ESCO MEDICAL

Scientific Evidence for

MIRI® Time-Lapse Incubator

The Next Generation of Time-Lapse Systems

This equipment is a CE-marked device and is in conformity with the essential requirements of the medical devices EU regulation 2017/745.

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MIRI® TL12

MIRI® TL6

Blastocyst Collapse and Re-Expansion Dynamics

The Effect of Pipette and Laser-Induced Blastocyst Collapse Before Vitrification on Their Re-Expansion and Clinical Outcome After Warming
Martínez-Rodero et al., 2025
Reproductive BioMedicine Online, 50(2), 104476

Key outcomes:

- **Precise monitoring after warming:** Continuous 5-minute imaging in MIRI® TL enabled accurate tracking of blastocyst re-expansion and hatching dynamics.
- **High embryo survival: 96.9%** post-warming survival rate confirmed MIRI® TL's stable culture environment.
- **Faster re-expansion detection:** Blastocysts collapsed by **laser re-expanded faster (tRE = 0.50 ± 0.37 h)** than those **collapsed mechanically (0.79 ± 0.56 h)** or **unmanipulated (1.22 ± 1.00 h)**.
- **Clear predictive insights:** Blastocysts showing earlier re-expansion **(approximately 0.6 h)** were strongly associated with higher live-birth outcomes.

Scientific Significance for User:

MIRI® TL provided precise, non-invasive tracking of post-warming dynamics, confirming early re-expansion as a key viability marker and demonstrating system's stability and sensitivity in embryo assessment.

MIRI® TL AI-Ready Imaging for Advanced Embryo Selection

A Novel Deep Learning Approach to Identify Embryo Morphokinetics in Multiple Time-Lapse Systems
Canat et al., 2024
Scientific Reports, 14(1), 29016.

Key outcomes:

- **High-quality, AI-ready imaging:** MIRI® TL provided high-resolution, biologically consistent imaging data that enabled AI-powered the deep learning model Biological Event Extraction (BEE) successfully recognized **11 key morphokinetic events** from the 1-cell stage to the blastocyst.
- **Reliable, clinically relevant performance:** The AI model, powered by high-quality MIRI® TL imaging, achieved a weighted average **F1-score of 52.3%** and showed excellent correlation with embryologist annotations **(R^2 = 0.95)**, and reached **96% accuracy** in predicting blastocyst formation.

Scientific Significance for User:

MIRI® TL provides AI-ready, high-quality imaging fully compatible with modern AI-driven embryo analysis tools, enabling accurate morphokinetic evaluation, blastocyst prediction, and improved precision and efficiency in automated embryo assessment.

