Long-term risks from medical ionizing radiation: cancer and cardiovascular disease

Maria Grazia Andreassi,
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IFC-CNR, Fondazione Toscana Gabriele Monasterio, Ospedale G. Pasquinucci, Massa
Sustainability of Medical Imaging: The Radiation Issue

Sustainability of medical imaging

Eugenio Picano

Doctors and patients should be more aware of the long term risks of radiological investigations

Contemporary medicine relies heavily on radiological and medicolegal investigations and procedures. However, the often essential information derived from such investigations is obtained at a risk that few doctors are fully aware of. Increased awareness among both doctors and patients would help reduce the number of inappropriate examinations and the avoidable biological burden on current and future generations. In this article, I outline the effect of ionizing testing in our society, review the possible detrimental public health effect based on current estimates of risk, and discuss simple ways of achieving a more cautious approach.

Exposure to medical radiation

Informed consent and communication of risk from radiological and nuclear medicine examinations: how to escape from a communication inferno

Eugenio Picano

Radiological and nuclear medicine examinations carry a definite albeit low long term risk of cancer. The patient undergoing such examinations often receive no or inaccurate information about these risks. Picano argues that this disregard of patient autonomy is no longer acceptable and suggests a practical way of communicating risk.

Communicating radiological risk

Every radiological or nuclear medicine examination involves the administration of radiation, with its inherent risk. In a risky business, however, any discussion of risk is complexified by patients' tendency to underestimate large risks such as the risk of dying from smoking tobacco, overestimate small risks (such as that of being struck by lightning), and be more willing to accept higher risks in situations where they think (usually wrongly) that they are in control, such as driving a car rather than being a passenger in an aeroplane. A risk of death of one in one million is generally ignored, since we face more risks of such magnitude every day, from travelling 100 miles by car or 1400 miles by aeroplane. It is now easy to ignore a risk of death of about one in 1000, which happens to be the long term risk of fatal cancer associated with a hole in computed tomography in a child or a thallium-201 myocardial perfusion test.

Informed consent: a right or a privilege?

Informed consent is not to mention radiological risk. Even for procedures with high radiation doses, such as interventions under fluoroscopic control, there is no explicit or implicit mention of long term risks. The risk exists and may be substantial, but it remains unknown (by the patient) and neglected (by the doctor). The basic argument is that radiologists are too busy to lose time in obtaining informed consent and too wise to undertake inappropriate examinations. Patients' legal right to information is eclipsed by the two forces of
Diagnostic exposure to radiation is a public health issue

Researchers Examine Long-term Risks of Exposure to Medical Radiation

Tracy Hampton, PhD

Because exposure to radiation is associated with potentially serious health risks, researchers are concerned about the increasing use of radiation for medical purposes. A double-edged sword, radiation can be used to effectively diagnose and treat individuals, but it can also cause subsequent cancer and other conditions. According to the United Nations Scientific Committee on the Effects of Atomic Radiation, medical use of radiation is not only growing, it is the largest man-made source of exposure to ionizing radiation. To learn more about long-term effects of radiation used in healthcare settings, epidemiologists are tracking people who have been exposed to medical radiation, noting details such as which individuals may be especially sensitive and whether interactions with other therapies, medical conditions, or lifestyle factors may come into play.

Diagnostic Radiation

Diagnostic procedures, particularly those that use x-rays, are the most common application of radiation in medicine and have increased considerably in recent years. Types of x-ray techniques include radiography, fluoroscopy, bone densitometry, and computed tomography (CT). “Clearly, we’re seeing a large increase in medical exposure, and a good part of the exposure is from CT,” said Elaine Ron, PhD, of the Radiation Epidemiology Branch at the National Cancer Institute, in Bethesda, Md. Speaking on the topic of medical radiation exposure at the recent Congress of Epidemiology, held in Seattle, Ron noted that CT scans are used to diagnose a wide range of conditions, from enlarged lymph nodes and internal bleeding to brain injuries and cancer. Of late, the technology has also been used by the “worried well” for whole-body health screenings. In most large hospitals in the US, CT scanning probably accounts for more than 10% of diagnostic radiology examinations and about two-thirds of the radiation dose (Oetler PA Jr. J Radiol Prot. 2002;20:353-359). “We have about 250 million diagnostic x-rays each year, which is close to one per person,” said Ron.


