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Review Article

Review On: Smart Nanomaterial in AI Assisted Reproductive Technologies

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ABSTRACT

The field of assisted reproductive technology (ART) is undergoing a significant transformation due to advancements in smart nanomaterials and artificial intelligence (AI). By addressing the subjectivity and variability of conventional methods, integrating AI into ART processes—such as gamete and embryo selection, personalized ovarian stimulation, sperm assessment, and embryo grading—improves ART success rates and allows for more individualized treatments. Both clinicians and embryologists can make more accurate and consistent decisions by using machine learning and deep learning algorithms to objectively analyze images and clinical data. The safety and effectiveness of drug delivery, cryopreservation, and the mitigation of oxidative stress in gametes and embryos have all increased as a result of nanotechnology's concurrent contributions. Nevertheless, there are significant issues with ethics, data quality, standardization, and regulatory oversight in spite of these technological advantages. To guarantee responsible and successful clinical translation, issues like skewed datasets, a dearth of generally recognized protocols, and inadequate regulatory guidance must be resolved. For these innovations to be implemented safely and fairly, ongoing research and ethical evaluation are crucial. The combination of AI and smart nanomaterials has the potential to revolutionize infertility treatment by enhancing treatment results, accessibility, and personalization in reproductive medicine.

INTRODUCTION

A range of medical techniques known as assisted reproductive technology (ART) are used to help when natural conception is impossible or difficult. In order to create a viable pregnancy, these methods frequently entail modifying the eggs, sperm, or embryos outside of the body. ART has transformed reproductive medicine and given millions of people and couples across the world hope when they struggle with infertility. [1]

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The scientific field of artificial intelligence (AI) is devoted to creating systems that provide outputs like information, forecasts, recommendations, or judgments that are in accordance with human-specific goals. Computer neural networks made up of linked nodes—also referred to as nodal points—that can transport data are used to do this. As a result, the computer may grow, learn, reason, process language, and solve problems.^[3] The purpose of the scientific discipline of artificial intelligence (AI) is to develop systems that produce information, predictions, suggestions, or judgments that align with the objectives of humans.^[4]

Thus, the computer can grow, learn, reason, understand language, and solve problems. The following are some important uses of AI in this field: 1) DNA analysis; 2) customized ovarian to evaluate and stimulation predict gonadotropin initiation dose; 3) evaluation of sperm properties like motility, morphology, and DNA integrity, as well as the selection of the best sperm for fertilization; 4) embryo selection for evaluation of their quality and outcome prediction, including the probability of success and overall result of various treatments; and 5) treatment protocol optimization by developing customized interventions that take age, fertility history, and genetic traits into consideration.^[5]

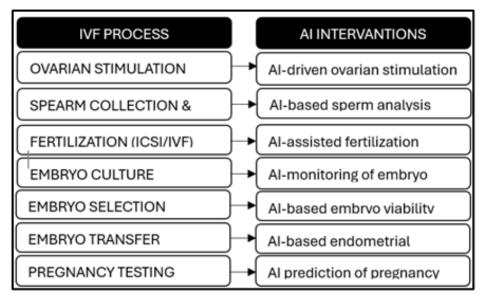


Figure 1: highlights areas where Artificial Intelligence (AI) can be used to improve accuracy and efficiency while summarizing the essential steps in the IVF (ART) process.^[5]

The primary steps of the IVF procedure (first column) and the AI-powered improvements at phases, where AI enhances accuracy, optimizes decision-making, and raises the likelihood of a successful pregnancy (second column).^[6]

Fertility treatments that work with eggs or embryos are referred to as assisted reproductive technology, or ART. This involves taking eggs out of a woman's ovaries surgically, fertilizing them in a lab, and then returning them to the original or another woman. [8] Pregnancy rates after ART have risen from 6% to 35% over the past 40 years, demonstrating how these biotechniques have radically changed how infertility treatments are administered to individuals (J. Wang & Sauer, 2006). [6]

Artificial intelligence (AI) is being used more in the medical industry for a variety of purposes. It contributes to accurate clinical decision making, helps with genetic analysis for individualized therapies, and enhances the interpretation of medical imaging. AI also facilitates patient monitoring, speeds up medication discovery, and improves surgical techniques with robotic support. [8]

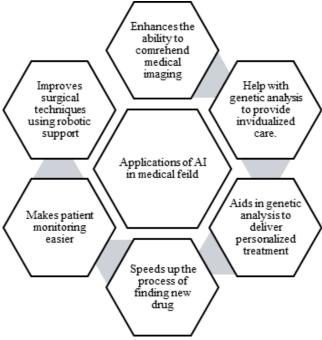


Figure 2: Applications of AI in medical field. [8]

Triptorelin is a synthetic decapeptide analogue of GnRh in which d-tryptophan is substituted at position 6 for the l-glycine of native GnRh. The activity of triptorelin is 100 times higher than that of GnRh. For ART, triptorelin has been used in three different regimens: an ultra-short protocol that uses the flare-up effect, a lengthy protocol that uses the downregulation effect, and a short protocol that uses both the flare-up and downregulation effects. ^[9]

