

19BIO103

Artificial Intelligence in IVF



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Introduction



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 (to exclude or banish) 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.

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.





Causes of female infertility

- Ovulation disorders
- Fallopian tube damage or blockage
- Uterine or cervical abnormalities
- Endometriosis
- Primary ovarian insufficiency (early menopause)
- Cancer and its treatment.



Causes of male infertility

- Abnormal sperm production or function
- Problems with the delivery of sperm
- Overexposure to certain environmental factors
- Damage related to cancer and its treatment



Solving the infertility problems

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.

ART includes procedures that make it easier for sperm to fertilize an egg, and help the egg implant in your uterine lining.

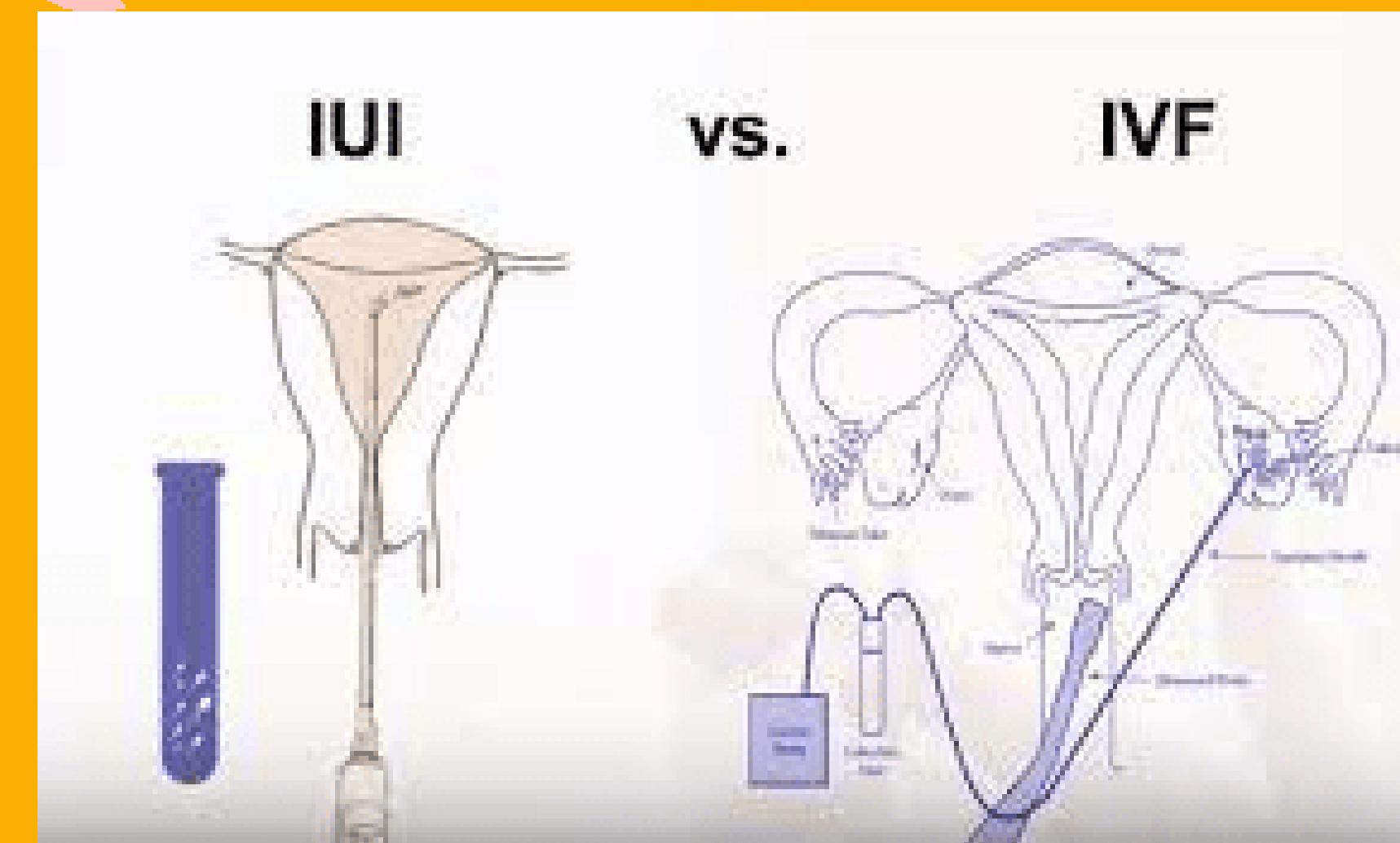
Assisted Reproductive Technology (ART) describes several kinds of procedures that can help you have a baby.

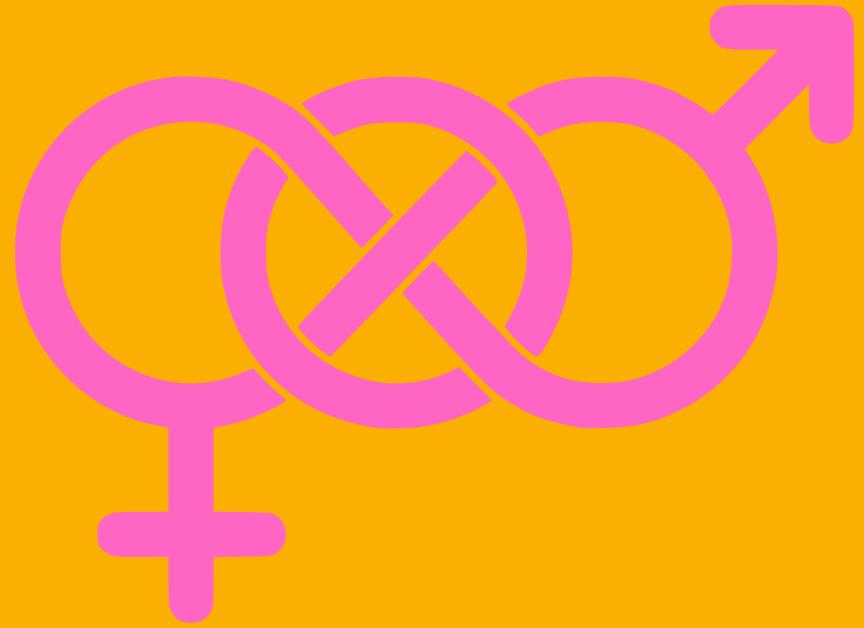


fertility treatment methods

Two of the most common fertility treatments are:

- intrauterine insemination (IUI)
- In vitro fertilization (IVF)
- Cryopreservation
- gestational carriers



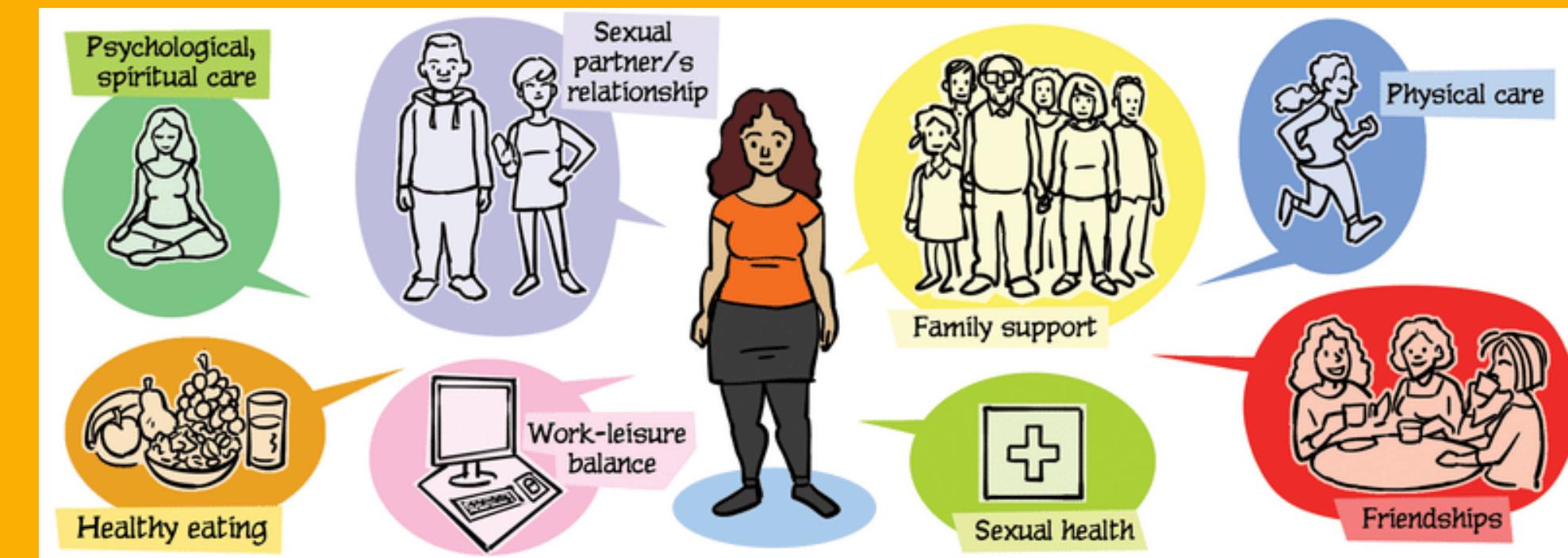


Sexual health

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

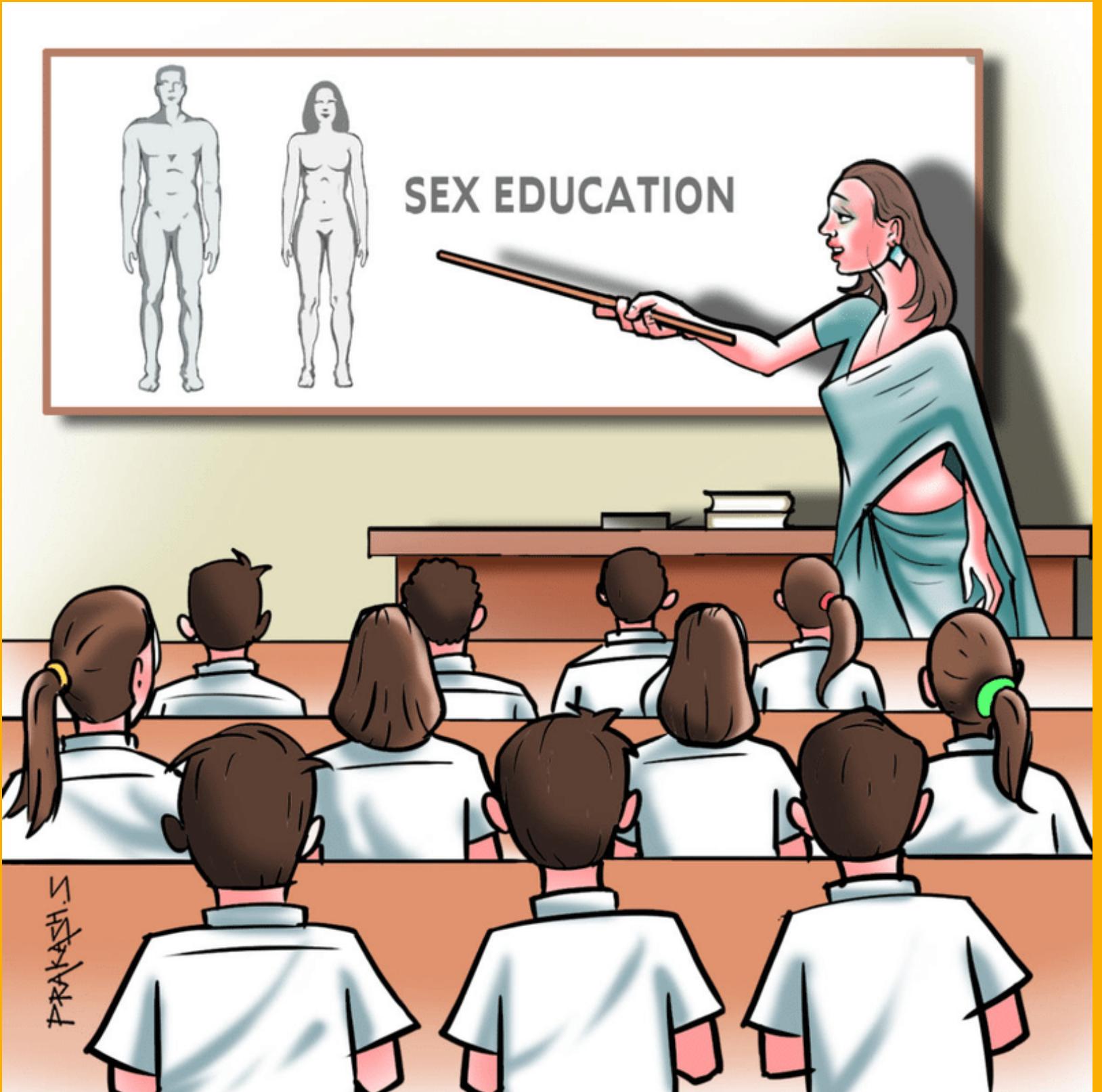
Key conceptual elements of sexual health When viewed holistically and positively

- 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.



Sex education

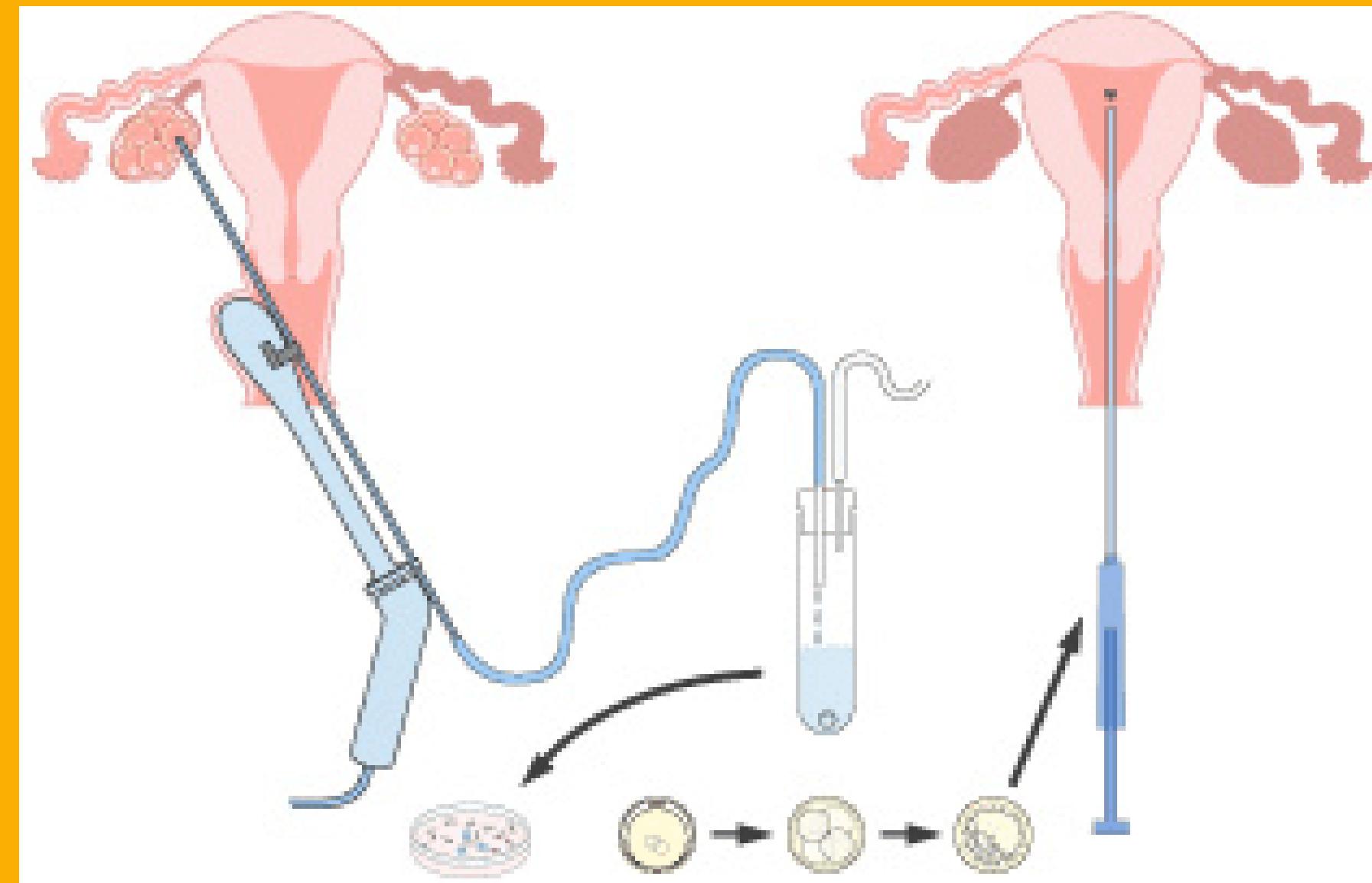
Sex education is learning about a broad variety of topics related to sex and sexuality, exploring values and beliefs about those topics, and gaining the skills that are needed to navigate relationships and manage one's own sexual health. Sex education may take place in schools, in community settings,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



Types of Assisted Reproductive Technologies

In vitro fertilization-embryo transfer (IVF-ET)

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.

