


Time-lapse systems by Vitrolife

Selected studies about embryo development and outcome



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Selected studies about embryo development and outcome

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Provided is a list of some of the studies about embryo development and clinical outcomes using EmbryoScope and EmbryoScope+ time-lapse systems.

 Find out more about Time-lapse systems by Vitrolife: www.vitrolife.com

Publications

Sibling oocytes cultured in a time-lapse versus benchtop incubator: how time-lapse incubators improve blastocyst development and euploid rate

Nobrega et al. Zygote 2023 Aug;31(4):402-409.
<https://pubmed.ncbi.nlm.nih.gov/37226769/>

Summary: Sibling oocyte study. Embryos cultured in the EmbryoScope or G185K benchtop. Embryos cultured in the EmbryoScope, had a significantly higher chance of being biopsied (64.8% vs 49.6%, $P < 0.001$). Moreover, a significantly higher blastocyst biopsy rate was observed on Day 5 in the EmbryoScope (67.8% vs 57.0%, $P = 0.037$), with a highly significant increased euploid rate (63.5% vs 37.4%, $P = 0.001$) and improved blastocyst quality ($P = 0.008$).

Improved embryonic development and utilization rates with EmbryoScope: a within-subject comparison versus a benchtop incubator

Setti et al. 2022 Zygote. 30(5): 633-637.
<https://pubmed.ncbi.nlm.nih.gov/35674243/>

Summary: There were significant differences in day 2 non-cleavage rates (OR:0.285, CI: 0.234-0.347), day 5 embryo rates (OR: 1.385, CI:1.331-1.442), blastocyst development rates (OR: 1.358, CI: 1.267-1.456), frozen blastocyst rates (OR: 1.163, CI: 1.085-1.248), Oocyte Utilisation Rate (OUR)(OR: 1.232, CI: 1.155-1.314), and Embryo Utilisation rate (EUR) (OR:1.269, CI: 1.202-1.341), all in favour of the TLI group versus culture in the G185K incubator.

Time-lapse technology improves total cumulative live birth rate and shortens time to live birth as compared to conventional incubation system in couples undergoing ICSI

Reignier et al. 2021 J. Assist. Reprod. Genet. 38:917-923 (note open access)
<https://link.springer.com/article/10.1007/s10815-021-02099-z>

Summary: Retrospective analysis of a total of 151 and 250 couples underwent their whole IVF care with the exclusive use of TLT and CI, respectively over a 5-year period, including all subsequent frozen-embryo transfers and ICSI cycles (if any). Total cumulative live birth (TCLB) and time to live birth (TTLB) were significantly improved with TLT over CI in couples undergoing ICSI for male factor. This study fuels the debate on the clinical benefit of using TLT. The use of time-related endpoints adds important information for both patients and practitioners.

Does embryonic culture environment affect ploidy rates in ART cycles: A single center study in UK

Rabi et al. 2022 J. Reprod. Infertil. 23(3): 169-176.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9666590/>

Summary: Retrospective single center cohort study, a total of 1099 blastocysts from 278 PGT-A cycles were analyzed. Inseminated oocytes were allocated in different incubators (benchtop and time lapse).The euploidy rate obtained from both groups showed a higher proportion of euploid embryos in the TLM incubator (37.03%, 95% CI 31.9-42.1) compared to those cultured in the BT incubator (30.4%, 95% CI 23.1-37.7).

Analysis showed a statistically significant proportion of “excellent” quality embryos in the TLM incubator when compared to the benchtop (34.5% vs. 21.4%). A sub analysis of 74 euploid single embryo transfers were included for clinical outcome analysis. Considering the limited sample size, pregnancy rates were comparable amongst both incubation systems (benchtop 73.3% vs. TLM 75%, $p=0.871$). There was a trend of improved outcome in the TL group, for clinical (86% vs. 96%) or ongoing (63.3% vs. 72.7%) pregnancy, however this was not significant at the 5% level.

