ICRP 2nd Symposium
Abu Dhabi

Paediatric CT and

Recent Epidemiological Studies

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October 24, 2013

National Council on Radiation Protection & Measurements

Views of a Radiation Epidemiologist

Personal views are presented and not necessarily those of the:

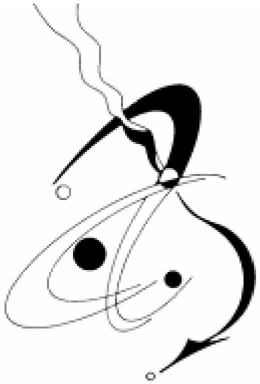
ICRP

NCRP (Report 171, 2012)

UNSCEAR (Annex B, 2013)

Outline - Epidemiology and CT Studies

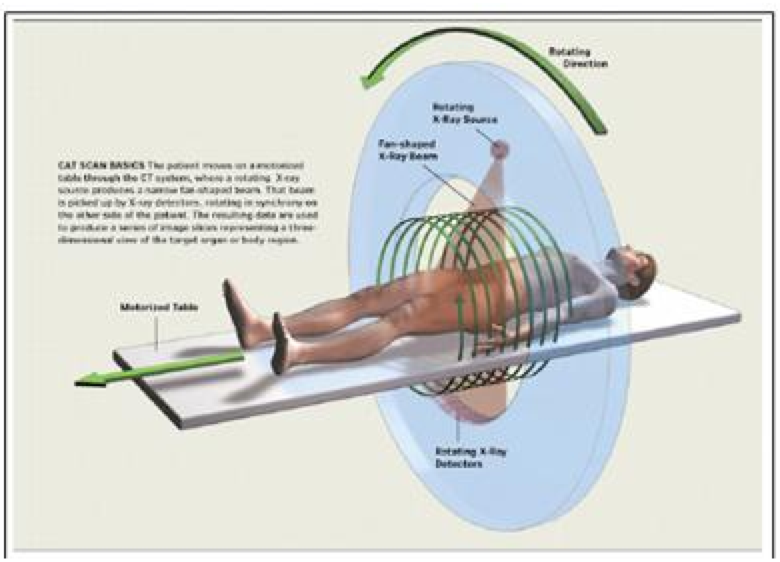
- Importance of CT Studies
- UK study (Pearce et al 2012)
- Reverse Causation
- Australian Study (Mathews et al 2013)
- Dosimetry Limitations
- Conclusions

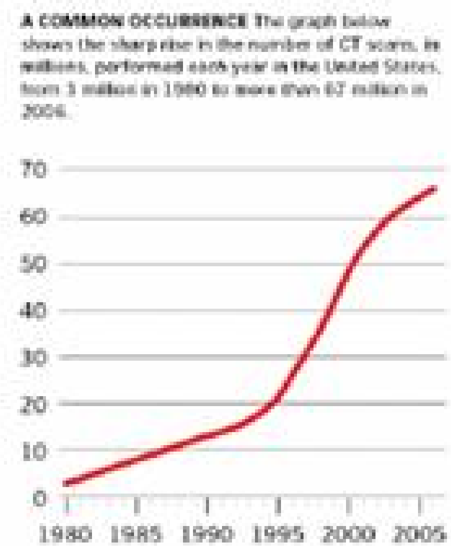


NCRP (Report 171, 2012)
UNSCEAR (Annex B, 2013)

CT Exams are Increasing each Year

- Over 84 million CT examinations were performed last year in the U.S. This is approximately one for every four U.S. citizens.





Radiation CT Doses are not Trivial

Table 1. Typical Organ Radiation Doses from Various Radiologic Studies.

Study Type	Relevant Organ	Relevant Organ Dose* (mGy or mSv)
Dental radiography	Brain	0.005
Posterior–anterior chest radiography	Lung	0.01
Lateral chest radiography	Lung	0.15
Screening mammography	Breast	3
Adult abdominal CT	Stomach	10
Barium enema	Colon	15
Neonatal abdominal CT	Stomach	20

- Brenner and Hall. NEJM 2007

CT Epidemiologic Studies are Important

- They have the potential to provide new information on the risk of cancer following exposures in childhood to ‘relatively’ high dose diagnostic procedures.

