



Start life with Nikon

Request a demonstration and let Nikon give your
IVF programme a great start in life





Pioneers in IVF

Nikon microscopes have played a key role in the development of Assisted Reproduction Techniques (ART) from the very start; the world's first in vitro fertilization (IVF) babies were conceived both in the UK and the US with the help of Nikon microscopes.

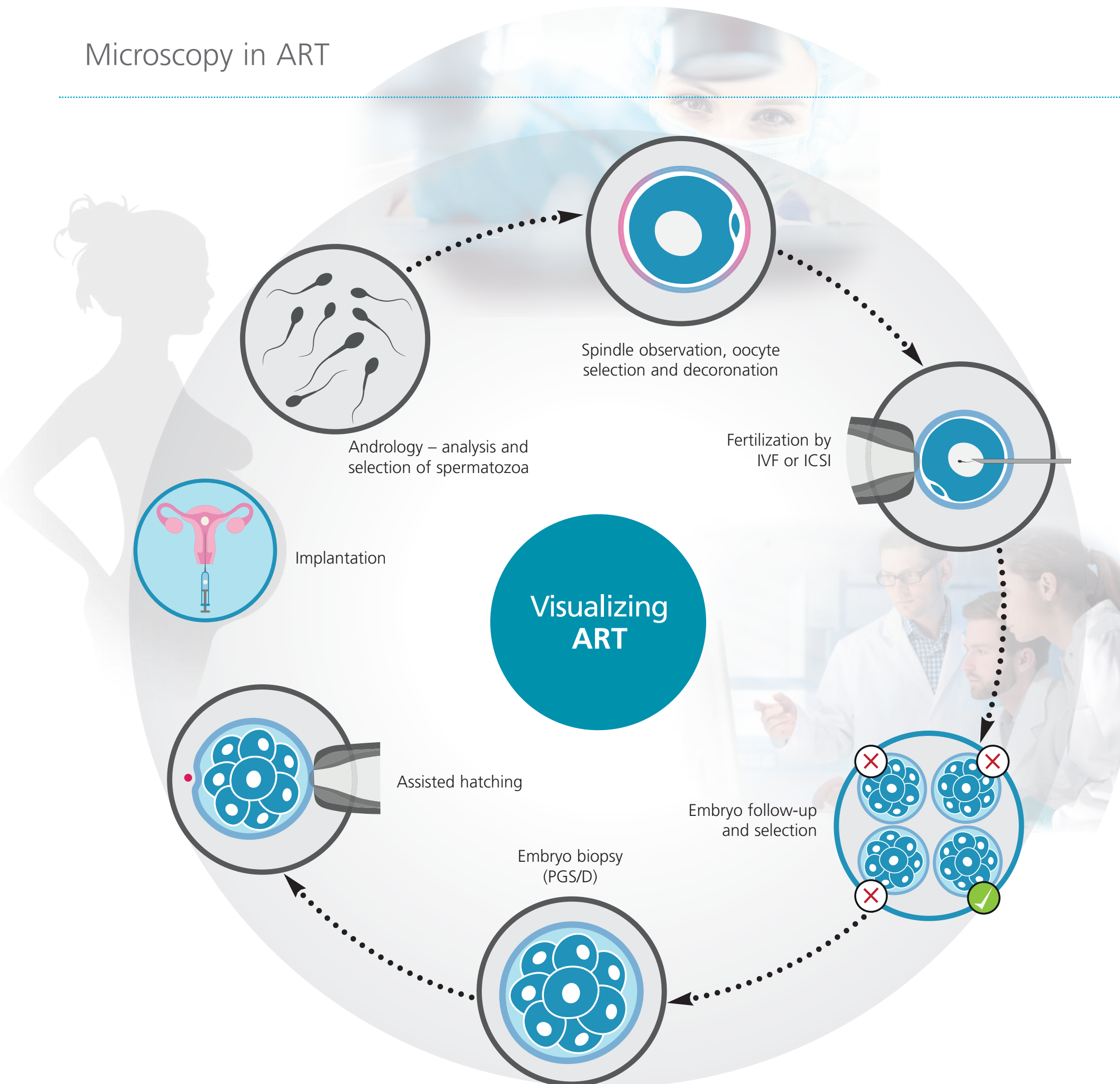
Since those pioneering days IVF has become a routine procedure. One in six couples worldwide experience some form of infertility problems at least once during their reproductive lifetime, and the current prevalence of infertility is estimated to be around 9% worldwide for women aged 20-44 (ESHRE), lasting for at least 12 months.