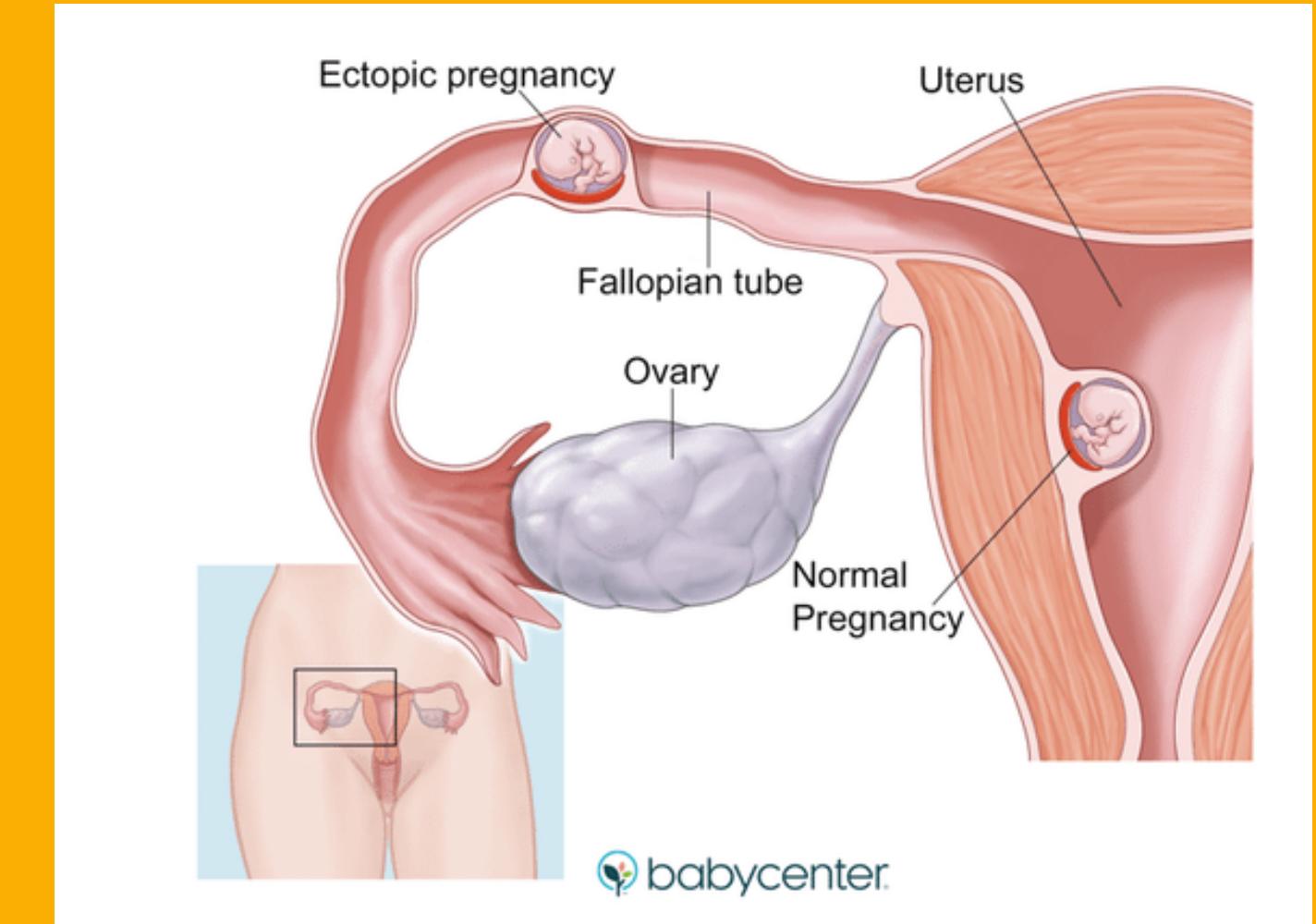


Benefits of IVF

Increased chance of fertilization and pregnancy.

Potential complications

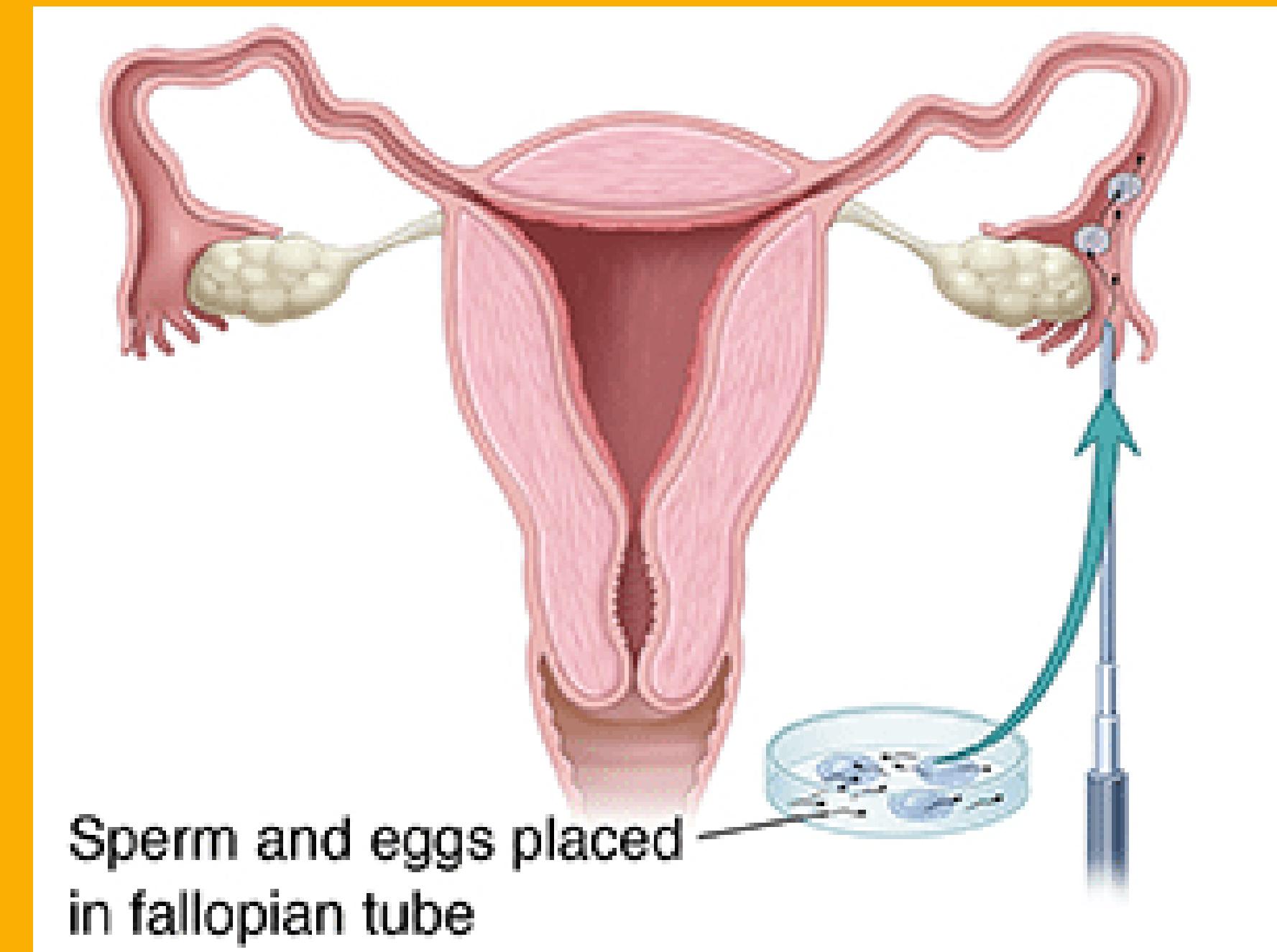
- multiple pregnancies, or two or more embryos implanting at a time
- side effects from fertility drugs, such as ovarian hyperstimulation syndrome
- ectopic pregnancy, where the embryo settles outside of the womb



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.

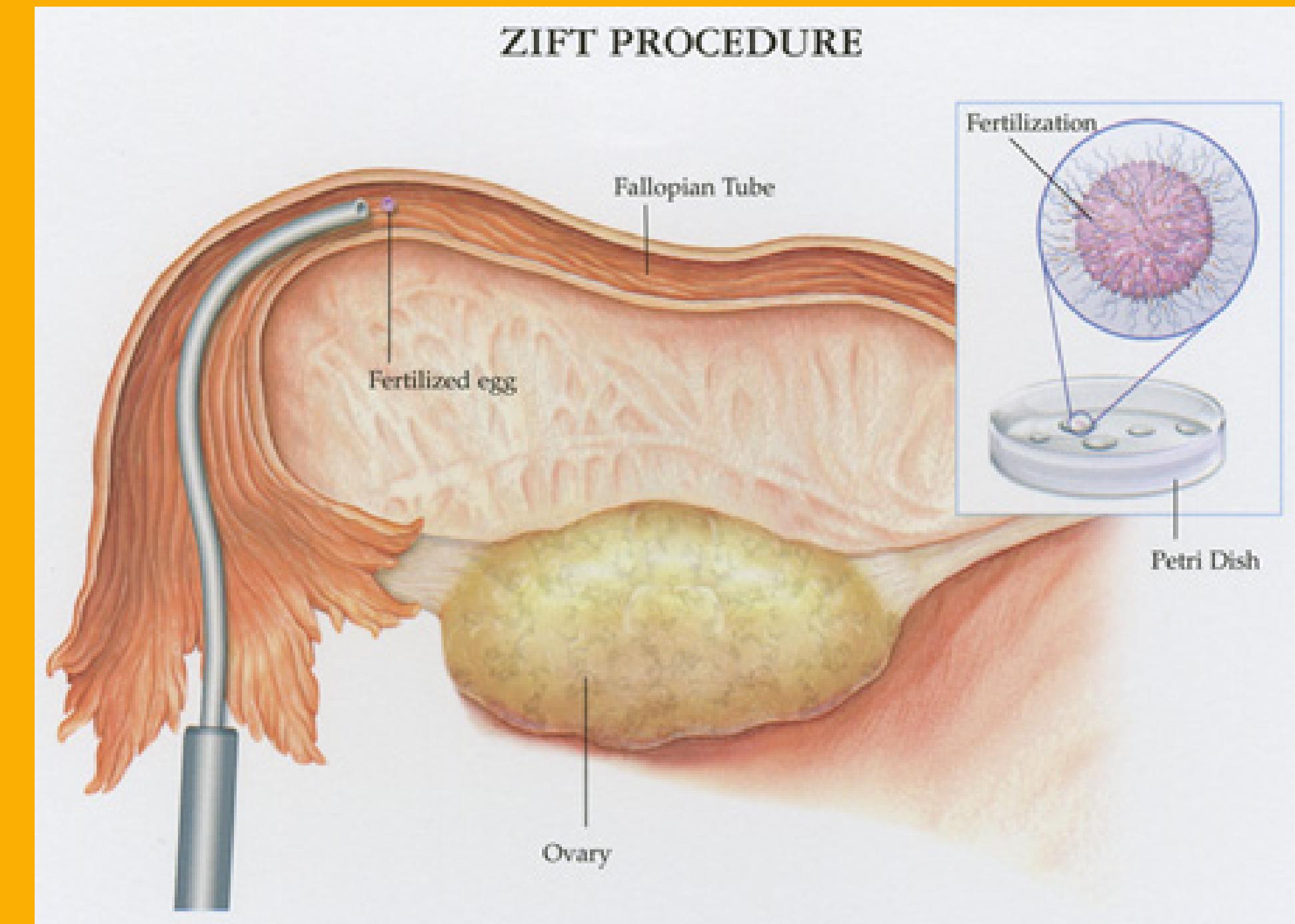
As there is no IVF procedure, a person does not have to choose which embryo to transfer.



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.



Frozen embryo transfer (FET).

Frozen embryo transfer (FET) involves thawing previously IVF frozen embryos and inserting them into a person's uterus.

Another possible risk of FET is that not all frozen embryos survive the thawing out process.



Intra Cytoplasmic 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 centre of an egg.



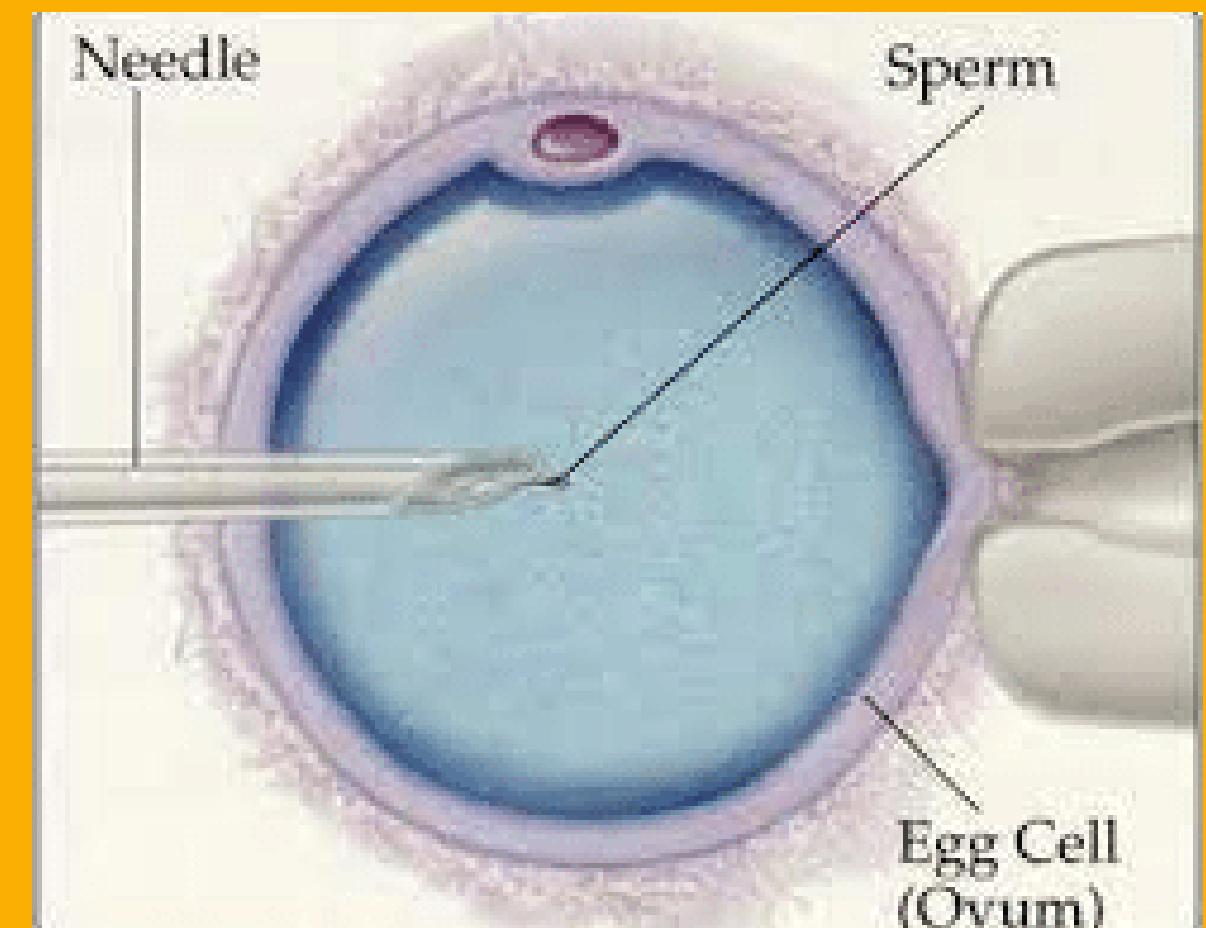
The involvement of AI in ART

Consider the highly manual and labour-intensive processes of ART as it is today.

Success rates depend on several variables.

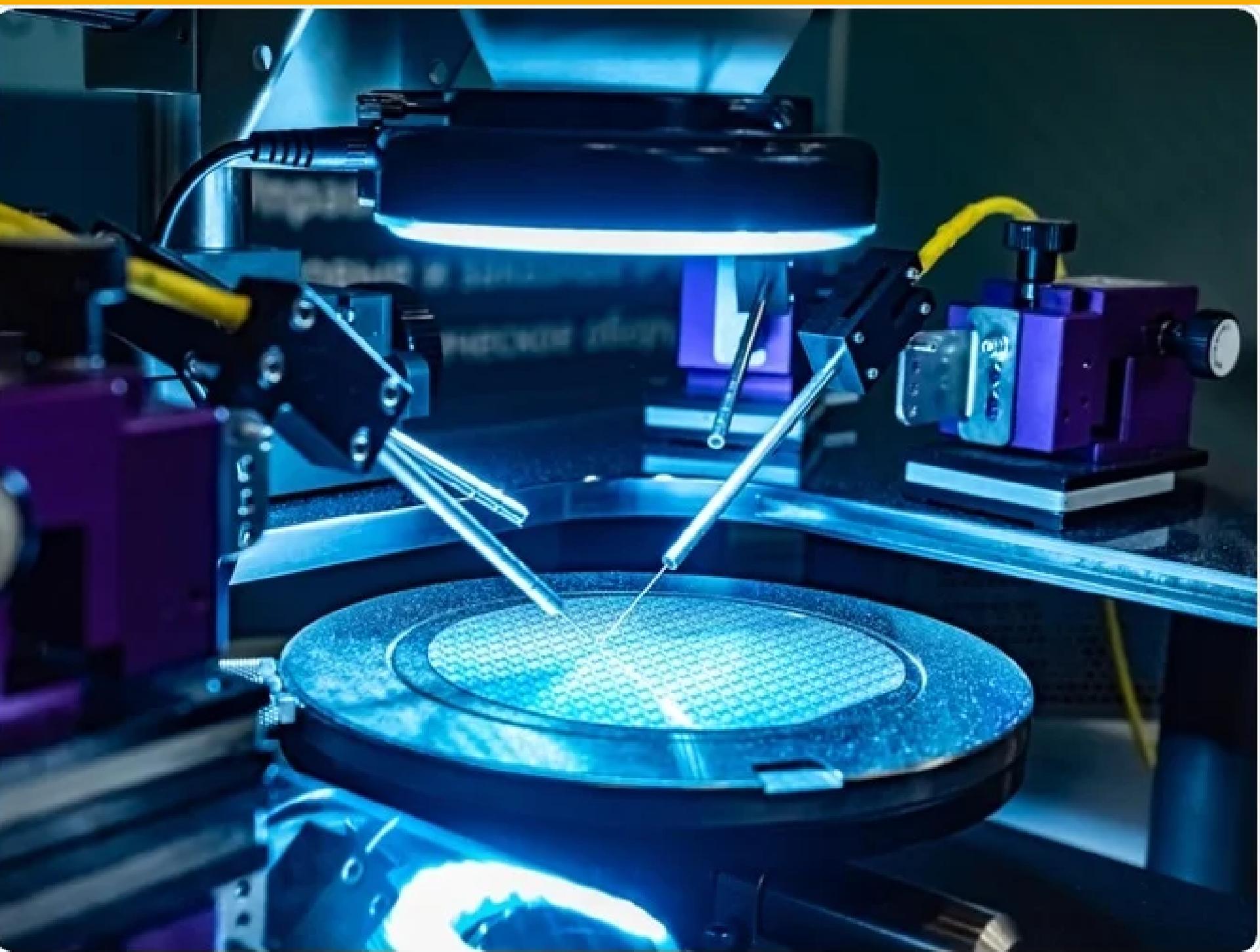
Some variables are patient-specific and (likely) uncontrollable, but many others are rooted in the process, including sperm, oocyte, and embryo selection to fertilization to implantation.

