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Treatment of Alzheimer disease
with CT scans --- a case report

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Alzheimer disease (AD)

- Neurodegenerative disorder --- of older adults
- AD is the cause of > 50% of dementia cases
- Cause and pathologic mechanism of AD are uncertain
- Earliest manifestation: selective memory impairment
- AD is a leading source of morbidity and death
- 5.2 million American over 65 y had AD in 2012
- Patient care costs $200 billion/y; will double by 2040
- Treatments can relieve some symptoms
- No cure or modifying therapy; it progresses inevitably
- Survival from 3 to 20 years; average is 8 to 10 years
- Young patients progress quickly; older ones slower
Alzheimer disease #2

- Incidence / prevalence rises exponentially with age
- Doubles every 5 years after age 65
- Over age 65, dementia was second to heart failure as a cause of mortality, accounting for 19% of deaths
- Advanced AD increases vulnerability to other disorders, (commonly infections), which result in death
- In addition to memory impairment: executive dysfunction and visuospatial impairment are observed early
- Deficits in language and behavior come later
- Then difficulty performing learned motor tasks (eating)
Alzheimer disease #3

- Brain changes *linked* to plaques - amyloid beta protein
- Biomarkers available to measure plaque changes
- Clinical trials underway evaluate (anti-amyloid) therapies
- AD does *not* occur in every amyloid brain
- Autopsies reveal plaque in people who do *not* have AD
- Brain imaging, CT and MRI, are used in AD evaluation
- Imaging can suggest alternative or additional diagnoses
- Process of AD begins *before* clinical symptoms appear
  - Early intervention would be the optimal time, if a disease-modifying therapy could be identified
Case Report: advanced AD patient

- 81 year old female; symptoms began 10 years ago
- Progressed gradually to final stages of AD
- April 8, 2015 to hospice; < 6 months life expectancy
- Examined May 21: “completely non-responsive”
- She refused medications, almost no communications
- No attempt to rise from her wheelchair in months
- Spouse knew low doses of x-rays stimulate patient’s protection systems against disease and aging
- He asked her physician to prescribe a CT scan to see anatomical changes and to stimulate neuroprotection
Treatments and observations

- **July 23** two scans @ 4 cGy each = 8 cGy total
- 2 days later caregiver reports noticeable improvement: wants “to get up and walk”; talks sense; feeds herself
- **Aug 6** one scan; Aug 11 she was very “interactive”
- Aug 12 much more talkative; reads words in book; asks questions, who people are; tries to stand; eats all food
- **Aug 20** one scan; big improvement; memory return; lifts leg and turns head in exercise class (in phase); talks
- **Oct 1** one scan; major setback occurs --- loss of almost entire gain; slow recovery, but to much better state
- **Nov 20** hospice care ends; back to day-care program
AD patient, spouse and author on Dec 4, 2015
Explanation of observations

• 3 treatments of x-rays stimulated natural adaptive neuroprotection systems
• Reversed some brain degeneration caused by aging
• Optimal total dose for stimulation is about 16 cGy from $2 + 1 + 1 = 4$ CT scans (each 4 cGy)
• 4th treatment inhibited the stimulation of protection systems --- caused a setback to recovery
• Booster CT scans, after 6 months, might re-stimulate protection systems against progressive deterioration and/or might promote further recovery
Radiation dose-response model

- Optimum
- Radiation-induced beneficial effects
- NOAEL
- Control group (natural radiation)
- Radiation-induced harmful effects

NOAEL: no observed adverse effects level

Absorbed radiation dose or dose-rate
Was this just one anecdotal case?

- Although only 1 patient, there were 4 treatments
- Within days after each scan, saw dramatic changes!
- 3 improvements, and 1 setback
- Slow, continuous recovery from setback into February
- It’s not over; booster course of treatments is an option
Discussion - Conclusions

- Did brain CT radiation really reverse AD?
- Do symptoms of advanced AD disappear naturally?
- Conforms to dose-response model: benefit vs. harm
- This case supports the radiation “hormesis” concept of low-dose stimulation and high-dose inhibition
- Upregulated protection of brain against degeneration
- Optimum cumulative dose is ~ 16 cGy or 16 rad
- No risk; CT scans are an accepted medical procedure
Recommendations

Since there is no other treatment for AD, then:

• Do same brain CT scan treatments on all AD patients
• Do proper randomized clinical studies, with “controls”
• Determine optimum protocol for AD treatment
• Treat when AD suspected; could delay onset of AD
• Booster treatment after ~ 6 months; prevent relapse
• Try CT scans on Parkinson and Huntington patients

