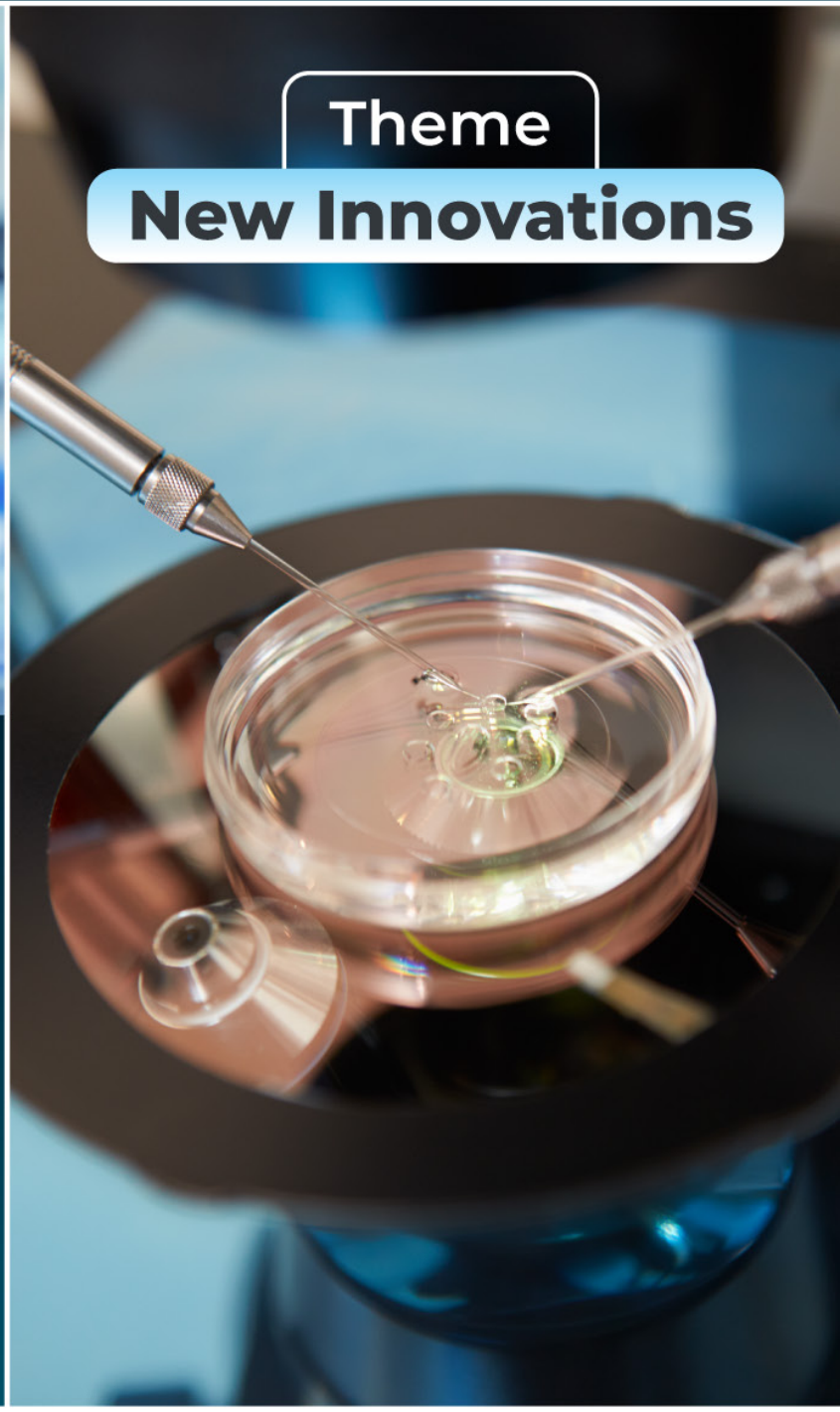
Indian Fertility Society

IFS Conversations

Vol 18



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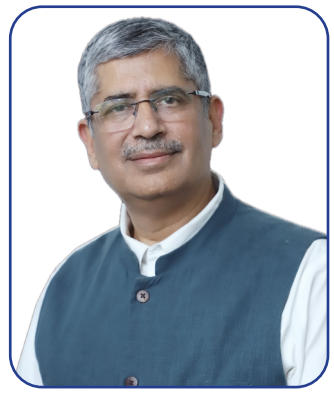
Message from the **President's Desk**



Dr Pankaj Talwar
President

Dear Friends,

It is indeed a pleasure to address you all on this issue of IFS Conversations. We look forward to seeing you all at Ahemdabad, from 6th to 8th Dec. 2024.

In this IFS conversation we have dealt with detailed new innovations. The editorial team and the authors have worked very hard towards it. Hope you all will find it very useful. The conversation also showcase various recent academic activities conducted by our extremely enthusiastic and committed members of state chapters and Special interest groups.

Wishing you all a very pleasant reading of this issue of IFS Conversation!

Message from the **Secretary Desk**

Dr Shweta Mittal
Secretary General

Dear Friends,

Greetings from team IFS
IFS conversations is the official newsletter, this particular issue focuses on the innovations in the fiield of Reproductive medicine and infertility. Hope all members enjoy reading and keeping them professionally updated.

Please go on to the IFS website and answer the surveys we have put in for pan India data collection We look forward to seeing you participate actively in Fertivision 2024 at Ahemdabad where you would see IFS at its best – academically, socially and culturally bringing together global and national leaders in the field and please go through the iterature published by IFS. Do not miss it!

Message from the **Editor's Desk**

Dr Rupali Bassi Goyal
Editor

Dear Friends,

Greetings from team IFS
We are pleased to release this edition of IFS Conversations which is based on theme "New innovation"
It has collection of articles on different aspects like AI, newer concepts in imaging, genetics, OTC, Yoga and sexology. It specially covers interviews of Lifetime awardees, President and Gen. Sec.

We sincerely thank all our authors for their wholehearted contribution towards this issue of IFS conversation. We would love to hear your comments and suggestions and encourage all our readers to contribute in our forth-coming issues of IFS conversations.

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Invited Articles

Vitrification: Fast and Furious

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Since the birth of first IVF baby in 1978,[1] assisted reproductive technology (ART) helped millions of couples dream of parenthood. [2] The advancements in the technologies including ovarian stimulation regimes, sperm preparation methods, embryo culture systems, laboratory standards, quality checks throughout the treatment cycle, and most importantly cryopreservation of gametes, embryos, and reproductive tissues were witnessed across the nations. Implementation of cryopreservation in the ART treatments significantly improved cumulative pregnancy rates and live birth rates. Also, it enabled the application of an elective single embryo transfer (eSET), which reduced the risk of multiple gestation.

Earlier, the human embryos were preserved using "slow freezing" procedure.[3] The technique of slow freezing was replaced by the "vitrification" procedure.[4]. The vitrification procedure was a real breakthrough technology in ART those days. High survival rates at warming, frozen Embryo Transfers (FETs) enhanced the quality of ART treatment by increasing the cumulative pregnancy outcomes. [5,6] Vitrification uses a high concentration of cryoprotective agents (CPAs) which increase viscosity and inhibit the ice crystal formation[7]. Successful vitrification correlates with several features like temperature during the vitrification and warming steps, concentration, time of exposure, and type of cryoprotective agents used (CPAs). The cooling rates and the warming rates are very important for the survival of gametes, embryos and reproductive tissues. At any stage, cryo-damage can occur, recrystallization during the warming step will affect the cryo-survival rates [8].

Cryoprotective agents - CPAs and Vitrification:

The choice of cryoprotective agents and their concentrations will have a direct influence on the outcomes. The CPAs are majorly of two types, penetrating and non-penetrating. The penetrating CPA has a smaller molecular weight (<400 Da). For example, CPAs like Dimethyl Sulfoxide (DMSO), Ethylene glycol (EG), Glycerol, propylene glycol, or 1,2 propanediol (PROH), etc. The nonpenetrating CPAs on the other hand have a higher molecular weight for example, Glucose, Sucrose, Galactose, Mannitol, Polyethylene glycol, polyvinylpyrrolidone, etc. The penetrating CPAs enter the cell membrane and protect the cell from any damage due to the low temperatures and the nonpenetrating CPAs create an osmotic gradient during the process which leads to the water diffusing out of the cell thereby minimizing the chance of intracellular ice formation.[9]

Indications for cryopreservation in ART treatment:

Several indications and the rationale for cryopreservation of the embryos in ART treatments are mentioned in Table1, which includes the risk of OHSS,[10,11] Pre-Implantation Genetic testings providing the required time interval between embryo biopsy and genetic analysis (12), Fertility preservation,[13,14] eSET (elective Single Embryo transfer) to reduce the no of embryos to transfer per cycle to minimize the risk of multiple pregnancies, [15,16,17] to avoid the negative impact of the elevated hormone (progesterone) levels in the late follicular phase[18] other medical conditions like Endometritis, Endometriosis, tubal factors etc.[19]

The vitrification protocol is based on the principle: exposure to small volumes of highly concentrated solution containing CPAs for a short time and a very high rate of cooling/warming which prevents intercellular and intracellular ice formation. [20] During the vitrification-warming process, the embryos get exposed to non-physiological oxygen tension, and a high concentration of oxygen may increase levels of ROS and events leading to apoptosis.[21,22,23,24]

Vitrification - Warming FAST and FURIOUS approach:

The vitrification and warming protocols currently applied are efficient and resulted in increasing live birth rates. Recently, new approaches were proposed to optimize the embryology lab workflow which helps improve the cumulative pregnancy rates. Currently, multi-step vitrification and warming protocols (Figure 1) are followed by many labs which involve exposing the embryos through a series of solutions containing cryoprotective agents (CPAs) during the vitrification procedure and passing through a series of solutions of decreasing osmolality during the warming procedure. The multi-step strategies have shown good survival rates as well as good outcomes. These multi-step procedures are time-demanding (10–15 min) and laborious as well. Quick removal of CPAs and allowing water to rehydrate the embryo gradually minimizes the damage during the vitrified-warming process. This reduces the overall time required during the vitrification-warming of embryos.[25,26,27]
This warming strategy involves neither DS (dilution solution) nor WS (washing solution) and only requires TS (thawing solution) for 1 min at 37° C. Later the embryo is transferred into culture media. This 1-min one-step rehydration strategy exhibited high survival rates and, significant implantation and pregnancy rates.[29] The new vitrification approach is quick and time-saving, the embryos and oocytes are exposed briefly (2 mins) to the equilibriation solution for 1 min and the vitrification solution for 1 min before loading into the vitrification device. The exposure time gradually reduced from 12-15 mins to 2 mins. Gallardo and colleagues advocated that reducing the duration of the procedure would improve the workflow in the laboratory and also reduce time of exposure to suboptimal temperature, a high concentration of oxygen, and toxicity of the CPAs, osmolality as well. They investigated a rehydration-based protocol with a short duration where the warming was performed with only 1-minute exposure in Thawing Solution (TS) using discarded human oocytes and abnormally fertilized zygotes.[28] The new short-duration protocol showed 100% survival rates 30 out of 30 (oocytes) and 27 out of 27 (zygotes), out of 27 survived abnormal zygotes, 24 (88.88%) cleaved after 24 hours.
In the largest published study so far by Liebermann and co-workers, the new one-step warming approach is not just quicker, less laborious and simpler than the multi-step protocol, but also with promising results. [28] 3,439 FETs were retrospectively analyzed and compared clinical outcomes between the one-step rehydration protocol and multi-step approach. Both the arms showed 99.5 % survival rates. The Clinical Pregnancy Rates were 63.0% for the one-step warming protocol and 59.9% for the multi-step rehydration protocol, which were comparable.
Ongoing pregnancy rates were 60.4 % and 55.4 % for the one-step warming protocol and multi-step rehydration protocol respectively. Also, lower spontaneous miscarriage rates (4% in one-step versus 7.6% in the multi-step arm, p = 0.0001) were observed. Liebermann et al also examined the fast and furious methods of vitrification and warming of oocytes by reducing the time of exposure to solutions and demonstrated successful survival and resumption of meiosis using a short protocol. 561 GVs(germinal vesicles) and 218 M1 (metaphase I) oocytes were frozen using the new freezing approach at room temperature for 2 min. The warming was done at 37°C for 2 min. After 24 and 48 hrs of culture, the resumption of meiotic activity was evaluated[30] The results were promising, 95% of GVs and 95.4% of the metaphase-I oocytes survived. Out of 533 GVs, 92.1% (491 out of 533)converted to metaphase I and after 48 hrs, 54.4% converted to metaphase II oocytes. The survival rates and the meiotic activity resumption were not compromised in the immature oocytes vitrified using a new strategy which is an absolute fast and furious approach.

To conclude, it was demonstrated that shortening the time of exposure to the CPAs during vitrification and a one-step approach during warming can contribute to higher survival rates as well as improved outcomes. A significant time-saving approach from 10–15 mins to 1 min of bench time for the embryologist, does not impact pregnancy or implantation rates negatively. This fast and furious approach towards the vitrification and warming of embryos and oocytes is surely going to bring a significant change in the laboratory workflow and reduce the embryologists bench time as well. Concerns regarding the duration of the procedure and reduced time of exposure during the vitrification and warming processes may impact the safety and acceptability of this new fast and furious strategy. Potential long-term follow-up is necessary. With the steady increase in the number of patients requiring cryopreservation during their fertility treatment, the laboratories need more efficient and

consistent protocols to minimize cryo-damage and maximize the outcomes.

