

# Cardiovascular Risk

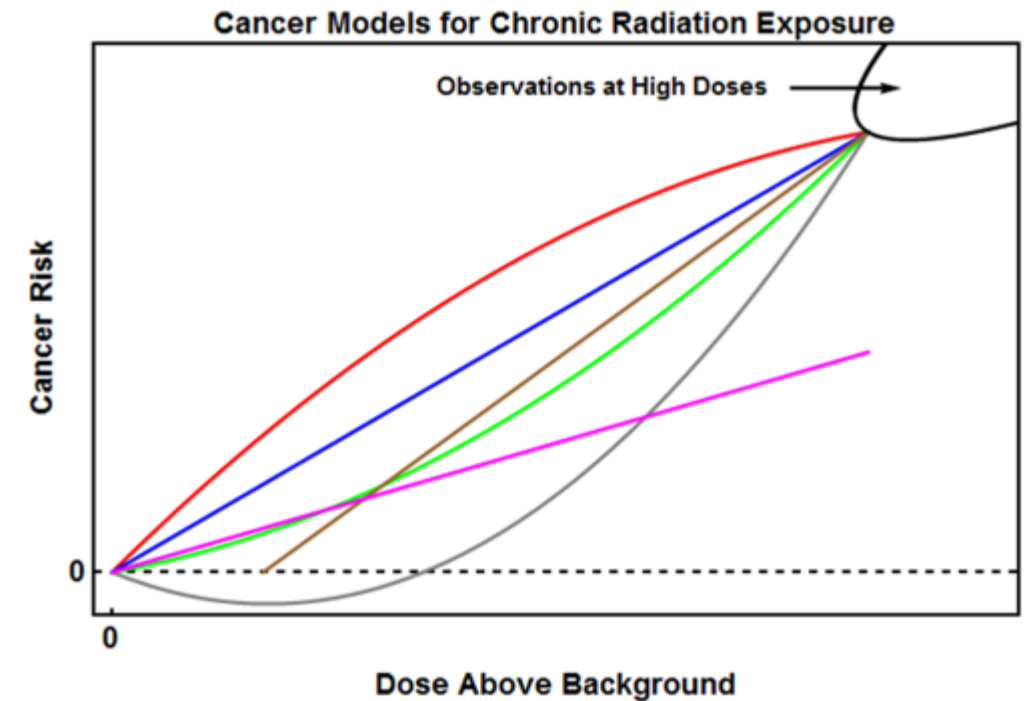
**Donald A. Cool**  
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Symposium**  
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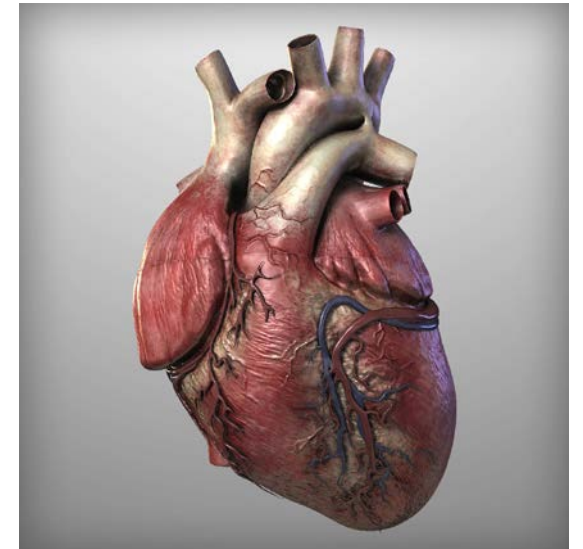
# Background

- Historical concerns about radiation exposure
  - Severe Tissue Reactions
  - Genetic
  - Cancer
- Non-cancer impacts now an issue to be investigated



# Cardio-Vascular Takeaways

- At high radiation doses, a variety of non-cancer effects have been observed such as damage to structures of the heart and to the coronary, carotid, and other large arteries
- An association between lower doses ( $<0.5$  Gy or  $< 50$  rad) and late circulatory disease has slowly been developing
- Controversy remains
- EPRI working to improve understanding
- EPRI Report anticipated late 2016



