The Adverse Effects of Occupational and Environmental Ionizing Radiation: Past, Present, and Future

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Presented at  UCSF OEM Conference
March 9, 2018

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• I have no conflicts of interest or disclosures related to this lecture

Issues to Discuss
• What do we know about cancer risk for workers exposed to ionizing radiation?

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• How much cancer risk is there to workers and patients from low dose radiation?
• Fukushima update: how are cytogenetics tests being used as a tool for dosimetry?

Types of Radiation Health Effects

• **Tissue (Deterministic) effects**: tissue damage that worsens with the dose and for which there is a threshold
  - Acute Radiation Syndrome
  - Skin Burns
  - Cataracts
• **Stochastic effects**: “probabilistic”—likelihood increases with dose, no lower threshold
  - Risk of Cancer
  - Heritable Genetic Defects (lab animal studies—not demonstrated in humans)

Modified from REAC/TS

Alpha, Beta, and Gamma Radiation All “Behave” Differently

- **Alpha Particles**: Dense energy deposition, but stopped by a sheet of paper or dead layer of skin
- **Beta Particles**: Lower energy deposition—stopped by a layer of clothing or a few mm of a substance (e.g. plastic)
- **Gamma Rays, X-rays**: Sparse energy deposition—stopped by inches to feet of concrete or mm to cm of lead
The distinction between external and internal exposure is important in radiation epidemiology.

- **External Exposure** –
  - Whole-body or partial-body

- **Internal Exposure** –
  - Internal radioactive material: inhaled, swallowed, absorbed through skin or wounds

- **Contamination**
  - External radioactive material: on the skin

Grays (Gy):
- Absorbed Dose: A measure of energy transfer used for external exposure from $\beta$, $\gamma$, X-ray
- 1 Gy = 100 Rad

Sieverts (Sv):
- Equivalent Dose: A more integrative measure that adds a weighting factor.
  - 20 for $\alpha$ particles
  - 1 for $\beta$, $\gamma$, X-ray. (so Gy=Sv in this case)
- Effective Dose: includes organ specific weightings
- 1 Sv = 100 Rem

**How much radiation dose is a millisievert?**
- US average natural background exposure 3 mSv
- US allowable annual exposure to a radiation worker 50 mSv
- Threshold for clinical signs of acute radiation sickness 1,000 mSv

**“Low Dose” Radiation is $\leq$ 100 mSv**

**What is the Cancer Risk to Workers Exposed to Ionizing Radiation?**
- Radiation is a known (IARC Type 1) carcinogen
  - Causality well established
    - Japanese Long Term Survivor Study
    - Patient Radiotherapy cohorts.
  - Increased risk for leukemias (except CLL)
  - Increased risk for major organ types of solid cancers
    - Some exceptions: pancreas, prostate, kidney, gallbladder, uterus...

Modified from Health Physics Society
Key Questions for radiation worker studies

• How closely does worker experience mirror Japanese Long Term Survivor Study (LSS)?
• How does cumulative exposure to workers compare to acute exposures in the LSS?
• What do worker studies tell us about the risk of low-dose radiation?
• How do the cancer risk profiles differ between worker populations with internal vs external radiation exposure

Two Key Occupational Groups:
Nuclear Energy/Defense and Medical Radiation Workers

Cancer studies of workers primarily exposed to external (whole body) ionizing radiation

• UK Radiation Worker Study
• US Savannah River and Shipyard Radiation workers
• Chernobyl
• INWORKS (US, UK, France)

United Kingdom Radiation Workers (NRRW-3) Mortality Study

• Included 174,000 monitored rad workers
  — Atomic energy and defense industries
• Dose-related increase in leukemias except CLL
  ERR/Sv = 1.71 (90% CI 0.06-4.29)
  — Strongest for CML
• Dose-related increase in all cancer excluding leukemia ERR/Sv = 0.28. (90% CI 0.02-0.56)


NRRW-3 Trends with Dose in RR for Mortality
All Cancers except Leukemia (90% CI)

