

# **Assisted Reproductive Technology**

Your Guide to Microscope Systems for the IVF Laboratory



# The moment you're absolutely clear about what you see.

This is the moment we work for.





# Add efficiency to your laboratory

Enjoy the convenience of ZEISS laboratory microscopes and solutions for your daily checks, every day. Efficiently apply your knowledge and methods with ergonomically designed microscopes, that adapt to you and your working procedures. Make the best of your tuition and choose a sturdy microscope, that is easy to use, has a long life and speeds up your daily routines.

www.zeiss.com/routine

# A Brief History of Assisted Reproductive Technology

Human assisted reproductive technology (ART) has a 170 years old history and has undergone a vivid expansion over recent years mainly due to the use of pioneering clinical techniques. Microscopes always had been essential to understand the roles of sperm and oocytes. Today the procedures of IVF and ICSI are worldwide established. Over one million treatments are performed globally each year, accounting for up to 7 % of all births in some developed countries.

"The ultimate goal of IVF is to achieve healthy single live births following each single embryo transfer."

Jacques Cohen et al, RBM Online (2012) 25, 585



### **Dr. William Pancoast**

inseminated the wife of the Quaker couple with the sperm of one of his medical students. The experiment resulted in the birth of a baby boy.



# Dr. Robert Edwards and Dr. Patrick Steptoe

successfully pioneered conception through IVF, which led to the birth of the first test tube baby in England on July 25th, 1978 via a Cesarean. Louise Joy Brown weighted in at 5 pounds, 12 ounces.



**First baby** born from an eight-cell frozen embryo. First baby born using a donated egg.



### **Dr. Robert Edwards**

earned the Nobel Price for his work on in-vitro insemination/conception of a human oocyte together with Dr. Patrick Steptoe.

1884

1965

1978

1981

1983

1992

2010



### **Dr. Robert Edwards**

successfully created a human embryo by adding his own semen to a human ovum in a Petri dish.



Introduction of Clomiphene Citrate and hMG in the IVF treatment protocol to stimulate the development of multiple eggs.



First successful pregnancy using ICSI.

# Where Every Success is so Significant, Leading-edge Technology is Essential.

In scarcely any other area the pressure to succeed and expectations are so high as in the field of assisted reproductive technology. The samples you handle in your IVF laboratory are precious. You have a dedicated time span, in which your workflow has to run smoothly. And all under controlled conditions, stable temperature and a clean environment. Furthermore, only the most healthy sperms, eggs and embryos lay the foundations for a successful fertilization.



### **Gynecology**

Screen gynecological smears for cytological and microbiological findings, e.g. parasites, bacterial vaginosis, chlamydial infections.

### **Recommended microscopes**

Upright light microscopes with brightfield and phase contrast.



### Semen Analysis Andrology

Create a seminogram to evaluate sperm concentration, motility/vitality and sperm morphology.

### **Recommended microscopes**

Upright light microscopes with magnification up to 100x and brightfield, phase contrast or fluorescence.



### **Oocyte/Embryo Handling**

Denude the oocytes by removing the outer somatic cell layer. Examine the oocytes and check for obvious morphological abnormalities. Transfer oocytes/embryos during IVF procedures or for vitrification.

### Recommended microscopes

Stereo microscopes with a heating plate inside a laminar flow box.



### **Fertilization**

Bring together oocyte and sperm by In vitro fertilization (IVF), Intracytoplasmic sperm injection (ICSI) or Intracytoplasmic morphologically-selected sperm injection (IMSI)

### **Recommended microscopes**

Inverted light microscopes with PlasDIC or iHMC contrast, micromanipulation and heating plate.



### **Embryo Development**

Monitor the embryonal growth and evaluate cell number, cell regularity, fragmentation/blebbing, multinucleation and the presence of vacuoles, granularity, thickness of the outer shell.

### **Recommended microscopes**

Inverted light microscopes with PlasDIC and/or iHMC.

