

## BIO END SEM PROJECT PROJECT

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NAME: ADITHYA KRISHNA                    ROLL NO: AM.EN.U4AIE21005

NAME: ADITHYA S NAIR                    ROLL NO: AM.EN.U4AIE21006

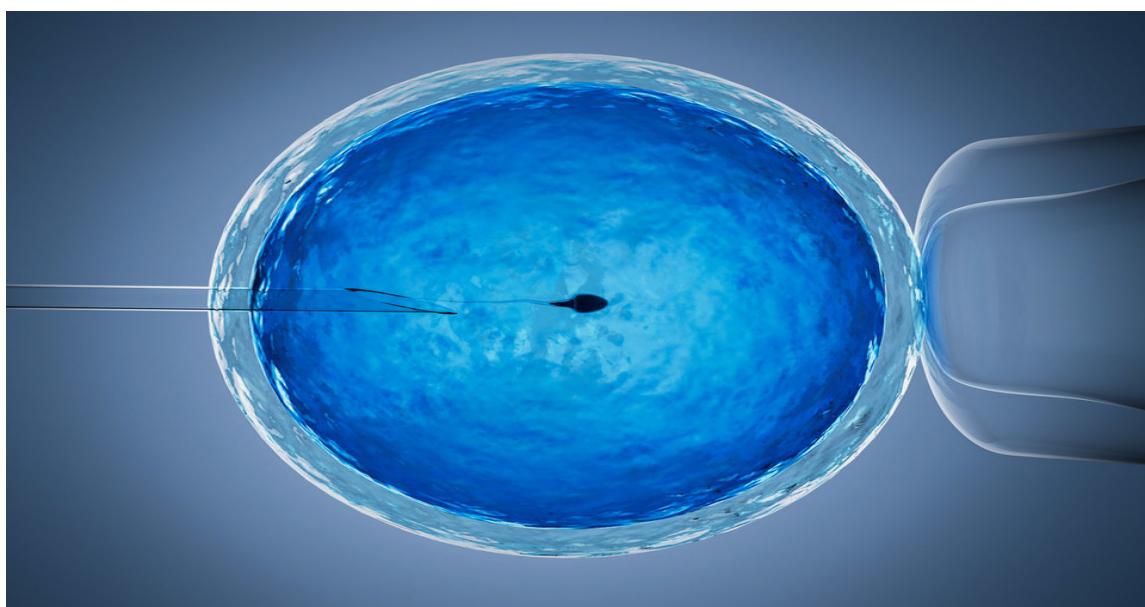
NAME: ANOOP BOBY MANUEL                ROLL NO: AM.EN.U4AIE21015

NAME: ATHUL GIREESH                    ROLL NO: AM.EN.U4AIE21020

NAME: NAVNEETH KRISHNA                ROLL NO: AM.EN.U4AIE21047

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## ARTIFICIAL INTELLIGENCE IN IN-VITRO FERTILISATION ( IVF )



## **Introduction**



<sup>1</sup>In India, social pressure on the woman to conceive soon after marriage is very high. Even if the problem lies with the man, the burden of infertility is mainly on the woman. She undergoes severe psychological pressure, depression, and social ostracisation while facing the problem of infertility. There are two main issues that need to be dealt with.

The first one is proper medical awareness among patients as well as the medical fraternity so that these patients get the right treatment at the right time. The second is social awareness to allow the couples to face this problem with dignity and privacy.

Many infertile couples end up going to quacks and astrologers who waste enormous amounts of precious time and money. If these couples are referred for the right medical intervention early on then the chance of successful pregnancy is higher. A woman is born with a fixed number of eggs and by the time she is 35, her ovarian reserve is low. It is better that she receives infertility treatment much before in order to have a successful outcome. Unfortunately, many medical practitioners continue treating these patients for years together with ineffective treatment when they should be referred for assisted conception. It is well known that the only treatment successful for patients with tubal block and low sperm count, is in-vitro fertilization. There is yet another group of couples in the cities nowadays that first delay marriage and then delay childbearing. It is important to convey the message that the best chance of childbearing in a woman is before the age of 32.

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<sup>1</sup> "Infertility – Social issues | AFGC - Advance Fertility and Gynaecology ...." 27 Jul. 2017, <https://www.advancefertility.in/infertility-social-issues/>. Accessed 7 Feb. 2022.

## **Causes of Infertility**

All of the steps during ovulation and fertilization need to happen correctly in order to get pregnant. Sometimes the issues that cause infertility in couples are present at birth, and sometimes they develop later in life. Infertility causes can affect one or both partners. Sometimes, no cause can be found.

### **²Causes of male infertility**



These may include:

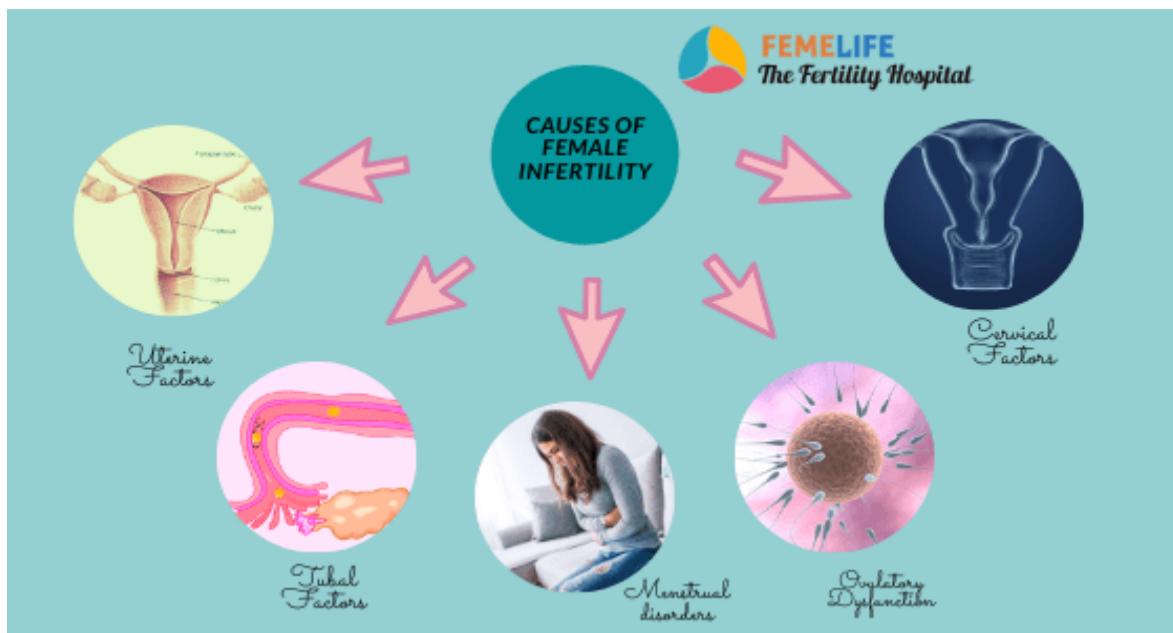
- **Abnormal sperm production or function** due to undescended testicles, genetic defects, health problems such as diabetes, or infections such as chlamydia, gonorrhea, mumps, or HIV. Enlarged veins in the testes (varicocele) also can affect the quality of sperm.
- **Problems with the delivery of sperm** due to sexual problems, such as premature ejaculation; certain genetic diseases, such as cystic fibrosis; structural problems, such as a blockage in the testicle; or damage or injury to the reproductive organs.
- **Overexposure to certain environmental factors**, such as pesticides and other chemicals, and radiation. Cigarette smoking, alcohol, marijuana, anabolic steroids, and taking medications to treat bacterial infections, high blood pressure, and depression also can affect fertility. Frequent exposure to heat, such as in saunas or hot tubs, can raise body temperature and may affect sperm production.

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<sup>2</sup> "Infertility - Symptoms and causes - Mayo Clinic." 1 Sep. 2021, <https://www.mayoclinic.org/diseases-conditions/infertility/symptoms-causes/syc-20354317>. Accessed 7 Feb. 2022.

- **Damage related to cancer and its treatment**, including radiation or chemotherapy. Treatment for cancer can impair sperm production, sometimes severely.

## Causes of female infertility



<sup>3</sup>Causes of female infertility may include:

- **Ovulation disorders** affect the release of eggs from the ovaries. These include hormonal disorders such as polycystic ovary syndrome. Hyperprolactinemia, a condition in which you have too much prolactin — the hormone that stimulates breast milk production — also may interfere with ovulation. Either too much thyroid hormone (hyperthyroidism) or too little (hypothyroidism) can affect the menstrual cycle or cause infertility. Other underlying causes may include too much exercise, eating disorders, or tumors.
- **Uterine or cervical abnormalities**, including abnormalities with the cervix, polyps in the uterus, or the shape of the uterus. Noncancerous (benign) tumors in the uterine wall (uterine fibroids) may cause infertility by blocking the fallopian tubes or stopping a fertilized egg from implanting in the uterus.

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<sup>3</sup> "Infertility - Symptoms and causes - Mayo Clinic." 1 Sep. 2021, <https://www.mayoclinic.org/diseases-conditions/infertility/symptoms-causes/syc-20354317>. Accessed 7 Feb. 2022.

- **Fallopian tube damage or blockage**, often caused by inflammation of the fallopian tube (salpingitis). This can result from pelvic inflammatory disease, which is usually caused by a sexually transmitted infection, endometriosis, or adhesions.
- **Endometriosis**, which occurs when endometrial tissue grows outside of the uterus, may affect the function of the ovaries, uterus, and fallopian tubes.
- **Primary ovarian insufficiency (early menopause)**, is when the ovaries stop working and menstruation ends before age 40. Although the cause is often unknown, certain factors are associated with early menopause, including immune system diseases, certain genetic conditions such as Turner syndrome or carriers of Fragile X syndrome, and radiation or chemotherapy treatment.
- **Pelvic adhesions** are bands of scar tissue that bind organs that can form after pelvic infection, appendicitis, endometriosis, or abdominal or pelvic surgery.
- **Cancer and its treatment.** Certain cancers — particularly reproductive cancers — often impair female fertility. Both radiation and chemotherapy may affect fertility.

## How to solve the problem

<sup>4</sup>Thanks to technology, there are lots of ways to help people with all kinds of fertility issues. The options that are best for you depend on your personal situation and what's causing your infertility.

Sometimes only one person needs treatment, other times both partners will use a combination of treatments together.

Fertility treatments often include medications that help with hormones and ovulation, sometimes combined with minor surgical procedures. Assisted Reproductive Technology (ART) describes several kinds of procedures that can help you have a baby. ART includes procedures that make it easier for sperm to fertilize an egg, and help the egg implant in your uterine lining.