Lack of automation leads to high inter-user variability.



Automating and streamlining the entire process should reduce overhead costs to fertility practices and increase access and reduce costs for patients.

Researchers have had nascent successes in using AI to identify and characterize the most viable oocytes and embryos.



**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.**

**Computer-aided sperm analysis
(CASA) assesses motile percentage and
kinematic parameters at the
population level of Sperm.**



AI could also help predict IVF outcomes to the patient level.

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.

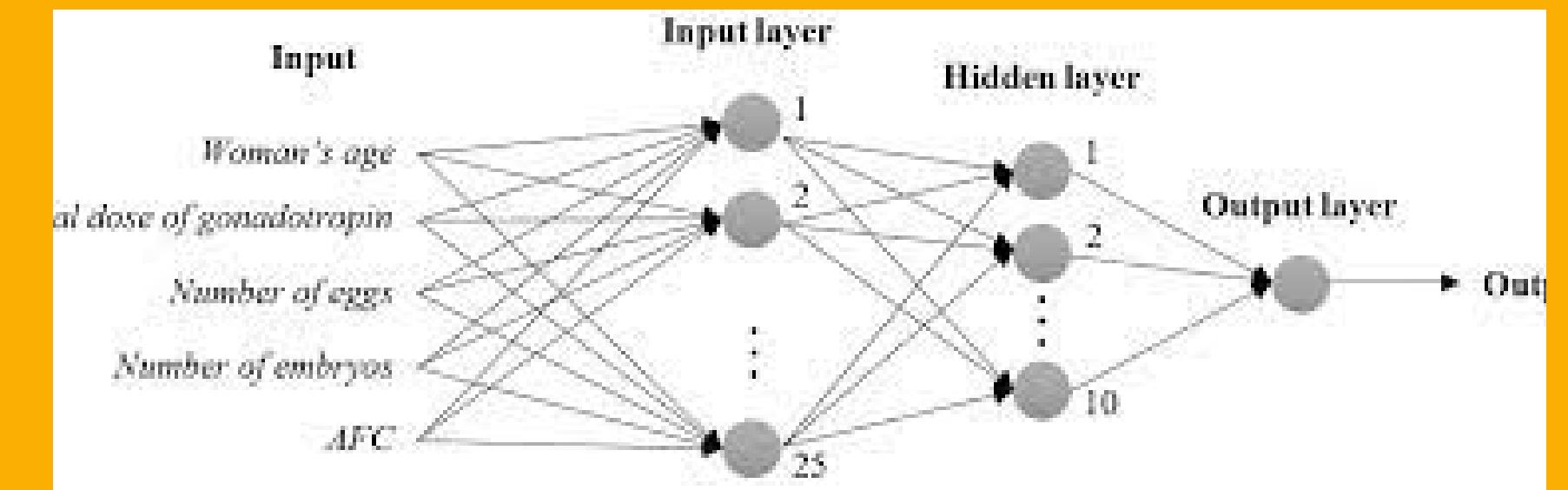
AI can begin to learn from partial, varied data and provide limited insights—insights limited by the quality of the data from which they learn.

Comprehensive note-taking, detailed outcomes reporting, and routine collection of high-quality imaging can accelerate this innovation.



Steps for doing IVF using AI

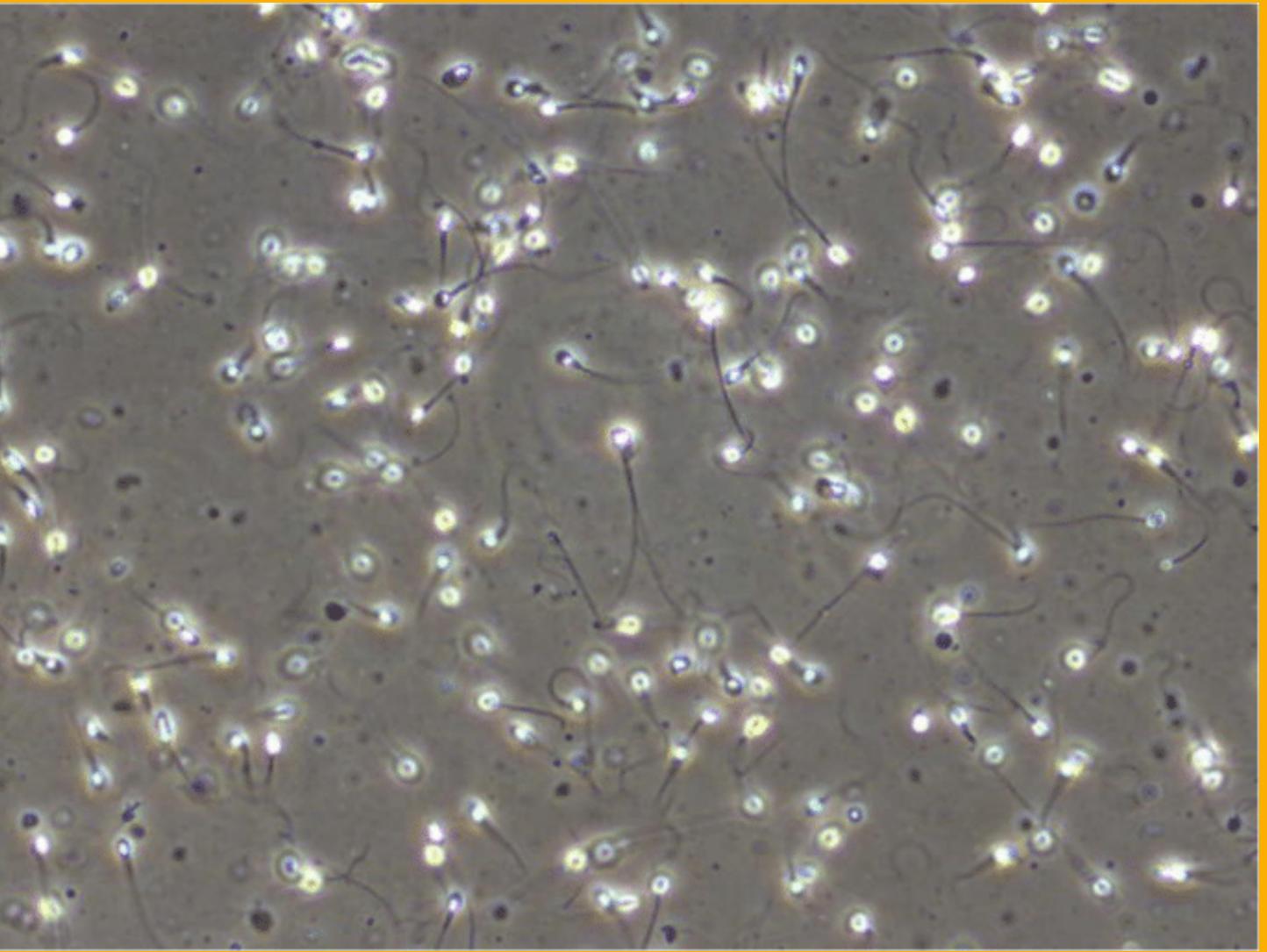
- Test the Sperm Quality Using AI
- Oocyte Assessment
- Performance of ICSI
- Cleavage state development
- Laser-assisted Hatching
- Blastocyst stage assessment
- Embryo Biopsy and Cryopreservation
- Implantation outcome prediction
- Embryo Tracking and witnessing
- Quality Control Monitoring



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)



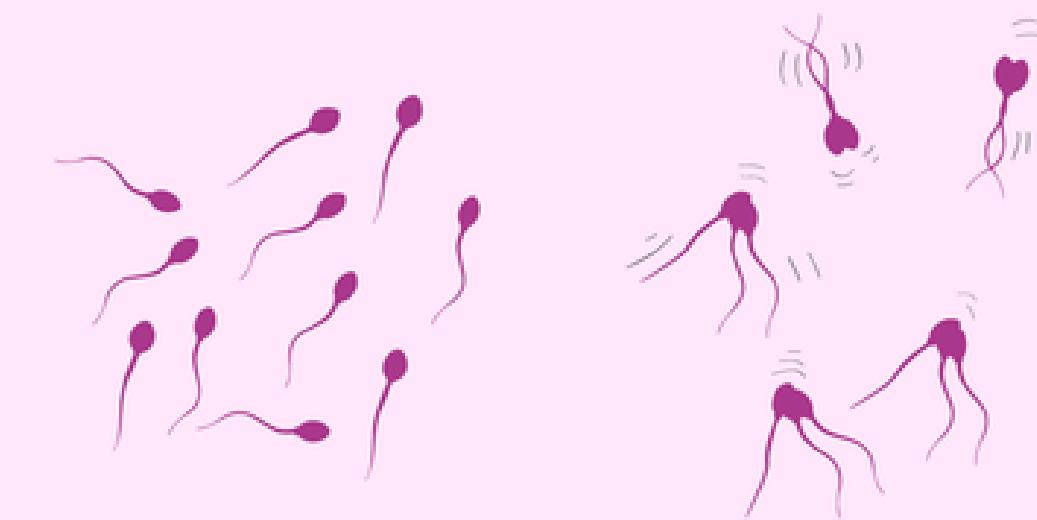
The range of adhesion is graded into 4 grades

Grade-0: No adhesion

Grade-1: Isolated or less than 10% adhesion

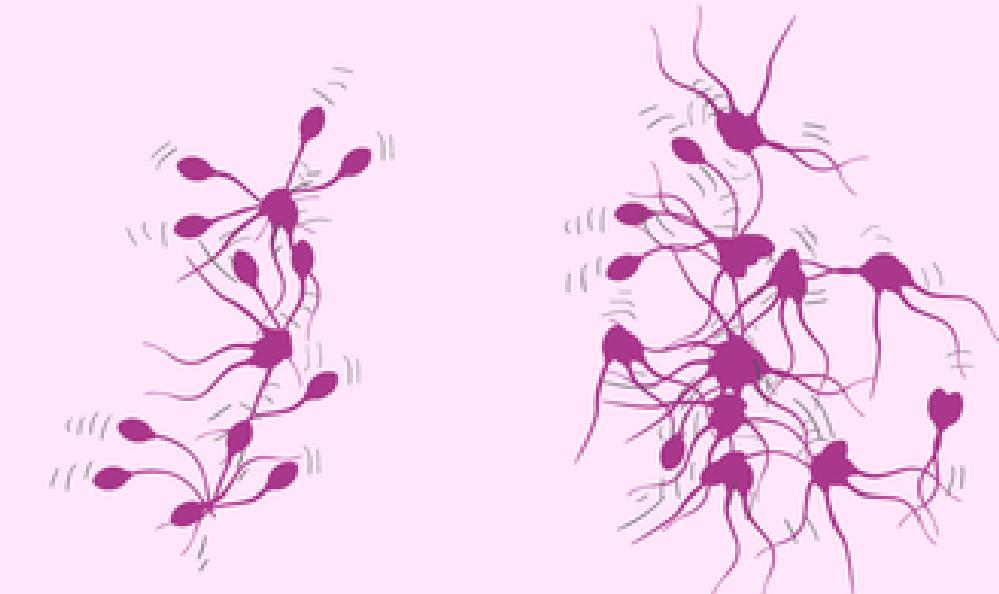
Grade-2: Moderate or less than 30% adhesion

Grade-3: Large or less than 50% adhesion



Grade 0
No adhesion

Grade 1
Isolated (<10%)



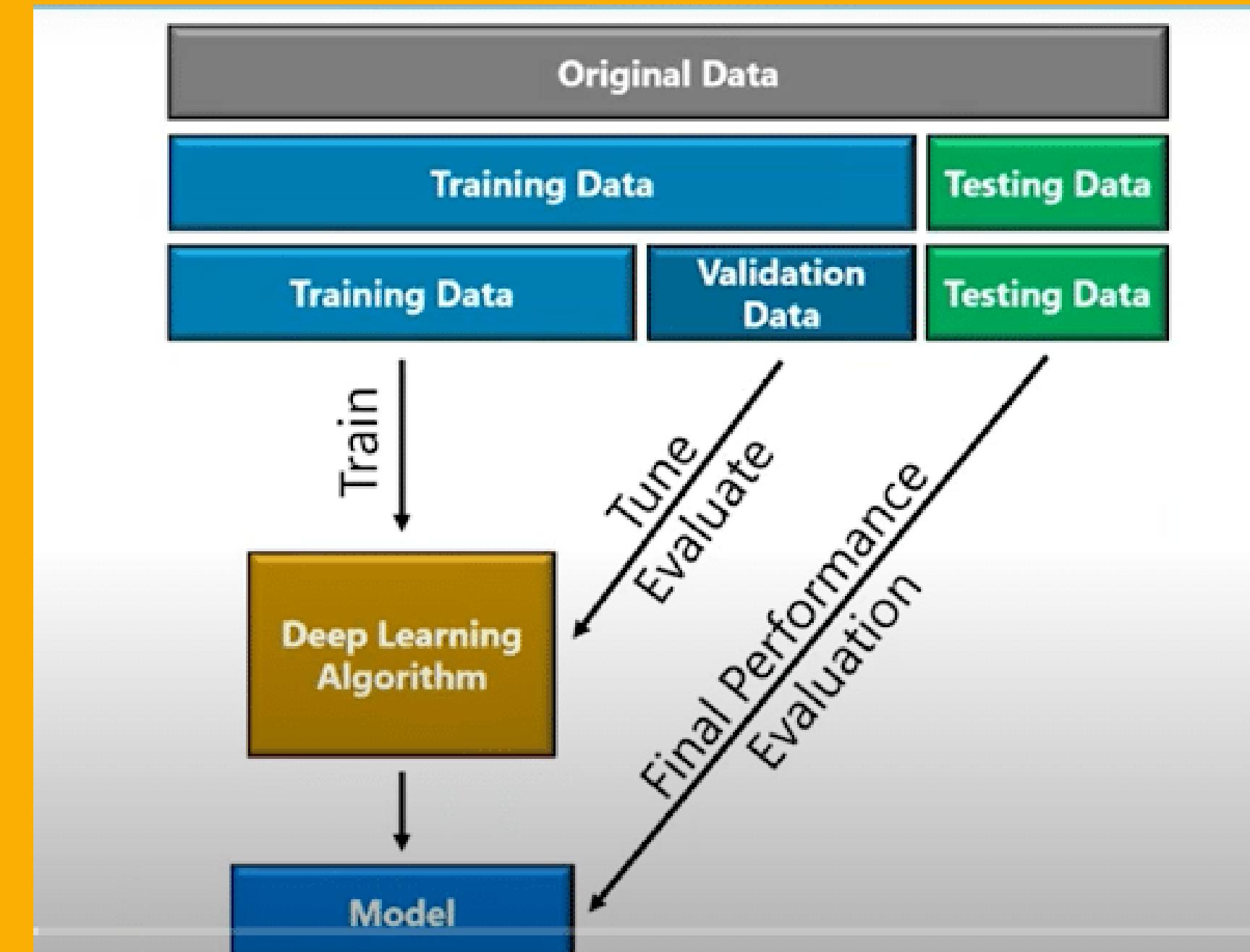
Grade 2
Moderate (<30%)

Grade 3
Large (<50%)

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..

