Biological Effects of Ionizing Radiation
Module 8 - AAPM/RSNA Curriculum

Basic Radiation Biology

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a copy of this lecture may be found at:
http://courses.washington.edu/radxphys/index.html
Why does a radiologist need to understand radiation biology?

- Assess the risk-benefit value from radiological and interventional procedures (increased number of radiation injuries to skin)
- Explain these risks to your colleagues and their patients
- The explosive growth in the use of computed tomography, nuclear imaging and other procedures has increased the radiation dose to the population
- The irradiation of the pregnant patient, either accidentally or intentionally, is another area where radiobiology is important in everyday practice
- An understanding of radiobiology, like an understanding of medical physics, gives radiologists another tool to add value to their practice
Radiation exposure to US population from all sources
The new pie chart!

US 1982 (NCRP 93)

- Medical: 0.54 mSv per capita
- Background: 83%
- Consumer products: 2%
- Occupational: 0.3%

Total: 3.6 mSv per capita

US 2006 (NCRP 160)

- Medical: 3.0 mSv per capita
- Background: 50%
- Consumer products: 2%
- Occupational: 0.1%

Total: 6.2 mSv per capita

*Slide courtesy: Dr. M. Mahesh, Johns Hopkins*
How are Biologic Effects Classified?

- **Stochastic Effect**
  - The probability of the effect, rather than its severity, ↑ with dose
  - Radiation-induced cancer and genetic effects
  - Basic assumption: risk ↑ with dose and no threshold
  - The principal health risk from low-dose radiation
How are Biologic Effects Classified?

- Deterministic or Non-stochastic Effect
  - Severity of the effect, rather than its probability, ↑ with dose
  - Requires much higher dose to produce an effect
  - Threshold dose below which the effect is not seen
  - Cataracts, erythyma, fibrosis, and hematopoietic damage are some deterministic effects
  - Dx radiology: only observed in some lengthy, fluoroscopically guided interventional procedures, CT perfusion (if not done carefully)
How does Radiation Interact with Tissue?

Indirect Action

Radiation → H_2O → H^+ + OH^- → Ionization and excitation → H^+; OH^-; HO_2^-; H_2O_2 → Free Radicals and Hydrogen Peroxide

Direct Action

Radiation → DNA → Molecular Damage → Mutation → Biological Response → Genetic → Somatic → Teratogenic

10^{-17} to 10^{-5} seconds → minutes to decades

In radiation therapy differences in the length of the cell cycle for tumors and normal tissues are important:

- Cells are most radiosensitive in M.
- They are relatively more sensitive in late G2.
- Least sensitive in S.
- The length of the cycle for quickly dividing mammalian cells is about 24 hours.

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c.f. RSNA/AAPM Web Module on Basic Radiation Biology
Sensitivity of Cells

- Law of Bergonié and Tribondéau:  
  - applies to most but not all cells
- The sensitivity of cells is directly proportional to their reproductive activity and inversely proportional to their degree of differentiation

<table>
<thead>
<tr>
<th>Resistant Cells</th>
<th>Sensitive Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cartilage</td>
<td>Epithelium of the GI tract</td>
</tr>
<tr>
<td>Bone</td>
<td>Hematopoietic tissues</td>
</tr>
<tr>
<td>Liver</td>
<td>Basal cells</td>
</tr>
<tr>
<td>Nervous tissue</td>
<td>Germinal cells</td>
</tr>
<tr>
<td>Kidney</td>
<td>Lymphoid tissues</td>
</tr>
<tr>
<td>Muscle</td>
<td></td>
</tr>
</tbody>
</table>
Exception: Peripheral lymphocytes are quite sensitive to radiation even though they are quite differentiated and do not divide. The peripheral lymphocyte count is used as a method to triage the severity of acute radiation exposure.
Cell Survival Curves

Note that the x-axis is linear and the y-axis is logarithmic
Cell Survival Curves

Sparsely Ionizing - x-rays or gamma rays

Densely Ionizing - alpha-particles

c.f. RSNA/AAPM Web Module on Basic Radiation Biology
Cell Survival Curves

Repair mechanisms create shoulder

- Fraction of Cells Surviving
- Dose (Gy)

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The radiation dose necessary to kill about 90% of the cells in the population is:

A) 1Gy
B) 7Gy
C) 10Gy
D) 20Gy

More radioresistant

More radiosensitive

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Review Question

NCRP 160 estimates that the average US population dose from medical exposure is about _______ of that from background sources.