Fig: 1 Diagram illustrates the multi-step Vitrification and Warming procedures

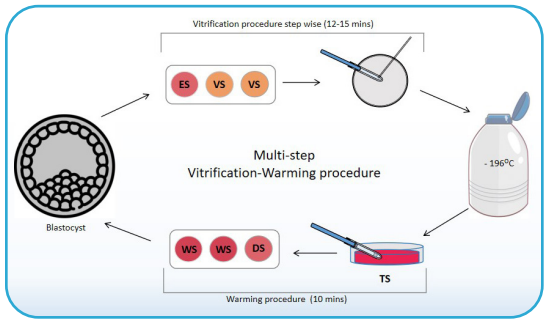

Table: 1 Indications for Cryopreservation in ART treatments

Indications	Rationale
Risk of OHSS	When a fresh embryo transfer cannot be carried out due to the risk of aggravated hyper stimulation
PGT	To provide time for checking the Genetic analysis of the embryo before transfer.
Surplus embryos	Surplus embryos preserved following fresh Embryo Transfer.
Fertility preservation	In women with a stable partner, about to go through gonadotoxic/chemotherapy treatments for cancer, there may be time in which to undergo a cycle of IVF and have embryos cryopreserved
eSET	To reduce the number of embryos transferred during a fresh cycle to minimize the risk of multiple pregnancy
Elevated hormone levels	To avoid the negative impact of the elevated hormone levels in the late follicular phase,
Medical pathology	Like hydrosalpinges, endometriosis, endometritis, fluid in endometrial cavity etc,.

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The A to Z of Witnessing in IVF

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Infertility affects approximately 50 million couples globally and patients are increasingly seeking medical intervention to conceive through IVF procedures.[1] Success rate depends upon numerous factors mainly patient related variables but also depends on new technologies and equipment incorporated in the laboratory. Sometimes, IVF procedural steps are susceptible to human errors with potentially deleterious consequences. For example, sample identification and mismatching errors may occur.

In fact, since the first known case of an ART mix-up in 1987 in Manhattan, USA, the accidental use of incorrect gametes or embryos during ART procedures has been reported in centres around the world.[2] Even though the occurrence of ART mix-ups is rare, their consequences are devastating for both the couples and fertility centres, leading to complex legal actions against the clinics. Therefore, mechanisms to prevent these unintended accidents are currently being sought by the fertility clinics.

Measures to prevent Assisted Reproductive Technologies (ART) mix-ups, such as labelling of all labware and manual double-witnessing protocols are currently in place in fertility clinics worldwide. Advanced cutting edge technological solutions for electronic witnessing are also being developed. One such recent innovation is the introduction of Electronic Witnessing System (EWS) in Infertility Clinical Practice.

The goal of Electronic Witnessing System is to ensure accurate identification and prevent mix ups. Critical Points during the clinical and laboratory IVF procedures are identified where mismatching of Gametes and Embryos may occur. These critical points are:[1]

1. Ovum Pick-up,
2. Sperm Collection,
3. Preparation of Sperm,
4. Insemination (IUI, IVF, ICSI),
5. Transferring Gametes and Embryos between tubes or dishes,
6. Embryo Transfer, and
7. Embryo or Gametes Cryopreservation.

Types of Witnessing Systems

1. Manual Witnessing: This is an old method used initially, a manual process where a healthcare professional verifies and documents each step of the process often using a paper checklist. It requires a trained Witness, usually a Fertility Specialist or an Embryologist. This person verifies the identity and handling of Gametes or Embryos at critical points. However, this mechanism of control has been shown to be vulnerable to human errors.[1]
2. Witnessing System based on Silicon Barcodes: In this type of system, Silicone barcodes are injected directly into Oocytes or Embryos.[3] [4]
3. Electronic Witnessing System (EWS): This new tracking system, also known as "Electronic Witnessing System", adds an extra layer of security to each step of the IVF process by assisting with the identification of patients and traceability of their reproductive cells or Gametes. Essentially, the tracking system ensures that the eggs, embryos and sperm belonging to you are used in your treatment. Every culture dish, specimen tube or plasticware consumables that are used at any point in the IVF process are labeled with a unique barcode or RFID tag that links each item to the intended patient's chart. Each time a patient's eggs, embryos or sperm are handled in the lab, the Embryologist will scan the barcode or RFID tag as additional confirmation that the dishes are correctly labeled and belong to the intended patient.

Electronic Witnessing Systems use Barcode scanning or RFID tags for patient and sample identification. RFID tags are a type of tracking system that uses radio frequency to search, identify, track, and communicate with items and people. These identification systems help mitigate the risk of human error during transfer or movement of samples from one dish or tube to the other, and safeguard every step of IVF cycle. RFID tags are circular or rectangular in shape and stick to the side of the plasticware used for clinical processing of IVF samples. They are patient specific and can record all credentials of the patient like name, personal data, blood group, fingerprint and face.

Principle of Electronic Witnessing Systems

Barcode based Electronic Witnessing System: Let us first understand the working of a barcode based Electronic Witnessing System. Barcodes are used for tracking patient and sample data for centralized recording in a computer software system. A Laser light from a scanner is shone on the barcode label surface and its reflection is captured by a sensor to read a barcode. However, barcodes have no read/write capabilities and hence have limitations. The systems are very labour intensive; as the samples must be scanned individually. The operator must remember the sequence of the process and manually scan each dish or plasticware during the process. This inconvenience resulted into skipping errors and hence lower adoption of these systems. More recently, there has been innovation in EWS development leading to the development of RFID based Electronic Witnessing Systems.

RFID (Radio Frequency Identification) based Electronic Witnessing System: Let us now understand the RFID (Radio Frequency Identification) based Electronic Witnessing System in detail. This system consists of hardware and software. Software processes and displays easy to understand visual interfaces on screen. It uses dual biometric recognition system which includes Face recognition and Fingerprint recognition, eliminating the need for manual double witnessing. It uses RFID tags to track and verify the identity of every patient and their sample involved in the process. Most RFID tags are incredibly small and moderate radio frequencies are used. The exposition time to gametes or embryos is limited to a few seconds hence safe. When in the incubator, the tags do not receive or emit any radio waves. It is a web-based witnessing system where real-time data is generated leaving no room for ambiguity or oversight.

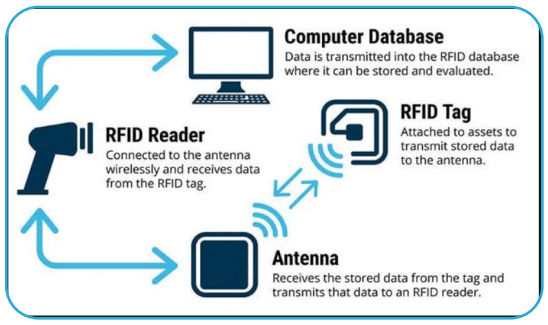
It keeps track of all events at all times, answers every question related to the ART process and events like Who, What, Where and When. Here the work area is the viewing area under the microscope. The system helps in avoiding unwanted mismatch errors in the work area. The EWS System triggers alarm (visual and audio), alerting the Embryologist for mismatch, thus preventing mixing of samples. These systems are configured as per the requirements and work flow of the clinic, monitoring each step in the IVF cycle.

Picture 1: A Typical Set-up of an Electronic Witnessing System

How does an Electronic Witnessing System work

- It starts with assigning Unique ID cards to the patients.
- Their data and Biometric credentials i.e. Fingerprint and Face are recorded on the system.
- Role of the patient is assigned as Patient, Recipient, or Donor.
- Each dish and plasticware holding patient's sample is tagged and assigned to their credentials.
- Egg collection and semen collection jars are linked to unique ID cards.
- Each dish and plasticware is connected and matched with previous dish or plasticware before starting the procedure.
- Every work area in the IVF lab detects wireless signals from these RFID tags. An antenna is built-in in the readers. This antenna emits the radio waves to transmit signals that activate the tag. The information present on the tag is translated to the detector. The software in the computer decodes that specific radio frequency and displays details of the patient/dish/tube which is then verified with the data in the software. One such system, SURETY™ Witness System has successfully filed a patent about the unique design of its compact RF Detector which consists of a circular antenna inserted in the light source itself. This unique compact design helps to avoid false mismatches which are prone to happen in other RFID based witness systems.

Here is a schematic of how the RFID tag information is passed to the computer.



Advantages of an RFID based witnessing system

There are 2 significant advantages of an RFID based witnessing over a Barcode based system:

- An RFID system safeguards against the users unintentionally working on multiple patients' eggs or sperms simultaneously.
- An RFID system records each step of the ART procedure, preventing the omission of crucial steps. The adoption of these types of EWS is swiftly expanding across the IVF clinics globally.[4]

Given below is a comparison between the 2 types of systems.

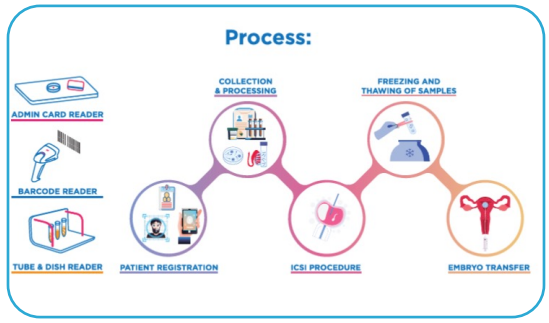
	Barcode Based System	RFID Based System
Ease of Scan	In a barcode based system, there is a need to scan each dish, lined up or individually placed side-by-side in the line of sight for scanner to read and verify that they are compatible. Samples are required to be moved out of the work area for scanning.	In an RFID based system dishes can be read simultaneously, automatically allowing the Embryologist to work uninterruptedly.
Dependency On The Operator	Barcode security relies on the operator remembering to perform check scans. There is no automatic alert or action if the Embryologist forgets to scan the barcode.	An RFID based system automatically monitors the work area under the microscope constantly so that there is no chance of oversight or escape.
Alerts Automatically	Using a barcode system, two unrelated samples can be placed in the same work area and may even be unintentionally manipulated.	In an RFID based system, work area is the viewing area under microscope. If two incompatible samples are placed under the microscope the RFID detector alerts the Embryologist about the mismatch, visually and audibly. It does not allow the Embryologist to proceed further until the error is resolved.
Interruption of Workflow	In both barcode and manual methods specific movements in the IVF cycle are logged manually. The workflow is interrupted during checks.	This is not the case in an RFID based systems as monitoring is done continuously whenever any activity is performed under the microscope.

Salient features of RFID based electronic witnessing system

- There are 2 significant advantages of an RFID based witnessing over a Barcode based system: Unique design of RF detector and placement to avoid false mismatch.
- AI based face recognition and fingerprint recognition for witnessing.
- Very small tags for uninterrupted view of the Embryologist.
- User friendly application.
- Flowchart, witness point diagram and protocols can be created according to the clinic's need.

- Substantial data is generated which helps in intralab or clinic-group comparisons.
- The signals are identified, tracked and recorded at each step of the ART process.
- An EWS can manage PGT procedures and Cryopreservation procedures as well as the tags can withstand cryopreservation temperatures (-196°C).

Given below is a schematic of an ART process.

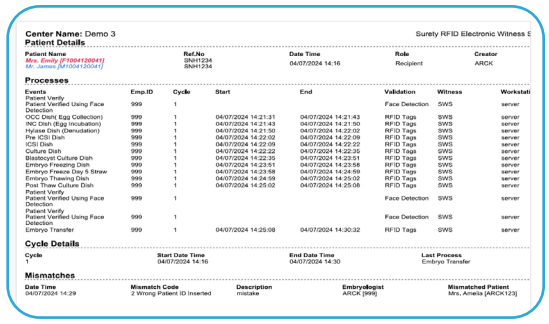


Picture 2: ART Process

On top of the security of gametes and embryos, these witness systems can also be used to improve other aspects of lab such as,

- Keeping patient records,
- Scheduling appointments,
- Daily overview of procedures,
- Inventory management, and
- Workflow management of staff.

Different Reports can be generated related to Patient cycles, Mismatch errors, and Consumable reports per cycle.



Picture 3: An Example of a Detailed Patient-wise Report

Benefits and ease of use of Electronic Witnessing System

Electronic Witnessing Systems are user friendly and it takes hardly any time to get acquainted. After getting initial information and confirmation from the clinic, mapping of locations for readers and sensors is carried out, followed by installation of hardware and software. A Witness Point Diagram in the form of flowchart is created according to the Centre's needs, requirements and the workflow. A demo is run to test the step-by-step process mentioned in the Witness Point Diagram. For a certain period, the system is validated where human double check and witnessing using RFID is carried out simultaneously.

Though mix-ups or mismatches are rare events, the necessity of incorporating witnessing systems is increasing. IVF Clinics could face legal challenges and regulatory sanctions while patients would have to cope with the psychological damage and loss of confidence in IVF process. A survey was carried out for "Patient's awareness and concerns about a possible mismatch error and their satisfaction level in response to integration of witnessing system in clinical procedures". It was observed that from psychological perspective witnessing system increased Patient's well-being and very importantly confidence in the clinic during IVF procedures and helped in minimizing additional stress that could overload patient's emotional balance while undergoing treatment[2]. On the other hand, considering mismatch of gametes can stake the reputation of clinic leading to catastrophic effects, the Clinician's and Embryologist's perspective also changed and they find complete peace of mind. It also helps Clinicians and Embryologist to keep transparency with Patient making them feel involved in the ART process[2]. The system and its reports generate useful data that can be used in productivity analysis of the clinic, and also helps in research activity.

