REVOLUTIONIZING SPERM PREPARATION

ZyMōt™ Sperm Separation Devices: Better for your patients. Better for your practice.

A better way to prepare sperm

Quality, accuracy and efficiency are central to the success of a fertility practice. Traditional, centrifugation-based sperm preparation methods are not only time-consuming and laborious, but cause additional sperm DNA fragmentation¹ and cellular stress,² lowering the odds of success.^{3,4} ZyMōt Sperm Separation Devices are a better way to prepare sperm for use in IUI and ICSI procedures. It's that simple.

Simple to adopt. Easy to use.

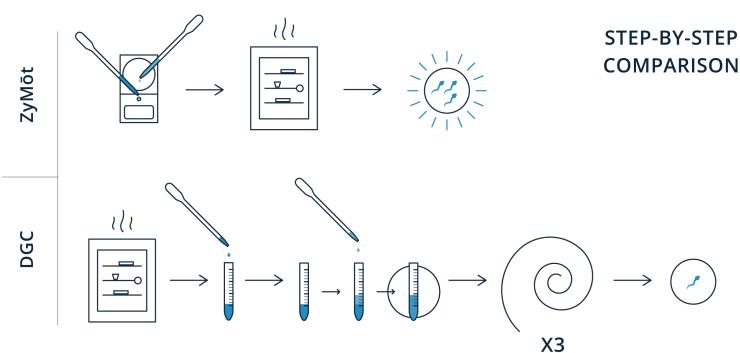
FDA-cleared, CE-certified and available worldwide, ZyMōt devices efficiently isolate the healthiest, rapidly progressive sperm, to help achieve outcomes that matter.⁵ Minimal training is required, with simple, standardized procedures that help users quickly achieve optimal performance.

Work on your timeline

ZyMōt devices enable processing whenever a sample is ready, eliminating delays caused by an equipment bottleneck. With **only 5 minutes of total hands-on tech time per sample**, every ZyMōt-processed specimen represents a significant time savings over traditional, centrifugation-based methods. Using ZyMōt devices frees staff for other critical tasks and improves lab productivity.

Fewer steps. More confidence.

A shorter chain of custody – fewer movements per sample – means that ZyMōt devices help minimize mismatching risk, reducing the potential for costly error. **Processing sperm with ZyMōt devices gives providers** more confidence and gives patients more peace of mind.



Comparison of major sperm separation steps when using ZyMōt Sperm Separation Devices (top) versus using traditional, centrifugation-based methods (bottom). ZyMōt requires fewer movements per sample, improving efficiency and productivity while reducing risk of costly errors.

Natural. Simple. Effective.

Try ZyMōt Sperm Separation Devices and realize immediate savings of time and resources, while providing premium quality sperm separation for your patients. **Learn more at zymotfertility.com.**

<u>References</u>

- 1. Zini, A., Finelli, A., et al. Urology (2000). doi: 10.1016/S0090-4295(00)00770-6
- 2. Aitken, R. J. and Clarkson, J. S. J Andrology (1988). doi: 10.1002/j.1939-4640.1988.tb01067.x
- 3. Dimakopoulou A., Jayasena C., et al. J Endocr Soc. (2019). doi: 10.1210/js.2019-OR18-5
- 4. Jayasena C.N., Radia, U.K. et al. Clin Chem (2019). doi: 10.1373/clinchem.2018.289348
- 5. Parrella, A., Keating, D. et al. J Assist Reprod Genet (2019). doi: 10.1007/s10815-019-01543-5





NATURE'S PRINCIPLES. PROVEN SUCCESS.

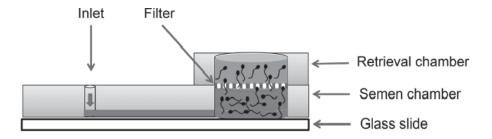
Understanding ZyMōt[™] Sperm Separation Devices

Better Sperm Selection by Mimicking Nature

DxNow has developed novel devices for use in ART procedures conducted by fertility clinics and OB/GYN practices. ZyMōt Multi Sperm Separation Devices prepare motile sperm from semen for use in IUI and ICSI procedures. These FDA-cleared, CE-certified devices are the first of their kind and available worldwide.