Relative risk trend mirrors Japanese LSS results

Several Studies of External Exposure to US Defense Radiation Workers

- Savannah River Site
  - Myeloid leukemia mortality (2007)
  - ERR/Sv = 12 (90% CI 2.35)
  - Highest in hourly paid
  - Lymphoma, NHL. Mortality (2009)

- Portsmouth Naval Shipyard (2 studies)
  - Leukemia mortality
  - Lung cancer mortality OR = 1.02 at 10 mSv (CI .99 - 1.04)
  - Corrected for Occ. Med. rad exposures OR = 1.0

- Matanoski (2008)—Multiple US Nuclear Shipyard Study
  - 28,000 workers
  - Dose-related increased incidence lympho-hematopoietic cancers RR 2.94 (95% CI 1.0-12)

Chernobyl Clean-up Workers

- Approximately 197 Deaths from Acute Radiation Sickness
- Zablotska: 111K remediation workers
  - Dose-related increased rate:
    - All Leukemias ERR/Gy 1.26 (95% CI .03-3.58)
    - Chronic Lymphocytic Leukemia ERR/Gy 2.58 (95% CI .02-8.43)
- Other studies of Chernobyl workers show no consistent increase in solid cancers


INWORKS Mortality Studies

- Cohort: 308,000 Workers in US, UK, France
- Low dose rate <10mGy/yr.
- All Cancer ERR 0.51/Gy (90% CI 0.2-0.79)
- Solid Cancer ERR 0.47/Gy. (90% CI 0.18-0.79)
- Leukemia ERR 2.96/Gy (90% CI 12.127-5.21)
- Risk of cancer similar to Japanese Atomic Bomb Survivors.

Richardson D et al: Risk of cancer from occupational exposure to IR (INWORKS)
BMJ 2015 351:h5359
Leuraud K et al. Ionizing Rad and Risk of Death from Leukemia (INWORKS)
Lancet Haematol 2105:2 e276-81

Internal Occupational Exposures α particles

- Radium Dial workers—Osteosarcoma of bone
  - But not Leukemia

- Uranium Miners (exposure to Radon progeny)
  - Decay products from Uranium found in rock
  - Radon gas decays to short-lived, alpha radiation emitting “progeny” (e.g., Polonium) that adsorb to airborne particulates
  - Now 20 different cohorts with lung cancer risk
    - Dose-response based on “Working Level Months”
    - Cancer risk elevated in non-smokers
    - More than additive in smokers
Internal Exposures and Atomic Weapons Development

- Internal deposition of U-235, Pu-239, and other transuranic radionuclides—mostly by inhalation
- US Hanford (WA) Workers with routine Pu-239 exposure potential show:
  - mortality from lung, liver, bone, and all cancers combined based on length of exposure
  - significant Healthy Worker Effect
- US Rocky Flats Workers—lung cancer


MAYAK: THE SITE OF THE WORLD’S THIRD LARGEST NUCLEAR ACCIDENT

Mayak (Russia) Plutonium Workers

- Part of Soviet Nuclear Weapons Complex
  In Western Siberia
- Multiple studies included reactor and electrochemical workers who were monitored for internal exposure
- Dose dependent increases in Lung, Liver, Bone cancers as well as overall solid tumors
  - Adjusted for smoking


“High Level” Messages from Nuclear Industry Worker Studies

- Dose-related leukemia, lymphoma, and overall solid cancer risk (external exposure)
- Lung Cancer and other organ specific cancers from internal exposure to Alpha emitters (Radon, Plutonium)
- Level of risk/dose similar to Japanese Atomic Bomb Survivors (Long Term Survivor Study)
- Cancer risk found with cumulative external low-dose exposure over time
  - Suggestion of risk at very low overall doses (<100mSv)
Neutron radiation and Flight Crews

- Airplane Pilots and Crew receive about 50% of their dose from neutrons (high energy transfer particulate)
- Average dose 3mSv/yr (up to 9.1 mSv)
  - US dose limit 50 mSv
- Increases in breast cancer, melanoma noted
  - Confounders: UV exposure, Circadian disruption
- Pilots have increased cytogenetic aberrations
  - More on this later