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Genomics in AI: Current Concepts

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Introduction

The intersection of genomics and artificial intelligence (AI) represents one of the most promising frontiers in modern science, driving significant advancements in personalized medicine, disease prevention, and therapeutic development. Genomics, the study of an organism's complete set of DNA, including all of its genes, has provided vast datasets that fuel the development of AI algorithms. This synergy between genomics and AI is revolutionizing how we understand, diagnose, and treat diseases, leading to more precise and effective healthcare solutions.

Genomics as a Catalyst for AI Evolution

The primary impact of genomics on AI lies in the sheer volume and complexity of data it generates. Human genomes consist of approximately 3 billion base pairs, and with the advent of high-throughput sequencing technologies, we can now sequence entire genomes quickly and affordably. These vast datasets are ideal for training AI models, which thrive on large-scale data to uncover patterns, predict outcomes, and identify anomalies. This synergy between genomics and AI is evidenced by studies highlighting the value of genomic data in advancing machine learning models and enhancing their performance in various tasks (Morris et al., 2021; Zeng et al., 2022). For instance, high-throughput sequencing technologies, such as those discussed by Mardis (2008), have revolutionized genomic research by enabling comprehensive analysis of genetic variations and contributing to the development of powerful AI tools.

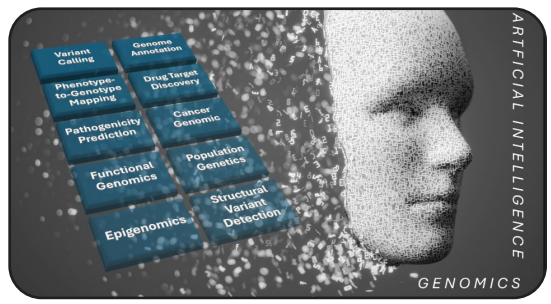
AI's ability to analyze and interpret genomic data has accelerated our understanding of the genetic basis of diseases. For instance, AI models can analyze genomic sequences to identify genetic variants associated with conditions like cancer, diabetes, and cardiovascular diseases (Koboldt et al., 2013; Li et al., 2021). These insights enable the development of targeted therapies and personalized medicine, tailoring treatments to an individual's genetic makeup for improved efficacy and reduced side effects (Miller et al., 2018; Collins & Varmus, 2015).

The integration of genomics into AI is profoundly shaping the future of artificial intelligence by providing vast, complex datasets that drive the development of more sophisticated algorithms. As AI models analyze genetic sequences, they uncover intricate patterns and relationships, enhancing their ability to predict outcomes, identify biomarkers, and enable personalized medicine (Zou et al., 2019; Libbrecht & Noble, 2015). This symbiotic relationship accelerates AI's evolution, fostering breakthroughs in fields such as precision medicine, drug discovery, and disease prevention (Chen et al., 2018; Topol, 2019). Ultimately, genomics not only expands the scope of AI applications but also enhances its accuracy, making AI a more powerful tool in healthcare and beyond.

The intersection of genomics and artificial intelligence (AI) is ushering in a new era of possibilities in both research and clinical diagnostics. As advancements in DNA sequencing technology generate unprecedented volumes of data, the challenge lies in effectively analyzing and interpreting this wealth of genetic information (Mardis, 2008; Goodwin et al., 2016). AI, with its unparalleled ability to process large datasets and identify complex patterns, is revolutionizing the field of genomics, paving the way for groundbreaking discoveries and innovations in healthcare (Esteva et al., 2019; Ghiassian et al., 2021).

Key applications of AI in genomics include:

- Variant Calling: AI algorithms are proficient at analyzing genomic data to identify genetic variants, such as single nucleotide polymorphisms (SNPs) and insertions/deletions, which are linked to various diseases. This application is crucial for personalized medicine, enabling precise risk assessments and tailored treatment strategies (Poplin et al., 2018).
- Genome Annotation: AI significantly enhances the annotation of genomic sequences by identifying genes, regulatory elements, and functional regions. This process is particularly vital for understanding the non-coding regions of the genome, which play key roles in gene regulation and expression (Yates et al., 2020).
- Phenotype-to-Genotype Mapping: AI models facilitate the correlation between phenotypic traits (observable characteristics) and specific genetic variations. This mapping is essential for deciphering the genetic basis of diseases and predicting susceptibility to various conditions (Wainberg et al., 2019).
- Drug Target Discovery: AI's ability to analyze genomic data allows for the prediction of potential drug targets by identifying relevant proteins or pathways involved in disease processes. This application is instrumental in the development of precision therapies and novel treatments (Wang et al., 2020).
- Pathogenicity Prediction: AI aids in assessing the pathogenicity of genetic variants by distinguishing between benign and disease-causing mutations. This capability is crucial for clinical decision-making and improving patient outcomes (Choi et al., 2015).
- Cancer Genomics: In cancer genomics, AI plays a pivotal role in analyzing tumor genomes to identify driver mutations, predict treatment responses, and guide personalized cancer therapies. Additionally, AI assists in tumor subtyping and prognosis, further enhancing the precision of cancer treatment (Chen et al., 2020).
- Functional Genomics: AI integrates multi-omics data (genomics, transcriptomics, proteomics) to provide a comprehensive understanding of gene function, regulatory networks, and disease mechanisms. This holistic approach reveals novel biomarkers and therapeutic targets (Sharma et al., 2021).
- Population Genetics: AI's ability to analyze genetic variation across populations offers valuable insights into evolutionary history, migration patterns, and disease prevalence. This application is critical for identifying population-specific risk factors and informing public health strategies (Martin et al., 2019).
- Epigenomics: AI investigates epigenetic modifications (such as DNA methylation and histone modifications) and their impact on gene expression. This research informs our understanding of disease mechanisms and potential interventions (Zhang et al., 2018).
- Structural Variant Detection: AI algorithms detect large-scale genomic rearrangements (such as deletions, duplications, and inversions) associated with genetic disorders. These algorithms complement traditional variant calling methods, offering a more comprehensive view of the genome (Chaisson et al., 2019).



Genomics and AI: A natural Alliance

As Genomics is enriching AI, Simultaneously, AI is rapidly establishing itself as an essential tool in genomics, transforming the study of genetic data and its implications for human health. Genomics, which involves the comprehensive analysis of an organism's DNA, provides critical insights into genetic risks, diseases, and personalized treatments. AI's capabilities in handling vast amounts of data and uncovering intricate patterns make it an invaluable asset in this domain. Among the AI tools, transformers have emerged as particularly powerful allies in this domain.

Transformers: A Breakthrough in DNA Sequence Analysis

Genomic data plays a significant role in advancing Artificial Intelligence (AI) by improving machine learning techniques, particularly through the use of Transformers (Yue T., 2023). The extensive DNA sequence data produced by evolving sequencing technologies serves as a valuable resource for developing robust AI tools. However, this data is prone to errors due to the challenges in accurately identifying DNA base pairs from electrochemical signals, leading to noise that complicates tasks such as classification, annotation, and sequence transformations (Adir et al., 2019).

Transformers, originally developed for natural language processing, are well-suited for genomic analysis because of their ability to model long-range dependencies in sequential data (Arima et al., 2020). Unlike traditional models, Transformers do not depend on fixed context windows, allowing them to capture complex relationships between distant elements in a sequence. This characteristic is particularly advantageous for DNA sequences where functional regions may be widely separated but still interact functionally (Wang et al., 2010). Transformers demonstrate noise resilience, thanks to self-attention mechanisms that enable them to focus on relevant sequence parts despite base pair errors. Their scalability makes them ideal for handling the vast amounts of DNA data generated by modern sequencing technologies (Kuai et al., 2018).

Furthermore, the versatility of Transformers enables their adaptation for various genomic tasks such as sequence classification, annotation, and transformation. Pre-trained models like BERT can be fine-tuned for specific DNA-related analyses, leveraging general features learned from extensive datasets for more specialized applications (Yanrong Ji., 2020). The integration of AI and genomics through Transformers opens up new possibilities for utilizing genomic data to enhance AI capabilities, leading to innovative advancements in both fields

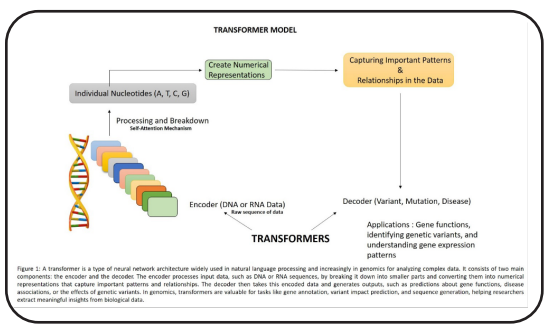


Figure 1: A transformer is a type of neural network architecture widely used in natural language processing and increasingly in genomics for analyzing complex data. It consists of two main components: the encoder and the decoder. The encoder processes input data, such as DNA or RNA sequences, by breaking it down into smaller parts and converting them into numerical representations that capture important patterns and relationships. The decoder then takes this encoded data and generates outputs, such as predictions about gene functions, disease associations, or the effects of genetic variants. In genomics, transformers are valuable for tasks like gene annotation, variant impact prediction, and sequence generation, helping researchers extract meaningful insights from biological data.

The ENBED Model: A Novel Approach to DNA Sequence Analysis

A prime example of Transformer-based innovation in genomics is the Ensemble Nucleotide Byte-level Encoder-Decoder (ENBED) model. This model, utilizing byte-level tokenization and an encoder-decoder architecture, is specifically designed for DNA sequence analysis. ENBED has outperformed state-of-the-art models in various genomic tasks, such as identifying enhancers, promoters, and splice sites, as well as generating mutations (Malusare et al., 2023).

The model's byte-level tokenization offers resilience to sequence variations, while its sub-quadratic attention implementation enhances processing efficiency. ENBED's architecture includes a modified T5 Transformer with specific adjustments tailored for DNA sequences, such as a unique tokenizer and an optimized encoder-decoder ratio.

Applications and Impact of the ENBED Model

ENBED excels in critical genomic tasks, including identifying enhancers, promoters, and splice sites, offering key insights into gene regulation. It accurately recognizes sequences with base call mismatches and insertion/deletion errors, maintaining precision where other models falter. ENBED also aids in annotating biological functions in genomic sequences, particularly in non-coding regions. Additionally, it can generate predictive analysis of microbial mutations and validate them against real-world data, providing valuable insights into microbial evolution. With a 95% accuracy in detecting erroneous DNA sequences and an F1 score of 0.71 for high-error regions, ENBED significantly advances AI in genomics.

Challenges and Considerations for Transformers

Despite their many advantages, the use of Transformers in genomics is not without challenges:

- Computational Cost: Transformers are computationally demanding, particularly when applied to very long sequences typical of genomic data. Techniques such as model pruning, distillation, and efficient attention mechanisms are necessary to mitigate these costs.
- Interpretability: While Transformers excel in prediction, understanding the biological relevance of their predictions and interpreting the learned features can be challenging. This remains an active area of research, with ongoing efforts to develop more interpretable models.

Ethical Considerations in Genomics Driven AI

While the impact of genomics on AI is undeniably transformative, it also raises important challenges and ethical considerations. The vast amounts of genetic data being generated and analyzed necessitate robust data privacy measures to protect individuals' sensitive information. Additionally, the integration of AI in genomics must be guided by ethical principles to ensure that advancements in personalized medicine do not exacerbate health disparities or lead to genetic discrimination.

Furthermore, the complexity of genomic data presents challenges in AI model interpretability. Understanding how AI algorithms arrive at specific predictions is crucial, especially in healthcare, where decisions based on these models can have significant consequences. Ongoing research is focused on developing more interpretable AI models that provide transparent and explainable insights into genetic data.

The sheer volume of genetic data being processed raises important questions about how this information is stored, shared, and utilized. Establishing robust ethical guidelines is essential to protect sensitive information and maintain public trust in these technologies.

Conclusion

The integration of genomics into AI represents a paradigm shift, offering unprecedented opportunities for personalized medicine, disease prevention, and enhanced clinical outcomes. While challenges such as computational costs and interpretability persist, the benefits of AI in genomics are clear. As genomics data increases, AI technology will continue to advance its applications, driving further innovation and transforming the landscape of healthcare. However, the integration of genomics and AI must be approached with careful consideration of ethical issues and challenges related to data privacy and model interpretability. With these considerations in mind, the synergy between genomics and AI promises to revolutionize healthcare, leading to more precise, effective, and personalized treatments for patients worldwide.

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Role of Hysteroscopy in Infertility - What's the current evidence?

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Abstract.
Hysteroscopy remains the gold standard for the evaluation of uterine cavity. Intra-uterine pathologies are seen in 25% of infertile patients. Hysteroscopy serves as "see and treat "as it can be both diagnostic and therapeutic in the same sitting and improves the reproductive outcome. It's a never-ending debate that use of Hysteroscopy be a part of infertility evaluation in all or in selective cases. Till now there has been no uniform consensus on the same. More systemic and Randomized studies are needed to assess its efficacy in infertile couples.

Introduction

The International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) define infertility as failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.

The basic evaluation of the infertile couple includes tests of ovulation and tubal patency, either by hysterosalpingography (HSG) / sonohysterography (SSG), or transvaginal sonography (TVS) and semen analysis for the male partner.

Intrauterine lesions are more common in infertile women, any abnormality in the uterine cavity decreases spontaneous fertility as well as impairs Implantation rates in assisted reproduction in 10-15% of cases and 50% in cases of recurrent Implantation Failure.[1] Hence it is important to evaluate endometrial cavity. Ultrasound (USG) or HSG are considered as the primary diagnostic tools for uterine cavity abnormalities.

2 'D' Ultrasound has 84.5% sensitivity, 98.7% specificity, 98% positive predictive value and 89.2% negative predictive value[2] but its accuracy is limited in diagnosing congenital uterine malformations, distinguishing submucosal fibroids in the presence of multiple fibroids and large polyps from hyperplasic endometrium.