Our revolutionary tools simulate the natural barriers of the cervical and uterine pathway that sperm must overcome to fertilize an egg. We enable separation of optimally functional sperm without the use of damaging chemicals or density gradient centrifugation (DGC).

ZyMōt Multi



The ZyMōt Multi is available in two processing volumes, 850µL and 3mL. A sample is applied through the device's inlet port, connected to a lower sample chamber. This chamber is separated from an upper collection chamber by an 8µm microporous filter. Filter size was determined after comparison between 3µm, 5µm and 8µm pore sizes. Incubation times of 15, 30 and 45 minutes were evaluated, with sperm saturation achieved at 30 minutes.¹ These parameters yielded optimal sperm collection efficiency and motility, with the 8µm pore demonstrating the highest degree of normal morphology.²

During sample incubation, the most motile and genomically competent sperm migrate upward through the filter, leaving less motile sperm behind. Separated sperm are then collected from the upper chamber for subsequent use in IUI or ICSI procedures. **No centrifugation is required.**

Simplifying and Standardizing Workflow

Easy to adopt and simple to use, ZyMōt Multi Sperm Separation Devices provide considerable time savings and standardization over traditional methods. ZyMōt devices avoid damaging DGC and preserve normal sperm morphology, significantly reducing DNA fragmentation and reactive oxygen species (ROS) production. Contact us for more information about how to evaluate ZyMōt Devices in your clinic. We offer comprehensive support with experts who are ready to help you incorporate our tools into your practice and extend your success. Learn more at zymotfertility.com.

References

- 1. Tasoglu, S., Safaee, H., Zhang, X., Kingsley, J. L., Catalano, P. N., Gurkan, U. A., Nureddin, A., Kayaalp, E., Anchan, R. M., Maas, R. L., Tüzel, E. and Demirci, U. (2013), Exhaustion of Racing Sperm in Nature Mimicking Microfluidic Channels During Sorting. Small, 9: 3374-3384. doi:10.1002/smll.201300020
- 2. Asghar, W., Velasco, V., Kingsley, J. L., Shoukat, M. S., Shafiee, H., Anchan, R. M., Mutter, G. L., Tüzel, E. and Demirci, U. (2014), Selection of Functional Human Sperm with Higher DNA Integrity and Fewer Reactive Oxygen Species. Adv. Healthcare Mater., 3: 1671-1679. doi:10.1002/adhm.201400058





ZYMŌT™ DATA SPOTLIGHT: DNA & ROS

Understanding the latest science in the ZyMot revolution

The Need for Healthy Sperm

Using healthy sperm for IUI and ICSI procedures is more important than ever. In new research¹ from scientists at Imperial College London, recurrent pregnancy loss was directly connected to the presence of elevated sperm DNA fragmentation and reactive oxygen species, along with a lower percentage of normal morphology. This follows a growing body of evidence that links improved sperm health to better pregnancy outcomes.² By avoiding sperm-damaging centrifugation, ZyMōt devices enable the separation of sperm with the lowest-possible levels of DNA fragmentation and oxidative stress. Improved sperm health means better clinical outcomes.

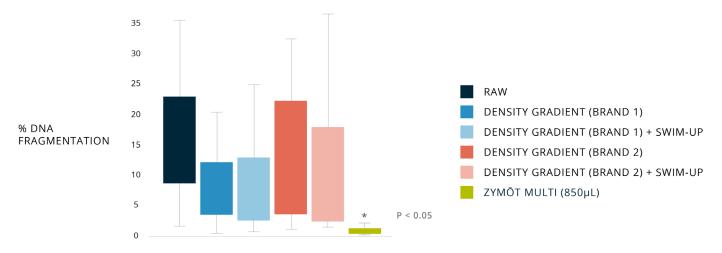
Avoiding DNA Fragmentation and Oxidative Stress

ZyMōt ICSI Sperm Separation Devices have been shown to separate sperm with near-zero DNA fragmentation, compared to density gradient centrifugation.³ In an independent study from Midwest Fertility Specialists, ZyMōt (850µL) Sperm Separation Devices were

directly compared to traditional sperm preparation techniques.⁴ This clinical research determined which approach resulted in improved DNA fragmentation index (DFI) and other sperm health biomarkers such as oxidative stress adducts (OSA) and high DNA stainability (HDS).

