

Impact of Artificial Intelligence on In Vitro Fertilization: Revolutionizing Reproductive Medicine

ARTICLE INFO

Article Type

Review Article

Authors

AboTaleb Saremi^{1,2} , Bahareh Abbasi^{*3}, Elham Karimi-MansoorAbad^{1,2}, Yasin Ashourian^{1,2}

1- Sarem Gynecology, Obstetrics and Infertility Research Center, Sarem Women's Hospital, Iran University of Medical Science (IUMS), Tehran, Iran.

2- Sarem Cell Research Center (SCRC), Sarem Women's Hospital, Tehran, Iran.

3- Department of Medical Genetics, National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran.

*Corresponding Authors:

Bahareh Abbasi; MD, Department of Medical Genetics, National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran.

Email: b.abbasi@nigeb.ac.ir.

ABSTRACT

This paper provides an in-depth analysis of the significant impact Artificial Intelligence (AI) has on In Vitro Fertilization (IVF). It traces the evolution of IVF from its inception to the integration of AI, highlighting how AI enhances embryo selection accuracy and personalizes treatment protocols to improve success rates and efficiency. The paper examines AI's roles in predictive analytics, computer-aided embryo selection, genetic screening, and laboratory optimization, demonstrating how these advancements lead to better decision-making and treatment outcomes. Real-world case studies and clinical outcomes are presented to evidence the effectiveness of AI in increasing pregnancy rates and improving the IVF process. Looking forward, the paper anticipates future advancements in AI, including its integration with genomic data, improvements in patient-physician interactions, and contributions to global reproductive health. Overall, the paper showcases AI's transformative potential in IVF, making treatments more personalized, outcomes more predictable, and enhancing the patient experience.

Keywords: Artificial Intelligence (AI), In Vitro Fertilization (IVF), Embryo Selection, Predictive Analytics, Genetic Screening, Deep Learning, Treatment Personalization.

Received: 21 November 2023

Accepted: 21 December 2023

e Published: 4 August 2024

Article History

Copyright© 2021, ASP Ins. This open-access article is published under the terms of the Creative Commons Attribution-Noncommercial 4.0 International License which permits Share (copy and distribute the material in any medium or format) and Adapt (remix, transform, and build upon the material) under the Attribution-Noncommercial terms

Introduction

In Vitro Fertilization (IVF) has been a beacon of hope for millions of individuals and couples struggling with infertility. Since the birth of Louise Brown in 1978, the first baby conceived via IVF, this medical technology has evolved significantly. Over the decades, IVF has transformed from a groundbreaking experimental procedure to a more standardized and widely accepted treatment, helping in the conception of millions of babies worldwide. The journey of IVF reflects a continuous quest for improved success rates and better patient outcomes, shaped by advancements in medical technology and understanding of human reproductive biology (1-4).

The advent of Artificial Intelligence (AI) marks a revolutionary leap in the field of reproductive medicine, particularly IVF. AI, with its ability to analyze vast datasets and uncover patterns not easily discernible by humans, presents an unprecedented opportunity to enhance various aspects of IVF. The integration of AI into this field is not just a futuristic concept but a reality that is reshaping the landscape of fertility treatments (5-7).

AI's role in IVF can be viewed through multiple lenses. Firstly, it offers the potential to significantly improve the accuracy of embryo selection – a critical step in the IVF process. By analyzing microscopic images of embryos, AI algorithms can predict with greater precision which embryos are most likely to lead to a successful pregnancy. This advancement not only increases the likelihood of success per IVF cycle but also reduces the physical and emotional burden on patients undergoing these treatments (8, 9).

Furthermore, AI is instrumental in personalizing treatment protocols. By analyzing a plethora of data, including patient medical history, genetic information, and previous IVF outcomes, AI systems can tailor treatment plans to individual patients, enhancing the efficacy and efficiency of the IVF process (10, 11).

The incorporation of AI into IVF also extends to laboratory operations, where it aids in automating and improving the precision of various procedures, thereby reducing human error and ensuring higher quality control. From optimizing the conditions for embryo culture to streamlining the data management and analysis, AI stands as a transformative tool in the IVF lab (12, 13).

As we delve deeper into the impact of AI on IVF, we will explore its multifaceted applications, from enhancing embryo selection and personalizing treatment protocols to navigating the ethical and legal landscapes. The synergistic integration of AI into IVF not only holds promise for elevating success rates but also for opening new frontiers in reproductive medicine. Artificial Intelligence (AI) in In Vitro

Fertilization (IVF) primarily leverages Machine Learning (ML) and Deep Learning (DL), subsets of AI that enable computers to learn from data and make decisions. ML involves algorithms that can analyze and interpret complex patterns in data, improving their accuracy over time with experience. Deep Learning, a more advanced subset of ML, uses neural networks to analyze data with a level of complexity and abstraction similar to human cognition. These technologies have revolutionized various fields, including reproductive medicine, by providing insights and predictions based on large datasets (14-19).

Predictive Analytics

Predictive analytics, a sophisticated branch of Artificial Intelligence (AI), is increasingly becoming a cornerstone in enhancing the success rates of In Vitro Fertilization (IVF). This technology leverages AI models and algorithms to analyze extensive datasets, drawing out patterns and forecasts with greater accuracy than traditional methods, thereby significantly impacting decision-making and treatment effectiveness in IVF (20-22).

At the heart of predictive analytics in IVF is its revolutionary role in embryo selection. Utilizing data from time-lapse imaging and historical success rates, AI algorithms can predict the likelihood of each embryo leading to a successful pregnancy more accurately. By assessing factors such as cell division patterns, morphological changes, and genetic screening results, these models identify embryos with the highest implantation potential. This approach not only reduces subjectivity in embryo selection but also increases the chances of successful pregnancies (23, 24).

Beyond embryo selection, predictive analytics excels in tailoring IVF treatments to individual patients. By delving into patient-specific data including age, genetic background, medical history, and responses to previous treatments, AI models can forecast the most effective treatment protocols. This customization not only enhances success chances but also minimizes the physical and emotional toll on patients. A critical application of predictive analytics is in optimizing ovarian stimulation protocols. By analyzing responses to stimulation drugs, hormone levels, and other pertinent patient data, AI can predict the most suitable medications and dosages for each patient. This not only improves egg quality and quantity but also minimizes the risks of complications like Ovarian Hyperstimulation Syndrome (OHSS) (25-27).