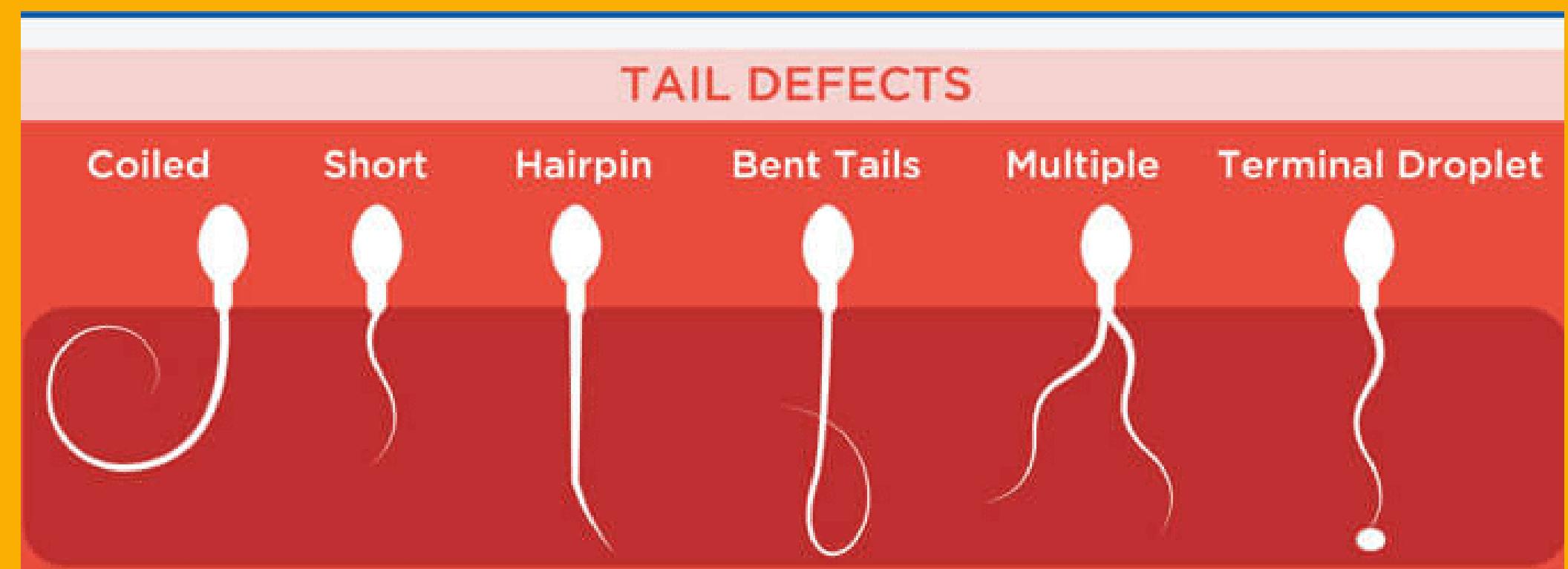
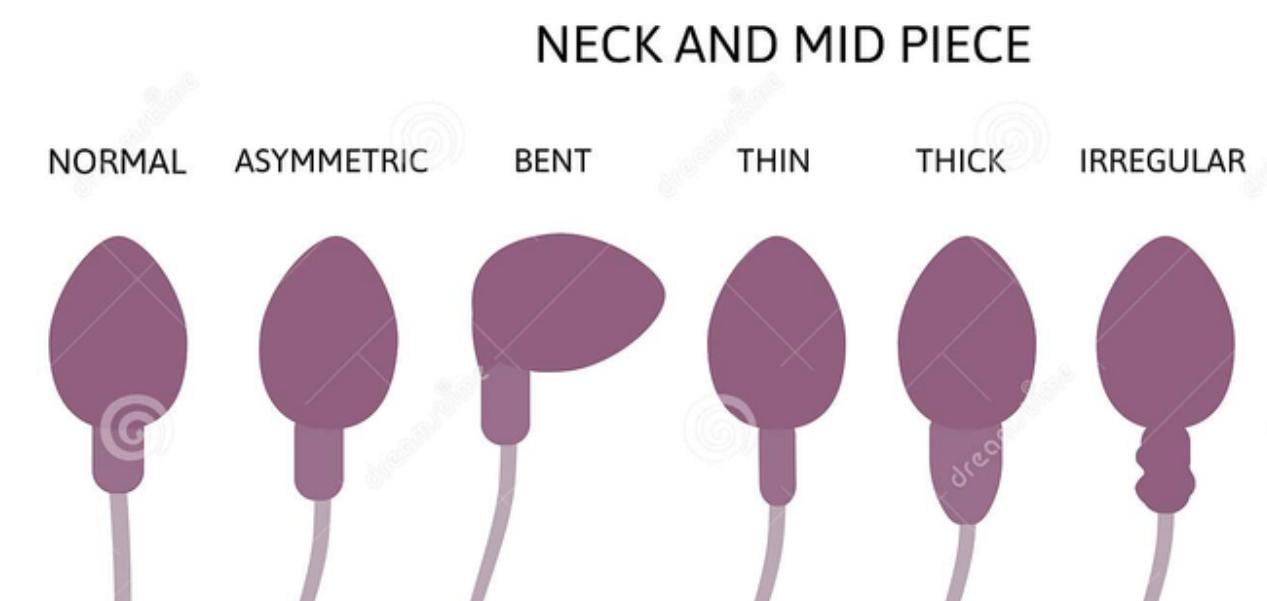
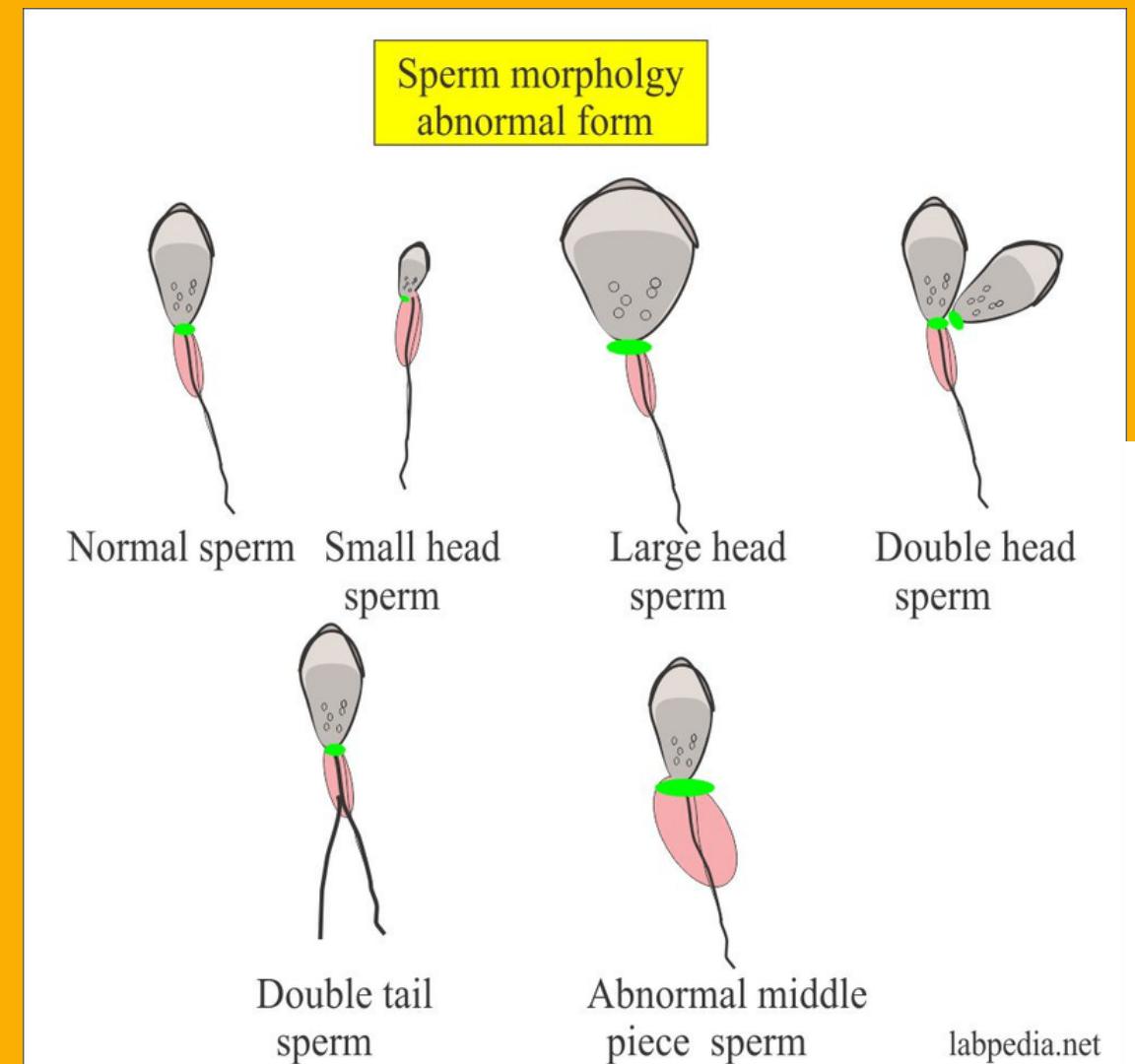
The ML algorithm used here is the CNN (Deep Convolved Neural Network) Which is effective in image classification programs.



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



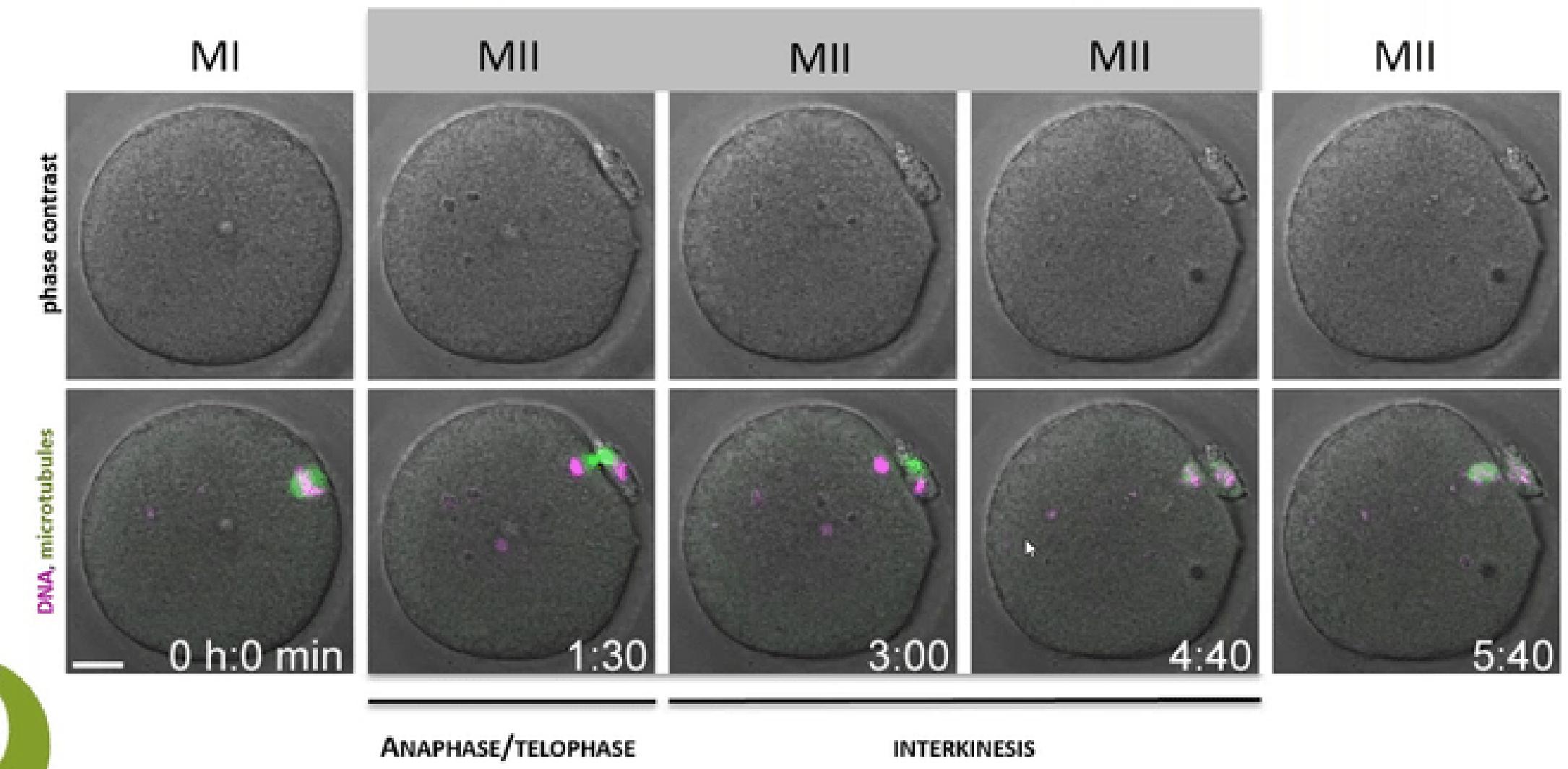
OOCYTE- ASSESSMENT

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

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



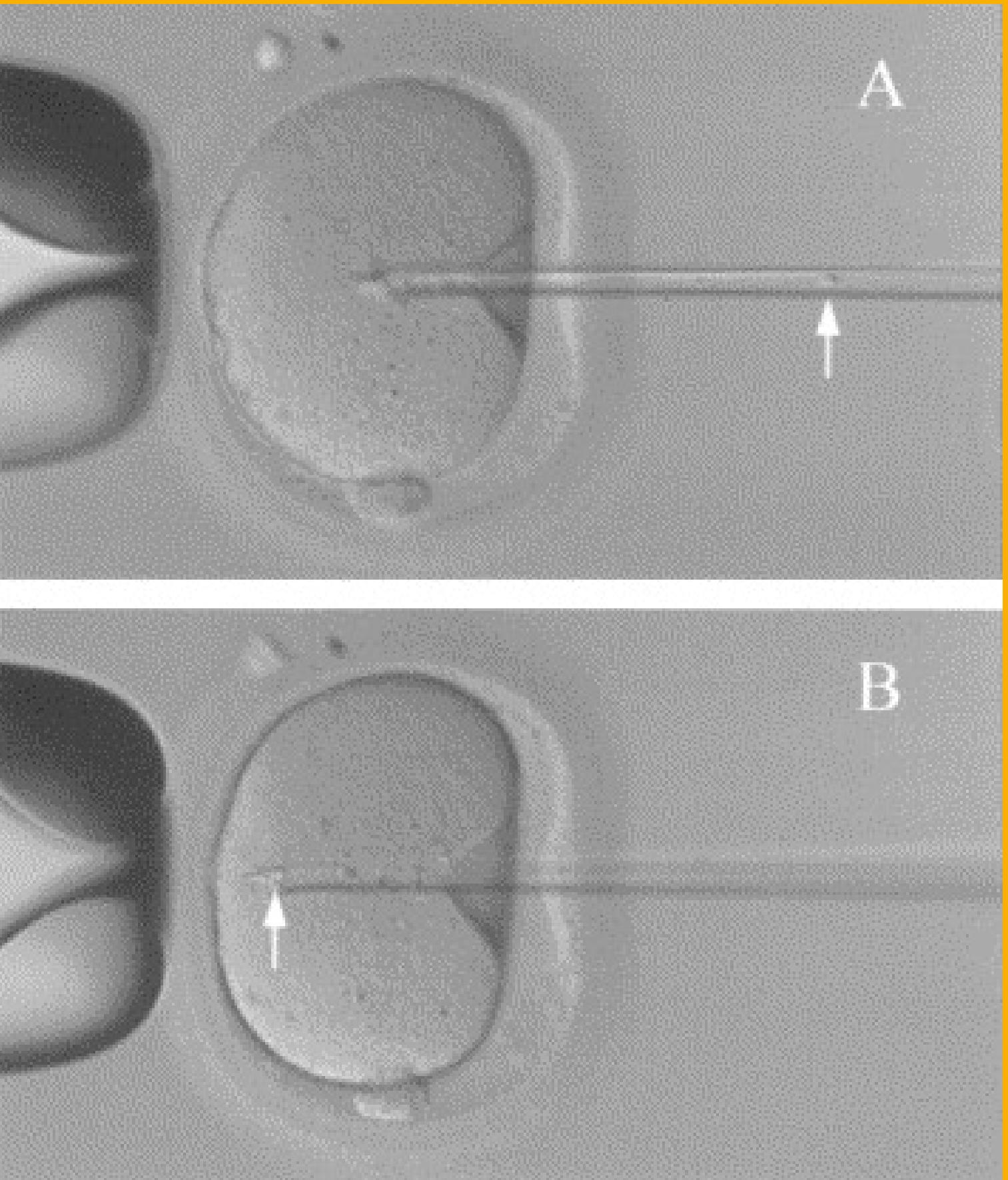
MI to MII stage transition



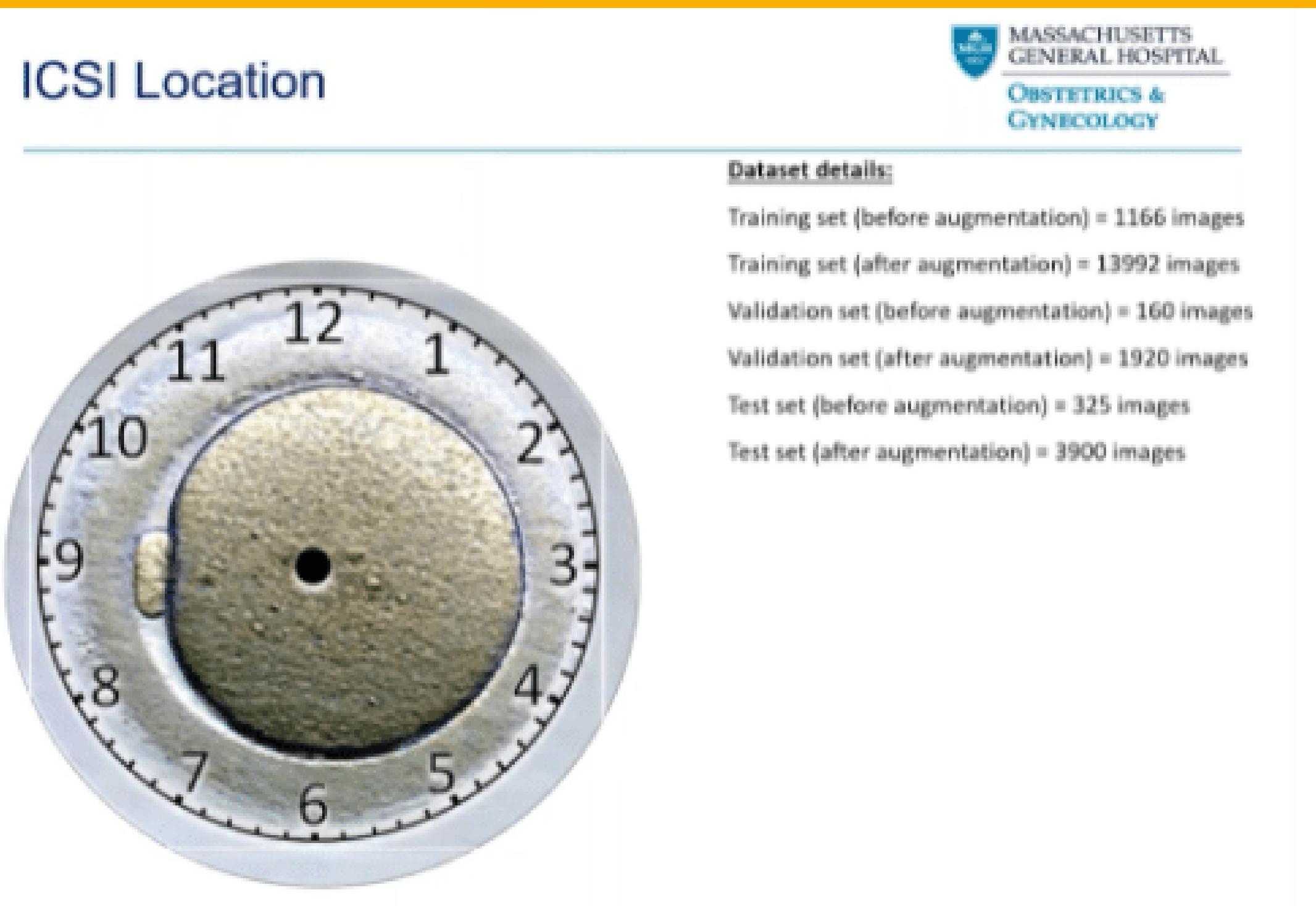
Performance of ICSI

On day-0 they analyze the oocyte and they perform the ICSI in optimized lab conditions.

