

# Automated Grading Of Early Stages Of The Human Embryo Development

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## Abstract

Assisted reproductive technology helps to reduce the couple who have infertility problems. In Vitro fertilization depends on the best selection of embryo quality. Embryo development and its impact on IVF is an essential step in ART. usually, we use an incubator for embryo development. And daily, embryologists remove embryos from the incubator to evaluate the stages of embryo development under the stereo microscope. Due to this embryo getting a lot of exposure, it may affect embryo quality. For some years, the time-lapse system (TLS) has been developed, which has the best feature for capturing digital pictures of the embryo at some time interval. This TLS helps without needing a computer system and to evaluate the quality of embryos without replacing the embryo from the incubator. TLS maintains the stability of the culture environment and limits embryo exposure. Using an incubator with a time-lapse system evaluates the best-automated embryo evaluation through digital pictures for ART procedures.

**Key Words:** Assisted reproductive technology, embryo stages, time-lapse system, embryo development.

## Introduction

In the world population, 15.0 % of couples face problems with having natural pregnancies(1). Infertility is an issue that is increasing globally nowadays(2). The ability of embryo implantation and success rate of pregnancy is evaluated by the grading system through the stereo microscope, which observes morphology. Seeing an embryo in one day at least once has limitations because more exposure is affected by temperature and P.H. The primary purpose is to evaluate and maintain the excellent culture surrounding. It provides a developed culture system such as an embryo scope incubator consisting of the time-lapse system without removing embryos from the incubator. T.L.S. gives an optimum cultural environment. Due to this, there are no disturbances to growth, and it enhances the formation of the blastocyst, rate of Implantation, and clinical pregnancy rate rather than the incubators with oxygen concentration levels in past years(3). In IVF procedures, the essential step is to develop fertilized oocyte and successive selection of one or two embryos for transfer(4). In Assisted reproductive technology, the time-lapse technology predicts the complete number of chromosome information within the embryo, which is essential for embryo implantation(5). An abnormal number of chromosomes, meiosis, and mitosis affect the usable embryo and its leading cause of IVF failure and abortions. From the start of the IVF procedure, embryo development correlated with the transfer outcome(6). Additionally, single embryo transfers will be promoted and made easier to conduct, improving the safety of both the mother and the baby. Time-lapse photography provides the idea of sustainable cultivation conditions and the chance to continuously monitor and observe an embryo's progress(7). The success rate of IVF depends on the IVF lab conditions and the performance of the embryologists. The essential part is to have well functioned and quality-controlled IVF laboratory. The main work in the lab is

to provide an optimal environment for manipulating gametes and embryos and to evaluate the embryos to maximize the assurance of achieving a live birth. The most challenging task is the cultivation of human embryos, including transferring gametes into the dishes and evaluating them at a specific time. Outside the incubator, culture media (pH, temperature) will change, which may produce stress in the metabolism and influence the quality of an embryo and developmental stage. Hence it's crucial that the time spent on manipulating oocytes and embryos outside the incubator is minimum.(8)

## Need for Research and invention story for Time-lapse system

In traditional embryo culture media outside the incubator, there is no accurate information about the timing of that developmental stage. Some events may miss out in these events consisting of irregular cell division such as direct cleavage and reverse cleavage. If we use a short assessment for the stages of embryos, then some embryos would not be correctly graded or properly ranked for quality(7). The time-lapse system provides a more stable environment for culturing embryos and embryo evaluation. It captures the image of the embryo continuously and has been introduced by the A.R.T. technique. It measures accurate time for cell division in embryos and electronic documentation for the embryo development process related to metabolic and genetic analysis. This helps us in embryo ranking and selection (7). The advantages of maintaining culture conditions include collecting images for embryo evaluation in a time-lapse system. It avoids the observation of the embryos from the traditional bench-top incubator to the microscopic system(laminar). This limits the amount of handling by people and exposure of the embryos to changes in the temperature and gas configuration of the air.

### Method:

#### a) The mechanism for the time-lapse system:

With the help of the most modern innovation, time-lapse embryo monitoring, embryologists can thoroughly evaluate the embryos during an IVF/ICSI procedure. This particular incubator has a built-in camera that periodically captures photos of the embryos as they develop. This camera device is linked to a microscope setup. A time-lapse video is created from the collected images by processing and combining them using software. This aids an embryologist's evaluation of each critical stage of an embryo's development(9).

