

Specialists In Reproductive Medicine & Surgery, P.A.

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Excellence, Experience & Ethics

Study Subject Consent for Participation in Oocyte Cryopreservation Study - 201

Human Oocyte Cryopreservation by Vitrification: Examination of Two Different Storage Devices

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Study Objectives:

The primary purpose of this research study is to cryopreserve (freeze) some or all of your oocytes (ovum or eggs) following retrieval. We will evaluate two different storage containers, each with a slightly different freezing protocol, with all of the containers eventually placed in liquid nitrogen for extended storage.

A secondary purpose of this study will be to evaluate oocyte survival rates with respect to the two storage containers should you choose to thaw your oocytes at a later date. If you also fertilize them with partner/donor

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sperm and then transfer some of these embryos into your uterus so that you may conceive, we will evaluate the pregnancy rates with respect to each of the two storage containers.

Study Sponsorship:

This study is sponsored by Specialists In Reproductive Medicine & Surgery, P.A. Dr. Papkov has volunteered his time to assist in the study.

Study Rationale:

There are many instances where it makes sense to cryopreserve (freeze) a woman's eggs, termed Oocyte Cryopreservation (OC). For example, if a woman had cancer and has to undergo radiation and chemotherapy, removal of some of her eggs may help her to have a child in the future should she become sterile following treatment.

It is a challenge to freeze the human egg for many reasons such as the large size of the cell, the large amount of water within the cell and the fact that the chromosomes are in transition preparing for fertilization. There is a growing body of data that suggests a rapid freezing technique, called vitrification, has the greatest promise of freezing and successfully thawing the human oocyte. The exact "recipe" of the process is still being investigated.

There are a growing number of storage containers designed to hold and store the oocyte. Some are easy to use while others are more difficult to work with. The success of the cryopreservation and warming process may also depend on the storage containers themselves. The main purpose of this study is to evaluate two different cryopreservation storage containers.

Inclusion Criteria:

The following are the study inclusion criteria:

1. Female, ages 13 (i.e., puberty) – 40, inclusive.
2. Meet the indications for OC (listed below) as determined by the Principal Investigator (PI).
3. Women not at high risk for complications of the medications used to stimulate the ovaries as determine by the PI.
4. Healthy enough to undergo analgesia/anesthesia for oocyte retrieval as determined by the PI.
5. At medium or low risk developing complications following retrieval as determined by the PI.
6. While there is no absolute limit to body mass index (BMI), BMI's 38 and above will be discouraged. As the BMI increases, it is difficult to maintain an airway under analgesia and the number of oocytes retrieved falls.
7. The study subject must be able to provide informed consent. If below the age of consent, we will require assent (agreement) of the young woman along with consent from their parent/legal guardian.

It is expected that up to 56 people will take part in this study.

Study Structure & General Procedure:

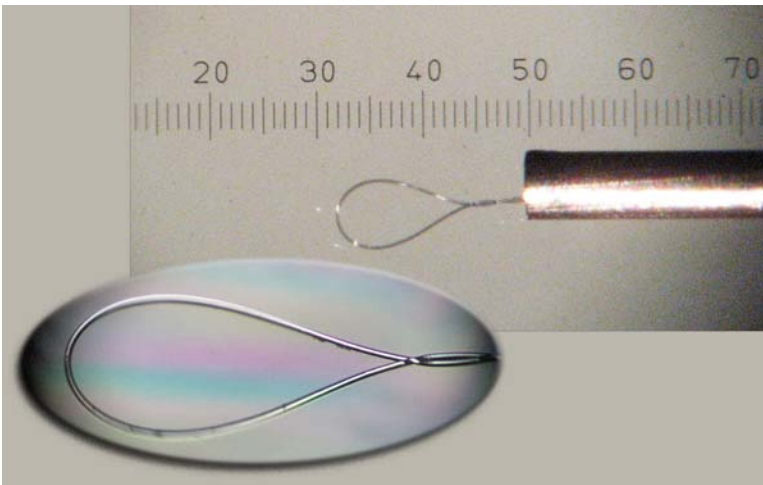
The process for preparing your ovaries to produce multiple oocytes and the retrieval process itself is covered in detail in other sections of the Oocyte Cryopreservation Packet. Following the retrieval, each of your oocytes will be carefully examined. Oocytes that are healthy and ready for fertilization (mature) will be divided between two different types of storage containers. Immature oocytes may also be cryopreserved in the hope that improved techniques will be available to mature the thawed oocytes in the laboratory so they too can also be