# What is Circulatory Disease?

- Cardiovascular disease (heart disease)
  - Ischaemic (coronary) heart disease (mainly MI)
  - Hypertensive heart disease
  - Valvular heart disease
- Cerebrovascular disease (stroke)
- Peripheral vascular disease



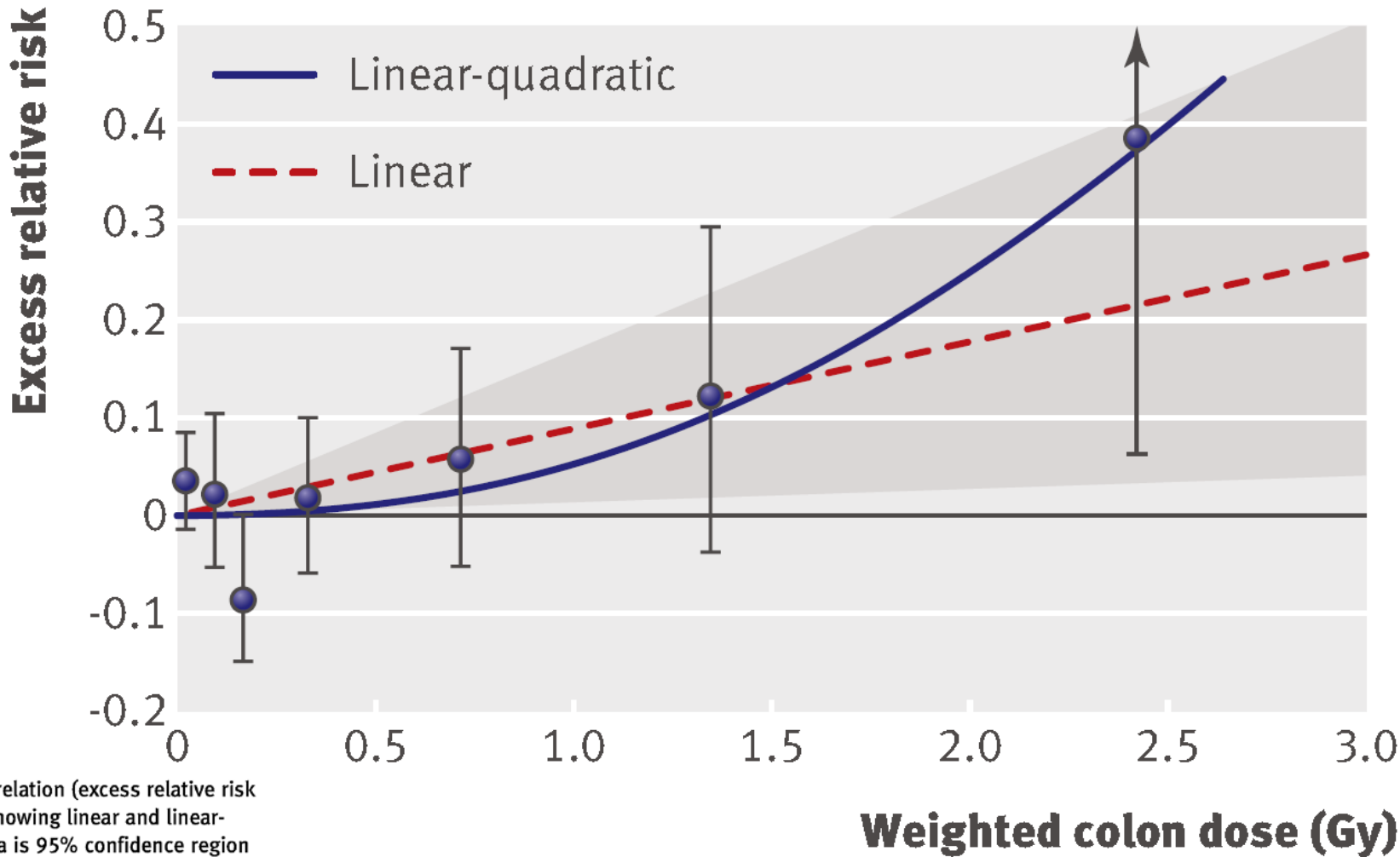


# History of Atomic Bomb Survivor Studies

- Suggestions of elevated circulatory disease risks
  - Life Span Study (LSS) mortality 1950-70 (Jablon et al, 1971)
    - Only in women
  - Adult Health Study (AHS) morbidity 1958-78 (Robertson et al, 1974, Kodama et al 1984)
    - Stroke and heart disease Hiroshima females only
  - LSS Report 11 1950-85 mortality (Shimizu et al, 1992)
    - Heart disease in men and women
  - Circulatory disease mortality 1968-1997
    - Significant effect for both heart disease and stroke
    - No indication of non-linearity in dose response
    - Narrowest dose range with significant effect is 0 to 0.5/1 Gy