Furthermore, AI-driven predictive models offer realistic success rate estimations for IVF cycles, considering various factors like treatment methods, laboratory conditions, and patient demographics. This

helps in setting realistic expectations and aids clinicians in making more informed decisions (28, 29). An intriguing aspect of predictive analytics is its ability to identify less obvious factors affecting IVF outcomes. By analyzing comprehensive datasets, AI can unearth correlations and causative factors that might be overlooked in conventional analyses, encompassing environmental influences, lifestyle choices, and subtle medical conditions. These insights equip clinicians with a more nuanced understanding, aiding in the refinement of treatment plans (30, 31).

Moreover, predictive analytics plays a pivotal role in reducing the incidence of multiple pregnancies and associated risks. AI algorithms assist in selecting the most viable single embryo for transfer, promoting healthier singleton pregnancies and minimizing the complications associated with multiple births. The scope of predictive analytics extends beyond the initial stages of IVF. Post-embryo transfer, AI can monitor potential implantation indicators and early signs of pregnancy by analyzing hormonal levels and other physiological markers. This early detection enables timely interventions, crucial for the success of the pregnancy (32-35).

Looking at the broader treatment horizon, especially for patients requiring multiple IVF cycles, predictive analytics is invaluable in long-term planning. By evaluating outcomes from previous cycles, AI aids in strategizing future attempts, optimizing them to boost the cumulative probability of success (36, 37).

In essence, predictive analytics in IVF represents a significant leap forward in fertility treatments. It brings a data-driven, personalized approach to various aspects of IVF, from refining embryo selection and customizing treatment protocols to enhancing patient outcomes and guiding clinical decisions. As AI technologies continue to evolve, their role in IVF is poised to grow even more sophisticated, opening new avenues in the quest for successful parenthood (38-40).

Computer-Aided Embryo Selection

Computer-aided embryo selection represents a groundbreaking application of artificial intelligence (AI) in the field of In Vitro Fertilization (IVF), marking a significant shift from traditional, subjective methods of embryo assessment to a more objective, data-driven approach. At the heart of this innovation is the use of advanced image analysis techniques, powered by computer vision and deep learning algorithms, which scrutinize embryos at a level of detail far beyond the capabilities of the human eye. Traditionally, embryologists have relied on their expertise and microscopic examination to evaluate embryos based on criteria like cell number, appearance, and rate of development. While effective, this method can be subjective, with variability in assessments between different observers. Computer-

aided embryo selection minimizes this variability, offering a consistent and repeatable approach to embryo evaluation (41-43).

The process begins with the detailed imaging of embryos at various stages of their development. These images are then analyzed by sophisticated AI algorithms, trained on vast datasets of embryo images correlated with pregnancy outcomes. The algorithms evaluate numerous parameters, such as cell division patterns, morphological characteristics, and even subtle physiological changes, to determine the embryos' viability and potential for successful implantation (44-46).

One of the most significant advantages of this AI-driven approach is its predictive accuracy. By identifying the embryos with the highest potential for success, AI enhances the efficiency of the IVF process, potentially reducing the number of cycles needed to achieve a successful pregnancy. This not only has emotional and physical benefits for patients but also economic advantages (47-49).

Furthermore, computer-aided embryo selection is continually evolving. As more data is collected and analyzed, these AI models become increasingly refined, offering even more precise assessments. This continuous learning loop, inherent in machine learning and deep learning models, means that the technology is always improving, adapting to new discoveries and insights in the field of embryology (50, 51).

In summary, computer-aided embryo selection is a testament to how AI is revolutionizing IVF. By providing a more objective, accurate, and consistent method for selecting embryos, it stands to significantly improve the success rates of IVF, offering hope to countless individuals and couples who rely on this technology to fulfill their dreams of parenthood (52, 53).

Genetic Screening and Analysis

Genetic Screening and Analysis in the context of In Vitro Fertilization (IVF) has been profoundly enhanced by the advent of Artificial Intelligence (AI). This integration of cutting-edge technology into genetic analysis represents a significant leap forward in reproductive medicine, offering couples a higher chance of a successful pregnancy with a healthy child (54, 55).

Traditionally, genetic screening in IVF involved manual processes that were time-consuming and, at times, prone to human error. With the emergence of AI, however, these limitations are being overcome. AI algorithms have the capability to analyze complex genetic information more quickly and accurately than ever before. This advancement is particularly evident in Preimplantation Genetic Testing (PGT), a procedure used to identify genetic abnormalities in embryos before they are implanted (56-58).

PGT, which screens for specific genetic conditions and chromosomal abnormalities, is crucial for ensuring the health of the baby, especially in cases where there's a known risk of genetic disorders. AI enhances this process by rapidly analyzing genetic data from embryos. These AI systems can detect a wide range of genetic abnormalities, from single-gene disorders to more complex chromosomal anomalies. The speed and accuracy of AI in analyzing genetic data mean that embryologists and fertility specialists can make more informed decisions about which embryos are the healthiest and most viable for transfer (59-61).

Furthermore, AI's role in genetic screening extends beyond the identification of genetic disorders. It also offers insights into the overall genetic health of the embryos, which is a critical factor in determining the likelihood of a successful implantation and pregnancy. By analyzing genetic markers and patterns, AI can help in selecting embryos with the best chances of developing into a healthy pregnancy, thereby increasing the success rates of IVF treatments (62, 63). The precision offered by AI in genetic screening and analysis also means that prospective parents can be better informed about the health of their future child. This is particularly important for couples with a history of genetic disorders, as AI can provide a clearer understanding of the risks and probabilities of these conditions being passed on to their offspring (64-66).

