Fetal Dose Calculation

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Conflicts of Interest: none

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Educational Objectives

Comprehensive review-collected and combined into one source

- Review of fetal risk levels
  - Ionizing and nonionizing risk
- Review of fetal dose calculation techniques
  - x-ray, fluoroscopy, CT, nuclear medicine/PET
- Provide material to develop discussion points for women
  - That may need to be imaged while pregnant
  - That have been imaged while pregnant

Take Home Message

- ICRP 84 "Pregnancy and Medical Radiation"
  - "Prenatal doses from most properly done diagnostic procedures present no measurably increased risk of prenatal death, malformation, or impairment of mental development over the background incidence of these entities."
- ICRP 79 (quoting 90 & 103)
  - "The overall conclusion from the limited available data, is that it is reasonable to assume that the overall lifetime risk of cancer from *in utero* irradiation is, at most, a few times that of the population as a whole, and the *in utero* risk is judged to be no greater than that following exposures in early childhood."

Take Home Message

- ICRP 84 "Pregnancy and Medical Radiation"
  - Radiation induced malformation threshold: 50 to 100 mGy (5-10 rad)
  - Fetal dose ≤ 100 mGy (10 rad) has a very small risk of radiation-induced cancer
    - 99% chance the fetus will not develop childhood cancer or leukemia
  - "Fetal doses below 100 mGy (10 rad) should not be considered a reason for terminating a pregnancy."
  - Fetal doses > 500 mGy (50 rad) can cause significant fetal damage
    - Magnitude and type of damage is dose and stage of the pregnancy dependent

Risk Models

- Risk models derived from
  - Animal models
    - Provide means to control experimental parameters
  - Human models
    - Historical exposure to medical radiation
    - Exposures to A-bomb (Hiroshima & Nagasaki 1945)
      - Largest cohort of pregnant women exposed ~ 2800
      - Estimated ~ 500 Conceptuses received > 10 mGy
      - CAVEAT: conceptus exposed to more than simply photons (e.g., neutrons)
    - Exposure to Chernobyl fall out
    - Limitations to human models
      - Causality is highly speculative
      - Data is conflicting at times

Terminology

- Prenatal [0-8 days]
  - Pre-implantation
- Embryo [8-56 days (1-8 weeks)]
  - Refers to prenantal offspring during most rapid development
- Fetus [> 56 days]
  - From beginning of 9th week until birth
- Conceptus:
  - Refers to both the embryo & fetus during the 9 month pregnancy term

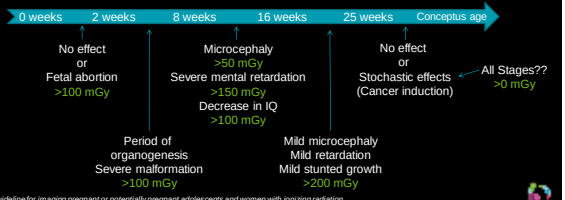
Ionizing Radiation Effects

- Potential risks from ionizing radiation
  - Termination of viability, non-recoverable growth retardation, microcephaly (w/ normal cognition), malformation, mental retardation, childhood cancer
- Natural occurrence of congenital abnormalities is ~5% of live births*
  - Making effect of medical x-rays difficult to evaluate
- Conceptus dose measurement uncertainty
  - Uncertainty of conceptus depth at time of exposure (except for CT, this is relatively unknown)
  - Conceptus depth error of ± 2 cm leads to dose uncertainties ~30-45%

*Pediatrics & Neonatology 56(1), 2015; 25-30

Deterministic/Stochastic Effects

- ACR practice guideline*
  - Dose < 100 mGy poses little to no deterministic effects
  - Casual effects difficult to determine due to statistical uncertainty of measurement



*Acr practice guideline for imaging pregnant or potentially pregnant adolescents and women with ionizing radiation
*Wagner, et al., Exposure of the pregnant patient to diagnostic radiations: a guide to medical management, 2ed