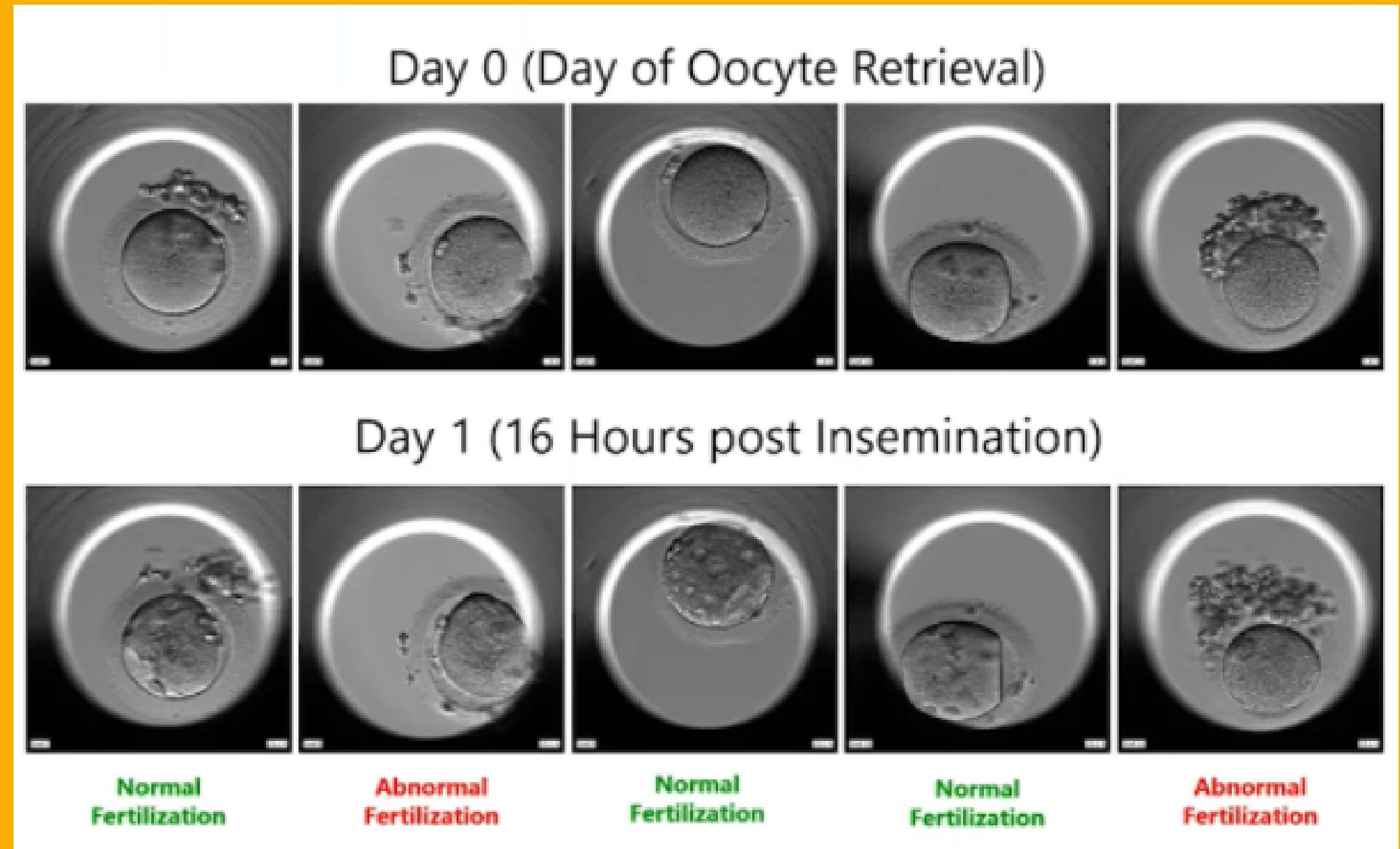
On doing the ICSI procedure the position is the the proper location to perform ICSI.



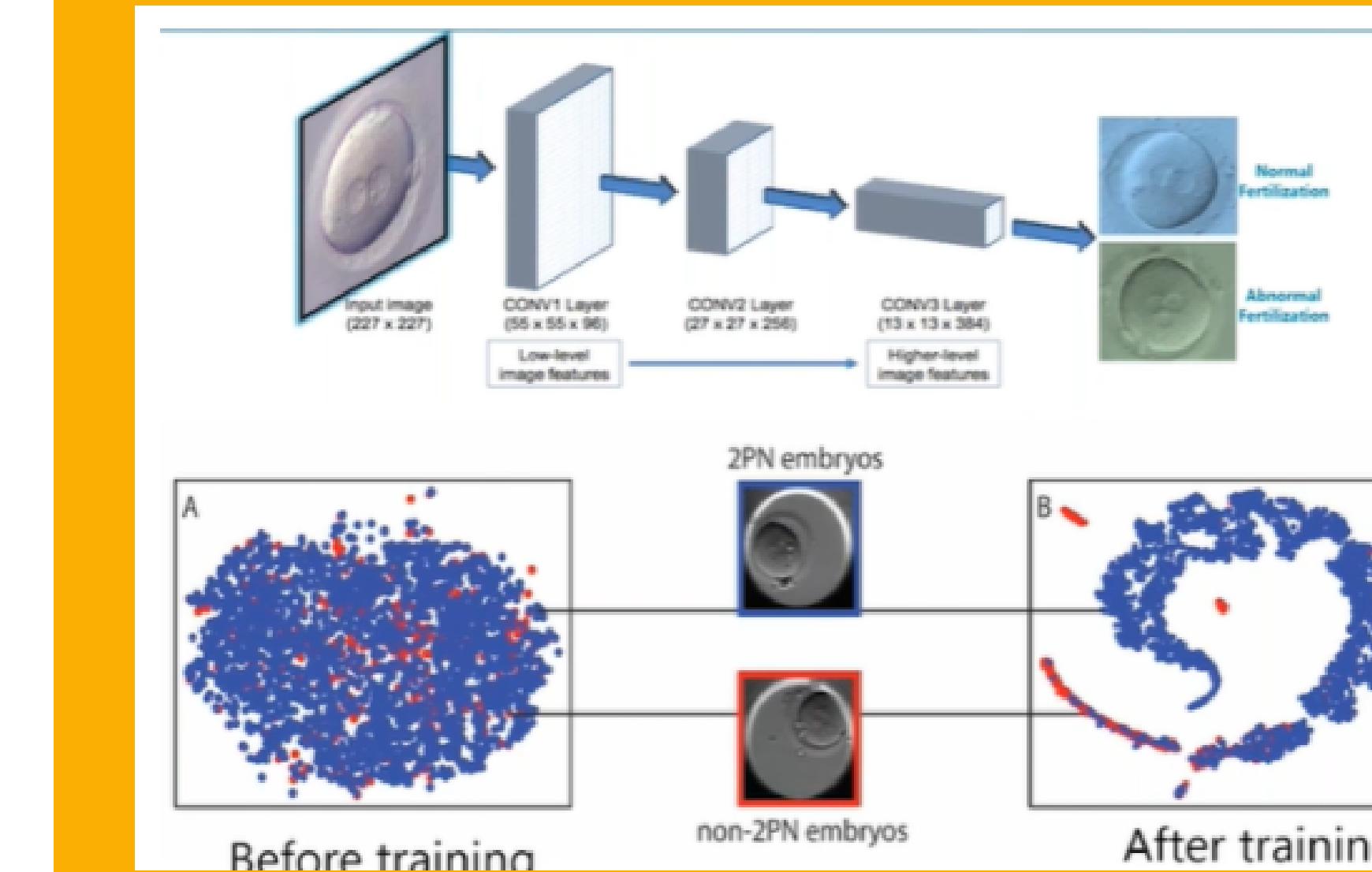
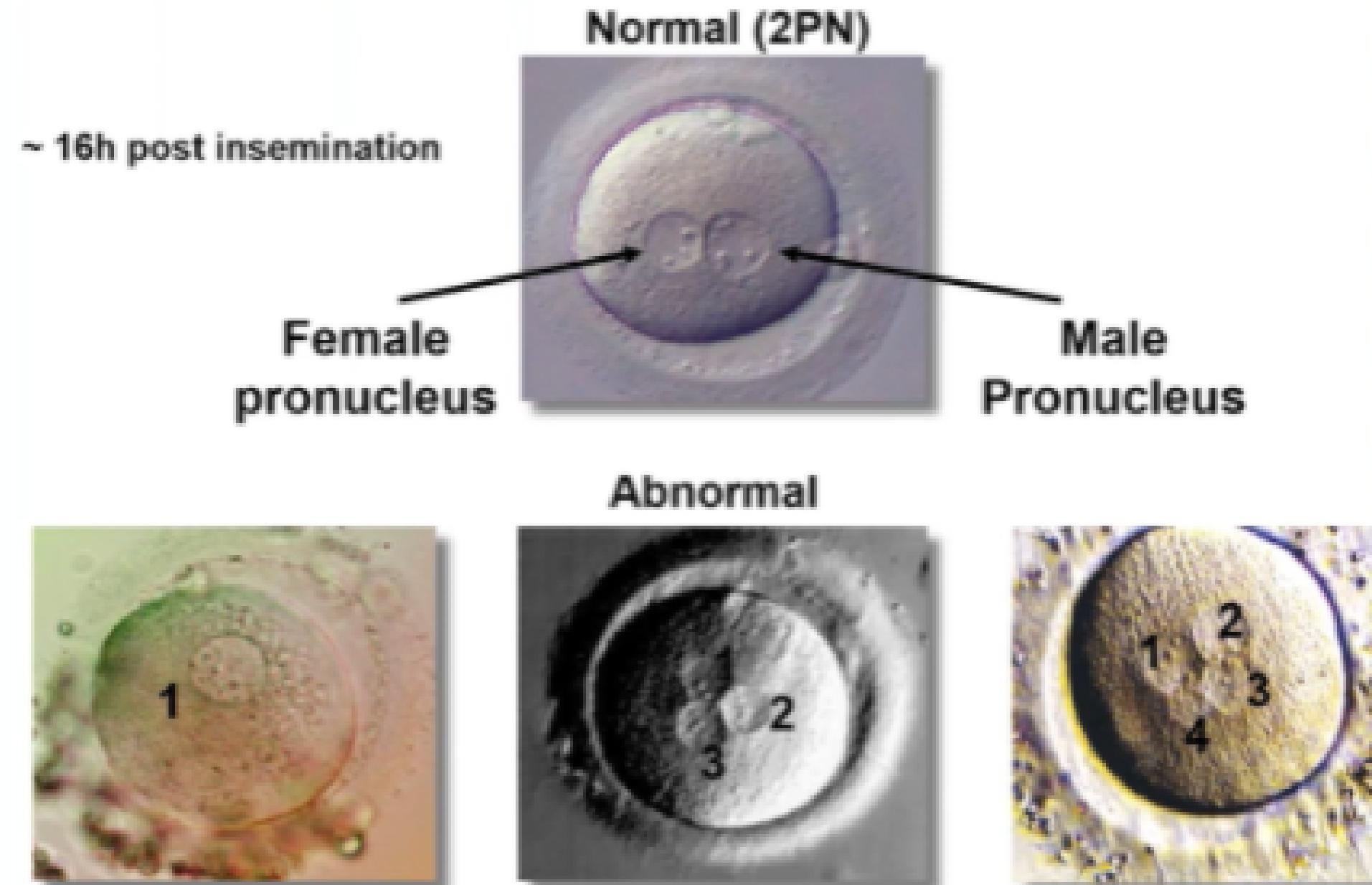
They use this Hour clock conventional method and trained AI to predict the accurate location to perform ICSI and found it as the extruded polar body to be near 5 hr mark and the training accuracy was 99.9%



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.



In the 16 hr post insemination check the embryos with 2PN (Pro Nucleus) is considered Normal and all others to be abnormal.

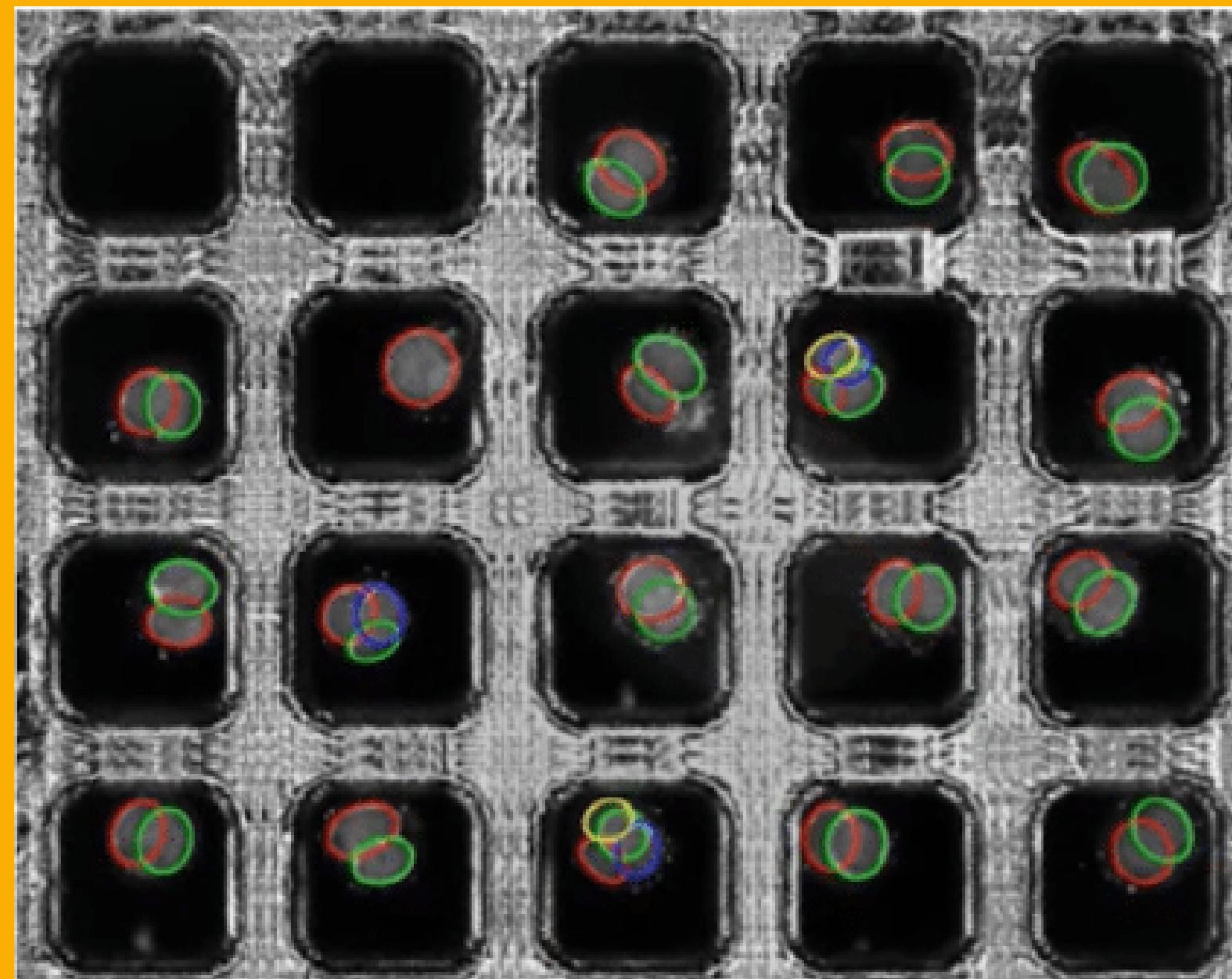


Analysis of the 2PN embryo in AI method.