The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

CURRENT CONCEPTS

Computed Tomography — An Increasing Source of Radiation Exposure


REVIEW ARTICLE

What are the risks from medical X-rays and other low dose radiation?

B F WALL, BSc; G M KENDALL, PhD; A A EDWARDS, MSc; S BOUFFLER, PhD; C R MUIRHEAD, MD and J R MEARA, MPH

Health Protection Agency, Radiation Protection Division, Centre for Radiation, Chemical and Environmental Hazards, Chilton, Didcot, Oxon. OX11 0RQ, UK

Circulation

American Heart Association
Learn and Live

AHA Science Advisory

Ionizing Radiation in Cardiac Imaging

A Science Advisory From the American Heart Association Committee on Cardiac Imaging of the Council on Clinical Cardiology and Committee on Cardiovascular Imaging and Intervention of the Council on Cardiovascular Radiology and Intervention

Thomas C. Gerber, MD, PhD, FAHA; Chair; J Jeffrey Carr, MD, MPH, Co-Chair; Andrew E. Arai, MD, FAHA; Robert L. Dixon, PhD; Victor A. Ferrani, MD, FAHA; Antoinette S. Gomes, MD, FAHA; Gary V. Heller, MD, FAHA; Cynthia H. McCollough, PhD; Michael F. McNitt-Gray, PhD; Fred A. Mettler, MD; Jennifer H. Mieres, MD, FAHA; Richard L. Morin, PhD; Michael V. Yester, PhD
“Medical exposures now dwarfs that of all other sources”

June 19th, 2007

~ 600% increase from 1980 to 2006

Modified and updated (Regulla D 2005, and Mettler FA 2007)
Picano E. BMJ, March 6 2004
Coronary procedure in Europe

Interventional procedures contribute to about 20% of the total collective dose per head per year.

The use of procedures continues to grow steadily, including pediatric cardiology.

**Coronary Angiography**

- PCI
- Stent coronarico

- Millions of procedures
- 92 93 94 95 96 97 98 99 00 01

**Togni M et al. Eur Heart J 2004**

**Picano et al. Int J Cardiovasc Imaging 2006**

Interventional procedures may give rise to deterministic effects

ICRP report 85 (2001): Avoidance of Radiation Injuries from Interventional Procedures

Ulcer 21 months after first procedure, base of ulcer exposes spinous process

Cataract in eye of interventionalist after improper working conditions related to high levels of scattered radiation.

FDA 1994: Public Health Advisory. Induced skin injuries in patient during fluoroscopically guided procedures
# Doses in interventional procedures

.Modified from Rehani, 2002; Hirschfeld, 2005; and Einstein, 2007

<table>
<thead>
<tr>
<th>Effect</th>
<th>Threshold dose (Gy)</th>
<th>Approx. onset</th>
<th>Minutes fluoro at 0.2 Gy/min</th>
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<tbody>
<tr>
<td>Transient erythema</td>
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<td>Hour</td>
<td>10</td>
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<tr>
<td>Permanent epilation</td>
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<td>3 weeks</td>
<td>35</td>
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<tr>
<td>Dry desquamation</td>
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<td>Telangiectasia</td>
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<td>&gt;1 year</td>
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<td>Skin cancer</td>
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(Rehani, 2002; Hirschfeld, 2005; and Einstein, 2007)
# Biological effects of radiation

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<td>Low</td>
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<tr>
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<tr>
<td><strong>Cell Biology</strong></td>
<td>Cell Death</td>
<td>DNA damage</td>
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<tr>
<td><strong>Clinical effects</strong></td>
<td>Erythema, ulcers</td>
<td>Cancer, genetic effects</td>
</tr>
</tbody>
</table>

![Graph showing risk vs. dose with threshold dose](image-url)
Stochastic effects:
DNA is the most important target of IR
From medical radiation dose to cancer risk

Source: Doll R and Peto R, 1981

Berrington de Gonzales and Darby, LANCET, 2004

Picano E, Lancet, letter 2005
BEIR VII report: the most up-to-date, comprehensive estimates for risk for cancer from low-dose radiation

The BEIR series are widely accepted as primary source of radiation risk estimates and protective regulations.