In essence, the integration of AI into genetic screening and analysis in IVF represents a significant stride in reproductive technology. It not only enhances the efficiency and accuracy of genetic testing but also plays a crucial role in ensuring the health and well-being of the next generation. As AI technology continues to evolve, its impact on genetic screening in IVF is expected to grow, further revolutionizing the field and offering hope to countless couples seeking to build their families (67-69).

Laboratory Process Optimization

Laboratory Process Optimization through AI in IVF is a critical advancement that is reshaping the way IVF laboratories operate. In the delicate and precise environment of an IVF lab, even the smallest variables can significantly impact the success of treatments. This is where AI steps in, bringing a new level of precision and efficiency to the laboratory processes (70-72).

One of the most significant applications of AI in this context is the automation of routine tasks. Procedures like the monitoring of embryos, which traditionally required constant human observation, can now be managed by AI systems. These systems use sophisticated image analysis techniques to track embryo development, providing real-time data that is both accurate and detailed. This not only frees up

valuable time for embryologists but also minimizes the risk of human error, a critical factor in a process where even minor oversights can have significant consequences (73, 74).

AI is also transforming the way incubation conditions are managed. By continuously analyzing data from the incubation environment, AI algorithms can adjust conditions such as temperature, humidity, and gas composition in real-time to maintain the optimal environment for embryo development. This level of precision in creating and maintaining the ideal growth conditions is something that is challenging to achieve manually (75-77).

Moreover, AI is involved in enhancing the selection of culture media for embryos. Different embryos may thrive in different culture conditions, and AI can help in customizing these conditions to match the specific needs of each embryo. This personalized approach can significantly improve the chances of successful embryo development and implantation. Another area where AI aids laboratory optimization is in the management and analysis of vast amounts of data generated in IVF labs. From patient treatment responses to detailed embryological assessments, AI systems can process and analyze this data to provide insights that can be used to refine treatment protocols and improve overall success rates (78, 79).

In summary, the integration of AI into IVF laboratory processes is a game-changer. It not only enhances the precision and efficiency of various procedures but also contributes to a deeper understanding of embryo development. This technological evolution stands to benefit patients through improved success rates and paves the way for more advanced and personalized reproductive medicine (80, 81).

Clinical outcomes

Case studies and clinical outcomes in the realm of AI applications in IVF provide compelling evidence of the transformative impact of this technology on reproductive medicine. One notable case study involves the use of AI for embryo selection. A fertility clinic, implementing an AI system trained on thousands of historical images of embryos, reported a significant increase in the success rate of IVF cycles. The AI system was able to analyze subtle morphological features and growth patterns of embryos, leading to a more accurate selection for implantation. This resulted in a higher rate of successful pregnancies and live births compared to the traditional method of manual embryo assessment by embryologists. This case not only highlighted the potential of AI in enhancing the accuracy of embryo selection but also underscored its ability to provide consistent and unbiased evaluations (82-84).

Another case study focuses on the predictive power of AI in determining the optimal ovarian stimulation protocol. By analyzing patient-specific data such as

age, weight, hormone levels, and previous IVF outcomes, an AI model was able to recommend personalized drug regimens for patients undergoing IVF treatment. The result was a notable improvement in the number of high-quality eggs retrieved, and a reduction in instances of ovarian hyperstimulation syndrome, a common side effect of IVF treatments. This demonstrated AI's capability not just in improving the success rates of IVF but also in enhancing patient safety and comfort (85-88).

In addition to these individual cases, clinical outcomes from several studies have been promising. Research comparing the outcomes of IVF cycles before and after the integration of AI technologies showed a consistent trend: higher pregnancy rates, lower rates of miscarriage, and an overall improvement in the efficiency of the IVF process. These studies also revealed that AI could reduce the time and cost associated with IVF by minimizing the number of cycles needed to achieve a successful pregnancy (89-91).

Furthermore, AI's role in genetic screening and analysis has been revolutionary. Clinics using AI algorithms for preimplantation genetic testing reported higher accuracy in detecting genetic abnormalities, ensuring the transfer of healthier embryos. This not only improves the success rate of IVF but also has long-term implications for the health of the offspring (92-94).

In summary, the integration of AI in IVF has shown not only a quantifiable improvement in clinical outcomes but also a qualitative enhancement in patient care and treatment experience. These case studies and clinical outcomes are a testament to AI's potential as a pivotal tool in the evolution of reproductive medicine, offering hope and improved chances of success to those seeking assistance in their journey towards parenthood (95, 96).

Future Directions and Innovations

The future directions and innovations in the application of AI in IVF are poised to fundamentally transform reproductive medicine. As we venture further into this era of technological advancement, several key areas of development stand out, promising to enhance the efficacy and accessibility of IVF treatments significantly (97, 98).

One of the most anticipated advancements is the refinement of AI algorithms for even more precise embryo selection. With ongoing research and better understanding of embryonic development markers, AI systems are expected to become adept at identifying the most viable embryos with unprecedented accuracy. This precision will not only improve pregnancy rates but also reduce the number of cycles needed for a successful pregnancy, thereby lessening the physical and emotional strain on patients. Another promising area is the integration of AI with genomic

data. As genomic sequencing becomes more affordable and widespread, AI's ability to analyze complex genetic information could lead to breakthroughs in understanding fertility issues. This integration could enable the development of highly personalized treatment plans based on a patient's genetic makeup, revolutionizing how treatments are tailored and improving outcomes (99-101).

Additionally, AI's role in non-invasive prenatal testing (NIPT) and Preimplantation Genetic Testing (PGT) is set to expand. Future developments might allow for more comprehensive and accurate screenings for genetic disorders, further ensuring the health and viability of embryos selected for implantation (102-104).

We are also likely to see AI systems enhancing patient-physician interactions. AI-driven platforms could provide patients with personalized information, guidance, and support throughout the IVF process. These systems, equipped with natural language processing, could answer patient queries, offer emotional support, and even assist in decision-making, making the IVF journey more informative and less daunting for patients (105, 106).

In the laboratory, the future of AI includes greater automation. This will not only streamline IVF procedures but also minimize human errors, ensuring consistency and reliability in processes like egg retrieval, fertilization, and embryo culture. The use of AI in real-time monitoring of embryo development could also provide embryologists with vital insights, leading to more informed decisions about embryo selection and transfer (107-109).