Correlating Morphokinetics with Live Birth Outcomes

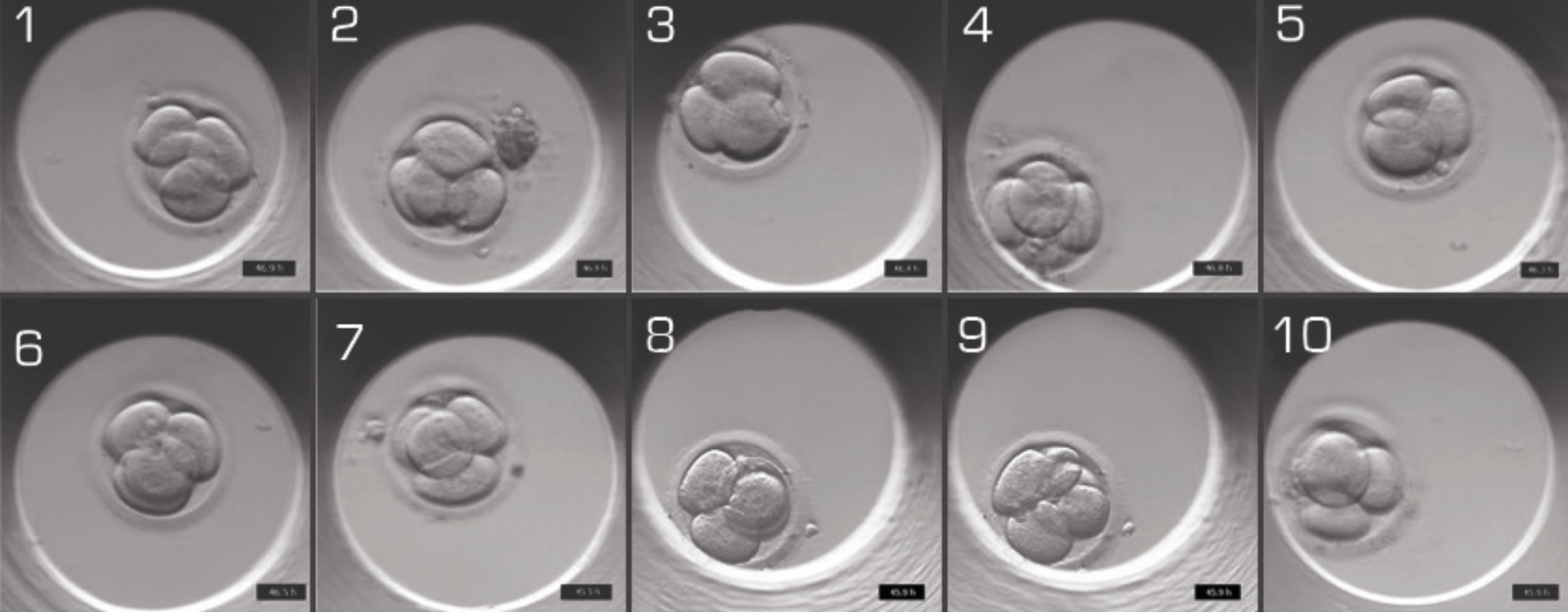
Correlation between Human Embryo Morphokinetics Observed through Time-Lapse Incubator and Life Birth Rate
Maghiar et al., 2024
Journal of Personalized Medicine, 14(10), 1045.

Key outcomes:

- **Efficient cell division dynamics:** Among 89 embryos analyzed, those resulting in **live births (n = 57)** progressed more rapidly through key stages **(t2–t8, CC2, CC3)** than **non-implanted embryos (n = 32).**
- **Correlation with embryo quality:** High-quality embryos (AA grade) exhibited superior morphokinetic timing and were significantly associated with implantation success ($p < 0.01$).

Scientific Significance for User:

MIRI® TL's continuous, non-invasive imaging provides precise and clinically relevant data to detect subtle morphokinetic differences and support more accurate embryo viability prediction of implantation potential in IVF laboratories.



Clinical Reliability and Environmental Stability

Time-Lapse Incubation for Embryo Culture—Morphokinetics and Environmental Stability May Not Be Enough: Results from a Pilot Randomized **Controlled Trial**
Sacks et al., 2024
Journal of Clinical Medicine, 13(6), 1701.

Key outcomes:

- **Consistent clinical outcomes:** Across 102 patients and 1061 oocytes, no significant differences were observed in live-birth rates **(24%–41.7%)**, blastulation rates **(37.6–48.1%)**, and cumulative pregnancy outcomes **(63.9%–73.5%)**, confirming that MIRI® TL system maintains optimal, undisturbed culture conditions for consistent embryo development.
- **Enhanced detection of abnormalities:** Continuous MIRI® TL monitoring detected subtle events such as multinucleation more frequently (**14.7%** in the morphokinetic and morphological assessment group and **14.2%** in the morphological assessment group) compared with **3.8%** in the conventional group (non-time-lapse imaging) (p = 0.003), demonstrating superior sensitivity for capturing subtle and dynamic abnormalities.

Scientific Significance for User:

MIRI® TL provides a precise and stable platform for detailed, non-invasive embryo monitoring, accurate annotation of developmental events, and superior detection of subtle dynamic abnormalities, offering deeper biological insights, supporting more informed decision-making, and improving outcomes in IVF laboratories.

Artificial Oocyte Activation and Morphokinetics

Ionophore Application for Artificial Oocyte Activation and Its Potential Effect on Morphokinetics: A Sibling Oocyte Study
Shelb et al., 2021
Journal of assisted reproduction and genetics, 38(12), 3125-3133.

