PICSI® Dish Clinical Outcome Data (2022)

A data sheet evidencing Physiological ICSI using the PICSI® Dish helps to improve outcomes for older couples and for patients with previous ICSI failure.

Large randomized control trials (RCTs) are the gold standard for effective research. Since hyaluronan-based sperm selection, so-called physiological ICSI, was introduced in the early 2000's *(Huszar et al., 2007)*, many articles, including small RCTs, have been published claiming benefits of the technique: improved embryo development, increased pregnancy and implantation rates and decreased miscarriage rates (*Avalos-Duran et al., 2018).*

However, the need for a properly planned and large RCT persisted. In this data sheet we explore the latest publications: a large RCT and a recent retrospective study, supporting improved outcomes for older couples and patients with previous ICSI failure.

Study One

Physiological, hyaluronan-selected intracytoplasmic sperm injection for infertility treatment (HABSelect): a parallel, two-group, randomized trial *(Miller et al., 2019).*

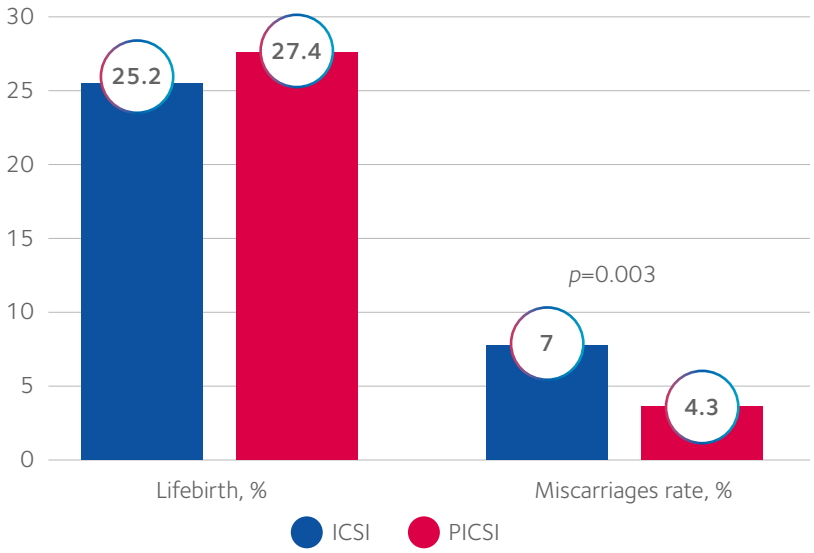
In 2019, Miller and colleagues published results from their HABSelect study – an RCT, supported by the UK National Institute for Health and Care Research.

- Carried out in 16 IVF centres in the UK
- Including 2,752 couples undergoing cycles of assisted reproduction
- Study compared physiological ICSI with PICSI® Dish with conventional ICSI

Outcomes of study

- Live birth rate was not significantly improved by physiological ICSI using the PICSI® Dish
- The use of PICSI® Dish led to a significant decrease in the miscarriage rate (secondary outcome) compared to conventional ICSI (Fig.1)

Figure 1: *Parallel, two-group, double-blinded RCT, carried out in 16 IVF clinics in the UK on 2,752 couples undergoing ICSI or PICSI*



HABSelect study primary and secondary outcomes. PICSI significantly reduces miscarriage rates compared to conventional ICSI

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Study Two

Sperm selection with hyaluronic acid improved live birth outcomes among older couples and was connected to sperm DNA quality, potentially affecting all treatment outcomes (*West et al., 2022*).

This publication detailed the results of the mechanistic part of the HABSelect study

- Researchers measured the ability of sperm to bind to hyaluronan and its correlation to DNA quality.
- A *post hoc* analysis of the original full HABSelect trial clinical outcomes by age was conducted.
- Authors built a predictive model from aggregation of the original HABSelect trial data into 10-year intervals for male and female age.

