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IMPROVING IVF SUCCESS

AI and robotics-based autonomous sperm selection for IVF

Company Presentation

October 2023

www.7design.co.il

Vision & Mission

Vision

To harness cutting-edge technologies to allow more people to have healthy BAIBYS™.

Mission

To leverage artificial intelligence, big data, micro-robotics, and automation to improve male fertility by revolutionizing Assisted Reproductive Technology (ART).

One-Liner

AI-based autonomous robotic system for selecting optimal sperm cells for IVF

BAIBYS™ develops an AI and robotics-based COMPLETELY AUTONOMOUS system for sperm selection at high magnification for ICSI (including the physical pick-up and isolation of the optimal cells), which will **improve success rates**, **reduce birth defects**, and **raise clinics' throughput**.

Capital

Disposables

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Fertility Crisis

Global Fertility Crisis Around Us

The New York Times

Opinion

What Are Sperm Telling Us?

Scientists are concerned by falling sperm counts and declining egg quality. Endocrine-disrupting chemica be the problem.

By Nicholas Kristof
Opinion Columnist

Feb. 20, 2

By Katherine Latham 28th March 2023

BBC

Sperm quality appears to be declining around the world but is a little discussed cause of infertility. Now scientists are narrowing in on what might be behind the problem.

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Falling sperm counts 'threaten human survival', expert warns

t Shanna Swan says low counts and changes to ment could endanger human species

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NEWS

Add falling sperm counts to the list of threats to human survival, epidemiologist warns

Grace Hauck USA TODAY

Published 4:58 p.m. ET Feb. 27, 2021 | Updated 12:12 p.m. ET Mar. 1, 2021

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Male Fertility Drops Dramatically

Sperm count

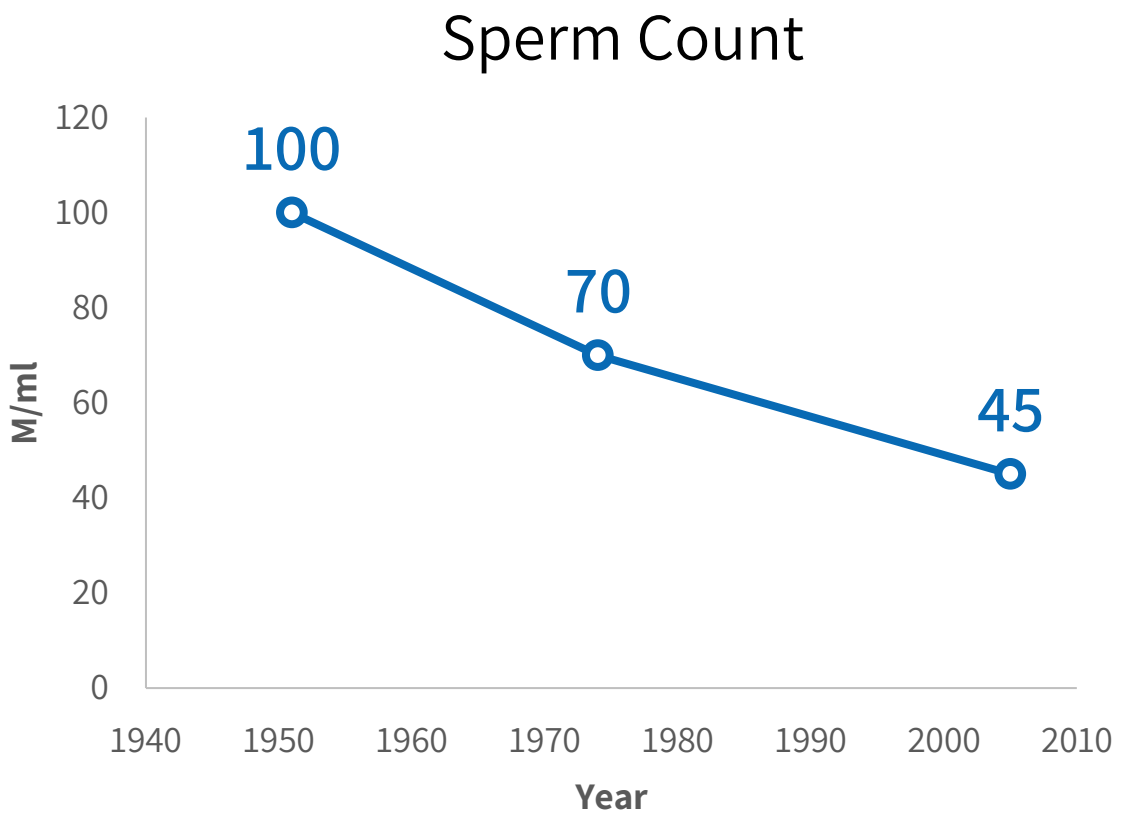
Decreased by 50% in 50 years and dropping

Sperm morphology

The criterion for “normal morphology” was changed since it became difficult to find “normal” based on the former definition –

Before 2010 – Definition of “normal sperm” was “>**14**% of cells have normal morphology” (WHO 4th Edition)

After 2010 – Definition of “normal sperm” changed to “>**4**% of cells have normal morphology” (WHO 5th Edition)



