Improving ART prognosis

For patients with recurrent implantation failure or pregnancy loss
Tailoring the IVF treatment approach for patients experiencing recurrent implantation failure or pregnancy loss

CooperSurgical Fertility and Genomics Solutions offer a range of innovative products to help improve IVF prognosis and optimize a couple’s chances of having a child.

ART prognosis is influenced by several factors, including maternal age, reproductive history and duration of infertility. Therefore, for patients experiencing recurrent implantation failure or recurrent miscarriage, it is likely that the etiology is equally multifactorial.

Factors involved in determining IVF prognosis

- Maternal age
- Duration of infertility
- Basal FSH and/or AMH
- Reproductive history
- Oocyte reserve
- Embryo quality
- Indication for IVF*
- Lifestyle
- Occupational/environmental exposure

* e.g. uterine factor, male factor, unexplained, immunological/hormonal factor

Recurrent implantation failure

Implantation failure is defined as no sign of implantation following embryo transfer (i.e. no detectable HCG production) or no visible intrauterine sac 5 weeks after the embryo was transferred, despite initial indicators of implantation. Recurrent implantation failure is commonly defined as failure to achieve clinical pregnancy after transfer of ≥4 good-quality embryos in ≥3 fresh or frozen cycles.

Recurrent miscarriage

Recurrent miscarriage is defined as ≥3 consecutive spontaneous pregnancy losses at less than 24 weeks of gestation. However, as some studies indicate, the risk of recurrent miscarriage after two consecutive losses is similar to the risk after three losses. Investigations may be started earlier, especially if the woman is >35 years, or if the couple have had difficulty conceiving either naturally or after IVF.
Tailored IVF treatments for challenging cases

<table>
<thead>
<tr>
<th>Enhanced fertility workup</th>
<th>Recurrent implantation failure</th>
<th>Recurrent miscarriage</th>
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<tr>
<td>Evaluate risk of sperm DNA fragmentation with HBA Assay®</td>
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<tr>
<th>Tailored IVF treatment options</th>
<th>Recurrent implantation failure</th>
<th>Recurrent miscarriage</th>
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<tbody>
<tr>
<td>Select sperm with PICS1 Dish® or SpermSlow™</td>
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<td>*</td>
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<tr>
<td>Culture embryos in GM-CSF enriched culture media</td>
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<tr>
<td>Screen embryos for aneuploidies with PGT-A</td>
<td>*</td>
<td>*</td>
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<tr>
<td>Screen embryos for rearrangements with PGT-SR</td>
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<tr>
<td>Identify the best time for transfer with ERPeak®SM endometrial receptivity test</td>
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</table>


CooperSurgical are global leaders in IVF, reproductive genetics, and women’s healthcare. With the widest range of products, services, and training, we aim to give every patient the personalized care and attention they deserve, regardless of their prognosis.
# Offering solutions to improve ART prognosis

<table>
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<th>Where to tailor</th>
<th>Options</th>
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<td>Sperm evaluation and selection</td>
<td>![Image] HBA Assay</td>
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<td>![Image] PICSi Dish</td>
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<td>![Image] SpermSlow</td>
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<td><strong>Embryo culture</strong></td>
<td>![Image] Culture Media with GM-CSF</td>
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<td>![Image] Culture Media with GM-CSF</td>
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4. CooperSurgical, data on file
Where to tailor Options

**Sperm evaluation and selection**

**HBA Assay**
Identifies patients with low HBA scores; a low score correlates with poorer fertilization, pregnancy and cleavage rates.¹

**PICSI Dish**

**SpermSlow**
Reduces implantation failure and miscarriage rates for patients with low HBA scores by selecting for sperm with high DNA integrity.² ³

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**Embryo culture**

**Culture Media with GM-CSF**
Increases ongoing implantation rates⁴ and significantly improves live birth rates⁵ for patients with a history of recurrent implantation failure or miscarriage.

**ERPeakSM Test**
Detects the receptivity status of the woman’s endometrium to provide information on the most suitable time for embryo transfer.

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**Embryo testing**

**PGT-A**
Improves implantation, while reducing time to pregnancy and miscarriage rates.⁶

**PGT-SR**
Identifies embryos with the correct amount of chromosomal material, which are most likely to lead to a healthy live birth.