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<sup>4</sup> "Fertility Treatments For Infertility - Planned Parenthood." <https://www.plannedparenthood.org/learn/pregnancy/fertility-treatments>. Accessed 7 Feb. 2022.

<sup>5</sup>Two of the most common fertility treatments are:

- intrauterine insemination (IUI) :

Healthy sperm is collected and inserted directly into your uterus when you're ovulating.

- In vitro fertilization (IVF):-

Eggs are taken from your ovaries and fertilized by sperm in a lab, where they develop into embryos. Then a doctor puts the embryos into your uterus.

Cryopreservation (aka freezing your eggs, sperm, or embryos at -196 degree C ), egg or embryo donation, and gestational carriers (aka surrogacy) are also forms of ART.

Donor sperm, donor eggs, and surrogates are often used by same-sex couples or single people who want to have a baby. You can also use sperm and/or eggs from a donor if a problem with your own sperm cells or eggs is causing infertility issues.

## Sexual health



<sup>5</sup> "Fertility Treatments For Infertility - Planned Parenthood."

<https://www.plannedparenthood.org/learn/pregnancy/fertility-treatments>. Accessed 7 Feb. 2022.

Sexual health is fundamental to the overall health and well-being of individuals, couples and families, and to the social and economic development of communities and countries. Sexual health, when viewed affirmatively, requires a positive and respectful approach to sexuality and sexual relationships, as well as the possibility of having pleasurable and safe sexual experiences, free of coercion, discrimination, and violence.

- access to comprehensive, good-quality information about sex and sexuality;
- knowledge about the risks they may face and their vulnerability to adverse consequences of unprotected sexual activity;
- ability to access sexual health care;
- living in an environment that affirms and promotes sexual health.

<sup>6</sup>The working definitions and framework for programming presented here are grounded in internationally recognized human rights and offer a rights-based approach to programming in sexual health

Key conceptual elements of sexual health When viewed holistically and positively:

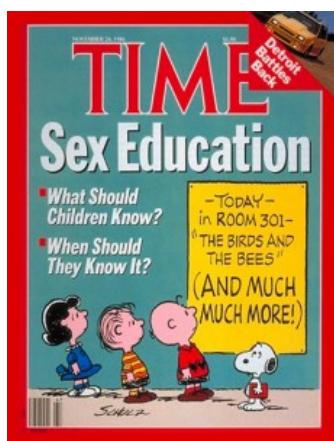
- Sexual health is about well-being, not merely the absence of disease.
- Sexual health involves respect, safety, and freedom from discrimination and violence.
- Sexual health depends on the fulfillment of certain human rights.
- Sexual health is relevant throughout the individual's lifespan, not only to those in the reproductive years but also to both the young and the elderly.
- Sexual health is expressed through diverse sexualities and forms of sexual expression.
- Sexual health is critically influenced by gender norms, roles, expectations, and power dynamics.

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<sup>6</sup> "Sexual health." <https://www.who.int/health-topics/sexual-health>. Accessed 7 Feb. 2022.

## Sex education

Sex education is high-quality teaching and learning about a broad variety of topics related to sex and sexuality, exploring values and beliefs about those topics, and gaining the skills that are needed to navigate relationships and manage one's own sexual health. Sex education may take place in schools, in community settings, or online.

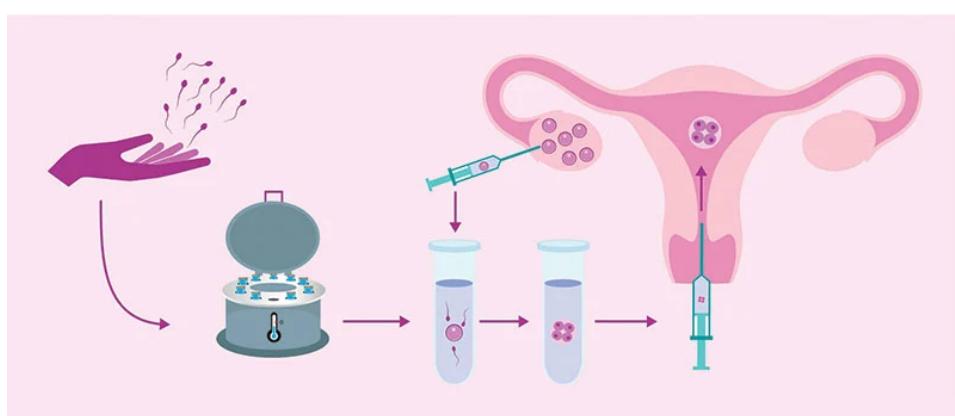


## Types of Assisted Reproductive Technologies

Assisted Reproductive Technology (ART) includes

### 1 ) In vitro fertilization-embryo transfer (IVF-ET)

#### **Embryo transfer and In-vitro fertilization (IVF)**



IVF involves a doctor extracting eggs and fertilizing them in a special lab. Specialists can combine this with an embryo transfer (IVF-ET) and transfer the resulting embryos into a person's uterus. The Society for Assisted Reproductive Technology states that IVF-ET accounts for 99% of ART procedures.

- 52% for people aged 35 or younger
- 38.1% for people aged 35–37
- 23.5% for people aged 38–40
- 7.6% for those over the age of 40

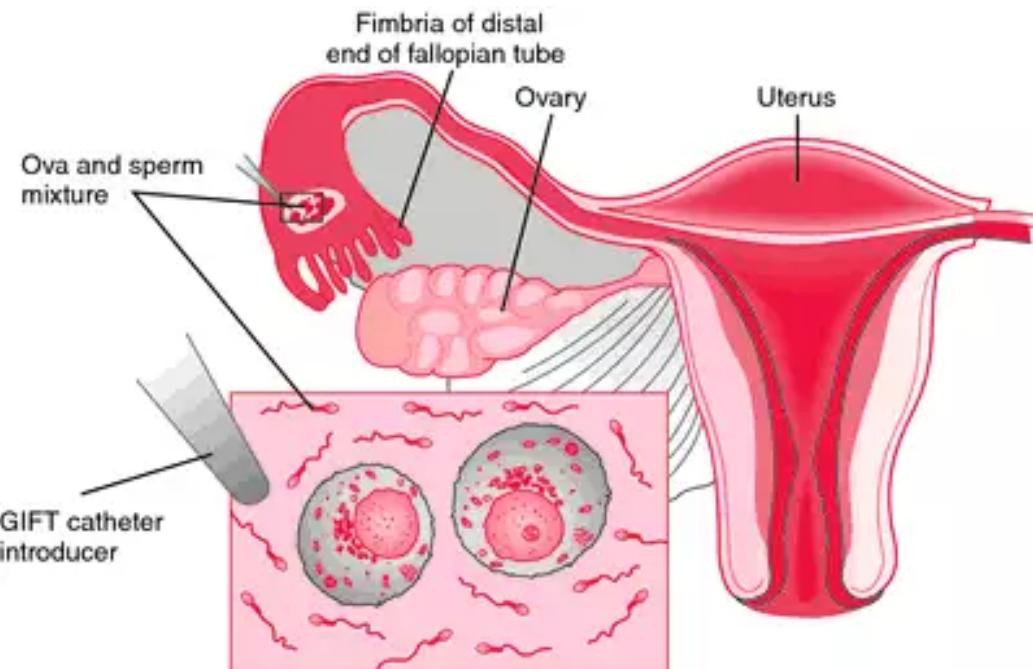
It may take more than one IVF cycle to result in pregnancy, and some people may not conceive with IVF at all. The benefits of IVF are an increased chance of fertilization and pregnancy.

Potential complications may include:

- multiple pregnancies, or two or more embryos implanting at a time
- side effects from fertility drugs, such as ovarian hyperstimulation syndrome
- ectopic pregnancy, where the embryo settles outside of the womb
- These techniques also apply to oocyte donation and gestational carriers. Approximately 99 percent of ART cycles performed are IVF-ET.

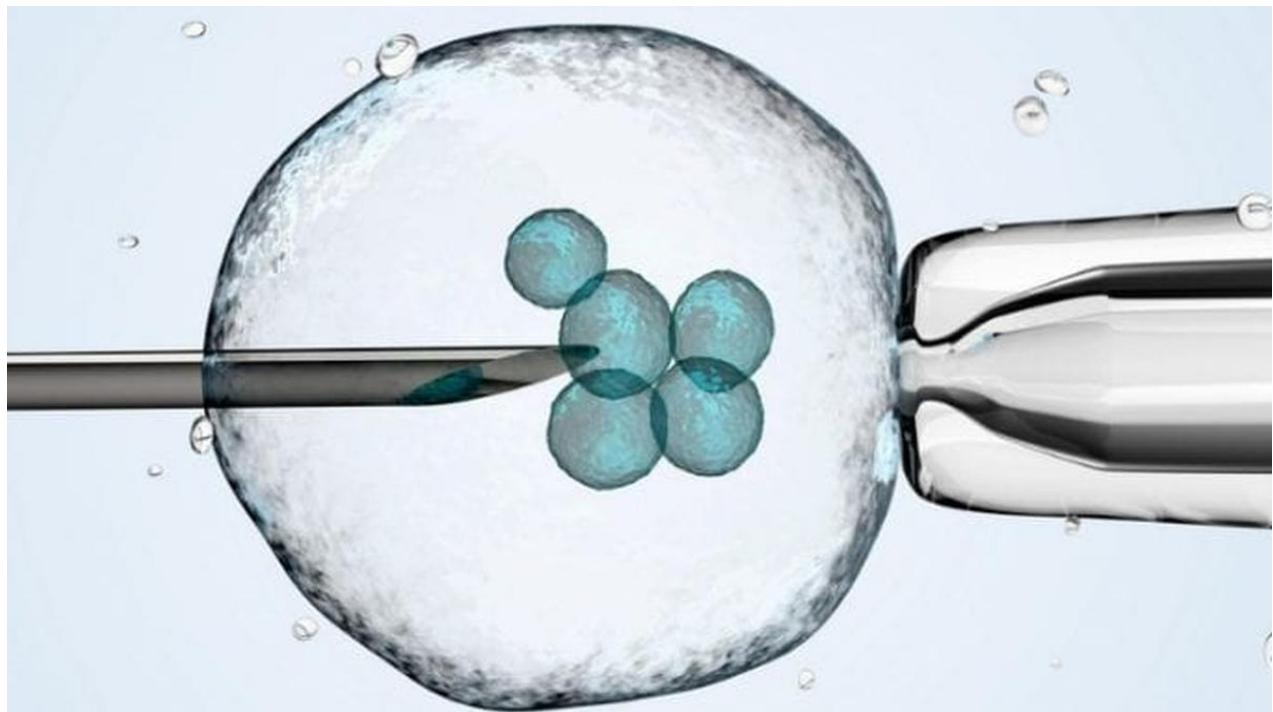
IVF-ET has helped many couples conceive successfully. ART may be recommended when other treatments (such as intrauterine insemination) have not been successful or when there is severe male factor infertility, severe endometriosis, or tubal obstruction.