HSG results are cycle dependent and results may vary during different days of cycle and different phases of the menstrual cycle, due to the variable growth of the endometrium. Menstrual debris, Mucus and air bubble may mimic filling defects, and thus obliterate shadows caused by small endometrial lesions.[3]

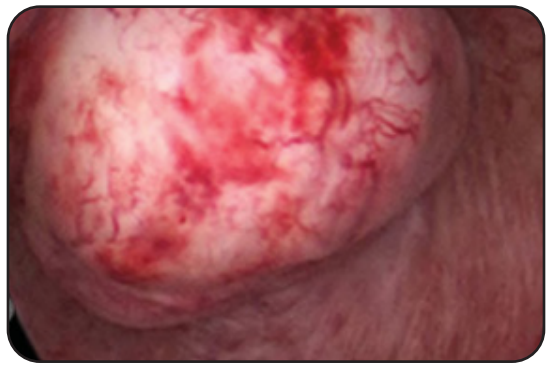
Abnormalities in approximately one-third of the patients are reported as normal on HSG and/ or Ultrasound, they may actually give false reassurance and may lead to failure of conception.

Hysteroscopy has evolved over years from direct visualization and diagnosing uterine cavity abnormalities to simultaneously diagnose and treat a multitude of intrauterine pathologies, hence is considered as the gold standard technique for uterine factor evaluation unlike the other indirect and purely diagnostic techniques, i.e. TVS, HSG and SSG. Nevertheless, the use of hysteroscopy as a routine procedure in the infertility work-up is still under debate and it is unclear at which specific step of the infertility work-up (e.g. at initial assessment as a routine in all infertile couple, prior to IUI, prior to first IVF/ICSI, when an intrauterine abnormality is suspected by non-invasive methods, or after one or more failed IVF/ICSI, etc.) hysteroscopy should be performed in order to maximize its beneficial effects on reproductive outcomes. These are

discussed below.

1. Hysteroscopy as a routine in the Fertility Workup in women with unexplained subfertility, who are trying to conceive spontaneously when ultrasound and HSG are normal. A recent systematic review of Cochrane Database by Kamath et al [4] included single RCT of 200 women with unexplained infertility of 2 years of duration, where 100 women were subjected to hysteroscopy vs no intervention in 100 women, clinical pregnancy rate (RR: 3.80, 95% CI: 2.31–6.24), miscarriage rate (RR: 2.80, 95% CI: 1.05–7.48) and the adverse effects were not statically different in both the groups. Thus there is no evidence for supporting routine hysteroscopy in primary fertility work-up of women with normal TVS or Sono hysterography , very low-quality evidence.
2. Role of Screening Hysteroscopy in unexplained infertility undergoing IUI or before first IVF/ICSI when ultrasound and HSG are normal. Hysteroscopy as a routine before IVF /ICSI increased the chances for a clinical pregnancy between 33 and 40% assuming 28% clinical pregnancy rate, relative risk 1.32 (95% CI: 1.20–1.45;), miscarriage rate (RR: 1.01, 95% CI: 0.67–1.50), both were not statistically difference ,low-quality evidence (systematic review of Cochrane Database by Kamath et al.[4]
3. In summary, there is no robust, high-quality evidence from 10 RCTs in 3,750 women that routine hysteroscopy before IVF/ICSI for various medical indications may offer a benefit for the outcomes of live birth or clinical pregnancy rate.
4. Hysteroscopies in Intrauterine pathologies Intrauterine abnormalities like endometrial polyps, submucous fibroids, uterine septa, or intrauterine adhesions are detected by hysteroscopy in 10 to 15% of infertile women seeking treatment.
   It's always a persistent dilemma -Should all Intrauterine pathologies always be removed in couples trying to conceive?

Submucous Myomas



Submucous Myoma

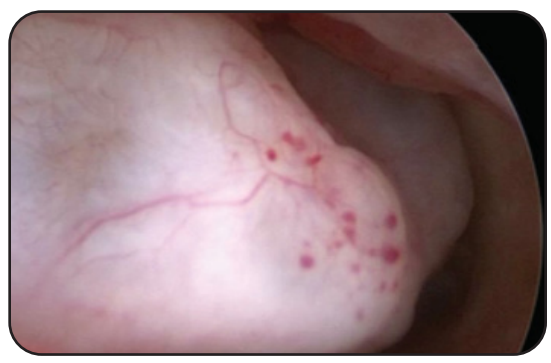
The incidence of submucosal myomas associated with infertility is estimated between 5% and 10%.

A meta-analysis by Pritts et al[5] reported that submucous myomas are associated with lower implantation rates and increased risk for pregnancy loss. Similarly Casini et al[6] reported that Pregnancy rates were statistically higher in the patients who underwent myomectomy with submucous fibroids (43.35% vs 27.2% in the nonsurgical group)

However Cochrane systemic review by bosteels et al[7] didn't show any clear benefits regarding operative myomectomy specially in couples with unexplained infertility trying to conceive normally with regular sexual intercourse (single RCT of 94 , pregnancy (OR (odds ratio) 2.44, 95% CI (confidence interval) 0.97 to 6.17; p = 0.06) and miscarriage rates (OR 1.54, 95% CI 0.47 to 5.00; p = 0.47) low quality evidence.

Nevertheless, according to the Practice Committee of the American Society for Reproductive Medicine (ASRM) and the updated French guidelines, in asymptomatic women with cavity-distorting myomas (intramural with a submucosal component or submucosal) and desire of pregnancy, myomectomy may be considered to improve pregnancy rates and reproductive outcomes.

Endometrial Polyps



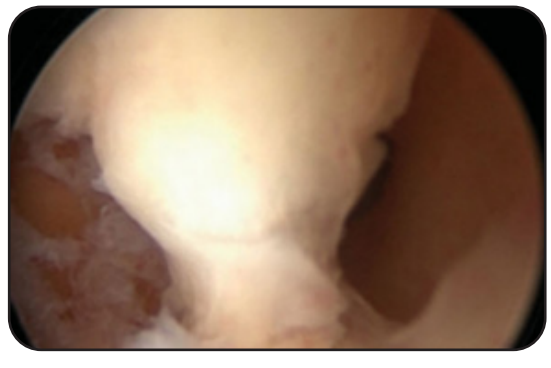
Endometrial Polyp

Perez-Medina et al[8] prospective study evaluating

204 women with 101 women underwent polypectomy prior to IUI, hysteroscopic removal of polyps showed a significant improvement in clinical PR (27). 65% of the study group achieved pregnancy before undergoing an intrauterine insemination cycle.

In another retrospective study of 230 women by Yahaihara et al (9) highest pregnancy rate, 50% to 60%, was achieved in those who had polyps removed from the utero-tubal junction, which could cause loss of function of the ostium and affect sperm passage.

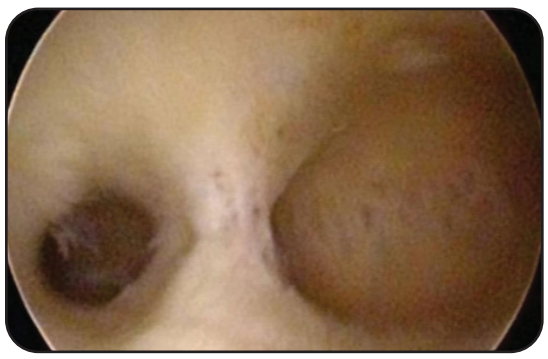
Uterine Septum



Of all the congenital anomalies, septate uterus is the most common uterine malformation, 0.2 to 2.3% of reproductive age women. Non-randomized prospective trials have shown that uterine septum is associated with 47% lower implantation rate and a 67% chance of miscarriage (10). Multiple observational studies indicate that hysteroscopic septum incision is associated with improved reproductive outcome. The uterine cavity is healed by approximately 8 weeks after hysteroscopic septum incision and this period seems to be appropriate for a woman to wait to conceive.

At present, the hysteroscopic resection is recommended by the American Society of Reproductive Medicine (ASRM) guidelines. Conversely, the European Society of Human Reproduction and Embryology (ESHRE), the National Institute for Health and Care Excellence (NICE) and the Royal College of Obstetricians and Gynaecologists (RCOG) do not support the routine use of this procedure.

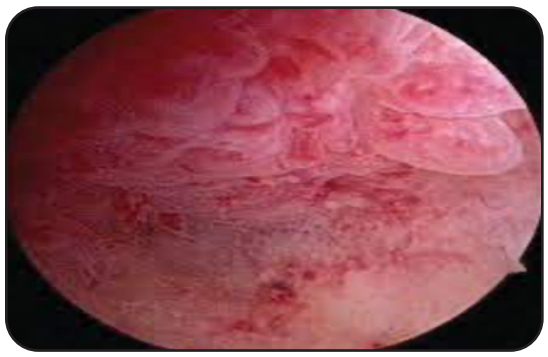
Uterine Synechiae



Intrauterine adhesions

Hysteroscopy represents the better technique for their evaluation, allowing the direct visualization of position, extent, and morphology of the adhesion. Hysteroscopic adhesiolysis has been shown to improve fertility rate and conception percentage by up to 48% (11)

Chronic Endometritis



The data on the clinical significance and implications for treatment of chronic endometritis is currently inconclusive, but there is some evidence that diagnosis and treatment based on hysteroscopy may improve outcomes in infertile patients.

Though the Cochrane data is inconclusive about operative hysteroscopy there is enough evidence in the multiple observational studies indicating improved clinical pregnancy rates in those women who undergoing operative hysteroscopy before an IVF cycle and thus examination of uterine cavity is a good practice point for the management of infertile women with a diagnosis of intrauterine abnormalities by ultrasound scan.

Should Hysteroscopy be a routine before Recurrent Implantation Failures?

Moderate quality of evidence has proven the beneficial effect of hysteroscopy for women experiencing one or more implantation failures after IVF/ICSI.

Benefits of hysteroscopy extend beyond the treatment of intrauterine abnormalities. The distending media like saline may remove anti-adhesive glycoprotein molecules on the endometrium [i.e. cyclooxygenase-2 (COX-2), mucin-1 (MUC-1) and integrin aVb3], These molecules play an important role in endometrial receptivity. Cervical dilation during pre-IVF hysteroscopy may facilitate easy entry of embryo catheter and thus may possibly improve implantation rate. Few authors have also proposed the beneficial role of endometrial scratching. The inflammatory reaction generated after endometrial scratch releases cytokines and growth factors required for implantation, such as glycodelin A,laminin alpha-4, integrin alpha-6 and matrix metalloproteinase-1 and thus enhances the endometrial receptivity thus improving clinical pregnancy rate after IVF.[12]

However, it is to be kept in mind that hysteroscopy requires general anesthesia, the operating room setting, skill of the surgeon and there is considerable cost involved in doing the procedure. Use of distention media composed of low osmolality and electrolyte-free for operative work, requires careful surveillance of fluid status to minimize complications due to fluid overload. These requirements may prohibit surgeons from considering hysteroscopy as a first-line test.

The National Institute for Health and Clinical Excellence (NICE guidelines, 2014) stated that hysteroscopy should not be offered during the initial infertility evaluation; as the effectiveness of this procedure as a routine in improving reproductive outcome has not been established.

On the other hand, according to the Practice Committee of the American Society for Reproductive Medicine (ASRM), hysteroscopy is a relatively expensive and invasive procedure. World Health Organization (WHO) recommends hysteroscopy when either clinical or diagnostic modalities like ultrasound or hysterosalpingogram (HSG) suggest intrauterine abnormality or after in vitro fertilization (IVF).

In contrast, the guidelines of the Italian Society of Gynaecological Endoscopy (SEGI), strictly recommend hysteroscopy as a screening procedure for the infertile couple as part of the primary work-up More profound emphasis is in patients undergoing in vitro fertilization/ intracytoplasmic sperm injection (IVF/ICSI) and recurrent miscarriages even if specific evidence of its usefulness in these cases is lacking.

Office Hysteroscopy

office hysteroscopy is strongly emerging as minimal invasive procedure allowing therapeutic procedure to be done in the same sitting. The use of office vaginoscopy hysteroscopy without a speculum and cervical tenaculum allows examination without the need for anesthesia and premedication. Vaginoscopy hysteroscopy is associated not only with minimal patient discomfort, but also with excellent visualization, and very low complication and failure rates (2% vs 5% with traditional hysteroscopes. The technological advances in terms of smaller diameters of the hysteroscope (2.9 mm vs 4 mm in traditional hysteroscope), better optical vision, decreased failure rate due to smaller diameter has made it a well-accepted procedure however it has its own limitations, it requires sufficient pretraining and good expertise with the traditional hysteroscopes proper skills and expertise, increased maintenance cost as they are more delicate wear out more easily, increased pain and discomfort makes the operative procedure little difficult, the visibility and distention is poor in patulous external os, and the visibility is poor in thickened endometrium, and the presence of blood inside the uterine cavity. for its diagnostic and therapeutic capacity of reliable the main intracavitary anomalies.

Its use in Indian scenario is still less as the office Hysteroscopy is not yet covered by the insurance company.