Comparison of pregnancy outcomes using a time-lapse monitoring system for embryo incubation versus a conventional incubator in vitro fertilization: An age-stratification analysis

Chera-aree et al. 2021 Clin. Exp. Reprod.Med. 2021;48(2):174-183
<https://ecerm.org/journal/view.php?doi=10.5653/cerm.2020.04091>

Summary: Retrospective analysis of 250 fertilized embryos from 141 patients over same time period. The TLS group had a significantly higher clinical pregnancy rate (46.4% vs. 27.2%, $p=0.002$), implantation rate (27.1% vs. 12.0%, $p=0.004$), and live birth rate (32.0% vs. 18.4%, $p=0.013$) than the CI group. Furthermore, subgroup analyses of the clinical pregnancy rate and live birth rate in the different age groups favored the TLS group. However, this difference only reached statistical significance in the live birth rate in women aged over 40 years and the clinical pregnancy rate in women aged 35–40 years ($p=0.048$ and $p=0.031$, respectively). The miscarriage rate, cleavage rate, and blastocyst rate were comparable. It should be noted that there were significantly more PGT cycles and fresh transfers in the TL group which could likely bias the overall results. When taken into consideration, there was still a trend to better outcomes.

Closed embryo culture system improved embryological and clinical outcome for single vitrified-warmed blastocyst transfer: A single-center large cohort study

Ueno et. al., 2019 Reprod. Biol. 19(2)139–144
<https://www.sciencedirect.com/science/article/abs/pii/S1642431X18304261?via%3Dihub>

Summary: 1402 patients were divided into two groups, CCS (EmbryoScope+) and STS (Astec). The main outcome measures in the two groups were embryological (blastocyst formation rates and utilized blastocyst rates) and clinical outcomes (ongoing pregnancy rates) after a single vitrified-warmed blastocyst transfer (SVBT). There were no significant differences in the blastocyst formation rates between the CCS and STS groups (59.6% versus 59.1%, $p=0.81$). However, there were significant differences in utilized blastocyst rates (51.0% 46.6%, $p<0.05$). Ongoing pregnancy rates per SVBT cycle were significantly higher in the CCS group than in the STS group (41.4% versus 34.4%, $p<0.05$). Moreover, after applying multi variable logistic regression analysis, the type of embryo culture system (CCS to STS, adjusted odds ratios: 1.41, 95% CI: 1.04–1.91) was correlated with ongoing pregnancy. Our study suggests that compared to STS, CCS could improve utilized blastocyst rates and ongoing pregnancy rates to a greater extent, following SVBT.

Embryo culture conditions are significantly improved during uninterrupted incubation: A randomized controlled trial

Alheloua, et al. 2018 Reprod Biol. 18(1):40-45
<https://pubmed.ncbi.nlm.nih.gov/29279181/>

Summary: RCT comparing EmbryoScope with standard incubator. The 8-cell development rate in all age groups combined ($p=0.016$), blastocyst development rate ($p=0.0022$) and the implantation rate ($p=0.0022$) were significantly higher for the uninterrupted culture in The EmbryoScope versus standard incubation. These findings demonstrated significant differences between the two incubation groups. It also indicated less efficacious embryonic development with age in both treatments which appeared more pronounced in the conventional incubator. In conclusion uninterrupted culture is superior compared to the interrupted incubation culture system.