## 2) Gamete intrafallopian transfer (GIFT)



GIFT involves collecting eggs and sperm in a tube before a doctor places the gametes directly into the fallopian tubes using laparoscopic surgery. As there is no IVF procedure, a person does not have to choose which embryo to transfer.

### **3 ) Zygote intrafallopian transfer (ZIFT)**



ZIFT is a combination of IVF and GIFT. Specialists stimulate and collect the eggs using IVF methods and mix the eggs with sperm in the lab before returning fertilized eggs or zygotes to the fallopian tubes. A benefit of ZIFT is that it may help those with damaged fallopian tubes or severe infertility issues become pregnant.

#### **4 ) Frozen embryo transfer (FET)**



Frozen embryo transfer (FET) has become increasingly common in the U.S. It involves thawing previously IVF frozen embryos and inserting them into a person's uterus. A 2017 study found that 52% of people who had FET had ongoing pregnancies.

According to the United Kingdom's Human Fertilisation and Embryology Authority, FET is as safe as using fresh embryos in treatment. However, some evidence suggests an increased risk of preterm birth with FET. Another possible risk of FET is that not all frozen embryos survive the thawing out process.

## 5 ) Intracytoplasmic Sperm Injection( ICSI)



Intracytoplasmic sperm injection (ICSI) is a procedure that specialists can perform alongside IVF to help fertilize an egg. An embryologist, or embryo specialist, uses a tiny needle to inject a single sperm directly into the center of an egg.

<sup>7</sup> ICSI fertilizes between 50–80% of eggs. The success rate of ICSI is similar to those of IVF, and it may be an effective method of ART for people with sperm-related infertility. ICSI is typically an add-on procedure to IVF, so it will be more costly than IVF alone.

Things to consider about ICSI include the following:

- The procedure may damage some or all of the eggs.
- The egg might not grow into an embryo even after being injected with sperm.

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<sup>7</sup> "Assisted reproductive technology: Definition, types, and ethics."

<https://www.medicalnewstoday.com/articles/assisted-reproductive-technology>. Accessed 7 Feb. 2022.

- If a person becomes pregnant naturally, there is a 1.5 to 3% chance that the baby will have a major birth defect. However, underlying infertility, rather than the treatment, may be the cause of the birth defect.

## The involvement of AI in ART



Andrew Moore, a former Dean of the School of Computer Science at Carnegie Mellon University defined Artificial Intelligence (AI) as “**The science and engineering of making computers behave in ways that, until recently, we thought required human intelligence.**” A branch of AI, Machine Learning (ML), is a system that can learn from vast amounts of clinical, demographic, pathology, laboratory, and imaging data to make connections and recommendations that humans cannot easily detect. In essence, ML is a set of algorithms that *learn how to learn* by seeing patterns and associations in large datasets. The learning can be guided or autonomous, but it produces outputs that can be used to guide decisions—including health care decisions.

AI and ML are rapidly changing the practice of medicine across various disciplines. Major inroads have already been made in disciplines where pattern recognition and classification are integral to the practice such as dermatology, radiology, and pathology. As a field, reproduction science has been slow to pursue opportunities in AI for reasons that are not at all clear. AI has remarkable potential to overcome the barriers of cost, access, and low success rates.

Consider the highly manual and labor-intensive processes of ART as it is today. Success rates depend on several variables. Some variables are patient-specific and (likely) uncontrollable, but many others are rooted in the process, including sperm, oocyte, and embryo selection to fertilization to implantation. Lack of automation leads to high inter-user variability. Indeed, gifted embryologists can be quite successful after years of training and practice; however, the learning curve and inconsistency across providers are rate-limiting. These factors are also a source of considerable costs for the practice. Automating and streamlining the entire process should reduce overhead costs to fertility practices and increase access and reduce costs for patients. Innovation does not reduce revenue for clinicians, quite the opposite: increased access, more efficient processing, and better outcomes should increase patient volume and revenue (and vastly improve patient outcomes) while reducing manual workload.

It is useful to highlight some examples of how AI can be applied to the practice of ART. For instance, researchers have had nascent successes in using AI to identify and characterize the most viable oocytes and embryos. Normally, embryologists select oocytes and embryos based on a subjective set of criteria, often developed from personal experience rather than evidence-based sources. To standardize, formalize and improve the selection process, researchers created and tested an AI system on two data sets of 269 oocytes and 269 corresponding embryos from 104 women. The AI was able to successfully identify and classify oocyte/embryo quality using the information it had learned through previous training.

Indeed, as the dataset expands and additional ML continues, the AI can hone its accuracy and predictive prowess. The algorithm gets “rewarded” for choosing features that are ultimately associated with better outcomes (live births, successful implantations, etc.). Put another way, the algorithm mathematically weights the features that lead to better outcomes. Conversely, the algorithm is “penalized” for identifying features associated with poorer outcomes (i.e. lower mathematical weight). In time, unsupervised, “deep learning” AI can detect patterns and features that the original programmers had not overtly considered or that embryologists may not use to subjectively assign the quality. Yet since AI is reinforced by outcomes, positive and negative, it creates a sort of inherent, evidence-based selection strategy. Moreover, the fully

trained AI could be standardized, commercialized, and marketed for use in fertility clinics. This would take the guesswork out of one of the major sources of variability in the ART process.

One could also envision AI used in a similar fashion to characterize spermatocyte quality. Computer-aided sperm analysis (CASA) systems are used in research and have been adopted in some clinics. CASA assesses motile percentage and kinematic parameters at the population level. Standard parameters include the amplitude of lateral head displacement, average path velocity, beat cross frequency, curvilinear velocity, straight-line velocity, straightness, and linearity. However, when a relatively simple AI algorithm was trained on 2817 spermatocytes from 18 individuals and tested, the AI was able to correctly classify sperm motility into five classes: progressive vigorous, intermediate vigorous, or hyperactivated vigorous, slow non-vigorous, or weakly motile non-vigorous. Overall accuracy was 89.9%.

Researchers have also had early success in using ML to digitally isolate sperm cell heads and characterize sperm head morphology as “good” or “bad.” The automatic analysis was trained on over 1,400 human sperm cells from 8 donors and reached precisions of 88% and higher.

<sup>8</sup>Large datasets (i.e. “big data”) allow ML to learn and develop best practices that can be applied to ART. For example, 80% of one large dataset can be used to train the AI while the remaining 20% is used to validate the model. Then a second large dataset can be used to test the AI algorithm and compare it to historical diagnostic pathways, assessments, treatments, and outcomes. Once trained, the AI could help the fertility specialist in several ways. AI can be used to hone ovarian stimulation protocols. The AI can crawl through thousands of electronic medical records to make associations between ovarian stimulation parameters and outcomes. In a similar way, AI could also help predict IVF outcomes to the patient level. Data mining has been used to identify factors that predict IVF outcomes such as the age of the woman, the number of the developed embryos, and the serum estradiol level on the day of human chorionic

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<sup>8</sup> "AI will revolutionize assisted reproductive technology (if we work ...." 1 Jul. 2020, <http://www.fertsterdialog.com/posts/ai-will-revolutionize-assisted-reproductive-technology-if-we-work-together>. Accessed 7 Feb. 2022.

gonadotropin administration. As these technologies are developed, the precision should increase to the point of being able to reliably assign an outcome probability on a patient-by-patient basis.

## **Challenges to AI in IVF**

- While the widespread use of electronic medical records will help pave the way for data mining and AI applications, the high variability of stimulation and embryology techniques across laboratories is a major barrier to ML.
- While newer AI algorithms can partially compensate for missing data, all ML systems work best when they can learn on vast, complete, codified data.
- Until reproductive specialists adopt a common clinical language and standard data acquisition criteria, data mining cannot occur to the degree required for off-the-shelf ART applications. Thus, the near-term will likely be an iterative process.
- AI can begin to learn from partial, varied data and provide limited insights—insights limited by the quality of the data from which they learn.
- Comprehensive note-taking, detailed outcomes reporting, and routine collection of high-quality imaging can accelerate this innovation.

## **Steps for doing IVF using AI**

- **Test the Sperm Quality Using AI**
- **Oocyte Assessment**
- **Performance of ICSI**
- **Cleavage state development**
- **Laser-assisted Hatching**
- **Blastocyst stage assessment**
- **Embryo Biopsy and Cryopreservation**
- **Implantation outcome prediction**
- **Embryo Tracking and witnessing**