#### b) Description of Time Lapse System:

Time-lapse system is known as embryo scope. It is an incubator. The Embryoscope is a material removal incubator that enables continuous, real-time observation of embryos. This incubator is used for in vitro fertilization or egg donation procedures because its camera can take pictures every ten minutes throughout the complete fetal development of those embryos grown in a dish. The embryos can undergo modifications that would be undiscovered in a traditional incubator, thanks to this reducing incubation technique. As a result, the Embryoscope provides additional information, which is a huge benefit when choosing embryos. All embryos are photographed using T.L.S. at various focus planes. T.L.S. captures photos of each embryo independently using excellent Hoffman modulation contrast optics. This produces images with exceptional quality that make it possible to see critical morphological details. The image capturing has undergone significant verification to provide safety about exposure to both light wavelength and total energy. Image data processing has been carefully considered to maintain data storage requirements to a minimal level while keeping the highest possible image quality. This provides continuous video playback. The time-lapse technique provides stability to the culture environment for embryos. In this system, temperature is controlled by direct heat contact, and the air is filtered by an H.E.P.A. filter continuously .an integrated gas mixer permit reduced oxygen conditions quickly. Studies indicate that improved culture conditions will allow for the development of more embryos into the blastocyst stage and that improved embryo selection will result in increased pregnancy rates. Compared to traditional culture and evaluation, there was a statistically significant difference in the rate of continuous pregnancy, the rate of live births, and the rate of premature pregnancy loss in the treatments that used the time-lapse system (7)

#### C) Parameter-related grading and morphology:

The second polar body extrusion (tPB2), pronuclear (P.N.) appearance (tPNa) and disappearance (tPNf), and cellular proliferation timing from 2- to 9-cell or more (t2, t3, t4, t5, t6, t7, t8, t9+) are the most often observed

morphological characteristics. T1 is the duration between the first mitotic division and the P.N. decreasing. The rounds of cleavage are also taken into account: the interval between the 2- and 3-cell stages (cc2, second round observed as t3-t2), the 3- to 5-cell stages (cc3, third round followed as t5-t3), and the 5- to 9-cell stages (cc4, fourth round observed as t9-t5) (10)

## Experiments:

### Data collection (Image capturing related morphology) :

The time of pronuclei fading (tPNf), time to cleavage into two (t2), three (t3), four (t4), five (t5), and eight (t8) cells, time to start of blastulation (T.B.), the inner cell mass (I.C.M.), and trophectoderm (T.E.) grade were the morphogenetic parameters evaluated by the embryologist. The embryo goes through perforation at this time, the blastocoel is large enough to push the trophectoderm up against the zona pellucida, and the latter begins to thin. This is when the time to cleavage is defined as the first observed frame in which the newly formed blastomeres are completely separated by epithelial cell membranes(11-20).

### Dataset Introduction

Infertile couples who underwent Intracytoplasmic Sperm Injection (ICSI) cycles provided the data. Previous studies presented the protocol for embryo cultivation and patient care. To maintain only videos with thorough descriptions and recordings corresponding to embryos with described stages. It is used to extract the images. (21-25)

### Result

According to our findings, the morphological quality of the produced blastocysts affected the timing of pronuclei fading (tPNf), cleavage into two (t2), four (t4), and eight (t8) cells, and the beginning of blastulation (tB). tPNf, t2, and t4 were used to distinguish between potential blastocysts of good (AA, AB, BA, and BB) and poor (CC) quality during the early stages of development. Regarding morphology, the 8-cell stage period distinguished blastocysts scored as an AA from those classified as BB. Early tB was associated with better-quality embryos (AA, AB, BA).

### Conclusion

This study solves any issues regarding the early stages of embryo development without exposure. This criterion comprises the detection of the embryo's location and the embryo's classification. We get the information from day 0 to day 5 without affecting pH and temperature. The time-lapse technique gives information about morphological characteristics and consequences of abnormal cell division during embryo development.