Medical Radiation Workers

- Increased risk of leukemia in Rad Techs and Radiologists working before 1950
  - Some studies also show melanoma, thyroid and breast cancer
- Ongoing Radiology Technologist Cohort Study (91,000)
  - Rad Techs overall show no increase in brain tumors...
  - But Rad Techs assisting in fluoroscopy do have elevated:
    - brain cancer mortality HR 23.55 (CI 1.48, 4.40)
    - breast cancer incidence HR 1.16 (CI 1.02, 1.32)
    - melanoma incidence HR 1.32 (CI 1.05, 1.61)

Radiologists rad dose has declined overall

Insufficient Information on cumulative dose from Fluoroscopy

Concern for exposure to fluoroscopy personnel

- Cumulative dose not well researched
- Cardiologist lifetime doses estimated 50-200 mSv
  - Wide dose ranges reported/procedure
  - 39 % Cardiologists report not using dosimeter
  - Equipment techniques and use of PPE vary widely globally
- Recent study of Interventional Fluoroscopists vs. Psychiatrists—no overall cancer mortality risk
  - Leukemia in older interventional radiologists
  - No dose measurements
Nuclear Medicine Technologists

• Use of radionuclides associated with:
  – All cause cancer mortality (HR 1.20; CI 1.01-1.43)
  – Breast Cancer (HR 2.68; CI 1.1-6.51)
  – Squamous Cell Skin Cancer (HR 1.29 CI 1.01-1.66)
• No increased risk of thyroid cancer in Nuc. Med. Techs
• Rad Techs holding patients >50 studies do have thyroid cancer increase (HR 1.47; CI 1.01-2.15)


Limitations of Ionizing Radiation
Cancer Studies on Medical Workers

• Limited follow-up, especially post-retirement years (latency)
• Lack of cumulative dose measurements—especially for fluoroscopically guided procedures
• Few good studies of Nuclear Medicine Personnel
  – Small numbers
  – Complexity of estimating internal and external dose

What new developments are there on tissue (deterministic) health effects?

Cataracts

• Posterior sub-capsular opacity most characteristic of radiation injury
• Atomic bomb survivor studies indicate excess cataract risk of 39% at 1Gy eye exposure
• Threshold much lower
Cataract and lens opacity risk in medical personnel exposed to ionizing radiation

- Multiple international studies showing increased risk for PSC cataracts in medical personnel
  - Meta-analysis of Cardiologists RR 3.21 (95% CI 2.1-4.8, p<.00001)*
  - Increases also in nurses, techs RR 2.76 (1.43, 5.31)
- US Rad Tech (self-reported) RR 3.0 (<1, 5.7)
- US National Council on Rad Protection lowers eye dose guideline
  - Annual dose limit lowered to 50mGy (formerly 150 mGy)


Cardiovascular disease

- Increased risk of cardiovascular death from high dose exposure is well established
  - Long-term atomic bomb survivor
  - Radiotherapy Patients
- Increasing evidence of CVD risk in low-dose occupational studies
  - CVD in INWORKS study (308K workers): ERR/Sv .22 (90% CI .08, .37)
  - Stroke in Rad Techs: HR 1.34 (95% CI 1.10, 1.64)
  - Worker studies indicate ↑CVD disease with 0.5 Gy cumulative dose threshold
- Possible mechanisms:
  - Microvascular damage
  - Inflammation

Stochastic Effects

HOW MUCH RISK OF CANCER IS THERE FROM LOW DOSE RADIATION?

Worker and Patient Populations

Linear No Threshold Model Supported by US and International Expert Committees

Source: BEIR VII 36
Newer Epidemiologic Evidence
Supportive of Cancer Risk Above 50 mSv

- Linear No Threshold (High Energy)
- Linear No Threshold (Low Energy)
- Linear Quadratic (leukemias)
- Linear with Threshold

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**EVOLVING EPIDEMIOLOGY**

Low-dose radiation cancer effects below 100 mSv are found in some human studies

- Japanese Long-Term Survivors Study
  - 80% of participants exposed to low dose
  - Significant cancer risk < 100 mSv
- INWORKS 3-Country Nuclear Worker Study
- Techa River Residents (Mayak, Russia)
- Medical Radiation Studies (Childhood CT)