⇨ Male infertility accounts for ~50% of infertility cases

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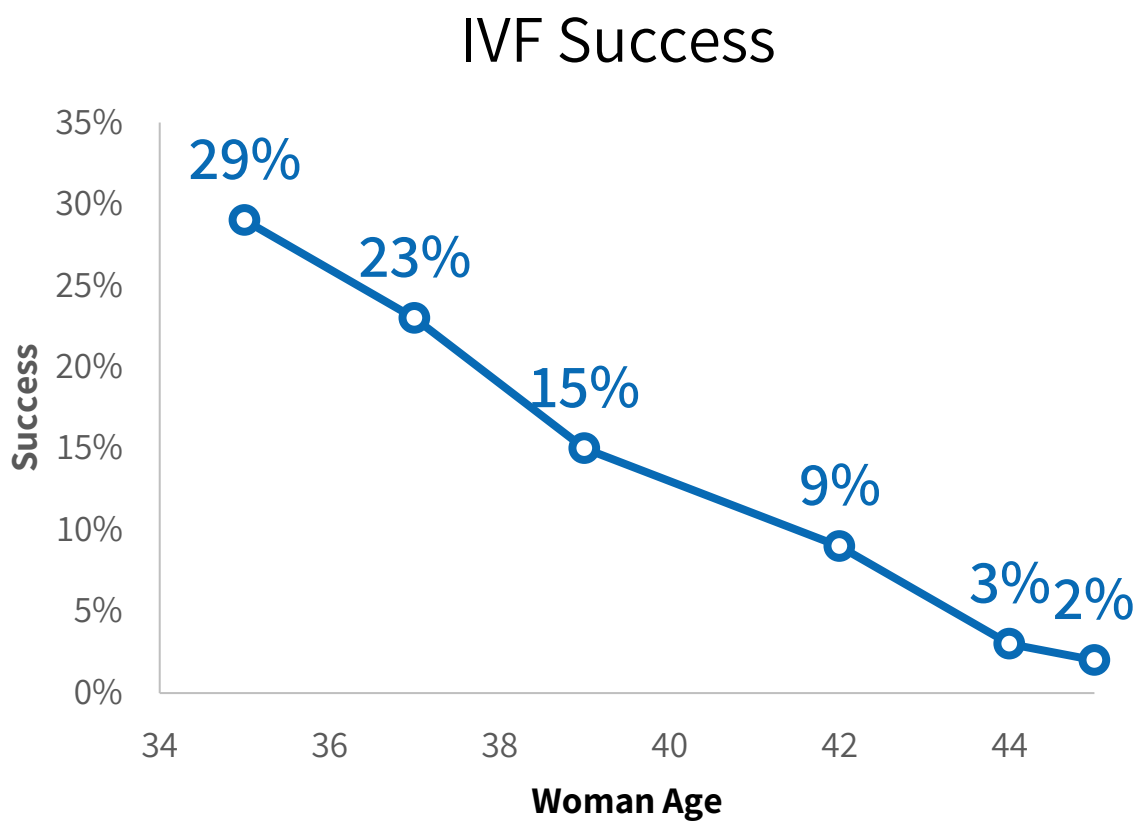
Women Give Birth Later

IVF success declines with age

In 2016, the U.S. tipping point

More women gave birth in their 30's than their 20's.



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IVF is Booming

* who.int/news/item/04-04-2023-1-in-6-people-globally-affected-by-infertility

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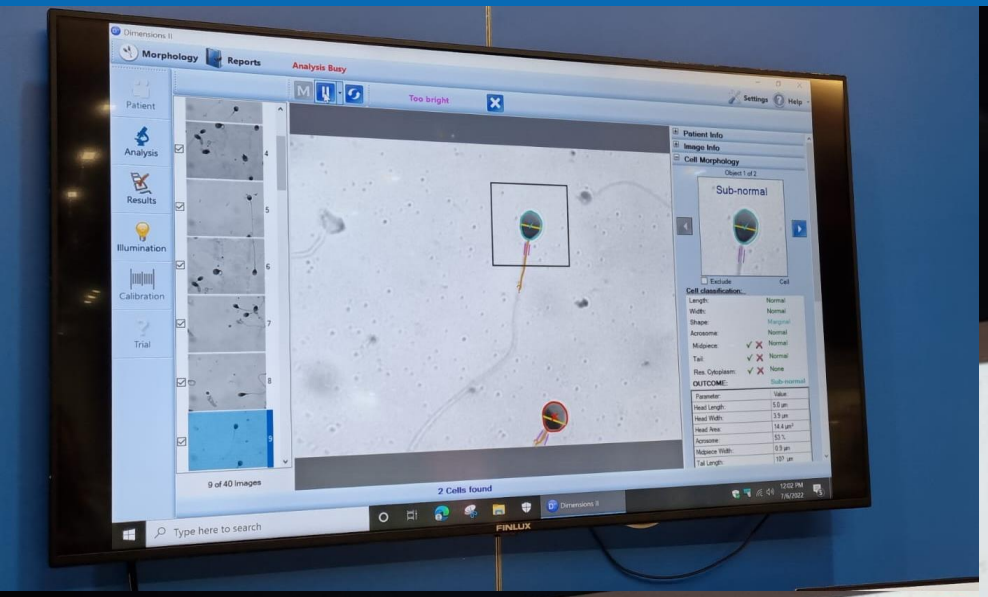
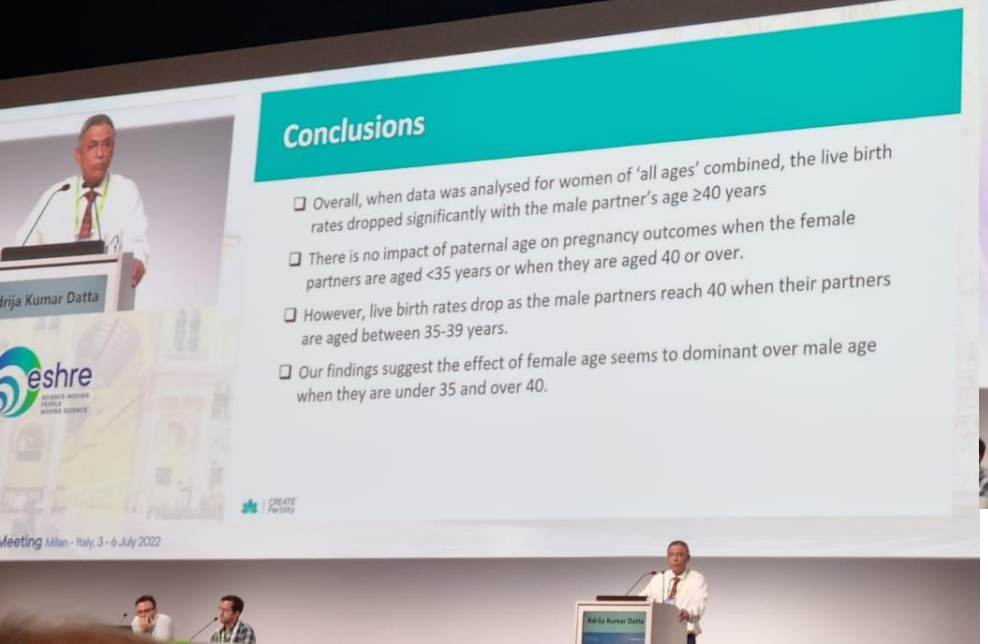
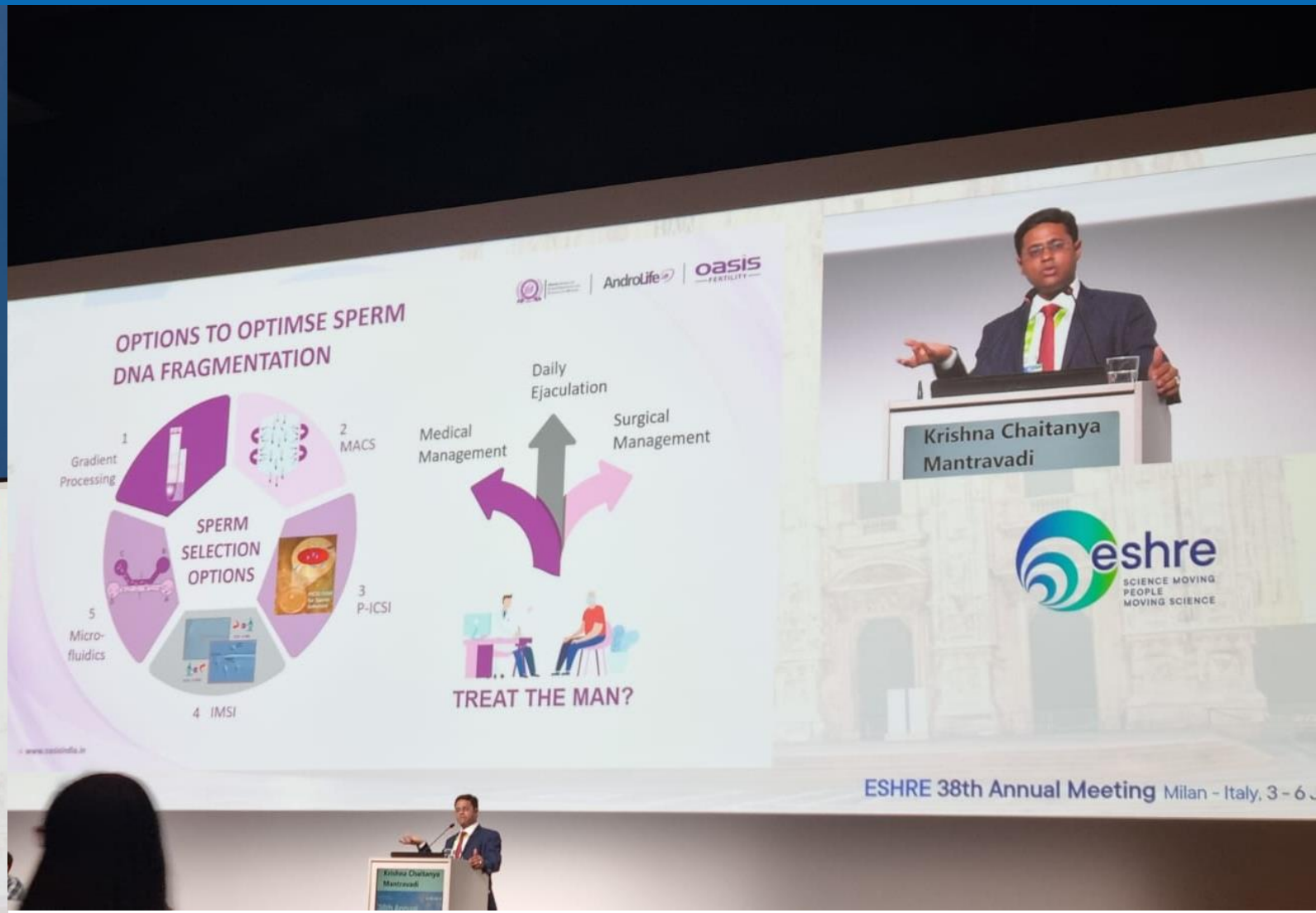
Male Infertility is Hot in Academic Conferences