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HBA Assay
Assess sperm sample quality in minutes
• Unique and innovative sperm diagnostic tool
• Designed with duplicate hyaluronan-coated chambers
• Calculates the proportion of mature sperm in a sample

HBA score positively correlates with fertilization, pregnancy and cleavage rates

Retrospective trial of 192 female patients and their male partners who underwent ICSI at Singapore General Hospital.
*p-value <0.05


HBA Assay allows you to determine your male patient’s prognosis in minutes helping you decide the best treatment approach
SPERM SELECTION

SpermSlow

- Physiological sperm selection product without PVP
- Semi-viscous medium containing hyaluronan (HA)
- Selects sperm with lower DNA fragmentation, leading to better embryo quality

Sperm selection with SpermSlow improves implantation rates compared to PVP

![Graph showing implantation rates for SpermSlow vs. PVP](image)

Retrospective observational study of couples treated with ICSI after sperm selection with either SpermSlow (N=293; 331 treatments performed) or PVP (N=86; 97 treatments performed); *p-value <0.05

Sperm selection for ICSI by HA binding mimics the natural selection of sperm with high DNA integrity by the zona pellucida. Lack of zona pellucida binding is a major cause of IVF fertilization failure

![Graph showing DNA Fragmentation Rate](image)

Prospective study of 20 men in a private ART center in Italy; *p-value <0.001

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Sperm selection by hyaluronan binding helps minimize unexplained ICSI failure by ensuring selection and injection of mature sperm with high DNA integrity.

**PICSI Dish**

- Unique ICSI dish with hyaluronan microdots
- Convenient and easy-to-use
- Decreases miscarriage rates for patients with poor sperm quality

**Sperm selection with PICSI Dish reduces clinical pregnancy loss for patients with low HBA scores**

 Five-fold improvement in pregnancy rates using the PICSI Dish compared to morphological assessment

<table>
<thead>
<tr>
<th>Rates</th>
<th>PICSi (HA Binding)</th>
<th>Conventional PVP</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fertilization</td>
<td>123/171 (71.93%)</td>
<td>127/198 (64.14%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Chemical pregnancy</td>
<td>12/19 (63.15%)</td>
<td>10/37 (27.03%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Clinical pregnancy</td>
<td>8/19 (42.10%)</td>
<td>6/37 (16.21%)</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Prospective study of 56 ICSI cycles using either the PICSI dish (n=19) or conventional ICSI techniques (n=37) for sperm selection.

**References**

EMBRYO CULTURE AND TRANSFER

Culture Media with GM-CSF
Create a more physiological culture environment

- Unique culture media system for poor prognosis patients
- Improves ongoing implantation and live birth rates for patients with a history of miscarriage and recurrent implantation failure
- Reduces embryonic stress and facilitates communication between embryo and endometrium

3 days of embryo culture in GM-CSF containing medium improved implantation rates and live birth rate for patients with a history of miscarriage

[Graph showing live birth rates and implantation rates with and without GM-CSF]

Subgroup analysis for previous miscarriage patients (n=289 embryo transfer cycles) from a multi-center, randomized, controlled parallel group, double blinded trial with 1,300+ patients from 14 centers. *p<0.01; **p<0.05

44% increase in ongoing implantation rate with EmbryoGen and BlastGen

3. CooperSurgical, data on file
Preimplantation Genetic Testing for Aneuploidies (PGT-A)

Identify embryos with the best chance of success

- High-resolution PGT-A performed via Next-Generation Sequencing technology and analysed with CooperGenomics’ unique PGTaiSM technology platform
- Provides the best detection of aneuploidy, partial (segmental) aneuploidy, unbalanced translocations, and some polyploidies
- Increases implantation rates and reduces miscarriage rates

The PGTaiSM technology platform is a ground-breaking algorithm harnessing the power of artificial intelligence and big data

![Graph showing PGT-A increases live birth rates](https://www.sart.org/

Sample size (number of transfers)

<table>
<thead>
<tr>
<th>Maternal Age</th>
<th>29,989</th>
<th>13,144</th>
<th>10,497</th>
<th>4,678</th>
<th>3,009</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVF without PGT-A</td>
<td>5,326</td>
<td>3,366</td>
<td>2,941</td>
<td>973</td>
<td>243</td>
</tr>
</tbody>
</table>
Preimplantation Genetic Testing for Structural Rearrangements (PGT-SR)

Screen embryos for inherited chromosome rearrangements

- Helps identify embryos with the correct amount of chromosomal material that are most likely to lead to a successful pregnancy and healthy live birth
- Performed using the most advanced technologies — Next-Generation Sequencing — for >98% accuracy
- Available for even the most complex cases, which others may turn away

