ± 0.6	55.6 ± 0.7	0.001
t8	56.2 ± 0.7	58.9 ± 0.8	0.017
tSB	97.5 ± 1.5	105.9 ± 1.7	0.002
tB	108.6 ± 0.8	112.4 ± 1.2	0.016

Table 1. Comparison of embryo morphokinetics

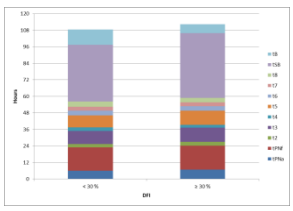


Fig 1. Comparison of cumulative morphokinetic development

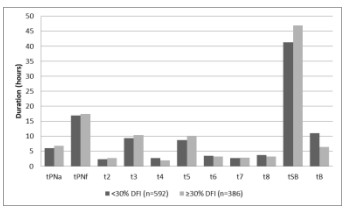


Fig 2. Comparison of the morphokinetic parameters

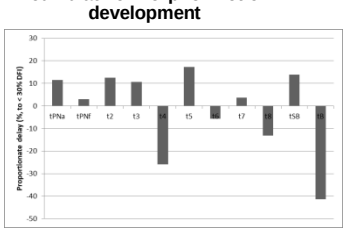


Fig 3. Proportionate delay (%) of morphokinetic development

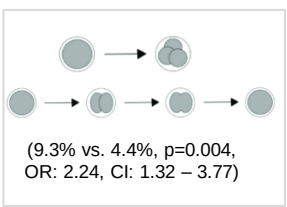


Fig 4. Direct and reverse cleavages incidence

The incidences of reverse or direct cleavages (Fig. 4) and multinucleation at 2-cell (18.9% vs. 12.0%, p=0.017, OR: 1.70, CI: 1.12 – 2.58) and 4-cell stages (14.2% vs. 6.4%, p<0.001, OR: 2.42, CI: 1.57 – 3.74) were significantly higher in embryos deriving from ≥30% DFI as compared to <30% DFI, respectively. The KIDScore ranked significantly different between embryos derived from samples with <30% or ≥30% DFI.

When DFI was treated as a continuous variable, positively correlations were observed with all timings of specific events (Table 2) and with the incidences of abnormal cleavage patterns (OR: 1.042, CI: 1.025 – 1.059) and multinucleation at 2-cell stage (OR: 1.053, CI: 1.030 – 1.076). An inverse correlation with the KIDScore rank (B: -0.218, CI: -0.044 - -0.007) was noted.

Morphokinetic data (hours)	B (95% CI)	p-value
tPNa	0.041 (0.020 – 0.062)	<0.001
tPNf	0.068 (0.034 – 0.102))	<0.001
t2	0.068 (0.036 – 0.100)	<0.001
t3	0.085 (0.047 – 0.124)	<0.001
t4	0.070 (0.029 – 0.110)	0.001
t5	0.120 (0.062 – 0.179)	<0.001
t6	0.117 (0.056 – 0.178)	<0.001
t7	0.104 (0.040 – 0.167)	0.001
t8	0.109 (0.037 – 0.181)	0.003
tSB	0.402 (0.203 – 0.602)	<0.001
tB	0.153 (0.038 – 0.268)	0.009

Table 2. Correlation between continuous DFI and embryo morphokinetics

Conclusions

Embryo morphokinetic parameters are negatively impacted by high sperm DFI, resulting in delayed cell cleavage and blastulation. It is possible that the deselection of those embryos might have led to similar clinical outcomes between the groups, nevertheless further studies are necessary to confirm this hypothesis.