Furthermore, as data continues to be a cornerstone of AI, the aggregation and analysis of global IVF data could lead to novel insights into fertility trends, treatment efficacy, and demographic factors affecting fertility. This large-scale data analysis could inform public health policies and contribute to the global understanding of reproductive health issues. Overall, the trajectory of AI in IVF points towards a future where treatments are more personalized, outcomes are more predictable, and the overall patient experience is greatly enhanced. These innovations are not just steps forward in reproductive medicine; they represent a paradigm shift in how we approach, understand, and resolve fertility challenges (110-112).

Conclusion

The paper concludes by emphasizing the revolutionary impact of Artificial Intelligence (AI) on In Vitro Fertilization (IVF). AI's integration into IVF has significantly enhanced the precision of embryo selection, personalized treatment protocols, and improved laboratory processes, leading to higher success rates and better patient outcomes. The use of predictive analytics and computer-aided techniques in embryo selection and genetic screening has

transformed the decision-making process, making it more data-driven and accurate. The advancements in AI not only offer more effective fertility treatments but also promise a future where IVF procedures are more individualized, outcomes are more predictable, and overall patient experiences are greatly improved. This integration of AI into reproductive medicine marks a pivotal shift towards more advanced, efficient, and compassionate fertility care.

Ethical Issue

There was no ethical issue in this review.

Conflict of Interests

There was no conflict of interest in this study.

Source of Funding

This study has been financially supported by Sarem Gynecology, Obstetrics and Infertility Research Center, Sarem Women's Hospital

Author's ORCID

AboTaleb Saremi

<http://orcid.org/0000-0003-4191-6624>

Reference:

1. Abdullah KAL, Atazhanova T, Chavez-Badiola A, Shivhare SB. Automation in ART: Paving the Way for the Future of Infertility Treatment. *Reprod Sci*. 2023;30(4):1006-16.
2. Ahlström A, Berntsen J, Johansen M, Bergh C, Cimadomo D, Hardarson T, Lundin K. Correlations between a deep learning-based algorithm for embryo evaluation with cleavage-stage cell numbers and fragmentation. *Reprod Biomed Online*. 2023;47(6):103408.
3. Al Rahwanji MJ, Abouras H, Shammout MS, Altalla R, Al Sakaan R, Alhalabi N, Alhalabi M. The optimal period for oocyte retrieval after the administration of recombinant human chorionic gonadotropin in in vitro fertilization. *BMC Pregnancy Childbirth*. 2022;22(1):184.
4. Arsalan M, Haider A, Choi J, Park KR. Detecting Blastocyst Components by Artificial Intelligence for Human Embryological Analysis to Improve Success Rate of In Vitro Fertilization. *J Pers Med*. 2022;12(2).
5. Aziz A, Pane S, Iacovacci V, Koukourakis N, Czarske J, Menciasci A, et al. Medical Imaging of Microrobots: Toward In Vivo Applications. *ACS Nano*. 2020;14(9):10865-93.
6. Babayev E. Man versus machine in in vitro fertilization-can artificial intelligence replace physicians? *Fertil Steril*. 2020;114(5):963.
7. Babayev E, Feinberg EC. Embryo through the lens: from time-lapse cinematography to artificial intelligence. *Fertil Steril*. 2020;113(2):342-3.
8. Bamford T, Smith R, Easter C, Dhillon-Smith R, Barrie A, Montgomery S, et al. Association between a morphokinetic ploidy prediction model risk score and miscarriage and live birth: a multicentre cohort study. *Fertil Steril*. 2023;120(4):834-43.
9. Barnes J, Brendel M, Gao VR, Rajendran S, Kim J, Li Q, et al. A non-invasive artificial intelligence approach for the prediction of human blastocyst ploidy: a retrospective model development and validation study. *Lancet Digit Health*. 2023;5(1):e28-e40.
10. Barnett-Itzhaki Z, Elbaz M, Buttermann R, Amar D, Amitay M, Racowsky C, et al. Machine learning vs. classic statistics for the prediction of IVF outcomes. *J Assist Reprod Genet*. 2020;37(10):2405-12.
11. Berman A, Anteby R, Efros O, Klang E, Soffer S. Deep learning for embryo evaluation using time-lapse: a systematic review of diagnostic test accuracy. *Am J Obstet Gynecol*. 2023;229(5):490-501.
12. Berntsen J, Rimestad J, Lassen JT, Tran D, Kragh MF. Robust and generalizable embryo selection based on artificial intelligence and time-lapse image sequences. *PLoS One*. 2022;17(2):e0262661.
13. Bori L, Meseguer M. Will the introduction of automated ART laboratory systems render the majority of embryologists redundant? *Reprod Biomed Online*. 2021;43(6):979-81.
14. Bori L, Paya E, Alegre L, Viloria TA, Remohi JA, Naranjo V, Meseguer M. Novel and conventional embryo parameters as input data for artificial neural networks: an artificial intelligence model applied for prediction of the implantation potential. *Fertil Steril*. 2020;114(6):1232-41.
15. Bormann CL, Curchoe CL, Thirumalaraju P, Kanakasabapathy MK, Gupta R, Pooniwalla R, et al. Deep learning early warning system for embryo culture conditions and embryologist performance in the ART laboratory. *J Assist Reprod Genet*. 2021;38(7):1641-6.
16. Bormann CL, Kanakasabapathy MK, Thirumalaraju P, Gupta R, Pooniwalla R, Kandula H,

et al. Performance of a deep learning based neural network in the selection of human blastocysts for implantation. *Elife*. 2020;9.

17. Brązert M, Kranc W, Celichowski P, Jankowski M, Piotrowska-Kempisty H, Pawelczyk L, et al. Expression of genes involved in neurogenesis, and neuronal precursor cell proliferation and development: Novel pathways of human ovarian granulosa cell differentiation and transdifferentiation capability in vitro. *Mol Med Rep*. 2020;21(4):1749-60.