Key outcomes:

- **Improved developmental kinetics:** The MIRI® TL system captured earlier pronuclei formation **(t2PNa = 8.2 h vs. 8.9 h, p = 0.002)** and more synchronized cleavage **(s3, p = 0.036)** following ionophore treatment, without an increase in abnormal division patterns.
- **Enhanced fertilization outcomes:** High precision time-lapse data linked ionophore activation with higher fertilization rates **(78.2% vs. 69.3%)** and improved blastocyst utilization **(54.6% vs. 48.2%, p = 0.05).**

Scientific Significance for User:

By providing detailed, objective development data, MIRI® TL enables the detection of subtle morphokinetic changes and supports the validation of new assisted fertilization techniques.

Advancing Insight into DNA Integrity and Embryo Development

Female Ageing Affects the DNA Repair Capacity of Oocytes in IVF Using a Controlled Model of Sperm DNA Damage in Mice
Horta et al., 2020
Human Reproduction, 35(3), 529-544.

Key outcomes:

- **Detection of developmental delays:** MIRI® TL imaging revealed delayed first cleavage **(t2 = 25.8–2.5 h)** and reduced blastocyst formation in embryos derived from DNA-damaged sperm.
- **Oocyte age-dependent outcomes:** Blastocyst formation was significantly lower with older oocytes **(70.4% in control vs. 0% after DNA damage)**, while younger oocytes maintained higher developmental potential **(86.9% control; 33.3% after mild DNA damage)**, indicating effective age-related DNA repair capacity.

Scientific Significance for User:

MIRI® TL's precision in detecting early morphokinetic alterations linked to DNA damage and oocyte competence, confirming its value as a non-invasive, high-sensitivity system for studying embryo viability and DNA repair dynamics.

AI-Driven Real-Time Embryo Assessment with MIRI® TL

Embryo Development Stage Prediction Algorithm for Automated Time-Lapse Incubators
Dirvanauskas et al., 2019
Computer methods and programs in biomedicine, 177, 161-174.

Key outcomes:

- **Supporting high AI performance:** The EMCA (Embryo Morphokinetic Classification Algorithm), trained on MIRI® TL imaging data, achieved up to **97.62%** overall accuracy, including **nearly 100%** in early (1- and 2 cell) stages and **96–98%** in later (4- and 8 cell) stages, and **over 93%** in detecting abnormal embryos.
- **Optimized for real-time AI analysis:** The high quality and biological consistency of MIRI® TL imaging allow novel AI models to operate in real time **(~0.1 s/image)**, facilitating fast processing and automated embryo assessment.

Scientific Significance for User:

MIRI® TL empowers next-generation AI models to deliver exceptional accuracy in embryo assessment and abnormality detection, while its real-time compatibility enables rapid, automated evaluation, driving smarter decision-making, greater efficiency, and improved outcomes in IVF laboratories.

High-Resolution Insights into Dynamic Cellular Processes with MIRI® TL

Time-Lapse Imaging of Cytoplasmic Strings at the Blastocyst Stage Suggests Their Association with Spontaneous Blastocoel Collapse
Ebner et al., 2020
Reproductive Biomedicine Online, 40(2), 191-199.

Key outcomes:

- **Comprehensive blastocyst visualization: :** MIRI® TL's high-resolution time-lapse imaging enabled continuous monitoring of 387 blastocysts, achieving a 62.4% blastocyst formation rate.
- **Detection of subtle cellular features:** Advanced optical quality and continuous monitoring allowed precise identification of cytoplasmic strings in 43.9% blastocysts.
- **Biological relevance:** High-precision imaging revealed a significant association between cytoplasmic strings and blastocoel collapses ($p < 0.001$) without negative impact on morphokinetic parameters or clinical outcomes.

Scientific Significance for User:

MIRI® TL is a reliable solution for advanced, non-invasive embryo assessment, providing continuous, high-quality visualization that reveals dynamic cellular processes and subtle morphokinetic behaviours undetectable with static observation, helping IVF laboratories enhance consistency and decision-making.