A) 1/10
B) ½
C) Equal
D) 2
E) 10
Deterministic or non-stochastic effects of radiation include all of the following except:

A) Bone marrow damage
B) Skin damage
C) Cataract induction
D) Leukemia
E) Infertility due to gonadal irradiation
Review Question

- Stochastic effects of radiation

(A) Can be recognized as caused by radiation
(B) Have a dose-dependent severity
(C) Have a threshold of 50 mSv/year
(D) Include carcinogenesis
(E) Involve cell killing
## Table 1

<table>
<thead>
<tr>
<th>Grade</th>
<th>NCI Skin Reaction</th>
<th>Approximate Time of Onset of Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>0–2</td>
<td>Single-Site Acute: prompt = no observable effects expected; early = no observable effects expected; midterm = no observable effects expected; long term = no observable effects expected</td>
</tr>
<tr>
<td>A2</td>
<td>2–5</td>
<td>B1: Epilation; B2: Recovery from hair loss; B3: No observable results expected</td>
</tr>
<tr>
<td>B</td>
<td>5–10</td>
<td>Erythema, epilation; Recovery at higher doses, prolonged erythema, permanent partial epilation; B3: Telangiectasia; dermal atrophy or induration; skin likely to be weak</td>
</tr>
<tr>
<td>C</td>
<td>10–15</td>
<td>Erythema, epilation; possible dry or moist desquamation; recovery from desquamation; C1: Prolonged erythema; C2: permanent epilation</td>
</tr>
<tr>
<td>D</td>
<td>&gt;15</td>
<td>Dermal atrophy; secondary ulceration due to failure of moist desquamation to heal; surgical intervention likely to be required; at higher doses, dermal necrosis, surgical intervention likely to be required; Telangiectasia; dermal atrophy or induration; possible late skin breakdown; wound might be persistent and progress into a deeper lesion; surgical intervention likely to be required</td>
</tr>
</tbody>
</table>

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**Note.** Applicable to normal range of patient radiosensitivities in absence of mitigating or aggravating physical or clinical factors. Data do not apply to the skin of the scalp. Dose and time bands are not rigid boundaries. Signs and symptoms are expected to appear earlier as skin dose increases. Prompt is <2 weeks; early, 2–6 weeks; midterm, 6–52 weeks; long term, >40 weeks.

* Skin dose refers to actual skin dose (including backscatter). This quantity is not the reference point air kerma described by Food and Drug Administration (21 CFR § 1020.32) or International Electrotechnical Commission (57). Skin dosimetry is unlikely to be more accurate than ± 50%. NA = not applicable.

1. NCI = National Cancer Institute
2. Refers to radiation-induced telangiectasia. Telangiectasia associated with area of initial moist desquamation or healing of ulceration may be present earlier.
Review Question

- Cells that are quite resistant to radiation are
  - A) Lymphocytes
  - B) Basal cells
  - C) Muscle cells
  - D) Hematopoietic cells
A skin dose of 3 Gy could lead to

A) Transient erythema
B) Permanent epilation
C) Wet desquamation
D) Skin necrosis
Skin Injuries – Case Reports

Two key articles from the American Journal of Roentgenology provide important background for the understanding of skin effects:

- Balter article referenced below

Figure 1: Radiation injury in a 60-year-old woman subsequent to successful neurointerventional procedure for the treatment of acute stroke. Estimated fluoroscopy time was more than 70 minutes; 43 imaging series were performed during course of the procedure. The head was not shaved. Note focal epilation on scalp and skin injury on neck but not on scalp. No dose estimates were available for this case.
### Skin Injuries – Degree of skin injury

<table>
<thead>
<tr>
<th>Factor</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>Increases linearly with time</td>
</tr>
<tr>
<td>Patient thickness</td>
<td>Increases exponentially with thickness</td>
</tr>
<tr>
<td>Distance to x-ray port</td>
<td>Decreases as the square of the distance</td>
</tr>
<tr>
<td>kV</td>
<td>Decreases with increasing kV</td>
</tr>
<tr>
<td>mA</td>
<td>Increases linearly with mA</td>
</tr>
</tbody>
</table>