Failing to conceive after a year or more of trying is known as infertility, and it affects 15% of couples worldwide. Even though up to 50% of instances may be due to male causes, women are often the ones who bear the societal stigma of infertility. The inability to conceive after an earlier pregnancy is known as secondary infertility, while the inability to conceive without a history of past conception is known as primary infertility. [11] Infertility affects an estimated 186 million

individuals and 48 million couples globally (WHO, 2020). Through ART procedures such in vitro fertilization, over 8 million children have been born globally. [9]

In order to improve drug efficiency, nanoparticles or drug formulations loaded with nanoparticles are currently being developed. These include: 1) preventing the gastrointestinal tract from breaking down and reducing intestinal absorption, which increases oral bioavailability; 2) circumventing blood-tissue barriers and delivering to specific target tissues, or even at the cellular level; 3) attaining a rapid onset and prolonged therapeutic action; 4) lowering the effective dose and side effects or toxicity; and 5) prolonging the half-life of medications in circulation. The expanding applications of nanotechnology in the drug delivery sector are comprehensively summarized in a number of literature reviews. [12]

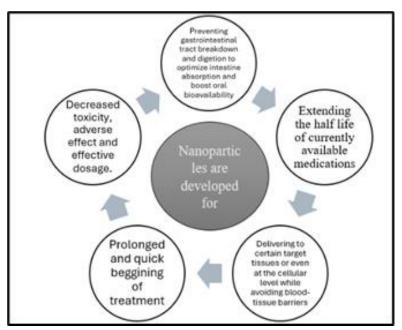


Figure 3: Nanoparticles are developed for applications such as. [12]

Applications of nanometric materials have grown in popularity and sophistication across a number of academic disciplines. Synthetic particles known as nanoparticles (NPs) have an extremely small size at the nanometer scale, a high surface-area ratio, and a variable manufacturing process. Materials that can be utilized to make nanoparticles include proteins, polysaccharides, and metals. Additionally, the drug delivery industry has made greater use of NPs to develop treatments for mutations in unstable hydrophilic or lipophilic

[12] The swift advancement molecules. innovative drug-delivery technologies has demonstrated that nanoparticles (NPs) serve as "shield" structures. shielding integrated medications enzymatic degradation. from Recently, polymeric microneedles encapsulated in nanoparticles (NPs-MNs) have emerged as appealing instruments that enable synergistic therapeutic methods for the treatment of cancer, diabetes mellitus, and dermatological conditions, as well as to support immunity.^[9]

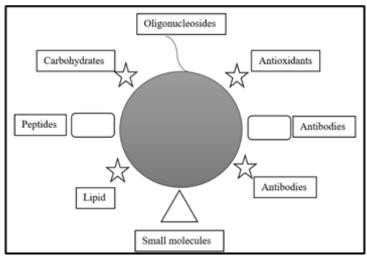


Figure 4: Biomolecules that nanoparticles can transport to cells include proteins, lipids, carbohydrates, RNAs, antioxidants, and tiny metabolite compounds.^[6]



HISTORY OF ART

When the initial "test-tube baby," Louise Brown, was born in 1978. In vitro fertilization (IVF), a revolutionary infertility treatment that gave hope to infertile couples, was introduced during this momentous occasion. [13] Intracytoplasmic sperm injection, or ICSI, is a novel treatment for male infertility. [15] ART research and invention are still going strong in the modern period. In order to maximize treatment results and enhance the patient experience, ongoing research investigates cutting-edge strategies such minimum stimulation regimens and gonadotropin-releasing hormone (GnRH) agonist cycle triggers. [14]

DIFFICULTIES USING CONVENTIONAL ART METHODS

The effectiveness of conventional techniques, such intracytoplasmic sperm injection and in vitro fertilization, is limited by several issues.^[16] The high cost of the treatments is another barrier to getting ART [9]. Furthermore, conventional ART methods usually take a onesize-fits-all approach, failing to take into consideration each patient's particular traits and preferences. [16] Another issue is that existing ART techniques heavily rely on human skill, which raises the possibility of human mistake and causes unpredictability in results.^[17] Because human judgment in embryology and clinical practice is subjective, more standardized and technologically advanced methods are required to improve the consistency and dependability of ART operations. illustrates the difficulties Figure 5 that conventional ART techniques confront.

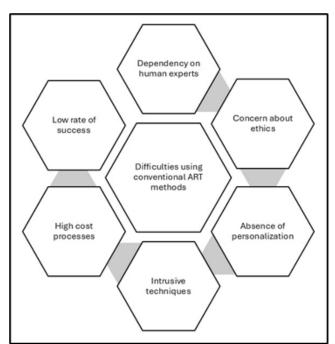


Figure 5: Having trouble with traditional ART techniques.^[1]

DEVELOPMENT OF AI IN ART

Over the past 20 years, AI has been used for a wider range of tasks, from simple tasks to more complex ones like ART. Instead of compromising doctors' clinical judgment, artificial intelligence

(AI) was included into healthcare systems to help with efficient decision-making during times of transition. ^[14] AI has the potential to revolutionize ART by decreasing subjectivity and boosting efficacy through the utilization of massive datasets. ^[13]