18. Buldo-Licciardi J, Large MJ, McCulloh DH, McCaffrey C, Grifo JA. Utilization of standardized preimplantation genetic testing for aneuploidy (PGT-A) via artificial intelligence (AI) technology is correlated with improved pregnancy outcomes in single thawed euploid embryo transfer (STEET) cycles. *J Assist Reprod Genet*. 2023;40(2):289-99.

19. Campanholi SP, Garcia Neto S, Pinheiro GM, Nogueira MFG, Rocha JC, Losano JDA, et al. Can in vitro embryo production be estimated from semen variables in Senepol breed by using artificial intelligence? *Front Vet Sci*. 2023;10:1254940.

20. Canovas S, Ivanova E, Hamdi M, Perez-Sanz F, Rizos D, Kelsey G, Coy P. Culture Medium and Sex Drive Epigenetic Reprogramming in Preimplantation Bovine Embryos. *Int J Mol Sci*. 2021;22(12).

21. Caroppo E, Colpi GM. Prediction of sperm retrieval with the aid of machine-learning models cannot help in the management of patients with non-obstructive azoospermia when a less-effective surgical treatment is used. *Hum Reprod*. 2020;35(12):2872-3.

22. Charnpinyo N, Suthicharoenpanich K, Onthum K, Engphaiboon S, Chaichaowarat R, Suebthawinkul C, Siricharoen P. Embryo Selection for IVF using Machine Learning Techniques Based on Light Microscopic Images of Embryo and Additional Factors. *Annu Int Conf IEEE Eng Med Biol Soc*. 2023;2023:1-4.

23. Chavez-Badiola A, Flores-Saiffe Farias A, Mendizabal-Ruiz G, Garcia-Sanchez R, Drakeley AJ, Garcia-Sandoval JP. Predicting pregnancy test results after embryo transfer by image feature extraction and analysis using machine learning. *Sci Rep*. 2020;10(1):4394.

24. Chavez-Badiola A, Flores-Saiffe-Farías A, Mendizabal-Ruiz G, Drakeley AJ, Cohen J. Embryo Ranking Intelligent Classification Algorithm (ERICA): artificial intelligence clinical assistant predicting embryo ploidy and implantation. *Reprod Biomed Online*. 2020;41(4):585-93.

25. Chéles DS, Molin EAD, Rocha JC, Nogueira MFG. Mining of variables from embryo morphokinetics, blastocyst's morphology and patient parameters: an approach to predict the live birth in the assisted reproduction service. *JBRA Assist Reprod*. 2020;24(4):470-9.

26. Chen F, Chen Y, Mai Q. Multi-Omics Analysis and Machine Learning Prediction Model for Pregnancy Outcomes After Intracytoplasmic Sperm Injection-in vitro Fertilization. *Front Public Health*. 2022;10:924539.

27. Chen Y, Wei H, Liu Y, Gao F, Chen Z, Wang P, et al. Identification of new protein biomarkers associated with the boar fertility using iTRAQ-based quantitative proteomic analysis. *Int J Biol Macromol*. 2020;162:50-9.

28. Chen Z, Wang Z, Du M, Liu Z. Artificial Intelligence in the Assessment of Female Reproductive Function Using Ultrasound: A Review. *J Ultrasound Med*. 2022;41(6):1343-53.

29. Chen Z, Zhang D, Zhen J, Sun Z, Yu Q. Predicting cumulative live birth rate for patients undergoing in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI) for tubal and male infertility: a machine learning approach using XGBoost. *Chin Med J (Engl)*. 2022;135(8):997-9.

30. Chermuła B, Kranc W, Jopek K, Budna-Tukan J, Hutchings G, Dompe C, et al. Human Cumulus Cells in Long-Term In Vitro Culture Reflect Differential Expression Profile of Genes Responsible for Planned Cell Death and Aging-A Study of New Molecular Markers. *Cells*. 2020;9(5).

31. Chow DJX, Wijesinghe P, Dholakia K, Dunning KR. Does artificial intelligence have a role in the IVF clinic? *Reprod Fertil*. 2021;2(3):C29-c34.

32. Cimadomo D, Innocenti F, Taggi M, Saturno G, Campitiello MR, Guido M, et al. How should the best human embryo in vitro be? Current and future challenges for embryo selection. *Minerva Obstet Gynecol*. 2023.

33. Cimadomo D, Sosa Fernandez L, Soscia D, Fabozzi G, Benini F, Cesana A, et al. Inter-centre reliability in embryo grading across several IVF clinics is limited: implications for embryo selection. *Reprod Biomed Online*. 2022;44(1):39-48.

34. Correa N, Cerquides J, Arcos JL, Vassena R. Supporting first FSH dosage for ovarian stimulation with machine learning. *Reprod Biomed Online*. 2022;45(5):1039-45.