Ionizing Radiation Effects

- Prenatal/early postnatal implantation < 2 weeks
  - Most sensitive time 0-8 days prior to implantation
    - 50-75% human pregnancies naturally abort/miscarriage
    - Generally are unrecognized since they occur within time window of menstruation
  - Miscarriage
    - 15-20% of clinically diagnosed pregnancies abort in 1st or early 2nd trimester
    - 1/3 implanted embryos naturally abort due to morphological abnormalities
  - Difficult to link causal effect from diagnostic radiation due to high natural abortion rate
  - Animal models suggest
    - Radiation induced prenatal death may occur > 50-100 mGy
  - Human extrapolation
    - Suggests radiation-induced prenatal death > 250 mGy

*Pediatrics & Neonatology 56(1), 2015; 25-30

Ionizing Radiation Effects

- Embryonic growth ~2-8 weeks (8-56 days)
  - Sensitive growth stage (organogenesis)
    - Most likely embryonic survival
  - A-bomb model
    - Exposed within 1500 meter blast radius (Dose > 250 mGy)
    - Birth records (as compared to normal population):
      - 2-3 cm shorter
      - ~3 kg lighter
      - 1 cm smaller head circumference (*most common morphologic effect*)
  - Animal models suggest similar effects but at doses < 100 mGy

Ionizing Radiation Effects

- Rapid neuronal development ~8-15 weeks (56-105 days)
  - Post embryonic stage
  - Neuronal development
  - A-bomb model
    - Sever mental retardation was seen between 10-100 mGy
      - "dose response seen in this group may overstate the risk for individuals exposed to x-rays…"*
    - Declining IQ test scores & scholastic performance
      - Doses > 100 mGy
      - Loss of IQ is estimated to be 30 points per Gy
  - Seizures
    - A-bomb model (Doses > 100 mGy)

**Wagner, et al., Exposure of the pregnant patient to diagnostic radiations: a guide to medical management, 2ed*

Ionizing Radiation Effects

- Malignancies (Assume LNT)
  - Evidence suggesting casual effect of *in utero* exposure
    - Primary cancer vector: leukemia
    - Correlation between increased incidence of childhood cancer *in utero* doses of > 20 mGy*
    - Increased likelihood childhood cancer 1-2 cases per 3000 children @ 10 mGy
    - 1 study showed: 2-3 times higher infant leukemia rates from fallout while *in utero***
      - 4 others did not
  - Data is conflicting and will probably not be resolved anytime soon
    - "Carcinogenicity of low-dose (~10 mGy) *in utero* irradiation is not likely to be resolved by further epidemiologic investigation"***

**Stewart, et al., Lancet 2 1956, 447*
**Kneale, et al., J Natl Cancer Inst 56:1976, 879*
***Peinidou, et al., Nature 382 1996, 352-53*
****Wagner, et al., Exposure of the pregnant patient to diagnostic radiations: a guide to medical management, 2ed*

How to Image a Pregnant Women?

- Pre-examination workup for pregnant women
  - Pregnancy does not necessarily preclude examination using ionizing radiation
    - Explore alternative exams: US or MRI (caveat: not recommended to use MR 1st trimester)
  - If x-ray/fluoro/CT is deemed necessary
    - Patient should provide consent for the examination
    - All precautions should be followed to MINIMIZE conceptus dose
    - Avoid cumulative and acute doses exceeding 100 mGy
    - Cumulative doses of 50 - 100 mGy are in gray zone for effects and should rarely occur
    - Doses less than 50 mGy are not associated with malformations, but carry risk of induced neoplasm (keep benefit/risk AHARA)
  - If woman is not pregnant
    - Old advice: NCRP ('71 & '77): do not become pregnant for at least two months after exposure
    - Current advice: "For exposures to ionizing radiation prior to conception, genetically heritable risks have never been identified in the human population. The heritable risks to progeny from diagnostic levels of radiation are not a realistic concern" *

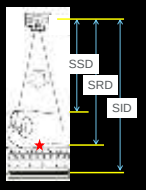
*McCollough et al. Radiographics 2007;27:909-917