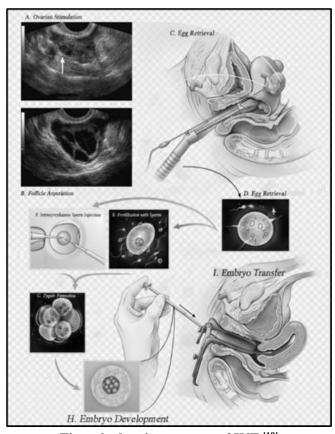


With the advent of alternative methods like gamete intrafallopian transfer (GIFT) and zygote intrafallopian transfer (ZIFT) in the 1980s, the scope of assisted reproductive technology (ART) procedures increased. By providing patients with additional options for fertility treatments, these methods influenced the evolution of reproductive medicine. [18]

ARTIFICIAL INTELLIGENCE IN ART TECHNIQUES

1. Fertilization within vitro

More than 48,000 babies were born in 2003 as a result of more than one lakh IVF cycles from four thousand US clinics. [19]. IVF (Fig. 6) entails ovarian stimulation, egg harvesting (see the video in the Supplementary Appendix, which is accessible at www.nejm.org along with the article's entire text), embryo cultivation, fertilization, and embryo transfer to the uterus. Eggs and sperm can be cultured together to fertilize them, or the more recent method of intracytoplasmic sperm injection can be used (Fig. 6).



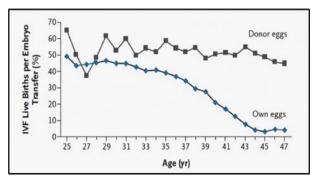
Figer 6: showing process of IVF [19]

Benefits of IVF

In 2003, 34% of IVF cycles in the US that used fresh, nondonor eggs ended in a clinical pregnancy. Due to frequent losses, In reality, there were 28 percent live births per cycle. [19] For women under 34 years old, the actual delivery rate

per embryo transfer ranges from 40 to 49 percent. After that, for every year that chronologic age increases, the live-birth percentage decreases by 2 to 6%. Only 5% of women give birth before the age of forty-three. On the other hand, IVF using young women's donation eggs is quite effective,

and the pregnancy rate seems to be rather constant regardless of the recipient's age (Fig. 7).^[19]



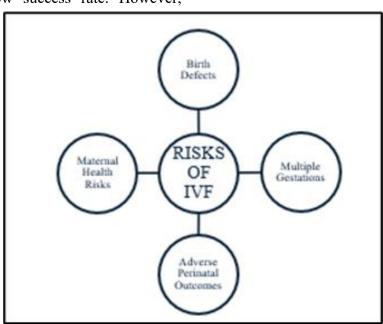
Figer 7: Age of the Woman Affects the Live Birth Rate per IVF Embryo Transfer.

In Vitro Fertilization Advancements

At first, the methods needed to carry out IVF were crude and had a low success rate. However,

significant advancements in IVF, such as the use of luteal phase support, controlled ovarian hyperstimulation, and enhanced culture medium, were made rapidly. [13] In the early 1980s, The concept of controlled ovarian hyperstimulation (COH) in connection with ART was developed by Howard and Georgeanna Jones. [13] In this first COH technique, one hundred IU of human menopausal gonadotropin (hMG) was used to recover an average of 3.7 oocytes per IVF cycle. [22] Higher dosages of gonadotropins were used in subsequent experiments at the same facility, which increased the number of recovered oocytes but had no effect on pregnancy rates. [13]

Risks of IVF



Figer 8: showing risk of IVF [19]

2. Intracytoplasmic sperm injection

Couples with male factor infertility have been treated with in vitro fertilization via insemination for more than ten years, with comparatively unsatisfactory outcomes. Fertilization failure is more likely to occur in patients with significantly aberrant semen parameters or when not enough spermatozoa are recovered. Fertilization rates have increased when the zona pellucida is opened by chemical, mechanical, or photoablation methods, avoiding sperm entry barriers when conventional in vitro insemination techniques have failed. has reached a fertilization rate of around 20% with consistent and repeatable outcomes.^[23]

limiting factors



The need for numerous functioning spermatozoa with adequate progressive motility, a normal acrosome, acrosomal content, and the dynamic of acrosomal loss are some of the limiting criteria, though. Additionally, when the quantity of injected spermatozoa was increased, these methods combined with a low fertilization rate showed a greater incidence of multiple sperm penetration.^[23]

3. Laboratory

The improvement of the embryo culture medium has likely been the most significant of these modifications. Pregnancy rates have, in fact, skyrocketed with the 1985 launch of the cultural media formula known as "Human Tubal Fluid.^[6] Numerous other changes are always being assessed to maximize embryology labs. The ideal oxygen (O2) content in embryo incubators is one such adjustment that is the focus of a lot of current study. Apart from media, several other methods have also been presented with improved results. For instance, ICSI and assisted hatching have proven to be quite beneficial.^[21]

4. Cryopreservation

A crucial component of ART is the cryopreservation of gametes and embryos. IVF procedures are now safer and more effective. In Europe, the percentage of cryopreserved embryo transfer cycles relative to fresh cycles is increasing. According to estimates, cryopreserved cycles accounted for 32% of transfers overall in 2011 as opposed to 28% in 2010. [26]

The oocyte is extremely challenging to cryopreserve since the extremely low temperature may inflict biological and physical harm to several cytoplasmic components, perhaps leading to cell death.^[25] Gametes and embryos may be stored for an extended period of time using cryopreservation,

which is very beneficial in several reproductive sectors.^[27]