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**What is the cancer risk to workers at the current US PEL?**

- International Commission for Radiation Protection (ICRP): Risk of Fatal Cancer 4.1%/Sv
- OSHA/NRC annual allowable dose: 50 mSv
- Lifetime US worker fatal cancer risk with 40 years of work at dose limit: 8.2%

**TOO HIGH!**

*ICRP Report #103. (2007)*

**Alternative Whole-Body Dose-Limit Guidelines**

- ICRP: 20 mSv/year averaged over 5 years
  - No single year exceeds 50 mSv
- US NCRP: 50 mSv/year with cumulative <10 mSv x (Age minus 18)

US Nuclear Regulatory Commission Staff Analysis:
"There is sufficient ... scientific basis to move the NRC’s framework to a greater degree of alignment with the ICRP recommendations."
Medical radiation dose to the public has been rising

- Average “population” dose now 3.2 mSv/pp
  - Increase of 600% since 1980
  - Driven by CT and Fluoroscopic Procedures
- Patient ionizing rad doses can be high
  - Abdominal CT Average 8 mSv (3.5-25)
  - Coronary PCTA, stent 15 mSv (6.9-57)

Mettler FA: Effective Doses in Radiology and Nuclear Medicine. Radiology 248(1) 2006

Hypothetical Fatal Cancer Risk from Low-Dose Radiation in Linear No-Threshold Model

- 0.04% risk of fatal cancer per 10 mSv (1 REM) external radiation dose above background (ICRP)
- CT scan = ~10 mSv
- Possible fatal cancer risk = 1/2500
- Uncertainties in making projections with low dose numbers, adding doses over time, etc.

ICRP 2007 Recommendations of the International Commission on Radiological Protection ICRP Publication103; Ann. ICRP 37 (2–4)

Childhood CT, Brain Tumors, and Leukemia

- Large UK National Health Service Study
- Excess Relative Risks for CT <10 years of age
- Brain tumor (Head CT) ERR 0.023/mGy (95% CI 0.10-0.49)
- Leukemia ERR 0.036/mGy (95% CI .005-.120)
- Absolute risks small:
  - 2 cases / 10,000 CT scans
  - (1 Leukemia/1 Brain Tumor)
- Follow-up period limited


How much radiation dose did your patient get?

- CTDIvol: 88.82 mGy
- DLP 1523.9 mGycm
Estimating the true CT Dose

- CTDI$_{vol}$ = A measure of the amount of energy deposited per unit mass in a standard plastic cylinder

- DLP (Dose Length Product) = product of CTDI$_{vol}$ X length of scan in centimeters

- For Effective Dose need to correct by:
  - A coefficient for patient size
  - By a tissue weighting factor. (e.g., .014 for Chest)

NOT Quick or Practical!

UC Davis CT Reporting: http://www.ucdmc.ucdavis.edu/radiology/RadiationDose.html

What are the effective doses in CT in Common Examinations?

- Smith-Bindman R. Arch. Intern Med. Dec 14 2009; 169(22) 2078-2086
- Mettler FA. Radiology 2008; 248:254-263

Fukushima update: how are cytogenetics tests being used as a tool for dosimetry?

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Follow-up on Exposure Concerns for >31,000 Fukushima Workers

- Exposure limits raised to 250mSv for some workers under ICRP emergency standards
- More than 1550 workers receive > 50 mSv annual allowable dose
- Exposure levels uncertain in initial phases
  - Shortage of dosimeters
  - Chaotic work situation
  - Multiple exposure sources
    - Internal
    - External

THE IMPORTANCE OF DOSE ESTIMATES

Follow-up on Exposure Concerns for >31,000 Fukushima Workers

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**DiCentric Chromosomes**
Interchange between two chromosomes forms a chromosome with two centromeres and fragment, followed by replication.

