Team Introductions

- Karen Burns, MD
  - Pediatric Oncology, Co-Director CFCPP
- Holly Hoefgen, MD
  - Pediatric Gynecology, Co-Director CFCPP
- Lesley Breech, MD
  - Pediatric Gynecology Division Director
- Janie Benoit, MD
  - Pediatric Gynecology Fellow
- Olivia Jaworek Frias, MSN
  - Fertility Navigator
- Julie Sroga, MD
  - Reproductive Endocrinology, University of Cincinnati
- Seth Risner, MS, PA(ASCP)
  - Pathology
- Tara Schafer-Kalkhoff, MA
  - Clinical Research Coordinator
- Abbey Franklin, PA
  - Pediatric Urology
- Mary Anne Lenk
  - Quality Improvement Consultant
Program History

• First established in 2009
  – Goal to see all eligible patients (new and relapsed)
  – Available Options:
    • Lupron
    • Sperm Banking

• Partnered with UC Reproductive Medicine
  – Embryo cryopreservation
  – Oocyte cryopreservation

• Ovarian Tissue Cryopreservation
  – Protocol opened at CCHMC (2012)

• Testicular Tissue Cryopreservation
  – Available via University of Pittsburgh (2014)
  – IRB pending at CCHMC
• Struggles with consults and timing
  – Which patients should be seen?
• Tremendous growth in institutional oncology program
  – Multiple teams within oncology
• Initially unable to track consults
• September 2013
  – Oncofertility Navigator Role Identified
    • Oncofertility database creation
  – New work flow established
    • Navigator to Care Manager communication
  – Fertility Consult Note created in Epic
• Staff education sessions beginning in 2014
• Formalized process for BMT patients 2015
• **Current Goal:** Fertility Consultation on all at risk patients in CBDI

• **Accepted Exclusions from Consultation**
  – Surgery only
  – Observation only
  – Palliative/Phase I treatment
  – *Second opinion/Consult only
  – Previous fertility consult completed
    • without change in infertility risk
  – Family declines fertility consultation
Eligible* Patients Receiving a Fertility Consult**
September 2013 - Present

*Ineligible criteria: observation only, palliative or <20% expected survival, phase I, previous fertility consult/intervention, consult only, surgery only, family declined, severe cognitive delay
**Fertility consult counted on date of documented consult
Percent of Eligible Patients Receiving a Fertility Consult*
September 2013 - Present

- FN began attending Onc weekly team mtgs.
- Began testing decision aids
- Began counting BMT pts in month conditioning started
- FN delivered Fertility Consult email education
- BMT pt list emailed to fertility consult email inbox
- Median baseline period Sep - Dec 2013 = 54%
- 4 pts missed during FN transition

Month of Tx Plan Made
- Median
- Goal

FN = Fertility Navigator
*Ineligible criteria: observation only, palliative or <20% expected survival, phase I, previous fertility consult/intervention, consult only, surgery only, family declined, severe cognitive delay
FERTILITY CONSULTATION WORKFLOW

**Fertility Navigator**
- Obtain initial contact information
- Review records for any previous fertility team contact
- Reach out to the Oncologist on-call to address Gonadotoxic Risk Calculation
- Reach out to the Gynecologist or Urologist On Call to make aware of pending consultation
- Assist with consultations as required and available

**Oncologist On Call**
- Assess risk calculation for previous cancer treatments
- Assess risk calculations for expected future treatments
- Discuss patient's plan of care with oncology colleagues
- Discuss findings with the Gynecologist or Urologist On Call

**Gynecologist and Urologist On Call**
- Review risk calculation with Oncologist On Call
- Discuss patient history and consultation request with Fertility Navigator
- Conduct Fertility consultation, document in Fertility Consult Notes, bill consultation

**Fertility Navigator**
- Contact Research Coordinator for any patients requesting research protocol treatment
- Contact University of Cincinnati for female REI services
- Contact appropriate sources for sperm banking
- Assure patients and families have all required contacts, direct to follow-up appointments and assist with further process steps as required
- **Follow up with "maybe" patients within 72 hours**