New Innovations in Office Hysteroscopy

A new device 'cryoprobe ' was used in office hysteroscopy for the removal of polyps and myomas with a diameter over 10 mm in 13 patients (aged 28 to 69) at the Department of Gynaecology , Military Institute of Medicine in Warsaw, Poland, from October 2017 to January 2018. The rigid Karl Storz Hysteroscope , Germany, with a width of 4 -5mm and working channel of 5Fr, was used for all patients[13]

Cryoprobe combines the functions of grasping and resecting . Low freezing temperature (around -70°C) at the end of the probe creates an adhesive force which allows pathological structure to get attached to the pointy end of the electrode-either after the structure has been resected or without a resection.[14] This adherence is created within a few seconds and lasts only during the freezing stage. After the tissue is connected to the probe, the hysteroscope is then removed with the probe and the attached sample from the uterine cavity. After a few seconds of the defrosting stage, the tissue is easily separated from the cryoprobe and sent for histopathology. A lower risk of bleeding due to the haemostatic features of cryotechnology is another advantage. [15]

Polyps, due to their flexibility, usually squeeze easily through the cervical canal .Small submucous myomas, the cryoprobe allows them to be totally enucleated from the uterus wall.

It is a less invasive alternative to the classical cervix dilatation using the 9mm resectoscope for small myomas; it is also easier and faster than enucleating them with the standard bipolar Twizzle tip electrode. The minimal invasiveness of the procedure is especially crucial for patients at a reproductive age, especially those who are treated due to infertility and thus may prove to be useful in office hysteroscopy.[16]

Thus cryoprobe used during ambulatory hysteroscopy may broaden the scope of possibilities of this technique by facilitating the resection of submucous myomas and endometrial polyps of a diameter above 10mm from the uterine cavity and may shorten the time of the procedure. However further studies in a bigger group are required on the safety and effectiveness of using the cryoprobe for hysteroscopic procedures.

Conclusion

". . . the womb is the field of generation; and if this field be corrupted it is in vain to expect any fruit though it be ever so well sown." Aristotle.

It is very important to have a healthy endometrial cavity for embryo to implant. Considering the cost effectiveness, routine hysteroscopy in all infertile women with unexplained infertility with normal USG and HSG/SSG findings and before first IVF is not routinely recommended. It's a good practice point that patients with

intrauterine pathologies should be individualized, counselled and decision should be taken after individualizing the benefits and adverse effects for the procedure. Patients with Recurrent Implantation Failure should be considered for hysteroscopy as uterine pathologies are seen in as high as 50% of these cases. Currently, the validity of the NICE guideline still holds: "Women should not be offered hysteroscopy on its own as part of the initial investigation unless clinically indicated because the effectiveness of surgical treatment of uterine abnormalities on improving pregnancy rates has not been established.". Large RCT's and metanalysis are needed to assess the effectiveness of Hysteroscopy in infertile cases.

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Declaration

Images are copied from the below mentioned article.

Georgi Stamenov Stamenov, Salvatore Giovanni Vitale, Luigi Della Corte, George Angelos Vilos, Dimitar Angelov Parvanov, Dragomira Nikolaeva Nikolova, Rumiana Rumenova Ganeva & Sergio Haimovich (2022) Hysteroscopy and female infertility: a fresh look to a busy corner, Human Fertility, 25:3, 430-446, DOI: 10.1080/14647273.2020.1851399

Role of 3D ultrasound and color doppler in early pregnancy

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Ultrasound is considered now an extension of gynecological examination. Most gynecologists are well versed with 2 D ultrasound. 3 D ultrasound in obstetrics is increasingly being used to diagnose complex fetal anomalies and in gynecology for the diagnosis of congenital and acquired uterine anomalies. This article is meant to explore the role of 3 d ultrasound in early pregnancy.

While performing 3 D ultrasound in early pregnancy color doppler especially power doppler should be used for minimum possible time and only if indicated i.e (ALARA-as low as reasonably achievable). This is because the heat exposure due to higher intensity of power and color doppler may impact embryological development. Thus, its use should be restricted to only if diagnostic uncertainty is there. There is displayed safety indices on the monitor which are to be adhered to. The TIS (thermal index) of soft tissue needs to be monitored in early pregnancy ultrasound, it should be kept below or equal to 1 when performing ultrasound in pregnancy <10wks.

Clinical Uses

To identify site and number of corpora lutea: Ring of fire appearance on 2 D ultrasound. Corpus lutea may appear solid, haemorrhagic or cystic and sometimes when it is solid it is difficult to see it against ovarian tissue, CD helps then. More than one corpora points towards multiple pregnancy.

Diagnose tubal ectopic -In ectopic pregnancy, the blood supply to trophoblast is seen as a separate area of increased vascularity from CL.

Detecting the fetal heartbeat as early as 6wks of gestation with color doppler provides reassurance in some selected patients.

Cervical and caesarean scar pregnancy.

In differentiating intrauterine pregnancy from

submucosal fibroid and endometrial polyp. Endometrial polyp has feeder vessel, submucosal fibroid has circular blood supply.
CD can confirm if caesarean scar or intramural pregnancy is breaching the endo myometrial junction. Presence of peripheral vasodilation in the absence of normal myometrial architecture as in scarred uterus, makes it prone to hemorrhage, the extent of vascularity is proportional to hemorrhage, so it is in ectopic too.

Pseudo AVM:

It is common physiological finding to find a

"AVM" in women where products of conception are retained over a prolonged period.
The risk of severe hemorrhage during evacuation is low as compared to previous beliefs. Normally implanted pregnancy with missed abortion showing increased flow does not have increased risk of hemorrhage.

True AVMs are a permanent feature present in nonpregnant women. They are associated with massive vasodilation of the uterine vessels, and are associated with heavy menstrual periods. They appear as areas of hypervascularity and strong turbulence in comparison with the normal myometrium around it.

Gestational trophoblastic disease

Villi in GTD are avascular on CD.GTD invading

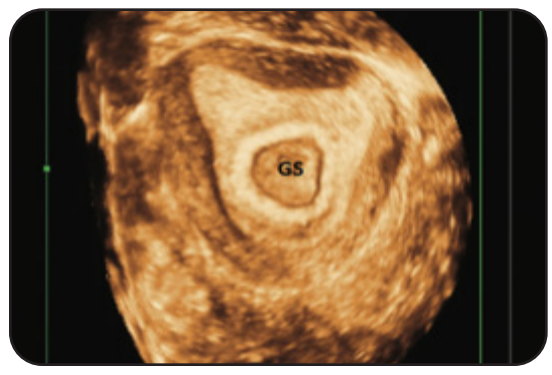
myometrium or if present for a prolonged time may show increased vascularity.

Use of 3D ultrasound in early pregnancy

Three-dimensional imaging allows clinicians

to obtain coronal views of the uterus, which is difficult using conventional two-dimensional imaging . Thus it helps in location of pregnancy.

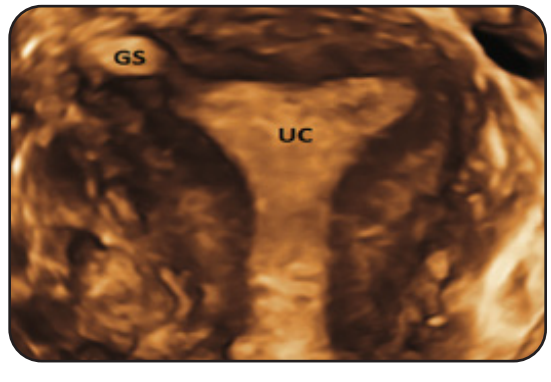
3D imaging very clearly demonstrates the endometrial myometrial junction. This is particularly useful in early pregnancy as it allows the clinician to establish the exact location of the pregnancy in relation to the uterine cavity and assess for invasion beyond said junction, thereby assisting the diagnosis of intramural, interstitial, cervical, or Caesarean scar ectopic pregnancies. A normal IUP is a pregnancy located within the uterine cavity with trophoblastic invasion that does not breach the endometrial myometrial junction.



Interstitial pregnancy

Three-dimensional imaging can better assess

interstitial pregnancies as it provides improved views of the interstitial portion of the tube and allows the clinician to better assess the position of pregnancy in relation to the uterine cavity to rule out uterine anomalies and aid management decisions



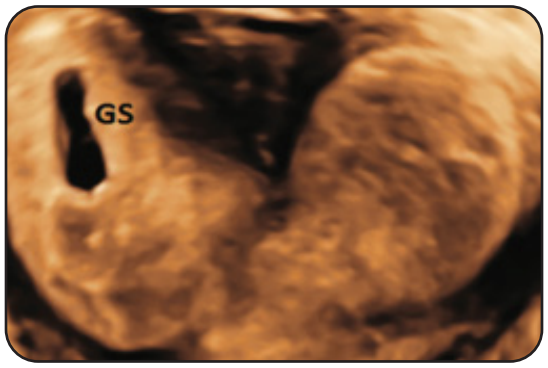
Interstitial pregnancy can be seen separate from the uterine cavity in the above picture.

Intramural Pregnancy

These pregnancies can either be partial (the trophoblast breaches the endometrial myometrial junction) or complete (the trophoblast lies entirely within the myometrium). The pregnancy is located above the internal os and medial to the interstitial tube there is a lack of decidual reaction in the surrounding tissue.

Cornual pregnancy

Presence of pregnancy in a horn of uterus separate from the uni cornuate uterus which shows a single interstitial fallopian tube within the main uterine body. A vascular pedicle can be seen joining the gestation sac to the unicornuate uterus.



Intrauterine pregnancy in one horn of bicornuate uterus can be seen with uterine myometrium lying between the two horns.

Caesarean Scar pregnancy

Caesarean scar pregnancies extend outside the uterine cavity and exhibit myometrial involvement. There is partial or complete absence of a decidual reaction and there must be evidence of functional peri trophoblastic flow. Three-dimensional ultrasound helps to assess the exact location of the Caesarean scar ectopic and whether there is any evidence of herniation, in order to establish the feasibility of surgical evacuation.

Fetal anatomy

3D enables the early detection of congenital anomalies such as neural tube defect, facial abnormalities, and limb deformities. It also useful for evaluation of chronicity in multiple pregnancy and detailed placental

Uterine anomalies

- Uterine anomalies can be an incidental finding during the ultrasound assessment of early pregnancy. It can at times be difficult to differentiate between an intra- uterine pregnancy and interstitial or cornual ectopic pregnancies in the presence of an underlying anomaly. Although diagnosis of a uterine anomaly can be compromised in pregnancy due to dilation of the uterine cavity by the presence of the pregnancy, 3D ultra- sound can undoubtedly aid diagnosis and especially help to rule out ectopic by examining the relationship between the uterine septum and the pregnancy.
- B-mode ultrasound is sufficient in providing diagnostic information in most women presenting with simple early pregnancy complications.
- Three-dimensional ultrasound and colour Doppler may help in the more complex and difficult cases, particularly in women with pregnancy incomplete miscarriage and those with uterine anomalies and ectopic pregnancies. In order to ensure safety, key protocols should be established in every scan department for its use to minimise the risk of exposing normal intrauterine pregnancy to the potentially harmful effects of colour Doppler.

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AI and Male Infertility

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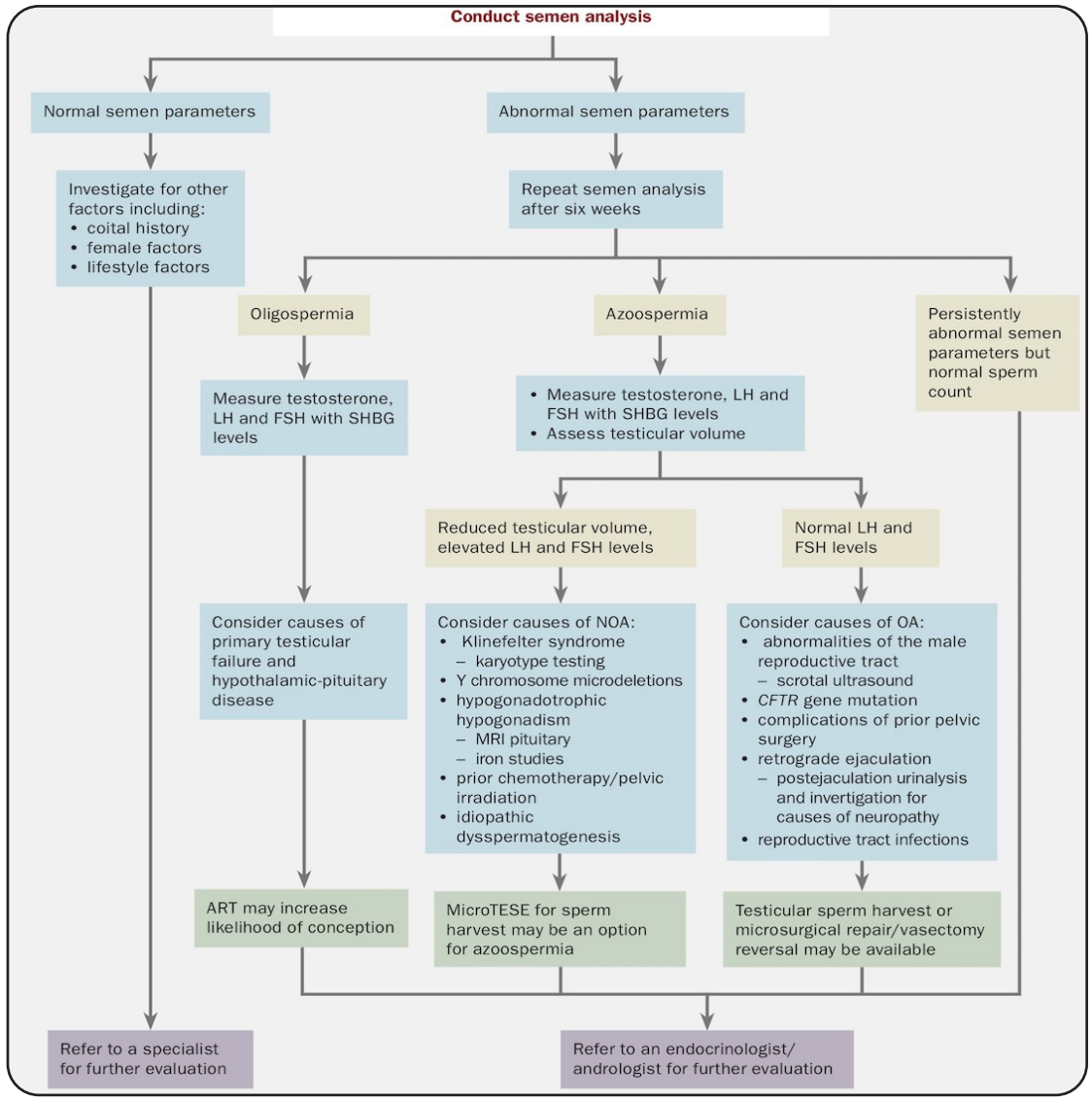
Introduction

Male infertility, affecting approximately 7% of all men, poses significant challenges in reproductive health. Traditional method of male infertility diagnosis relies on manual semen analysis and physical examinations wherein an embryologists assess sperm count, motility, and morphology using microscopy and standardized criteria. With the advancement in medical science, artificial intelligence (AI) is emerging as a powerful tool in addressing this complex issue.