Non-Invasive Monitoring Across Species

Equine Non-Invasive Time-Lapse Imaging and Blastocyst Development
Mayers et al., 2019
Reproduction, Fertility and Development, 31(12), 1874-1884

Key outcomes:

- **Non-invasive, continuous imaging:** MIRI® TL provided uninterrupted, **5-minute interval** monitoring of equine embryos under precisely controlled temperature and gas conditions for up to **10 days** after ICSI.
- **Precise morphokinetic annotation:** High-frequency MIRI® TL's imaging system captured exact timings of early mitotic events – debris extrusion (approximately 20 h post ICSI), first cleavage (t2 = 24.9 ± 1.1 h), and blastocyst formation (t8 = 79.1 ± 3.3 h).
- **Predictive developmental insights:** Embryos reaching the blastocyst stage showed shorter cleavage intervals with **t2 (23–32 h)** and **t8 (62–96 h)** timing predicting blastocyst formation with **>50% probability**, while delayed divisions were linked to failed development ($p < 0.05$).
- **Dynamic developmental features:** Thanks to its exceptional imaging sensitivity, MIRI® TL uniquely captured **rhythmic blastocyst pulsation** approximately **every 10 minutes**, as a potential indicator of healthy development.
- **Safe imaging technology:** Despite generating approximately **1750 images** per embryo, total light exposure remained below phototoxic thresholds, confirming MIRI® TL's system safety.

Scientific Significance for User:

MIRI® TL's precision, stability, safety and cross-species reliability for detailed morphokinetic analysis, establishing it an ideal system for developmental research and optimization of assisted reproduction in animals.

Identifying Abnormal Embryo Development Patterns

Time-Lapse Imaging Provides Further Evidence that Planar Arrangement of Blastomeres is Highly Abnormal
Ebner et al., 2016
Archives of Gynecology and Obstetrics, 296(6), 1199-1205.

Key outcomes:

- **Precise cleavage pattern evaluation:** Continuous time-lapse monitoring MIRI® TL enabled accurate assessment of early embryo cleavage dynamics **in 115 ICSI cycles**, distinguishing **planar (5.5%)** and **tetrahedral (17.4%)** 4-cell embryos.
- **Accurate detection of timing and irregularities:** The system's stable culture environment and multi-focal imaging allowed precise identification of cleavage timing and irregular events.
- **Revealing developmental differences:** MIRI® TL imaging demonstrated that planar embryos exhibited a significantly reduced **blastocyst formation rates (37.5% vs. 58.8%)**, higher **bi/multinucleation (40.6% vs. 7.8%, $p < 0.001$)**, and greater frequency of **abnormal cleavages events ($p < 0.0001$)**.
- **Detection of subtle delays:** Detailed morphokinetic analysis revealed developmental delays between **t2–t4 and t8**, detectable only through continuous observation.
- **Proven biological neutrality:** Planar embryos were also observed in **conventional incubators**, confirming that MIRI® TL does not induce planar cleavage and ensuring **biological neutrality** and **reliability**.

Scientific Significance for User:

Continuous monitoring with MIRI® TL enables early detection of subtle developmental abnormalities in planar embryos, enhancing selection accuracy and clinical decision-making without disrupting optimal culture conditions.

Temperature Control and Morphokinetic Stability

Impact of a Controlled Culture Temperature Gradient on Mouse Embryo Development and Morphokinetics
Walters et al., 2020
Reproductive BioMedicine Online, 40(4), 494-499.

Key outcomes:

- **High-precision monitoring:** A stable culture environment with uninterrupted 5-minute imaging across six independent chambers allowed precise monitoring of developmental changes under different temperature conditions **(35.0–37.5 °C).**
- **Sensitivity to subtle changes:** The MIRI® TL's high accuracy detected significant developmental effects from even 0.5 °C variations, which significantly affected blastocyst formation and cell division timing, confirming the need for strict temperature uniformity.
- **Optimized outcomes:** Optimal embryonic development was observed precisely at **37.0 °C**, while lower temperatures **(35.0–36.0 °C)** resulted in slowed cell division, and higher temperatures led to accelerated cleavage dynamics.

Scientific Significance for User:

By isolating temperature as a single variable, MIRI® TL demonstrates chamber-level temperature accuracy, generating standardized and reproducible morphokinetic data to support consistent embryo assessment and evidence-based selection decisions.