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fertilized. It is estimated that one or two oocytes will be stored in each container. Essentially half of your eggs will be placed in one type of container and the other half in the other.

Your oocytes will undergo a process to remove water from the cell. If very much water is in the oocyte at the time of vitrification, ice crystals will form potentially damaging the egg. Cryoprotectants replace the water and help to keep the oocyte safe during vitrification. All of your eggs will undergo the same preparation process.

One of the storage containers is called a VitroLoop™ and is considered an “open system,” a storage system that comes into direct contact with liquid nitrogen. A nylon loop is formed which holds a small amount of media and the oocytes themselves. This is plunged into liquid nitrogen. Once frozen, the device itself is placed inside a cryo-vial full of liquid nitrogen and the entire assembly is plunged into liquid nitrogen for storage.



The actual nylon loop is shown above with the scale on the tape in tenths of millimeters. The loop with steel tube is inserted into the VitroLoop™ on the right.



The VitroLoop™ storage container is pictured above. Units are in cm.

The second storage container is called a CryoLock, and is also considered an “open system”. This system is composed of a two piece straw. The main piece consists of a handle portion with a very small angled well on one end. The second piece consist of a “cap” that covers and “locks” over the angled well end of the straw. The oocytes are loaded onto the angled well and the straw is then plunged into liquid nitrogen. The angled well containing the oocytes is then covered with the cap while remaining under liquid nitrogen. This combined unit is then transferred into larger containers for long-term storage. It is truly uncertain which storage unit works best.

This study is separated into three different phases:

Phase I: Cryopreservation, Ease-of-Use

The laboratory staff will rate ease-of-use of each container type during the vitrification process via a questionnaire. The amount of time the procedure takes for each container will also be reported.

Phase II: Warming, Ease-of-Use

The laboratory staff will rate the ease of use of each container type during the warming process via a questionnaire. The amount of time it takes to warm and the survival rates of the oocytes will be tallied. This phase will occur when you are ready to become pregnant with your oocytes, you donate them or you simply decide to have them thawed and discarded.

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Phase III: Efficacy

The primary endpoint of this segment of the study will be survival rate following thaw. Secondary endpoints will include fertilization rates, embryonic growth rates, embryo quality, blastocyst rates, implantation rates, pregnancy rates, spontaneous loss rates and multiple pregnancy rates will be calculated between the two types of storage containers.

Storage of your cryopreserved oocytes at distant facilities may be encouraged (out of the way of hurricanes). Because this is an actual study, however, the cryopreserved oocytes should not be transferred to other facilities for thawing. It is essential that SRMS track the success and failures of the OC process and adding another facility to the process significantly complicates the data analysis. Any patients who transfer their oocytes will be considered to have incurred a protocol violation and their data may not be able to be included in the study.

General Indications for Oocyte Cryopreservation:

- Lack of Sperm*- Following a routine In Vitro Fertilization (IVF) procedure wherein the partner is unable to provide a semen specimen or there are too few sperm to fertilize the available oocytes.
- Cancer⁺ - Prior to new/recurrent cancer treatment.
- Delaying Reproduction - Should a woman prefer to freeze her oocytes for use at a later date when she fears her reproductive capabilities may otherwise be compromised.
- Prior to medical treatment – Prior to medical treatments that may impair fertility.
- Do not want excess cryopreserved embryos- Due to ethical or religious reasons, some patients do not want to freeze excess embryos during IVF so the alternative would be to freeze excess oocytes.
- Quarantine – Although not necessary at this time, some programs quarantine oocytes prior to donation.
- At risk for premature menopause- There may be a family history or genetic reasons why a woman may be at risk of entering menopause earlier.

