DOSIMETRIC AND BIOKINETIC MODELS OF THE PREGNANT FEMALE FOR RADIOLOGICAL PROTECTION

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Fetal Radiation Exposure

Medical Sources

- **Computed Tomography (CT)**
  - pulmonary embolism, acute appendicitis, trauma, etc.
- **Fluoroscopy**
  - typically for life-saving procedures
  - embolization of organs and blood vessels due to trauma, others
- **Nuclear Medicine**
  - planned: ventilation-perfusion, thyroid, bone and renal scans
  - un-planned: isolated cases of I-131 administration (Graves’ disease) and F-18 administration via FDG (Hodgkin's lymphoma)

Non-Medical Sources

- **Environmental / Occupational**
- **Atomic Bomb Survivors**
- **Techa River Offspring Cohorts**
  - Studied under SOLO – Epidemiological Studies of Exposed Southern Urals Populations
Fetal Computational Phantom Development

- Performed CT and 1.5 T MR scanning on 21-week preserved fetal specimen
- Performed 4.7 T MR scanning on 12-week preserved fetal specimen
- Gathered CT image sets of pregnant women at various stages of gestation
- Images hand-contoured and reviewed by radiologist and anatomist
- Contours rendered into 3D polygon meshes and converted to flexible surfaces
- Fetal and maternal tissue masses and morphometry matched to literature sources
- Implemented volumetric scaling methodology to create phantoms at other ages
Completed Fetal Computational Phantom Series

Fetal age (weeks post-conception)

A  B  C  D  E  F  G  H

8  10  15  20  25  30  35  38
Pregnant Female Phantom Development

The UF family of hybrid phantoms of the developing human fetus for computational radiation dosimetry

Matthew R Maynard¹, John W Geyer¹, John P Aris², Roger Y Shifrin³ and Wesley Bolch¹,4,5

doi:10.1088/0031-9155/56/15/014
Pregnant Female Computational Phantom Development
Pregnant Female Computational Phantom Development

Contoured anatomy

Adult female organs removed

With pregnant anatomy

After NURBS conv.
Uterus visible (D)
Uterus not visible (E)
Completed Pregnant Female Computational Phantom Series

A  B  C  D  E  F  G  H
8 weeks  10 weeks  15 weeks  20 weeks  25 weeks  30 weeks  35 weeks  38 weeks
The UF Family of hybrid phantoms of the pregnant female for computational radiation dosimetry

Matthew R Maynard\textsuperscript{1}, Nelia S Long\textsuperscript{1}, Nash S Moawad\textsuperscript{2}, Roger Y Shifrin\textsuperscript{3}, Amy M Geyer\textsuperscript{1}, Grant Fong\textsuperscript{4} and Wesley E Bolch\textsuperscript{1,5}
Application: In-Utero Radiation Epidemiology

**Project Background**

- Urals, Russia: 1949 - 1956
- Significant radionuclide exposure to workers in the Mayak nuclear weapons plant and surrounding populations/villages along the Techa River
- ~30,000 exposed individuals living along the Techa River
- Sr-90/Y-90, Sr-89, I-131, Cs-137/Ba-137m, Pu-239
- Increased incidence of leukemia, solid cancers, other health effects in populations that were exposed *in utero*
- **Aim:** to quantify the excess health risks associated with protracted, low dose rate radiation exposures

**Need**

- Radiation-induced cancer is cellular-level phenomenon (organ dose as surrogate)
- Doses (S-values) to individual organs are needed to calculate associated risk
- S-value – dose to target tissue per nuclear transformation in source tissue
Application: In-Utero Radiation Epidemiology

**Summary of Transport And Calculation Methods**

- **MCNPX v2.7 – Monte Carlo radiation transport**
- Utilized *F8 tally exclusively (MeV/starting source particle)
- **Directly sampled from respective radionuclide spectrums**
- Post-processing – mathematically combine simulations to yield total S-value

\[
S \left( r_T \leftarrow r_S \right) = \frac{k}{m_T} \sum_n Y_n \ast F8_n \left( r_T \leftarrow r_S, \sum_i E_i Y_i \right)
\]

- Where \( m_T \) is target mass, \( n \) is particle type, \( i \) is nuclear transition, and \( k \) is a conversion constant

- **Acceptable tally uncertainty: 3% intra-fetal sources, 10% maternal sources**
- **Dual-lattice representation of pregnant mother (lattice overlay)**
  - coarse resolution maternal tissues, fine-resolution fetal tissues
- Particle histories (NPS) determined iteratively – ranged: 100 mil. to 650 mil.
- >1000 individual simulations
MCNPX Visualization of Dual-Resolution Anatomy
Fetal organ dosimetry for the Techa River and Ozyorsk offspring cohorts, part 1: a Urals-based series of fetal computational phantoms

Matthew R. Maynard · Natalia B. Shagina · Evgenia I. Tolstykh · Marina O. Degteva · Tim P. Fell · Wesley E. Bolch

Fetal organ dosimetry for the Techa River and Ozyorsk Offspring Cohorts, part 2: radionuclide $S$ values for fetal self-dose and maternal cross-dose

Matthew R. Maynard · Natalia B. Shagina · Evgenia I. Tolstykh · Marina O. Degteva · Tim P. Fell · Wesley E. Bolch
Biokinetic Model: Introduction

• Biokinetic Model: Model of how a given material moves through a biological organism.