**Conclusions**
- Likely worker cancer risk from low dose radiation (< 100 mSv)
- Risk from workers’ cumulative dose over time similar to risk seen in Japanese LSS
- Current US PEL for whole body exposure (50 mSv/yr) allows substantial cancer risk
- Growing evidence for tissue effects causing cataracts and CVD in the work environment
1. In studies of workers exposed to external radiation the most consistently increased type of malignancy is:
   - A. Prostate Cancer
   - B. Brain Cancer
   - C. Leukemia
   - D. Bone Cancer

2. Which dose-response model for radiation-related cancer is most consistent with the scientific evidence?
   - A. Threshold model
   - B. Hormesis model
   - C. Linear no-threshold model
   - D. The indeterminate model

3. The OSHA PEL for whole body exposure to ionizing radiation:
   - A. Limits workers to 50 mSv/year exposure
   - B. Allows substantial lifetime cancer risk
   - C. Is higher than international and US national expert committee recommendations
   - D. All of the above

Questions?
Ongoing Water Leaks Are an Environmental Threat

Residents of the most contaminated areas may never return home. Returning residents may receive up to 2 REM (20 mSv)/year from radiocesium.

Very limited return zones
Approx. 136K residents still displaced

Lagniappe

Radon Gas and Radon Progeny

- Decay products from Uranium found in rock, soil...ubiquitous
- Radon gas decays to short-lived, alpha radiation emitting “daughters” (e.g., Polonium) that adsorb to particulates in air
- Deposited in lungs—high local dose
- Well established cause of lung cancer in miners
  - Synergism with smoking
  - Current exposure limit not protective
  - NIOSH recommended 4x reduction (1988)
Residential Radon Exposure is a Significant Public Health Concern

- Second most important cause of lung cancer
- Estimated 21,000 deaths/year (13.4% of total lung Ca)
- EPA remediation level: 4 picocurie/liter of air
  - 148 Bq/L of air
  - Balances feasibility with health protection
  - 0.73% lifetime risk for non-smoker at EPA level
  - 4.1% lifetime risk for smokers
- WHO recommends 100Bq/L (2.7pCi/L)

Residential Radon Progeny

- Risk established in multiple residential studies and by extrapolation from miners
- Estimated Attributable Risk: 8-15% of Lung Cancers in Europe and North America
- US EPA 4 pCi/L (148 Bq/m3 or .1WL) air is a remediation level, not a “safety level”
  - Risk 62 cases lung cancer/1000. (US EPA)
- WHO recommends 100Bq/L (2.7pCi/L)

California Radon Distribution

- Regional variability can be wide
- Adjacent homes can have very different readings
- Importance of testing
- Longer term measurement devices preferred (alpha track)
- Remediation includes sealing basements, venting, and negative pressure under foundation slabs
Percent Radon Tests > 4 PiCi/L by County

California Indoor Radon Test Results

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<tr>
<th>Zip Code</th>
<th>#Tests</th>
<th># &gt;=4 PiCi/L</th>
<th>% Pos</th>
<th>Max PiCi/L</th>
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<td>94221</td>
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<td>0</td>
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https://www.cdph.ca.gov/Programs/CEH/DRSEM/CDPH%20Document%20Library/EMB/Radon/Radon%20Test%20Results.pdf

California Interactive Radon Map
http://maps.conservation.ca.gov/radon/

Measures of Risk

- **ERR** = (0.00045 – 0.00015) / 0.00015 = 2
- **EAR** = 0.00045 – 0.00015 = 0.0003

Human Epidemiology Shows Increased Cancer Risk Above 100 mSv

Modified from: BEIR VII
Newer Epidemiologic Evidence
Supportive of Cancer Risk Above 50 mSv

<table>
<thead>
<tr>
<th>Radiation-related cancer risk</th>
<th>Linear No Threshold (High Energy)</th>
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<th>Linear Quadratic (leukemias)</th>
<th>Linear with Threshold</th>
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Low-dose radiation cancer effects below 100 mSv are found in some human studies:

- Japanese Atomic Bomb Survivors Study
- INWORKS 3-Country Nuclear Worker Study
- Techa River Residents (Mayak, Russia)
- Medical Radiation Studies (Childhood CT)

But studies in high natural background areas in Yangjiang, China and Kerala, India do not show increased risk.