

Centre for Reproductive Medicine

Embryoscope Monitoring

Embryoscope monitoring uses ‘time-lapse’ imaging and has been classed by the HFEA as a so-called treatment ‘add-on’. It is an optional extra to your treatment. It is not an integral part of your treatment and you do not have to have it.

The Human Fertilisation and Embryology Authority (HFEA) reviews evidence on ‘add-ons’ and scores them using a ‘traffic light’ system as red or amber. The HFEA reviews can be seen at the following link

<https://www.hfea.gov.uk/treatments/treatment-add-ons/>

The HFEA has graded time-lapse as ‘amber’. The HFEA states that “There is a conflicting body of evidence for this add-on, further research is required.”

This information sheet explains why CRM offers Embryoscope. Based upon the scientific literature, we find evidence that time-lapse imaging provides valuable additional information to embryologists about how embryos are growing in the laboratory. We have found no evidence to suggest that it is unsafe.

We offer Embryoscope monitoring within a research clinic setting and we undertake research and audit using Embryoscope data in order to expand knowledge for the future.

What is Embryoscope monitoring?

The embryoscope is a specially designed incubator that takes computer pictures of each embryo while it is in the laboratory. These pictures, taken approximately every 10 minutes, give embryologists very detailed information about what the embryo looks like as it grows, precisely when certain events in development take place, and can reveal many small but important changes that would otherwise be missed.

Why might embryoscope monitoring help me?

Research around the world has shown that the embryoscope is suitable for incubating embryos for IVF and ICSI treatment, and that taking regular images for time-lapse analysis is not harmful (1). Researchers who have used the embryoscope to culture embryos for many patients reported that it increased the pregnancy rate by more than 10% relative to a group of patients whose embryos were cultured in a regular incubator(2) which they believed was due to a combination of improved embryo selection and more stable culture conditions. Improved embryo selection was based upon the extra information available about embryo development, which changed the embryologists’ decisions about which embryo was the most suitable for transfer. Some researchers also reported that the embryoscope could help to choose embryos that carry the right number of chromosomes, even though it does not do genetic testing (3). Another possible benefit is that the culture conditions are more stable in an embryoscope, because the embryos do not need to be moved out of the incubator to be

viewed on a microscope. However, not all researchers have found an increased pregnancy rate in embryoscope (1). It is important to understand that embryoscope monitoring is relatively new and currently there is limited information available about it because there are few well designed large randomised controlled trials (RCTs) done. RCTs are extremely expensive and challenging in the IVF clinic setting, and their results often come too late, when technology has already moved on. Moreover, some options may work in some clinics but not in others, because there are different practices. Many patients and clinicians perceive that certain options may be advantageous, so treatments are often offered before evidence is available.

TABLE: Clinical pregnancy rates per embryo transfer, with and without Embryoscope CRM data, January 2016-August 2020

A clinical pregnancy is one that is recognised on an ultrasound scan 5 weeks after the embryo transfer.

| | Number of patients using Embryoscope | Clinical pregnancy rate in Embryoscope | Number of patients using other incubator (BT37) | Clinical pregnancy rate in other incubator (BT37) | Difference between Embryoscope and other incubator |
|--|--------------------------------------|--|---|---|--|
| All patients all ages | 1700 | 44.5% | 281 | 35.9% | 8.6%** |
| Female age up to 35 | 970 | 53.2% | 163 | 43.6% | 9.6%* |
| Female age 36-39 | 493 | 37.3% | 76 | 32.9% | 4.4% |
| Female age 40 or more | 236 | 23.3% | 42 | 11.9% | 11.4% |
| Quality control group (age less than 37, 1 st attempt, negative for viral diseases, at least 3 eggs fertilised) | 638 | 59.1% | 113 | 44.3% | 14.8%** |

The difference in pregnancy rate for rows marked ** is 'significant at $p < 0.01$ ' which means that this result could occur by chance fewer than 1 in 100 times.

The difference in pregnancy rate for the row marked * is 'significant at $p < 0.05$ ' which means that this result could occur by chance fewer than 1 in 20 times.

Rows not marked with a * are not significant results. These rows have lower numbers of transfers overall and more data is needed before we can draw conclusions for these groups.