- **Quality Control Monitoring**

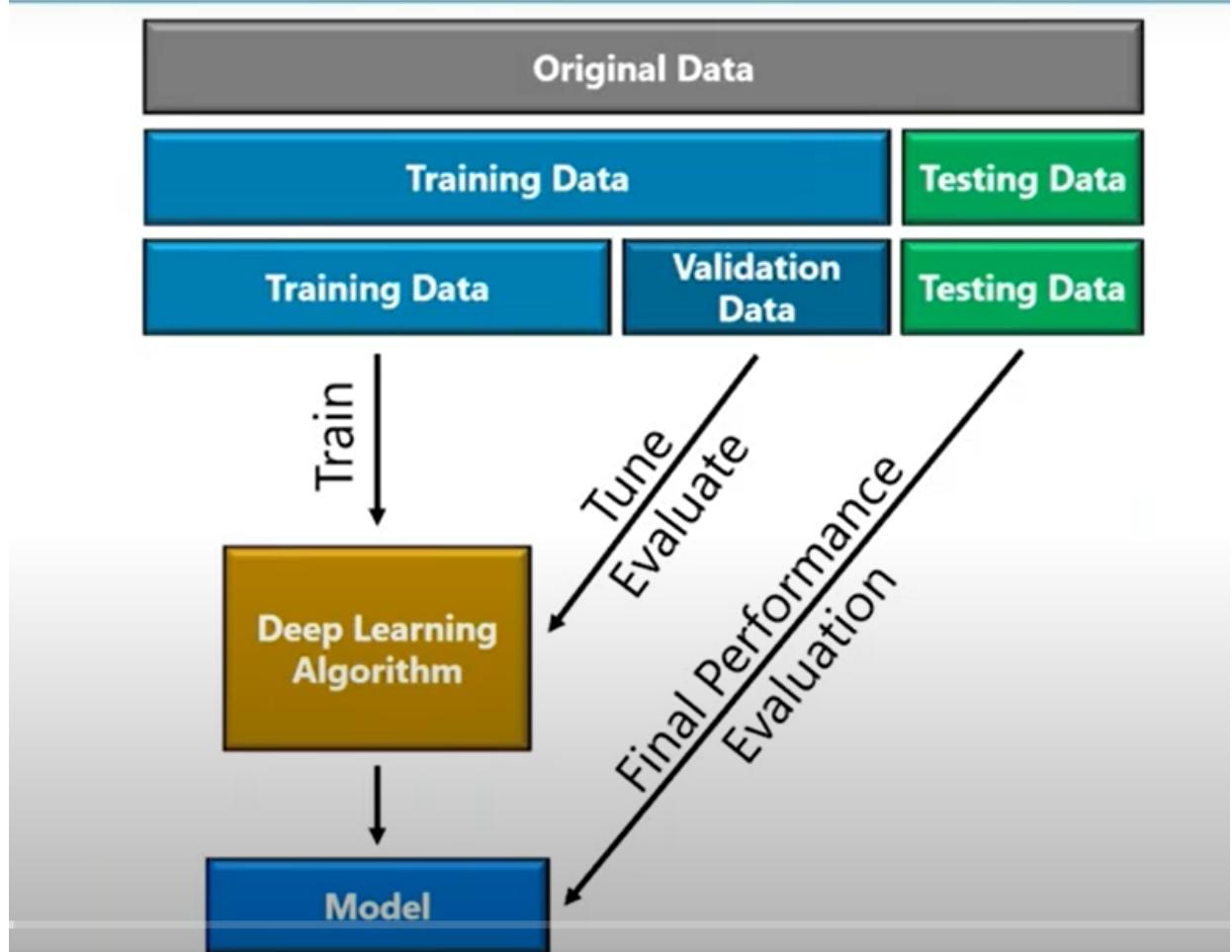
### **Test the Sperm Quality Using AI**

To test the sperm quality using AI it uses the constraints like:-

- If the semen is Acidic, Alkaline, or Neutral.
- Normal, or Low sperm count.
- Less Motility, Normal motility, and Vigorous motility.
- Pink cell ( Dead-cell ) or white cell ( Live-cell )
- The range of adhesion is graded into 4 grades ( Grade-1, Grade-2, Grade-3, Grade-4 )
- Grade-1 (No adhesion)
- Grade-2 (Isolated or less than 10% adhesion)
- Grade-3 (Moderate or less than 30% adhesion)
- Grade-4 (Large or less than 50% adhesion)

In a similar case, the Scientists from the Massachusetts General Hospital made an application that uses a 3D printed case to take the semen input and predict the Sperm Concentration, Motility, Sperm count, and forward progression. Through this application, we can see the sperm movement and the concentration which can't be seen with a naked eye. All of this causes under 3 dollars. The ML algorithm used here is the CNN ( Deep Convolved Neural Network ) Which is effective in image classification programs.

To build and Train the Algorithm They took some data and split it into the test and the train data set. The train data set is used for training the data and the test for testing the data set.



This application packed 98% accuracy in the 5th edition of WHO.

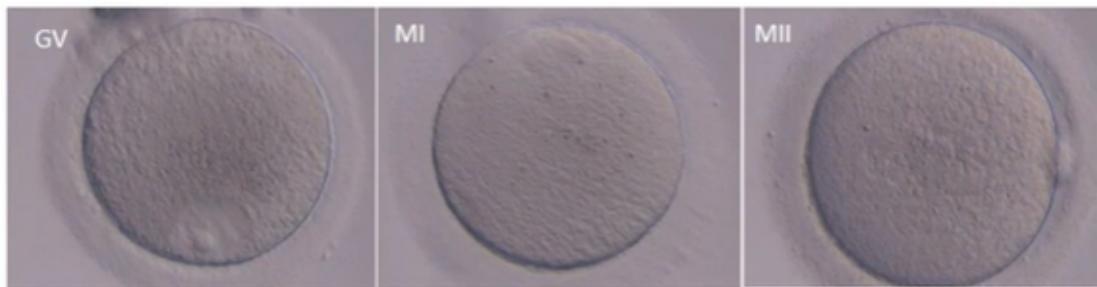
The sperm Morphology Grading is done by classifying the sperm into 4 classes that are

- Normal
- Head defect
- Neck defect
- Tail defect

The input image for the classification is 227x227 and later on, it is zoomed into 1x1x11 (Low-level image features —> High-level image features)

## OOCYTE ASSESSMENT

The oocyte assessment is done when the oocytes are mature and 3 kinds of mature oocyte is given here - GV, MI, MII



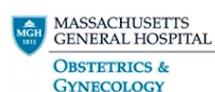
In this case the MII can also be different patient by patient.

## Performance of ICSI

At day 0 they analyse the oocyte and they perform the ICSI in optimised lab conditions .

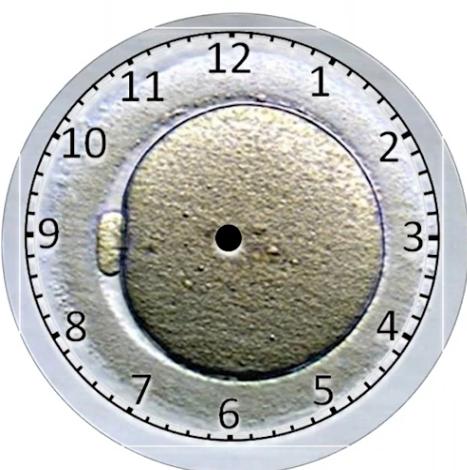
On doing the ICSI procedure the position is the proper location to perform ICSI .

### ICSI Location



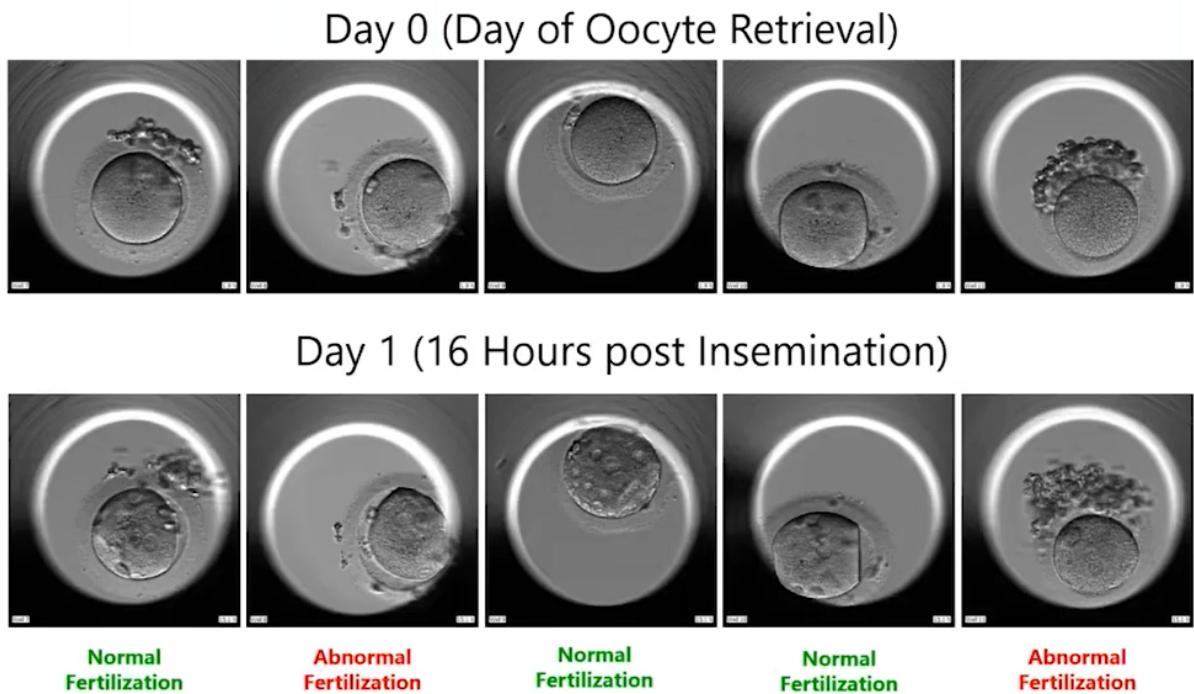
#### Dataset details:

Training set (before augmentation) = 1166 images  
Training set (after augmentation) = 13992 images  
Validation set (before augmentation) = 160 images  
Validation set (after augmentation) = 1920 images  
Test set (before augmentation) = 325 images  
Test set (after augmentation) = 3900 images



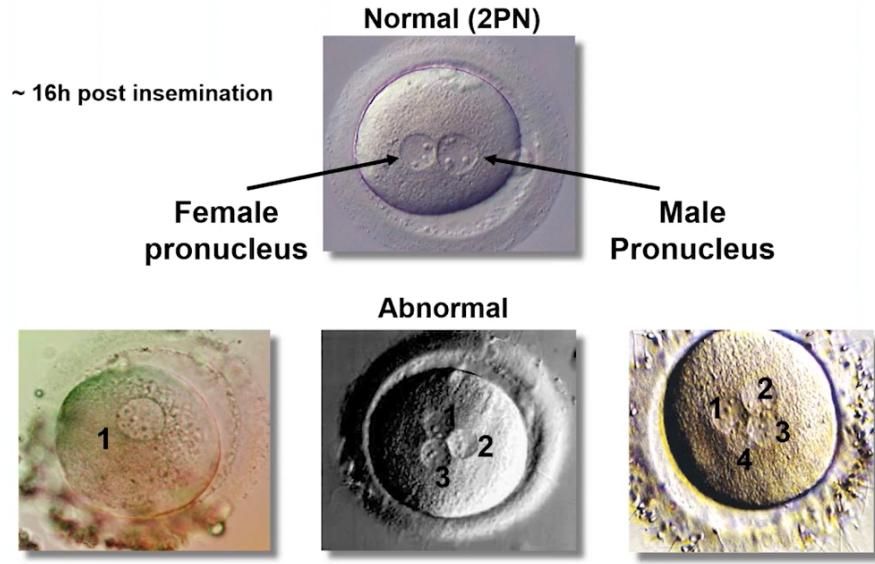
They used this Hour clock conventional method and trained AI to predict the accurate location to perform ICSI and found it as the extruded polar body to be near 5 hr mark and the training accuracy was 99.9%

After performing the ICSI and 16 hr of post insemination they examine the fertilized egg and run it through an AI model to predict if the egg is Normally or Abnormally Fertilized.