* European Society of Human Reproduction & Embryology 2022

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IVF’s High Personal Toll

Emotional roller-coaster

Enormous financial burden

Prolonged and tedious process of several years

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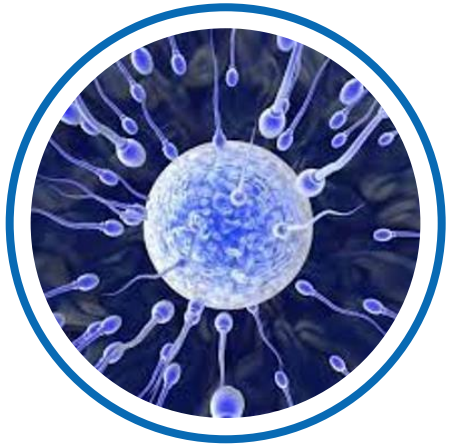
IVF Evolvement

The Challenge



Classic IVF
Sperm cells compete to fertilize the egg – Natural selection

- Normal birth defects
- Low success rate

In ~80% of current IVF – Random sperm cell is injected into the egg (ICSI) to ensure penetration

- Higher birth defects
- Moderate success rate

Sperm Selection at High Magnification – Detailed evaluation of sperm cell morphology and motility

- Normal birth defects
- Higher success rate

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Manual Sperm Selection at High Magnification

Trained embryologist **manually selects a single sperm** cell out of millions using a special microscope with **high magnification** (×6,100).

Selection of Spermatozoa with Normal Nuclei to Improve the Pregnancy Rate with Intracytoplasmic Sperm Injection

To the Editor: Intracytoplasmic injection of sperm is th recommended treatment for male infertility, associated witl an average pregnancy rate per cycle of about 30 percent. Although sperm count and motility were found to have nc effect on the outcome of intracytoplasmic sperm injection, scanning and transmission electron microscopy indicatec that the achievement of pregnancy may depend on norma

N Engl J Med. Vol. 345. No. 14 · October 4. 2001

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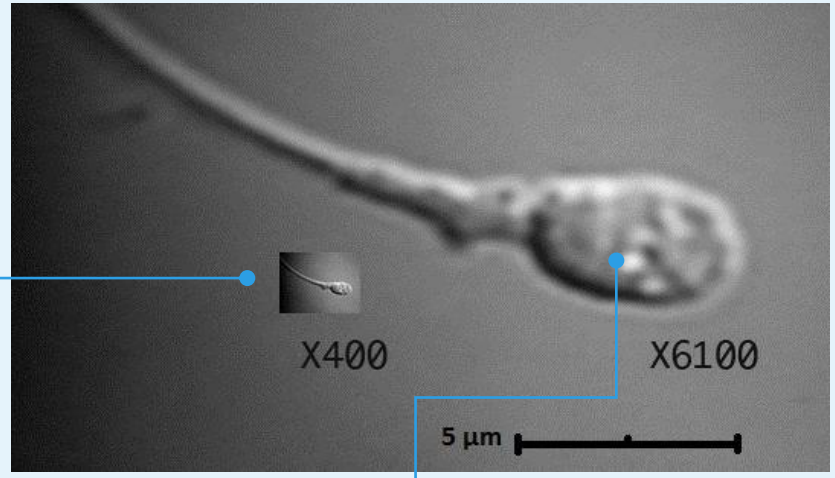
Why is High Magnification Critical?