Epidemiology

Radiation Dangerous Even at Lowest Doses

A new National Research Council (NRC) report finds that although the risks of low-dose radiation are small, there is no safe level. That conclusion has grown stronger over the past 15 years, says the NRC committee, dismissing the hypothesis that tiny amounts of radiation are harmless or even beneficial.

The risk of low-level radiation has huge economic implications because it affects standards for protecting nuclear workers and for cleaning up radioactive waste. The Biological Effects of Ionizing Radiation VII (BEIR VII) panel examined radiation doses of 0.1 sieverts (Sv), which is about twice the yearly limit for workers and 40 times the natural background amount the average person is exposed to each year. The typical American's 82% of exposure stems from natural sources such as radon gas seeping from Earth; the rest is hematogenous, coming mostly from medical procedures such as scans.

In its last report on the topic, in 1990, a BEIR panel calculated risks by dividing cancer cases and deaths among the two atomic bombs dropped on Japan in World War II. Risks appeared to increase linearly with the dose. Based on evidence that even a single "hit" of radiation can damage a cell's DNA, the panel extrapolated this relationship to very low doses produced with microtens in the bone marrow or heart of an adult.

Some scientists have challenged this LNT model, however, noting that some epidemiologic and lab studies suggest that a little radiation is harmless and could even stimulate DNA repair enzymes and other processes that protect against later insults, an idea known as hormesis (Science, 17 October 2003, p. 779).

But the 712-page BEIR VII report finds that the LNT model still holds. The panel had the latest cancer incidence data on the bomb survivors, as well as new dose information.

Committee members also reviewed fresh studies on nuclear workers and people exposed to medical radiation, all of which supported the LNT relationship. The model predicts that a single 0.1-Sv dose would cause cancer in 1% of 100 people over their lifetime. Such risks should be taken into account, the report cautioned, when people consider full-body computed tomography scans, a recent fact that delivers a radiation dose of 0.123 Sv.

At the same time, notes panelist Ethel Gilbert, an epidemiologist at the National Cancer Institute in Bethesda, Maryland, "we can't really quantify" the risk at the lowest doses. The BEIR VII panel examined the limits of zero for a threshold. But found that "ecologic" studies suggesting that people in areas with naturally high background radiation levels do not have elevated rates of disease are of limited use because they don't include direct measures of radiation exposure. The panel also concluded that animal and cell studies suggesting benefits or a threshold for harm are not "compelling," although mechanisms for possible "hormetic effects" should be studied further.

Toxicologist Ed Calabrese of the University of Massachusetts, Amherst, a vocal proponent of the hormesis hypothesis, says the panel didn't examine enough studies. "I would bet more of the data were left out instead of [inclusion] just being summarily dismissed."

The panel's chair, Stanford epidemiologist Richard Monroe, acknowledges that the long-running debate over the LNT model won't end with this report, noting that "some minds will be changed, others won't." — Jason Kodsi

www.sciencemag.org SCIENCE VOL 309 8 JULY 2005

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Risk of cancer (fatal and non-fatal) for exposure to one 15 mSv MSCT

- Elderly: 1 in 1,500
- Adult man: 1 in 750
- Adult woman: 1 in 500
- Male child (<1 year): 1 in 200
- Female child (<1 year): 1 in 100

Equivalent number of chest x-rays

(Einstein A, et al. JAMA 2007)
Risk increases with decreasing age

Children exposed to ionizing radiation have a (3-4 times) greater cancer risk than adults, as they have more rapidly dividing cells and have longer life expectancy.

Figure 4. Estimated Dependence of Lifetime Radiation-Induced Risk of Cancer on Age at Exposure for Two of the Most Common Radiogenic Cancers.