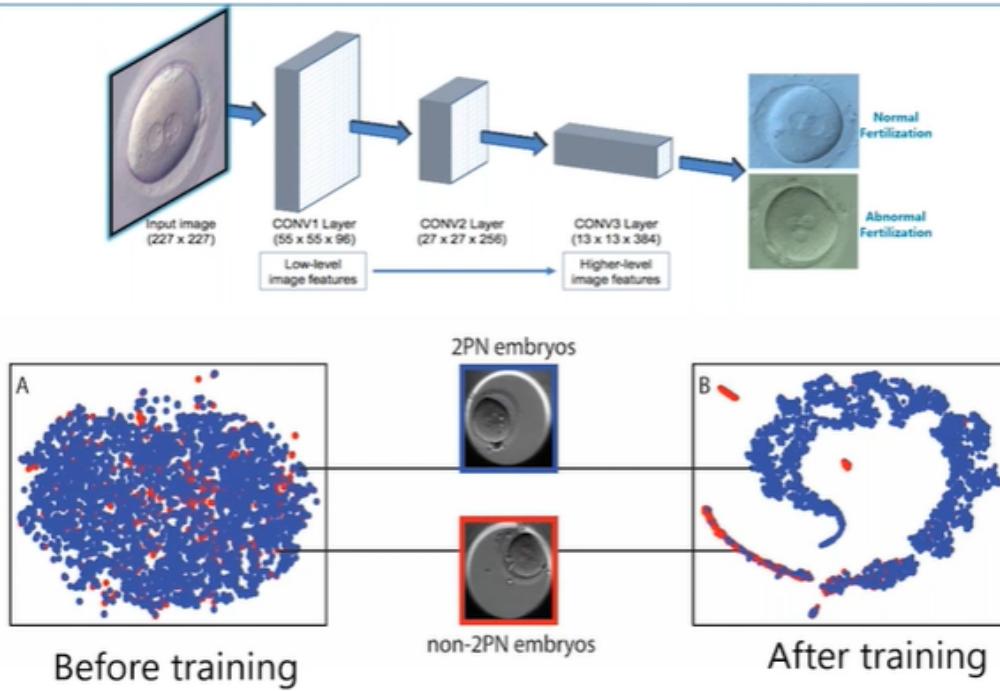


Method of doing ICSI:-

<https://drive.google.com/file/d/1Sns43lqPnU8FkhG9tqZJIVHUs-8Q9b6C/view?usp=sharing>



Analysis of the 2PN embryo in AI method.

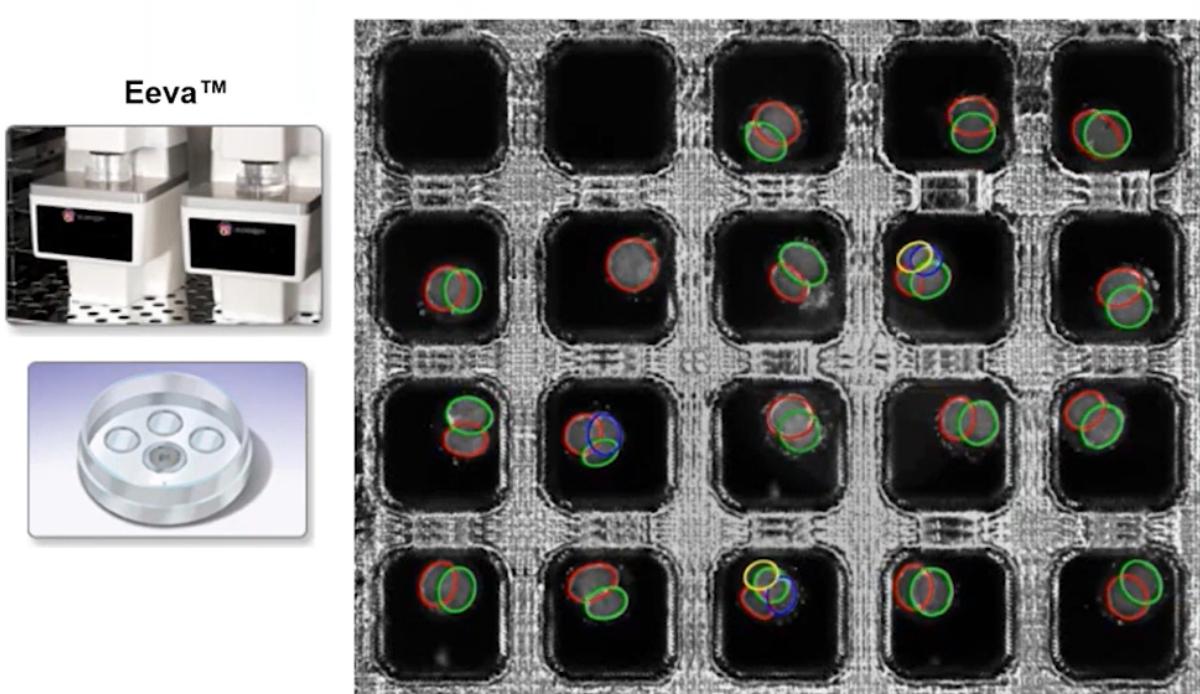


## **Cleavage state development**

On day 3 they look for the cleavage state development they look for:-

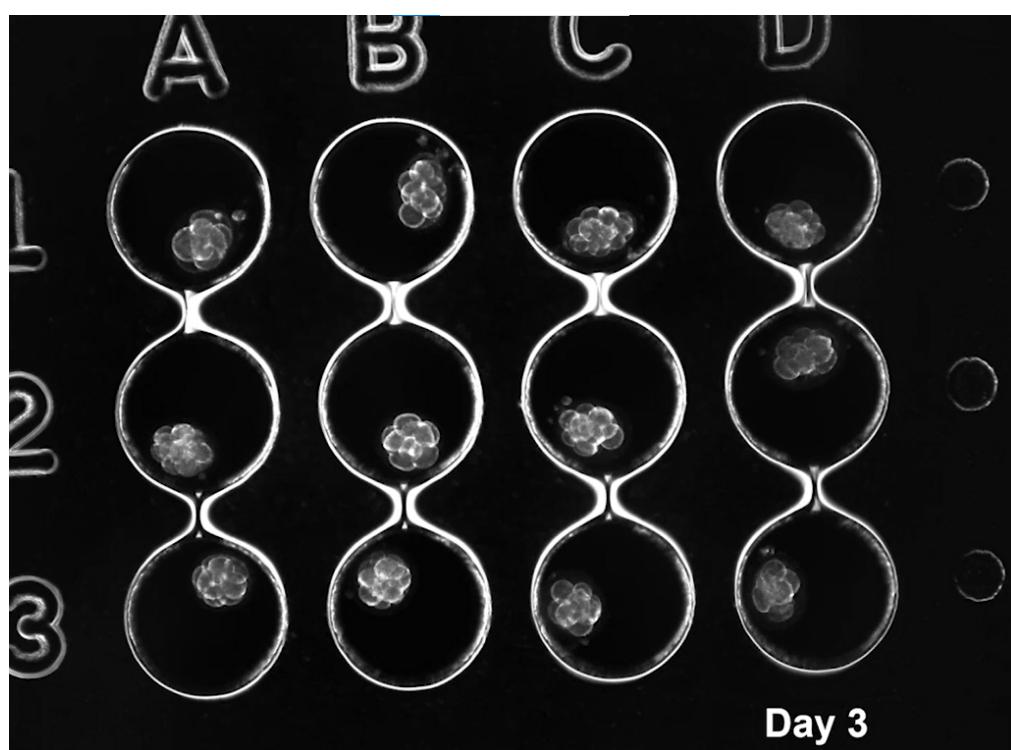
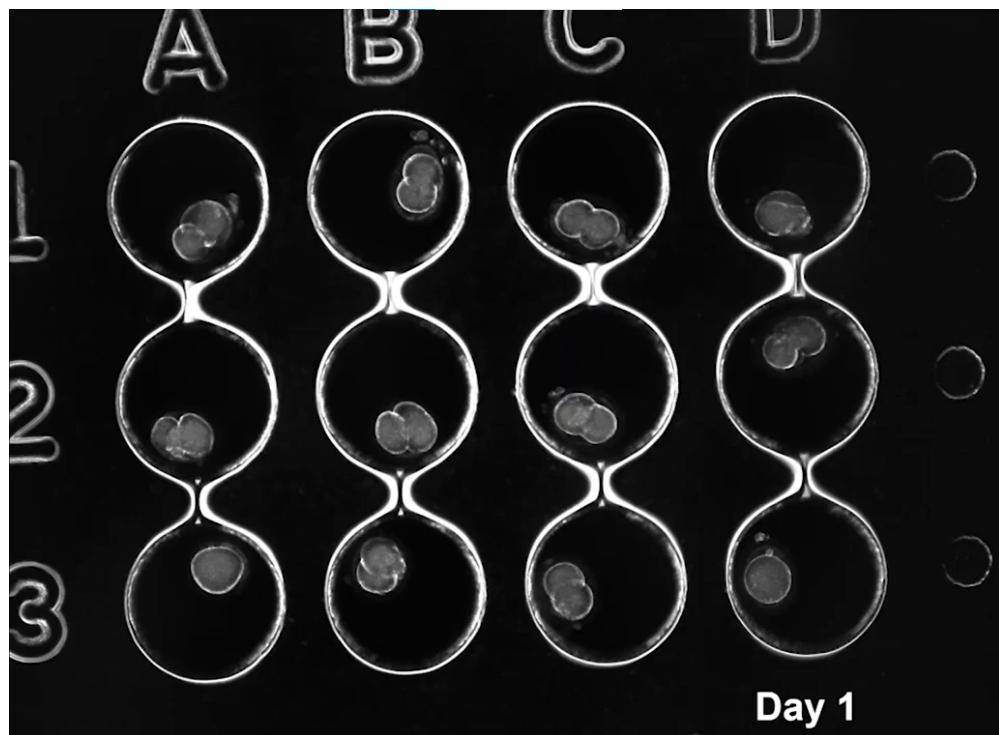
- Cell number
- % of fragmentation
- %Asymmetry