Conceptus Dose Calculation-Digital X-ray

- DR/CR-calculate direct fetus exposure
  - Entrance skin dole (ESD*) for the mother

$$ESD(mGy) = K_{air} \cdot \left(\frac{mAs_{exam}}{mAs_{air}}\right) \cdot \left(\frac{SRD}{SSD}\right)^2 \cdot \left(\frac{\mu_{en}}{\rho}\right)_{air}^{tissue} \cdot B$$

  - Measure air KERMA (K_{air}) at the reference point (SRD)
  - Scale by mAs
  - Scale by entrance skin dose (use inverse square law)
  - Apply soft tissue dose correction factor
    - Typically ~ 1.06
  - Apply backscatter (*B*) correction factor**
    - Typically ~ 1.3 ± 0.1



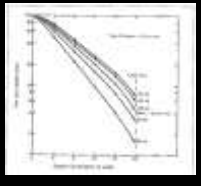
*Brady & Kaufman Med Phys 2015;42(5):2489-2497
*Wagner, et al., Exposure of the pregnant patient to diagnostic radiations: a guide to medical management, 2ed

Conceptus Dose Calculation-Digital X-ray

- Calculate conceptus dose (CD)

$$CD(mGy) = ESD(mGy) * PDD$$

  - Scale ESD from mother
  - Look up percent depth dose (PDD)
    - Measure depth using US
  - Rules of Thumb
    - Half value depth (HVD) in tissue is ~ 4-5 cm
    - Or estimate depth to be ~ 6 cm from anterior surface (~40% of ESD)
    - Depths can vary depending on bladder fill
      - Variation of gestational sac ± 3 cm
      - Conceptus dose varies ~40% over ~3 cm



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Conceptus Dose Calculation-Digital X-ray

- EXAMPLE Patient in early pregnancy undergoes AP KUB radiography
  - Technique was 70 kVp, 35 mAs, & 112-cm SID
  - The patient measures 23 cm thick over the uterus w/ 8 cm deep conceptus
  - The detector is 5 cm below the table top
  - Output (*measured by ion chamber*) is 4.2 mR/mAs @ 100 cm and HVL = 2.8 mm Al
  - 8 cm conceptus depth @ 70 kV ~ 30% of ESD

$$ESD = 4.2\frac{mR}{mAs} * 8.76\frac{mGy}{R} * 35\ mAs * \left(\frac{100\ cm}{112 - 5 - 23\ cm}\right)^2 * 1.06 * 1.3 = 2.5\ mGy$$

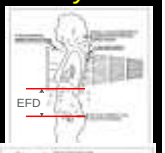
$$CD = 2.5\ mGy * 0.3 \sim 0.8\ mGy$$

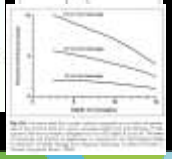
Conceptus Dose Calculation-Digital X-ray

- DR/CR-calculate indirect fetus exposure
  - Only scatter radiation is incident on conceptus
  - Conceptus dose depends on FOV area and distance from FOV border
    - Edge field distance (EFD)

$$CD(mGy) = ESD(mGy) * EFD$$

    - Rule of thumb
      - If EFD > 10 cm; CD = 2%*ESD
      - If EFD > 25 cm (i.e., CXR) CD is negligible
        - » May not be negligible if a very large number of images were taken (*unlikely*)

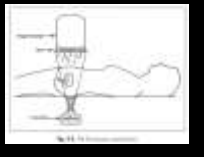




*Wagner, et al., Exposure of the pregnant patient to diagnostic radiations: a guide to medical management, 2ed

Conceptus Dose Calculation-Fluoroscopy

- General fluoroscopy calculations
  - Calculations are similar to planar x-ray
  - If fluoro is a PA procedure, conceptus will typically be deeper
  - Need to calculate peak skin dose
    - From dose rate
    - Total time exposure



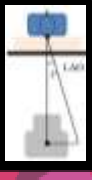
$$ESD(mGy) = K_{air}\left(\frac{mGy}{\min}\right)\left(\frac{mA_{exam}}{mA_{lab}}\right)\cdot t(\min)\cdot\left(\frac{SRD}{SSD}\right)^2\cdot\left(\frac{\mu_{en}}{\rho}\right)^{tissue}_{air}\cdot B$$

$$CD(mGy) = ESD(mGy) * PDD$$

*Wagner, et al., Exposure of the pregnant patient to diagnostic radiations: a guide to medical management, 2ed