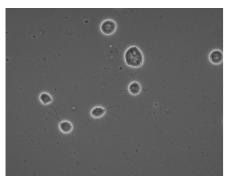


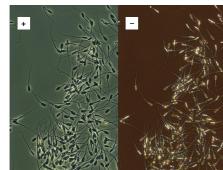
# Embryo Biopsy & Assisted Hatching

Use the laser to thin or open the zona pellucida and take biopsies from blastocyst or trophectoderm for genetic tests.

### Recommended microscopes

Inverted light microscopes with PlasDIC or iHMC contrast, micromanipulation, heating plate and laser module.













Courtesy of Hamilton Thorne, US

# **Upright Light Microscopes**



# **Stereo Microscopes**



# **Inverted Light Microscopes**



### Accessories





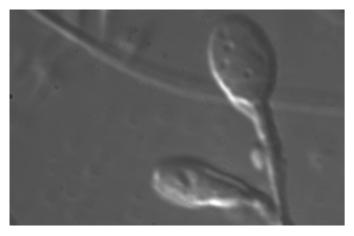
# **Select Your ZEISS Microscope System aligned with Your IVF Workflow to Maximize Your Success Rates**

The samples you handle in your laboratory are precious. You have a dedicated time span, in which your workflow has to run smoothly. And all under controlled conditions, stable temperature and a clean environment. In assisted reproductive technology you use different methods involving microscopes. ZEISS microscopes are designed exactly to your IVF workflow needs and deliver crisp images. They all have one purpose – enable precise reproductive work to maximize success rates for your clients.

	ZEISS Axio Lab.A1	ZEISS Axio Scope.A1	ZEISS Stemi 508	ZEISS SteREO Discovery.V8	ZEISS Axio Vert.A1	ZEISS Axio Observer
ART procedure	Semen analysis	Semen analysis	Oocyte/Embryo handling	Oocyte/Embryo handling	Fertilization Embryo development Embryo biopsy Assisted hatching	Fertilization Embryo development Embryo biopsy Assisted hatching
Description	Axio Lab.A1 is compact and attaches great importance to ergonomics, which allows for fatigue-proof working. The excellent optics with the options of phase positive and phase negative contrast allows you to visualize sperm cells with highest contrast. Axio Lab.A1 can be used for manual semen analysis. Furthermore, it also builds the basis for many computer assisted sperm analysis systems, such as CEROS from Hamilton Thorne.	Axio Scope.A1 offers flexibility and modularity to fit your advanced semen analysis needs. By combining brightfield, phase contrast and fluorescence you can perform different morphology and vitality checks with one system. The ergonomic design provides fatigue-proof working with the microscope. The integrated fluorescence LEDs are maintainance-free and keep the overall footprint of the system compact. Axio Scope.A1 is your reliable semen analysis system, when it goes beyond routine brightfield and phase contrast observation.	Stemi 508 is your compact stereo microscope, that fits any standard laminar flow box.  The large working distance offers convenient handling and manipulation of oocytes or embryos. The operation of the microscope is easy and intuitive leading to increased productivity. Due to the optional heating plates you can keep your samples at 37 °C while they are outside the incubator.	SteREO Discovery.V8 is equipped with open interfaces, that allows for integration into a laminar flow box. Its modular design and extensive accessories offer you a variety of options to set up your workplace to your exact requirements. The impressive stereoscopic image helps you to better observe and manipulate your oocytes and embryos. You get a high-resolution, high-contrast, and apochromatically corrected microscopic image – that is key for taking the right decisions. With its 8x zoom, you can quickly change from the overview down to the magnified detail, while staying perfectly in focus.	Axio Vert.A1 is perfectly suited as basis for a standard ICSI system. This compact inverted microscope is particularly impressive in terms of its price-performance ratio. Choose your preferred micromanipulation system since the system is compatible with all common models. Even laser-assisted hatching or embryo biopsies for PGT can be performed, e.g. with Hamilton Thorne's laser system. Use all relevant contrast techniques: with Axio Vert.A1 you have access to PlasDIC, iHMC, phase contrast and DIC ideal for routine IVF / ICSI and even IMSI. Plus, Axio Vert.A1 fits completely into your laminar flow box.	Axio Observer provides all relevant contrasting techniques in one single stand. iHMC, PlasDIC and DIC are all possible. Additionally, you can combine phase contrast with all methods. Axio Observer is readily compatible with all major laser systems to perform laser-assisted hatching or embryo biopsies for preimplantation genetic testing (PGT). Additionally, this robust and powerful microscope offers encoding and motorization options for higher user comfort. The Optovar allows you to change magnification without switching objectives, which can be extremely helpful, e.g. for IMSI. This future proof microscope leaves nothing to be desired.
Documentation	•	•	•	•	•	•
Contrasting techniques	Brightfield, phase contrast (±), LED fluorescence	Brightfield, phase contrast (±), LED fluorescence	Brightfield, darkfield, oblique light	Brightfield, darkfield, oblique light	iHMC, PlasDIC, DIC, phase contrast	iHMC, PlasDIC, DIC, phase contrast
Micromanipulation	-	-	•	•	•	•
Heating plate	optionally available from e.g. Tokai Hit	optionally available from e.g. Tokai Hit	optionally available from e.g. Tokai Hit	optionally available from e.g. Tokai Hit	•	•