At CRM, Embryoscope monitoring is a popular option that has been available since 2012. The alternative to Embryoscope is a specialised IVF/ICSI incubator (BT37) containing an identical environment, but without the ability to take pictures. In our experience, the average pregnancy rate for people who choose Embryoscope is consistently higher than for those who do not choose it. We have analysed our own data to reach this conclusion and our

results are presented in the table. On average, 8.6% more patients became pregnant following an embryo transfer in the embryoscope group than the non-embryoscope group.

The table also shows results for patients who meet a certain set of characteristics. We call this our 'quality control' group. This helps us to undertake 'like-for-like' comparison, in similar types of patients, which makes the comparison fairer. For the 'quality control' group, use or not of embryoscope is the key point of comparison. On average, 14.8% more such patients became pregnant if they used embryoscope.

Based upon our analysis, we expect that embryoscope monitoring of your embryos might improve the chances of pregnancy. There is no evidence available that suggests it would cause any harm.

Advantages of embryoscope monitoring?

Embryoscope monitoring may increase the pregnancy rate after IVF or ICSI. This is its main advantage.

Embryoscope provides detailed information about each embryo, which may be useful in understanding your personal embryo quality, but it does not interfere with your routine IVF or ICSI treatment. Non-transferred embryos that are good enough quality to store frozen will be stored as normal for your use later on.

Disadvantages of embryoscope monitoring?

The main disadvantage is that the embryoscope is a new technology, so there may still be questions about whether it could cause problems that we don't know about, for example, problems with later development. However, all the evidence available so far suggests that the embryoscope is safe.

A further disadvantage is that embryoscope monitoring will require you to pay a fee to cover its running costs (as shown on the price list).

In addition, you will need to attend an extra appointment with our research nurse in order to consent to embryoscope. Both partners (where applicable) need to attend since consent has to be provided in person.

If you need help to understand whether embryoscope is suitable for you, please bring this up at your consultation or information session and staff will be pleased to assist.

Planning to use the embryoscope

If you wish to consider using the embryoscope, you will be referred to the 'Embryoscope Clinic', which is a research clinic, where you will be able to discuss the points outlined to decide whether you might benefit from taking up this option.

Both partners (where applicable) need to attend the Embryoscope Clinic appointment, because consent has to be given in person at the CRM. If it is impossible for you both to attend at the same time, you can arrange separate appointments.

You are under no obligation to use Embryoscope. Even if you sign up to have embryoscope, you can still change your mind as long as you let us know.

Please note, during the Covid 19 pandemic, all appointments are taking place remotely by telephone or video link, so there is no requirement to attend CRM for the embryoscope appointments.

Embryoscope Follow-up

You are welcome to come back to the Embryoscope Clinic after your treatment cycle for a follow-up consultation to review the embryoscope findings. This can help to explain any embryological factors seen or to reassure you if your embryo development is as expected. It may be particularly useful if you are considering your future options if treatment has not been successful. The follow-up consultation is free of charge.

Research and embryoscope monitoring

Charitable funding for the embryoscope was provided in order to support our research programme which aims to improve the success of treatments and to increase understanding of embryo development and early pregnancy in general.

1. Research use of eggs and embryos not suitable for use in treatment

Patients attending embryoscope clinics will be asked to consider research participation by providing any unfertilised eggs, embryos or sperm which cannot be used in your own treatment for research use. Such research is voluntary and has absolutely no effect upon the treatment itself, which will proceed in the same way regardless of your decision about research. But participating in research will allow us to make progress towards better treatments in the future. The types of research that we are undertaking are outlined on patient information sheets and consent forms which are specific for each particular project and which may change from time to time. You will be provided with a copy of these. Please be reassured that all our research is fully approved by Research Ethics Committees and UHCW NHS Trust. Where it is required, the research is also approved by the Human Fertilisation and Embryology Authority. Unless you are a participant in our egg sharing to research programme, our research only makes use of materials that cannot be used in treatment and which would normally be discarded.

2. Research use of images and data collected on the embryoscope

The embryoscope collects thousands of digital images of embryos as well as numerical data, for example, the time at which an embryo gets to a certain stage. We use these pictures and data for research and analysis to try to understand many different aspects of embryo growth and to improve IVF for the future.

We do not specifically ask for your consent for this type of research but if you have any objections, please let us know.

Who can have embryoscope monitoring?

