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How the Felix™ System compares with the most common sperm separation methods used in IVF clinics

Assisted Reproductive Technology and Sperm Separation Methods

The introduction of assisted reproductive technology (ART), especially *in vitro* fertilisation (IVF) during the 1980s, led to the development of a wide range of different sperm separation methods [1-3] . In the early years of ART, the focus was on obtaining motile spermatozoa. However, the focus has since shifted to the isolation of functional sperm, not only for IVF but also for intracytoplasmic spermatozoa injection (ICSI) ART procedures.

In parallel with ART development, the Swim Up (SU) and density gradient centrifugation (DGC) methods for spermatozoa separation were also developed in the 1980's. Forty years on, these remain the two most common global sperm separation methods used in the global market today.

In the 1990's, novel spermatozoa separation methods based upon electrophoresis, and the inherent negative charge in the mature spermatozoa, were investigated for their ability to decrease spermatozoa DNA fragmentation in the sperm separation process, and its ultimate potential to improve ART success.

The DGC Method for Sperm Separation

In the DGC method**,** the density gradient selects morphologically normal sperm cells based on their specific density [6-8]. However, exposing sperm to several centrifugation steps during this procedure may damage sperm DNA. So dense sperm can still have poor DNA, even if they are progressively motile [8-11].

The Swim Up method for Sperm Separation

The Swim Up method separates sperm with good progressive motility which correlates with good DNA quality [12, 13]. Good sperm motility is also essential for successfully engaging with the zona pellucida for oocyte fertilisation whether insemination is by natural conception or by IVF. However, any centrifugation steps , if used in the swim up procdedure, can increase levels of reactive oxygen species production which has been demonstrated to impair sperm quality and DNA [8, 14].

Generally, the Swim Up method provides a smaller yield of sperm than the DGC method [12].

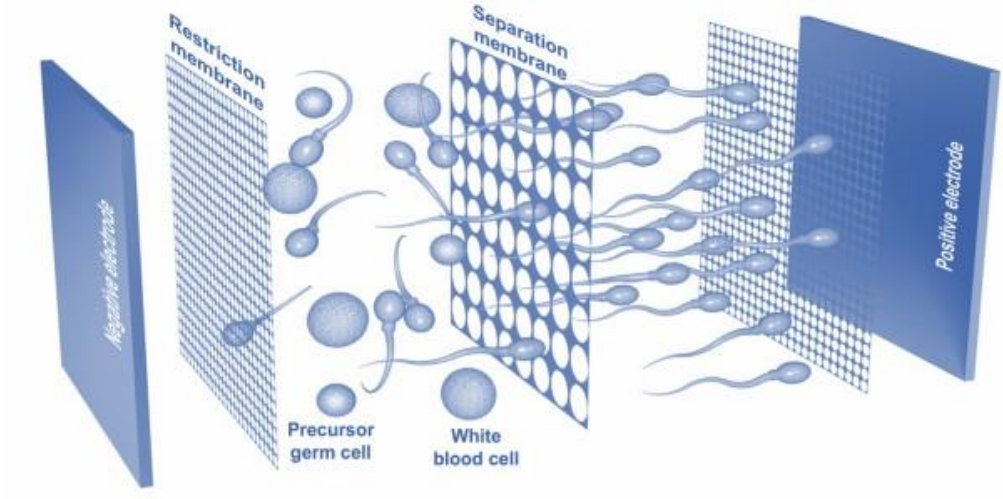
Depending on the semen sample, the quantity of sperm may not be sufficient for a natural IVF process[7]. The Swim Up method has further limitations: it cannot be

used on some semen samples such as those with very low sperm counts, highly viscous samples and/or those with poorly motile sperm.

The Felix™ System for sperm separation

Finally developed in 2020, the new Felix™ System uses electrophoretic and membrane size exclusion to separate the sperm based on their charge and size. This contrasts with the swim-up (SU) and density gradient centrifugation (DGC) methods which separate sperm based on their motility and density respectively.

Felix™ is a rapid, easy to use, automated membrane-based electrophoretic device. The Felix™ System separates high quality sperm [4, 5] from raw semen by a proprietary process combining electrophoresis and size exclusion membranes that allow high quality sperm into the harvest chamber while excluding cellular contaminants such as leukocytes and precursor germ cells.