Comparison of the development of human embryos cultured in either an EmbryoScope or benchtop incubator

Sciorio et al. (2018) J. Assist. Reprod. Genet, 35(3): 515–522
<https://pubmed.ncbi.nlm.nih.gov/29243141/>

Summary: The development of sibling human zygotes was compared after culture in either a benchtop incubator (SI) or an EmbryoScope time-lapse incubator (ES). Between May 2015 to April 2016, a total of 581 normally fertilized 2PN, pronuclear-stage embryos, from 47 patients were allocated to culture in either a benchtop incubator (SI) or an EmbryoScope incubator (ES). The proportion of good quality embryos was higher in the ES group compared to the SI on day 2 (66.8 vs. 50.5%, $P = 0.014$) and on day 3 (75.1 vs. 56.0%, $P = 0.006$). Those differences were statistically significant. A higher proportion of embryos developed to good quality blastocysts when cultured in the EmbryoScope compared to the benchtop (49.4 vs. 42.0%, $P = 0.24$ (Authors noted a higher proportion of top quality D3 embryos transferred in EmbryoScope group, some of these which would likely have progressed to top quality blastocysts).

Cumulative live birth rates and perinatal outcomes with the use of time-lapse imaging incubators for embryo culture: a retrospective cohort study of 1882 ART cycles

Mascarenhas et al. 2018 BJOG 126(2):280-286.
<https://pubmed.ncbi.nlm.nih.gov/29443441/>

Summary: Comparison was done between 1064 IVF cycles using TLI (TLI cycles) and 818 IVF cycles using SC (SC cycles). The fresh embryo transfer live birth rate was noted to be higher for TLI cycles [TLI 36.8 versus SC 33.9%. The age was significantly higher in the TL group and there were significantly more older patients in the TL group. The adjusted odds ratio (aOR) for live birth was 1.28, 95% CI 1.05–1.57], but the frozen embryo transfer live birth rates were not significantly different. In supplementary data, in the under 37 patient group, Live birth per retrieval and cumulative live birth per retrieval was significantly higher in the TL groups (43.1%, 36.3% $p = 0.0099$, and 62.2% versus 56.8% $p = 0.0416$) Continuous embryo culture elicits higher blastulation but similar cumulative delivery rates than sequential: a large prospective study.

Continuous embryo culture elicits higher blastulation but similar cumulative delivery rates than sequential: a large prospective study

Cimadomo et al. 2018 J. Assist. Reprod. Genet 35(7): 1329–1338
<https://pubmed.ncbi.nlm.nih.gov/29725911/>

Summary: Study was primarily to look at effect of single or sequential media including effect in different incubator types. In this study, a sub analysis comparing the effect of undisturbed culture in non-disturbed Embryoscope versus standard incubation showed a positive effect of an undisturbed culture system upon blastocyst formation (OR= 1.22; $p < 0.01$). Conclusion: Continuous embryo culture in a time-lapse undisturbed system seems then the safest strategy. Possibly, by extensively reducing the need for embryo manipulation, it also limits the related environmental fluctuations (in temperature, humidity, gas, and hence pH) and risks for embryo damage or loss [27–29]. Moreover, costs and time-consuming labor are associated with the daily check of embryo culture and media changeover in day 3, matters which should not be disregarded in the definition of the ideal management of an IVF lab.

Incubator type affects human blastocyst formation and embryo metabolism: a randomized controlled trial

Kermack et al. Publication following Abstract presentation in 2017 by Lowen et al. (see reference below)
Hum. Reprod., 37(12): 2757–2767,
<https://academic.oup.com/humrep/article-abstract/37/12/2757/6775035?redirectedFrom=fulltext>

Summary: Overall, blastocyst formation rate on Day 5 was significantly higher in embryos cultured in the TLS (55%) compared to the standard incubator (45%; $P = 0.013$). Similarly, there was an increase in the number of blastocysts suitable for cryopreservation in the TLS (31%) compared to the standard incubator (23%; $P = 0.032$). There was a significant difference in the utilization of 12 amino acids by blastocysts cultured from Day 3 to Day 5 in the TLS compared to the standard incubator. Embryos cultured in the TLS displayed an increased total amino acid utilization ($P < 0.001$) and reduced amino acid production ($P < 0.001$) compared to those in the standard incubator.