Figure 1: Timeline of male infertility diagnosis and treatment methods



AI's most significant impact in male infertility is in the realm of diagnostics. Advanced algorithms improve semen analysis by accurately assessing sperm count, motility, and morphology, thus providing comprehensive evaluations critical for diagnosing infertility. Additionally, AI enhances genetic testing by identifying mutations related to infertility, which vary based on race and ethnicity, thereby supporting personalized diagnostic approaches. Another notable application is in sperm aneuploidy testing, where AI improves the detection of chromosomal abnormalities that can lead to recurrent pregnancy loss.[3] Despite these advancements, the field is not without its controversies, particularly concerning the risk of bias in AI models and the necessity of transparent reporting guidelines.[4] Therapeutic applications of AI in male infertility are also noteworthy as it assists in optimizing sperm retrieval techniques, pharmacological interventions, and surgical options. This article explores the intersection of male

pharmacological interventions, and surgical options. This article explores the intersection of male infertility and AI, examining how intelligent algorithms are transforming diagnosis, treatment, and patient care.

Machine Learning

AI is built on algorithms, with machine learning (ML) at its core. These problem-solving procedures allow computers to learn from data. For human language processing, AI uses natural language processing (NLP) techniques. NLP, linking AI to linguistics, enables machines to understand and analyze human communication. ML algorithms are crucial in developing these NLP capabilities. **(Fig. 2)**
Machine learning (ML) is classified in three main groups: ML capable of recognizing patterns (unsupervised ML), ML that has algorithms and predicts the outcome based on the pre-existing input-output correlations (supervised ML), and Machine learning (ML) that employs an approach that utilizes positive and negative feedback mechanisms to develop problem-solving strategies. (reinforcement learning)[2],[4]

AI has revolutionized the diagnostic process for male infertility. Machine learning algorithms can now analyze semen samples with unprecedented accuracy and speed. For instance, a 2013 study published in Biol Reprod demonstrated that AI system is capable of assessing sperm concentration with 90% accuracy, outperforming manual methods.[7]
Computer vision techniques, coupled with deep learning, enable automated morphology assessment of sperm cells. These AI-powered systems can identify subtle abnormalities that might be missed by human observers, leading to more precise diagnosis.**(Fig. 3)**

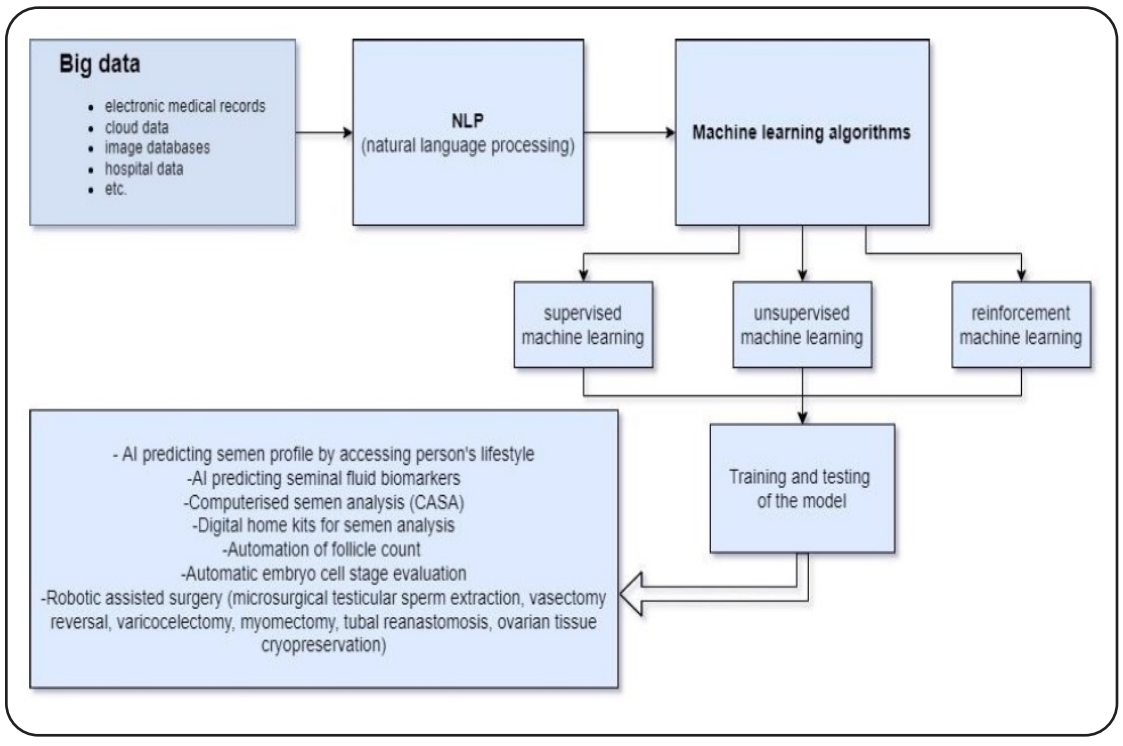


Figure 2: Use of AI in Reproductive Medicine (2)

AI, evolved around the 1950s, and it wasn't until the early 2010s that researchers began applying AI to male reproductive health issues Current AI algorithms analyze factors like age, abstinence time, semen quality, and lifestyle to predict sperm DNA damage and infertility. Machine learning, combined with advanced microscopy, assesses oxidative stress effects on sperm. Recent years have seen increased AI use in sperm morphology and motility analysis, improving sperm selection for assisted reproduction.(7)

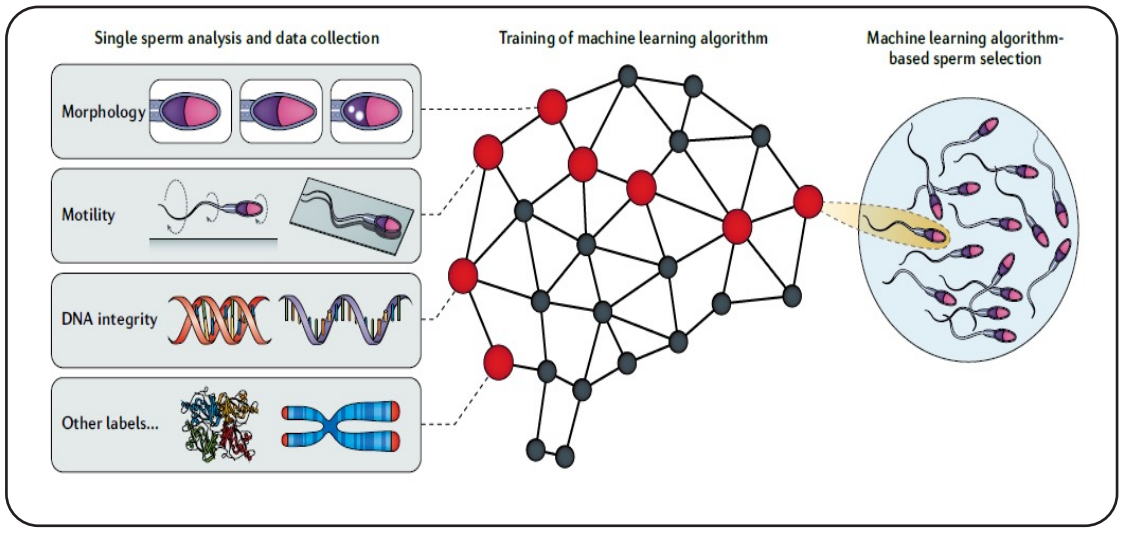


Figure 3: Machine learning algorithms can be trained on sperm quality metrics like morphology, motility, and DNA integrity to automate sperm selection at the single-cell level. This application drives further research into individual sperm characteristics. (4)

AI and Sperm Motility

Sperm motility is described as the ability of the sperm to swim towards the oocyte during natural fertilisation. There are various AI tools that help select the motile sperms, few of them are:

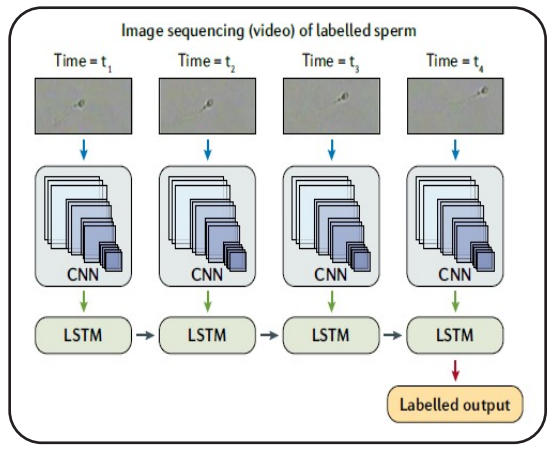
CASA (Computer-Aided Sperm Analysis):
It has been 40 years since the development of CASA wherein images of sperm are assessed and captured from microscopy and data regarding motility is extracted through amplitude of lateral head displacement or average path and curvilinear velocity. This system offers sample-level motility data, but tracking individual sperm to correlate motility with morphology or DNA integrity remains challenging.(21)

SpermQ and FAST:
These computer softwares use high-speed imaging (500 and 332 fps respectively) to trace sperm tail movements, providing beating patterns and frequencies. However, their requirement for dark backgrounds limits analysis of multiple individual sperm simultaneously. (4)

Holographic Imaging:
This technique has also been used to track the tail beat and motility of individual sperms

Convolutional neural networks (CNNs):
Machine learning models effectively analyze sperm motility, with Convolutional Neural Networks (CNNs) showing the highest accuracy, particularly in video analysis. Support Vector Machines (SVMs) and Artificial Neural Networks (ANNs) offer complementary capabilities in classifying motility types and analyzing concentration, respectively (Fig. 4). AI-smartphone integration provides accurate on-the-go assessments. These diverse approaches enhance sperm quality evaluation, with CNNs leading in performance due to their strength in visual data processing. (7)

A.



B.

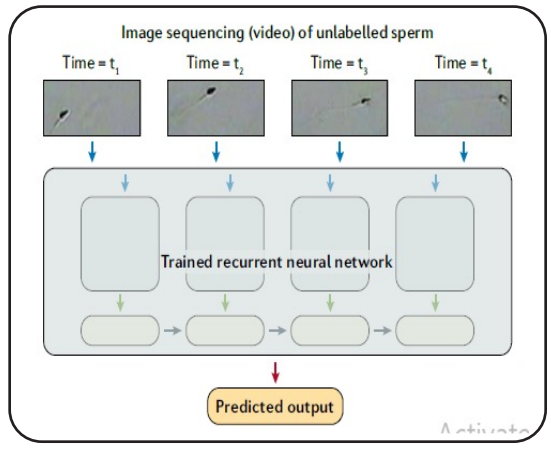


Figure 4: RNNs (recurrent neural networks) analyze sperm swimming videos, exploiting their sequential nature. They automatically extract individual sperm tail-beating patterns and motility by detecting frame-to-frame changes.
*CNN- convolutional neural network , LSTM- long short- term memory

Microfluidics:

Both microfluidic platforms represent significant advancements in single-sperm analysis, but they differ in their approach and capabilities. The first platform uses electrical impedance to measure tail-beating patterns, focusing on distinguishing hyperactivated from non-hyperactivated sperm based on their movement characteristics(22),(23). The second platform is more comprehensive, featuring 2,400 traps and the ability to assess multiple parameters (morphology, tail beating, and DNA integrity) simultaneously for up to 400 live sperm.
This latter platform's use of rheotaxis for trapping ensures only motile sperm are analyzed. While the first platform provides detailed insights into sperm motility patterns, the second offers a more holistic analysis of individual sperm qualities, making it potentially more suitable for generating diverse datasets for machine learning applications in sperm selection. (Fig. 5)