# LSS Stroke (Shimizu et al. 2010)

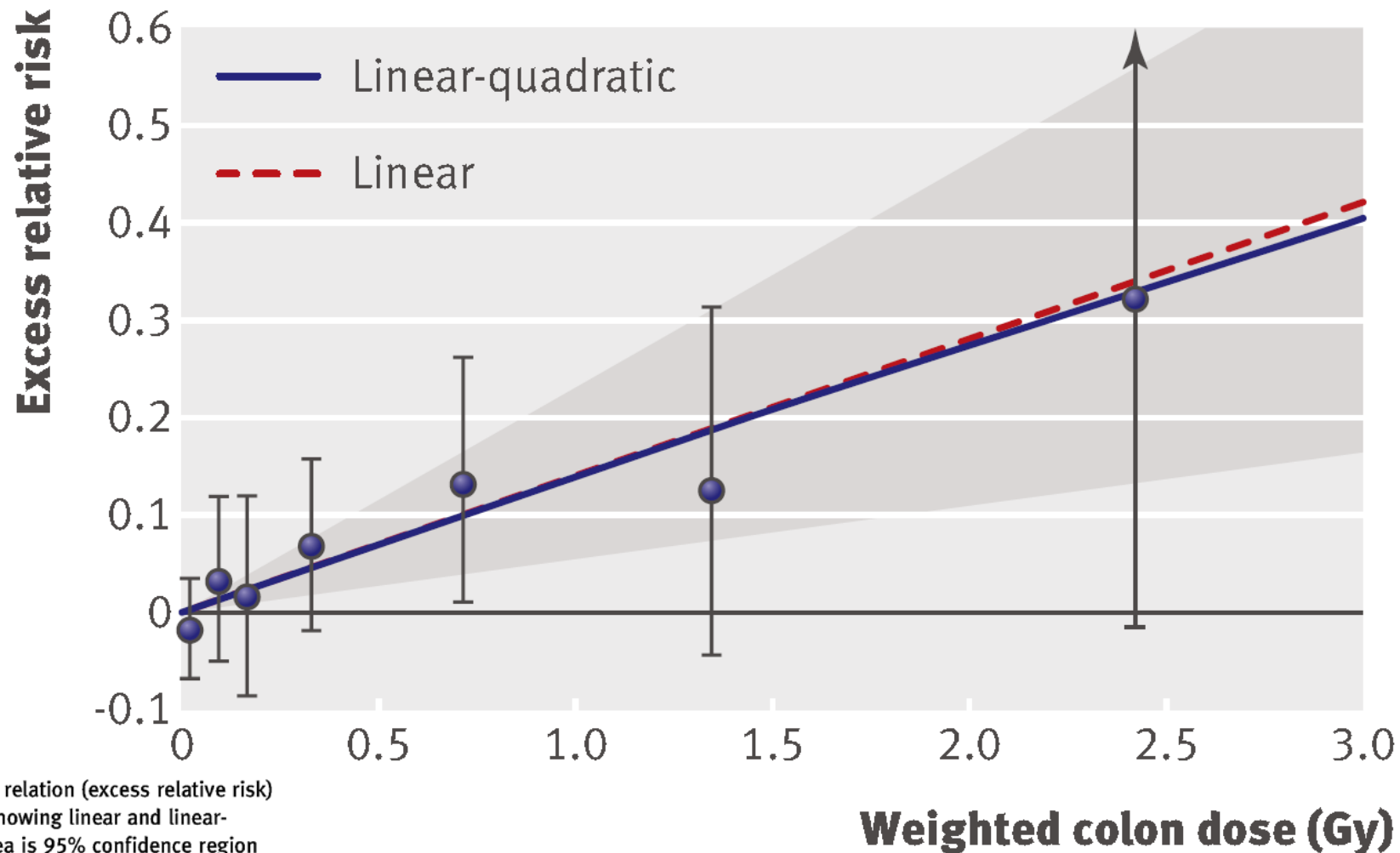


**Fig 1** | Radiation dose-response relation (excess relative risk per Gy) for death from stroke, showing linear and linear-quadratic functions. Shaded area is 95% confidence region for fitted linear line. Vertical lines are 95% confidence intervals for specific dose category risks. Point estimates of risk for each dose category are indicated by circles

Figure 1: Stroke

BMJ 2010;340:b5349

# LSS Heart Disease (Shimizu et al. 2010)

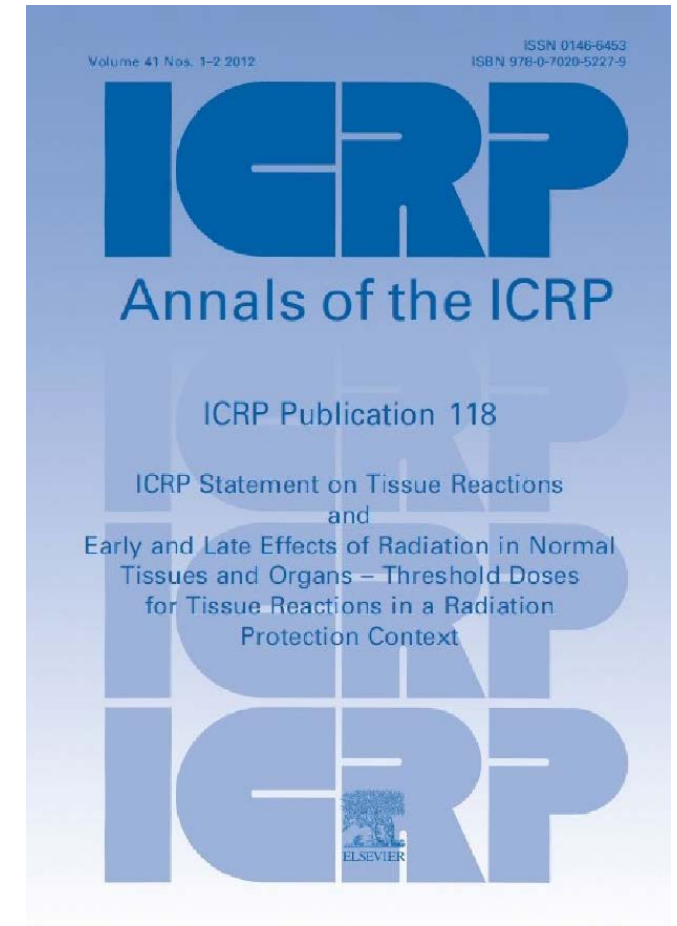


**Fig 2 |** Radiation dose-response relation (excess relative risk) for death from heart disease, showing linear and linear-quadratic functions. Shaded area is 95% confidence region for fitted linear line. Vertical lines are 95% confidence intervals for specific dose category risks. Point estimates of risk for each dose category are indicated by circles

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# ICRP Publication 118

- "...the absorbed dose **threshold** for circulatory disease may be **as low as** 0.5 Gy, with approximately **1% of exposed individuals** developing cardiovascular or cerebral diseases **>10 years** after exposure."
- "However, it is unclear whether or not the threshold is the same for acute, fractionated, and chronic exposures, and in the absence of evidence, it is assumed that the threshold dose is the same in all cases."
- ICRP 118 includes a cautionary statement on circulatory effects, but did not introduce any new dose limit.