* Where there is a lack of sperm, this will often not be known until after the patient will have undergone analgesia and oocyte retrieval. Obtaining informed consent with these medications on board may be challenging. Whenever possible, the study will be presented ahead of time. In reality, risks of the procedure under these circumstances will be minimal since the retrieval will have already taken place and discarding the unfertilized oocytes may be more traumatic than cryopreserving the viable ones. Regardless, if informed consent cannot be obtained due to impairment, the patient will not be included in the study.

⁺ In the case of cancer, some oncologists will feel uncomfortable with the brief elevations of hormones as well as the inevitable delay that will ultimately occur as the ovaries develop oocytes. A consensus with the study patient's cancer physicians will be needed before oocyte retrieval can take place.

Study Benefits:

Oocyte cryopreservation may provide the study patient with an option for fertility preservation. It is possible, however, that you may not directly benefit from taking part in this study. It is hoped that in the future, the information gained from this study will also help others who are undergoing oocyte cryopreservation.

Study Risks:

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The risks of the ART procedure are covered in the general information materials. Risks particular to this study are as follow:

- It is possible that no mature oocytes will be available for cryopreservation.
- It is possible that you will never want to have the oocytes thawed and used.
- It is possible that none of the cryopreserved oocytes will survive warming.
- It is possible that any immature oocytes frozen will not advance and be available for fertilization.
- It is possible that none of the thawed oocytes will fertilize.
- It is possible that none of the resulting embryos will grow.
- It is possible that none of the transferred embryos will implant, grow and result the delivery of a healthy and normal child.
- The study patient pays for the majority of the fees of the procedures. Your funds may be spent with an uncertain outcome.

Alternatives to Participation in The Study:

- Freeze embryos rather than oocytes.
- See if reproductive capacity remains intact regardless of your pending treatments and age.
- Egg donation
- Be a recipient of donated embryos
- Adoption
- Childlessness

Patient Rights:

You will not be paid for your participation in this study. You have been told that no monetary compensation from Specialists In Reproductive Medicine & Surgery, P.A. (SRMS) will be made in the event of a physical injury or illness resulting from participation in the research study. Medical treatment for any complications will certainly be made available to you, the costs of that treatment will be at your own expense or at the expense of your health care insurer, which may or may not provide coverage.

Taking part in the study is purely voluntary, and your decision not to participate in the study will not incur any penalties or loss of benefits to which you might otherwise be entitled. If you decide to take part, you may change your mind about being in the study anytime without penalty or loss of benefits regarding future health care here at SRMS.

Likewise your doctor has the responsibility and right to take you out of the study without regard to your prior consent, should it be determined that continuing the study would be detrimental to your health in any way. If you withdraw voluntarily or are asked to withdraw by your doctor, you may be asked to cooperate in having the requisite laboratory tests and examinations completed as determined by your doctor to be necessary for your good health and safety.

Study Costs:

The specific fees involved in this process are covered in detail in the available Oocyte Cryopreservation Price List.

Many tests, procedures and medical exams that may be required as participant in the study are part of the standards of medical care identified for similar patients and may or may not be covered by most insurance companies. Medications and all physician and hospital related costs incurred during your treatment and, as a

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participant in the study, will be charged to you much the same way you would be charged if you were not a participant in this study.

If your health care insurer does not pay for your cost, you will be responsible for the cost of the medical care related to any condition including and not limited to labs, co-pays, physician fees, hospitalization and procedures.