Research Need 8: Future medical radiation studies

Most studies of medical radiation should rely on exposure information collected prospectively, including cohort studies as well as nested case-control studies. Future studies should continue to include individual dose estimation for the site of interest, as well as an evaluation of the uncertainty in dose estimation.
Cumulative patient effective dose in children with congenital heart disease

Ait-Ali et al. ESC Congress 2008, Munich

<table>
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<th>Variable</th>
<th>Value</th>
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<tr>
<td>Age, mean ±SD, years (range)</td>
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<td>(1 month-16 years)</td>
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<td>Gender, n</td>
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<tr>
<td>Male/female</td>
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<tr>
<td>BMI, kg/m² (range)</td>
<td>11.5±15</td>
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<td>(2.1-75)</td>
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<td>Coarctation of the aorta (+ventricular septal defect)</td>
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<td>Pulmonary stenosis</td>
<td>6</td>
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<td>Functionally univentricular heart</td>
<td>5</td>
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<td>Pulmonary atresia (+ventricular septal defect)</td>
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<td>Patent ductus arteriosus</td>
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<td>Other complex CHD</td>
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</table>
Methods: Lifetime radiological estimated dose

Dose Reference values in pediatric cardiology

<table>
<thead>
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<th>Examination</th>
<th>Effective dose (mSv)</th>
<th>Equivalent n. of chest x-rays</th>
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</thead>
<tbody>
<tr>
<td>CONVENTIONAL RADIOLOGY</td>
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<tr>
<td>Chest x ray (single postero-anterior)</td>
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<td>1</td>
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<tr>
<td>COMPUTED TOMOGRAPHY</td>
<td></td>
<td></td>
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<tr>
<td>Head CT</td>
<td>4</td>
<td>200</td>
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<tr>
<td>Chest CT</td>
<td>3</td>
<td>150</td>
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<tr>
<td>Abdomen CT</td>
<td>5</td>
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<td>INTERVENTIONAL RADIOLOGY</td>
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<tr>
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<td>140</td>
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<td>PDA closure</td>
<td>7.6</td>
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</tr>
<tr>
<td>Ballon dilatation</td>
<td>8.1</td>
<td>405</td>
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</tbody>
</table>

From Bacher et al. Patient-specific dose and radiation risk estimation in pediatric cardiac catheterization. Circulation 2005
Radiological exposure

Total examinations: 1548
Mean examinations: 26.2 ±26.3 per patient

Frequency of examinations:
- X-rays: 93%
- Computed Tomography: 2.5%
- Diagnostic cath: 1%
- Interventional cath: 3.5%

Total collective dose:
- X-rays: 41%
- Computed Tomography: 5%
- Diagnostic cath: 43%
- Interventional cath: 11%
Cumulative Effective Dose and Lifetime Attributable Risk of Cancer

Mortality excess per Sv all cancers (BEIR VII)

Effective dose, mSv
median (25th-75th)

- Males: 7.1 (5.1-12.5) (LAR <1 year)
- Females: 9.4 (6.5-18.1)

1 in 282 (1 in 431-1 in 117) 1 in 156 (1 in 239-1 in 83)
Exposure for cath lab workers

Eg. Exposure from 300 procedures/year

Effective dose
9-44 mSv/year
(lead protective apron)

4-20 mSv/year
(protective apron + thyroid shield)

R. Padovani - SENTINEL Project: Interventional Radiology and Cardiology Course, Budapest, 5-6 July 2006

Cancer risk from professional exposure in staff working in cardiac catheterization laboratory: Insights from the National Research Council's Biological Effects of Ionizing Radiation VII Report

Lucia Venneri, MD, PhD, Francesco Rossi, BSc, Nicoletta Botto, Bsc, Maria Grazia Andreassi, BSc, PhD, Nicoletta Salcone, BSc, Ahmed Emad, MD, Mauro Lazzeri, MD, Cesare Gori, Bsc, Eliseo Vano, Bsc, PhD, and Eugenio Picano, MD, PhD Pisa, Florence, Italy; and Madrid, Spain

Background Occupational doses from fluoroscopy-guided interventional procedures are the highest ones registered among medical staff using x-rays. The aim of the present study was to evaluate the order of magnitude of cancer risk caused by professional radiation exposure in modern invasive cardiology practice.