Although IVF was originally used in women who had difficulty conceiving, today it is relevant to almost all fertility problems in both men and women when combined with ICSI (intracytoplasmic sperm injection) and similar techniques. Today, more than 1.5 million ART cycles are reported every year worldwide and Europe plays a leading role in ART, initiating almost 50% of reported treatments (ESHRE).

At the heart of Nikon's offering in ART is an understanding of the needs of IVF today – excellent optical quality and cell-friendly imaging technologies which minimize environmental stress and optimize cell viability during imaging.

Today, Nikon continues to be a leader in IVF by providing embryologists with diverse tools to support every step of the ART cycle: from upright microscopes for andrology studies, through stereomicroscopes for monitoring and selection, to inverted systems for live cell imaging and manipulation.

Microscopy in ART



Assisted Reproductive Technologies (ART) are primarily used for infertility treatments that aim to achieve pregnancy. They belong to the field of reproductive endocrinology and infertility, and they may include intracytoplasmic sperm injection (ICSI), genetic embryo selection (pre-implantation genetic screening/diagnosis, PGS/D) and cryopreservation (frozen embryo transfer, FET) amongst others. ART is also used for couples who are at risk of transmitting some genetic diseases to their progeny, such as cystic fibrosis.

Microscopy has a pivotal role within the exogenous steps of the ART cycle: from spermatozoa assessment and oocyte selection after retrieval, through fertilization, to the final selection of the embryos for implantation.

After oocytes are decoronated and selected, standard IVF might not be enough to warranty fertilization and pregnancy, and nowadays, more than 67% of those procedures are performed using ICSI together with methods developed for analyzing and selecting the most suitable sperm for ICSI, such as IMSI (intracytoplasmic morphology selected sperm injection), PICSI (physiological intracytoplasmic sperm injection) or MACS (magnetic activated cell selection) followed by ICSI.

Not every implanted embryo results in a live birth. Average deliveries per aspiration cycle vary from 21.9% for IVF, to 20.1% in ICSI (Calhaz-Jorge et al 2016), and further techniques have been implemented to ultimately increase the rate of pregnancy and delivery success that aim at selecting the best embryo to implant and assist its development through PGS/D and assisted hatching.

All these techniques are delicate procedures requiring sample manipulation carried out under microscopic observation. Clear, high resolution imaging coupled to the embryologist's expertise is of paramount importance.