Results: Using ZyMōt effectively reduced DFI (P<0.05) compared to standard protocols: two commercially available gradients, and gradients followed by swim-up. The device also significantly reduced (P<0.05) OSA levels, a measurement of oxidative stress, and HDS, a measurement of immature cells and high histone retention. "Overall, the quality of the sperm obtained post-processing was improved by the use of the separation device," wrote the study author.

Conclusion: Using ZyMōt devices shows statistically significant improvements in three DNA- and stress-focused indicators of sperm health and function, when compared to traditional, centrifugation-based methods.



Comparison of DNA fragmentation levels for raw semen, and after processing with commercially available gradients (with and without swim-up) and ZyMōt Sperm Separation Devices.

Improving Efficiency and Outcomes

ZyMōt devices are easy to adopt and simple to use, helping labs quickly achieve optimal performance. With only 5 minutes of total hands-on tech time per sample, every ZyMōt-processed specimen represents a significant time savings over traditional, centrifugation-based methods. In addition to increased efficiency, ZyMōt devices deliver improved sperm performance to achieve the best possible outcomes in IUI and ICSI procedures. Learn more at zymotfertility.com.

References

- A.P. Dimakopoulou et al. Elevated semen oxidative stress in male partners as novel marker of recurrent pregnancy loss. ENDO 2019, New Orleans, March 24, 2019.
- C.N. Jayasena et al. Reduced testicular steroidogenesis and increased semen oxidative stress in male partners as novel markers of recurrent miscarriage. Clinical Chemistry. Volume 65. January 2019. p. 161.
- M.M. Quinn et al. Microfluidic sorting selects sperm for clinical use with reduced DNA damage compared to density gradient centrifugation with swim-up in split semen samples. Hum Reprod. July 10, 2018. doi: 10.1093/humrep/dey239.
- Broussard A et al. Sperm DNA fragmentation (SDF) was most effectively improved by a sperm separation device compared to different gradient and swim-up methods. Fertility and Sterility, Volume 111, Issue 4, e15.





ZYMŌT™ DATA SPOTLIGHT: MOTILITY & MORPHOLOGY

Understanding the latest science in the ZyMōt revolution

Delivering Superior Motility and Morphology

ZyMōt™ Sperm Separation Devices were designed and developed to aid reproductive medicine professionals in the selection of the healthiest and best performing sperm for use in assisted reproductive technology (ART) procedures. ZyMōt enables the separation of sperm with the lowest possible levels of DNA fragmentation and oxidative stress, while increasing fertilization and euploidy rates. Processing with ZyMōt has also been shown to increase the proportion of sperm with normal morphology. Improved sperm health means better clinical outcomes.

In an internal study of sperm health, ZyMōt Multi Sperm Separation Devices (850 μ L) was evaluated in a heterogeneous population of more than two dozen samples.

Results: Median motility increased significantly (P<0.01) after processing with ZyMōt devices (below, left). Similarly, progressive motility showed a significant increase (P<0.01) after processing (below, right). ZyMōt processing also improved the proportion of sperm with normal morphology.

Conclusion: Using ZyMōt devices shows statistically significant improvements in sperm motility and progression, enriching a sample for improved sperm performance.



In an internal study of a heterogeneous population of more than two dozen samples, ZyMōt devices were shown to significantly increase motility (left), and progressive motility (right).

Improving Efficiency and Outcomes

ZyMōt devices are simple to use, helping labs quickly achieve optimal performance. With only 5 minutes of total hands-on tech time per sample, every ZyMōt-processed specimen represents a significant time savings over traditional, centrifugation-based methods. In addition to increased efficiency, ZyMōt devices deliver improved sperm performance to achieve the best possible outcomes in IUI and ICSI procedures. Learn more at zymotfertility.com.