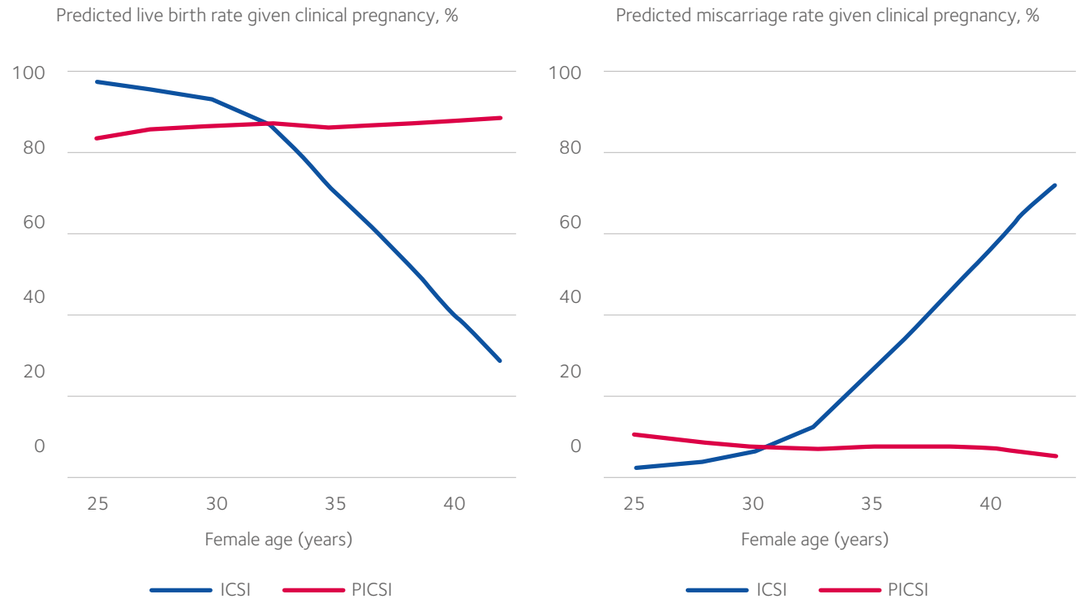
Outcomes of study

- Hyaluronan-binding score (HBS) correlated with sperm DNA quality, showing that sperm capable of binding to hyaluronan are more likely to have compact chromatin and intact DNA (Table 1).
- Older men and women randomized to the physiological ICSI group using PICSI® Dish had the same live birth rates and same low miscarriage rates as younger patients (Fig. 2), most likely due to avoidance of sperm with damaged DNA.
- The modeled live birth and miscarriage data strongly suggest that physiological ICSI using PICSI® Dish particularly mitigates the poor prognosis usually ascribed to women of "advanced maternal age."
- Post hoc analysis confirmed female age and treatment allocation to ICSI or physiological ICSI using PICSI® Dish to be significant factors with strong effects upon the establishment of a clinical pregnancy, continuing to a live birth, and the odds of miscarriage, particularly in those patients 35 years of age or older (Fig.3)

Table 1: *Correlations between 1247 semen samples assayed for the HBS and sperm DNA integrity*

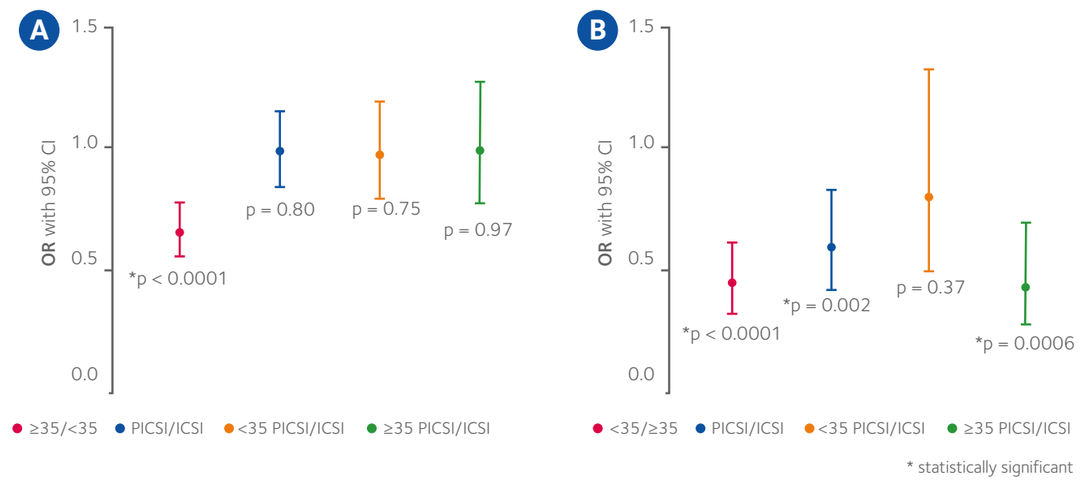
Method	What does this method detect?	Findings
Alkaline Comet	Mostly DNA single-strand breaks	Spermatozoa capable of binding to hyaluronan are more likely to have intact DNA
TUNEL	DNA single-strand and double-strand breaks	
Acridine Orange	DNA single-strand and double-strand breaks	
Sperm Chromatin Dispersion Assay	DNA single-strand and double-strand breaks	