Patient Confidentiality:

As part of this study, your Protected Health Information (medical records including but not limited to laboratory reports, radiology reports, pathology reports, diagnostic procedure reports, hospital records, physician notes and other reports or documents that may contain your protected health information) may be used and disclosed (looked at, copied or given to others involved in the research study) to compile data related to your participation in this research study. These records may contain information that can identify you such as name, birth date, social security number, etc. If you (or your child) decide that you do not want this information released to any of the individuals below, then you will not be able to participate in the research study.

Who will have access to your medical records?

Organizations that may examine and/or copy your medical records for research, quality assurance, and data analysis include:

- Lee Memorial Health System Institutional Review Committee
- Dr. Craig Sweet and his research study staff
- Dr. Galen I. Papkov of Florida Gulf Coast University (Statistician) or his designee
- Governmental regulatory agencies including, but not necessarily limited to, the department of Health and Human Services, the Food and Drug Administration & Medicare/Medicaid Authorities
- Your Insurance Company

Additionally, parts of your medical records that pertain to any participation in this study may be photocopied and sent to a central location for clinical reviews. Confidentiality will be maintained by using a study number and/or your initials as an identifier on the medical data. Your identity will never be divulged unless you have given express permission.

This authorization (permission to use your protected health information for research purposes) has no expiration date. However, you can change your mind and withdraw your authorization at any time. You can withdraw or take away your consent to have this information viewed by any other individual at any time. You do not have to give an explanation as to why you are withdrawing your permission and you will not lose any benefits to which you are entitled and you will continue to receive care.

You will be removed from the study should you choose to withdraw your consent for release of your protected health information. If you choose to take away your permission to use and disclose your health information, you must notify the investigator in charge of this study in writing. The information that has already been shared with others in relation to this research study cannot be removed; however, no new information will be released.

If you wish to withdraw your permission please contact the office below. They will make sure your written request to withdraw your permission is processed correctly.

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12611 World Plaza Lane, Building 53
Fort Myers, FL 33907

The results of this research may be published in journals or other forums and/or presented at meetings; however, individual identifying information will not be revealed in any publication or presentation that may result from this study.

Notification of Results:

You will be informed about any new significant findings that might become available in the scientific community, which may effect your decision to continue participation in this study.

Phase I of the study is expected to be presented or published first while phases II & III will be delayed for an extended period of time as patients decide to eventually thaw or donate oocytes. It will be your responsibility to provide up-to-date contact information so that you may be informed of the results. We encourage you to keep your contact information up-to-date.

Questions:

If you have any questions regarding this study, you may call SRMS at 239-275-8118. If you have any questions regarding your rights as a research subject, you may call the Lee Memorial Hospital Institutional Review Committee at (239) 424-3383.

Voluntary Consent:

I have read this informed consent. I have been informed of the risks and benefits involved in participation in the research study. All my questions have been answered to the best of my satisfaction. I further understand the following:

- If I have any further questions or concerns at any time, the study investigators will address them as needed.
- I am encouraged to review this consent with family and friends. With my permission, the staff of SRMS are free to answer any questions they have regarding the study.
- I will receive a copy of this consent form.
- I have not been coerced in any way to participate in this study.
- I have been given adequate time to decide to participate or decline this study.
- I voluntarily consent to take part in this research study and I am free to withdraw my consent and stop my participation in the study at any time.
- Withdrawal from the study will not influence the care I receive at SRMS in any way.
- By signing this form, I have not given up any legal rights that I would otherwise have as a subject of a scientific study.

- Please notify me of the results of this study.
- You need not notify me the results of this study.

Signature of the Participant or Legal Guardian

Date

Participant's printed name

Date

Participant's Initials _____ Date: ____/____/_____

Personnel explaining consent to participant

Date

Investigator only:

I verify that voluntary consent was obtained from this patient (or parent/legal guardian) for participation in this study by one or more members of my research staff.

Investigator's signature

Date

Investigator's printed name

Date

Child's Assent (when applicable)

You have had this study explained to you and you understand what will happen to you and agree to participate.

Signature of Adolescent

Date

Signature of Person Obtaining Assent

Date

Updated: 7/23/2013

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