**Research Coordinator**
- Work with research institutions (Pitt, Northwestern)
- Consent patients for research protocol procedures
- Assure all appropriate paperwork completed for research portion of procedures
Goal: Assist the patient/family through the Oncofertility process as seamlessly as possible

• Obtain initial consult information:
  – Fertilityconsult@cchmc.org
  – Pager
  – Desk phone / Message line
  – Interdisciplinary meetings
  – EPIC in-basket
  – Review of weekly patient lists (Oncology)
  – Review of BMT schedule/calendar
  – Tumor Board

• Initiate fertility consult/process chart review
  – Identify previous treatment & future treatment
  – Identify urgency of consult (Solids, Liquids, Neuro-Onc, BMT)
• Contact the on call fertility oncologist for risk assessment
• Coordinate fertility consult with patient’s care manager
  – CBDI clinic / GYN clinic / Inpatient
• Contact GYN/Urology on call to notify of pending fertility consult
• Prep consult
  – Shared Decision Making Tool
  – Patient folder (male / female)
• Facilitate in the actual Fertility Consultation
  – Ensure appropriate lab testing is performed
  – Review financial considerations
• Navigate the research Process
  – Contact research coordinator with potential research candidates
• Notify Pathology/Surgery Scheduling of OTC patients
• Contact REI (oocytes/embryos/sperm) - fax notes and labs
Oncofertility Risk Assessment

• Provided by oncology members of CFCPP
• New patient plan is discussed with primary oncology team
  – Identify protocol, address any protocol deviation
  – Determine window of time before initiation of therapy
• Cumulative doses of chemotherapy and/or radiation in protocol
• Provide assessment of previous and planned treatment regimens
Oncofertility Risk Assessment

• Tools for calculating risk:
  – SaveMyFertility
  – Fertile Hope
  – Summed Alkylating Agent (SAA score)
  – Cyclophosphamide Equivalent Dosing (CED) calculation
  – Literature searches on new / unfamiliar medications & protocols
What is Cyclophosphamide Equivalent Dosing?

- **Cyclophosphamide equivalent dose (CED) calculation:**
  
  - 1.0 * (cumulative cyclophosphamide dose (mg/m²))
  - + 0.244 * (cumulative ifosfamide dose (mg/m²))
  - + 0.857 * (cumulative procarbazine dose (mg/m²))
  - + 14.286 * (cumulative chlorambucil dose (mg/m²))
  - + 15.0 * (cumulative BCNU dose (mg/m²))
  - + 16.0 * (cumulative CCNU dose (mg/m²))
  - + 40 * (cumulative melphalan dose (mg/m²))
  - + 50 * (cumulative Thio-TEPA dose (mg/m²))
  - + 100 * (cumulative nitrogen mustard dose (mg/m²))
  - + 8.823 * (cumulative busulfan dose (mg/m²))

Green et al. 2014
Oncofertility Risk Assessment

- Identify Risk Category:
  - Low
    - (<20% develop infertility)
  - Intermediate
    - (20-80% develop infertility)
  - High
    - (>80% develop infertility)
Fertility Preservation Options

- **Egg Freezing** (Oocyte Cryopreservation): 2-6 weeks
- **Embryo Freezing** (Embryo Cryopreservation): 2-6 weeks
- **Ovary Freezing** (Ovarian Tissue Cryopreservation): 2-3 days
- **Depo-Lupron Injection** (Ovarian Suppression): 0 days

Time required for fertility option:

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Day 0 to Day 42.
Fertility Preservation Options

- Initiation of Shared Decision Making
Follow Up Process

• **Goal**: follow up call within 72 hours
  – Decision time frame dependent of care

• Fertility Navigator contact information given

• Patients may request follow up consult with Fertility Navigator / Providers

• Survivors
  – Goal: Annual GYN/Fertility follow up
Percent of Eligible Patients Electing a Fertility Preservation Option
September 2013 - Present