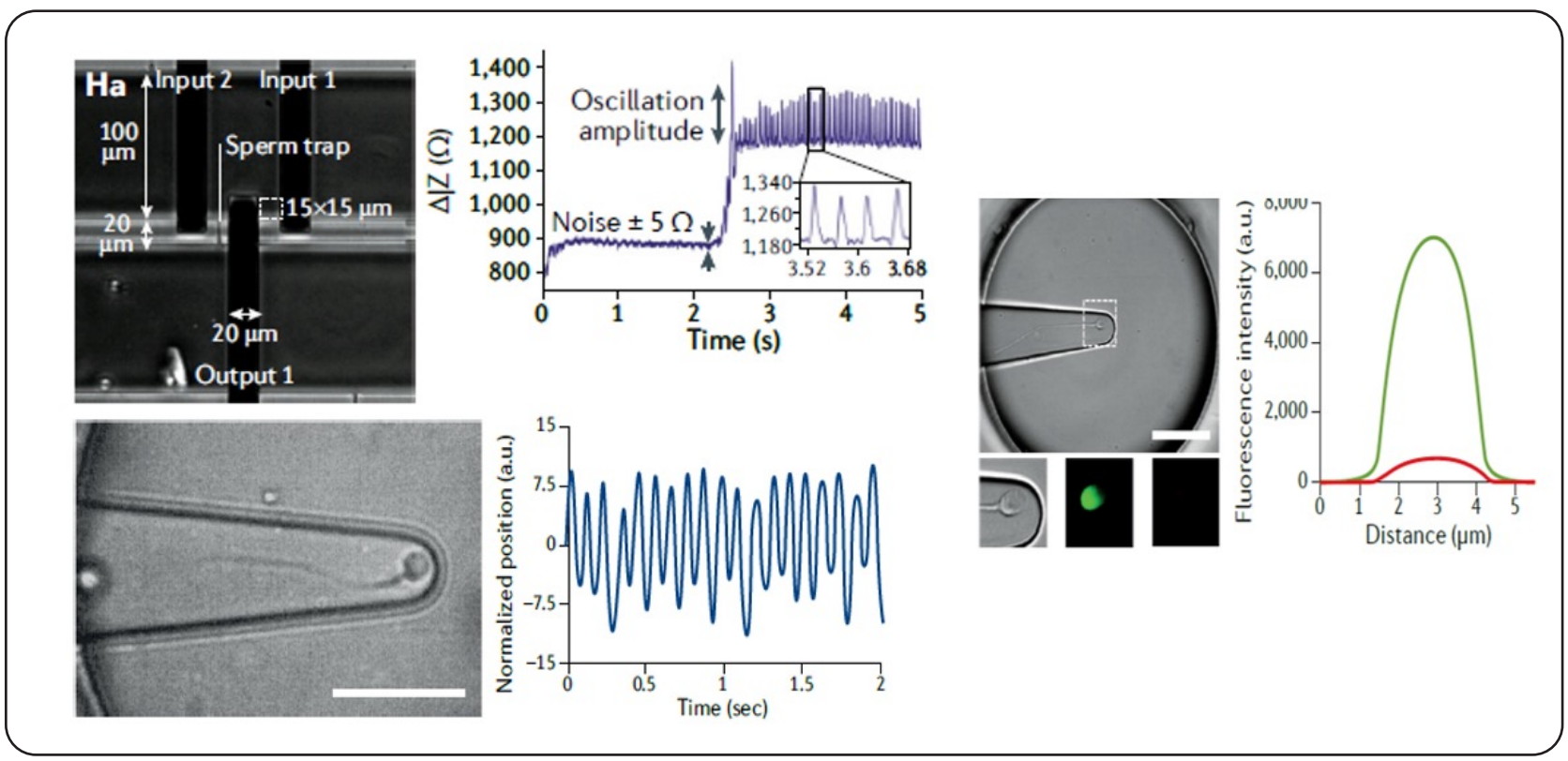


Figure 5: Principle of a Microfluidic device for Single-Sperm Tail Movement Analysis (4)

AI and Sperm morphology

Table 1: Few tools

Tools	Working/Algorithm	Reference
FERTEC	1. Processes 100x magnified sperm images 2. Classifies according to WHO strict criteria 3. Removes background 4. Identifies objects in image 5. Extracts sperm head	You et al. (4), You et al (8), Kruger et al. (9)
IVOS (Integrated Visual Optical System)	1. Hamilton Thorne Research IVOS: An automated semen analyzer 2. Showed promising association between automated normal sperm morphology outcomes and IVF 3. IVOS repeatability (accuracy) comparable to experienced manual observers 4. Accuracy depends on quality of slide preparation	Coetzee et al. (10)
SVM (Support Vector Machine)	1. It can help in classification of sperm head morphology 2. According to a paper published in 2019, its precision is more than 90% 3. A study conducted in 2017 used the subset of extracted sperm head morphology features (extracted using Interferometric phase microscopy(IPM)) and the precision was found to be >90% and good accuracy with AUC = 89.59%	Cherouveim et al. (3), Mirsky et al. (11)

Tools	Working/Algorithm	Reference
CNN (Convolutional Neural Network)	**Advantages of Deep Learning** 1. Gained popularity due to ability to extract information directly from images 2. Provides higher prediction accuracy compared to other machine learning approaches 3. Eliminates potential errors during feature extraction **Convolutional Neural Network (CNN)** 1. Applied for sperm classification 2. Highly effective in image recognition and classification **Visual Geometry Group 16 Algorithm** 1. Pre-trained on human-annotated stock images from ImageNet database 2. Retrained for sperm classification **Performance Comparison** 1. Achieved 94% true-positive rate 2. Outperformed cascade ensemble SVM method 3. Eliminated excessive computation required for training by using pre-trained network **Specific Application Example** 1. Classification of sperm acrosome, head, and vacoule 2. Used images from ×40 or ×60 objective lens (final magnification ×400 and ×600) **Performance Metrics** 1. Accuracy in identifying sperm heads: 77.00% 2. Precision in identifying sperm heads: 83.48%	Shaker.F et al (24) Javadi.S et al (13) Ghasemian F et al (14)

AI and Sperm Integrity

DNA fragmentation assays (SCSA, TUNEL, SCD, and Comet) use fluorescent staining to assess sperm DNA integrity, but their invasive nature precludes clinical use of analyzed sperm. AI offers potential solutions, with current applications in DFI prediction and CASA assisted evaluations showing promise. Callum et al. (15) developed a CNN deep learning algorithm VGG16 as mentioned above which can predict the the sperm DNA integrity based on the morphology.

Table 2: Other AI algorithms designed for sperm DNA integrity

Algorithm	Outcome	Reference
CNN	New sperm DNA fragmentation test (R10) with AI-aided evaluation (X12) was studied. Manual and AI methods showed strong correlation ($r = 0.97$, $p < 0.001$), suggesting AI's potential in sperm analysis.	Koruda et al. (16)
MobileNet CNN	New stain-free imaging with MobileNet CNN predicts sperm DNA fragmentation (mean error: 0.05, 90th percentile: 0.1). Potential application in improving ICSI sperm selection.	Noy et al. (17)
Logistic Regression	A single-cell DNA fragmentation index (DFI) assay combines acridine orange test and SCSA to create DFI-scored brightfield images. Regression models correlate sperm morphology with DFI ($r = 0.558$-0.620), while classification model categorizes sperm with 82.7% accuracy. This study pioneers correlation of sperm DNA integrity with morphology at single-cell level.	Wang et al. (18)

Recent Research Developments

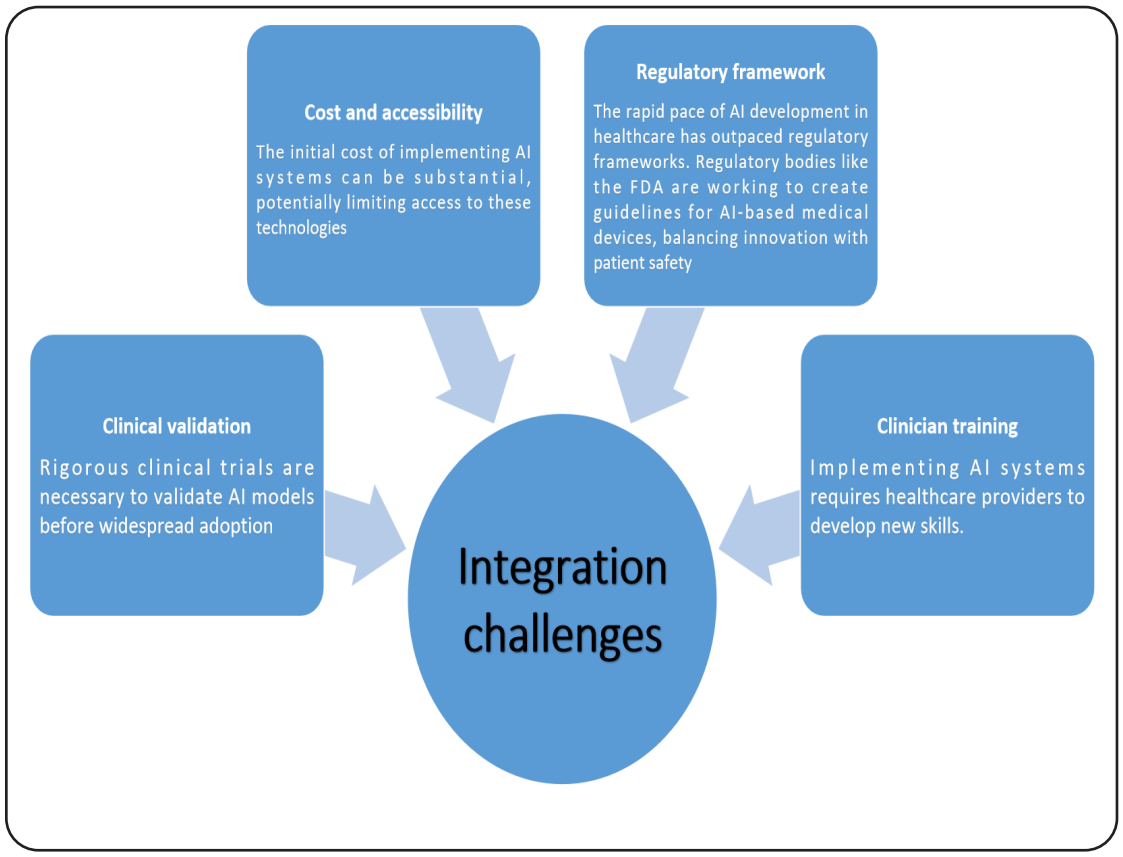
The field of AI in male infertility is rapidly evolving, with new studies constantly pushing the boundaries of what's possible. Some recent developments include:

1. Predicting Sperm Retrieval Success: A retrospective study of 430 micro-TESE patients developed an AI model to predict sperm retrieval in non-obstructive azoospermia. The model, using artificial neural networks, achieved an AUC of 0.7246 and 85% accuracy in a 20-patient validation set. T/E2 (Testosterone/Estrogen) ratio emerged as the most significant predictor. This AI tool offers potential for predicting micro-TESE outcomes in NOA patients, emphasizing the importance of T/E2 ratio in sperm retrieval prediction. (19)
2. AI in Epigenetic Analysis: AI-driven systems biology approaches offer a comprehensive framework for understanding male infertility's complex, multifactorial nature. By integrating genetic, epigenetic, and functional data through computational modeling, these methods can simulate system behavior and uncover intricate causal relationships. This approach, exemplified by Zhu et al.'s work on yeast populations, has potential to provide novel insights into male infertility mechanisms. (20)

Integration Challenges

While AI shows immense promise in male infertility care, integrating these technologies into clinical practice presents several challenges

Figure 6: Challenges in AI integration:



Future Prospects and Challenges

1. AI-Guided Genetic Screening: Machine learning models could potentially predict the impact of specific genetic variations on fertility, guiding targeted therapies or counseling.
2. Robotic-Assisted Microsurgery: AI-powered robotic systems may enhance the precision of surgical interventions for male infertility, such as varicocele repair or vasectomy reversal.
3. AI in Sperm Selection for ART: Advanced image analysis and predictive modeling could identify sperm with the highest potential for successful fertilization and healthy embryo development.

Ethical Considerations and Limitations

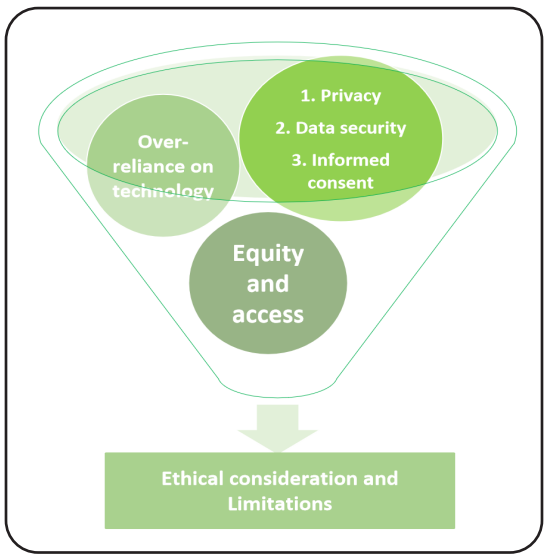


Figure 7: Ethical considerations in AI-assisted fertility care

Conclusion

The integration of AI in male infertility diagnosis and treatment represents a paradigm shift in reproductive medicine. From enhancing diagnostic accuracy to personalizing treatment plans, AI technologies offer the potential for significantly improved outcomes. However, the path to fully realizing the benefits of AI in this field is not without challenges. Integrating these advanced technologies into clinical practice requires overcoming hurdles in validation, training, regulation, and accessibility. The future of male infertility care lies in the thoughtful and responsible integration of AI technologies with human expertise. By embracing innovation while carefully navigating the associated challenges and ethical considerations, we can offer new hope to millions of couples struggling with infertility.

