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3D/4D ultrasound guided embryo transfer vs clinical touch technique

Submission date	Recruitment status	[X] Prospectively registered
15/12/2017	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
06/02/2018	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
06/03/2024	Urological and Genital Diseases	

Plain English Summary

Background and study aims

In vitro fertilisation (IVF) is a technique that is used to help people with fertility problems to have a baby. During IVF, an egg is taken from the woman's ovaries and fertilised with sperm in a laboratory. The fertilised egg (embryo) is then returned to the woman's uterus (womb). Current embryo transfer techniques have remained largely unchanged since IVF treatment began. Traditionally there have been two techniques: a “clinical touch” method used to guide the transfer catheter (tube) to within 10mm of the uterine fundus (top of the uterus) before injection of the embryo. This is essentially a “blind” procedure and works on tactile sensation (touch). Similarly some clinicians transfer the embryos at a fixed distance from the external cervical opening (about 6cm), but this works on the assumption that the uterine dimensions including the cervix are the same for all women. If the catheter damages the endometrium (the lining of the uterus) or touches the fundus, this causes uterine contractions which lead to lower embryo implantation rates. The use of ultrasound during embryo transfer was first discussed in 1995 to allow accurate positioning of the catheter tip near the uterine fundus and hence improve pregnancy rates. The technique has often been described as “cleaner” with the ability to tailor the placement of the embryo to the individual. Ultrasound guided embryo transfer is recommended by NICE and is used in 77% of embryo transfers worldwide. Traditionally, ultrasound guided embryo transfer has been performed using trans-abdominal 2D ultrasound. More recently, ultrasound technology and capabilities have advanced so that 3D and 4D imaging of the uterus can now be achieved, showing finer detail with greater clarity, as well as enabling spatial awareness in terms of the dimensions and volume of the uterus. It is reasonable to assume that more accurate placement of the transfer catheter and the embryo(s) could result in higher pregnancy rates. In a small study, transabdominal 3D ultrasound was used to confirm the correct placement of a trial catheter before embryo transfer, which was not subsequently performed under ultrasound guidance. A second study also confirmed the ability to ensure correct catheter placement using 3D and 4D ultrasound using transabdominal ultrasound, and reported an increase in pregnancy rate from 36.66% to 65%. With the availability of the Kitazato embryo transfer catheter, the ability to perform an embryo transfer using a transvaginal 3D/4D ultrasound scan has become possible. The resolution of images obtained using transvaginal ultrasound appears superior to similar images obtained through transabdominal scanning. The aim of this study is to find out whether this technique results in better pregnancy rates and outcomes.

Who can participate?
Women undergoing fresh or frozen embryo transfer

What does the study involve?
Participants are randomly allocated into either the intervention group or the control group. In the intervention group, a transvaginal ultrasound is performed to guide the embryo transfer. In the control group the embryo placement is carried out using the clinical touch technique. All participants are followed up for 10 months to record the number of live births.

What are the possible benefits and risks of participating?
Benefits may include an improved pregnancy rate. Ultrasound guidance may also reduce the number of failed embryo transfers due to better catheter placement. Risks between the groups should be similar. Ectopic pregnancy rates should be similar between groups and there is likely still to be a miscarriage risk. Intervention group transfers may take slightly longer than control group transfers. Discomfort is likely to be similar in both groups.

Where is the study run from?
Liverpool Women's NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
February 2018 to September 2020

Who is funding the study?
Liverpool Women's NHS Foundation Trust (UK)

Who is the main contact?
1. Dr Lewis Nancarrow (public)
2. Mr Richard Russell (scientific)
3. Miss Louise Hardman (public)

Contact information

Type(s)
Public

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number
202857

ClinicalTrials.gov number

Secondary identifying numbers
Version 3.0, IRAS 202857

Study information

Scientific Title
3D/4D ultrasound guided embryo transfer vs clinical touch technique: a randomised controlled trial

Acronym
3D/4D UGET

Study hypothesis
Does the use of advanced ultrasound techniques during embryo transfer improve the pregnancy rate and outcome for patients undergoing IVF treatment?
Embryo implantation is a critical step in successful IVF treatment. Correct placement of the embryo(s) within the uterine cavity can result in improved implantation. If the uterine cavity can be assessed in greater detail, is the more accurate placement of the embryo possible and will this improve implantation and pregnancy rates?

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West - Liverpool Central Research Ethics Committee, 09/12/2016, REC ref: 16/NW/0588

Study design
Prospective randomized parallel trial (unblinded)

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Condition
Infertility

Interventions
In a non-randomised pilot study of an unselected population (50 patients), an increase in live birth rate biochemical pregnancy rate of 15% was observed in the intervention group compared with a control group. The sample size in this study assumes an expected response rate in the study group of 40% and in the control group of 25%. To achieve an 80% power to detect the difference, with a significance level of 5%, it is calculated that 149 subjects per group will be required. With a withdraw/non-evaluable subject rate of 5%, a total of 157 subjects per group will need to be recruited, leading to a total required sample size of 314 subjects.

Patients will be randomized to the study group or control group using computer generated numbers. The study group will have embryo replacement done under 3D/4D vaginal ultrasound guidance whereas the control group will have the embryo placement done by the clinical touch technique, where the embryo catheter is inserted to 6 cm to the uterine cavity from the external cervical os. The total duration of follow up is 10 months.

Intervention Type
Procedure/Surgery

Primary outcome measure
Live births, recorded at follow up at 10 months

Secondary outcome measures

1. Biochemical pregnancy, defined as urinary pregnancy test positive, at 2 weeks after embryo transfer
2. Clinical pregnancy, defined as presence of intrauterine pregnancy with fetal heart rate >100bpm between 6-8 weeks pregnancy, at 5 weeks after embryo transfer
3. Miscarriage, recorded at 20 weeks after embryo transfer
4. Ectopic pregnancy, recorded at 8 weeks after embryo transfer
5. Multiple pregnancies, recorded at 5 weeks after embryo transfer
6. Failed embryo transfer, recorded at time of procedure
7. Grading of ease of procedure (Easy 1 to Difficult 5), recorded at time of procedure
8. Duration of procedure, recorded at time of procedure
9. Patient experience, assessed by questionnaire following procedure

Overall study start date
01/02/2018

Overall study end date
30/09/2020

Eligibility

Participant inclusion criteria
1. All women undergoing fresh or frozen embryo transfer
2. All women able to provide written informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
314

Total final enrolment
320

Participant exclusion criteria
1. Known or suspected hydrosalpinx
2. Fluid within the endometrial cavity
3. Gross distortion of endometrium (e.g. fibroids etc)
4. Previous myomectomy
5. Previous randomization
6. Significant health issues, e.g. HIV, Hepatitis C, Hepatitis B, previous trachelectomy

Recruitment start date
01/03/2018

Recruitment end date
30/01/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Liverpool Women's NHS Foundation Trust
Crown Street
Liverpool
United Kingdom
L8 7SS

Sponsor information

Organisation
Liverpool Women’s NHS Foundation Trust

Sponsor details
Crown Street
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04q5r0746

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Hewitt Fertility Centre, Liverpool Women's NHS Foundation Trust

Results and Publications

Publication and dissemination plan
Dissemination will occur through departmental meeting including research meetings. This potentially will extend to national/international conferences and publications in the field of fertility.

Intention to publish date
01/02/2021

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version V3	21/03/2016	02/04/2019	No	No
Abstract results		15/10/2020	20/01/2022	No	No
Abstract results		06/08/2021	20/01/2022	No	No
HRA research summary			28/06/2023	No	No
Results article		08/09/2023	06/03/2024	Yes	No