EMBRYOLOGY IN THE ERA OF TIME LAPSE

It is estimated that today, more than 10% of couples are subfertile. Social, genetic and environmental factors may be the reason for this situation. For some couples facing infertility, IVF is their only way of achieving their dream of having a baby. More than three decades have passed since the birth of the first child conceived using the in vitro fertilization (IVF) method. Tremendous progress has been made on the IVF field, regarding stimulation protocols, culture media composition laboratory equipment and methods such as ICSI and vitrification, which has brought a vast improvement in the effectiveness of IVF treatment and pregnancy outcomes.
Despite the progress and wide availability of infertility treatment using IVF many issues remain unresolved and unexplained. Consequently, further improvements to increase treatment efficacy and effectiveness are difficult to achieve. One of the key problems is the difficulty with the precise evaluation of the developmental potential of embryos obtained after in vitro fertilization. Therefore, embryos of unknown implantation potential are frequently transferred. Pregnancy rates can be significantly improved by transferring a greater number of embryos, but this may produce an undesirable increase in the incidence of multiple pregnancies and related gestational complications.
Currently, the success rate of ART has been standardized at approximately 40%. After achieving such high pregnancy rates, clinical practice efforts have been directed toward minimizing multiple pregnancies by single embryo transfer.

The only way of doing this is by improving embryo selection. The ability to identify embryos with a higher capacity for implantation means we can reduce the number of embryos for transfer without reducing the chances of pregnancy in a cycle of assisted reproduction.
Embryonic potential for implantation and successful pregnancy in IVF cycles has traditionally been assessed by means of microscopic examination with the use of a grading system based on morphology. The visualization of embryonic development has been limited to a brief evaluation once a day under the microscope, exposing our embryos to temperature and pH fluctuations outside of the incubator. In addition, evaluation of morphology under microscope is subject to observer subjectivity. It is therefore crucial to develop new, non-invasive biomarkers of embryo developmental potential other than those based on morphological criteria. Different non invasive embryo selection methods have been proposed in the past, such as metabolomics, that provide information on how to distinguish embryos with better prognosis which failed to become a diagnostic tool on embryologists hands on everyday practice.
One of the noninvasive embryo evaluation methods to have come into the light in recent years using morphokinetics ,is the time-lapse monitoring systems (TMS). Image capturing with time-lapse devices is a non invasive method that offers the possibility of 24-hour monitoring of embryo development and of increasing the quantity and quality of information without disturbing the culture conditions. Time-lapse imaging in combination with microscopes within the incubation unit allows keeping embryos in the incubator in an undisturbed environment during the whole culture period. Embryo development for each individual embryo can be

assessed at the same time by taking pictures at defined time intervals. For each embryo, these pictures can be viewed in sequence as a video and allow to follow exactly how the embryos grow over time. In combination with a single step culture medium that allows undisturbed blastocyst culture without media change, there is no longer any need to remove the dish or the embryos out of the incubator. Hence embryos can grow completely undisturbed from the time of insemination until to the time of embryo transfer on any day of development.

The goal of frequent monitoring, while maintaining an optimal culture environment, has led to the development of specialized culture systems, such as the Embryoscope incubato, primo vision and other systems that enables time-lapse photography without removing embryos from the incubator.

The use of morphokinetics, or timing of embryonic developmental events and visualization of dynamic morphology, available through continuous time-lapse monitoring, has added another dimension to current traditional morphology classification scores. These systems generate unique determinations that combine the morphologic assessment with the timing of embryonic cleavages, thus diminishing observer subjectivity. The safety of these systems has also been demonstrated.

Time lapse has become the ultimate tool on predicting embryo implantation potential and this can lead to an increase of IVF treatment effectiveness by using only single embryo transfers.