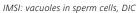
# **Recommended Contrasting Techniques for ART**

Historically, microscopy has played an important role in our understanding of the morphology and role of sperm and ova in reproduction, elucidating their behavior before and during their fusion, and helping us understand the early stages of zygote development. Appropriate transmitted light microscopy contrast techniques that are specialized for living and unstained samples are essential in the field of ART.



### DIC delivers brilliant images for IMSI

Top marks to DIC for IMSI for producing brilliant images at high magnifications. You can easily assess the shape and vacuole count of sperm cells.

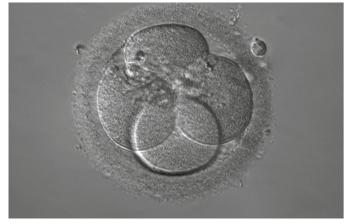




### PlasDIC improves your ICSI results

Structures such as the zona pellucida of oocytes are brought out particularly well by PlasDIC contrast technique. You can judge precisely where to inject, thanks to the strong and brilliant relief effect

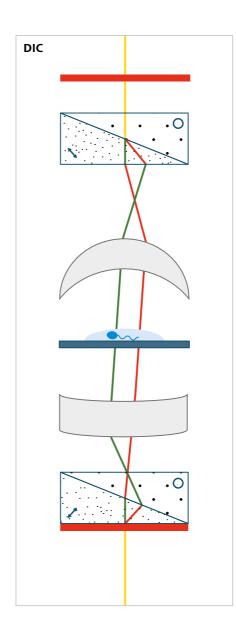
ICSI: oocyte with zona pellucida, PlasDIC



Embryo: nucleus with nucleoli visible in right cell, iHMC

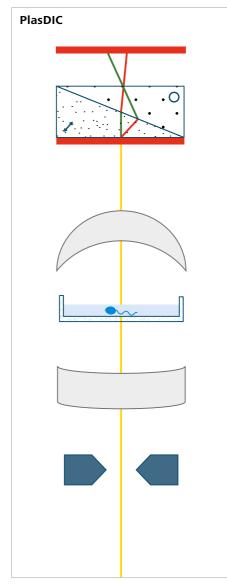
### iHMC reveals even finest structures in the cell nucleus

You examine embryos and assess cell nuclei? iHMC shows nucleus shape and nucleoli brilliantly.