Predicting Implantation Potential after Vitrification

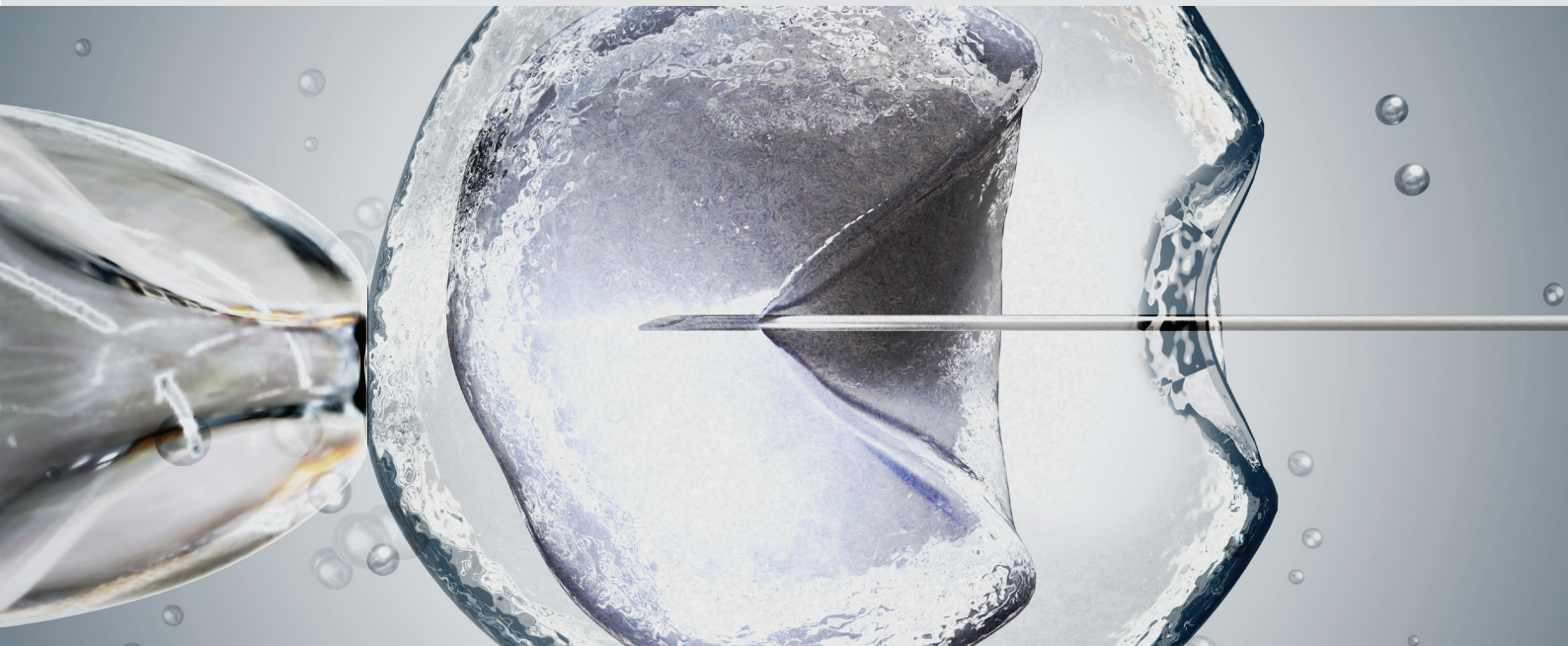
Morphokinetics of Vitrified and Warmed Blastocysts Predicts Implantation Potential
Ebner et al., 2016
Journal of assisted reproduction and genetics, 34(2), 239-244.

Key outcomes:

- **New morphokinetic insights:** Precise annotations of three new post-warming events – tRE (start of re-expansion), tCRE (completion of re-expansion), and tAH (start of artificial hatching) – expands understanding of embryo behaviour.
- **Identification of key viability indicators:** Continuous, high-resolution monitoring revealed that blastocysts associated with higher implantation and live-birth rates re-expanded earlier **(approximately 0.7 h after warming)** and completed re-expansion faster **(tCRE = 2.16 ± 0.94 h)** than those that did not result in pregnancy.

Scientific Significance for User:

MIRI® TL's continuous, high-resolution imaging enabled precise monitoring of these subtle post-warming dynamics, establishing early re-expansion as a reliable, non-invasive marker of embryo viability and supporting improved embryo selection and clinical outcomes.