Figure 2: *Modeled, predicted live birth rate and miscarriage rate with female age following ICSI or physiologic ICSI using PICSI® Dish*



The model demonstrated that PICSI helps to overcome negative effect of advanced maternal age on live birth and miscarriage rates

Figure 3: *HABSelect trial odds ratios (with female age and treatment allocation to ICSI or PICSI) of a clinical pregnancy continuing to a live birth (A) and miscarriage (B) as clinical outcomes*



Female age and treatment allocation to ICSI or PICSI are significant factors affecting live birth and miscarriage rates

Study Three

Hyaluronic acid-sperm selection significantly improves the clinical outcome of couples with previous ICSI cycles failure *(Scaruffi et al., 2022).*

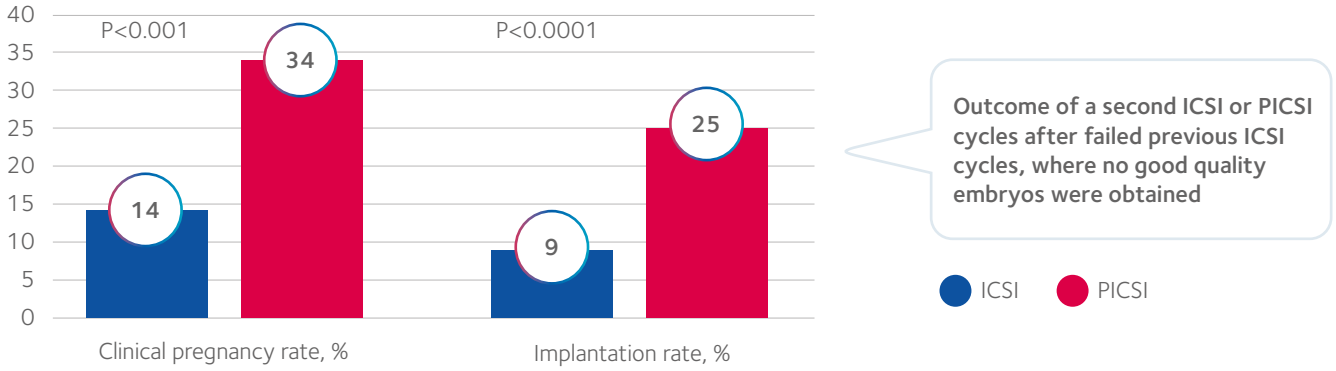
A retrospective study indicating hyaluronan-based sperm selection brings real value to IVF treatment, especially following previous unsuccessful ICSI cycles.

- A study of 167 couples with one failed ICSI attempt with low fertilization rate and poor embryo quality

Outcomes of study

- Cleavage rate, embryo quality, pregnancy and implantation rates were significantly higher in the group undergoing physiological ICSI with the PICSI® Dish compared to conventional ICSI

Figure 4: *Clinical pregnancy and implantation rates with standard ICSI or physiological ICSI using PICSI® Dish following one previous failed ICSI attempt characterized by low fertilization rate and poor embryo quality*



Conclusions

The ability of sperm to bind to hyaluronic acid is connected to sperm DNA quality, potentially affecting all treatment outcomes.

Sperm selection with hyaluronan significantly decreases miscarriage rates. Among older couples it improves live birth outcomes and helps to mitigate the poor prognosis usually ascribed to "advanced maternal age."

The use of hyaluronan for sperm selection may provide better treatment outcomes after previous failed ICSI cycle.

Hyaluronan-based selection of sperm for ICSI could be considered as part of the treatment plan for advanced-age couples and patients with previous unsuccessful ICSI attempts.

References

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4.West R, Coomarasamy A, Frew L, et al. Sperm selection with hyaluronic acid improved live birth outcomes among older couples and was connected to sperm DNA quality, potentially affecting all treatment outcomes. *Hum Reprod 2022*;37: 1106-25.

5.Scaruffi P, Bovis F, Casciano I, Maccarini E, De Leo C, Gazzo I, Massarotti C, Sozzi F, Stigliani S, Anserini P. Hyaluronic acid-sperm selection significantly improves the clinical outcome of couples with previous ICSI cycles failure. *Andrology 2022*; 10(4):677-685.