Randomized controlled trial comparing embryo culture in two incubator systems: G185 K-System versus EmbryoScope

Barberet et al. 2017 Fert. Steril. 109(2):302–309
<https://pubmed.ncbi.nlm.nih.gov/29175066/>

Summary: Study primary outcome was powered to detect a 48% relative increase in implantation rates. Secondary measures were embryo quality. The proportion of high-grade embryos on day 2 was significantly higher in the TLI group compared with the G185 group (40.4% vs. 35.2%). The number of viable embryos (% of all embryos) was significantly higher in the EmbryoScope G185K (40.9%) EmbryoScope (47.8%) $p < 0.01$.

The impact of the incubator on embryo morphology remained significant in multivariate analysis, which took into account the woman's age, the rank of attempt, and the smoking status (TLI vs. G185: odds ratio 1.27; 95% confidence interval, [1.04–1.55]). Odds of TOP grade embryo ($n = 3097$ embryos) TLI vs G185* O.R. 1.26 [1.02-1.54] $P = 0.03$. No difference was found in the mean number of frozen embryos, even though the total proportion of frozen embryos was significantly higher in the TLI group than in the G185 group (29.5% vs. 24.8%). NOTE: clinical outcome measures were powered to detect a 48% increase, although there was a clear trend, in increase in outcome it was not significantly different. CPR/ Per ET G185K (41.3%) EmbryoScope (48.6%).

Live birth rate following undisturbed embryo culture at low oxygen in a time-lapse incubator compared to a high-quality benchtop incubator

Kalleas et al. 2022. Fertil. (Camb)(1):147-153.
<https://pubmed.ncbi.nlm.nih.gov/32098536/>

Summary: The EmbryoScope group had an increased chance of a live birth (43.2% vs. 34.5%; OR= 1.43 [95%CI: 0.96–2.13]) with significantly reduced early pregnancy loss (5.8% vs. 13.8%; OR= 0.37 [0.19–0.74]) compared to the K-System incubator. There was a higher proportion of 4-cell embryos on day 2 and 8-cell embryos on day 3 in the EmbryoScope, compared to the K-Systems. The use of TL incubators is appropriate in ART by virtue of their high specification, facility for low oxygen culture and provision of minimally disturbed culture conditions which limit exposure of human embryos to environmental stress.

Time-lapse culture with morphokinetic embryo selection improves pregnancy and live birth chances and reduces early pregnancy loss: a meta-analysis

Pribenszky et al. 2017 Reprod. Biomed. Online 35(5):511-520.
<https://pubmed.ncbi.nlm.nih.gov/28736152/>

Summary: Meta analysis Studies where undisturbed culture and use of time-lapse information appropriate to transfer day was actively used to make embryo transfer decisions. Study showed that there was a statistically significant effect in Ongoing PR OR 1.542 CI (1.211-1.965) $P < 0.001$, Live Birth OR 1.668 (CI 1.134-2.455) $P = 0.009$ Early Pregnancy Loss OR 0.662 (CI 0.469-0.935) $P = 0.01$.

Embryos cultured in a time-lapse system result in superior treatment outcomes: a strict matched pair analysis

Barrie et al. 2017 Hum. Fertil., 20(3), 179–185
<https://www.tandfonline.com/doi/full/10.1080/14647273.2016.1258735>

Summary: A retrospective strict matched-pair analysis of 728 treatment cycles between January 2011 and September 2014 was performed. A total of 364 treatment cycles, where all embryos were cultured and examined in EmbryoScope®, were matched to treatment cycles where all the embryos were cultured in a standard incubator with conventional morphological examination. Matching was performed for patient age, number of oocytes collected, treatment type and date of oocyte collection (\pm six months). CPR, IR and LBR were found to be significantly higher in the time-lapse system (TLS) group compared to the standard incubation group (CPR = 44.8% versus 36.5%, $p = 0.02$; IR = 39.3% versus 32.2%, $p = 0.03$; and LBR = 43.1% versus 33.8%, $p = 0.01$). Although there was a 5.5% decrease in the MR for the TLS group when compared to the standard incubation group, this result was not statistically significant (18.9% versus 24.4%, $p = 0.19$).