Examining sperm cells at **high magnification shows morphological defects**, which correlate with low success rate and birth defects



At standard magnification no morphological details can be shown

At high magnification morphological defects are clearly shown

Higher IVF success rate & lower birth defects

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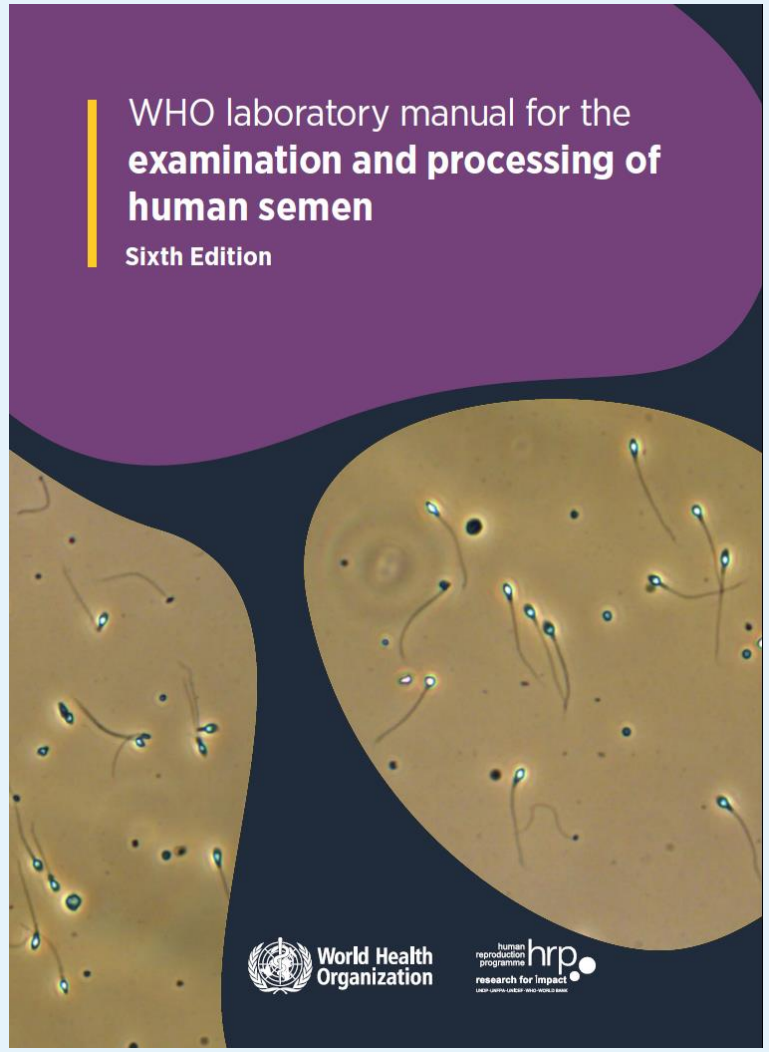
Why is Morphology Important?

WHO Guidelines (6th Edition, 2021)

"Abnormal spermatozoa generally have a **lower fertilizing potential**, depending on the types of anomalies, and may also have **abnormal DNA**. Morphological defects have been associated with **increased DNA fragmentation**, an **increased incidence of structural chromosomal aberrations**, **immature chromatin** and **aneuploidy**. Emphasis is therefore given to the form of the head, although the sperm tail (midpiece and principal piece) is also important to consider for the understanding of the male reproductive tract".



* WHO Laboratory Manual, 2021, page 49

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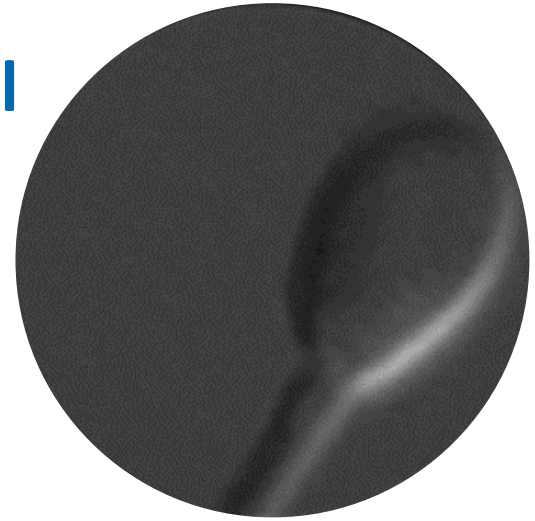
Benefits of Sperm Selection

- Higher fertilization rate
- Sperm quality is a critical factor for embryo development to blastocyst stage
- Higher pregnancy and birth rates
- Decrease birth defects
- The sperm cell delivers a novel epigenetic signature to the egg (Miller et al 2010)

Results According to Injected Sperm

Good sperm cell

Symmetric
Proportional
No morphology defects

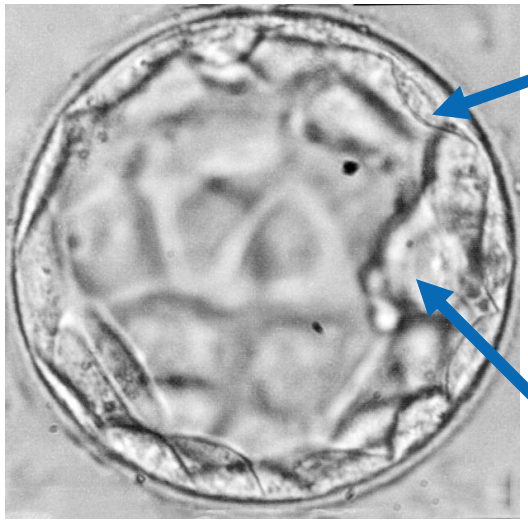


Bad sperm cell

Asymmetric
Non-proportional
Has morphological defects (vacuoles)