APPLICATIONS OF AI IN ART

1. Sperm assessment using AI

a. CASA

A computerized method for evaluating sperm properties including concentration, morphology, and motility is called computer aided semen analysis, or CASA. Compared to manual assessment, this method of semen analysis yields precise and repeatable findings.^[34] Standardized protocols across laboratories are made possible by CASA, which minimizes observer bias and offers extremely precise and dependable data. CASA is still a fundamental and important technique for assessing male infertility function in spite of these and sperm requirements.[3]

b. Automated analysis of sperm using AI

Beyond conventional CASA, sperm analysis systems are using AI, namely ML and DL algorithms, to increase precision, effectiveness, and consistency. By autonomously classifying sperm based on motility, morphology, and viability, AI models are trained on massive datasets of sperm photos or videos. This improves diagnostic consistency and lowers operator mistakes. [35]

2. AI in oocyte selection

AI DL models enable objective and automatic analysis of high-resolution oocyte images. These models can be programmed to recognize changes in the oocytes such as oocyte maturation, fertilization potential and embryo development outcomes which can be missed by the observing embryologist. Some approaches integrate time



lapse imaging, polar body morphology, or metabolic profiles with AI-based analysis to improve predictive performance.^[3]

3. AI in embryo grading

Al's use in ART gamete and embryo selection is a quickly developing topic that has significant promise to increase ART operation success rates. By using AI technology, which can analyze large amounts of data, especially photos and videos, sperm, oocytes, and embryos may be evaluated more accurately and objectively.^[4]

4. Ethical Concerns with AI in Reproductive Medicine

The integration of artificial intelligence (AI) with reproductive health raises complex and critical ethical issues. Numerous normative issues arise when AI is incorporated into ART increasingly, especially in relation to the proof of efficacy, informed permission, possible hazards for progeny, and the effect on patient autonomy and wellbeing. [36]

5. ART's Prediction Analytics and Systems for Decision Support

By enabling doctors and embryologists to make better judgments, these cutting-edge technologies improve patient care and results.^[1] Additionally, after IVF-embryo transfer, machine learning algorithms play a critical role in predicting live birth outcomes and early pregnancy loss, providing doctors with crucial information.^[37]

6. AI in personalized treatment plan

AI is now heavily relied upon for creating individualized treatment regimens, particularly for ART. Its goal is to maximize results while lowering the mistake that occurs during clinical decision-making. Large multidimensional data sets are analyzed using ML models, which consider genetic information, ovarian reserve indicators, hormonal profiles, population demographics, stimulation history, and treatment results. [3]

Table 1: lists the benefits and drawbacks of AI algorithms included into ART. [5]

AI Tool	Application in ART	Advantages	Limitations
LR	A simple technique for predicting the likelihood of pregnancy		Limited accuracy for highly complex data
ANNs	Optimizing therapy and adjusting gonadotropin dosage	Capacity to understand intricate connections between data	High processing power and challenging interpretation of the results
LSTM	Time-series analysis to track the course of therapy	Perfect for time series and dynamic data analysis	Expensive computing and susceptibility to data noise
SVM	Analysis of fertility factors and forecasting success	Robustness with small datasets, high generalization	requires that input features be carefully chosen.
RF	Predicting treatment outcomes and classifying data	Excellent results in classification and analysis of large amounts of data	may be more likely to overfit if not adjusted appropriately.
CNNs	Analysis of sperm and embryos using imaging	High image analysis accuracy and automated feature identification	requires training graphics processing units and big datasets.
Gradient boosting (XGBoost, LightGBM)	Predicting the success of embryo transfer and implantation result	Reduction in overfitting risk when applied to nonlinear data	For best results, the parameters must be properly adjusted.

ROLES OF AI IN ART

1. Assessment of the reproductive system in females

The assessment of female reproductive function, including ovarian reserve and endometrial receptivity, is one of the most crucial stages in the infertility. Artificial intelligence-assisted diagnosis may be one of the best methods for evaluating female function and reproductive offering recommendations for identifying infertility problems.^[2]

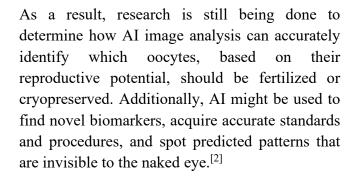
2. Ovarian stimulation

Customized regulated ovarian stimulation is now possible thanks to the application of machine learning techniques to forecast the prognostic outcomes for ovarian response; [39] as well as to suggest initial dosages of follicle stimulation hormones for ovarian stimulation. [40] Because retrospective results show that over half of IVF cycles had potential early or late trigger injections that impacted the outcomes of oocyte retrieval, researchers have developed a decision support system with an algorithm trained to determine the best time for oocyte retrieval and an interpretable machine learning model to optimize the day of trigger. [41]

3. AI in gamete selection

Gamete health has a significant impact on the outcome of ART, hence it's critical to find early indicators of quality. These are now assessed by highly qualified individuals, However, automated techniques based on AI image analysis could produce more trustworthy and impartial outcomes..^[2]