Selected abstracts

Does the addition of time-lapse morphokinetics in the selection of embryos for transfer improve pregnancy rates? A randomized controlled trial

Goodman et al. 2016 Fert.Steril 105(2), 275-285
<https://pubmed.ncbi.nlm.nih.gov/26522611/>

Summary: This RCT was designed to detect improvements in clinical outcome based solely on use of a morphokinetic model, while controlling for positive effects due to improved incubation in a time-lapse setting. The sample size for this trial was determined by the primary trial end point of CPR based on the recent Cleveland Clinic overall clinical pregnancy rate of 50% at the time. To detect a 10% increase in clinical pregnancy rate with a power of 80%, it was determined that they needed to randomize 232 patients, 116 in each group. Starting CP in the “control” group was 63% rather than 50%, likely due to improved incubation experienced using the non-disturbed environment. This study was therefore underpowered to detect expected increased based on baseline pregnancy rates. As an example, 680 patients would have been required to detect a 10% difference from 63-73%, and 2836 would have been required to detect a 5% absolute increase.

Although CPR and IR were similar overall with a trend favouring TLM. (TLM vs. CS, respectively: CPR 68% vs. 63%; IR 51% vs. 45%) and with blastocyst transfers (CPR 74% vs. 67%; IR 56% vs. 51%). CPR with day 5 transfer was threefold higher than day 3 transfer, but group (TLM vs. CS) was not a significant predictor of clinical pregnancy or implantation. These data indicate that there may in fact be a clinically relevant tendency toward higher success rates with the time-lapse technology, but larger studies are required to achieve the power needed to detect a significant smaller magnitude of difference. In addition, there were a mix of day 3 and day 5 transfers as well as SET and DET.

Increased live birth rate, blastocyst formation and quality when embryos were cultured in EmbryoScope time-lapse incubators compared to MINC™ benchtop incubators

Lee et al. 2023 Hum. Reprod., 39(Supplement 1) (abstract ESHRE 2023)
<https://doi.org/10.1093/humrep/dead093.621>

Summary: There was an increase in Day 5 top quality blastocysts (AA) from embryos in the Embryoscope compared to the MINC (15.3% vs.9.7%, $p < 0.0001$), and Day 5 good quality blastocysts (\geq BB, 24.4% vs.16.9%, $p < 0.0001$). Overall, the utilisation rate was significantly higher from embryos in the Embryoscope (51.3% vs.46.0%, $p < 0.0001$). From fresh single blastocyst transfers, there was a significant increase in detection of fetal heart by ultrasound (34.7% vs 28.0% $p < 0.01$) and live birth rate (30.9% vs 24.6%, $p < 0.01$) from embryos cultured in the Embryoscope ($n = 972$) compared to the MINC ($n = 633$).

Evaluation of clinical and laboratory outcomes between two embryo incubator systems: Conventional Tri-gas versus Time-lapse

Cunegatto et al. 2021 Fert. Steril. 116(3) Supplement e147–e148
[https://www.fertstert.org/article/S0015-0282\(21\)01783-0/fulltext](https://www.fertstert.org/article/S0015-0282(21)01783-0/fulltext)

Summary: 526 fresh cycles. Same culture media. The blastocyst rate was significantly higher in the TL group with 57.1 versus 50%. $P=0.006$. There was a non-significant increase in clinical outcomes in the TL group, however transfer numbers were low. Pregnancy rate per fresh embryo transfer (TL, $n=72$ and SI, $n=118$) (38,3% vs. 33,9%, $p=0.532$), ongoing/birth rate from clinical pregnancy (92,9% vs. 85,0%, $p=0.322$).