Conceptus Dose Calculation-Fluoroscopy

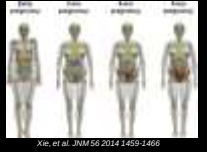
- C-arm fluoroscopy
  - Calculate ESD similar as general fluoro
  - May require accounting for
    - Rotation (LAO or RAO)
    - Angulation (Cran & Caud)



$$Dist_{runs\ 3-7} = \frac{66\ cm}{cos(3^\circ)} = 66.1\ \text{cm}$$

Conceptus Dose Calculation-CT

- Pregnancy and CT
  - ACR* indicates for most abdominal pain, US then MR should be first options before CT
  - Iodinated contrast is generally safe for the conceptus**
- Pregnant computational phantoms
  - Variety of software options exist for dose calculations
  - Advantage
    - Provides dose calculation to fetus for direct and indirect irradiation
  - Disadvantage
    - NCIST phantoms must be requested from NIST & purchased elsewhere
    - Need software to use phantoms



Xie, et al. JNM 56 2014 1459-1466

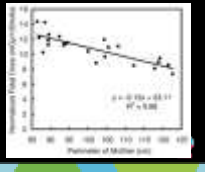
** ACR Practice Guideline for imaging pregnant or potentially pregnant adolescents and women with ionizing radiation. 2008*
***ImageWisely website: https://www.imagewisely.org/Imaging-Modalities/Computed-Tomography/Medical-Physicists/Articles/The-Pregnant-Patient*

Conceptus Dose Calculation-CT

- An empirical derived formula is used to estimate CD*
  - Perimeter (P) of mother
  - Depth to most anterior portion of conceptus (d_c)

$$CD(mGy) = (-0.119(P) - 0.029(d_c) + 24.56) \cdot mAs$$

  - Advantages:
    - Based on modern MDCT (2002-06) technology
      - As accurate as Felmlee methodology (AJR; 154: 185-190, 1990)
    - Based on MC calculations
  - Disadvantages:
    - May not represent pregnant women population
      - Single institution study
    - Assumes full coverage of uterus
      - No partial volume dose estimates are available



** Angel et al. Radiology 249 (1) 2008, 221-227*

Conceptus Dose Calculation-NM/PET

- Diagnostic Nuclear Medicine
  - Standard nuclear medicine procedures << 50 mSv*
  - Greatest risk comes from full mother's bladder externally irradiating the conceptus
    - Pregnant mothers should drink a lot of water and keep their bladder empty as best they can over the 10 half life decay of the radionuclide
- Calculate conceptus dose
  - MIRD formula: assume dose to uterus as 1st order approximation

$$d(r_T, T_D) = \sum_{r_S} \left(\frac{1}{\lambda_0} \int_0^{T_D} A(r_S, t)\,dt\right) \cdot \left(\frac{1}{M(r_S,t)} \sum_i E_i Y_i \phi(r_S \leftarrow r_S, E_i, t)\right)$$

  - Use Olinda/EXM 1.1 or Olinda 2.0 software
  - Compiled look up tables*

Conceptus Age [Units mrads (mGy)]

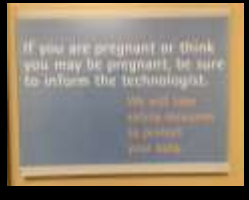
*Bural et al. Mol Imaging Radionul Ther.21(1) 2012, 1-5

Discussion Points

- Counsel patient on dose and risk (Be MINDFUL)
  - You are either breaking the news to a women that she is pregnant
  - You are pointing out something that she knew about, but elected not to tell you
  - Should abatement (abortion) be considered?
    - In 1959 abortion was recommended for doses > 100 mGy (Hammer-Jacobsen)
    - As of 1994, abortion is rarely justified because of radiation risk to embryo/fetus (ACR)
    - E.g., highest risk level (i.e., exposure > 150 mGy between 8-15 weeks, 57-105 days)
      - Only 6% chance of mental retardation
      - < 3% chance of cancer
      - 15% chance of microcephaly