A. Oocyte selection



B. Sperm selection and semen analysis

AI may therefore be used to evaluate and choose the most suitable samples for reproductive treatments. To improve male fertility prediction, some researchers have applied five artificial intelligence (AI) techniques to eight feature selection methods, Others, however, have employed data mining to forecast human sperm concentration and motility from lifestyle and environmental questionnaires, offering a useful alternative to more expensive laboratory testing. [2]

4. Embryo selection

AI may therefore be used to evaluate and choose the most suitable samples for reproductive treatments. To improve male fertility prediction, some researchers have applied five artificial intelligence (AI) techniques to eight feature selection methods, while others have used data mining to predict human sperm concentration and motility from questionnaires on lifestyle and environmental factors, providing a helpful substitute for more costly laboratory tests.^[2]

5. Analysis of cell free DNA

Researchers have been examining their profiles and relationships, as well as speculating on the range of processes from which they emerge. They are mostly found in serum, follicular fluid, seminal plasma, wasted culture medium, and blastocoel fluid in a reproductive context. Therefore, cfDNA



may be utilized for the diagnosis of infertility diseases, the identification of reliable biomarkers to predict the outcome of ART, and non-invasive genetic or epigenetic diagnostics, which are now carried out by highly qualified specialists using expensive equipment.^[42]

6. The onset of the age of omics

The selection of gametes and embryos as well as the timing of embryo implantation are critical to the effectiveness of ART. ^[2] Omics analysis can differentiate between morphologically identical embryos and potentially establish ploidy status non-invasively by eliminating the need for biopsies and reducing the number of cycles, reducing the risk of harming embryos and their environment while also saving money. However, one of the biggest problems for researchers is the volume of data that omics produces from a sample.^[42]

7. Workflow in Clinical Practice

Future AI applications will extend beyond clinical care to operational management and workflow, encompassing data entry, processing, and management, all of which will become more efficient and error-free. For instance, radio frequency identification technologies, barcodes, or manual identification are now used to monitor and identify embryos particular to a patient.^[2]

8. Moving toward a customized care plan

AI is ideally suited as a technique to address complicated, multifaceted issues including implantation failure, inadequate stimulation response, and recurrent miscarriages.^[2] Recognition of faces AI in donor selection may make it possible for IVF offspring to "pass" as a person's own biological kid.^[43]

ADVANTAGES OF AI IN ART



Embryo implantation potential

When it comes to predicting implantation success, machine learning models that use time-lapse imaging, morphokinetics, and patient background data have demonstrated encouraging results. In certain cases, these algorithms have even outperformed seasoned embryologists in terms of evaluating embryo quality.^[44]

Ovarian response

By looking at variables including age, antral follicle count, hormone levels, and previous stimulation history, AI systems may predict ovarian response with more sensitivity and specificity than traditional models. These projections can assist in enhancing stimulation techniques and tailoring dose of gonadotropin [45]

Risk of treatment failure or complications (e.g., OHSS)

By using patient-specific data (such as AMH, BMI, PCOS status, and follicle counts), AI models may predict cycle cancellation or unfavourable outcomes and stratify the risk of adverse events such ovarian hyperstimulation syndrome (OHSS), allowing for prophylactic actions.^[3]

Improves selection of optimal treatment protocols, embryo quality, and timing

A Chinese clinical AI system demonstrated decision-level support and significantly improved prediction accuracy for cycle success and optimal protocol selection by uncovering hidden patterns in large amounts of IVF data.^[24]

DISADVANTAGES OF ALIN ART

Lack of standardization

The generalizability of AI models is restricted by variations in imaging methods, laboratory procedures, and data labelling between clinics. External validity is significantly diminished by the fact that many models are trained exclusively on clinic-specific information.^[3]

"Black box" problem

Because DL models frequently lack interpretability, it might be challenging to comprehend the decision-making process. Lack of clarity in the situation might make regulatory clearance more difficult and erode clinician trust [3]

Data quality and bias

The quantity, variety, and quality of incoming data are critical to AI. Inaccurate or unfair results may be produced by models trained on biased datasets (such as a single ethnicity, a particular piece of equipment, or a geographic area), particularly if the case population is not entered into the model's database.^[3]

Limited regulatory oversight

There is presently no ART-specific guidelines for AI applications from regulatory agencies such as the FDA (USA), EMA (EU), and CDSCO (India). Reproductive technologies are not specifically covered under the generic "software as a medical device" (SaMD) law that apply to such instruments under current frameworks.^[38]

Clinical integration challenges

It takes a large investment in infrastructure, training, and compatibility with current systems to integrate AI into healthcare operations. The physicians' inability to adjust to technology because of their lack of faith in it.^[3]

APPLICATIONS OF SMART NANOMATERIALS IN ART

1. In vitro impacts of nanoparticles on spermatozoa

Nanoparticles have been used to improve cryopreservation, semen sexing, and sperm selection in a number of farm animal species. [6] Both swine and bovine species benefit from the use of magnetic iron oxide nanoparticles for sexing semen. [28] Additionally, apoptosis and acrosome reactive spermatozoa were efficiently eliminated by conjugating magnetic nanoparticles with lectins or annexin V.[29] In pig sperm, silver nanoparticles function as an antibacterial agent, offering a substitute for antibiotics in the preservation and storage of semen. [30] In order to reach and pierce the egg, sperm need ATP to sustain cell viability, functioning, acrosome response, and movement. [31]