The Felix™ sperm separation method offers potential benefits over the two traditional sperm separation methods – DGC and Swim Up . The Felix™ system separates on an entirely different principal based on the negative charge of the sperm, which are the sperm likely to have high quality DNA [5] . No centrifugation is required. The Felix™ system is not reliant on sperm motility or density and can process samples with poor sperm counts, poor motility and high viscosity.

The major operational advantage of the Felix™ System in the IVF clinic is the considerable efficiency gain, requiring only 6 minutes of processing to achieve sperm separation outcomes compared with the methods such as the double DGC-swim up technique, which takes at least 1 hour to perform [15]

In summary, the Felix™ System is a unique sperm isolation technique that efficiently selects sperm on the basis of their size and charge rather than the traditional criteria of sperm density or motility.

References

1. Jameel, T., *Spermatozoa swim-up: a simple and effective technique of semen processing for intrauterine insemination.* J Pak Med Assoc, 2008. 58(2): p. 71-4.
2. DeAngelis, A.M., A.E. Martini, and C.M. Owen, *Assisted Reproductive Technology and Epigenetics.* Semin Reprod Med, 2018. 36(3-04): p. 221-232.
3. Kushnir, V.A., et al., *Systematic review of worldwide trends in assisted reproductive technology 2004-2013.* Reprod Biol Endocrinol, 2017. 15(1): p. 6.
4. WHO. Laboratory manual for the examination of human semen and sperm–cervical mucus interaction, 4th ed. Cambridge, Cambridge University Press. 2010.
5. FEL-200 Report-Felix sperm separation validation report - Data on File.
6. Muratori M, Tarozzi N, Cambi M, Boni L, Iorio AL, Passaro C, et al. Variation of DNA Fragmentation Levels During Density Gradient Sperm Selection for Assisted Reproduction Techniques: A Possible New Male Predictive Parameter of Pregnancy? Medicine (Baltimore). 2016;95(20):e3624.
7. Pinto S, Carrageta DF, Alves MG, Rocha A, Agarwal A, Barros A, et al. Sperm selection strategies and their impact on assisted reproductive technology outcomes. Andrologia. 2021;53(2):e13725.
8. Raad G, Bakos HW, Bazzi M, Mourad Y, Fakih F, Shayya S, et al. Differential impact of four sperm preparation techniques on sperm motility, morphology, DNA fragmentation, acrosome status, oxidative stress, and mitochondrial activity: A prospective study. Andrology. 2021;9(5):1549-59.
9. Morrell JM, Rodriguez-Martinez H. Practical applications of sperm selection techniques as a tool for improving reproductive efficiency. Vet Med Int. 2010;2011.
10. Ghaleno LR, Valojerdi MR, Janzamin E, Chehrazi M, Sharbatoghli M, Yazdi RS. Evaluation of conventional semen parameters, intracellular reactive oxygen species, DNA fragmentation and dysfunction of mitochondrial membrane potential after semen preparation techniques: a flow cytometric study. Arch Gynecol Obstet. 2014;289(1):173-80.
11. Matson PL, Myssonski K, Yovich S, Morrison L, Irving J, Bakos HW. The density of human semen and the validation of weight as an indicator of volume: a multicentre study. Reprod Biol. 2010;10(2):141-53.
12. Henkel RR, Schill WB. Sperm preparation for ART. Reprod Biol Endocrinol. 2003;1:108.
13. Simon L, Lewis SE. Sperm DNA damage or progressive motility: which one is the better predictor of fertilization in vitro? Syst Biol Reprod Med. 2011;57(3):133-8.

14. Younglai EV, Holt D, Brown P, Jurisicova A, Casper RF. Sperm swim-up techniques and DNA fragmentation. Hum Reprod. 2001;16(9):1950-3.

15. Yamanaka M, Tomita K, Hashimoto S, Matsumoto H et al Combination of density gradient centrifugation and swim-up methods effectively decreases morphologically abnormal sperms. J Reprod Dev. 2016;62(6):599-606.

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The Felix™ System is not included on the Australian Register of Therapeutic Goods (ARTG) and is not available for clinical use in Australia.

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