Monitoring and selection

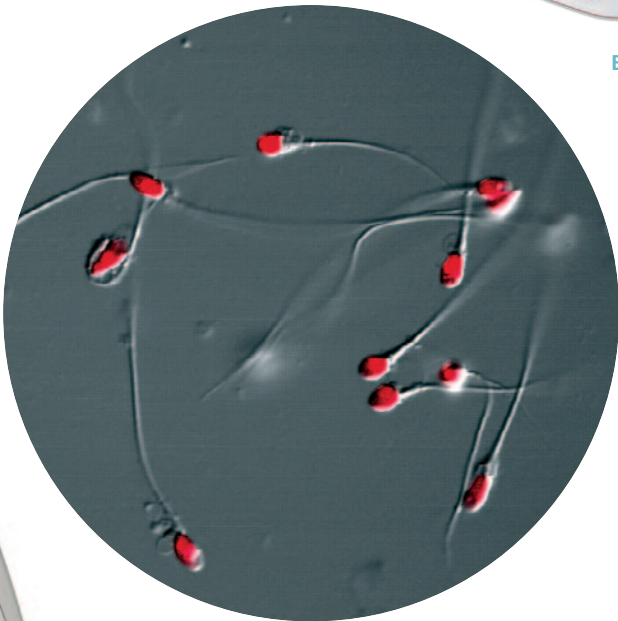
Andrology

IVF and ICSI require the preparation and selection of optimal spermatozoa for IVF incubation or direct injection into eggs. Sperm is concentrated and initially selected by density gradient centrifugation, generally followed by swim-up test. Recent studies recommend the additional use of MACS to select non-apoptotic sperm cells (Ziarati et al 2018). Other tests that determine the proper functioning of the sperm cells quality may be evaluated microscopically through criteria such as maturity, sperm count, motility and morphology, especially of the head region containing the nucleus. Abnormal head shapes such as 'pin', 'amorphous', 'tapered', 'round' and 'multinucleated' are associated with reduced IVF success rates and can be identified with relatively low microscope magnification.

Perform optimal sperm counting, maturity, motility, vitality and morphological studies with excellent phase contrast and fluorescence observation with Nikon's Eclipse upright microscopes. Choose Eclipse Si or Ci-L for your andrology studies and let us enable your success.



Eclipse Si



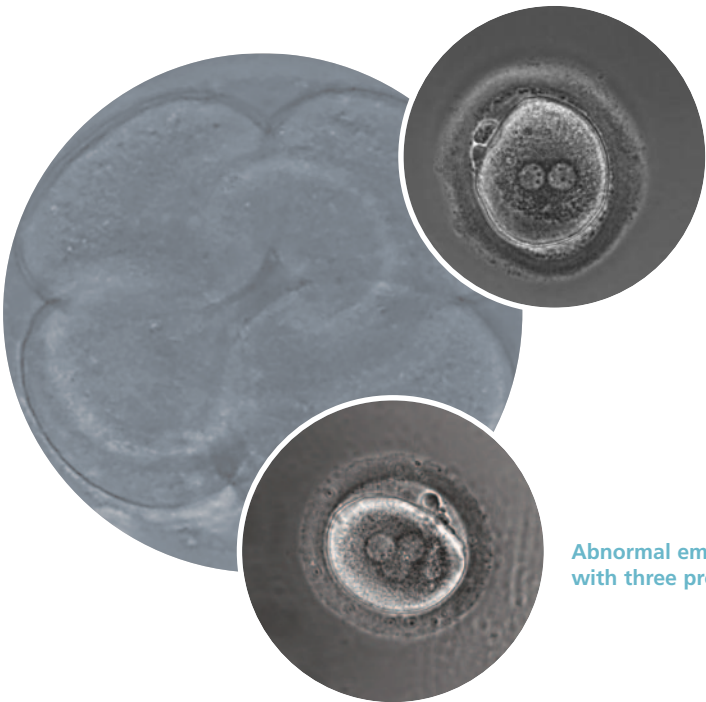
Eclipse Ci-L plus

Oocyte and embryo follow-up

Following retrieval, eggs are usually examined under the microscope to select appropriate eggs for fertilization. Morphological features taken into account include size, degree of vacuolation, fragmentation and granulation, polar body and spindle morphology, integrity and thickness of the zona pellucida, as well as the presence and health of cumulus cells around the egg. The main criterion for selection is maturation stage (metaphase II oocytes are optimal for ICSI) as mature eggs are more likely to support normal embryo development.

Embryo quality is generally assessed by cell number at defined time points, regularity of cells in terms of size and shape, and degree of cytoplasmic fragmentation. Other factors may include multinucleation, presence of vacuoles, granularity, and thickness of the zona pellucida. Decisions on which embryo(s) to implant or to freeze for future FET are usually made on day three, although some laboratories may maintain embryos in vitro for up to 5 days to aid the selection process.

Comfortably monitor your oocytes and embryos at your preferred magnification with Nikon's SMZ series of stereo microscopes, which offer zoom ratios from 4.4:1 to 25:1 with exceptional optical quality and ergonomic design for a variety of embryology and ART applications. Choose your preferred magnification of work and we will advise and coordinate the installation in your cabinets.

