

## HYLIGHT

Prototyping a light-sheet microscope for the diagnostic of embryo implantation based on hyperspectral phasor analysis

## PUBLIC SUMMARY

One out of seven couples in Europe experience subfertility problems. In vitro fertilization (IVF) has overcome many underlying causes by crossing sperm with isolated eggs to generate an embryo in vitro. Typically, five to ten embryos are produced per cycle, and one or two will be then transferred into the uterus of a woman. However, the number of initial embryos leading to a live birth is relatively low (~18%), and repeated unsuccessful IVF cycles imply significant emotional and physical distress for women. Often, pregnancy rates are artificially increased by transferring multiple embryos to the mother.

However, this procedure has the undesirable effect of multiple pregnancies, which generate remarkable obstetrical and neonatal complications, including prematurity and underweight and 40-fold increase in the risk of dying in early infancy. Mothers carrying multiple foetuses have higher rates of hospitalization and caesarean delivery.

In this context, identifying the embryos that are competent for implantation and development is a critical technological roadblock to increase the efficiency of IVF and therefore reduce the so called "time to pregnancy". Nowadays, time-lapse incubators, the state-of-the-art technology, allow to monitor the morphological changes of the developing embryo; alternatively, pre-implantation genetic testing serves to discard embryos with genetic alterations, but in an invasive way.

However, in retrospective studies, none of these two methods showed a significant increase in pregnancy rates. Therefore, current technologies are not useful to properly identify competent embryos. To overcome this limitation, we propose to develop a diagnostic device based on an imaging method of our invention, which classifies competent embryos on the basis of their metabolic profile, in a non-invasive way. In agreement with other researchers, we observed a robust correlation between embryo metabolism and its viability.

Our novel method takes advantage of the intrinsic fluorescence of key metabolites (i.e., NADH or FADH), thus allowing to image live embryos in physiological conditions. We already built a Proof-of-Concept (PoC) device, in collaboration with our partner M-Squared. The PoC device combines light-sheet microscopy, multiphoton (MP) imaging, and a novel hyperspectral (HS) phasor analysis, accelerated by artificial intelligence (AI), herein referred to as HYLIGHT.

This breakthrough technology overcomes classical limitations of hyperspectral imaging applied to biological samples, namely: speed, phototoxicity, and resolution. Finally, we propose a project to thoroughly test the PoC device to transform it into a first prototype. With this aim, we partnered with DEXEUS, a pioneer IVF clinic, to make sure that this prototype will meet all the needs of the clinical practice; moreover, our market analysis and interest from venture capital strongly supports the incorporation of a profitable spin-off for the commercialization of our technology.





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