2. Impact of nanoparticles on preantral follicles grown in vitro

Glutamate, glycine, and cysteine combine to produce the tripeptide GSH, which is crucial in the fight against oxidative stress. [33] Therefore, raising GSH during preantral follicle in vitro culture is crucial for enhancing follicle development and vitality as well as lowering oxidative stress in the cells. In mice with dehydroepiandrosterone-induced polycystic ovarian syndrome, mice's preantral ovarian follicles were protected by curcumin-loaded superparamagnetic iron oxide (Fe3O4) nanoparticles. [6]

3. Effects of nanoparticles on cumulus-oocyte complexes that have matured in vitro

According to recent research by Jahanbin et al. (2021), adding zinc nanoparticles to in vitro maturation conditions increases the activity of



superoxide dismutase (SOD) in cumulus cells, decreases DNA damage and apoptosis in COC, and ultimately speeds up embryonic development. Superoxide is converted to hydrogen peroxide and oxygen by the enzymes catalase (CAT) and SOD. By controlling their levels through its activity, SOD reduces the potential toxicity of reactive oxygen species (ROS) and reactive nitrogen species. [32]

Increased glutathione levels are essential for controlling oxidative stress in cultured cells.^[10] Pig oocytes were co-incubated with BSA-coated gold nanoparticles, and while the oocytes absorbed the gold nanoparticles preferentially, no toxicity was seen.^[7] Lactic acid, which can be utilized as a

metabolic substrate and improve the cells' antioxidant capacity, is produced when PLGA nanoparticles break down in in vitro-cultivated COC.^[6]

The intracellular glutathione level of cumulus cells was elevated in bovine COCs that developed in vitro with copper and ZnO nanoparticles, which promoted embryo development in vitro. [20] In cultured cells, elevated glutathione levels are crucial for regulating oxidative stress. [10] Pig oocytes were co-incubated with BSA-coated gold nanoparticles, and while the oocytes absorbed the gold nanoparticles preferentially, no toxicity was seen. [7]

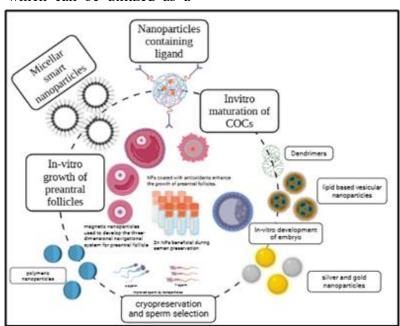


Figure 9: Nanotechnology's advantages for assisted reproduction.

4. Nanoparticles' effects on the development of embryos in vitro

Exogenous antioxidants connected to nanoparticles have been introduced to the embryonic culture media to facilitate rapid penetration and protect the embryo from oxidative damage. Accordingly, melatonin-associated lipid nucleic nanoparticles decreased ROS, mRNA for BAX, and caspase 3 levels as well as cell death

while improving the in vitro development of bovine embryos.^[51]

CONCLUSION

A revolutionary development in the field of reproductive medicine is the incorporation of artificial intelligence and smart nanomaterials into assisted reproductive technologies. The overall effectiveness of ART procedures like IVF, the precision of gamete and embryo selection, and the personalization of treatment are all greatly enhanced by these technologies. By overcoming limitations of conventional methods—including low success rates, high costs, invasiveness, and ethical complexities—AI and nanotechnology collectively enhance reproductive outcomes while reducing treatment burdens. Despite challenges such as data biases, standardization issues, and regulatory gaps, ongoing research and ethical considerations will be crucial in guiding their application. Ultimately, responsible these innovations hold great promise for increasing the accessibility, safety, and success of fertility treatments, paving the way for a new era of personalized reproductive healthcare.

REFERENCES

- 1. Mapari, Smruti A et al. "Revolutionizing Reproduction: The Impact of Robotics and Artificial Intelligence (AI) in Assisted Reproductive Technology: A Comprehensive Review." Cureus vol. 16,6 e63072. 24 Jun. 2024, doi:10.7759/cureus.63072
- Zammit, Raymond. "Ethical issues of artificial intelligence & assisted reproductive technologies." International Journal of Prenatal and Life Sciences DOI: 10.24946/IJPLS (2023): 1-24.
- 3. Hynniewta, Barry Cooper, Ferrill Navas, and Kathrina Marbaniang. "Artificial intelligence in assisted reproduction: the future for reproductive medicine." International Journal of Reproduction, Contraception, Obstetrics and Gynecology 14.9: 3182.
- 4. Naser, M., M. N. Mohamed, and L. H. Shehata. "Artificial intelligence in assisted reproductive technology review." Int J Progress Sci Technol 25 (2021): 507-11.
- 5. More, Akash, et al. "Advancing Assisted Reproduction Technology: The Role of