• Transfer Rates (t): Fraction of material that is exchanged along one pathway of exchange between two compartments per unit time.
  - Typically expressed in units of [1/day]
Background: ICRP Publication No. 88

- International Commission on Radiological Protection: Publication No. 88
  - Fetomaternal dosimetry for internal exposures
    - Doses for most radionuclides determined by estimating activity concentration ratios between the mother and the fetus (CM:CF ratios)
  - Limited knowledge on intrafetal exchange
    - Intrafetal activity distribution being modelled as that of a 3-month old infant
  - Amniotic fluid exchange not modelled
Iterative Method of Model Development

1. Fetomaternal Exchange and Biokinetic Model Structure
2. Bulk Physiological Adjustment of Adult Biokinetics
3. Element, and Organ, Specific Transfer Rate Adjustment
4. Tissue Concentration Matching
Fetomaternal Blood-flow Model
Adult Blood-flow Model

• “Reference values for resting blood flow to organs of man” – Williams, Leggettt 1989

• “A Blood Circulation Model For Reference Man” – Leggettt, Williams, Eckerman 1995
Fetomaternal Blood-Volume

- Munro and Eckerman (1998) Maternal blood-volume trends applied to baseline values provided by ICRP Publication No. 89

- 123 ml/kg as observed by Pasman (2009) Fetal blood-volume applied to ICRP Publication No. 89 reference masses

<table>
<thead>
<tr>
<th>Associated Data</th>
<th>$R^2$</th>
<th>Trend-line Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal plasma volume</td>
<td>1.00</td>
<td>$PV = -7.66E-02 \times GA^3 + 4.28E+00 \times GA^2 - 2.04E+01 \times GA + 2.40E+03$</td>
</tr>
<tr>
<td>Maternal red blood cell volume</td>
<td>0.99</td>
<td>$RBCV = -1.77E-02 \times GA^3 + 1.16E+00 \times GA^2 - 1.24E+01 \times GA + 1.50E+03$</td>
</tr>
<tr>
<td>Fetal blood volume</td>
<td>0.99</td>
<td>$FBV = (4.41E-03 \times GA^2 - 1.07E-01 \times GA + 6.69E-01) \times 1.23E+02$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Blood volume (ml)</th>
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<tbody>
<tr>
<td>P1 Fetal</td>
<td>1.14E+01</td>
</tr>
<tr>
<td>P2 Fetal</td>
<td>7.48E+01</td>
</tr>
<tr>
<td>P3 Fetal</td>
<td>2.58E+02</td>
</tr>
<tr>
<td>P1 Maternal</td>
<td>7.51E+03</td>
</tr>
<tr>
<td>P2 Maternal</td>
<td>7.72E+03</td>
</tr>
<tr>
<td>P3 Maternal</td>
<td>7.79E+03</td>
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</table>
### Fetal Blood Flow

- Fetal blood-flow based on data acquired from 2001-2014
- New data available due to 3D-Ultrasound technology

<table>
<thead>
<tr>
<th>Associated Data</th>
<th>Representative Function</th>
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<tbody>
<tr>
<td>Right ventricle</td>
<td>RVF = 3.04E-03×GA³ + 1.05E+00×GA² - 2.84E+01×GA + 2.02E+02</td>
</tr>
<tr>
<td>Left ventricle</td>
<td>LVF = -2.34E-02×GA³ + 2.50E+00×GA² - 5.92E+01×GA + 4.23E+02</td>
</tr>
<tr>
<td>Combined cardiac output</td>
<td>CCO = -3.71E-02×GA³ + 4.74E+00×GA² - 1.16E+02×GA + 8.39E+02</td>
</tr>
<tr>
<td>Ductus arteriosus</td>
<td>DuArF = 2.12E-02×GA³ - 6.54E-01×GA² + 1.35E+01×GA - 1.17E+02</td>
</tr>
<tr>
<td>Placental (Early gestation)</td>
<td>PF = ((1.38E+00 - 1.03E+01×GA⁻²)¹⁰)/100</td>
</tr>
<tr>
<td>Placental (Mid and late gestation)</td>
<td>PF = EXP(3.35E+00 + 6.06E-5×GA³ - 1.87E-05×GA³×ln(GA))/100</td>
</tr>
<tr>
<td>Upper body (Early gestation)</td>
<td>UBF = ((8.24E+00 - 4.67E-02×GA² + 1.91E-03×GA³)¹⁰⁶)/100</td>
</tr>
<tr>
<td>Upper body (Late gestation)</td>
<td>UBF = LVF/CCO - ((1.32E-01×GA – 5.90E-02)×0.1)²×π×60×28.94/CCO</td>
</tr>
<tr>
<td>Descending aorta</td>
<td>DeAoF = LVF + DuArF - UBF</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>PF = 0.11</td>
</tr>
</tbody>
</table>