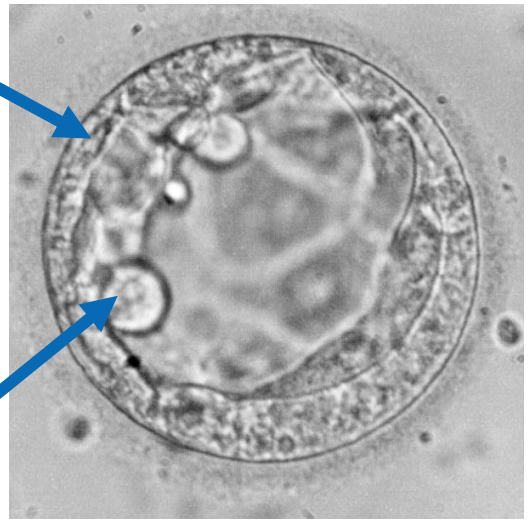
Good blastocyst

Embryo cells mass penetrates the blastocell cavity
Many placenta cells surround the blastocyst
Distinguished differentiation between them



Trophectoderm (TE) = Placenta cells

Inner Cell Mass (ICM) = Embryo cells



Bad blastocyst

Little to no embryo cells mass
Few placenta cells, most of them atretic

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Limitations of Current Technology

Manual solution is limited

- Time consuming ~3h
- Subjective & inconsistent
- Requires extensive training
- Expensive

Not widely adopted

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BAIBYS' Solution

BAIBYS™ Solution

AI-based autonomous robotic sperm selection platform

- Fast
- Objective, consistent, & **more accurate**
- Fully automated
- Affordable

The smart future of IVF

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How Does It Work? AI Classification

AI classifies sperm cells morphology at high magnification

- **Proprietary algorithm processes** the video stream of “live” sperm in real time
- **Autonomously classifies sperm** cells based on their morphology & motility at high-magnification (×6,100)
- **The algorithm controls** the motorized X-Y stage in real time to maintain the selected sperm cell in the middle of the field of view to allow reviewing the cell from all sides

Watch the video at
youtube.com/watch?v=cRwpi_0r4Tg

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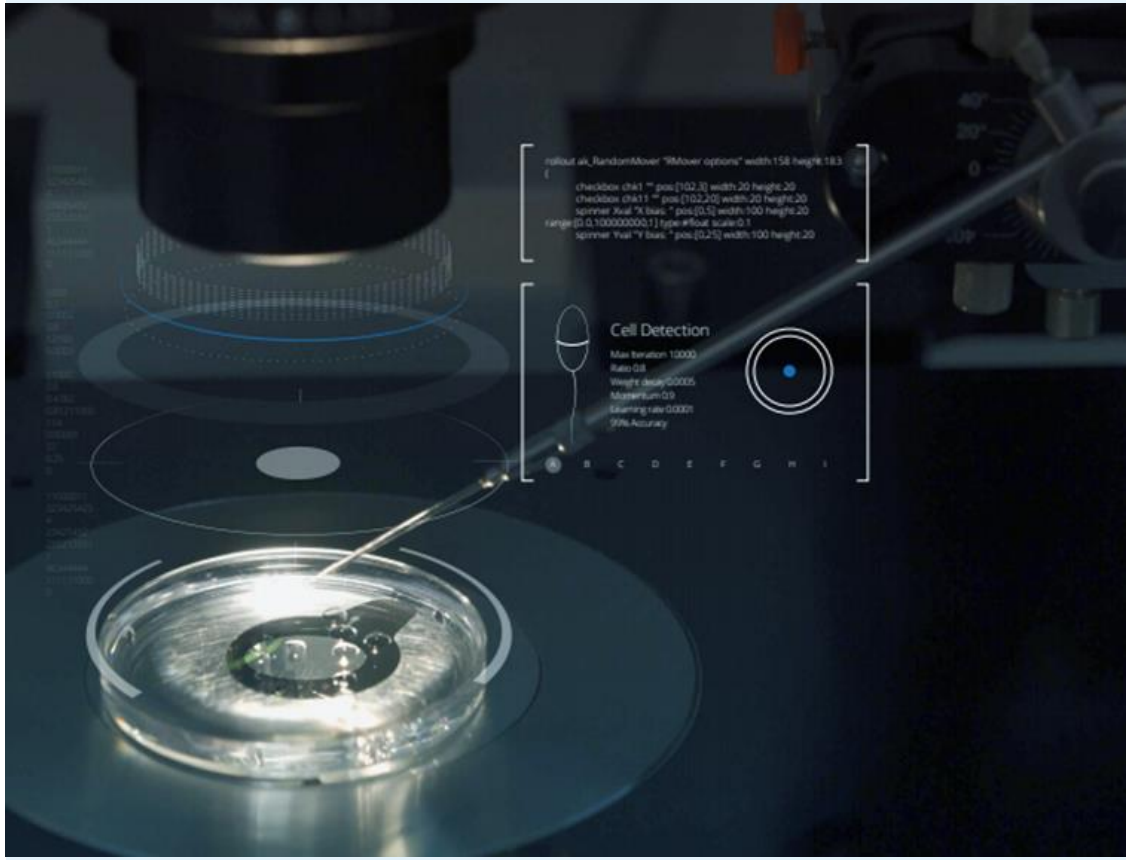
How Does It Work? Robotic Selection

Robotic platform scans sperm and extract optimal cells autonomously

- Sub-micrometer motorized X-Y stage
- Intelligent Scanning Technology (IST)
- Controlled micro-manipulator
- Automated isolation of the selected sperm
- Controlled pump extracts cells
- Fully autonomous from A to Z



Watch the video at youtube.com/watch?v=VwDQRZflKjo

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What does Science Say? (1)

> *Conclusions: IMSI* [a method of sperm selection at high magnification] *seems to be* ***an effective tool at reducing the incidence of structural defects*** *compared to ICSI…*

Itoi et al, 2021

> *The* ***incidence of birth defects*** *was statistically different, with* ***2.5% (32/1280) in IMSI and 4.5% (119/2627) in ICSI****. The results demonstrated that IMSI decreased the incidence of structural defects compared to ICSI – 2.2% (18/830) vs. 3.8% (78/2049) – in a statistically significant manner.*

Dieamant et al, 2021

> *We found a significant* ***differential DNA methylation and expression of many genes*** *in sperm with poor and good morphology.*