ZYMŌT™ DATA SPOTLIGHT: IMPROVING OUTCOMES

Understanding the latest science in the ZyMōt revolution

Increasing Fertilization and Euploidy Rates

ZyMōt™ Sperm Separation Devices have been designed and developed to aid reproductive medicine professionals in the selection of the healthiest and best performing sperm for use in assisted reproductive technology (ART) procedures. ZyMōt devices enable the separation of sperm with the lowest possible levels of DNA fragmentation and oxidative stress. Improved sperm health means better clinical outcomes.

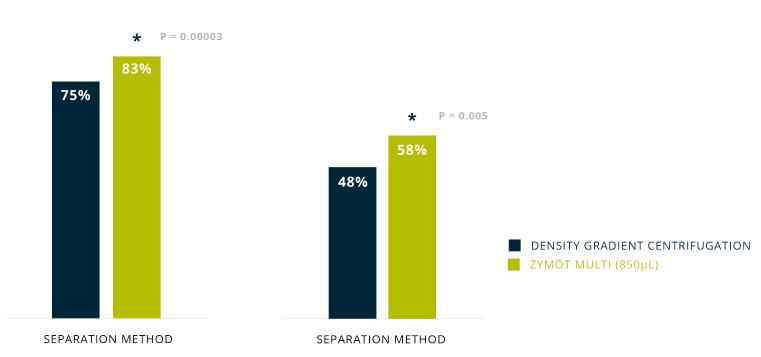
Results: In a study of over 3600 oocytes at The Fertility & IVF Center of Miami, the center observed a significant increase in fertilization rates, from 75% using their traditional sperm preparation methods to 83%

when using ZyMōt devices, an 11% increase (P=0.05) over the baseline rate (below, left). Following the biopsy of over 1300 embryos, traditional methods yielded a 48% euploidy rate, which improved significantly to 58% when using ZyMōt devices, an increase of 21% (P<0.05) over baseline (below, right).

Conclusion: The ZyMōt Multi (850µL) Sperm Separation Device resulted in significantly improved fertilization and euploidy rates. ZyMōt devices offer a competitive advantage to lab workflow and patient outcomes.

FERTILIZATION RATE

EUPLOIDY RATE



At The Fertility & IVF Center of Miami, using the ZyMōt Multi (850μ L) Sperm Separation Device resulted in an 11% increase over the baseline fertilization rate (left) and a 21% increase over the baseline euploidy rate (right).

Improving Efficiency and Outcomes

ZyMōt devices are simple to use, helping labs quickly achieve optimal performance. With only 5 minutes of total hands-on tech time per sample, every ZyMōt-processed specimen represents a significant time savings over traditional, centrifugation-based methods. In addition to increased efficiency, ZyMōt devices deliver improved sperm performance to achieve the best possible outcomes in IUI and ICSI procedures. Learn more at zymotfertility.com.





HIGHER GENOMIC COMPETENCE IMPROVES OUTCOMES

Understanding the latest sperm science in the ZyMōt™ revolution

Not all sperm are created equal

Using the best sperm helps increase the odds of a successful fertility treatment cycle. **But not all sperm are created equal**: up to 11% of men with a normal semen analysis have a measurable problem with sperm chromatin (DNA) fragmentation, and thus reduced motility.¹

ZyMōt Sperm Separation Devices are a better way to process sperm, without harmful centrifugation.^{2,3} ZyMōt devices enable the separation of sperm with nearly undetectable levels of DNA fragmentation and oxidative stress.⁴ Improved sperm health means better clinical outcomes.^{5,6}

In research¹ from scientists at Weill-Cornell Medical College, ZyMōt devices were directly compared to density gradient centrifugation (DGC), evaluating parameters of sperm health and clinical outcomes.

Results

In a collection of 23 patients, semen samples were split and processed by either DGC or the ZyMōt Multi 850µL device, with analyses before and after processing. Highly statistically significant results were observed in the ZyMōt-processed samples, when compared to DGC: **Sperm motility and normal morphology increased. DNA fragmentation decreased.**

Similar processing was applied to another 25 couples undergoing intracytoplasmic sperm injection (ICSI). Again, statistically significant results were observed when ZyMōt processing was compared to DGC: improved sample motility, progression and normal morphology. There was a dramatic decrease in DNA fragmentation.

