

Ovarian tissue cryopreservation

Information for healthcare professionals



Working in partnership with:
University Hospital Southampton
NHS Foundation Trust and
Complete Fertility Centre, Southampton

The method used in Southampton has been adopted from a leading Copenhagen centre, with over a decade's experience in the freezing technique, evidenced with successful pregnancy outcomes years later when tissue has been re-implanted. ^(2, 3)

What do I need to do?

If your female patient is aged below 37-38 years, carries a significant risk of irreversible damage to ovarian function due to proposed chemo/radiotherapy, but has a good overall survival prognosis and is otherwise surgically fit, you may refer her to the fertility centre at University Hospital Southampton.

For NHS staff, a medical referral form is available at: <http://tinyurl.com/OTS-referral>

OR

Fax an urgent referral letter to Dr Mili Saran, Consultant in Reproductive Medicine, Complete Fertility, Princess Anne Hospital on **02381 208715**.

Please state the patient's cancer and staging and the treatment carried out so far including the proposed timeframe for the start of chemo/radiotherapy. It would assist the fertility team further to be informed of any further pending imaging, (e.g. CT abdomen/pelvis).

OR

Contact Dr Claire Wiggins, NHS Blood and Transplant on SCI.Southampton@nhs.net

References

- Children born after autotransplantation of cryopreserved ovarian tissue. A review of 13 live births. Jacques Donnez, Sherman Silber, Claus Yding Andersen, Isabelle Demeestere, Pascal Piver, Dror Meirou, Antonio Pellicer, and Marie-Madeleine Dolmans. *Annals Of Medicine*, Volume 43, Issue 6, 2011.
- Restoration of ovarian activity and pregnancy after transplantation of cryopreserved ovarian tissue: a review of 60 cases of reimplantation.
 - Jacques Donnez, M.D., Ph.D.^a
 - Marie-Madeleine Dolmans, M.D., Ph.D.^b
 - Antonio Pellicer, M.D., Ph.D.^c
 - Cesar Diaz-Garcia, M.D.^c
 - Maria Sanchez Serrano, M.D.^c
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 - Valérie Luyckx, M.D.^b
 - Claus Yding Andersen, M.Sc., D.M.Sc.^e

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- Cryopreservation of ovarian tissue for a decade in Denmark: a view of the technique.
 - Mikkel Rosendahl^{a, b, c}
 - Kirsten Tryde Schmidt^{b, c}
 - Erik Ernst^d
 - Per Emil Rasmussen^d
 - Anne Loft^c
 - Anne Grethe Byskov^a
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Introduction

Premature ovarian failure (POF) can arise without a clear medical cause at an early age or be caused by iatrogenic agents like chemo or radiotherapy for cancer⁽¹⁾. Other conditions that can cause POF are:

- autoimmune diseases requiring chemotherapy (e.g. systemic lupus erythematosus)
- endocrine (e.g. galactosemia)
- genetic diseases (e.g. Turner's syndrome)

The ovaries are very sensitive to cytotoxic treatment, especially to radiation and alkylating agents.⁽¹⁾

Several options are currently available to preserve fertility in cancer patients and allow them to conceive when they have overcome their disease:

- embryo cryopreservation
- oocyte cryopreservation
- ovarian tissue cryopreservation (OTC)⁽¹⁾

Cryopreservation of ovarian tissue is the only option available for pre-pubertal girls and women who cannot delay the start of chemotherapy.⁽¹⁾

What is ovarian tissue cryopreservation?

Ovarian tissue cryopreservation (OTC) is a process whereby, after preparing the ovarian cortex (concentrated with primordial follicles) into smaller sections, the sections are safely frozen at very low temperatures using liquid nitrogen. Human ovarian tissue stored in this way allows preservation of hormonal as well as fertility potential for several years (25 years or more).

How successful is OTC?

The technique was first introduced in 1996 for cancer patients in some of the large centres worldwide. Since then a large amount of data has been published demonstrating successful return of ovarian function, both hormonal and fertility, with reports of successful natural as well as in vitro fertilisation (IVF) conceived pregnancies.^(1,2,3)

Worldwide over 70 births have been recorded so far after orthotopic ovarian tissue transplantation to either the existing non-functional ovary or to the pelvic peritoneum. Hence, whilst this technology is still relatively new, it is now an established clinical option that can bring a new hope, in particular, to adolescent cancer patients and those with aggressive high risk cancer requiring urgent cancer treatment.

Why not in vitro fertilisation (IVF) instead?

The IVF procedure is suitable only for women and post pubertal girls where the cancer chemo/radiotherapy treatment can be safely delayed by at least 2-3 weeks, and where the cancer and related comorbidities are not a contraindication themselves for IVF drugs.

For prepubertal girls and women who are in need of urgent cancer treatment, and are otherwise fit to go through a laparoscopic surgical procedure, the better placed option is that of ovarian tissue cryopreservation. Many women who could go through IVF may still prefer ovarian cryopreservation.

What does the OTC procedure involve?

Once the patient is referred on to the fertility team, she is thoroughly counselled and her wishes are respected at all times. The patient's suitability for the procedure is further assessed and certain investigations, such as hormonal tests, ovarian reserve tests and ultrasound, are carried out.

The gynaecologist will then liaise with the specialist team from NHS Blood and Transplant and arrange the patient's surgery as a day case. Routine procedure involves laparoscopic unilateral oophorectomy under general anaesthetic. The tissue is then transported to the lab where a specialist biomedical scientist prepares the tissue for freezing. The cortex of the ovary is separated from ovarian medulla and divided into strips. These tissue pieces are put in a cryoprotectant that will keep the tissue viable during cryopreservation and storage at below -150 degree centigrade.