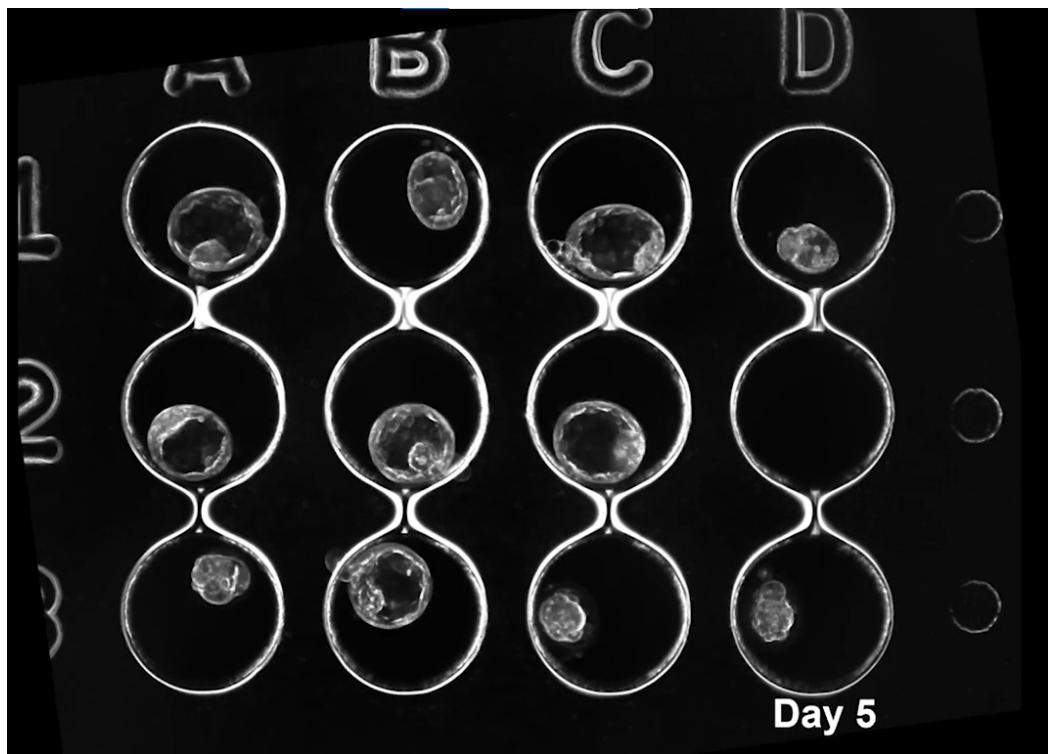
But in 2010 the culture changed to Timelapse video imaging as it will give a close look and it uses this footage to clearly visualize what is happening and how it is happening. This led to the upliftment of lots of Algorithms to classify the best embryo that will be capable of baby-making.



This tool helps to make the visualisation and this figure we can see the division of cells and can be seen by different colours.

## The usage of Time-lapse Imaging in AI

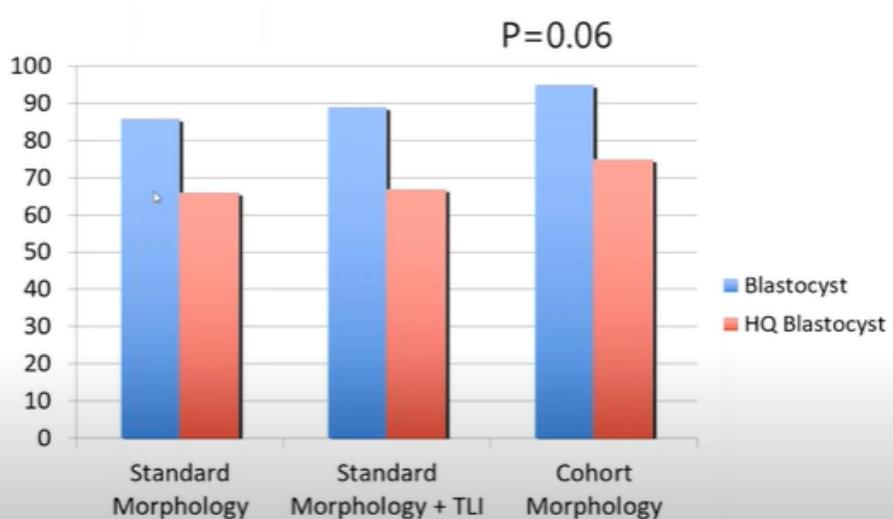




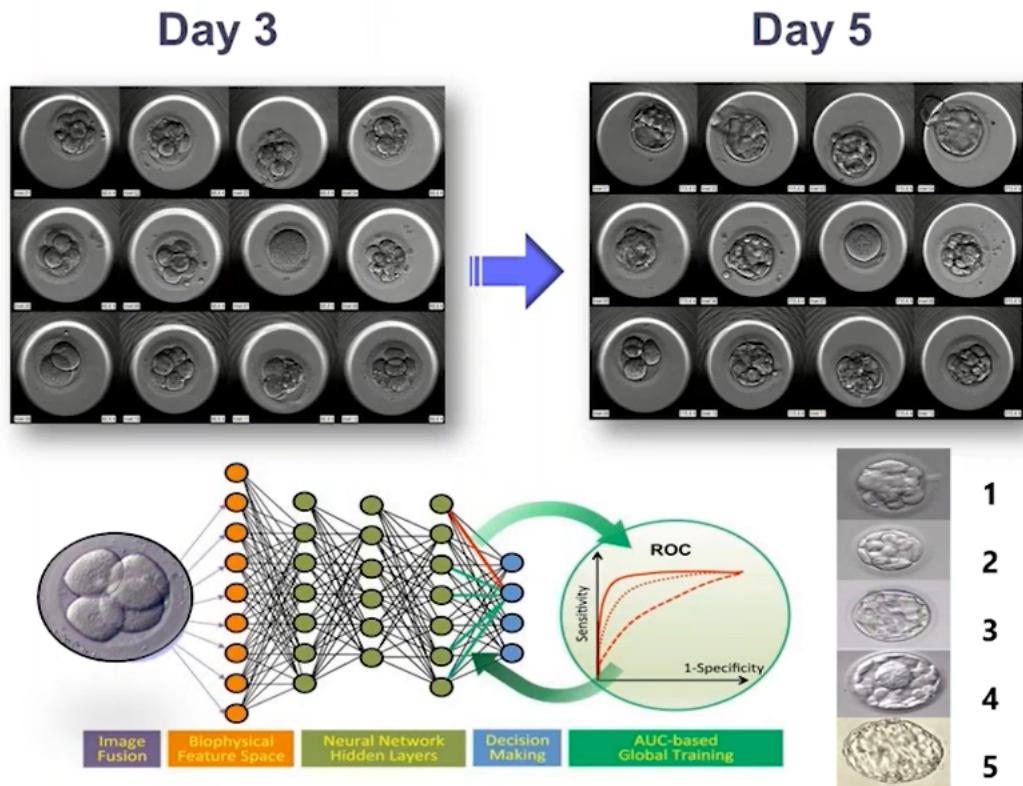
These images were put through a test by 3 ML algorithm to find the optimized one in which the first algorithm chose only Standard Morphological characters, the second one took the Standard Morphological characters and Time-lapse imaging, and at last, took only cohort Morphology. (Similar Morphological Characters to the test data, along with Cell number, fragmentation, and Symmetry).

## Day 3 Selection Methods

MASSACHUSETTS  
GENERAL HOSPITAL  
OBSTETRICS &  
GYNECOLOGY



But the main problem is that Cohort Morphology selection has low Consistency in the selection process, so they trained the AI to get the imaging of day 5 using the day3 imaging and hence they can get a good idea about what is going to happen with embryos in cohorts.



So by this method AI could pick some embryos in which 90 % and above became perfect Blastocyst after.

## Laser-assisted hatching

Laser-assisted hatching is done on day-3, this is done to prepare for hatching, to prepare for PGT (Preimplantation Genetic Testing) ( a genetic test performed on embryos to identify numerical chromosomal abnormalities (aneuploidy)) so that the Trophectoderm ( first cell type that emerges during development and plays pivotal roles in the viviparous mode of reproduction in placental mammals) have an easy time herniating outside the zona pellucida

This method is used for purposes such as Polar body biopsy, blastomere biopsy, assisted hatching, trophectoderm biopsy, blastocoel collapse

This method uses laser pulses and these are applied on a zone where there is the greatest distance between the zona pellucida and healthy blastomere

**Laser Assisted Hatching**

MASSACHUSETTS GENERAL HOSPITAL  
OBSTETRICS & GYNECOLOGY

Polar Body Biopsy      Assisted Hatching      Blastomere Biopsy      Trophectoderm Biopsy      Blastocoele Collapse

Laser pulses are applied on zona where there is the greatest distance between the zona pellucida and healthy blastomeres

Isotherm Color Key

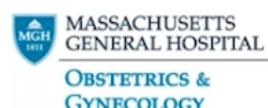
Laser Beam
140°C (Hole Size)
100°C
80°C
60°C
50°C

Navigation icons: back, forward, search, etc.

## Automated assisted hatching

They try to train a system or model to select the best location to perform laser-assisted hatching. So again They use the Hour clock conventional method. They numbered it like 1 to 12 and they had 12 classification time points to train the system and they got an accuracy of 99%. Again this is another step to automation.

### Automated Assisted Hatching



#### Dataset details:

Training set (before augmentation) = 1159 images

Training set (after augmentation) = 13908 images

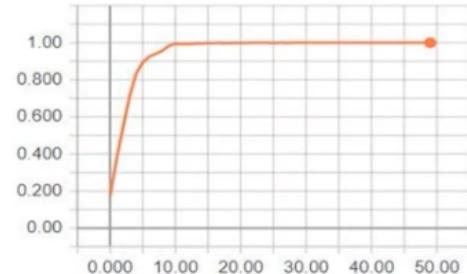
Validation set (before augmentation) = 159 images

Validation set (after augmentation) = 1908 images

Test set (before augmentation) = 324 images

Test set (after augmentation) = 3888 images

Training Accuracy : 99.87 %



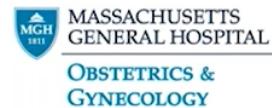
Kelly et al., Fertility and Sterility. 2020



## Blastocyst Stage Assessment

After the hatching is done they move to the blastocyst assessment stage and they use the Gardner grading system to evaluate the quality. The Gardner blastocyst grading system assigns 3 separate quality scores to each blastocyst embryo: Blastocyst development stage – expansion and hatching status. Inner cell mass (ICM) score, or quality. Trophectoderm (TE) score, or quality.