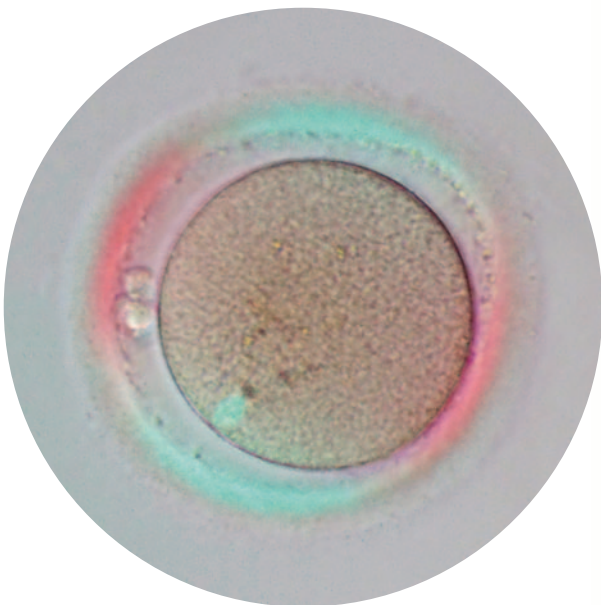
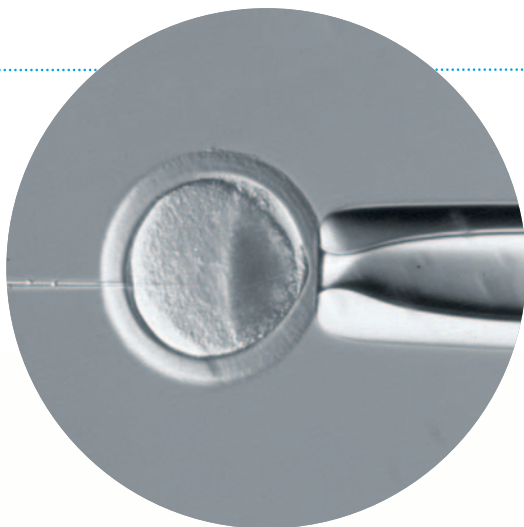


Normal embryo with two pro nuclei*

Abnormal embryo with three pro nuclei*

Fertilization

Several methodologies are available for fertilization within the ART cycle, standard IVF and ICSI being the most common ones. ICSI is the process by which the sperm head is injected into the oocyte's cytoplasm, mimicking fertilization, with the aid of micromanipulators. Several techniques have been developed to increase fertilization success. For example, by selecting the sperm that will be injected by morphological features (motile sperm organelle morphology examination, MSOME), or by physiological properties (PICS). Selecting oocytes with spindle present and avoiding perturbation of these spindles further increases fertilization success. The spindle can be visualized in color in any orientation using Nikon's Spindle Observation System.



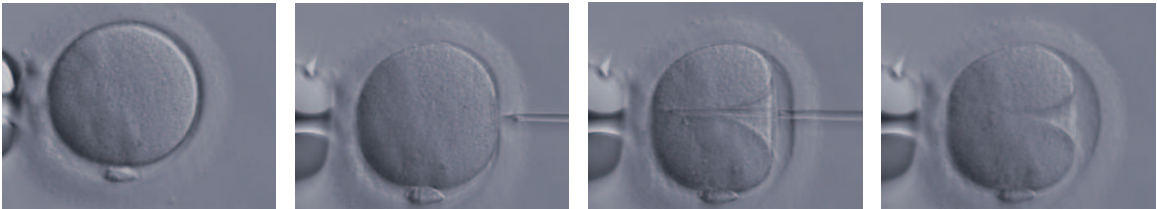
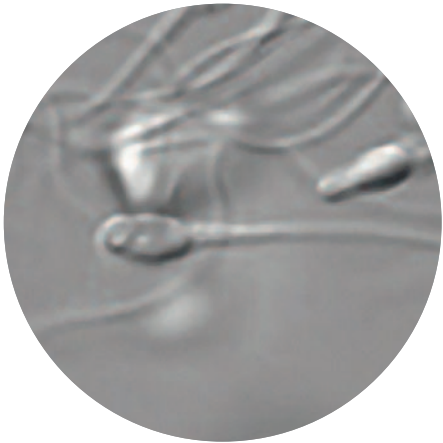
360 Spindle observation system