- They draw attention to the need to reduce unnecessary exams and

- They draw attention to the need to reduce dose per exam commensurate with desired quality for clinical benefit.

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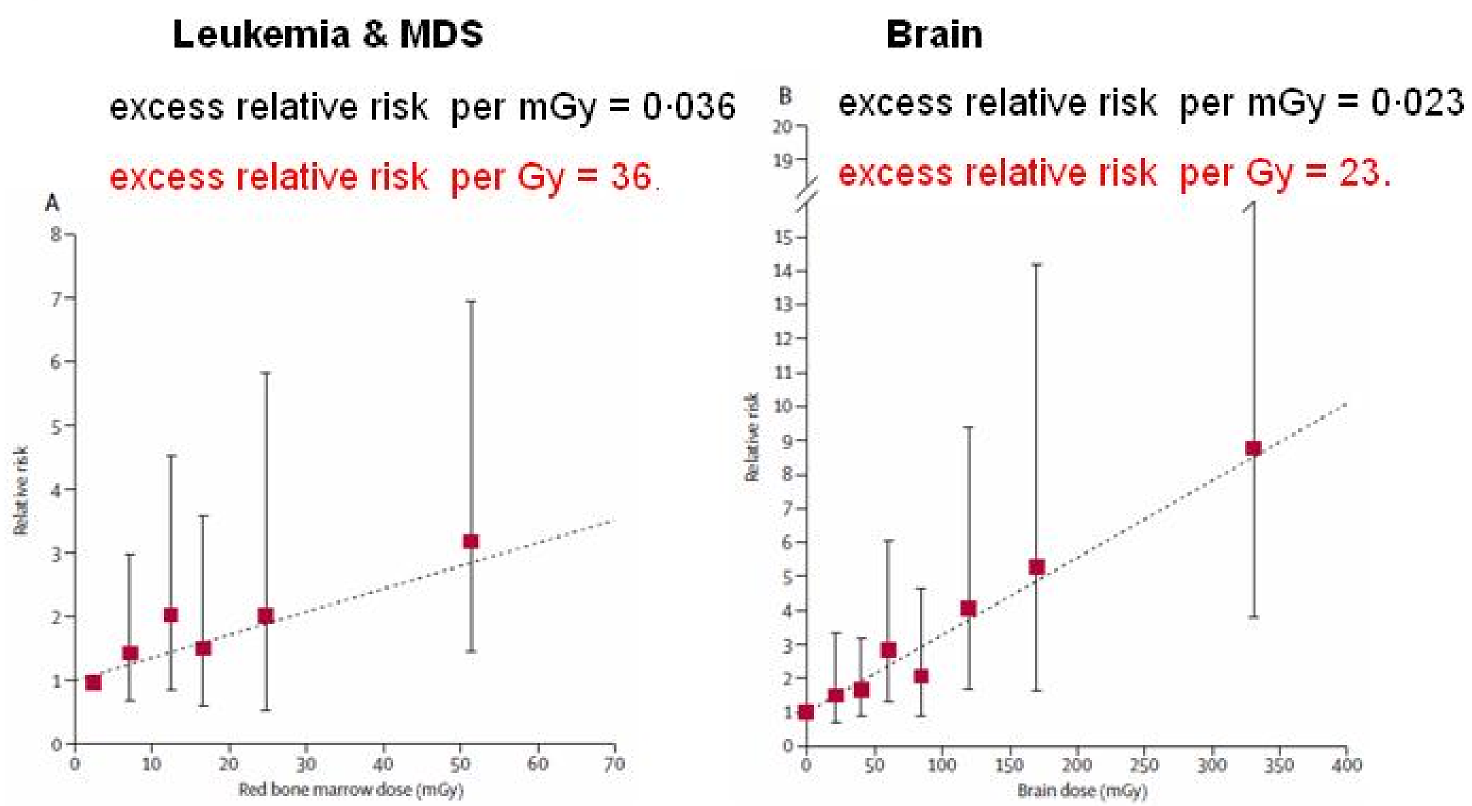
United Kingdom CT Study