- Nanotechnology in Enhancing Fertility Treatments and Diagnostics." Journal of Pharmacy and Bioallied Sciences (2025): 10-4103.
- 6. Silva, José Roberto Viana, Pedro Alves Aguiar Barroso, Danisvânia Ripardo Nascimento, Ciro Siqueira Figueira, Venância Antonia Nunes Azevedo, Bianca R. Silva, and Ricardo Pires dos Santos. "Benefits and challenges of nanomaterials in assisted reproductive technologies." Molecular Reproduction and Development 88, no. 11 (2021): 707-717.
- Komninou, E. R., Remião, M. H., Lucas, C. G., Domingues, W. B., Basso, A. C., Jornada, D. S., ... & Collares, T. (2016). Effects of two types of melatonin-loaded nanocapsules with distinct supramolecular structures: polymeric (NC) and lipid-core nanocapsules (LNC) on bovine embryo culture model. PloS one, 11(6), e0157561.sss
- 8. Wu, Y. C., Su, E. C. Y., Hou, J. H., Lin, C. J., Lin, K. B., & Chen, C. H. (2025). Artificial intelligence and assisted reproductive technology: A comprehensive systematic review. Taiwanese Journal of Obstetrics and Gynecology, 64(1), 11-26.
- 9. Lu, X., Sun, Y., Han, M., Chen, D., He, X., Wang, S., & Sun, K. (2023). Triptorelin nanoparticle-loaded microneedles for use in assisted reproductive technology. Drug delivery, 30(1), 2226367.
- 10. Adeoye, O., Olawumi, J., Opeyemi, A., & Christiania, O. (2018). Review on the role of glutathione on oxidative stress and infertility. JBRA assisted reproduction, 22(1), 61
- 11. Hanassab, S., Abbara, A., Yeung, A. C., Voliotis, M., Tsaneva-Atanasova, K., Kelsey, T. W., ... & Dhillo, W. S. (2024). The prospect of artificial intelligence to personalize assisted reproductive technology. Npj digital medicine, 7(1), 55.

- 12. More, A., Mahajan, S., Dakre, S., Anjankar, N., & More, D. (2025). Advancing Assisted Reproduction Technology: The Role of Nanotechnology in Enhancing Fertility Treatments and Diagnostics. Journal of Pharmacy and Bioallied Sciences, 10-4103.
- 13. Falchi, L., Khalil, W. A., Hassan, M., & Marei, W. F. (2018). Perspectives of nanotechnology in male fertility and sperm function. International Journal of Veterinary Science and Medicine, 6(2), 265-269.
- 14. Brezina PR, Ning N, Mitchell E, Zacur HA, Baramki TA, Zhao Y: Recent advances in assisted reproductive technology. Curr Obstet Gynecol Rep. 2012, 1:166-73. 10.1007/s13669-012-0019-2
- 15. Gamete and zygote intrafallopian transfer (GIFT And ZIFT). (2023). Accessed: April 26, 2024:
- 16. Feldman B, Aizer A, Brengauz M, Dotan K, Levron J, Schiff E, Orvieto R: Preimplantation genetic diagnosis should we use ICSI for all?. J Assist Reprod Genet. 2017, 34:1179-83. 10.1007/s10815-017-0966-7
- 17. Mat MF, Baharuddin MN: Issues and problems in Malaysian contemporary visual arts. J Vis Art Des. 2016, 7:131-43. 10.5614/j.vad.2016.7.2.4
- 18. Mekonnen H, Bires Z, Berhanu K: Practices and challenges of cultural heritage conservation in historical and religious heritage sites: evidence from North Shoa Zone, Amhara Region, Ethiopia. Herit Sci. 2022, 10:172. 10.1186/s40494-022-00802-6
- 19. Letterie G. Artificial intelligence and assisted reproductive technologies: 2023. Ready for prime time? Or not. Fertil Steril. 2023;120(1):32-7.
- 20. Wang, Y., Branicky, R., Noë, A., & Hekimi, S. (2018). Superoxide dismutases: Dual roles in controlling ROS damage and regulating ROS

- signaling. Journal of Cell Biology, 217(6), 1915-1928.
- 21. Shvetha M. Zarek, Suheil J. Muasher, Mild/minimal stimulation for in vitro fertilization: an old idea that needs to be revisited, Fertility and Sterility, Volume 95, Issue 8, 2011, Pages 2449-2455, ISSN 0015-0282,
 - https://doi.org/10.1016/j.fertnstert.2011.04.04
- Van Steirteghem, A. C., Nagy, Z., Joris, H., Liu, J., Staessen, C., Smitz, J., ... & Devroey, P. (1993). High fertilization and implantation rates after intracytoplasmic sperm injection. Human reproduction, 8(7), 1061-1066.
- 23. Xu, X., Jiang, Y., Du, J., Sun, H., Wang, X., & Zhang, C. (2024). Development and validation of a prediction model for suboptimal ovarian response in polycystic ovary syndrome (PCOS) patients undergoing GnRH-antagonist protocol in IVF/ICSI cycles. Journal of Ovarian Research, 17(1), 116.
- 24. Sciorio, R., Pluchino, N., & Fuller, B. J. (2023). Review of human oocyte cryopreservation in ART programs: Current challenges and opportunities. Cryobiology, 113, 104590.
- 25. Rienzi, L., Gracia, C., Maggiulli, R., LaBarbera, A. R., Kaser, D. J., Ubaldi, F. M., ... & Racowsky, C. (2017). Oocyte, embryo and blastocyst cryopreservation in ART: systematic review and meta-analysis comparing slow freezing versus vitrification to produce evidence for the development of global guidance. Human reproduction update, 23(2), 139-155.
- 26. Larman, M. G., Hashimoto, S., Morimoto, Y., & Gardner, D. K. (2014). Cryopreservation in ART and concerns with contamination during cryobanking. Reproductive medicine and biology, 13(3), 107-117.