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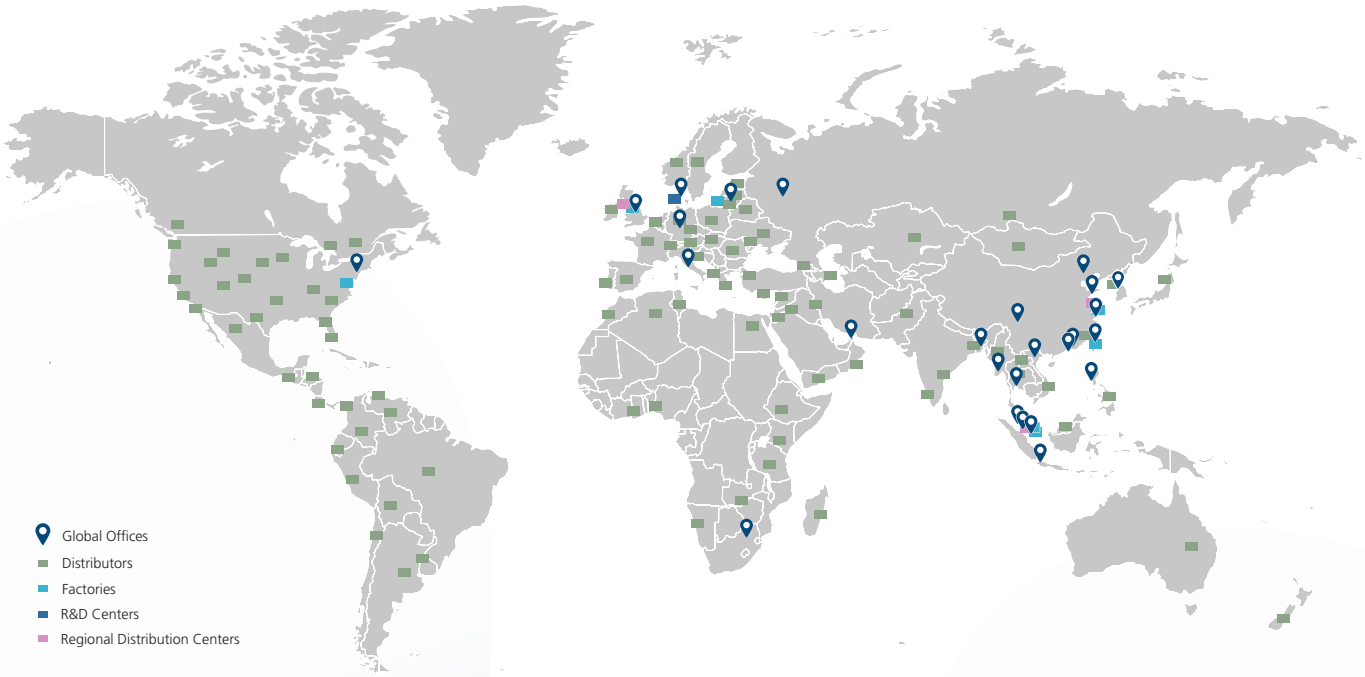

Esco Medical Products:

MIRI® M Multiroom Incubator
MIRI® Multiroom Incubator
MIRI® Humidity Multiroom Incubator
MIRI® II-12 Multiroom Incubator
Mini MIRI® Dry Multiroom Incubator
Mini MIRI® Humidity Multiroom Incubator
MIRI® TL6 Time-Lapse Incubator
MIRI® TL12 Time-Lapse Incubator
Multi-Zone ART Workstation
MIRI® Laminar Flow Cabinet
MIRI® Evidence RFID Witnessing & Traceability System
CelCulture® CO_2 Incubator
MIRI® GA (Gas and Temperature Validation Unit)
MIRI® AVT
CultureCoin®

Infertility is a problem that has a significant social, psychological, and economic impact on afflicted individuals and couples. It is a global concern that knows no race or creed. It has been estimated that 1 in 6 couples struggle with infertility at least once in their lifetime.

Esco Medical is one of the divisions of the Esco Lifesciences Group. We provide innovative technological solutions for fertility clinics and laboratories. We aim to become the leading manufacturer of high-quality equipment such as long-term embryo incubators, ART workstations, anti-vibration tables, and time-lapse incubators.

Our products are designed with the Silent Embryo Hypothesis as a guiding principle. The Silent Embryo Hypothesis states that the less disturbed an embryo can remain, the better its developmental potential will be. Most of our products are designed in Denmark and made in the EU. Our primary focus is to increase pregnancy success rates and patient satisfaction.

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Designed and Made in the E.U.