RVF = right ventricular flow, LVF = left ventricular flow, CCO = combined cardiac output, DuArF = ductus arteriosus flow, PF = placental flow as a fraction of CCO, UBF = upper body flow as a fraction of CCO, DeAoF = descending aortic flow as a fraction of CCO, PF = pulmonary flow as a fraction of CCO, GA = gestational age in units of weeks. All flows and CCO are given in units of milliliters per minute.
Fetal Blood-Flow

• Fraction of incoming blood shunted away from the fetal liver, and going directly to the fetal heart

• Prior estimates held that the shunted fraction was higher than the un-shunted fraction

<table>
<thead>
<tr>
<th>Gestational period</th>
<th>Shunted fraction</th>
</tr>
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<tbody>
<tr>
<td>P1</td>
<td>0.486</td>
</tr>
<tr>
<td>P2</td>
<td>0.219</td>
</tr>
<tr>
<td>P3</td>
<td>0.184</td>
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</tbody>
</table>
Amniotic Fluid: Introduction

Uterine Wall

- Intramembranous
- Swallowing
- Lung Fluid
- Urination
- Transmembranous

AF

Fetus
Amniotic Fluid Flow: Intramembranous Transfer

- Concentration gradient component deemed negligible for radiation dosimetry

- \[ t = 1.6337 \times 10^{-6} \times VF \], where \( t \) is the transfer rate in units of inverse days, and \( VF \) is the intramembranous volume flux in units of milliliters per day.
Current Efforts

- Carbon
- Cesium
- Thallium
- Technetium
- Lead
- Plutonium
- Radon
- Ruthenium

- Physiological adjustment of adult parameters based on fetal growth and development
- Physiological adjustment of adult parameters based on maternal observed maternal changes
QUESTIONS?
Implementation of First Iteration Modeling for Cesium
Implementation of First Modeling Iteration – A Fetomaternal Biokinetic Model of Cesium

Fetal Tissue Retention

![Graph showing fetal tissue retention over gestational age for different tissues: Bone, GI, Brain, Liver.](image-url)
Implementation of First Modeling Iteration – A Fetomaternal Biokinetic Model of Cesium

Amniotic Fluid Retention

Fraction of Injected Cesium vs. Gestational Age (days)
Implementation of First Modeling Iteration – A Fetomaternal Biokinetic Model of Cesium

Placental Retention

Fraction of Injected Cesium

Gestational Age (days)
Implementation of First Modeling Iteration – A Fetomaternal Biokinetic Model of Cesium

Short-Term Maternal Tissue Retention

![Graph showing short-term maternal tissue retention for various organs over gestational age.](image)
Implementation of First Modeling Iteration– A Fetomaternal Biokinetic Model of Cesium

Maternal Retention

![Graph showing the relationship between Fraction of Injected Cesium and Gestational Age (days)]
Implementation of First Modeling Iteration – A Fetomaternal Biokinetic Model of Cesium

Fetal Retention

Fraction of Injected Cesium

Gestational Age (days)
Bulk Physiological Adjustment of Adult Biokinetics: Amniotic Fluid Flow – Intramembranous Transfer

Concentration Gradient Dependent Component of Molar Solute Flux

Concentration Component of Solute Transfer Rate [mmol/8hr]

Intramembranous Concentration Gradient [mmol/l]

(solutes)

(solutes)
Bulk Physiological Adjustment of Adult Biokinetics: Amniotic Fluid Flow – Intramembranous Transfer

Volume Flux Dependent Component of Fractional Solute Flux

- Fractional Solute Transfer Rate [1/hr]
- Volume Flux [ml/8hr]

Graph showing the relationship between fractional solute transfer rate and volume flux for sodium, chloride, and calcium.

- Points for sodium and chloride are marked with squares and triangles, respectively.
- Points for calcium are marked with diamonds.

Scale:
- Y-axis: 2.00E-04 to 6.00E-04
- X-axis: 2.50E+01 to 2.25E+02