Discussion Points

- The signage around the department may induce unnecessary fear



Thank you

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Ultrasound

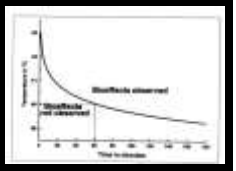
- Ultrasound (US) is a nonionizing procedure
  - You may be asked to assess US risk for pregnancy
  - Number of studies* linking use of US *in utero* to sequelae later in life
    - Miscarriages
    - Preterm birth
    - Autism
    - ADHD
    - Etc…

*Davies, et al. Lancet 340(8831 1992 1299-303
*Webb, et al. Autism Research 10(3) 2017 472-84

Ultrasound

- Potential bio effects of diagnostic US
  - Over entire history of diagnostic US
    - No consistent pattern in bio effects research suggest risk to Conceptus
    - As long as heating is maintained below threshold for such effects
  - Impossible to prove diagnostic US is w/o risk
    - FDA recommended that in utero US imaging be limited to clinically ordered procedures
      - Based on physician judgment
      - Risk vs. benefit model still applicable
  - US intensities beyond diagnostic levels have been shown to cause deleterious effects
    - Hence, new technologies such as Doppler, and or 3D/4D should be sufficiently tested for safety

Ultrasound



- Ultrasound deposits energy per time (1 W = 1 $\frac{J}{sec}$)
  - Absorbed energy is converted to tissue heating
  - Tissue heating is dependent on tissue type
    - A thermal index (TIS) = 1 for ↑1° C
  - Bones absorb most energy
    - TIB = 1 for ↑1° C
    - Fetal bones are primary concern for potential thermal effects
    - Fetus is more susceptible to bone heating compared to embryo
- Hyperthermic mammalian teratogenic effects
  - Demonstrated at temperatures approaching 40° C
  - No bioeffects for ultrasound < 1 hour

Ultrasound

- Ultrasound waves propagate longitudinally into tissue
  - Produce areas of tissue compression (high pressure) and rarefaction (low pressure)
  - Cavitation Effect
    - Sound wave "jostle" micron-sized gas bubbles within tissue
    - Bubbles grow in size
      - Vibratory motion of bubble attracts diffused gases to feed and enlarge
      - Pulsating bubble is forced to collapse
      - Releases free radicals formed from bubble gas
    - A mechanical index (MI) = 1, the patient is at an elevated risk for cavitation
- Cavitation unlikely to occur in patient tissue
  - Diagnostic levels are not intense enough
  - Too much time between ultrasound echo pulses to sustain phenomenon

MRI

- Recommended not to receive elective MRI study during 1st trimester
  - MR study of 1st trimester should be limited to cases in which unique diagnostic info can be obtained
    - Exposure limited to minimum for diagnostic info
- Not recommended to perform MR study using contrast agent w/ pregnant patient**
  - MR contrast agents (Gd) cross the placenta and remain in amniotic fluid for some time

**ImageWisely website: https://www.imagewisely.org/Imaging-Modalities/Computed-Tomography/Medical-Physicists/Articles/The-Pregnant-Patient

MRI

- MRI immerses patient and conceptus in strong magnetic field
  - Static B-field has not been shown to cause bio effects
  - Rapidly changing B-fields are used to create MR image
    - Nerve ending stimulation
    - Electric currents can be induced
    - No knowledge of effect on conceptus

MRI

- Radiofrequency (RF) fields are used to encode MR signal
  - The patient/conceptus is exposed to RF fields
  - Heating generation is primary mechanism for potential bioeffects
  - Heating is dependent on
    - Frequency
    - RF intensity
    - Manner of pulse deposition (image acquisition)
  - Energy absorbed in tissue is estimated using specific absorption rate (SAR)
    - Amount of RF energy absorbed per unit time per unit mass of tissue
    - RF energy averaged over whole body: $\frac{W}{kg}$