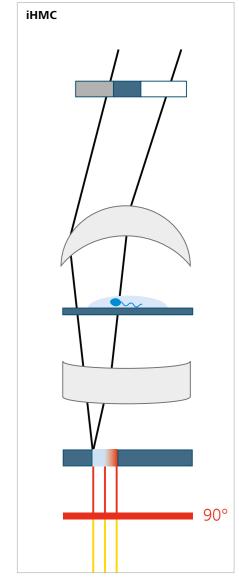
### Highest structural resolution

- For the smallest structures (e.g. good contrast sperm morphology)
- Optical sections possible
- No plastic vessels, only glass bottom and cover slip



### Strongest contrast

- For large objects (e.g. oocytes)
- No optical sections possible
- For highest ease of use
- Chosen contrast setting is memorized
- Lower structural resolution
- Plastic or glass vessels



### Best compromise

- Between DIC and PlasDIC
- Easier alignment and contrast memory only with iHMC
- Moderate optical sectioning
- Plastic or glass vessels

# **Expand Your Possibilities**

Selecting only the most healthy eggs, sperm and embryos is essential. Microscopes are indispensible tools in this selection process. Embryo care during laboratory incubation also becomes more important to ensure embryo viability is not compromised before embryo transfer. Whenever IVF samples are incubated, observed or manipulated, optional accessories help to maintain them in a contamination-free, cellfriendly environment that mimics in vivo conditions as far as possible.

Variations from the optimum can result in irreversible cell damage and failure of the whole process.

Besides the microscope the right accessories are important to guarantee a smooth and optimum workflow. This includes temperature control and incubation during various IVF procedures, such as embryo grading; micromanipulation equipment for ICSI; laser modules for embryo biopsies; and cameras for digital documentation.



### Micromanipulation

A stable, vibration-free microscope environment is essential for precise work, as well as the requirement for enough space around the specimen to position micromanipulation equipment. Long working distance condensers are required for convenient micromanipulation. ZEISS microscopes are compatible with all common micromanipulation equipment (e.g. from Narishige and Eppendorf) to support procedures such as ICSI or embryo biopsies.

### **Laser modules**

Preimplantation genetic testing (PGT) is becoming increasingly important in IVF. Laser systems are state of the art to perform embryo biopsies of blastocyst, trophectoderm and for assisted hatching. Axio Observer is compatible to all major laser system solutions and guarantees a broad application range.





### **Heating plates and incubation**

For various IVF procedures, such as the examination of the quality and development of the oocytes and embryos, the microscopes need to be equipped with heating plates. These plates maintain the temperature of the specimen at 37°C during observation. Heating plates are available for inverted as well as for stereo microscopes from ZEISS. For Axio Observer a stage top incubator with optional pH control is available.

# A stable temperature and clean environment is critical to maximize the success rate in IVF, embryo development and

ZEISS stereo microscopes for ART can be directly mounted in a laminar flow box for optimized conditions, allowing a seamless

### **Digital documentation**

Wether you go for connectivity and remote monitoring or for documentation with high resolution, e.g. important for IMSI, ZEISS offers the right solution with its broad Axiocam portfolio.

workflow of all necessary sample handling steps.

implantation.

# **Smart Connected Laboratory**

### **ZEISS Labscope**

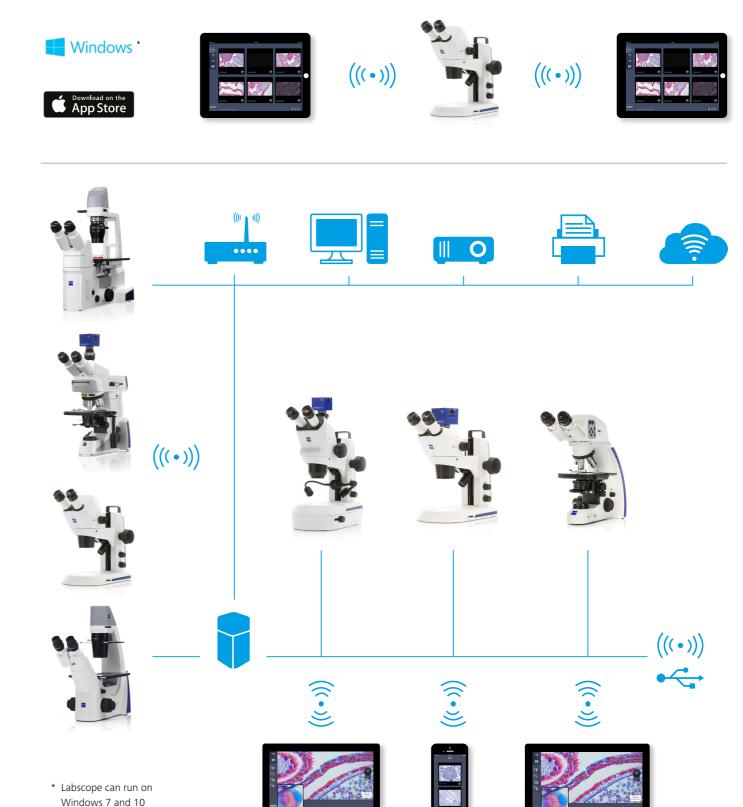
Easy lab management with remote monitoring possibility