Cassuto et al, 2021

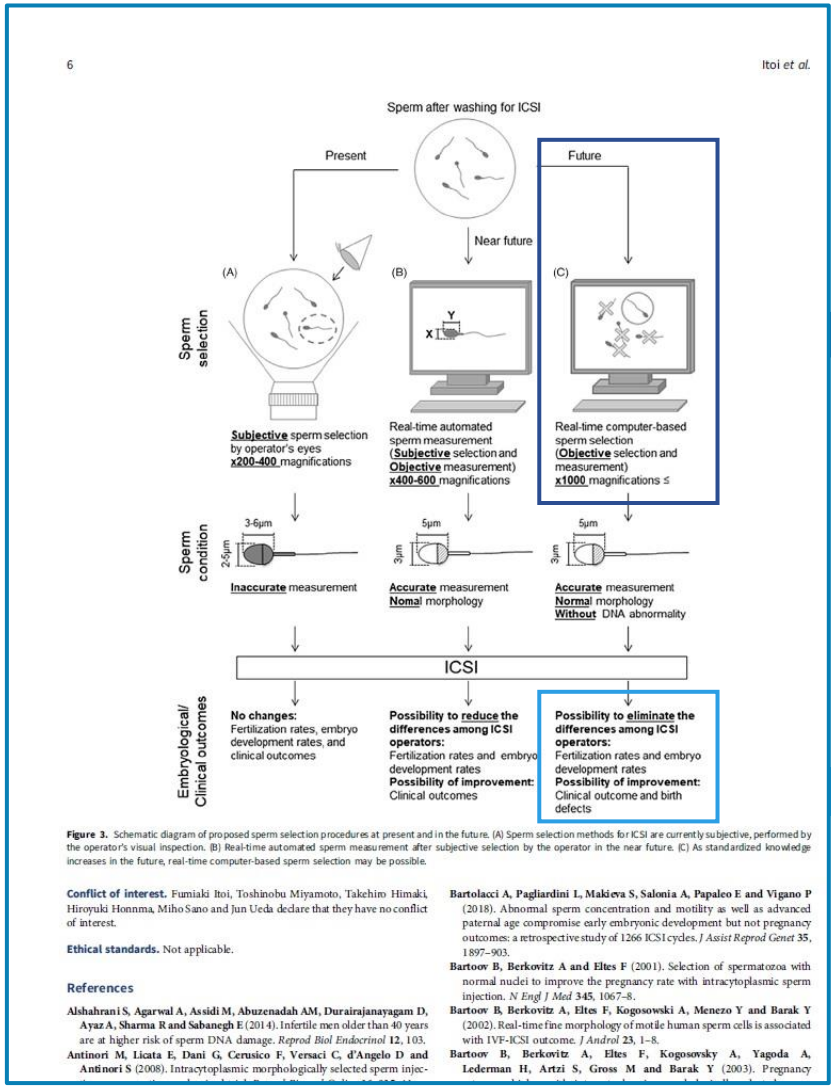
> ***Tremendous opportunities exist for machine learning to advance male fertility treatments.*** *The fundamental challenge of sperm selection — selecting the most promising candidate from 100,000,000 gametes — presents a challenge that is uniquely well-suited to the high-throughput capabilities of machine learning algorithms paired with modern data processing capabilities.*

You et al, 2021

> *This study demonstrates* ***the value of analyzing sperm morphology using the criteria recommended in terms of predicting fertilization and perhaps pregnancy outcome****… If the morphology is not evaluated with care, a diagnosis of unexplained infertility can be made incorrectly and lead to much frustration for both the patient and the physician.*

Kruger et al, 1987

What Science Says (2)



6 Itoi et al.

Sperm after washing for ICSI

Present | Near future | Future

(A) Subjective sperm selection by operator's eyes x200-400 magnifications

(B) Real-time automated sperm measurement (Subjective selection and Objective measurement) x400-600 magnifications

(C) Real-time computer-based sperm selection (Objective selection and measurement) x1000 magnifications ≤

Sperm selection

Sperm condition: 3-6μm, 2-5μm; 5μm, 3μm; 5μm, 3μm

Inaccurate measurement

Accurate measurement Nomal morphology

Accurate measurement Normal morphology Without DNA abnormality

ICSI

Embryological/ Clinical outcomes

No changes: Fertilization rates, embryo development rates, and clinical outcomes

Possibility to reduce the differences among ICSI operators: Fertilization rates and embryo development rates
Possibility of improvement: Clinical outcomes

Possibility to eliminate the differences among ICSI operators: Fertilization rates and embryo development rates
Possibility of improvement: Clinical outcome and birth defects

Figure 3. Schematic diagram of proposed sperm selection procedures at present and in the future. (A) Sperm selection methods for ICSI are currently subjective, performed by the operator's visual inspection. (B) Real-time automated sperm measurement after subjective selection by the operator in the near future. (C) As standardized knowledge increases in the future, real-time computer-based sperm selection may be possible.

Conflict of interest. Fumiaki Itoi, Toshinobu Miyamoto, Takehiro Himaki, Hiroyuki Honnma, Miho Sano and Jun Ueda declare that they have no conflict of interest.

Ethical standards. Not applicable.

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Bartolacci A, Pagliardini L, Makieva S, Salonia A, Papaleo E and Vigano P (2018). Abnormal sperm concentration and motility as well as advanced paternal age compromise early embryonic development but not pregnancy outcomes: a retrospective study of 1266 ICSI cycles. *J Assist Reprod Genet* **35**, 1897–903.

Bartoov B, Berkovitz A and Eltes F (2001). Selection of spermatozoa with normal nuclei to improve the pregnancy rate with intracytoplasmic sperm injection. *N Engl J Med* **345**, 1067–8.

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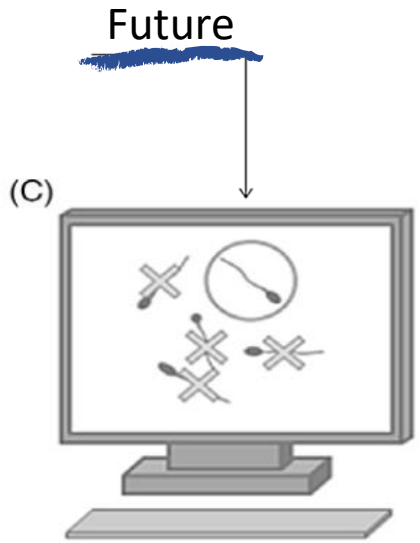

Real-time computer-based sperm selection (**Objective** selection and measurement)
x1000 magnification ≤

Possibility to eliminate the differences among ICSI operators:
Fertilization rates and embryo development rates
Possibility of improvement:
Clinical outcome and birth defects