In studying clinical outcomes within a cohort of 16 patients with a history of recurrent implantation failure, ZyMōt device use followed by fresh embryo transfer in 9 patients resulted in a **50% clinical pregnancy rate**. This group of patients had experienced a 0% implantation rate in their previous cycles, which used density gradient centrifugation.

The remaining 7 patients in the cohort underwent PGT-A prior to a frozen embryo transfer. These patients saw a statistically significant increase in the number of euploid embryos following the use of a ZyMōt Multi (850 μ L) Sperm Separation Device. Additionally, they experienced an **80% ongoing pregnancy rate**.



The ZyMōt Multi (850µL) device delivers a processed sperm sample with significantly reduced DNA fragmentation, increased motility and normal morphology, leading to improved euploid rates and more healthy pregnancies.

Conclusion

Processing with ZyMōt enhanced sperm sample motility, progression and morphology, along with providing a "remarkable reduction" of DNA fragmentation. ZyMōt devices yielded sperm with "higher genomic competence" demonstrated by their improved euploid rate and ability to establish healthy pregnancies. ZyMōt devices are suitable for use with IUI and ICSI procedures. Learn more at zymotfertility.com.

References

- Parrella, A., Keating, D., Cheung, S. et al. J Assist Reprod Genet 36, 2057–2066 (2019). doi: 10.1007/s10815-019-01543-5
- 2. Zini, A., Finelli, A., et al. Urology (2000). doi: 10.1016/S0090-4295(00)00770-6
- 3. Aitken, R. J. and Clarkson, J. S. J Andrology (1988). doi: 10.1002/j.1939-4640.1988.tb01067.x
- Broussard, A., Leader B., et al. PCRS 2019 (2019).
- 5. Dimakopoulou A., Jayasena C., et al. J Endocr Soc. (2019). doi: 10.1210/js.2019-OR18-5
- 5. Jayasena C.N., Radia, U.K. et al. Clin Chem (2019). doi: 10.1373/clinchem.2018.289348





IMPROVING IUI OUTCOMES

Understanding the latest sperm science in the ZyMōt™ revolution

Intrauterine insemination (IUI) is routinely used as the first line of treatment for infertility patients. The procedure is less invasive, requires little or no medication, and amounts to a fraction of the cost of an IVF cycle. Pregnancy rates following IUI treatment have historically been low, and it is common for patients to complete multiple IUIs prior to moving on to an IVF cycle.¹

A Better Way to Process Sperm for IUI

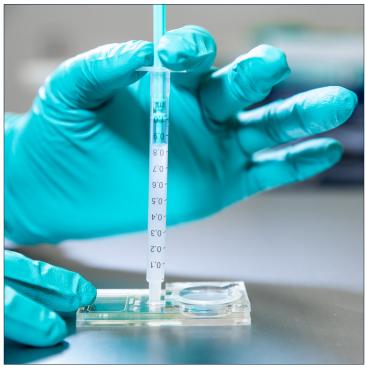
ZyMōt Sperm Separation Devices offer an alternative preparation method that allows for **simple**, **natural**, **and effective isolation of motile sperm with the greatest chromatin integrity**. Previous studies have demonstrated a reduction in IUI pregnancy rates in couples with elevated levels of DNA fragmentation.² **ZyMōt devices have been shown to reduce sperm DNA fragmentation and cellular stress**.³

Results: In a retrospective study of 265 IUI patients with unexplained infertility, patients whose semen samples were processed using ZyMōt Sperm Separation Devices were 3.5 times more likely to achieve an ongoing pregnancy than the age-matched control group, where sperm was processed with the traditional, centrifugation-based method.⁴ In this study, the ZyMōt IUI treatment group also experienced a reduced miscarriage rate when compared to patients whose semen samples were processed by density gradient (0% vs. 5% respectively).⁴

9.1% DENSITY GRADIENT CENTRIFUGATION ZYMŌT MULTI (850µL)

The effect of IUI sperm preparation method on pregnancy outcomes: ZyMōt improved treatment prognosis.