### Further recommendations:

'Time-lapse technique' produces a lot of data that will presumably use to help choose the best embryos. Numerous IVF clinics supplied their laboratories with T.L.T. systems and a wealth of scientific papers to identify the morphological parameters associated with favorable predictive biological and clinical results. In the future, we might be able to develop more precise and reliable methods thanks to further standardization and in-depth examinations of the numerous datasets made available by the time-lapse documentation. The most useful morphokinetic variables, particularly t8, t9, and tEB to be included in future version development. of morphological and morphokinetic correlations with chromosome sets status.

### References:

1. Raudonis V, Paulauskaite-Taraseviciene A, Sutiene K, Jonaitis D. Towards the automation of early-stage human embryo development detection. *BioMedical Engineering OnLine*. 2019 Dec 12;18(1):120.
2. Agarwal A, Mulgund A, Hamada A, Chyatte MR. A unique view on male infertility around the globe. *Reproductive Biology and Endocrinology*. 2015 Dec 26;13(1):37.
3. Goodman LR, Goldberg J, Falcone T, Austin C, Desai N. Does the addition of time-lapse morphokinetics in the selection of embryos for transfer improve pregnancy rates? A randomized controlled trial. *Fertility and Sterility*. 2016 Feb;105(2):275-285.e10.

4. Huang B, Tan W, Li Z, Jin L. An artificial intelligence model (euploid prediction algorithm) can predict embryo ploidy status based on time-lapse data. *Reproductive Biology and Endocrinology*. 2021 Dec 13;19(1):185.
5. Meseguer M, Rubio I, Cruz M, Basile N, Marcos J, Requena A. Embryo incubation and selection in a time-lapse monitoring system improves pregnancy outcome compared with a standard incubator: a retrospective cohort study. *Fertility and Sterility*. 2012 Dec;98(6):1481-1489.e10.
6. Campbell A, Fishel S, Bowman N, Duffy S, Sedler M, Thornton S. Retrospective analysis of outcomes after IVF using an aneuploidy risk model derived from time-lapse imaging without PGS. *Reproductive BioMedicine Online*. 2013 Aug;27(2):140–6.
7. Lundin K, Park H. Time-lapse technology for embryo culture and selection. *Upsala Journal of Medical Sciences*. 2020 Apr 2;125(2):77–84.
8. Motato Y, de los Santos MJ, Escriba MJ, Ruiz BA, Remohí J, Meseguer M. Morphokinetic analysis and embryonic prediction for blastocyst formation through an integrated time-lapse system. *Fertility and Sterility*. 2016 Feb;105(2):376-384.e9.
9. Tran D, Cooke S, Illingworth PJ, Gardner DK. Deep learning as a predictive tool for fetal heart pregnancy following time-lapse incubation and blastocyst transfer. *Human Reproduction*. 2019 Jun 4;34(6):1011–8.
10. Armstrong S, Bhide P, Jordan V, Pacey A, Farquhar C. Time-lapse systems for embryo incubation and assessment in assisted reproduction. *Cochrane Database Syst Rev*. 2018;5:CD011320.
11. Bamford T, Barrie A, Montgomery S, Dhillon-Smith R, Campbell A, Easter C, et al. Morphological and morphokinetic associations with aneuploidy: a systematic review and meta-analysis. *Human Reproduction Update*. 2022 May 25;
12. Chaple, Jagruti N., and Punam Sawarkar. "Protocol - Assessment about Knowledge of Panchakarma in Asha Workers and Their Sensitization with Panchakarma Module in Wardha Taluka." *Journal of Pharmaceutical Research International*, June 2, 2021, 1–6. <https://doi.org/10.9734/jpri/2021/v33i30B31633>.
13. Chaple, Jagruti, and Dhirajsingh S. Rajput. "Retrospective Monocentric Study on Career Preferred by Ayurveda Alumni." *Journal of Pharmaceutical Research International*, July 7, 2021, 169–74. <https://doi.org/10.9734/jpri/2021/v33i35B31916>.