Methods From the dosimetric Tuscany Health Physics data bank of 2006, we selected dosimetric data of the 26 (7 women, 19 men; age 46 ± 9 years) workers of the cardiovascular catheterization laboratory with effective dose >2 mSv. Effective dose (E) was expressed in milliSievert, calculated from personal dose equivalent registered by the thermoluminescent dosimeter, at waist or chest, under the apron, according to the recommendations of National Council of Radiation Protection. Lifetime attributable risk of cancer was estimated using the approach of Biological Effects of Ionizing Radiation 2006 report VII.

Results Cardiac catheterization laboratory staff represented 67% of the 6 workers with yearly exposure >6 mSv. Of the 26 workers with 2006 exposure >2 mSv, 15 of them had complete records of at least 10 (up to 25) consecutive years. For these 15 subjects having a more complete lifetime dosimetric history, the median individual effective dose was 46 mSv (interquartile range = 24-64). The median risk of (fatal and nonfatal) cancer (Biological Effects of Ionizing Radiation 2006) was 1 in 192 (interquartile range = 1 in 137-1 in 370).

Conclusions Cumulative professional radiological exposure is associated with a non-negligible Lifetime attributable risk of cancer for the most exposed contemporary cardiac catheterization laboratory staff. (Am Heart J 2009;157:118-24.)
Dose exposure in all medical staff censored in Tuscany (Florence-Pisa) Health Physics data bank year 2006
Cancer risk from professional exposure in staff working in cardiac catheterization laboratory

**Figure 4**

Median LAR = 1 in 192
(range = 1 in 137-1 in 370)
42 spontaneous cancers

100 mSv for 100 patients

+ 1, Radiation induced

(1 in 100)

Range of uncertainty

BEIR VII, 2006
An epidemiological study of 5 million people is required to quantify directly the risk of cancer from exposure of 10 mSv (500 chest X-rays) or less.


Range of uncertainty

** ** **

BEIR VII, 2006
RECOMMENDED RESEARCH NEEDS

A more detailed listing of the BEIR VII recommended research needs can be found at the end of Chapter 13.

Research Need 1: Determination of the level of various molecular markers of DNA damage as a function of low-dose ionizing radiation

Currently identified molecular markers of DNA damage and other biomarkers that can be identified in the future should be used to quantify low levels of DNA damage and to identify the chemical nature and repair characteristics of the damage to the DNA molecule.

Research Need 6: Genetic factors in radiation cancer risk

Further work is needed in humans and mice on gene mutations and functional polymorphisms that influence radiation response and cancer risk.
Biodosimetry shrinks uncertainty

15% increase in adult patients after invasive cardiovascular interventions
(Andreassi MG et al. Eur Heart J, 2007)

200% long-term increase in children with congenital heart disease (Andreassi MG et al. Eur Heart J 2006)

50% increase in interventional cardiologists
(Andreassi MG et al, FASEB J, 2005)

Intermediate endpoint for carcinogenesis

Long-term predictor of cancer

Bonassi et al. Carcinogenesis 2006
Chromosomal damage, radiation exposure and congenital heart disease

European Heart Journal
doi:10.1093/eurheartj/ehl014

Clinical research

Cardiac catheterization and long-term chromosomal damage in children with congenital heart disease

Maria Grazia Andreassi1*, Lamia Ait-Ali1,2, Nicoletta Botto1, Samantha Manfredi1, Gaetano Mottola3, and Eugenio Picano1,3

1CNR, Institute of Clinical Physiology, Pisa, Italy; 2Scuola Superiore S. Anna, Pisa, Italy; and 3Clinica Cardiologica MonteVergine, Mercogliano, Avellino, Italy
Congenital Heart Disease, Cardiac Catheterization and Chromosome Aberrations

Mean cumulative estimated dose: 19.4± 1.6 mSv (1000 Xrays) per patient

200% long-term increase in children with CHD
Acute chromosomal DNA damage in human lymphocytes after radiation exposure in invasive cardiovascular procedures