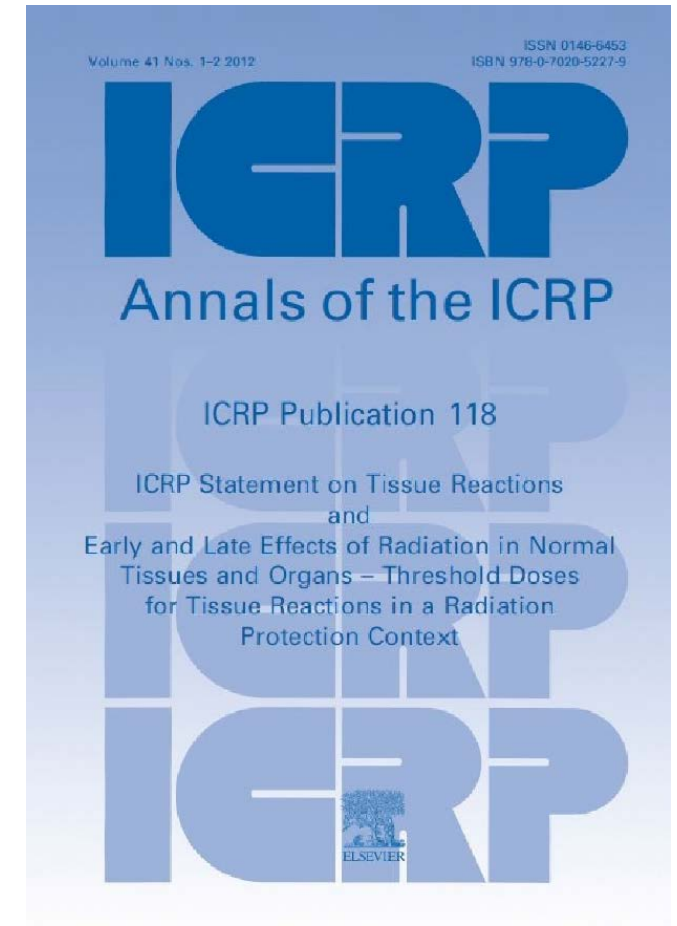


ICRP Publication 118. Ann. ICRP 41(1/2) 2012



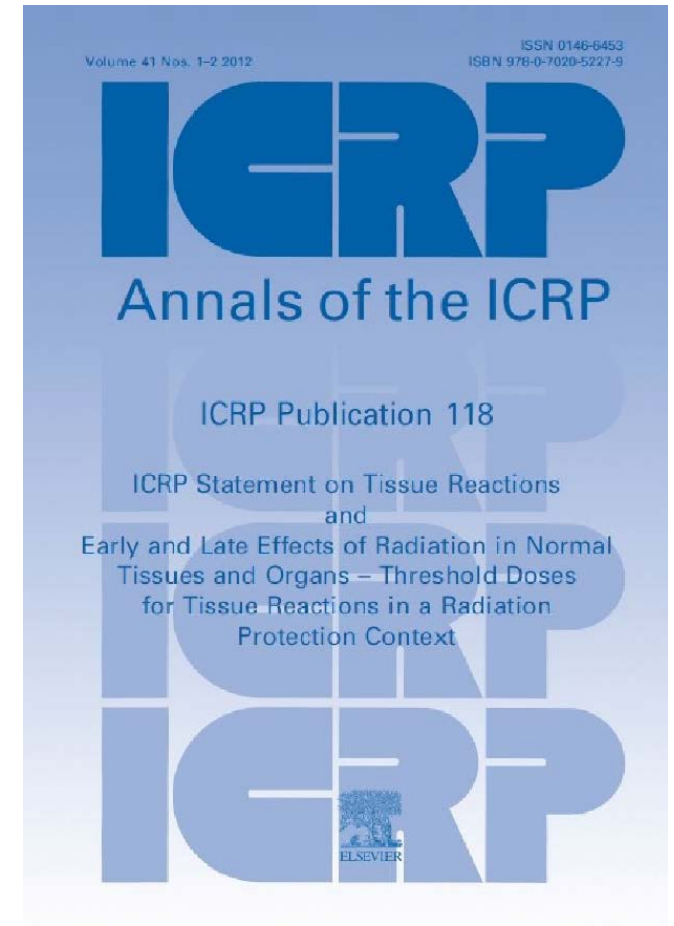
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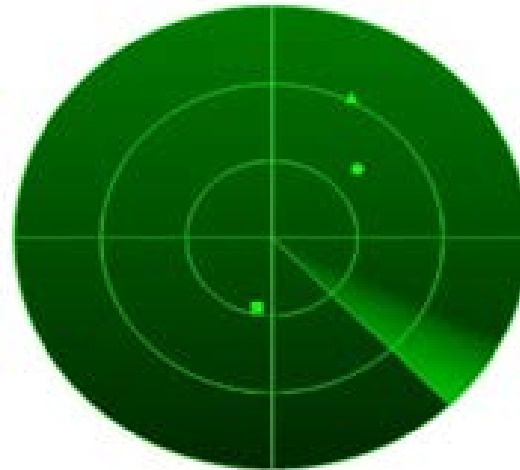
# MELODI Workshop 2015