*Ineligible criteria: observation only, palliative or <20% expected survival, phase I, previous fertility consult/intervention, consult only, surgery only, family declined, severe cognitive delay*
# of Patients Electing Fertility Preservation by Option
Sep. 2013 - Present

Count (# of Patients)

Month

Sperm Cryopreservation  Ovarian Tissue Cryopreservation  Testicular Tissue Cryopreservation
Preservations Options Completed
(Based on currently available date)

• Females
  – Ovarian Tissue Cryopreservation: 44
    • 22 since 1/2015
  – Oocyte Cryopreservation: 8
  – Embryo Cryopreservation: 0

• Males
  – Sperm Cryopreservation: 22
  – Testicular Tissue Cryopreservation: 8
    • 6 since 1/2015
STEPS TO OVARIAN TISSUE CRYOPRESERVATION …
Determine patient eligibility based on the study’s inclusion and exclusion criteria.
1) Females, $\geq 1$ month and $\leq 41$ years of age.

2) Undergo surgery, chemotherapy, drug treatment, and/or radiation for the treatment or prevention of a medical condition or malignancy expected to result in permanent and complete loss of subsequent ovarian function.

3) Or, have a medical condition or malignancy that requires removal of all or part of one or both ovaries.

4) Subject may have newly diagnosed or recurrent disease.

5) Subject who already has stored cryopreserved ovarian tissue in a frozen state prior to undergoing cancer treatments (surgery, chemotherapy or radiation) will be eligible for enrollment with informed consent.

6) Signed an approved informed consent and authorization permitting the release of personal health information. The subject and/or the subject’s legally authorized guardian must acknowledge in writing that consent for specimen collection has been obtained, in accordance with institutional policies approved by the U.S. Department of Health and Human Services.

7) Is not a candidate for or chooses not to utilize embryo or oocyte banking.
1) Females, \( \geq 1 \text{ month} \) and \( \leq 41 \text{ years of age} \).

2) Undergo surgery, chemotherapy, drug treatment, and/or radiation for the treatment or prevention of a medical condition or malignancy expected to result in permanent and complete loss of subsequent ovarian function.

3) Or, have a medical condition or malignancy that requires removal of all or part of one or both ovaries.

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7) Is not a candidate for or chooses not to utilize embryo or oocyte banking.

- Completed pre-treatment, recurrence, & post-treatment survivors
- No restrictions based on risk assessment
- Allows for case by case evaluation
- Final decision left with the CFCPP team and the patient’s family
Exclusion Criteria

1) Women with psychological, psychiatric or other conditions which prevent giving fully informed consent.

2) Women whose underlying medical condition significantly increases their risk of complications from anesthesia and surgery.

3) Women who have a large mass in the ovary that is being removed will not be enrolled in the study. That is, ovarian tissue cryopreservation will not be performed on portions of the ovary that contained a large mass as the tissue may not be suitable for future use due to limited or no follicles.

4) Serum FSH levels above 20 mIU/ml.
Patient Consent Process
OTC Consent Preparation

- Prepare patient folder with OTC Study paperwork.

Consent the Patient

- Consent Forms used based on age: Adult Consent Parental Permission, Assent
  - ≥ 18 years: Adult Consent completed by patient
  - ≤ 17 years old
    - For all: parent or legal guardian completes Parental Permission
    - ≤ 10 years: patient asked for verbal assent, if age appropriate
    - 11 to 17 years: patient asked to provide written Assent
    - 16 to 17 years: patient asked to sign Adult Consent as well as Assent

- Consent Forms used based on language spoken: Full or Short Form Consent
  - Full Consent Form: used for English speaking patients
  - Short Form Consent Form: used for non-English speaking patients
    - Currently translated into Arabic and Spanish.
Ovarian Tissue Cryopreservation – Procedure
– Combined vs Solo procedure
– Laparoscopic (Open option available)
– Remove Single Whole Ovary
– Ovary removed via easiest accessible direction
Ovarian Tissue Cryopreservation - Processing.