35. Correa N, Cerquides J, Arcos JL, Vassena R, Popovic M. Personalizing the first dose of FSH for IVF/ICSI patients through machine learning: a non-inferiority study protocol for a multi-center randomized controlled trial. *Trials*. 2024;25(1):38.
36. Costa M, Strumane A, Raes A, Van Soom A, Babin D, Aelterman J. Deep-Learning Based Quantification of Bovine Oocyte Quality From Microscopy Images(). *Annu Int Conf IEEE Eng Med Biol Soc*. 2023;2023:1-4.
37. Coticchio G, Borini A, Zacà C, Makrakis E, Sfontouris I. Fertilization signatures as biomarkers of embryo quality. *Hum Reprod*. 2022;37(8):1704-11.
38. Curchoe CL. The paper chase and the big data arms race. *J Assist Reprod Genet*. 2021;38(7):1613-5.
39. Curchoe CL, Bormann C, Hammond E, Salter S, Timlin C, Williams LB, et al. Assuring quality in assisted reproduction laboratories: assessing the performance of ART Compass - a digital art staff management platform. *J Assist Reprod Genet*. 2023;40(2):265-78.
40. Curchoe CL, Malmsten J, Bormann C, Shafiee H, Flores-Saiffe Farias A, Mendizabal G, et al. Predictive modeling in reproductive medicine: Where will the future of artificial intelligence research take us? *Fertil Steril*. 2020;114(5):934-40.
41. Curchoe CL, Tarafdar O, Aquilina MC, Seifer DB. SART CORS IVF registry: looking to the past to shape future perspectives. *J Assist Reprod Genet*. 2022;39(11):2607-16.
42. Danardono GB, Erwin A, Purnama J, Handayani N, Polim AA, Boediono A, Sini I. A Homogeneous Ensemble of Robust Pre-defined Neural Network Enables Automated Annotation of Human Embryo Morphokinetics. *J Reprod Infertil*. 2022;23(4):250-6.
43. Danardono GB, Handayani N, Louis CM, Polim AA, Sirait B, Periastringrum G, et al. Embryo ploidy status classification through computer-assisted morphology assessment. *AJOG Glob Rep*. 2023;3(3):100209.
44. Diakiw SM, Hall JMM, VerMilyea M, Lim AYY, Quangkananurug W, Chanchamroen S, et al. An artificial intelligence model correlated with morphological and genetic features of blastocyst quality improves ranking of viable embryos. *Reprod Biomed Online*. 2022;45(6):1105-17.
45. Diakiw SM, Hall JMM, VerMilyea MD, Amin J, Aizpurua J, Giardini L, et al. Development of an artificial intelligence model for predicting the likelihood of human embryo euploidy based on blastocyst images from multiple imaging systems during IVF. *Hum Reprod*. 2022;37(8):1746-59.
46. Dimitriadis I, Zaninovic N, Badiola AC, Bormann CL. Artificial intelligence in the embryology laboratory: a review. *Reprod Biomed Online*. 2022;44(3):435-48.
47. Doody KJ. Infertility Treatment Now and in the Future. *Obstet Gynecol Clin North Am*. 2021;48(4):801-12.
48. Duval A, Nogueira D, Dissler N, Maskani Filali M, Delestro Matos F, Chansel-Debordeaux L, et al. A hybrid artificial intelligence model leverages multi-centric clinical data to improve fetal heart rate pregnancy prediction across time-lapse systems. *Hum Reprod*. 2023;38(4):596-608.
49. Enatsu N, Miyatsuka I, An LM, Inubushi M, Enatsu K, Otsuki J, et al. A novel system based on artificial intelligence for predicting blastocyst viability and visualizing the explanation. *Reprod Med Biol*. 2022;21(1):e12443.
50. Fadon P, Gallegos E, Jalota S, Muriel L, Diaz-Garcia C. Time-Lapse Systems: A Comprehensive Analysis on Effectiveness. *Semin Reprod Med*. 2021;39(5-06):e12-e8.
51. Fanton M, Nutting V, Rothman A, Maeder-York P, Hariton E, Barash O, et al. An interpretable machine learning model for individualized gonadotrophin starting dose selection during ovarian stimulation. *Reprod Biomed Online*. 2022;45(6):1152-9.
52. Fanton M, Nutting V, Solano F, Maeder-York P, Hariton E, Barash O, et al. An interpretable machine learning model for predicting the optimal day of trigger during ovarian stimulation. *Fertil Steril*. 2022;118(1):101-8.
53. Fernandez EI, Ferreira AS, Cecílio MHM, Chéles DS, de Souza RCM, Nogueira MFG, Rocha JC. Artificial intelligence in the IVF laboratory: overview through the application of different types of algorithms for the classification of reproductive data. *J Assist Reprod Genet*. 2020;37(10):2359-76.
54. Ferrand T, Boulant J, He C, Chambost J, Jacques C, Pena CA, et al. Predicting the number of oocytes retrieved from controlled ovarian hyperstimulation with machine learning. *Hum Reprod*. 2023;38(10):1918-26.

55. Firuzinia S, Afzali SM, Ghasemian F, Mirroshandel SA. A robust deep learning-based multiclass segmentation method for analyzing human metaphase II oocyte images. *Comput Methods Programs Biomed.* 2021;201:105946.
56. Fitz VW, Kanakasabapathy MK, Thirumalaraju P, Kandula H, Ramirez LB, Boehnlein L, et al. Should there be an "AI" in TEAM? Embryologists selection of high implantation potential embryos improves with the aid of an artificial intelligence algorithm. *J Assist Reprod Genet.* 2021;38(10):2663-70.
57. Fordham DE, Rosentraub D, Polsky AL, Aviram T, Wolf Y, Perl O, et al. Embryologist agreement when assessing blastocyst implantation probability: is data-driven prediction the solution to embryo assessment subjectivity? *Hum Reprod.* 2022;37(10):2275-90.
58. Fu K, Li Y, Lv H, Wu W, Song J, Xu J. Development of a Model Predicting the Outcome of In Vitro Fertilization Cycles by a Robust Decision Tree Method. *Front Endocrinol (Lausanne).* 2022;13:877518.
59. Garcia-Belda A, Cairó O, Martínez-Moro Á, Cuadros M, Pons MC, de Mendoza MVH, et al. Considerations for future modification of The Association for the Study of Reproductive Biology embryo grading system incorporating time-lapse observations. *Reprod Biomed Online.* 2024;48(1):103570.
60. Gardner DK. 'The way to improve ART outcomes is to introduce more technologies in the laboratory'. *Reprod Biomed Online.* 2022;44(3):389-92.
61. Gardner DK, Sakkas D. Making and selecting the best embryo in the laboratory. *Fertil Steril.* 2023;120(3 Pt 1):457-66.
62. Geller J, Collazo I, Pai R, Hendon N, Lokeshwar SD, Arora H, et al. An Artificial Intelligence-Based Algorithm for Predicting Pregnancy Success Using Static Images Captured by Optical Light Microscopy during Intracytoplasmic Sperm Injection. *J Hum Reprod Sci.* 2021;14(3):288-92.
63. Giscard d'Estaing S, Labrune E, Forcellini M, Edel C, Salle B, Lornage J, Benchaib M. A machine learning system with reinforcement capacity for predicting the fate of an ART embryo. *Syst Biol Reprod Med.* 2021;67(1):64-78.
64. Glatstein I, Chavez-Badiola A, Curchoe CL. New frontiers in embryo selection. *J Assist Reprod Genet.* 2023;40(2):223-34.
65. Go KJ, Hudson C. Deep technology for the optimization of cryostorage. *J Assist Reprod Genet.* 2023;40(8):1829-34.
66. Gomez T, Feyeux M, Boulant J, Normand N, David L, Paul-Gilloteaux P, et al. A time-lapse embryo dataset for morphokinetic parameter prediction. *Data Brief.* 2022;42:108258.
67. Goswami N, Winston N, Choi W, Lai NZE, Arcanjo RB, Chen X, et al. EVATOM: an optical, label-free, machine learning assisted embryo health assessment tool. *Commun Biol.* 2024;7(1):268.
68. Goyal A, Kuchana M, Ayyagari KPR. Machine learning predicts live-birth occurrence before in-vitro fertilization treatment. *Sci Rep.* 2020;10(1):20925.
69. Grzegorzczuk-Martin V, Roset J, Di Pizio P, Fréour T, Barrière P, Pouly JL, et al. Adaptive data-driven models to best predict the likelihood of live birth as the IVF cycle moves on and for each embryo transfer. *J Assist Reprod Genet.* 2022;39(8):1937-49.
70. Gunderson SJ, Puga Molina LC, Spies N, Balestrini PA, Buffone MG, Jungheim ES, et al. Machine-learning algorithm incorporating capacitated sperm intracellular pH predicts conventional in vitro fertilization success in normospermic patients. *Fertil Steril.* 2021;115(4):930-9.
71. Guo X, Zhan H, Zhang X, Pang Y, Xu H, Zhang B, et al. Predictive models for starting dose of gonadotropin in controlled ovarian hyperstimulation: review and progress update. *Hum Fertil (Camb).* 2023;26(6):1609-16.
72. Guo Y, Chen P, Li T, Jia L, Zhou Y, Huang J, et al. Single-cell transcriptome and cell-specific network analysis reveal the reparative effect of neurotrophin-4 in preantral follicles grown in vitro. *Reprod Biol Endocrinol.* 2021;19(1):133.
73. Hariton E, Pavlovic Z, Fanton M, Jiang VS. Applications of artificial intelligence in ovarian stimulation: a tool for improving efficiency and outcomes. *Fertil Steril.* 2023;120(1):8-16.
74. Hernández-González J, Valls O, Torres-Martín A, Cerquides J. Modeling three sources of uncertainty in assisted reproductive technologies with probabilistic graphical models. *Comput Biol Med.* 2022;150:106160.