* Itoi et al, 2021, page 6

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Business Model

Reoccurring revenue from disposable components

IVF is mainly a private market

- Most clinics are “for profit”
- For manual sperm selection couples currently pay ~ $1,000 out-of-pocket
- Thus, BAIBYS’ product is mostly independent of reimbursement.
- The clinic’s costs for BAIBYS’ product are lower, allowing a higher margins and access to more customers

Capital

Disposables

* Illustration

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Product Benefits

Cost saving, fast, fully autonomous, objective, and accurate

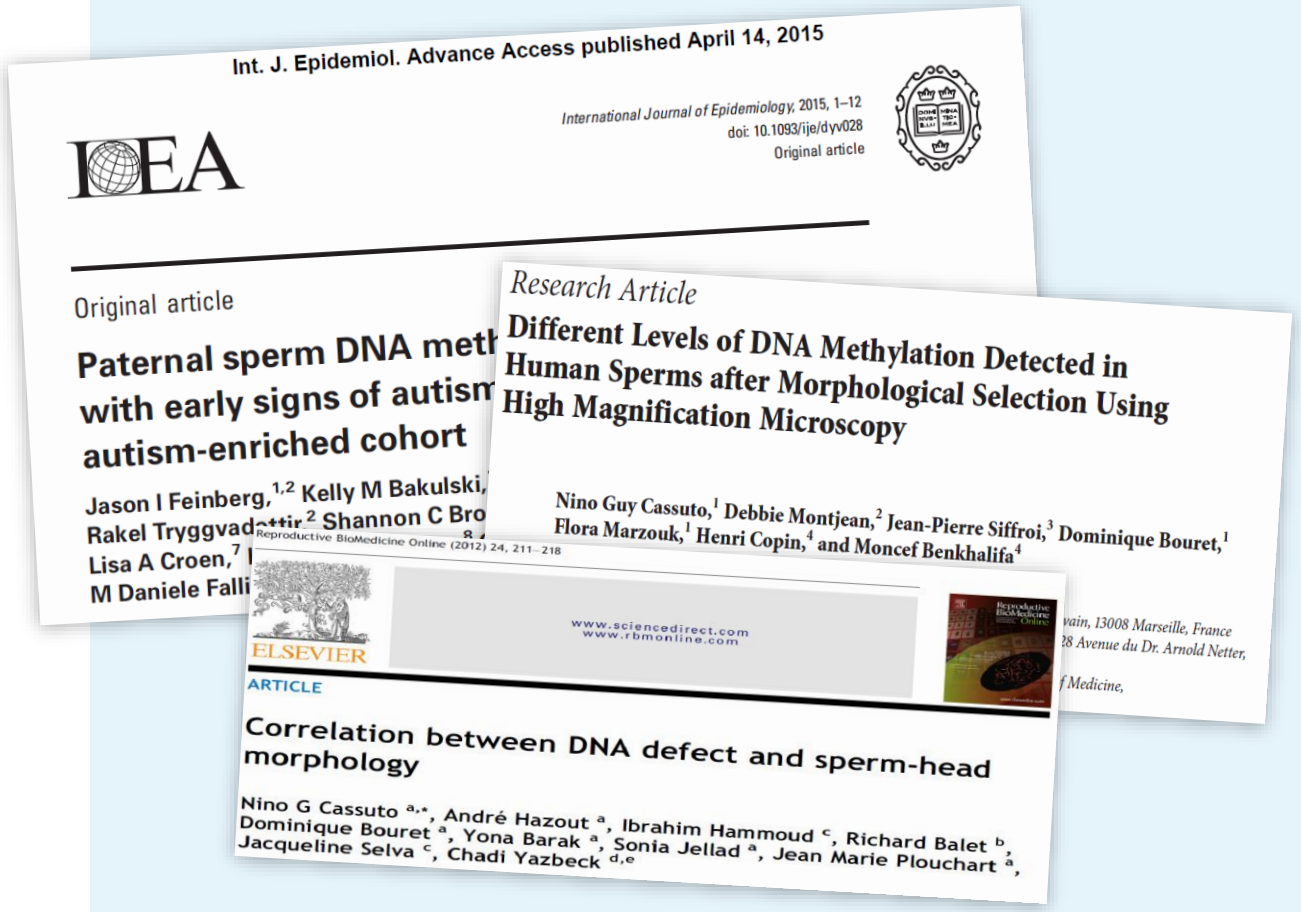
- **Complete solution** – BAIBYS™ system is a complete and integrated solution
- **Time saving** – Fully autonomous procedure at high magnification in minutes
- **Low cost** – Reduced costs by saving long work of a highly qualified embryologists
- **Increasing lab throughput** – By shortening procedure overall time
- **Fully autonomous** – Objective technique, independent of human limitation such as subjective interpretation, fatigue, and distraction
- **State-of-the-art technology** – AI and robotic based revolutionary product
- **Latest development** – The newest high-tech tool for IVF centers that routinely perform ICSI
- **Achieves the ultimate goal** – Higher pregnancy rates while reducing major birth defects

Clinical & Regulatory Validity

Essential clinical data already published (refer to baibys.com/resources)

Regulatory safe and recognizable – FDA 510k

Shorter time-to-market



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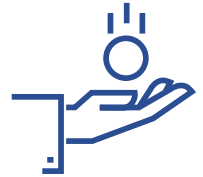
Total Addressable Market