## Blastocyst Grading System



Grade	Stage	Description
1	Early Blastocyst	Blastocoel less than half the volume of the embryo, little or no expansion in overall size; ZP thick
2	Expanding Blastocyst	Blastocoel more than half the volume of the embryo, some expansion in overall size; ZP beginning to thin
3	Full Blastocyst	Blastocoel completely filling embryo; ZP not completely thinned
4	Expanded Blastocyst	Blastocoel completely filling embryo; fully expanded embryo and ZP very thin
5	Hatching Blastocyst	Hatching blastocyst, TE starting to herniate through the ZP
6	Hatched Blastocyst	Blastocyst completely hatched (i.e. completely out of the ZP)

## Gardner Grading System

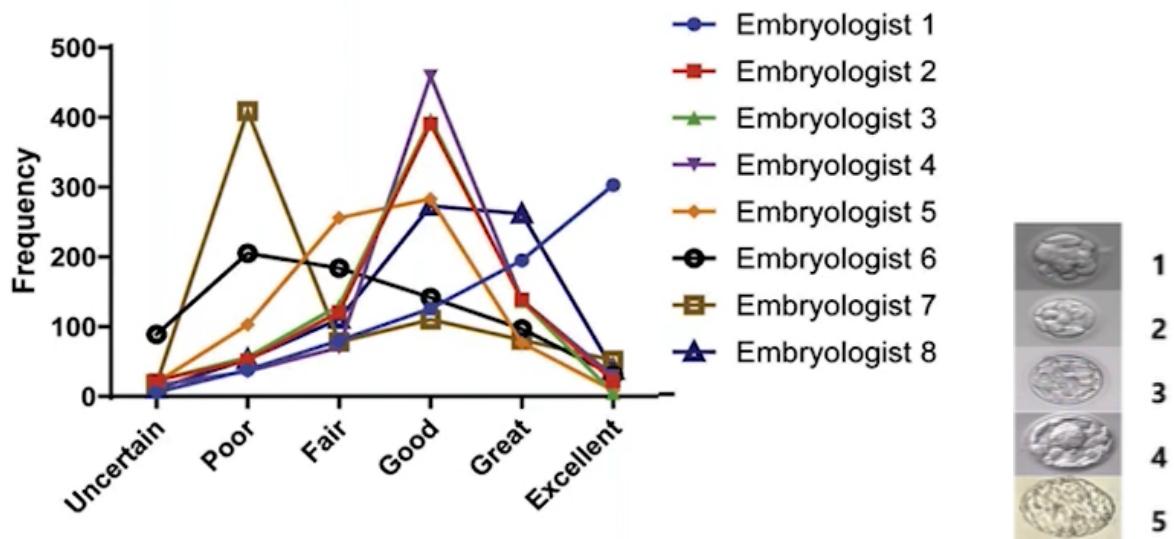
For grading, they have a mobile application based in AI which can grade the Blastocyst development stage – expansion and hatching status. Inner cell mass (ICM) score, or quality. Trophectoderm (TE) score, or quality.



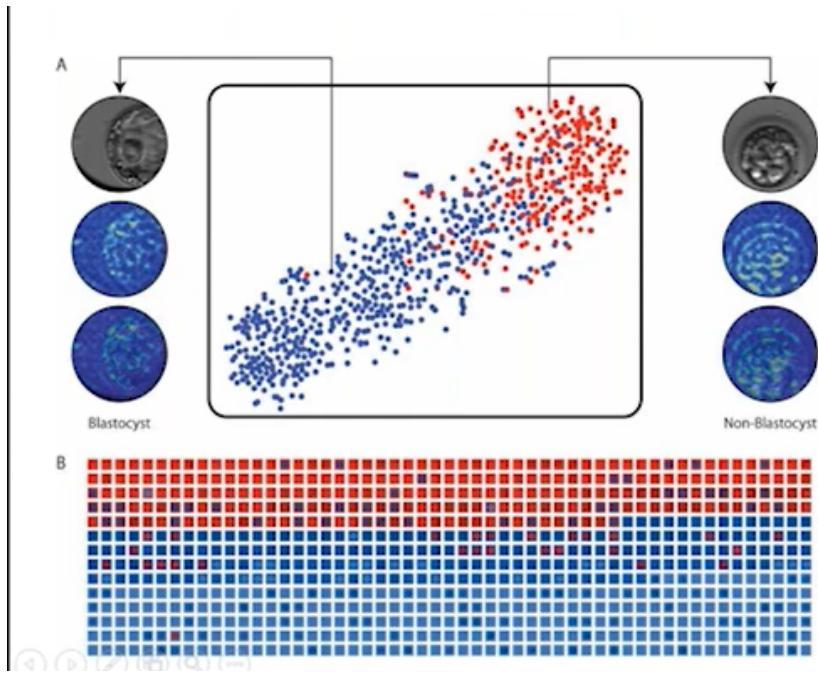
### High Quality Blastocyst: $\geq 3BB$

① ② ③ ④ ⑤ ⑥

The usage of this application is proven that when a group of 8 embryologists were to select the good quality blastocyst everyone was having a hard time or every person selected a different one.

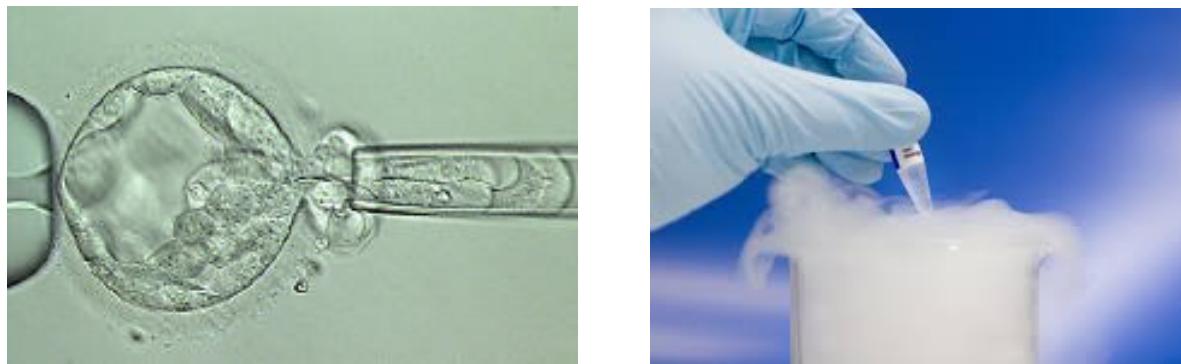


By using this AI model which can Predict the best blastocyst by training the model with 5 images from worst blastocyst to the good one, it was able to predict the best one from the Blastocyst in the group they provided to the model.

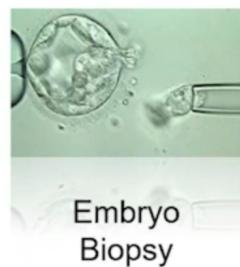


This is the AI predicted model in which the Blue represents the blastocyst and another to be non-blastocyst.

## EMBRYO BIOPSY AND CRYOPRESERVATION



Embryologists had inconsistencies in the embryos that they would perform biopsy and similarly there were inconsistencies in embryos they would vitrify. So there was an overall inconsistency in some of the clinical decision making.

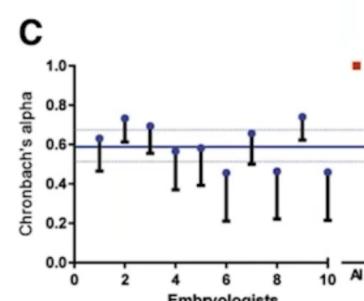
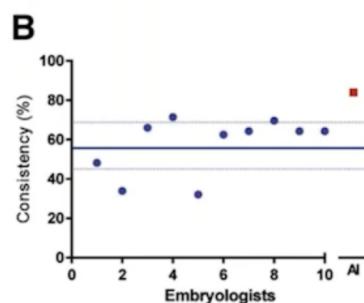
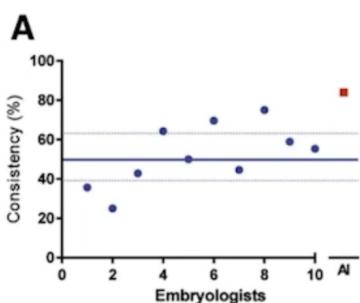


Embryo Biopsy



Embryo Freezing

Overall Consistency



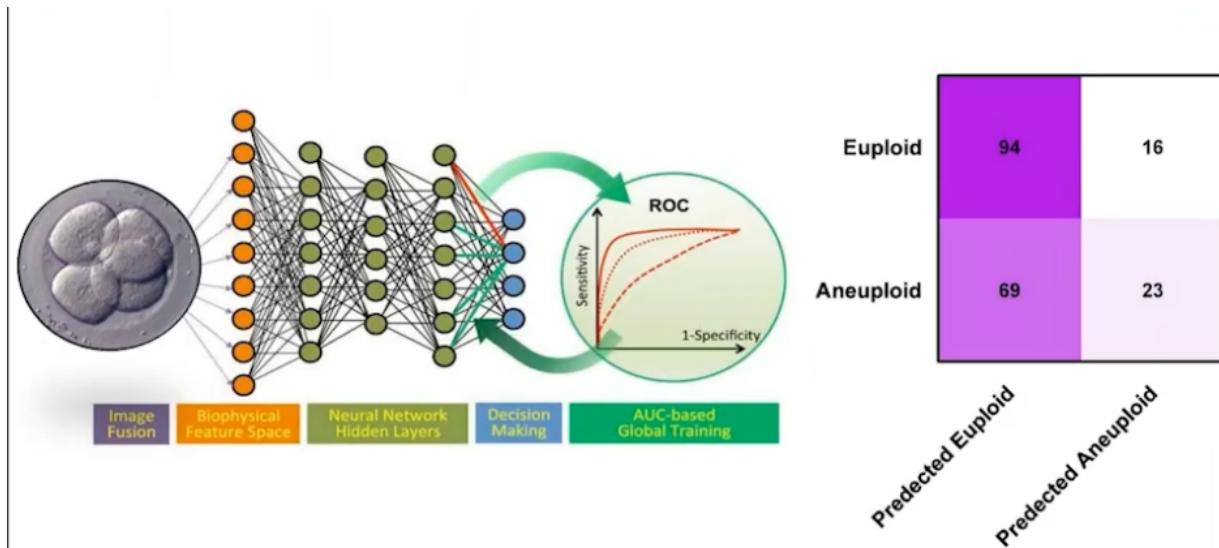
But Artificial Intelligence made the same calls every time and was not biased on what our decision is and reduced the inconsistency found earlier.