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Calender of Events

April & May 2024

Date	Chapter/SIG	Topic	Attendees	Offline/Online
1.04.2024	Puducherry	PG clinics initiative of IFS chapter	40	Physical Meet
1.04.2024	Maharashta	Newer frontiers in POI	70+	Offline
02.04.2024	MP	"Arambh" orientation to human embryology	70	Physical Meet
05.04.2024	UP	Installation	70	Physical Meet
06.04.2024	TN	Installation	250	Physical Meet
07.04.2024	Orrisa with Roukela OGS	Male infertility & IUI workshop	60	Physical Meet
07.04.2024	Karnataka	Correlation of USG & Laparoscopy	100	Physical Meet
10.04.2024	MP	Endocrinological Evaluation in Infertility	190+	Physical Meet
10.04.2024	Odisha with BOGS	Masterclass series	60+	Online
17.04.2024	MP	Masterclass series	170	Online
18.04.2024	Central	Intelligence Empowerment programme (IEP)	110+	Online
19.04.2024	Central	Youth empowerment program	100+	Online
19.04.2024	Central	Monthly quiz on Kahoot	80+	Online
20.04.2024	Central	Installation ceremony	50+	Physical Meet
20.04.2024	2 SIG+ MP Chapter	Patient Counseling & Holistic Medicine	70+	Online
23.04.2024	Puducherry with South TN	Diagnosis of endometriosis	40+	Physical Meet
26.04.2024	Haryana	Installation ceremony	75+158	Hybrid
27.04.2024	Puducherry	PG clinics series 2	40	Physical Meet
01.05.2024	MP	Polaris-myometrial evaluation on USG	256+	Online
01.05.2024	SIG Early Pregnancy /AOGD	Update on ART regulations	345	Online
02.05.2024	Haryana with Rewari OGS	Filling the lacunae	120+	Online
04.05.2024	Odisha Chapter	Semen analysis made easy	50	Physical Meet
04.05.2024	IFS Chhattisgarh	Installation Ceremony with talk on PRP in ART	80+	Physical Meet
05.05.2024	IFS Bihar	Installation Ceremony & CME on male infertility	58	Physical Meet
08.05.2024	IFS MP	Master Classes	190	Online
10.05.2024	Central	Youth empowerment program	156	Online
12.05.2024	Gujrat	Installation Ceremony with Spermicon	120	Physical Meet
13.05.2024	IFS Puducherry/AOGD	Exploring the enigmatic disease	60+	Online
16.05.2024	SIG: KPI	KPIs in focus	90+	Online
16.05.2024	Central	Nightingale (IVF Nurses)	90+	Online
17.05.2024	Central	Executive Body Meet	20+	Hybrid
19.05.2024	SIG	Endoscopy	60	Physical Meet
19.05.2024	Central	Fertility Preservation & Cancer Patients	50+	Physical Meet
24.05.2024	Central	Young Turks journal club	125+	Online

Date	Chapter/SIG	Topic	Attendees	Offline/Online
24.05.2024	Central	Monthly quiz on Kahoot	70+	Online
26.05.2024	IFS Jharkhand Chapter	Jharkhand Installation Ceremony	70+	Physical Meet
26.05.2024	IFS Kashmir Chapter	IUI workshop	90	Offline
26.05.2024	SIG	Ultrasound & Endoscopy in infertility	40	Offline
28.05.2024	Central	Counselor empowerment programme (CEP)	60+	Online
28.05.2024	Chapter	Kashmir Installation Ceremony	40+	Physical Meet
29.05.2024	IFS MP, Bihar & Karnataka	Deconding Basis essential PCOS (Bharat Sangam)	228	Online
29.05.2024	IFS Maharashtra with AMOGS	Infertility pathshala	50+	Online
30.05.2024	Central Central	AI in ART	112+	Online
30.05.2024	Central Celagenix Pharma CME (Delhi)	Male and female infertility realm beyond antioxidants	30+	Physical Meet

June 2024

Date	Chapter/SIG	Topic	Attendees	Offline/Online
1.06.2024	IFS UP East & SIG CLNICAL EMBRYOLOGY	Installation and Embryology talk	60+	Offline
2.06.2024	IFS Vidarbha	Installation Ceremony	75+	Offline
5.06.2024	IFS MP	Imaging in Gynaecology & infertility	120+	Online
5.06.2024	IFS MP	Polaris	275+	Online
7.06.2024	Bhubaneshwar - Pharma CME	"Male and Female Fertility Realm beyond antioxidants"	160+	Offline
9.06.2024	IFS UP East	Chapter Quiz	120+	Online
9.06.2024	Rajasthan	Fertility CME and Installation Ceremony	90+	Offline
11.06.2024	Rajasthan	Symposium	50+	Offline
13.06.2024	Punjab/ SIG Andrology (SAR)	Semen preparation	70+	Offline
13.06.2024	Chandigarh/ SIG endoscopy	Endoscopy	120+	Online
14.06.2024	Hyatt Residency	Voice of Healthcare	200+	Offline
14.06.2024	central	Youth Empowerment Program (YEP)	190+	Offline
16.06.2024	IFS Bengal	Installation Ceremony	40+	Offline
20.06.2024	IFS Haryana/ SIG PCOS, IFS Collaboration, endocrinology committee AOGD	Reproductive endocrinology in ART	90+	Online
20.06.2024	IFS Madhya Pradesh	Master class -instruments and equipment in IVF	130+	Online
20.06.2024	IFS Tamil Nadu/ SIG: Reproductive Endocrinology	Mastering Ovarian Stimulation	180+	Online
21.06.2024	Central	CEP	110+	Online
29.06.2024	Central	NEP	80+	Online
21.06.2024	Central	Self Empowerment Pilot Project, SEP	135+	Online
21.06.2024	Central	E.B.M Monthly Meet	20+	Offline
23.06.2024	Andhra Pradesh	Installation		Offline
26.06.2024	Kashmir	IUI Workshop		Offline

Date	Chapter/SIG	Topic	Attendees	Offline/Online
27.06.2024	Chhattisgarh/ SIG Embryology IFS	Embryology for clinicians	165	Online
28.06.2024	Uttarakhand IFS/ SIG Endoscopy	Endoscopy in infertility	185	Online
28.06.2024	Madhya Pradesh	Bharat Sangam	879	Offline
28.06.2024	Central	Youth Empowerment Program (YEP)	130+	Online
28.06.2024	Central	Quiz on Kahoot	90+	Online
30.06.2024	Bihar/ Samarth Pharma CME	Ovulation Induction in IUI	130+	Offline
30.06.2024	Pondicherry	Navigation Uterus, Fibroids, Endometriosis & Adenomyosis		Offline
30.06.2024	Vidarbha Chapter (IFS-VC)	Semen analysis and preparation - Hands on workshop	40+	Offline
30.06.2024	Uttar Pradesh E IFS	Silvete – Art troubleshooting		Offline
30.06.2024	SIG Endometrirosis /RCOG./ AOGD	Endometriosis management	62	Offline

July 2024

Date	Chapter/SIG	Topic	Attendees	Offline/Online
02.07.2024	Central	IEP	90+	Online
03.07.2024	IFS Madhya Pradesh	Imaging in gynaecology	456	Online
03.07.2024	SIG reproductive endocrinology	Reproductive endocrinology in ART	104	Online
04.07.2024	Chandigarh IFS, SIG Fertility Preservation	Fertility preservation	74	Offline
05.07.2024	SIG Endoscopy	Endoscopy in ART	456	Offline
05-07-2024	SIG Research Methodology	Data Types and Measures of Association	115	Online
06-07-2024	Rajasthan	National Series Physical CMES	50+	Offline
09.07.2024	Tamil Nadu Ifs / AP Chapter IFS	Ovulation Induction in different clinical scenarios	80+	Online
10.07.2024	Madhya Pradesh IFS	"Suraksha" Laparoscopy in Pregnancy clinical, surgical and Medicolegal Aspects	290+	Online
10.07.2024	Asterdam	ASRM with ISAR & IFS Session	100+	Offline
11.07.2024	Tamil Nadu	Anrology Workshop	80+	Offline
12.07.2024	Central	Youth Empowerment Program (YEP)	140+	Online
13.07.2024	SIG Early Pregnancy	Ovulation Induction and IUI	150	Offline
14.07.2024	Jammu SIG Early Pregnancy	"Dealing with Repeated pregnancy loss: Evidence based Management"	115	Online
14.07.2024	Jharkhand Celagenix Pharma CME	Antioxidants in male and female infertility organised	60+	Offline
15.07.2024	Madhya Pradesh	PCOS Awareness Camp	100+	Offline
16.07.2024	New Delhi	CEP	90+	Offline
17.07.2024	SIG Endoscopy	Endoscopy in ART	30+	Offline
18.07.2024	Chhattisgarh & Bihar/ SIG POR	POR and ART	110+	Online
18.07.2024	SIG Endoscopy	Endoscopy in ART	45+	Offline
19.07.2024	Central	EBM (Monthly Meet)	20+	Hybrid
21.07.2024	Central	SEP	150+	Online

Date	Chapter/SIG	Topic	Attendees	Offline/Online
21.07.2024	Chandigarh	Installation Ceremony	70+	Offline
24.07.2024	Haryana	Infertility & Endometriosis	60+	Offline
24.07.2024	Chandigarh, Jammu, Karnataka & Pondicherry	SIG-Ultrasound	350+	Online
25.07.2024	IFS Central with IFS Bihar, Kashmir, Gujarat, Haryana & Tamilnadu	Patient Empowerment Program (PEP) Camp	500+	Online
25.07.2024	Central	PEP (world IVF Day) "Sanjeevni"	18+	Online
26.07.2024	Central	Youth Empowerment Program (YEP)	120+	Online
28.06.2024	Mumbai	SIG Applied Genetics	60+	Offline
28.07.2024	IFS UP East Celagenix Pharma CME	Male and female infertility realm beyond antioxidants	50+	Offline
29.07.2024	IFS MP	Bharat Sangam	320+	Online
30.07.2024	Central	2nd NEP Nursing Empowerment Program	60+	Online
31.07.2024	SIG: Counseling	Psychology care during recurrent implantation failure RIF	70+	Online

August 2024

Date	Chapter/SIG	Topic	Attendees	Offline/Online
1.08.2024	SIG: PCOS with UP East Chapter	Nuances in Ovulation Induction in PCOS	280+	Online
2.08.2024	SIG: Counseling with ASRM Academy	Psychology care in Fertility Treatment	220+	Online
5.08.2024	North-East and SIG: Endoscopy & Endometriosis	Endometriosis clinical management	60+	Online
6.08.2024	SIG: Research & Methodology	Making Sense of Sensitivity & Specificity	90+	Online
7.08.2024	IFS MP	Polaris	350+	Online
7.08.2024	IFS MP with Jharkhand & Kerala	Bharat Sangam	410+	Online
7.08.2024	SIG: KPI with Vidarbha Chapter	Fertilization Rate	220+	Online
8.08.2024	SIG: Embryology with Tamilnadu chapter	What we should know about IVF lab	260+	Online
8.08.2024	SIG: Environment & Fertility with Holistic Medicine	Impact of Environment facts on Infertility	190+	Online
9.08.2024	IFS Haryana with InterMedics Pharma CME	Understanding IVF Laboratory for Clinicians	70+	Offline
9.08.2024	Central	Youth Empowerment Program (YEP)	140+	Online
10.08.2024	SIG:Fertility Preservation			
11.08.2024	Odisha chapter	Installation Ceremony	70+	Offline
11.08.2024	Celagenix Pharma CME - MP Chapter	Male and female infertility realm beyond antioxidants	50+	Online
11.08.2024	Sun Pharma CME - Chhattisgarh	Letrozole in ovulation Induction	60+	Offline
11.08.2024	Central	Nurses Empowerment Program (NEP)	70+	Online
11.08.2024	IFS UP East	Quiz on Kahoot	80+	Online
12.08.2024	IFS Uttarakhand	Updater on Infertility	140+	Online
12.08.2024	Central	Counselor Empowerment Program (CEP)	90+	Online

Date	Chapter/SIG	Topic	Attendees	Offline/Online
14.08.2024	Central	i-EP Revise AI tools	140+	Online
16.08.2024	IG: Endoscopy with IFS MP	Hands on Workshop	60+	Offline
18.08.2024	Central	IFS Mid Term Meet	80+	Hybrid
20.08.2024	Central	Self Empowerment Program (SEP)	100+	Online
21.08.2024	SIG: Endoscopy with IFS TN	Endoscopy in Infertility	80+	Online
21.08.2024	IFS Odisha	Male & Female Infertility	50+	Offline
22.08.2024	IFS Pondicherry	Surgical Managements of Endometriosis	90+	Online
23.08.2024	IFS Uttarakhand	Installation Ceremony	50+	Offline
23.08.2024	SIG Ultrasound with Endoscopy &x IFS South TN Chapter	Just Fibroids	270+	Online
24.08.2024 25.08.2024	IFS Bihar	2nd Annual Conference	200+	Offline
28.08.2024	SIG: POR	Evidence Basis Mangement of POR	110+	Online
28.08.2024	SIG: QA&QC with SIG Embryology	Quality Assurance & Quality Control in ART	140+	Online
28.08.2024	Central with IFS West Bengal, Jammu, Punjab, Maharashtra, Andhra & Odisha	Patient Empowerment Program (PEP) Phase 2	400+	Hybrid
29.08.2024	Central	IFS Trade Meeting for Fertivision 2024	60+	Offline
29.08.2024	SIG: Genital Tuberculosis	Enigma of TB	150+	Online
30.08.2024	IFS MP	Masterclasses on Quality Management in IVF Lab	200+	Online
30.08.2024	Central	Youth Empowerment Program (YEP)	160+	Online
30.08.2024	Central	Quiz on Kahoot	100+	Online
30.08.2024	IFS Haryana	Quiz on Kahoot	60+	Online
31.08.2024	IFS Karnataka	Installation Ceremony	70+	Offline

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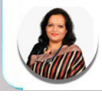

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