Ti2-U ICSI station with Fi3 camera

The aim in selected IMSI is to select the sperm with the greatest potential for success in ICSI. The development of MSOME, utilizing a powerful microscope, facilitated the introduction of IMSI. IMSI using magnifications of >6000x has resulted in higher pregnancy and delivery rates and lower abortion rates in some reports (Bartoov et al 2003, Berkovitz et al 2005 and 2006, Luna et al 2015). During IMSI, sperm are observed and selected in a glass-bottomed dish at high magnifications, which enable the detection of subtle defects in sperm organelles such as the acrosome, mitochondria, and nucleus. Another common defect is abnormal vacuolation. Nuclear chromatin is considered abnormal if it contains more than one vacuole. Sperm examination normally uses DIC with 60x or 100x oil objectives, while Nikon also offers the possibility for 100x dry IMSI, making the process smoother and faster. Following sperm selection, Hoffman modulation or Emboss contrast at 20x or 40x non-oil objectives are used for ICSI. In cases of severe male infertility, there might not be "normal" spermatozoa and second-best ones need to be selected.

Nikon's renowned Advanced Modulation Contrast (NAMC) optics, as well as the newly developed simple Emboss Contrast technique, enable optimal contrast levels for fine detail observation during ICSI procedures. To support ICSI and IMSI procedures, you can choose from Nikon's compatible micromanipulation equipment, featuring Narishige and Eppendorf products. Nikon's inverted observation microscopes, the Ts2R and Ti2 systems, are the mainstay of IVF procedures, offering exceptional optical quality and robust, vibration-resistant design.



ICSI sequence - Images courtesy of Dr Pierre Boyer, Laboratoire d'AMP, Hôpital Saint Joseph, Marseille, France

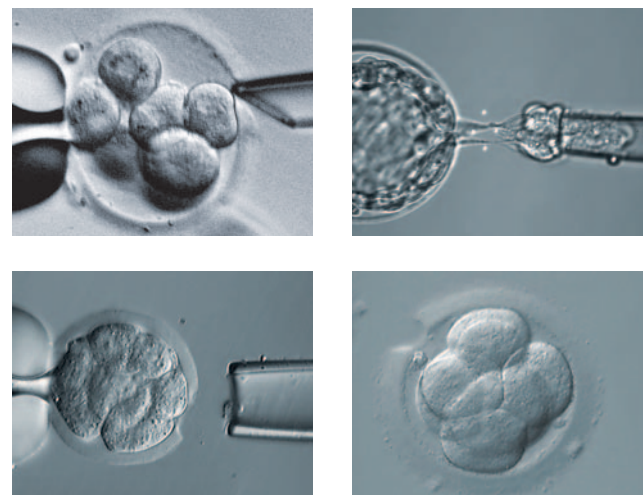
Embryo biopsy and assisted hatching

After fertilization has taken place, further steps might be required for the success of the ART cycle by further manipulation of the embryo through assisted hatching and/or PGS/D. For both techniques, lasers are used to disrupt the external layer of the embryo for different purposes.

On the one hand, assisted hatching aims to open the zona pellucida around the embryo to assist its naturally occurring hatching. It was developed when fertility experts reported that embryos with a thin zona pellucida had higher rates of implantation during IVF, and has been further confirmed (Li et al 2016). Although this process can be chemically mediated, mechanical and laser mediated techniques have been shown to be more successful (Park et al 2014).