Embryoscope monitoring is suitable for most patients, but there are some factors that may affect your decision:

Attending the Embryoscope Clinic. Your information session with the nurse about your IVF or ICSI treatment will proceed as normal. For embryoscope monitoring, you also need an appointment in the Embryoscope Clinic.

Number of embryos available. Patients with several embryos who need to choose the best one for transfer will probably benefit most. If there are only one or two embryos, the embryoscope would provide detailed information that might be relevant to your diagnosis or clinical advice, but it would not affect the selection of embryos or the chances of successful treatment.

If there are several embryos to choose from, we usually recommend blastocyst culture, so you would expect to have a transfer on day 5 after egg collection. If you need to have embryos transferred at an earlier stage (day 2, 3 or 4), for example because the number of embryos available is low, then we can still use the embryoscope, but there would be less information available because the embryos were in the Embryoscope for a shorter time.

Patients willing to pay the fee. The fee is payable at baseline scan. A chip and pin facility is available.

If for any reason you wish to change your mind after you have signed up to using the embryoscope, you can cancel but you must let us know.

If you have not used the embryoscope, we will refund any payment you have made for it. However, if you have used the embryoscope, regardless of the number of eggs collected or the length of time, then the fee will remain payable.

Capacity of the embryoscope

Occasionally there may be capacity issues.

For embryos:

There is enough space in the embryoscope for up to 12 eggs/embryos for a particular couple. If you have more than 12 embryos, those in excess of 12 will be cultured in a regular incubator in the usual way, and will still be available for you to use.

For patients:

We have two embryoscopes and each can hold embryos for up to 6 couples.

It is difficult to predict exactly which day patients are going to be ready for egg collection.

Therefore, occasionally there could be more than twelve couples who need embryoscope monitoring at the same time. We do our utmost to schedule cycles so that capacity is available, but unfortunately, we cannot absolutely guarantee that space will be available.

The likelihood that embryoscope is not available when you need it is less than 1 in 100. We will let you know if any problems of this sort arise.

Unfortunately, patients with active viral conditions are not suitable to use the embryoscope, in order to avoid any risk of transmission of viruses.

Can I have the photos?

If you wish, we can provide you with a memory stick with a video of each embryo that you had transferred. You should think carefully about whether you would like this or not, and also, when would be the right time for you. If you decide that you would like to receive the embryo video, you will need to ask for it by contacting the unit in writing or email. We have a form for this purpose that you will be given at the Embryoscope Clinic and you can return it to the CRM at an appointment or by post, or you can just email us to ask for your video. There is no charge for the video and there is no time limit on your request.

Cancellations?

Sometimes treatment is cancelled before the stage when the embryoscope is used. For example, if you have under- or over-response to the medications, or if you do not have any eggs that fertilise. In this case, we are happy to either refund you the fee that you have paid for embryoscope, or to carry it over to another treatment cycle, whichever you prefer.

What do I have to do?

Please read this information sheet carefully.

To arrange an appointment to discuss embryoscope monitoring, please contact the Embryoscope Clinic secretary on 02476 967528, embryoscope@uhcw.nhs.uk

This appointment needs to be arranged for after you have attended the CRM for your nurse information session.

References:

- (1) Kirkegaard K, Hindkjaer JJ, Grøndahl ML, Kesmodel US, Ingerslev HJ. A randomized clinical trial comparing embryo culture in a conventional incubator with a time-lapse incubator. *J Assist Reprod Genet.* 2012 Jun;29(6):565-72. Epub 2012 Mar 30. PubMed PMID: 22460082; PubMed Central PMCID: PMC3370049.
- (2) Meseguer M, Rubio I, Cruz M, Basile N, Marcos J, Requena A. Embryo incubation and selection in a time-lapse monitoring system improves pregnancy outcome compared with a standard incubator: a retrospective cohort study. *Fertil Steril.* 2012 Sep 10. pii: S0015-0282(12)02068-7. doi: 10.1016/j.fertnstert.2012.08.016. [Epub ahead of print] PubMed PMID: 22975113.
- (3) Campbell A, Fishel S, Bowman N, Duffy S, Sedler M, Hickman CF. Modelling a risk classification of aneuploidy in human embryos using non-invasive morphokinetics. *Reprod Biomed Online.* 2013 May;26(5):477-85. doi: 10.1016/j.rbmo.2013.02.006. Epub 2013 Feb 19. PubMed PMID: 23518033.

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