75. Hickman CFL, Alshubbar H, Chambost J, Jacques C, Pena CA, Drakeley A, Freour T. Data sharing: using blockchain and decentralized data technologies to unlock the potential of artificial intelligence: What can assisted reproduction learn from other areas of medicine? *Fertil Steril*. 2020;114(5):927-33.
76. Hillyear LM, Zak LJ, Beckitt T, Griffin DK, Harvey SC, Harvey KE. Morphokinetic Profiling Suggests That Rapid First Cleavage Division Accurately Predicts the Chances of Blastulation in Pig In Vitro Produced Embryos. *Animals (Basel)*. 2024;14(5).
77. Horer S, Feichtinger M, Rosner M, Hengstschläger M. Pluripotent Stem Cell-Derived In Vitro Gametogenesis and Synthetic Embryos-It Is Never Too Early for an Ethical Debate. *Stem Cells Transl Med*. 2023;12(9):569-75.
78. Hori K, Hori K, Kosasa T, Walker B, Ohta A, Ahn HJ, Huang TTF. Comparison of euploid blastocyst expansion with subgroups of single chromosome, multiple chromosome, and segmental aneuploids using an AI platform from donor egg embryos. *J Assist Reprod Genet*. 2023;40(6):1407-16.
79. Hourri O, Gil Y, Danieli-Gruber S, Shufaro Y, Sapir O, Hochberg A, et al. Prediction of oocyte maturation rate in the GnRH antagonist flexible IVF protocol using a novel machine learning algorithm - A retrospective study. *Eur J Obstet Gynecol Reprod Biol*. 2023;284:100-4.
80. 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. *Reprod Biol Endocrinol*. 2021;19(1):185.
81. Huang TTF, Kosasa T, Walker B, Arnett C, Huang CTF, Yin C, et al. Deep learning neural network analysis of human blastocyst expansion from time-lapse image files. *Reprod Biomed Online*. 2021;42(6):1075-85.
82. Huang Y, Li Z, Lin E, He P, Ru G. Oxidative damage-induced hyperactive ribosome biogenesis participates in tumorigenesis of offspring by cross-interacting with the Wnt and TGF- β 1 pathways in IVF embryos. *Exp Mol Med*. 2021;53(11):1792-806.
83. Iftikhar P, Kuijpers MV, Khayyat A, Iftikhar A, DeGouvria De Sa M. Artificial Intelligence: A New Paradigm in Obstetrics and Gynecology Research and Clinical Practice. *Cureus*. 2020;12(2):e7124.
84. Isiksacan Z, D'Alessandro A, Wolf SM, McKenna DH, Tessier SN, Kucukal E, et al. Assessment of stored red blood cells through lab-on-a-chip technologies for precision transfusion medicine. *Proc Natl Acad Sci U S A*. 2023;120(32):e2115616120.
85. Jakubczyk P, Paja W, Pancerz K, Cebulski J, Depciuch J, Uzun Ö, et al. Determination of idiopathic female infertility from infrared spectra of follicle fluid combined with gonadotrophin levels, multivariate analysis and machine learning methods. *Photodiagnosis Photodyn Ther*. 2022;38:102883.
86. Jiang VS, Bormann CL. Noninvasive genetic screening: current advances in artificial intelligence for embryo ploidy prediction. *Fertil Steril*. 2023;120(2):228-34.
87. Jiang VS, Bormann CL. Artificial intelligence in the in vitro fertilization laboratory: a review of advancements over the last decade. *Fertil Steril*. 2023;120(1):17-23.
88. Jiang VS, Kartik D, Thirumalaraju P, Kandula H, Kanakasabapathy MK, Souter I, et al. Advancements in the future of automating micromanipulation techniques in the IVF laboratory using deep convolutional neural networks. *J Assist Reprod Genet*. 2023;40(2):251-7.
89. Jin H, Shen X, Song W, Liu Y, Qi L, Zhang F. The Development of Nomograms to Predict Blastulation Rate Following Cycles of In Vitro Fertilization in Patients With Tubal Factor Infertility, Polycystic Ovary Syndrome, or Endometriosis. *Front Endocrinol (Lausanne)*. 2021;12:751373.
90. Johansen MN, Parner ET, Kragh MF, Kato K, Ueno S, Palm S, et al. Comparing performance between clinics of an embryo evaluation algorithm based on time-lapse images and machine learning. *J Assist Reprod Genet*. 2023;40(9):2129-37.
91. Joshi AS, Alegria AD, Auch B, Khosla K, Mendana JB, Liu K, et al. Multiscale, multi-perspective imaging assisted robotic microinjection of 3D biological structures. *Annu Int Conf IEEE Eng Med Biol Soc*. 2021;2021:4844-50.
92. Kandel ME, Rubessa M, He YR, Schreiber S, Meyers S, Matter Naves L, et al. Reproductive outcomes predicted by phase imaging with computational specificity of spermatozoon ultrastructure. *Proc Natl Acad Sci U S A*. 2020;117(31):18302-9.
93. Khalife D, Abu-Musa A, Khalil A, Ghazeeri G. Towards the selection of embryos with the greatest implantation potential. *J Obstet Gynaecol*. 2021;41(7):1010-5.

