Fertility Preservation Options for Cancer Patients

OPTIONS FOR FEMALE AND MALE CANCER PATIENTS UNDER 40 YEARS OLD PRIOR TO CHEMOTHERAPY, RADIATION THERAPY, AND BONE MARROW TREATMENTS

PART 1

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What is Oncofertility?

Oncofertility is a new term that describes the effort to preserve fertility for young people with cancer.

This new field includes basic reproductive biology, clinical science, ethics, law, economics, pediatric surgery, and education sciences.
1 in 49 human females in the USA between the ages of birth and 40 are diagnosed annually with cancer.

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>5 Year Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Cancers</td>
<td>64%</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>90%</td>
</tr>
<tr>
<td>Childhood Cancers</td>
<td>80%</td>
</tr>
</tbody>
</table>

2015 – 1 person in 285 children in the USA will be diagnosed with cancer before age 20.

Microsoft Clip Art Provided by Fotolia
70,000 cancer patients are exposed to chemotherapy and radiation therapy and half are breast cancer patients.

<table>
<thead>
<tr>
<th>Incidence of Cancer</th>
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</thead>
<tbody>
<tr>
<td>Breast Cancer</td>
<td>30,000</td>
</tr>
<tr>
<td>Lymphoid Malignancies</td>
<td>30,000</td>
</tr>
<tr>
<td>Childhood Cancers</td>
<td>6,500</td>
</tr>
<tr>
<td>Solid Tumors (Cervical, Osteosarcoma)</td>
<td>5,000</td>
</tr>
</tbody>
</table>
Options for Men

- Sperm Bank
- Donor Sperm
- Adoption
Male Fertility Preservation

**Adult Males**

Store sperm → Cryopreserve → Unthaw sperm → Insert into oocyte by Intra-Cytoplasmic Sperm Injection (ICSI) then In Vitro Fertilization (IVF)

**Adult Males with Partner**

Combine → Cryopreserve → Unthaw embryo → IVF
sperm & oocyte to form embryo

**Prepubescent Males**

Testis → Cryopreserve → Unthaw tissue → Autograft → ICSI → IVF
tissue biopsy
Cancer Therapy Often Damages the Ovary and Leads to Infertility

Chemotherapy or Radiation Therapy

Apoptosis (cell death)

Can Fertility Be Preserved in Female Cancer Patients?

Photos: Mary Zelinski, PhD, ONPRC
Options for Women

Options for women are fewer because:

- the **number** of oocytes is finite.
- mature oocytes are **difficult** to freeze.
- mature oocytes are only **available** on certain days of a woman’s cycle.
- immature eggs can be frozen but are difficult to **mature** **in vitro**.
The goals of Oncofertility are to:

- understand the **fundamentals** of follicle development.
- develop methods to **mature** follicles in vitro
- provide germline preservation as an **option** to:
  - female cancer patients
  - NASA deep space astronauts
  - endangered and threatened species
Novel Strategies for Fertility Preservation in Women

- Ovarian protection
- Follicle culture
- Ovarian auto-grafts
- Cryopreservation – See Cryobiology section, Chapter 8.
Bioengineering Primate Follicles: From Immature Eggs to Live Births
Ovarian Protection

Female Rhesus Macaque
*Macaca mulatta*

http://upload.wikimedia.org/wikipedia/commons/2/2d/Macaca_mulatta_in_Guiyang.jpg
http://creativecommons.org/licenses/by-sa/2.0/deed.en  No changes were made.
Reduce or eliminate the gametotoxic effects of cancer therapy on the ovary \textit{in vivo} by applying intraovarian Sphingosine-1-phosphate (S1P) before X-irradiation.

**Hypothesis:** S1P-based strategies are feasible for preserving ovarian function and fertility in primates after cancer therapies.

**Specific Aim:** To determine if S1P delivered directly into rhesus monkey ovaries can protect follicles and oocytes from radiotherapy-induced damage and preserve ovarian function.
The Sphingomyelin Pathway and Cell Death

Sphingomyelin – Membrane Lipid

Sphingomyelinase

Sphingomyelinase

Ceramide Synthase

Ceramide

Sphingosine

Sphingosine 1-Phosphate (S1P)

Apoptosis

http://www.nature.com/nrm/journal/v2/n11/full/nrm1101-838a.html

Drawing: Mary Zelinski, PhD, ONPRC and Lynda Jones, MS, ONPRC
Experimental Procedure and Results

Rhesus Females
Ages 6 – 9
Normal menstrual cycles

Osmotic Minipump

Method
2 osmotic minipumps sc
1 pump in each ovary
Intra-ovarian catheters

Vehicle (solution without S1P)
S1P
FTY720 (long-acting S1P)

7 days
Pumps removed

One ovary removed, Before X-ray

One ovary removed, After X-ray
9 – 11 months

Photos: Mary Zelinski, PhD, ONPRC