On the other hand, PGS/D can help embryologists make informed decisions on which embryo(s) to select for implantation. In addition to morphological assessment of sperm, eggs and embryos, PGS/D is often used when couples are affected by genetic disease or in cases where couples experience repeated, unexplained IVF failures. PGS/D identifies chromosomal abnormalities using fluorescence in situ hybridization (FISH), comparative genomic hybridization (CGH) or PCR-based DNA ~ It is generally performed with the aid of a laser to facilitate reaching the cells with the micromanipulators under microscope observation. The embryo is positioned using a round ended micropipette and the zona pellucida is perforated using a laser, enzymes or acid tyrode solution. A second pipette is then inserted into the embryo through the perforation to gently aspirate cells for analysis.

Nikon's Eclipse Ti2 inverted observation microscope is designed laser safe for the best protection of the embryos during laser procedures. NAMC optics enable optimal contrast levels for fine detail observation during embryo biopsy procedures as well as assisted hatching.

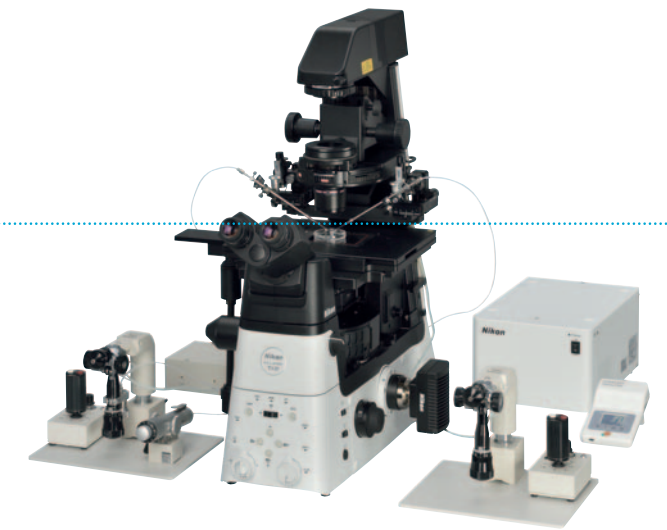


Embryo biopsy and assisted hatching - images courtesy of Vitrolife and Dr Mary Herbert, Newcastle Fertility Centre at Life



Ts2R ICSI station

Supporting IVF



As well as its comprehensive range of microscopes for IVF, Nikon also supplies specialized objectives for live cell imaging, digital imaging equipment and software to enhance IVF procedures.

Objectives

Long working distances are essential. Nikon's CFI60 optical system provides both long working distances as well as high N.A.s, enabling high resolution observation of living unstained cells. Benefit from apodized phase contrast objectives that dramatically reduce halo effects compared with conventional lenses. A correction collar is also available for live cell work that compensates for the effects of working at physiological temperatures.



Imaging

Nikon's digital cameras can be incorporated into IVF imaging systems to enable immediate image display, capture and archiving and immediate image sharing via network. The DS-Fi3 camera is the camera of choice for IMSI because its high definition, high sensitivity and fast capture rates are able to 'freeze' fast moving sperm.



NIS-Elements

Nikon's intuitive NIS-Elements software enables image acquisition while providing features such as image annotation, stitching, object counting and display. It is a powerful image management tool, which integrates cameras, components and peripherals with image acquisition, archiving and visualization tools.

Micromanipulators

Nikon supplies Narishige and Eppendorf micromanipulator equipment to support ART procedures such as ICSI, IMSI, embryo biopsies and assisted hatching. The Narishige products offer compact design to provide a reduced distance from manipulator mount to microelectrode tip thereby increasing stability. Eppendorf's TransferMan@NK 2 offers an excellent combination of automatic processes and intuitive operation to allow the most complex of micromanipulation techniques to be carried out rapidly and precisely.



Environmental control

The highest quality, temperature controlled heated stages from Okolab and Tokai Hit are offered with Nikon microscopes and stereomicroscopes. Nikon microscopes and stereomicroscopes can be easily fitted into your IVF cabinet or workstation.



Laser systems

Nikon inverted microscopes can be coupled with laser systems required for ART procedures such as embryo biopsy and assisted hatching procedures.