Maria Grazia Andreassi¹,*, Angelo Cioppa², Samantha Manfredi¹, Cataldo Palmieri¹, Nicoletta Botto¹, and Eugenio Picano¹,²

¹CNR Institute of Clinical Physiology, G. Pasquinucci Hospital, Via Aurelia Sud-Montereppe, 54100 Massa, Italy and ²Department of Invasive Cardiology, Montevergine Clinic, Mercogliano, Italy

15 % increase in adult patients after invasive cardiovascular interventions
Somatic DNA damage in interventional cardiologists: a case-control study

Maria Grazia Andreassi,* Angelo Cioppa,† Nicoletta Botto,* Gordana Joksic,‡ Samantha Manfredi,* Chiara Federici,* Miodrag Ostojic, ‡ Paolo Rubino, † and Eugenio Picano*, †
**DNA repair genes and cancer**

Web registry on DNA repair polymorphisms and cancer risk:
www.perseus.isi.it/huge

<table>
<thead>
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<th>Study</th>
<th>Date</th>
<th>Polymorphisms</th>
<th>Cancer Site</th>
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<th>Freq_co</th>
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XRCC3 gene polymorphism influence chromosomal DNA damage in Interventional Cardiologists

Accurate repair of DNA DSBs is critical in preserving the genomic integrity of cells

Biomarkers of DNA damage susceptibility as Newton's prism

FROM POPULATION RISK

Physical dosimetry

TO INDIVIDUAL RISK

BIOLOGICAL DOSIMETRY

LOWER RISK

Higher risk

Genetic polymorphism?
Micronutrients?
Oxydant antioxydant balance?

(Andreassi MG et al, FASEB J, 2005)
Parveen Bhatti, Alice J Sigurdson and Kiyohiko Mabuchi

Can low-dose radiation increase risk of cardiovascular disease?

Risk of heart disease increases after high-dose therapeutical radiation (typically >30–40 Gy), such as that received for treatment of Hodgkin’s lymphoma and breast cancer. The radiation dose-response for cardiovascular disease in Japanese survivors of the atomic bomb at doses less than 5 Gy sparked assessments of human and mechanistic data on the unexpected cardiovascular effects at subtherapeutic doses. Patients with certain non-malignant diseases have received therapeutic radiation (eg, ankylosing spondylitis) or
Radiation-induced coronary artery disease

LF Fajardo

Chest 1977;71;563-564

The online version of this article, along with updated information and services can be found online on the World Wide Web at:
http://chestjournals.org
Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials

Early Breast Cancer Trialists’ Collaborative Group (EBCTCG)
CVD is probably associated with dose, volume and technique of irradiation. Actually, the average median dose is 2.3 Gy to the heart and 7.6 Gy to the left anterior descending coronary artery. However, part of the heart still receives >20 Gy.

<table>
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<td>106</td>
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<tr>
<td>&gt;15</td>
<td>234</td>
<td>145</td>
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</table>
Cardiovascular mortality after radiotherapy for peptic ulcer

Cohort study on 1470 patients treated between 1936 and 1965 for peptic ulcer with radiotherapy compared with 1568 patients treated with drugs

Radiation doses to the stomach were 8 – 18 Gy in fractions of 1.5 Gy
Radiation doses to the heart were 1.6 – 3.9 Gy in fractions of 0.33 Gy


Significant effect for both heart disease and stroke (whole-body uniform doses in the range 0-4 Sv)

Revealed a dose response relationship that was highly significant statistically and appeared linear with no threshold, with each additional Sv of radiation increasing the mortality rate by a factor of 0.17

**Occupational studies and circulatory disease mortality**

“No clear evidence in the range 0-4 Sv”