- Studies at Semipalatinsk Nuclear Test Site seem to show very high relative risk of cardiovascular disease
- ProCardio case controlled study project initiated.
- Studies of Chernobyl workers also found increased risk, with indication of linear model
- Modeling of data from atomic bomb survivors shows that shape of response must be analyzed with care, and models besides LNT must be tested



# Why is this Important?

- Cardio Vascular Disease (CVD) is a **recognized issue** that is **not yet addressed** in recommendations or standards
- Life-threatening, and viewed by most people like a cancer
- Conclusions **may impact dose limits**, radiation protection programs, and communications



## Research Studies

- EPRI Reports
- Publications in peer-reviewed journals

**Findings**

## Scientific Committees

- Review latest science and trends
- Consider Experience, Ethics, Prudence

**Recommendations**

## Regulatory Agencies

- Review Recommendations
- Procedural and Public Processes

**Standards**

## EPRI Role

- Basic Research
- Critical review and analysis of data
- Science to inform development of recommendations
- Science to inform development of standards



# EPRI Research



- Analyze the rapidly changing state of science with regard to low dose radiogenic circulatory and cerebrovascular diseases.
- Determine if there is evidence for a linear no-threshold risk response model for such effects.
- Recommend other meaningful research to help the industry proactively engage in regulatory and scientific discussions that may result in significant changes to future radiation safety standards.
- ***Specific objective*** is to evaluate the current epidemiological and toxicological radiation effects data with respect to possible low dose non-cancer health effects of the cardiovascular and cerebrovascular systems to inform decisions on adequate worker protection.

# Status

- Identified reference literature on CVD effects of radiation is significantly larger than was found for the lens of the eye
- A total of **621** independent publications have been identified on the radiation epidemiology of cardiovascular and cerebrovascular effects (CVD) and mechanistic studies in the literature, including those from the DOE, NASA, Life Span Study, and others



# Observations

## ■ LSS Doses

- All heart disease risks could be seen as approximately linear from 0-3 Gy overall,
  - 0-1 Gy is perhaps statistically significant increased risk,
  - 0-0.5 Gy is not statistically significant.
- BUT there is large uncertainty:
  - Japan vs. US heart disease (US has more ischemic heart disease for example)
  - Japan population baseline risks have varied a lot over time making estimates very difficult.
  - LSS data for ischemic heart disease only does not at all appear to vary by dose



# Observations

- Medical Therapy – higher doses ( $>30\text{Gy}$ ) cause CVD issues, but not directly applicable to low dose, low dose rate
- Occupational Studies (e.g. Radiation workers, x-ray techs, nuclear workers, Mayak workers, etc. etc.) all suffer from significant potential confounding of background risk factors for CVD
- There is still no accepted radiobiological mechanism for CVD effects



# Next Steps

- Detailed review of ICRP-118 radiation effects statements on cardiovascular and cerebrovascular systems, with special emphasis on statements, evaluations, and recommendations is underway
- Mechanism for systematic review of the compiled literature developed
- Product to be EPRI Technical Report and peer review journal submittal
- Objective: Inform ongoing discussions by ICRP, NCRP, regulatory organizations







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