Conclusion: Processing sperm with ZyMōt devices can improve a patients' IUI treatment prognosis at the onset of their infertility journey, offering the greatest chance of success with the lowest risk treatment option.



The ZyMōt Multi (850μ L) device accepts 850μ L of raw semen input, and yields a final sample volume of 500μ L — directly suitable for IUI procedures. No centrifugation is required.

Simple to Adopt. Easy to Use.

FDA-cleared, CE-certified and available worldwide, ZyMōt Sperm Separation Devices efficiently isolate the healthiest, rapidly progressive sperm, to help achieve outcomes that matter. Minimal training is required, with simple, standardized procedures that help users quickly achieve optimal performance. ZyMōt Sperm Separation Devices are a better way to prepare sperm. It's that simple. Learn more at zymotfertility.com.

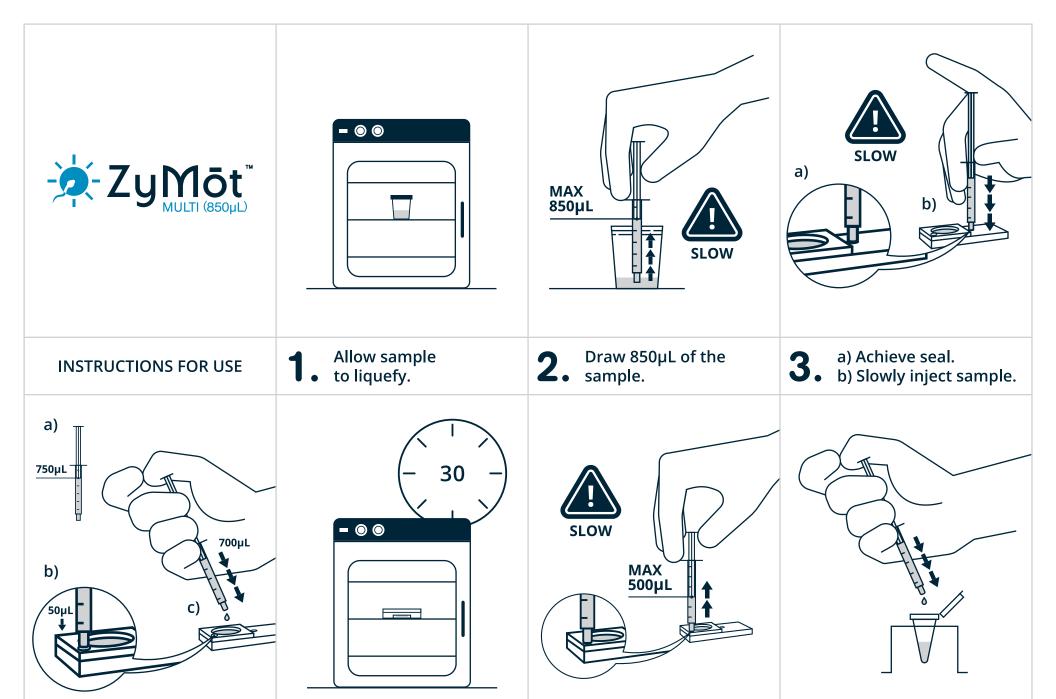
References

- 1. Cohlen, B., et al. Hum Reprod Update (2018). doi: 10.1093/humupd/dmx041
- Evenson, D. and Wixon, R. Reprod Biomed Online (2006). doi: 10.1016/s1472-6483(10)62000-7
- 3. Broussard, A., et al. Fertility and Sterility, Volume 111, Issue 4, e15. (2019).
- 4. Gode, F., et al. Fertil Steril (2019). doi: 10.1016/j.fertnstert.2019.06.037
- 5. Parrella, A., et al. J Assist Reprod Genet (2019). doi: 10.1007/s10815-019-01543-5



SPERM SEPARATION METHOD





a) Draw 750μL of media.b) Prime outlet channel.c) Cover membrane.

5. Incubate at 37°C for 30 minutes.

6. Slowly aspirate a maximum of 500μL.

7. Transfer the collected material for later use.