- 27. Taylor, U., Garrels, W., Barchanski, A., Peterson, S., Sajti, L., Lucas-Hahn, A., ... & Rath, D. (2014). Injection of ligand-free gold and silver nanoparticles into murine embryos does not impact pre-implantation development. Beilstein journal of nanotechnology, 5(1), 677-688.
- 28. Durfey, C. L., Swistek, S. E., Liao, S. F., Crenshaw, M. A., Clemente, H. J., Thirumalai, R. V., ... & Feugang, J. M. (2019). Nanotechnology-based approach for safer enrichment of semen with best spermatozoa. Journal of animal science and biotechnology, 10(1), 14.
- 29. Pérez-Duran, F., Acosta-Torres, L. S., Serrano-Díaz, P. N., Toscano-Torres, I. A., Olivo-Zepeda, I. B., García-Caxin, E., & Nuñez-Anita, R. E. (2020). Toxicity and antimicrobial effect of silver nanoparticles in swine sperms. Systems biology in reproductive medicine, 66(4), 281-289.
- 30. Piomboni, P., Focarelli, R., Stendardi, A., Ferramosca, A., & Zara, V. (2012). The role of mitochondria in energy production for human sperm motility. International journal of andrology, 35(2), 109-124.
- 31. Falchi, L., Galleri, G., Dore, G. M., Zedda, M. T., Pau, S., Bogliolo, L., ... & Ledda, S. (2018). Effect of exposure to CeO2 nanoparticles on ram spermatozoa during storage at 4 C for 96 hours. Reproductive Biology and Endocrinology, 16(1), 19.
- 32. Remião, M. H., Lucas, C. G., Domingues, W. B., Silveira, T., Barther, N. N., Komninou, E. R., ... & Collares, T. (2016). Melatonin delivery by nanocapsules during in vitro bovine oocyte maturation decreased the reactive oxygen species of oocytes and embryos. Reproductive toxicology, 63, 70-81.
- 33. Amann, R. P., & Waberski, D. (2014). Computer-assisted sperm analysis (CASA):

- Capabilities and potential developments. Theriogenology, 81(1), 5-17.
- 34. Wang, R., Pan, W., Jin, L., Li, Y., Geng, Y., Gao, C., ... & Liao, S. (2019). Artificial intelligence in reproductive medicine. Reproduction, 158(4), R139-R154.
- 35. Rolfes, V., Bittner, U., Gerhards, H., Krüssel, J. S., Fehm, T., Ranisch, R., & Fangerau, H. (2023). Artificial intelligence in reproductive medicine—an ethical perspective. Geburtshilfe und Frauenheilkunde, 83(01), 106-115.
- 36. Letterie, G. (2023). Artificial intelligence and assisted reproductive technologies: 2023. Ready for prime time? Or not. Fertility and Sterility, 120(1), 32-37.
- 37. Canon, C., Leibner, L., Fanton, M., Chang, Z., Suraj, V., Lee, J. A., ... & Hoffman, D. (2024). Optimizing oocyte yield utilizing a machine learning model for dose and trigger decisions, a multi-center, prospective study. Scientific Reports, 14(1), 18721.
- 38. Adeoye, O., Olawumi, J., Opeyemi, A., & Christiania, O. (2018). Review on the role of glutathione on oxidative stress and infertility. JBRA assisted reproduction, 22(1), 61.
- 39. Correa, N., Cerquides, J., Vassena, R., Popovic, M., & Arcos, J. L. (2024). IDoser: Improving individualized dosing policies with clinical practice and machine learning. Expert Systems with Applications, 238, 121796.
- 40. Letterie, G., & Mac Donald, A. (2020). Artificial intelligence in in vitro fertilization: a computer decision support system for day-to-day management of ovarian stimulation during in vitro fertilization. Fertility and Sterility, 114(5), 1026-1031.
- 41. Zmuidinaite, R., Sharara, F. I., & Iles, R. K. (2021). Current advancements in noninvasive profiling of the embryo culture media secretome. International Journal of Molecular Sciences, 22(5), 2513.



- 42. Close, R. (2024). The fertility fix: The boom in facial-matching algorithms for donor selection in assisted reproduction in Spain. The New Bioethics, 1-17.
- 43. VerMilyea, M., Hall, J. M. M., Diakiw, S. M., Johnston, A., Nguyen, T., Perugini, D., ... & Perugini, M. (2020). Development of an artificial intelligence-based assessment model for prediction of embryo viability using static images captured by optical light microscopy during IVF. Human Reproduction, 35(4), 770-784.
- 44. Rodríguez-Fuentes, A., Rouleau, J. P., Vásquez, D., Hernández, J., Naftolin, F., & Palumbo, A. (2022). Volume-based follicular output rate improves prediction of the number of mature oocytes: a prospective comparative study. Fertility and sterility, 118(5), 885-892.
- 45. Benjamens, S., Dhunnoo, P., & Meskó, B. (2020). The state of artificial intelligence-based FDA-approved medical devices and algorithms: an online database. NPJ digital medicine, 3(1), 118.

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