14. Chaturvedi, Anuj, Sunil Kumar, Sourya Acharya, Shilpa A Gaidhane, Anil Wanjari, and Dhruv Talwar. "Myocardial Performance Index Among Patients of Sick Cell Disorder in Rural Teaching Hospital: A Case-Control Study." *Cureus*, November 1, 2021. <https://doi.org/10.7759/cureus.19175>.
15. Chaudhari, Mahesh K., Shiwani P. Dandade, Saurabh D. Borkar, Shivani K. Borkar, and Archana Teltumbde. "A Study to Assess the Effectiveness of Planned Teaching Programme on the Knowledge Regarding Management of Pre-Eclampsia among Antenatal Mothers." *Journal of Pharmaceutical Research International*, December 15, 2021, 595–603. <https://doi.org/10.9734/jpri/2021/v33i58A34156>.
16. Chaudhari, Payal Sandeep, Manoj Ghanshyam Chandak, Kajol Naresh Relan, Pooja Ghanshyam Chandak, Chanchal Harikishor Rathi, Madhulika Shyamsundar Chandak, and Abhilasha Dass. "Lasers in Diagnosis, Interception and Management of White Spot Lesions and Dental Caries - A Review." *Journal of Evolution of Medical and Dental Sciences* 10, no. 9 (March 1, 2021): 624–31. <https://doi.org/10.14260/jemds/2021/134>.
17. Chaudhary, Konika, Shivali Vaibhav Kashikar, and Rajasbala Pradeep Dhande. "MRI Assessment of Paediatric Developmental Delay." *Journal of Evolution of Medical and Dental Sciences* 10, no. 8 (February 22, 2021): 479–83. <https://doi.org/10.14260/jemds/2021/105>.
18. Chaudhary, Rahul, Nitin Samal, and Sanjeev Chaudhary. "Ipsilateral Neck/Inter-Trochanteric and Mid-Shaft Femoral Fractures Treated with Dual Construct Implants." *Journal of Pharmaceutical Research International*, December 15, 2021, 426–34. <https://doi.org/10.9734/jpri/2021/v33i58A34134>.
19. Chaudhary, Richa, Karthikeya Nagula, and Amar Taksande. "Modified Glasgow Coma Scale and the Alert Verbal Painful Unresponsive Scale for Assessing the Level of Consciousness in Pediatric Critical Care Patients—A Comparative Study." *Journal of Pediatric Neurology*, March 16, 2021, s-0041-1725981. <https://doi.org/10.1055/s-0041-1725981>.
20. Chaudhary, Shruti, Gyanavelu Injeti, Amar Taksande, Revat Meshram, and Amol Lohkare. "Right Sided Facial Nerve Palsy, Bilateral Microtia with Polydactyly in an Infant – A Rare Case Report." *Journal of Evolution of Medical and Dental Sciences* 10, no. 18 (May 3, 2021): 1353–55. <https://doi.org/10.14260/jemds/2021/285>.
21. Chaurasia, Tanvi, Deepti Shrivastava, Himanshi Agarwal, and Geeta Chaurasia. "Acute Polyhydromnios: A Rare Entity." *Journal of Pharmaceutical Research International*, July 3, 2021, 88–92. <https://doi.org/10.9734/jpri/2021/v33i35A31877>.
22. Chavan, Aparna, Rakesh Maran, and Gajanan Chavan. "Dysphonia: Epidemiology, Diagnosis and Risk Factors at Tertiary Health Care Center." *Indian Journal of Otolaryngology and Head & Neck Surgery*, October 25, 2021. <https://doi.org/10.1007/s12070-021-02952-8>.
23. Chaware, SachinHaribhau, SurekhaGodbole Dubey, Vinay Kakatkar, Ajit Jankar, Swati Pustake, and Abhishek Darekar. "The Systematic Review and Meta-Analysis of Oral Sensory Challenges in Children and Adolescents with Autism Spectrum Disorder." *Journal of International Society of Preventive and Community Dentistry* 0, no. 0 (2021): 0. [https://doi.org/10.4103/jispcd.JISPCD\\_135\\_21](https://doi.org/10.4103/jispcd.JISPCD_135_21).
24. Chhabadia, Gazal. "COVID-19 Pandemic: Health Impact and Social Responsibility." *Journal of Pharmaceutical Research International*, July 21, 2021, 68–74. <https://doi.org/10.9734/jpri/2021/v33i38A32061>.
25. Chimurkar, Vilas K., Vaibhav Anjankar, Prajakta Ghewade, and Anil J. Anjankar. "Morphometric Study of Cadaveric Spleen in Vidarbha Region." *Journal of Pharmaceutical Research International*, December 9, 2021, 132–37. <https://doi.org/10.9734/jpri/2021/v33i54A33728>.