Easily connect and manage your ZEISS microscopes with the imaging app Labscope. You can select and switch between connected microscopes with just one simple click. Even multiple users can access the same microscope and see the live image. With a single laptop or tablet in your lab you already can control all connected microscope and manage the storage of images and data. This saves costs and time.

The architecture allows for remote monitoring of your samples. So you can provide your clients the opportunity to remotely observe the actual ICSI process or the successful harvesting of oocytes and to take part in this exciting moment.

Embryologists also have the benefit that they can monitor embryos remotely via Wi-Fi or LAN at anytime and from anywhere – thereby allowing them to keep an eye on embryo status without having to be tied to the laboratory.

ZEISS microscopes equipped with Axiocam ERc 5s and Labscope build the perfect teaching environment. In a digital classroom, the teacher can project the live image to a screen and discuss with the whole class.



16 17

(both 32-bit and 64-bit).

# **ZEISS Axio Observer: Successful Fertilization with ICSI**

fiore institute St. Gallen, Switzerland

# "Success and safety are our focus."

**Felix Roth** 

### **Visiting the Fertility Center**

"Success and safety are our focus – and for the procedure to be as minimally invasive as possible. There's nothing better than when a woman becomes pregnant naturally after the first consultation because her mind is relaxed. The greatest feeling of success is when we have to intervene as little as possible," says Felix Roth of Fiore. Fiore is a private institute for reproductive medicine and gynecological endocrinology with a total of four centers in Switzerland. Approximately 400 procedures are performed annually at the main center in St. Gallen. The success rate is extremely high. Three laboratory technicians and a manager ensure that everything runs smoothly.

Their range of services includes fertility assessment, hormone therapy, insemination, IVF, ICSI, TESE (testicular sperm extraction), cryopreservation, psychosomatic consultation, and microendoscopic reconstructive surgery.

### The Challenges

The temperature must be kept constant throughout the entire process. If the temperature exceeds or falls below 37°C, the risk of damage to the egg and sperm cells increases. The process takes place in a limited window of time – unless the cells are frozen. Sometimes there is only one egg, so you only have one try. Everything comes down to one thing – the workflow cannot be interrupted and the devices must function perfectly. The laboratory cannot afford failures. Individual support and service staff who come quickly when needed play a critical role.

The workflows and techniques have become established over the course of many years. The physician doesn't have time to learn new techniques. The micromanipulators must be very finely adjusted; the doctor must be able to work with them more or less "blindly."



The microscopes should be stable and vibration-free. "ZEISS Axio Observer is simply a fantastic device. The optics are very, very good – incredibly good," emphasizes Walter Diethelm of Mikroskop Technik Diethelm. He is responsible for Fiore as a ZEISS dealer in Switzerland. For example, details of the zona pellucida on the egg cell can be viewed easily with the microscope. The same goes for the individual sperm cells.

In hardly any other field are expectations and the pressure to succeed as high as in reproductive medicine. The samples are very precious. Only healthy sperm, eggs, and embryos lay the foundation for successful fertilization. In addition, you have a specific period of time in which your workflow must be carried out smoothly. And all of this under controlled conditions, at a constant temperature, and in a clean environment. The best support for the responsible work carried out by the attending physicians and their MTAs is a microscope system that enables the use of state-of-the-art techniques while simultaneously being easy to operate with excellent ergonomics. ZEISS microscopes offer highly accurate results when working in the field of reproductive medicine – for successful fertilization.