– Recently moved to in-house processing
– Requires FDA licensing and oversight
Pathology
Pathology
Other Female Options

• Provided via University of Cincinnati Center for Reproductive Health
  – Oocyte Cryopreservation
  – Embryo Cryopreservation
• Oocyte and embryo cryopreservation
  – Explanation of process: ovarian hyperstimulation and oocyte retrieval, cryopreservation, and storage
    • Pregnancy rates for oocytes and embryos
  – Determine cycle stimulation start based on cancer treatment
    • Traditional follicular phase start
    • Immediate start for late follicular-luteal phase
  – Financial counseling for cryopreservation and storage
  – Special considerations in adolescent/young adult population
    • Virginal status with transvaginal monitoring/aspiration
    • Relationship status – counseling in regards to legal implication to embryo cryopreservation

• Options for using gametes in the future
  – Uterine radiation – need for gestation carrier
    • FDA labs obtained if at risk for needing gestational carrier

• Contraception and Hormone replacement discussions
• 19 patients referred for gamete cryopreservation since 1/2014
• 13 pre-treatment and 6 post-treatment consults
• Age: 17-26
• AMH: Pretreatment 0.88-3.9; post treatment 0.03-0.7
• 8 proceeded with oocyte cryopreservation with 3 canceled cycles
  – 5 to 22 oocyte cryopreserved
  – Cancelled per patient desire, poor response, enlarging complex ovarian mass
  – 0 embryo cryopreservation cases
• 4 pending stimulation starts for post treatment patients
• Testicular Tissue Cryopreservation
  – Counseled for all pre-pubertal males who meet study criteria
  – Currently made available through the University of Pittsburgh

• Sperm Cryopreservation
  – Counseled for all pubertal male patient’s regardless of risk stratification
  – Made available through University of Cincinnati
  – In-house room available for banking at CCHMC
New Oncology Patient Order Set
EPIC Fertility Synopsis (Testing Phase)
• Currently using Excel Spreadsheets
• Considering REDCap vs other Data Management options
  – Interested in multi-center shared database
Initial Programmatic Barriers

- Process for capturing consults
- Coordination of fertility care (No fertility navigator)
- Data management / Monitoring of completed consults
- Lack of fertility team specific contact information
- Tissue processing in outside facilities
  - Time to processing, Scheduling
- Lack of Research Assistant
- Lack of Institutional support & oncology buy-in
- Need for overall staff education
- Logistics of 3 oncology services + BMT
- Financial Barriers
Ongoing Programmatic Barriers

• Data management
  – Remains in Excel
• Unable to process sequential ovaries in a single day
• Continued education throughout departments
• Resource management
  – faculty/fellow time, staff time, OR time, clinic utilization
• Funding
Recent Updates

• Protocol & consent improvements
• Increased participation in Oncofertility Consortium
• Initiation of Shared Decision Making Tool
• New Name, New Website
• Hiring of Clinical Research Coordinator
New in 2015!!

- New gynecology lead / Co-Director
- Protocol & Consent Updated
- Amendments & Updates accepted by IRB
- Increased participation in Oncofertility Consortium
  - Monthly pediatric specific meetings
  - Participation in consortium website updates
  - TWO chapters in the upcoming Pediatric and Adolescent Oncofertility: Best Practices and Emerging Technologies textbook
- Initiation of Shared Decision Making Tool
- New Name, New Website
- Hiring of Clinical Research Coordinator
Fertility Preservation – Future Direction

• Patient centered-improvements
  – Continue testing, improvement and spread of SDM tool
  – Increase information available to our international patients in their preferred language
  – Increased presence in survivor population

• Increase our national presence

• Expand & improve workflow model
  – Increased participation of urology with male consults
  – Defined roles of Fertility Navigator, CRC, etc …

• Expand data-driven decision making & QI
  – Measure timely consults, Follow up of patient receiving fertility preservation methods, Monitoring the role of finances on decision

• Expand research protocols
  – TTC protocol currently with IRB for approval at CCHMC