ACCF/AHA/HRS/SCAI Clinical Competence Statement on Physician Knowledge to Optimize Patient Safety and Image Quality in Fluoroscopically Guided Invasive Cardiovascular Procedures: A Report of the American College of Cardiology Foundation/American Heart Association/American College of Physicians Task Force on Clinical Competence and Training:  
[http://circ.ahajournals.org/content/111/4/511.short](http://circ.ahajournals.org/content/111/4/511.short)
Figure 2: Radiation injury in a 40-year-old man who underwent multiple coronary angiography and angioplasty procedures. Images show time sequence of a major radiation injury (7). These images often provide the first hint to individual patients that injury is related to a previous fluoroscopic procedure. (a) At 6–8 weeks after exposure, prolonged erythema with mauve central area appears, suggestive of ischemia. (b) At 16–21 weeks, depigmented skin with central area of necrosis is seen. (c) At 18–21 months, deep necrosis with atrophic borders is seen. (This sequence is available on the Food and Drug Administration Web site and is in the public domain (61).)
CT Perfusion Over Exposure

Hair loss after a CT perfusion scan
Dose estimate of 4-5 Gy

Hair loss after a CT perfusion scan to detect a possible stroke.
Organ Systems Response: Reproductive Organs

- Gonads are very radiosensitive
- Females
  - Temporary sterility: 1.5 Gy acute dose
  - Permanent sterility: 6.0 Gy acute dose*
    - *reported for doses as low as 3.2 Gy
- Males
  - Temporary sterility: 2.5 Gy acute dose*
    - *reported for doses as low as 1.5 Gy
  - Permanent sterility: 5.0 Gy acute dose
  - Reduced fertility 20-50 mGy/wk when total dose > 2.5 Gy
Organ Systems Response: Ocular Effects

- Eye lens contains a population of radiosensitive cells

- Unlike senile cataracts that typically develop in the anterior pole of the lens, radiation-induced cataracts begin with a small opacity in the posterior pole and migrate anteriorly.

- Based on studies of patients and occupational workers, the International Commission on Radiological Protection (ICRP) recently released a statement indicating lens opacities occur at doses of $0.5 \text{ Gy}$.
Organ Systems Response: Ocular Effects

- This threshold dose is much lower than previously thought
- Studies also show that the threshold dose for lens opacities does not change if the dose is received chronically over many years or acutely, as in patient exams

**Current ICRP Dose Threshold**
0.5 Gy for acute and chronic exposure with latent period inversely related to dose

**Previous Lens Dose Thresholds**
4 Gy for acute exposure with a latent period of ~ 4yrs
8 Gy for chronic exposure with a latent period from 8-35 years
Acute Radiation Syndrome (ARS)

- Characteristic clinical response when whole body (or large part thereof) is subjected to a large acute external radiation exposure
- Organism response quite distinct from isolated local radiation injuries such as epilation or skin ulcerations
- Combination of subsyndromes occurring in stages over hours to weeks as the injury to various tissues and organs is expressed
- In order of their occurrence with increasing radiation dose:
  - Hematopoietic syndrome
  - Gastrointestinal syndrome
  - Neurovascular syndrome

- Acute Radiation Syndrome: A Fact Sheet for Physicians
### TABLE 25-5. SUMMARY OF THE STAGES, DOSE RANGE, MAJOR CLINICAL SYMPTOMS, AND EFFECT OF MEDICAL INTERVENTION ON THE ACUTE RADIATION SYNDROME