Cleavage state development

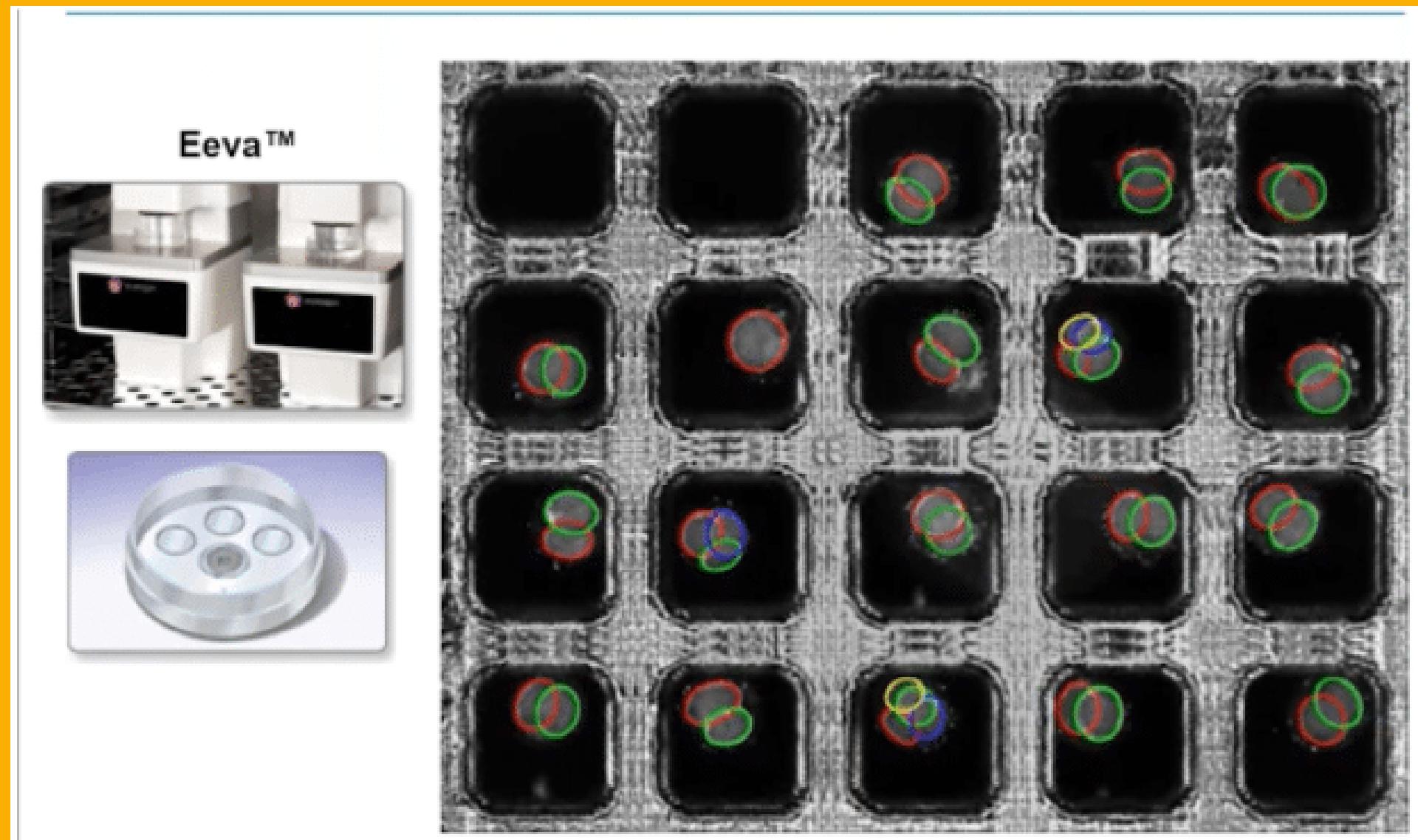
On day 3 they look for the cleavage state development they look for:

- Cell number
- % of fragmentation
- % Asymmetry

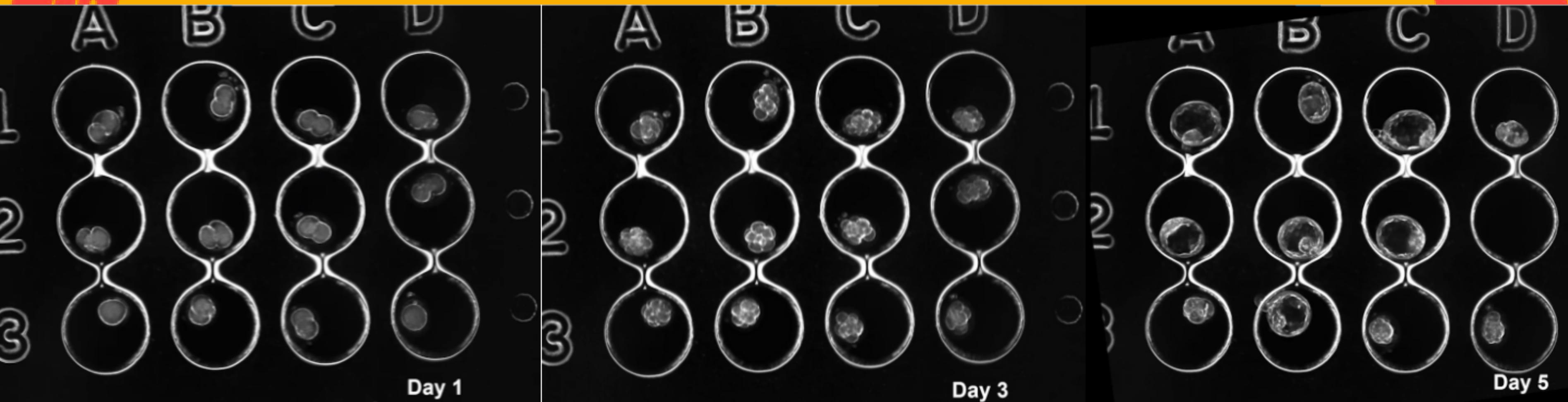


But in 2010 the culture changed to Timelapse video imaging as it will give a close look and it uses this footage to clearly visualize what is happening and how it is happening.

This led to the upliftment of lots of Algorithms to classify the best embryo that will be capable of baby-making.



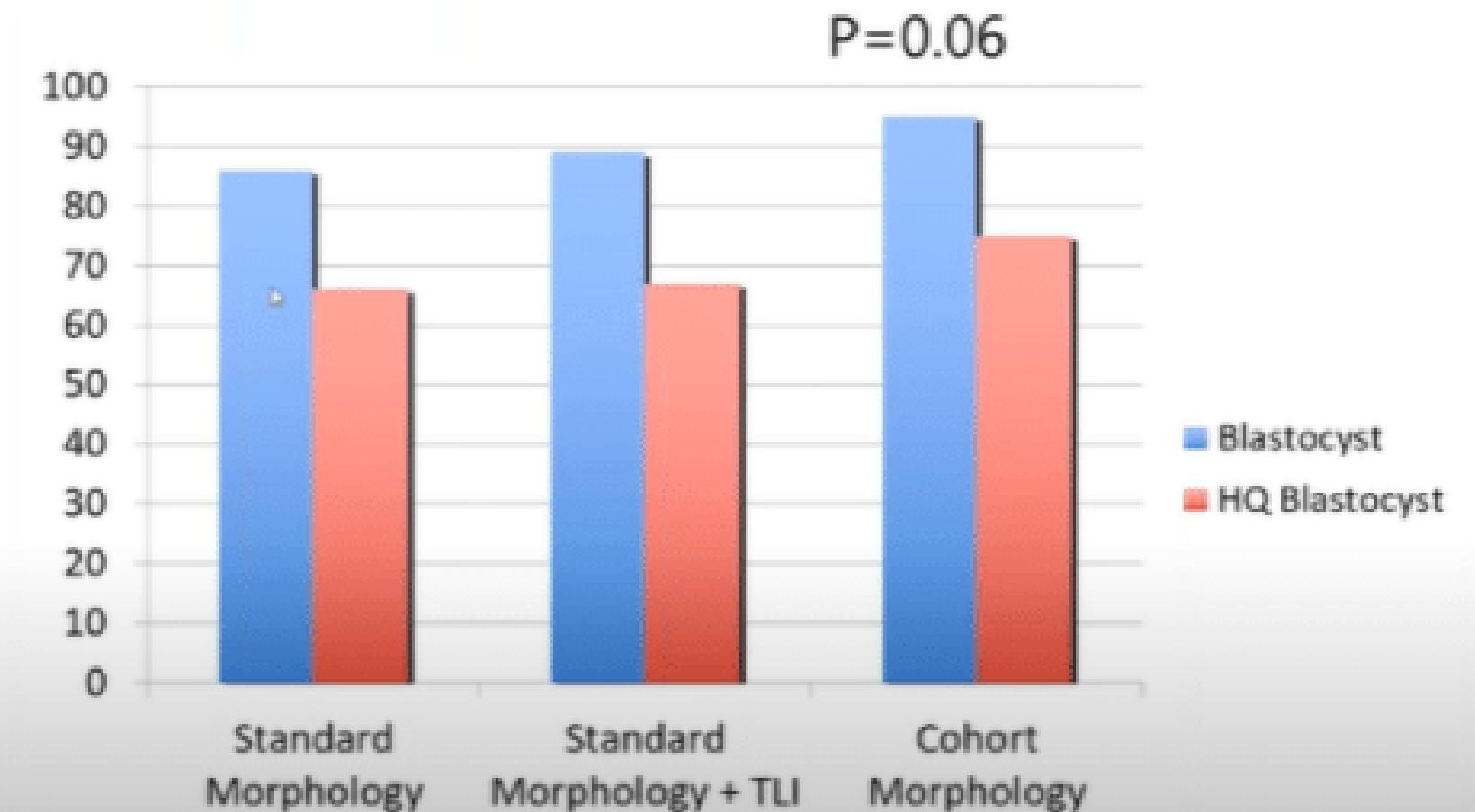
The usage of Time-lapse Imaging in AI



These images were put through a test by a 3 ML algorithm to find the optimized one.

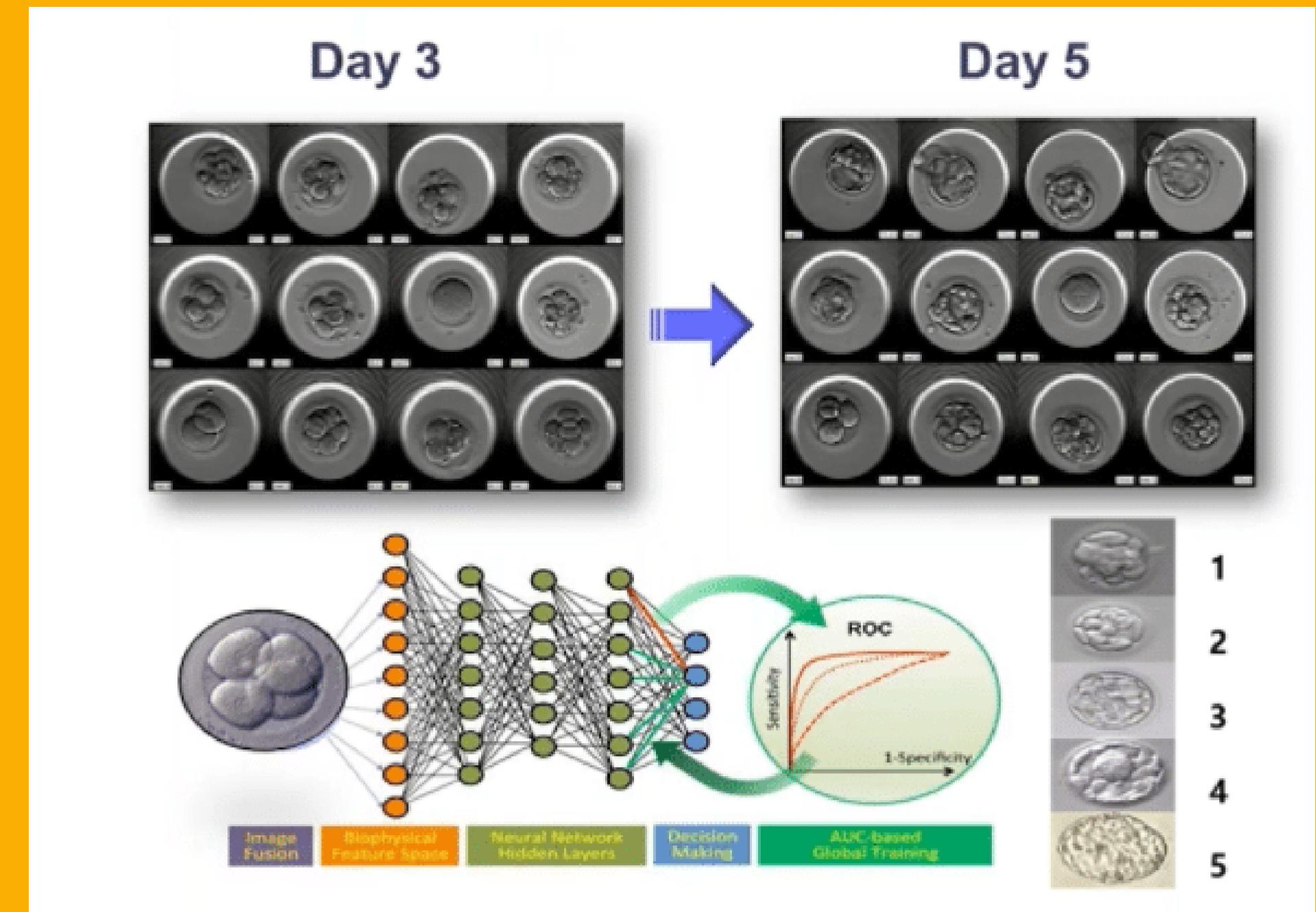
The first algorithm choose only Standard Morphological characters, the second one took the Standard Morphological characters and Time-lapse imaging and the last took only cohort Morphology. (Similar Morphological Characters to the test data, along with Cell number, fragmentation, and Symmetry).

Day 3 Selection Methods



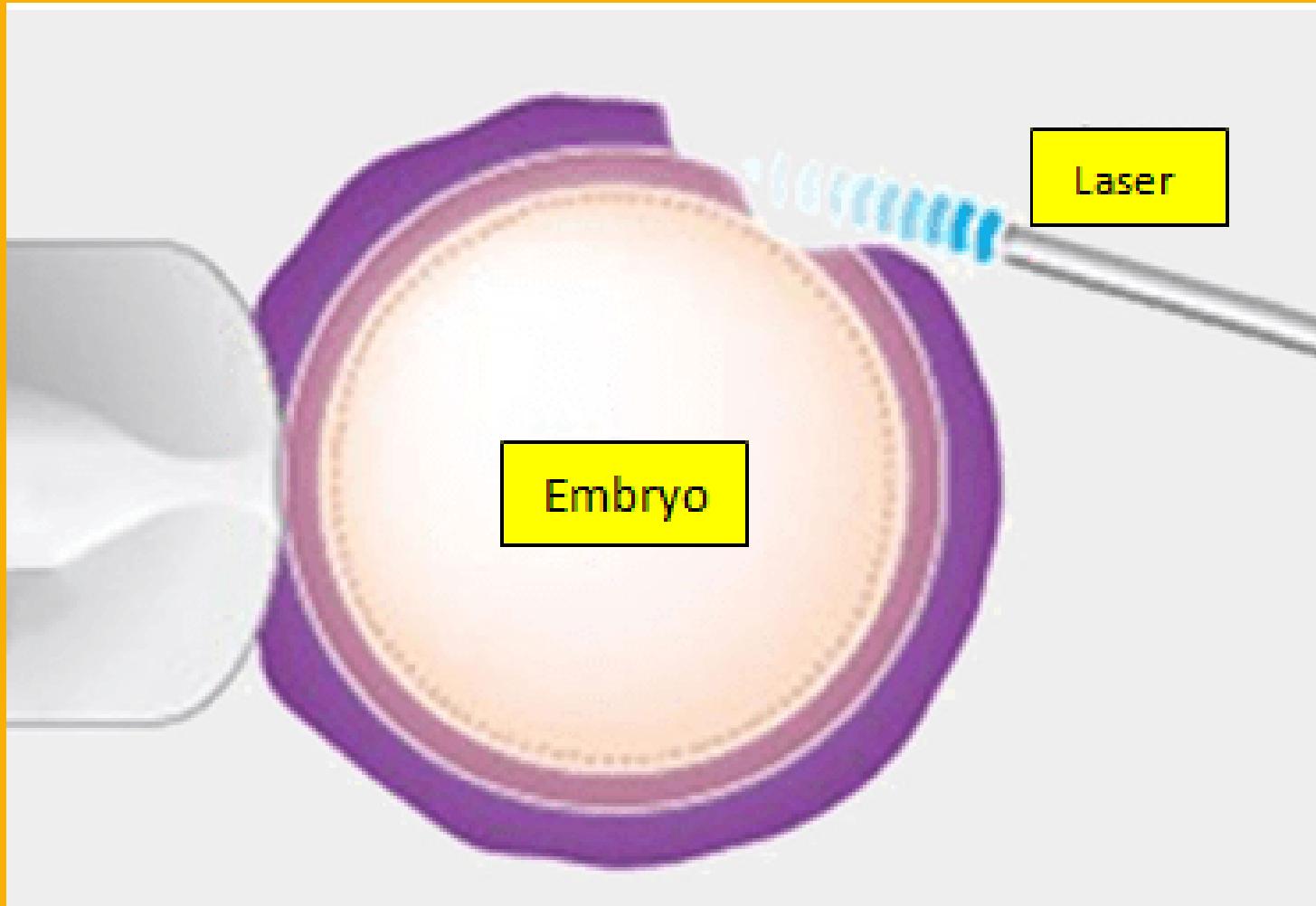
But the main problem that is Cohort Morphology selection has low Consistency in the selection process, so what they did is they trained the AI to get the imaging of day 5 using the day3 imaging, and hence they can get a good idea about what is going to happen with embryo in cohorts.