Potential benefits are enormous; costs are very low
Other beneficial effects of low radiation

Medical practitioners used radiation ~1900 to ~1960, to:

• Eliminate metastases or slow cancer growth
• Accelerate healing of wounds
• Stop infections: gas gangrene, carbuncles and boils, sinus, inner ear, etc.
• Relieve arthritis and other inflammatory conditions
• Cure swollen lymph glands
• Cure pneumonia
• Cure asthma

with no apparent increase of cancer incidence
Longevity best measure of radiation effects

• Radiation scare: Cancer risk increase with more dose
• **Cancer** is ideal antinuclear scare. It is very complex, many causes, confounding factors, uncertain, not well understood, difficult to predict, and **we dread cancer**
• However, **longevity is best** indicator of radiation effects
• Cameron: early radiologists, nuclear shipyard workers
• Calabrese-Baldwin: gamma radiation increases median life span of low-dose group by 10 to 30% over “controls”
• Radiation stimulates the adaptive protection systems against the enormous spontaneous rate of cell damage and organism damage by all other causes
Backup slides
RADIOBIOLOGY SPECIAL FEATURE: COMMENTARY

What we know and what we don’t know about cancer risks associated with radiation doses from radiological imaging

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ABSTRACT

Quantifying radiation-induced cancer risks associated with radiological examinations is not easy, which has resulted in much controversy. We can clarify the situation by distinguishing between higher dose examinations, such as CT, positron emission tomography—CT or fluoroscopically guided interventions, and lower dose “conventional” X-ray examinations. For higher dose examinations, the epidemiological data, from atomic bomb survivors exposed to low doses and from direct epidemiological studies of paediatric CT, are reasonably consistent, suggesting that we do have a reasonable quantitative understanding of the individual risks: in summary, very small but unlikely to be zero. For lower dose examinations, we have very little data, and the situation is much less certain, however, the collective dose from these lower dose examinations is comparatively unimportant from a public health perspective.
Blood system is very sensitive

HEMOPOIETIC RESPONSE TO LOW DOSE-RATES OF IONIZING RADIATION SHOWS STEM CELL TOLERANCE AND ADAPTATION

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Viktor Meineke □ Bundeswehr Institute of Radiobiology Affiliated to the University of Ulm, Germany;

Ludwig E. Feinendegen □ Heinrich-Heine-Universität Düsseldorf, Germany, and Brookhaven National Laboratory, Upton, NY, USA

□ Chronic exposure of mammals to low dose-rates of ionizing radiation affects proliferating cell systems as a function of both dose-rate and the total dose accumulated. The lower the dose-rate the higher needs to be the total dose for a deterministic effect, i.e., tissue reaction to appear. Stem cells provide for proliferating, maturing and functional cells. Stem cells usually are particularly radiosensitive and damage to them may propagate to cause failure of functional cells. The paper revisits 1) medical histories with emphasis on the hemopoietic system of the victims of ten accidental chronic radiation exposures, 2) published hematological findings of long-term chronically gamma-irradiated rodents, and 3) such findings in dogs chronically exposed in large life-span studies. The data are consistent with the hypothesis that hemopoietic stem and early progenitor cells have the capacity to tolerate and adapt to being repetitively hit by energy deposition events. The data are compatible with the “injured stem cell hypothesis”, stating that radiation–injured stem cells, depending on dose-rate, may continue to deliver clones of functional cells that maintain homeostasis of hemopoiesis throughout life. Further studies perhaps on separated hemopoietic stem cells may unravel the molecular-biology mechanisms causing radiation tolerance and adaptation.
Chronic radiation affects blood system

- Reviewed histories of *humans* in 10 radiation accidents (28,000 in Techa, 1,800 in Mayak); studied rats, dogs
- Effect is a function of dose-rate *and* total dose
- Blood stem cells are very radiosensitive, but tolerate and adapt to *chronic* radiation --- better at *lower* dose rate
- Get clones of functioning cells → a lifetime of service
- Dogs at 0.3 cGy/day: *same* cancer rate as control dogs
- 1934 ICRP: “tolerance dose” 0.2 R/day or 70 cGy/y *okay*
- ICRP recommendations (LNT & ALARA) *not* justified
Continuous Co-60 irradiation of dogs