In 2023,
the IVF market is
expected to reach
$54.1B

The Business Research Company

Through 2027
Annual growth rate
(CAGR)
13.6%

The Business Research Company



By 2025,
BAIBYS' TAM
> $1B/yr

5M cycles × $200

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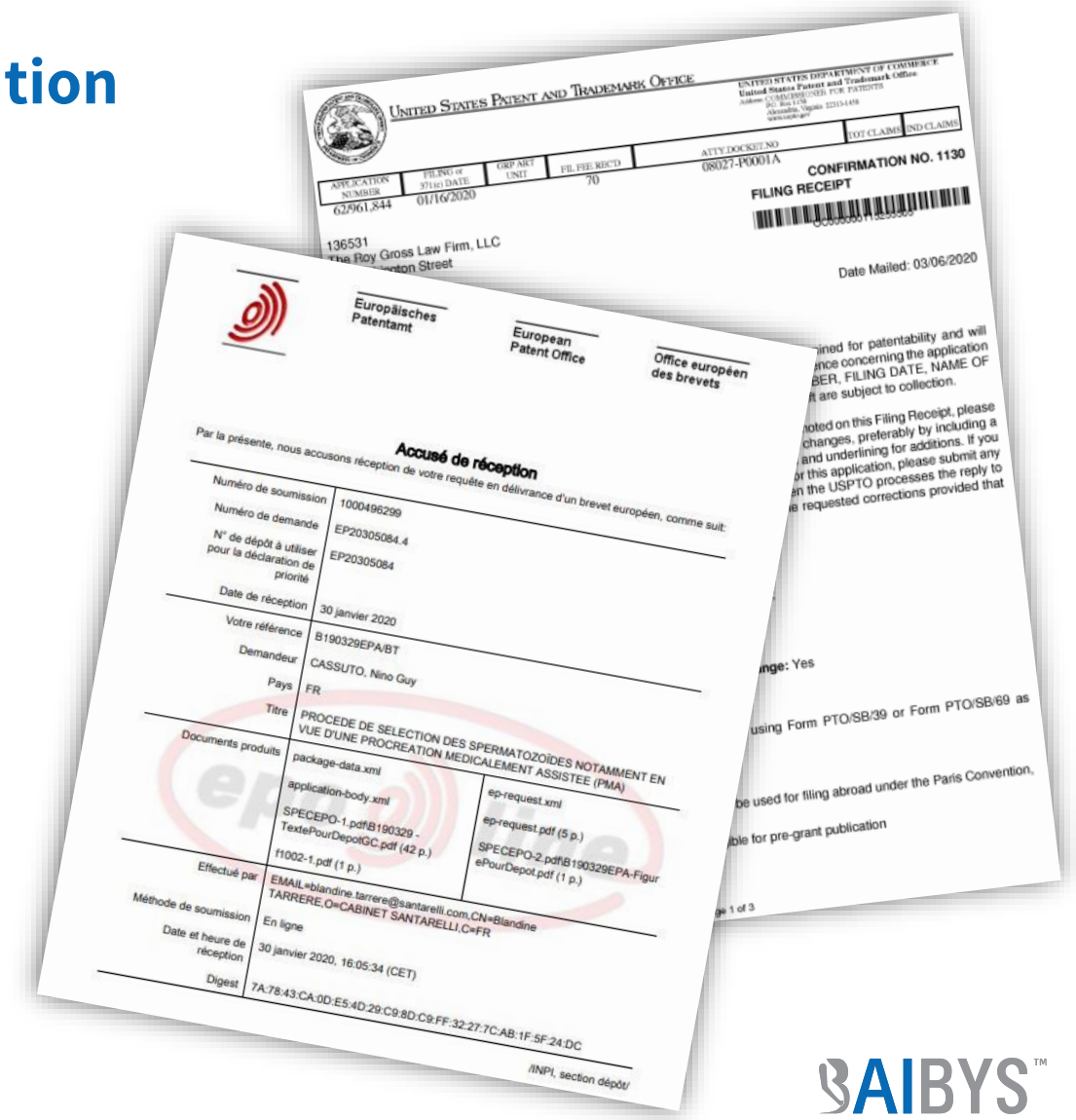
Intellectual Property

Automated spermatozoa candidate identification

- Stage – National
- Priority – January 16th, 2020

Process for selecting spermatozoa in particular view of a MAP

- Stage – Granted (France)
- Priority – January 30th, 2020



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BAIBYS™ Team

Itay Itzhaky
Chairman of the Board

2x exits for $270M

30+ years as CEO in medical device industry

Gal Golov
Co-Founder & Co-CEO

Electro-optical engineer

20+ years experience in R&D & business roles

Dr. Yaron Silberman
CEO

PhD in AI, MBA

25+ years in BioMed business roles

Recent position – CEO of a 40-employee company

Dr. Nino Guy Cassuto
Co-Founder & Chief Medical Officer

IVF KOL & expert in male fertility

Owner of global IVF clinics network

Nahum Budin
Sr. VP R&D

30+ years of R&D management

Managed teams of 100+ employees

Betty Meiri-Farber
Clinical Director

Senior embryologist, MSc

25+ years experience in managing int'l IVF clinics

Scientific Advisory Board – Investors

All are fertility experts and clinic owners – Providing access to knowledge & big-data
Invested $2M Seed Round

Prof.
Shlomo Mashiach

Dr. Nino
Guy Cassuto

Dr.
Djedik Diakite

Prof.
Martha Dirnfeld

Dr.
Stephane Eimer RIP

Dr.
Eric Konyaole

Dr. Fernando
Sánchez Martín

Dr. Pascual
Sánchez Martín

Prof.
Adrian Shulman

Dr.
Athanase Sodjiedo

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Achievements

x2 Israel Innovation Authority grants $700k – *the maximum possible!*

Innovation showcase finalist at Reproductive Health Innovation Summit 2023 (12 out of 55)

Selected for IBM's Hadassah Accelerator (5 out of >100 candidates)

Semi-finalist StartUp+ competition (20 out of 200 start-ups)

Accepted to NVIDIA Inception Program for AI-based Start Ups

Selected to present at the Japan-Israel conference in Tokyo

רשות החדשנות
Israel Innovation Authority

Women's Health Innovation Series
REPRODUCTIVE HEALTH INNOVATION SUMMIT

IBM

המרכז הרפואי האוניברסיטאי הדסה
מיסודו של ארגון נשות הדסה
מרגישים הדסה חדשה

STARTUP+

כלכליסט

bank hapoalim

NVIDIA INCEPTION PROGRAM

כלכליסט

ISRAEL DISCOUNT BANK

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BAIBYS™ Value Proposition

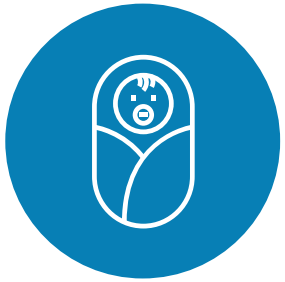
Feasible technology

Based on already-proven technological components

Working prototype completed

Simple, fast, objective, affordable solution

Increase clinic throughput & revenue



Increased birth rate & decreased birth defects

AI where it matters

In normal sperm, 96% of sperm cells are abnormal

While AI in IVF commonly used to select embryo, if the sperm used for fertilization is abnormal, likelihood for good embryos is low

Substantial & fast growing market

Exp. $54.1B in 2023
CAGR 13.6%

Company de-risked

$2M seed raised from clinic owners (target customers)

$2M raised in Round A from Israeli VC

Profound clinical & regulatory validation

Prominent KOLs & experienced team

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Thank You

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