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



Laser-assisted hatching

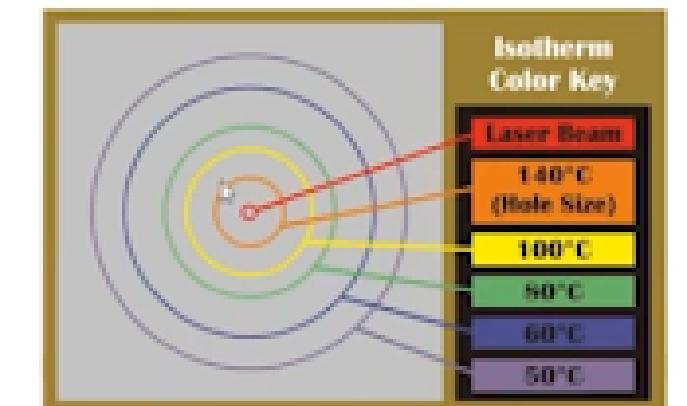
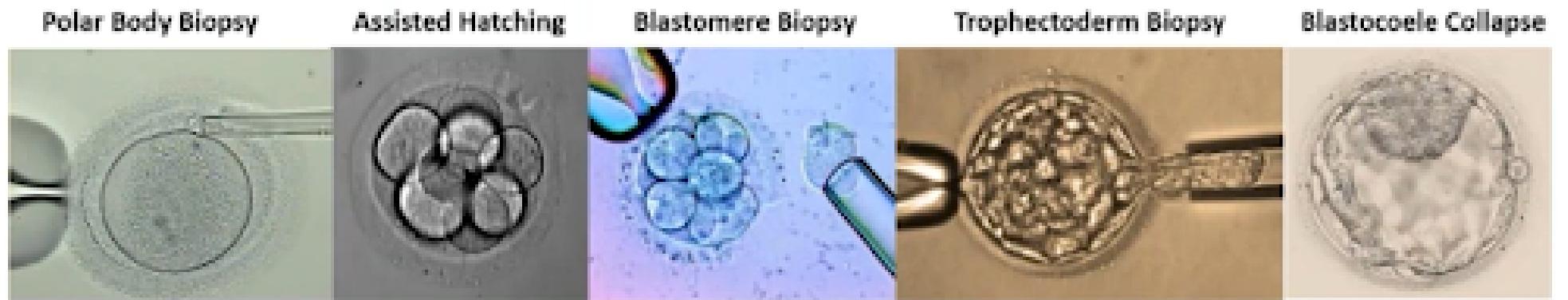
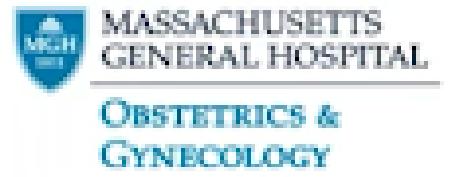
Laser-assisted hatching is done on day-3, this is done to prepare for hatching, to prepare for PGT so that the Trophectoderm have an easy time herniating outside the zona pellucida



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



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

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 this 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.

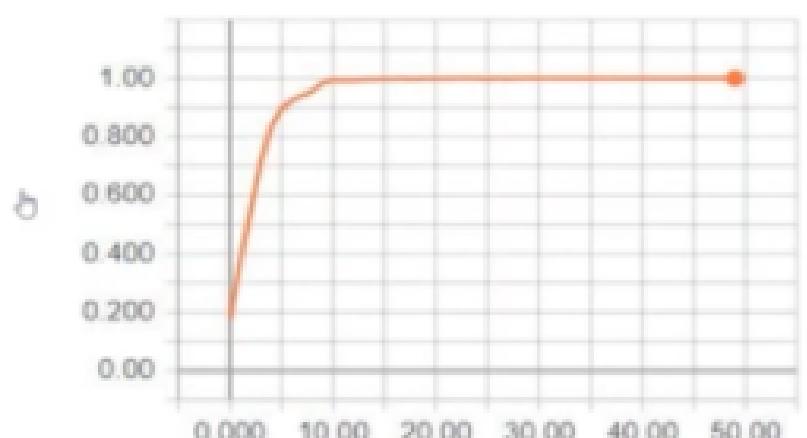
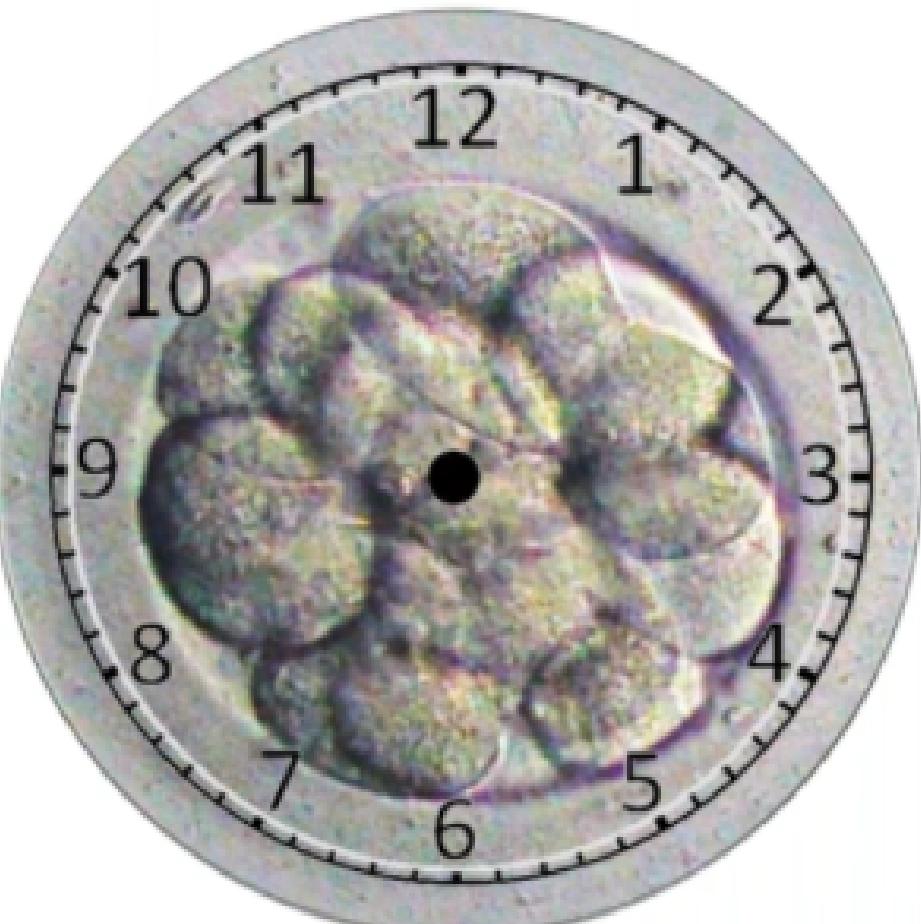
Automated Assisted Hatching



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. 202

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, TE starting to herniate through the ZP
6		Hatched Blastocyst Blastocyst completely hatched (i.e. completely out of the ZP)

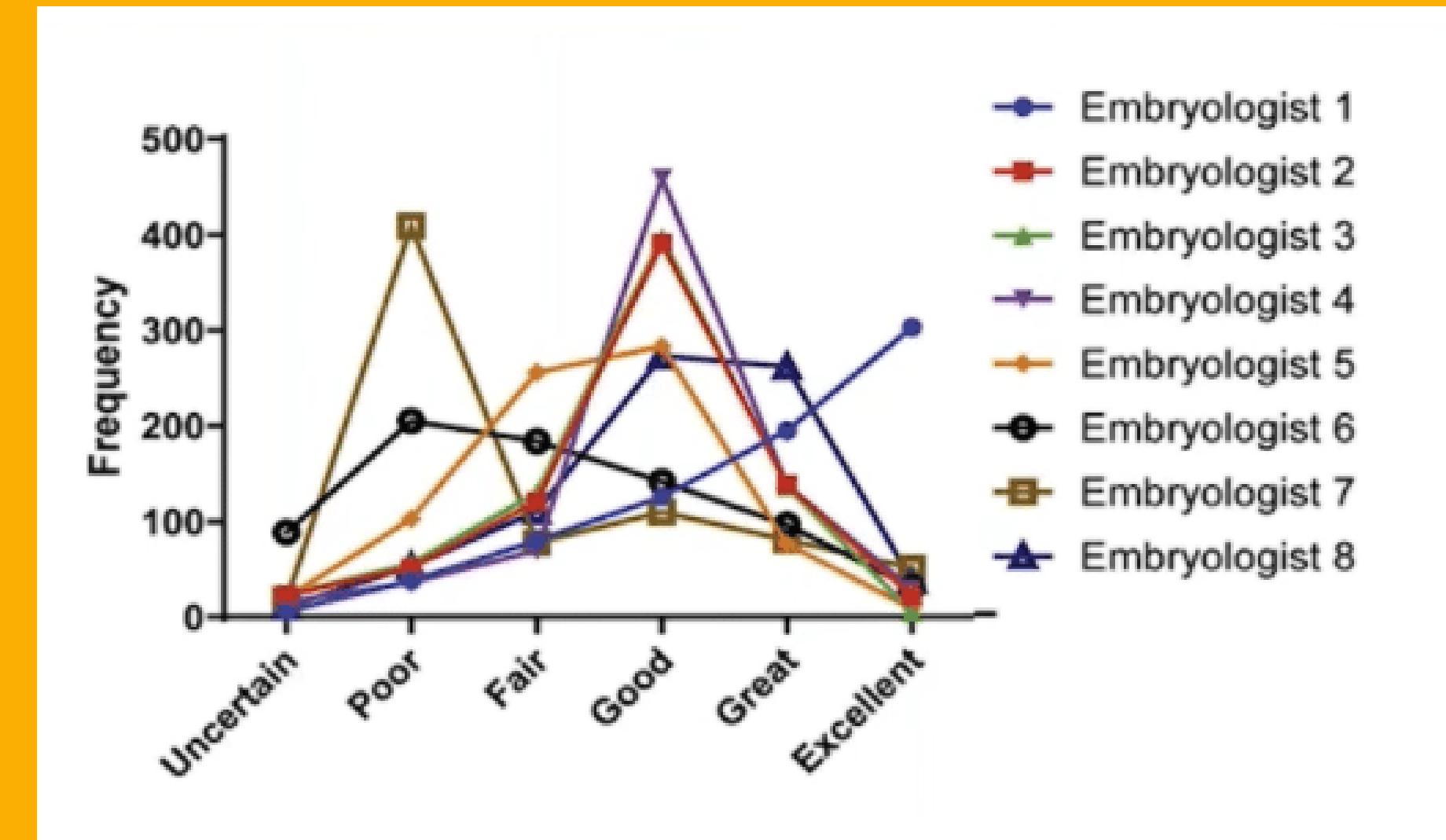
Gardner Grading System

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

Trophectoderm (TE) score, or quality.



The Importance of AI has been realised when a group of 8 embryologists struggled to pick out a good quality blastocyst from a given group of blastocysts.



An artificial intelligence (AI) model has been developed which can predict the best blastocyst from a group of blastocysts given to it

The AI model has been trained to identify the best blastocyst from the worst by using five images that indicate best to worst blastocyst



1

2

3

4

5

EMBRYO BIOPSY AND CRYOPRESERVATION

There was an overall inconsistency in some of the clinical decision making.

Embryologists had inconsistencies in the embryos that they would perform biopsy and similarly there were inconsistencies in embryos they would vitrify,





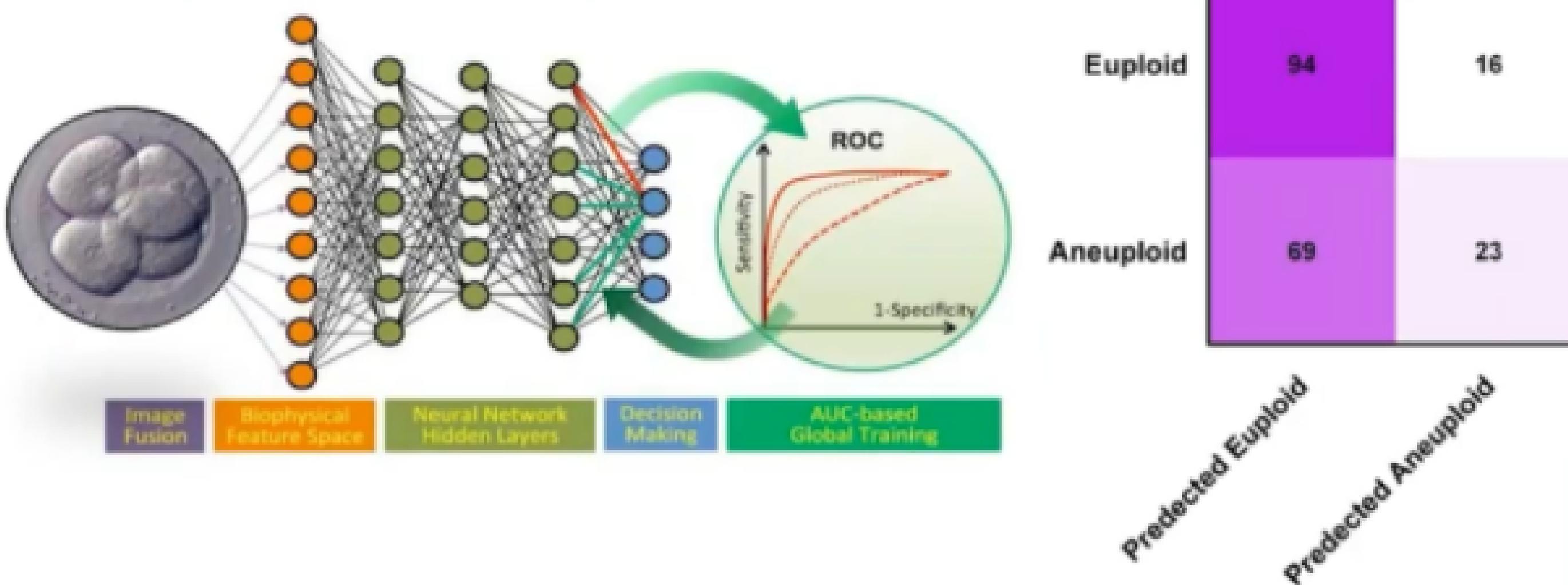
Embryo Ploidy Prediction

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

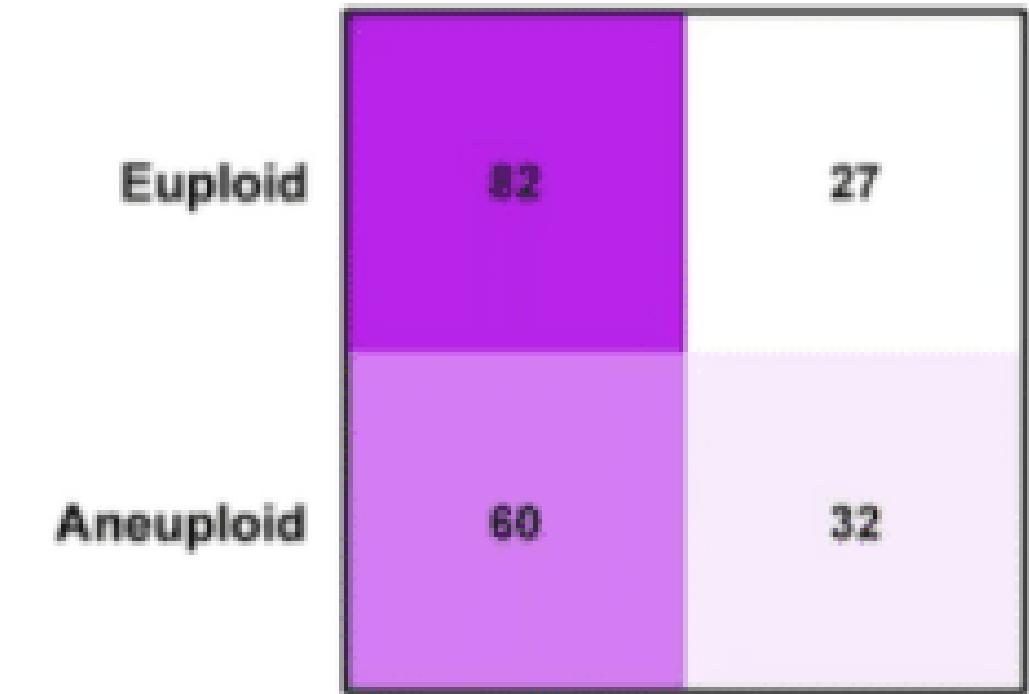
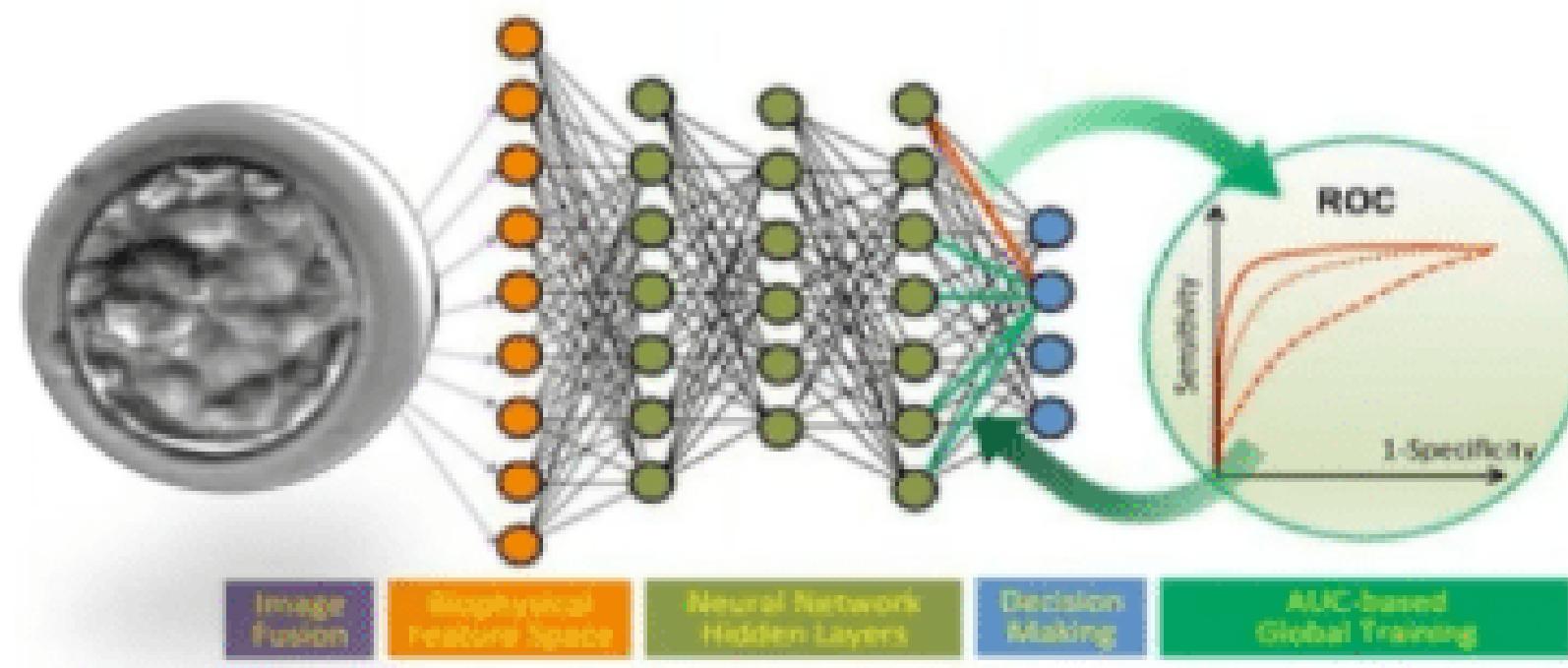