0.3 cGy/d = 110 cGy/year = 110 rad/year

Blood counts of 0.3 cGy/d same as 0 cGy/d

Fatal tumors of 0.3 cGy/d same as 0 cGy/d
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<th>Dose Rate (cGy/day)</th>
<th>Dose Rate (mGy/year)</th>
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Median lifespan versus Co-60 radiation level

Threshold for shorter lifespan ~ 70 cGy/year
Radiotoxicity of Inhaled $^{239}$PuO$_2$ in Dogs

Bruce A. Muggenburg,a Raymond A. Guilmette,a Fletcher F. Hahn,a Joseph H. Diel,a Joe L. Mauderly,a Steven K. Seilkopb and Bruce B. Boecker*a,1

aData: Lovelace Respiratory Research Institute, Albuquerque, New Mexico 87108; andb SKS Consulting Services, Siler City, North Carolina 27344


Beagle dogs inhaled graded exposure levels of insoluble plutonium dioxide ($^{239}$PuO$_2$) aerosols in one of three monodisperse particle sizes at the Lovelace Respiratory Research Institute (LRRRI) to study the life-span health effects of different degrees of $\alpha$-particle dose non-uniformity in the lung. The primary noncancerous effects seen were lymphopenia, atrophy and fibrosis of the thoracic lymph nodes, and radiation pneumonitis and pulmonary fibrosis. Radiation pneumonitis/pulmonary fibrosis occurred from 105 days to more than 11 years after exposure, with the lowest associated $\alpha$-particle dose being 5.9 Gy. The primary carcinogenic effects also occurred almost exclusively in the lung because of the short range of the $\alpha$-particle emissions. The earliest lung cancer was...
Radiotoxicity of inhaled $^{239}$PuO$_2$ in beagle dogs
<table>
<thead>
<tr>
<th>Exposure Level</th>
<th>Initial Lung Burden kBq/kg</th>
<th>Lung Dose to Death cGy</th>
<th>Age to Death days</th>
<th>Normalized Lifespan 50% mortality</th>
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Median lifespan versus $^{239}\text{PuO}_2$ lung burden

Normalized Lifespan (50% mortality)

Initial Lung Burden (kBq/kg)

Lung dose to death – cGy

Threshold

- 160
- 620
- 1300
- 2500
- 3500
- 4500
- 5900
Hormesis by Low Dose Radiation Effects: Low-Dose Cancer Risk Modeling Must Recognize Up-Regulation of Protection

Ludwig E. Feinendegen, Myron Pollycove, and Ronald D. Neumann

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Abstract
Ionizing radiation primarily perturbs the basic molecular level proportional to dose, with potential damage propagation to higher levels: cells, tissues, organs, and whole body. There are three types of defenses against damage propagation. These operate deterministically and below a certain impact threshold there is no propagation. Physical static defenses precede metabolic-dynamic defenses acting immediately: scavenging of toxins;—molecular repair, especially of DNA;—removal of damaged cells either by apoptosis, necrosis, phagocytosis, cell differentiation-senescence, or by immune responses,—followed by replacement of lost elements. Another metabolic-dynamic defense arises delayed by up-regulating immediately operating defense mechanisms. Some of these adaptive protections may last beyond a year and all create temporary protection against renewed potentially toxic impacts also from nonradiogenic endogenous sources. Adaptive protections have a maximum after single tissue absorbed doses around 100–200 mSv and
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- Studies ignore spontaneous (internal) DNA damage rate
- Natural rate very high compared to radiation-induced rate
- Average number of DNA alterations /average cell /per day
  Natural (due to metabolic ROS): total ~ $10^6$, DSB ~ $10^{-1}$
  Rad-induced (1 mGy/y, γ bkgnd): total ~ $10^{-2}$, DSB ~ $10^{-4}$
- Ratio of natural/rad’n alterations: total ~ $10^8$, DSB ~ $10^3$

Adapted from Pollycove and Feinendegen 2003
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- Low radiation up-regulates adaptive protection systems
- *Fast defences* act immediately to remove toxins, repair DNA, remove/replace damaged cells and tissue, then …

- *Delayed defences* of up-regulated adaptive systems (>150 genes) that may last more than a year and protect against toxic impacts from *both* radiation sources and non-radiation sources

- 150 mGy acute highly stimulates adaptive protections
- Chronic or repetitive rad’n initiates lower level protection
- Adaptive protection less risks ➔ longer life, less cancer
Adaptive response
Low radiation dose up-regulates cell repair capability
Decreases risk of the 4 Gy challenging dose