## Embryo Ploidy Prediction

- A deep neural network model was trained and tested using 3112 images to classify embryos as aneuploid and euploid.
- Embryos images captured on day 3 and day 5 were used to classify embryos based on karyotype.
- The algorithm was tested using 201 blastocyst images.

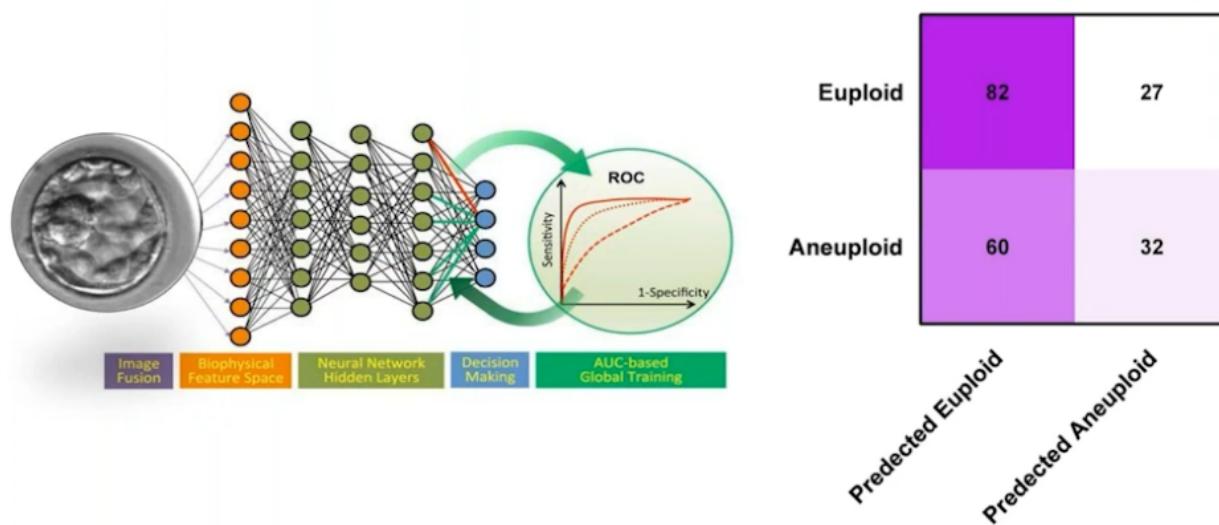


## Day 3 Karyotype Prediction



The deep learning CNN trained to classify day 3 embryos as aneuploid and euploid was able to identify 85.4% of aneuploid embryos.

## Day 5 Karyotype Prediction

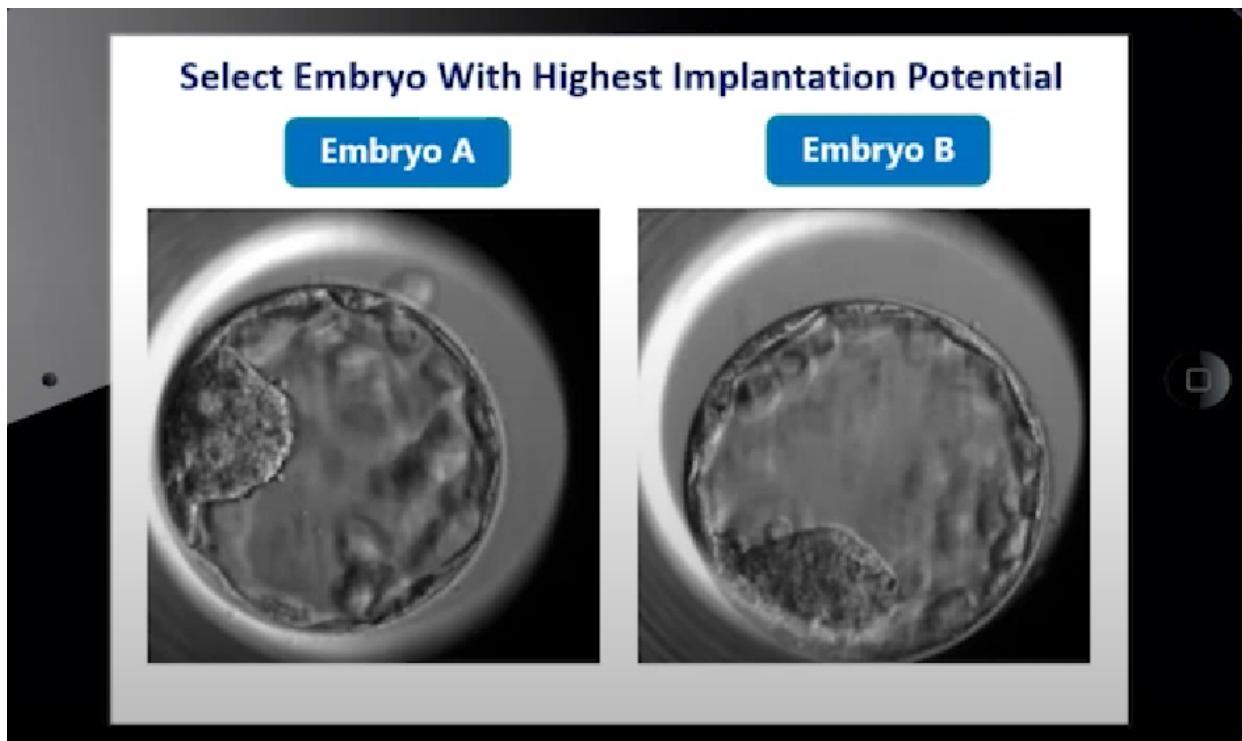


- CNN classified that karyotype on day 5 of development had specificity of 72.5%.
- Results show that networks can identify non-invasive markers for genetically abnormal embryos, the need for non-invasive markers in selecting genetically normal embryos for transfer still exist.

## IMPLANTATION OUTCOME PREDICTION

They trained an algorithm to predict implantation so in this we took images of day 5 embryos that were transferred and the output is whether or not they would have an continuing pregnancy.

It had a high accuracy of 79 percent in determining whether which gametes we are going to implant or not

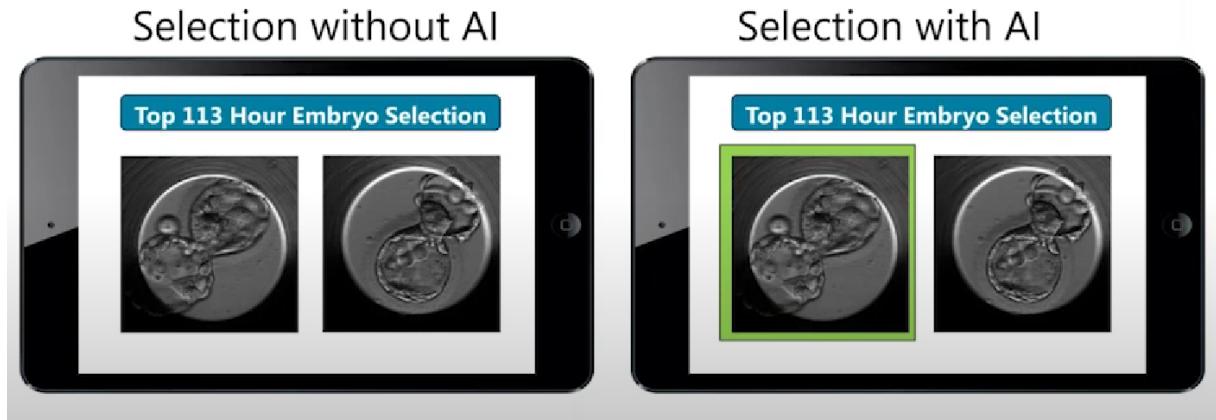


Then, using two embryos of comparable quality and grade, a module was created in which all of the embryos in the module are euploid Embryo on transfer as an eset (Elective single embryo transfer ) and with known implantation results.

The cnn outperformed the embryologists in differentiating 200 euploid embryos based on their implantation outcomes

Embryologists average accuracy was 67.4 while the CNN(Artificial intelligence) was 75.3 percent

## Embryo selection with Assistance



Additional 200 Euploid eSET embryo transfer test set with known outcomes. The staff without ai selected the embryos which were going to be implanted

The average selection by the staff without AI assistance was 65.5 percent .The AI correctly selected embryos 78 percent of time



The embryologists had the information of which all embryos were selected by the AI. Everyone improved in identifying the embryo for implantation and there was an average improvement rate of 8.1 percent

## **Embryo tracking and Witnessing**

Through this process, it ensures that the embryo and the gamete belong to the specified couples. By matching up with patient information. The AI innovation, in this case, is that they try to match the embryo characters to the patient's and so can identify the embryo with basic signatures and also match the patient id with patient cohorts.



## **Quality Control Monitoring**

AI is widely used in laboratories for quality control. This aims to set the laboratory up in a perfect cultural condition.

The culture condition in a lab mostly relies on:

- Internal and external temperatures of Incubators
- Surface temperatures
- Refrigerator and freezer temperatures
- Contact materials

Numerous KPIs or Key Performance Indicators are used to set up the quality of the lab. KPIs are essentially a set of Quantity based measurements that are used to measure a laboratory overall performance. One of the Pregnancy outcome KPI is the delay in results, the delay in outcome results makes it difficult to identify and correct the variables affecting embryo culture in a consistent way and timely way.

Therefore KPIs are very important in this aspect and the need to identify an early KPI measure is very important, as it can be used to assess cultural conditions and predict outcomes.

## **How the AI can be improved in IVF**

- Using big data sets and long-term training of the AI model can be used to improve the accuracy and chances of High-quality embryo selection.
- All IVF clinics can make a change in inputting the patient data, ie rather than keeping the IVF data to one clinic and making it accessible to every clinic by using Cloud storage, so from that AI can be used to study the various cases and the outcomes and also can be used to classify different images.
- Can be used to create a unified medical record along with all the clinics and can be accessed by using Cloud technologies.
- If this kind of Cloud is used to do so, the AI will be also capable of predicting the Medications for Infertility and post fertility care.

## **CONCLUSION**

- The AI system could learn how embryos develop over time and then use this information to select the best embryos to implant from just a single image. This would offer a cheaper alternative to current analysis tools that are only available at the most expensive IVF clinics.
- Advanced freezing technology allows more patients to have multiple children as a result of one IVF cycle, thereby reducing the cost and easing the process for patients.
- Artificial intelligence can predict how likely an embryo is to develop as far as the stage of having a fetal heart and can thus help the embryologist to select the best embryo for transfer.

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