Day 3 Karyotype Prediction



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



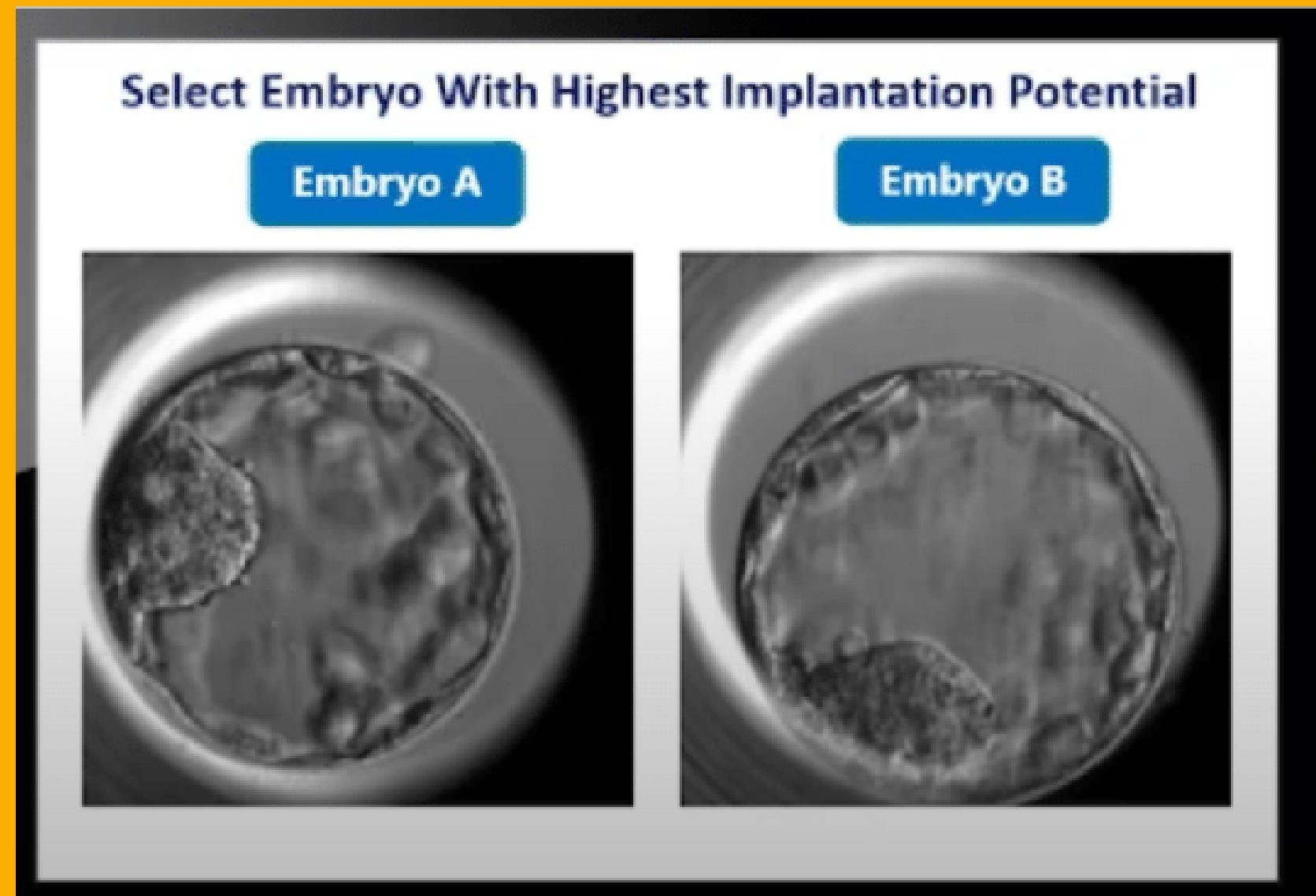
Predicted Euploid
Predicted Aneuploid

- CNN classified that karyotype on day 5 of development had specificity of 72.5%.

IMPLANTATION OUTCOME PREDICTION

They used photos of day 5 embryos that were transferred to train an algorithm to predict implantation, and the outcome was whether or not they would have a continuing pregnancy.

It showed a high accuracy of 79 percent in determining whether we should implant gametes or not.



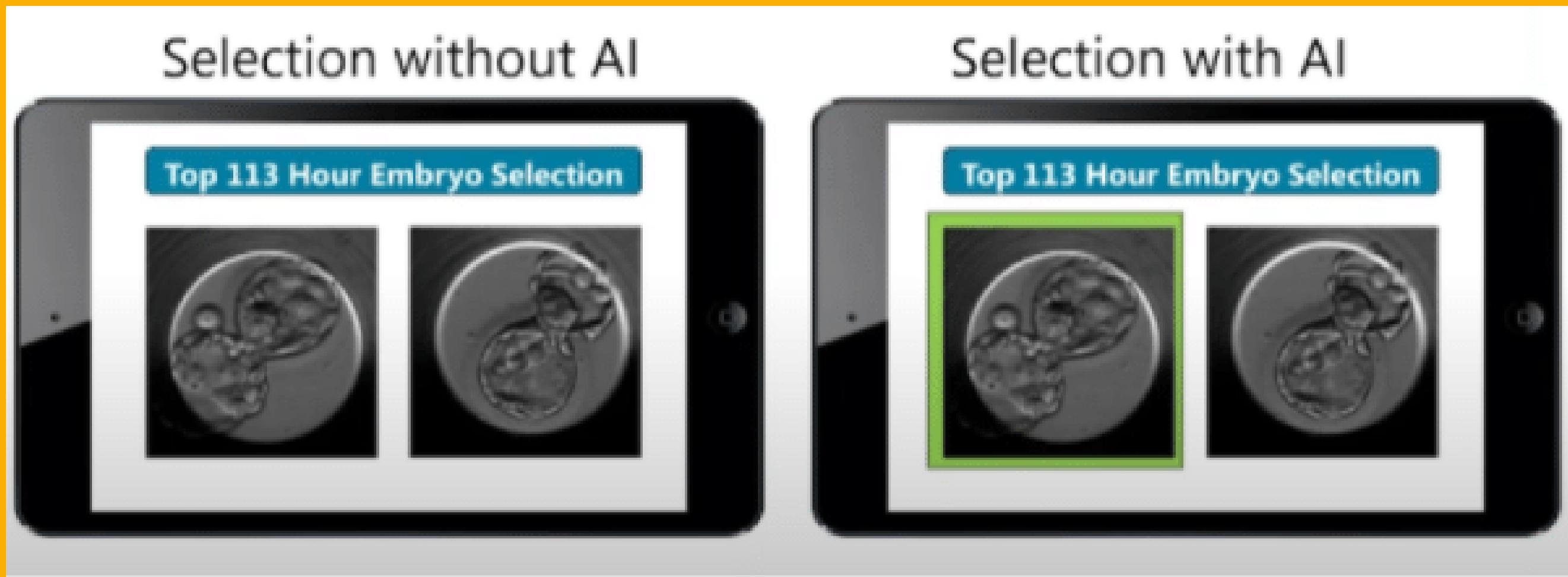
Then, using two embryos of comparable quality and grade, a module was created in which all of the embryos in the module are euploid Embryo on transfer as an eset and with known implantation results.

In differentiating 200 euploid embryos based on their implantation outcomes, the CNN surpassed the embryologists. The average accuracy of embryologists was 67.4%, whereas CNN (artificial intelligence) was 75.3 percent.



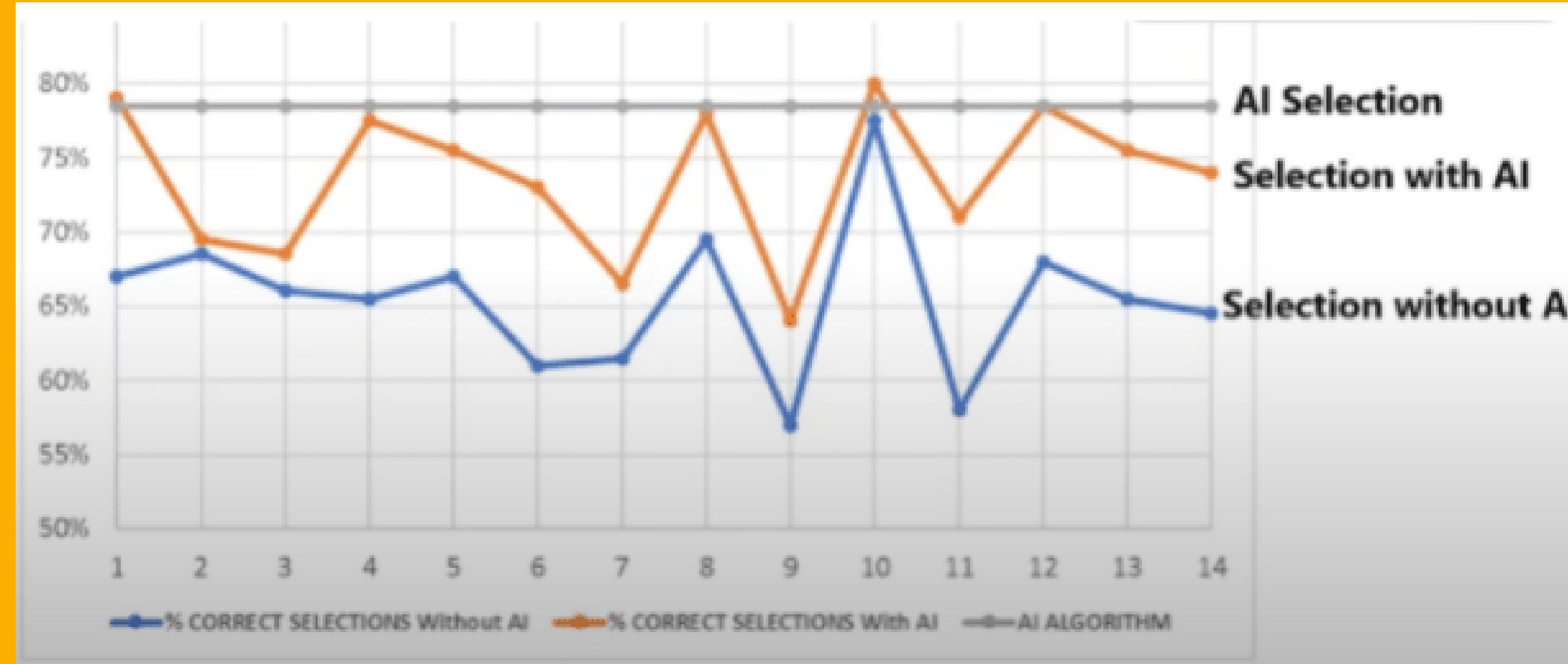
Embryo selection with Assistance

On Differentiating an additional set of 200 euploid embryos



The average selection by the staff without AI assistance was 65.5 percent

The AI correctly selected embryos 78 % of the 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 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 perfect cultural conditions such as,

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





KPIs



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

Big data sets and long-term training of the AI model can improve the accuracy and chances of High-quality embryo selection.

All IVF clinics can make a change in inputting the patient data.

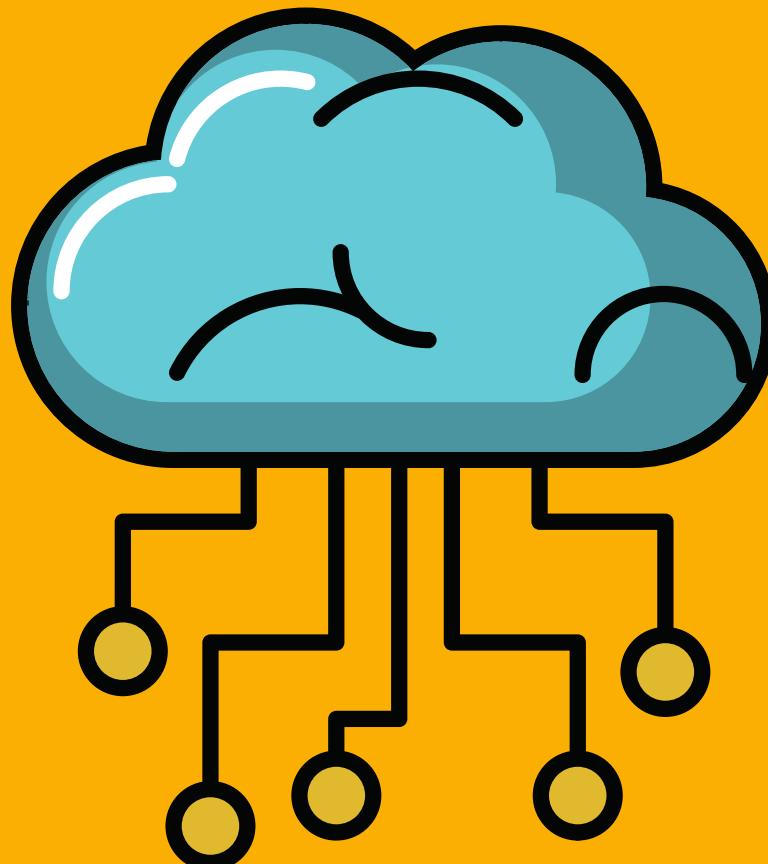
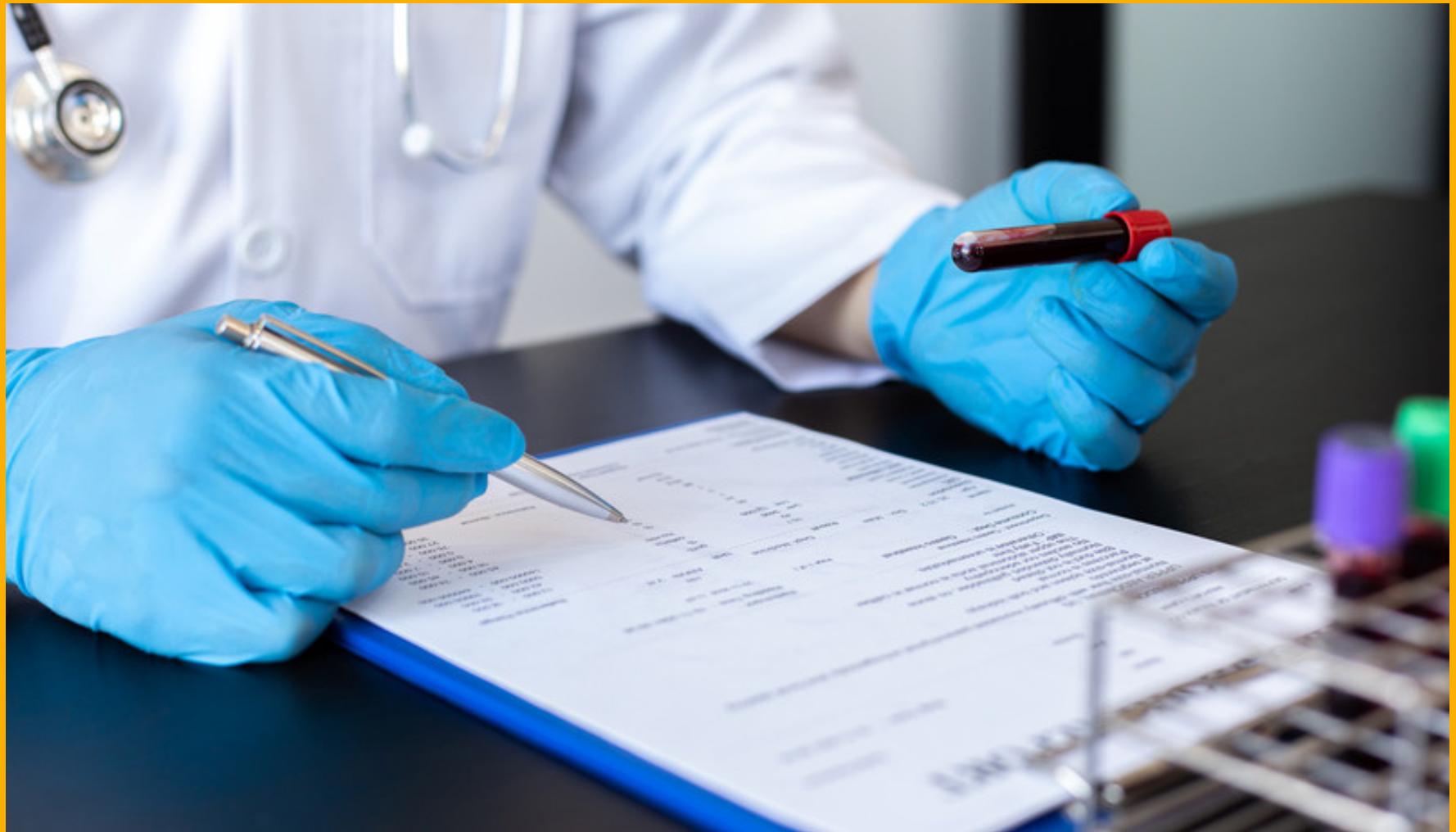
Rather than keeping the IVF data to one clinic, we can make it accessible to every clinic by using Cloud storage.

So from that, AI can study the various cases and their outcomes and also can 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.

Unified data from the cloud can be used to train the AI to make it 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.



Thank
you!