Many individuals with balanced chromosome rearrangements are unaware of their carrier status until they try to start a family. For those with repeated implantation failure or repeated miscarriage, a karyotype can inform whether they have a rearrangement and could be a candidate for PGT-SR

80% If one parent is a carrier of a reciprocal translocation, approximately 80% of resulting embryos will be unavailable for transfer

2. CooperSurgical, data on file
EMBRYO TRANSFER

ERPeak\textsuperscript{SM} Endometrial Receptivity test

Test for precision embryo transfer

- Detects the receptivity status of the woman’s endometrium
- Measures the expression of relevant hormone-regulated genes to identify the most suitable time for embryo transfer to increase the likelihood of implantation
- Processed on CooperGenomics’ custom-developed and validated platform\textsuperscript{1}

The Window of Implantation (WOI) is the short time period during which the endometrium is at its most receptive for implantation

The WOI is typically between 8-10\textsuperscript{2} days after ovulation in a natural menstrual cycle or five days after progesterone exposure in an ART cycle. It is shifted in approximately 30% of women undergoing IVF,\textsuperscript{3} occurring either slightly earlier or later than five days after progesterone exposure. Studies have shown a 51.7-63.2% pregnancy rate in patients with recurrent implantation failure (RIF) who have undergone endometrial receptivity testing\textsuperscript{4,5}

\textsuperscript{1} CooperSurgical, data on file
CooperSurgical Fertility and Genomic Solutions is the global leader in IVF, reproductive genetics and women’s healthcare, providing innovative solutions for the entire ART journey.

Working together, we offer a trusted system of consumables and equipment as well as a full suite of reproductive tests and services.
Training program

In addition to helping you optimize your success rates, we strive to drive progress and innovation in the field of ART. We invite customers and partners to learn new techniques and share best practices in our fully equipped training laboratories.

Our global network of training laboratories provide evidence-based training by skilled, experienced embryologists. Sessions include demonstrations and hands-on learning in a comprehensive range of Assisted Reproductive Technologies (ART) and culture media processes.

By undertaking our biopsy technique course, you can upgrade your skill levels through comprehensive hands-on training and the sharing of best practice lab techniques.

If you or your staff could benefit from training, see our website coopersurgical.com for more information and bookings.

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1. Data from participant evaluation forms
# Product range

## Diagnostic Devices

<table>
<thead>
<tr>
<th>Device</th>
<th>Order Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBA slide</td>
<td>BCT-HBA-10</td>
</tr>
</tbody>
</table>

## Sperm Selection

<table>
<thead>
<tr>
<th>Device</th>
<th>Description</th>
<th>Order Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>PICSI Dish</td>
<td>Box of 20, individually packaged, sterile</td>
<td>BCT-PICSI-20</td>
</tr>
<tr>
<td>SpermSlow</td>
<td>4 x 0.1ml</td>
<td>10944000</td>
</tr>
</tbody>
</table>

## Embryo Culture and Transfer

<table>
<thead>
<tr>
<th>Device</th>
<th>Order Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>EmbryoGen &amp; BlastGen</td>
<td>12062003</td>
</tr>
<tr>
<td>EmbryoGen</td>
<td>12040003</td>
</tr>
<tr>
<td>BlastGen</td>
<td>12050003</td>
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</tbody>
</table>

## Genetic Testing

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Description</th>
<th>Order Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGT-A</td>
<td>Embryo Biopsy Kit and Aneuploidy Screening</td>
<td>N/A</td>
</tr>
<tr>
<td>PGT-SR</td>
<td>Embryo Biopsy Kit and Structural Chromosome Rearrangement Testing</td>
<td>N/A</td>
</tr>
<tr>
<td>ERPeak&lt;sup&gt;3BH&lt;/sup&gt; Endometrial Receptivity Test</td>
<td>Endometrial Biopsy Kit and Receptivity Testing</td>
<td>N/A</td>
</tr>
</tbody>
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Availability of a device for clinical use is dependent on the regulatory approval status of that device within the country the device is intended to be sold into.
Train with CooperSurgical and optimize your performance, learn new skills and network with international peers.

We invite customers and partners to learn new techniques and share best practices in our fully equipped laboratory.

We provide evidence-based training by skilled, experienced embryologists which includes demonstrations and hands-on training in a comprehensive range of ART techniques and procedures.