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Dose range</th>
<th>Prodromal effects</th>
<th>Manifest-illness effects</th>
<th>Survival without treatment</th>
<th>Survival with treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematological</td>
<td>0.5–1.0 Gy</td>
<td>Mild</td>
<td>Slight decrease in blood cell count</td>
<td>Almost certain</td>
<td>Almost certain</td>
</tr>
<tr>
<td></td>
<td>(50–100 rad)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.0–2.0 Gy</td>
<td>Mild to moderate</td>
<td>Early symptoms of bone-marrow damage</td>
<td>Probable (&gt;90%)</td>
<td>Almost certain</td>
</tr>
<tr>
<td></td>
<td>(100–200 rad)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.0–3.5 Gy</td>
<td>Moderate</td>
<td>Moderate to severe bone-marrow damage</td>
<td>Possible</td>
<td>Probable</td>
</tr>
<tr>
<td></td>
<td>(200–350 rad)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.5–5.5 Gy*</td>
<td>Moderate to severe</td>
<td>Severe bone-marrow damage; slight intestinal damage</td>
<td>Death likely within 3–6 wk</td>
<td>Possible</td>
</tr>
<tr>
<td></td>
<td>(350–550 rad)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5.5–8.0 Gy</td>
<td>Severe</td>
<td>Bone-marrow pancytopenia and moderate intestinal</td>
<td>Death likely within 2–3 wk</td>
<td>Possible if stem cell support or replacement is successful</td>
</tr>
<tr>
<td></td>
<td>(550–800 rad)</td>
<td></td>
<td>damage</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8.0–10.0 Gy</td>
<td>Severe</td>
<td>Combined gastrointestinal and bone-marrow damage;</td>
<td>Death within 1.0–2.5 wk</td>
<td>Death likely, but survival possible if stem cell support or replacement is successful</td>
</tr>
<tr>
<td></td>
<td>(800–1000 rad)</td>
<td></td>
<td>hypotension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>10.0–50.0 Gy</td>
<td>Severe prodromal symptoms, hematological syndrome</td>
<td>Severe prodromal symptoms which overlap with</td>
<td>Death within 5–12 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1,000–5,000 rad)</td>
<td>which overlaps with severe gastrointestinal damage;</td>
<td>central nervous system effects, Ataxia, severe</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>electrolyte imbalance; fatigue, gastrointestinal</td>
<td>edema, neurovascular damage, shock</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurovascular</td>
<td>&gt;50 Gy (5,000 rad)</td>
<td>Severe prodromal symptoms which overlap with central</td>
<td></td>
<td>Death within 2–5 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>nervous system effects, Ataxia, severe edema,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>neurovascular damage, shock</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The LD50/60 is 3–4 Gy (300–400 rad).*
LD_{50/60} 

- LD_{50/60} means the dose that would kill 50% of the exposed individuals within 60 days
- The LD_{50/60} for humans is somewhere between 3.5 and 7 Gy depending on the level of care
Diagnosis and Treatment of Radiation Injuries

- Radiation injury is a complex medical event. Accidents are rare so most physicians will seldom see a case. Physicians should be able to diagnose and triage patients so appropriate care can be delivered.

- The IAEA Report on the diagnosis and treatment of radiation injuries can be found here:
  
  http:\www-pub.iaea.org/MTCD/publications/PDF/P040_scr.pdf
<table>
<thead>
<tr>
<th>Clinical Signs</th>
<th>Dose (Gy)</th>
<th>Decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Body (WB)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No vomiting</td>
<td>No early erythema</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Local Exposure (LE)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting two to three hours after exposure</td>
<td>Early erythema</td>
<td>1-2</td>
</tr>
<tr>
<td>Vomiting in one to two hours after exposure</td>
<td>Early erythema</td>
<td>8-15</td>
</tr>
<tr>
<td>Vomiting in less than one hour, or other severe symptoms</td>
<td>Early erythema</td>
<td>&gt;4</td>
</tr>
</tbody>
</table>
Review Question

● Which cells are considered to be the most radio-resistant?

● (A) Bone marrow cells
● (B) Lymphoid tissues
● (C) Neuronal cells
● (D) Skin cells
● (E) Spermatids
Review Question

A patient is brought to the hospital with an estimated whole body dose of 4 Gy. The most likely radiation syndrome would be

A) Bone Marrow Syndrome
B) Gastrointestinal Syndrome
C) Central Nervous System Syndrome
Review Question

- Skin ulcers are most commonly seen
- A) Following CT
- B) Following GI fluoroscopy
- C) Following interventional neurological procedures
- D) Following interventional cardiac procedures