(Pearce et al., Lancet 2012)

- Record linkage study of leukaemia and brain cancer incidence following CT scans to 178,000 persons at ages 0ï 21.
- Collection of scan data for individual patients was not possible. Average CT machine settings from two national surveys were used.
- Significant dose responses reported



Major Epidemiology Limitation
No Information on Why Scans Performed

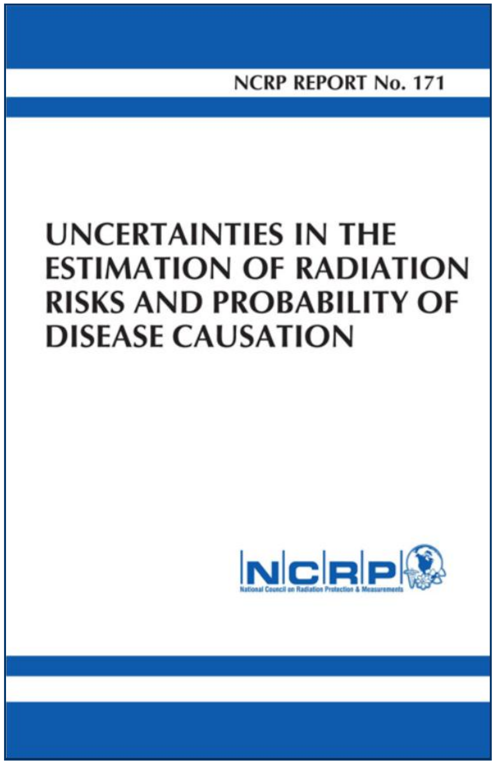
UNSCEAR 2013: EFFECTS OF RADIATION EXPOSURE OF CHILDREN
(Consultant: Fred Mettler – Former C3 Chair)

ñé there are concerns about the risk estimates because of lack of information about indications for the CT scans and the consequent potential for **ó reverse causationô** (i.e. cancers may have been caused by the medical conditions prompting the CT scans rather than by the CT dose) and **lack of individual dosimetry**. ñ

Major Epidemiology Limitation
No Information on Why Scans Performed

NCRP Report 171 (2012): UNCERTAINTIES IN THE ESTIMATION OF RADIATION RISKS (Chair: Julian Preston – former C1 Chair)

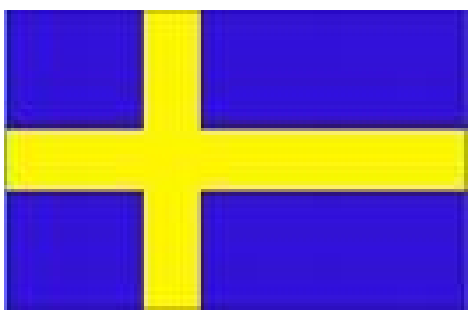
ñ**Children who receive frequent examinations** may have some underlying disability related to the outcome of interest. That is, a child who receives multiple CT exams of the head may have a central nervous system disorder that is prompting such examinations that eventually results in a cancer diagnosis.ò



Example of Reverse Causation

- Thyroid cancer following I-131 scans for evaluation of suspected tumor in Sweden among 35,000 adults (ave thyroid dose 0.94 Gy)

Dickman PW, Holm LE (former Chair MC), Lundell G, Boice JD Jr, Hall P. Thyroid cancer risk after thyroid examination with 131I: A population-based cohort study in Sweden. Int J Cancer 106(4):580–587; 2003.



We abstracted clinical data for all 35,000 patients, including thyroid size, I-131 activity administered and the reason for the examination.