<table>
<thead>
<tr>
<th>Study</th>
<th>Workers (circulatory deaths)</th>
<th>ERR* per Sv</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.K. radiologists (Berrington 2001)</td>
<td>2,698 (514)</td>
<td>&lt;0</td>
<td>Time trend in cancer but not in CVD</td>
</tr>
<tr>
<td>U.S. radiologists (Matanoski 1975)</td>
<td>30,084 (1,070)</td>
<td>0.2</td>
<td>Time trend in cancer but not in CVD</td>
</tr>
<tr>
<td>U.S. radiology techs (Hauptmann 2003)</td>
<td>90,284 (1,070)</td>
<td>0.01–0.42</td>
<td>Time trend in both stroke and CHD</td>
</tr>
<tr>
<td>Nuclear workers study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IARC 3 country study (Cardis 1995)</td>
<td>95,673 (7,885)</td>
<td>0.26</td>
<td>5% workers &gt; 0.2 Sv</td>
</tr>
<tr>
<td>U.S. power reactors (Howe 2004)</td>
<td>53,698 (350)</td>
<td>8.3</td>
<td>2% workers &gt; 0.4 Sv</td>
</tr>
<tr>
<td>Mayak workers (Bolotnikova 1994)</td>
<td>9,373 (749)</td>
<td>0.01</td>
<td>95% CI: (2.3, 18.2)</td>
</tr>
<tr>
<td>Chernobyl emergency (Ivanov 2001)</td>
<td>65,905 (1,728)</td>
<td>0.79</td>
<td>Exposures 0 to 0.35 Sv</td>
</tr>
</tbody>
</table>

*Excess relative risk*
MORTALITY

The non-cancer mortality experience of male workers at British Nuclear Fuels plc, 1946–2005

Dave McGeoghegan, Keith Binks, Michael Gillies, Steve Jones* and Steve Whaley

Accepted 14 January 2008

For male radiation workers, there is an apparent dose response for mortality from circulatory system disease \( [P<0.001, \text{ERR}=0.65/Sv (90\% \text{CI 0.36–0.98})] \).

Int J Epidemiol 2008; 37:506-518
Current State of Knowledge

Epidemiological evidence indicate radiation induced cardiovascular effects for moderate doses (0.5 - 2 Gy)

"whilst recognizing the potential importance of observations on non-cancer diseases - particularly heart disease and stroke - the Commission judges that the present available data does not allow for inclusion in the estimation of detriment following radiation doses in the range up to few tens of mSv (100 ≤ mSv)"
Carotid IMT and risk in patients without history of CVD

P < 0.001

O'Leary et al. NEJM 1999; 340: 14 - 22

Quintile Carotid IMT

Incidences MI/Stroke per 1000 Person-year

CCA-IMT
ICA-IMT
CCA + ICA IMT
Endothelial dysfunction and CV events

Brachial endothelial function study

- Cuff inflation
- Cuff deflation
- 5 min
- Basal before nitrate

Al Suwaidi et al, (157) 28
Schachinger et al, (147) 92
Neunteufi et al, (73) 60
Perticone et al, (225) 32
Heitzer et al, (281) 54
Halcox et al, (308) 46
Modena et al, (400) 67
Schindler et al, (130) 45
Gokce et al, (187) 1
Targonski et al, (503) 16

Duration of follow up (months)

-8.0 -6.0 -4.0 -2.0 0.0 2.0 4.0 6.0 8.0

Standardized effect

Coronary
Brachial

n= 2500

Lerman A et al. Circulation, 2005
Atherosclerotic effects associated with environmental radiation exposure: the Chernobyl cancer children study

Young adults (n=18, 25.3±2.7 y vs 10 controls) exposed as children to environmental (Chernobyl area) and therapeutic (radioiodine ablation) radiation show signs of early atherosclerosis, mirrored by depressed FMD and increased CIMT

Venneri et al. preliminary results
Cardiovascular effects associated with low Radiation Doses assessed with an integrated clinical, cellular and experimental approach: The Interventional Cardiologist Study

Cardiorad Study

Cath lab exposed workers (aged 26-60 yrs)

(>50 mSv lifetime cumulative exposure)

Unexposed age and gender matched controls

Primary endpoint:

% FMD and Carotid IMT

Potential mechanisms for atherosclerosis initiation:

a) inflammation-coagulation; b) apoptosis and oxyradical stress balance; c) genetic instability and d) endothelial dysfunction.
Thank you for your attention