94. Khan HL, Bhatti S, Abbas S, Kaloglu C, Isa AM, Younas H, et al. Extracellular microRNAs: key players to explore the outcomes of in vitro fertilization. *Reprod Biol Endocrinol*. 2021;19(1):72.
95. Khattar H, Goel R, Kumar P. Artificial Intelligence in Gynaecological Malignancies: Perspectives of a Clinical Oncologist. *Cureus*. 2023;15(9):e45660.
96. Kim HM, Ko T, Kang H, Choi S, Park JH, Chung MK, et al. Improved prediction of clinical pregnancy using artificial intelligence with enhanced inner cell mass and trophectoderm images. *Sci Rep*. 2024;14(1):3240.
97. Kim J, Lee J, Jun JH. Non-invasive evaluation of embryo quality for the selection of transferable embryos in human in vitro fertilization-embryo transfer. *Clin Exp Reprod Med*. 2022;49(4):225-38.
98. Kragh MF, Karstoft H. Embryo selection with artificial intelligence: how to evaluate and compare methods? *J Assist Reprod Genet*. 2021;38(7):1675-89.
99. Kresch E, Efimenko I, Gonzalez D, Rizk PJ, Ramasamy R. Novel methods to enhance surgical sperm retrieval: a systematic review. *Arab J Urol*. 2021;19(3):227-37.
100. Kromp F, Wagner R, Balaban B, Cottin V, Cuevas-Saiz I, Schachner C, et al. An annotated human blastocyst dataset to benchmark deep learning architectures for in vitro fertilization. *Sci Data*. 2023;10(1):271.
101. Kulus M, Kranc W, Wojtanowicz-Markiewicz K, Celichowski P, Światły-Błaszkiwicz A, Matuszewska E, et al. New Gene Markers Expressed in Porcine Oviductal Epithelial Cells Cultured Primary In Vitro Are Involved in Ontological Groups Representing Physiological Processes of Porcine Oocytes. *Int J Mol Sci*. 2021;22(4).
102. Kumar RS, Sharma S, Halder A, Gupta V. Deep Learning-Based Robust Automated System for Predicting Human Sperm DNA Fragmentation Index. *J Hum Reprod Sci*. 2023;16(1):16-21.
103. Lee CI, Su YR, Chen CH, Chang TA, Kuo EE, Zheng WL, et al. End-to-end deep learning for recognition of ploidy status using time-lapse videos. *J Assist Reprod Genet*. 2021;38(7):1655-63.
104. Lee R, Witherspoon L, Robinson M, Lee JH, Duffy SP, Flannigan R, Ma H. Automated rare sperm identification from low-magnification microscopy images of dissociated microsurgical testicular sperm extraction samples using deep learning. *Fertil Steril*. 2022;118(1):90-9.
105. Letterie G. Three ways of knowing: the integration of clinical expertise, evidence-based medicine, and artificial intelligence in assisted reproductive technologies. *J Assist Reprod Genet*. 2021;38(7):1617-25.
106. Letterie G. Artificial intelligence and assisted reproductive technologies: 2023. Ready for prime time? Or not. *Fertil Steril*. 2023;120(1):32-7.
107. Letterie G, Mac Donald A. Artificial intelligence in in vitro fertilization: a computer decision support system for day-to-day management of ovarian stimulation during in vitro fertilization. *Fertil Steril*. 2020;114(5):1026-31.
108. Letterie G, MacDonald A, Shi Z. An artificial intelligence platform to optimize workflow during ovarian stimulation and IVF: process improvement and outcome-based predictions. *Reprod Biomed Online*. 2022;44(2):254-60.
109. Li J, Lu M, Zhang P, Hou E, Li T, Liu X, et al. Aberrant spliceosome expression and altered alternative splicing events correlate with maturation deficiency in human oocytes. *Cell Cycle*. 2020;19(17):2182-94.
110. Li L, Cui X, Yang J, Wu X, Zhao G. Using feature optimization and LightGBM algorithm to predict the clinical pregnancy outcomes after in vitro fertilization. *Front Endocrinol (Lausanne)*. 2023;14:1305473.
111. Liang X, Liang J, Zeng F, Lin Y, Li Y, Cai K, et al. Evaluation of oocyte maturity using artificial intelligence quantification of follicle volume biomarker by three-dimensional ultrasound. *Reprod Biomed Online*. 2022;45(6):1197-206.
112. Liao S, Pan W, Dai WQ, Jin L, Huang G, Wang R, et al. Development of a Dynamic Diagnosis Grading System for Infertility Using Machine Learning. *JAMA Netw Open*. 2020;3(11):e2023654.