Embryo culture in time-lapse system provides better rates of blastocyst formation, decreases embryo development arrest rate compared to traditional triple-gas culture system

Nicolielo et al. 2021 Fert. Steril. Vol. 112 Issue 3 Supplement e125–e126
[https://www.fertstert.org/article/S0015-0282\(19\)31052-0/fulltext](https://www.fertstert.org/article/S0015-0282(19)31052-0/fulltext)

Summary: A total of 9,482 mature oocytes followed in vitro fertilization, 4,936 in the triple-gas group and 4,546 in the time-lapse group. From those, 1,791 blastocysts were formed in the traditional incubator group and 1,942 in the time-lapse group (50.2% versus 56.7%, $p=0.001$, chi-square test). Blastocyst mean number formed in the time-lapse group were generally higher than the control group (3.4 ± 2.8 versus 2.7 ± 2.8 $p < 0.0001$, t-test). Mean number of blastocysts formed in the time-lapse group was higher in age groups 35 to 37 years ($p=0.02$), 38 to 40 years ($p=0.0003$); 41 to 42 years ($p=0.001$). Embryo developmental arrest rate was also lower in the time-lapse group (11% versus 15%, respectively; $p=0.05$, chi-square test). The uninterrupted culture available at the time-lapse system produced better blastocyst formation rates, especially between 35 and 42 years old, lower embryo arrest rate and mainly with the ability to produce approximately 01 (one) extra blastocyst per cycle, which could increase the cumulative pregnancy rates.

Most effective incubator to improve blastocyst formation rate and implantation rate time-lapse benchtop or standard benchtop: A case referent study

Brahmbhatt et al. 2021 Fert. Steril. 116(3) Supplement: E133
[https://www.fertstert.org/article/S0015-0282\(21\)00969-9/fulltext](https://www.fertstert.org/article/S0015-0282(21)00969-9/fulltext)

Summary: Group A ($n=170$) patients whose embryos were cultured in Timelapse (EmbryoScope) and Group B ($n=180$) patients whose embryos were cultured in standard benchtop incubator(MINC In the time lapse benchtop incubator selected by morphokinetics (KIDScore) and in benchtop incubator selected by morphology assessment (according to Istanbul consensus 2010). Blastocyst formation rate in group A with timelapse is (42.6% vs 39.9 %) vs in group B with standard benchtop ,which is non-significant with $p > 0.05$ but implantation rate is significantly higher in group A with Timelapse (68.4% vs 48.6%)vs group B with standard benchtop with $p=0.01$.

A prospective randomised trial comparing embryo development in the MINC incubator versus the EmbryoScope incubator

Lowen et al. 2017 Hum. Reprod. 32(suppl 1):i210
https://academic.oup.com/humrep/article/32/suppl_1/i1/3926642

Summary: The proportion of embryos cultured in the EmbryoScope that developed into blastocysts on day 5 was significantly higher than those allocated to the MINC incubator (159/289 (55%) EmbryoScope versus 133/296 (45%) MINC; $P = 0.015$). The same applied to the total number of blastocysts (192/289 (66%) EmbryoScope versus 170/296 (57%) MINC; $P = 0.025$). Furthermore, significantly more embryos formed blastocysts suitable for cryopreservation on D5 following culture in the Embryoscope (90/289 (31%)) versus MINC (69/296 (23%), $p = 0.033$). Outcomes not SS different but not powered to detect outcome.

Does culture in a time-lapse incubator improve blastocyst outcomes?

Wale et al., 2014 Fert. Steril. 102(3) Supplement: e212
[https://www.fertstert.org/article/S0015-0282\(14\)01344-2/fulltext](https://www.fertstert.org/article/S0015-0282(14)01344-2/fulltext)

Summary: Embryos cultured in a time-lapse incubator using standard protocols were significantly more likely to develop into a usable blastocyst when compared to embryos cultured in MINCs. This study demonstrates that blastocysts originating from ultra-minimal disturbance culture through the use of a time-lapse incubator are more likely to be of higher quality and potentially result in improved clinical outcomes. Supported by: Melbourne IV.



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