### **ICSI**

Intracytoplasmic Sperm Injection

- is an assisted reproductive technology (ART)
- to treat sperm-related infertility problems
- to enhance the fertilization phase of in vitro fertilization (IVF)

### How does ICSI work?

Ovulation and egg retrieval

- Stimulation of ovaries to produce multiple eggs (appr. 2 weeks)
- Stimulation of follicles to mature (hCG)
- Collection of mature eggs 34 36 hours after hCG treatment









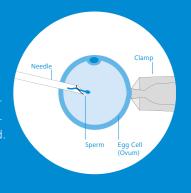


### Sperm collection

■ Masturbation or removal from a testicle through incision

### Sperm injection

- The embryologists uses micromanipulation tools and equipment on an inverted microscopes.
- A very delicate, sharp and hollow needle is used to immobilize and pick up a single sperm
- The needle is carefully inserted through the outer shell of the egg and the egg membrane.
- The sperm is injected into the inner part of the egg (cytoplasm) and the needle is removed.
- Then the fertilized egg grows in a laboratory for one to five days.









### Embryo transfer

■ The fertilized egg is then placed in a woman's uterus.



# Service and Support for Your ZEISS Microscope System

ZEISS Moments are about passion. The same passion that drives us to support and accompany you and your ZEISS microscope over its life cycle ensures that your work will lead systematically to success.

### You work hard. We make sure your microscope keeps pace with you.

High imaging quality, reliable results and instrument availability are the parameters of your day-to-day working life. Your ZEISS microscope integrates seamlessly into this demanding workflow. It provides you with insights and results that you can trust: thorough, comprehensive and reproducible. With our Life Cycle Management we help you keep your microscope in optimum condition to get these optimum results.

### Life Cycle Management comes with your microscope.

Life Cycle Management from ZEISS backs up our solutions throughout the working life of your ZEISS microscope system. From the procurement phase onward, you can count on our support with site surveys to optimize the location for your microscope system. Throughout the operational phase we will complement our service with support for relocations and upgrade opportunities that enhance or expand your possibilities. As soon as you think about replacing your long-serving microscope with a new one, we will take care of the disassembly and disposal of systems that are no longer needed. Rely on our service features: our employees analyze the status of your system and solve problems via remote maintenance or directly at your location.

### From expert to expert

Never hesitate to ask our application specialists to support your specific tasks. Take advantage of our training sessions for any colleagues or employees who will be working with your ZEISS microscope.

### Peace of mind and availability with regular maintenance

Your service plan is tailor-made for you. Make sure you take advantage of all the opportunities your ZEISS microscope system offers. Get optimized performance, instrument reliability and availability, all at predictable costs. Choose from different service levels of our Protect-Service Plans, ranging from Protect preventive, via Protect advanced, to Protect premium. We look forward to discussing your ideal Service Plan personally.









The moment you see something that has been hidden from you until now. This is the moment we work for.

How will doctors treat their patients in the future? How far can we go with the miniaturization of semiconductor structures? What role will photographs and videos play in the way we communicate in years to come? These and many other questions are what drive us every day at ZEISS. Only those who ask will find the answers.

As pioneers in the industry and one of today's worldwide leaders in the field of optics and optoelectronics, we have always pushed the limits of the imagination at ZEISS.

The questions for medicine in the future are already being worked on by our people – with boldness, passion and innovation. From this impetus will come medical instruments that optimize the success of treatments and laboratory devices that will underpin medical advances.

The many challenges that industry faces also motivate us to continue setting new standards in technology. As we do, quality in all components is being safeguarded by ZEISS. Just as it will be in the smaller, higher-performance and low-priced microchip of the future.

ZEISS researchers and developers are working with equal determination to realize their quality standards for moving and fixed images. Whether in the largest planetarium in the world or in the smallest smartphone that has ever been built, it's going to happen and you will see it. This passion for topmost performance links all business areas at ZEISS. That's how we create advantages for our customers and inspire the world to look for things that have been hidden until now.









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