Reason for I-131 Scan
All Reasons

Reason for I-131 Scan (No. Cancers)	RR of Thyroid Cancer by Years After I-131 Scan				
	2-	5-	10-	>20	All
All Reasons (105)	3.1*	2.5*	1.2	1.7*	1.8*

ÅSignificant thyroid cancer risk overall (RR 1.8*)

Note that the adult thyroid gland is not considered a radiosensitive.

Reason for I-131
Suspicion of Tumour

Reason for I-131 Scan (No. Cancers)	RR of Thyroid Cancer by Years After I-131 Scan				
	2-	5-	10-	>20	All
All Reasons (105)	3.1*	2.5*	1.2	1.7*	1.8*
Suspicion of Tumour (69)	6.3*	4.8*	2.3*	3.5*	3.5*

ÅRisk very high when reason for Scan was a suspicion of tumour (RR 3.5*)

Reason for I-131 Other Than Suspicion of Tumour

Reason for I-131 Scan (No. Cancers)	RR of Thyroid Cancer by Years After I-131 Scan 2-	5-	10-	>20	All
All Reasons (105)	3.1*	2.5*	1.2	1.7*	1.8*
Suspicion of Tumour (69)	6.3*	4.8*	2.3*	3.5*	3.5*
Other Reasons (36)	1.3	1.5	0.6	0.9	0.9

ÅNo excess risk if Scan performed for ñother reasonsò (RR 0.9)

Reverse Causation Bias Lasted for More than 20 years after 131-I Exam

Reason for Scan (No. Cancers)	RR of Thyroid Cancer by Years After Scan				
	2-	5-	10-	>20	All
All Reasons (105)	3.1*	2.5*	1.2	1.7*	1.8*
Suspicion of Tumour (69)	6.3*	4.8*	2.3*	3.5*	3.5*
Other Reasons (36)	1.3	1.5	0.6	0.9	0.9

ÅThe ñsuspicion of tumourò predicted future diagnoses of cancer even 20 years after examination

Radiation exposure from CT scans in 'childhood'.. <22 years of age

Mother and 21 year old son

Radiation exposure from CT scans in 'childhood'.. <22 years of age

Mother and 21 year old son

Å A 21 year old is not a child

Age at Exposure Effect in UK Study the Reverse of Previous Studies

Age at exam	ERR/Gy
0-	5
5-	28
10-	37
15-	41

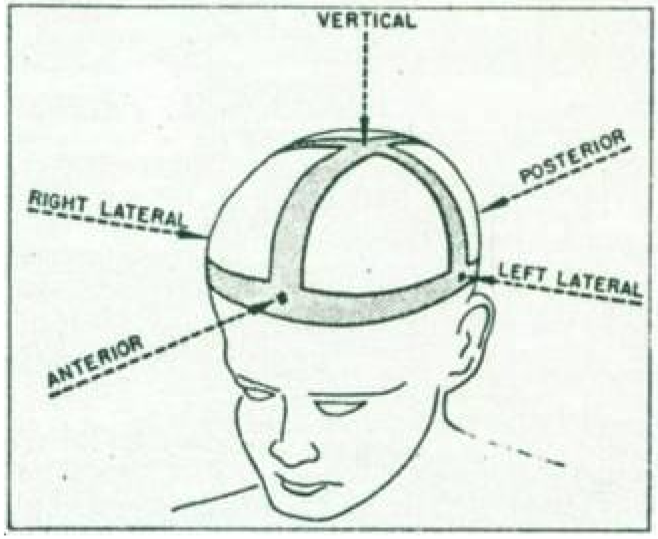
UNSCEAR 2013:
ñThe risk of glioma is highest at < 5 years at irradiation and seems to largely disappear at the age of 20 years or more at irradiation, suggesting that **susceptibility decreases as brain development nears completion**.ò

Radiation Risk Implausibly High for Brain and Inconsistent with Previous Studies

Study	ERR/Gy
CT (Pearce 2012)	23
Tinea Capitis (Ron 1988)	2
Childhood Cancer (Neglia 2006)	0.33
A-Bomb Survivors <10 y (UNSCEAR 2008)	0.88

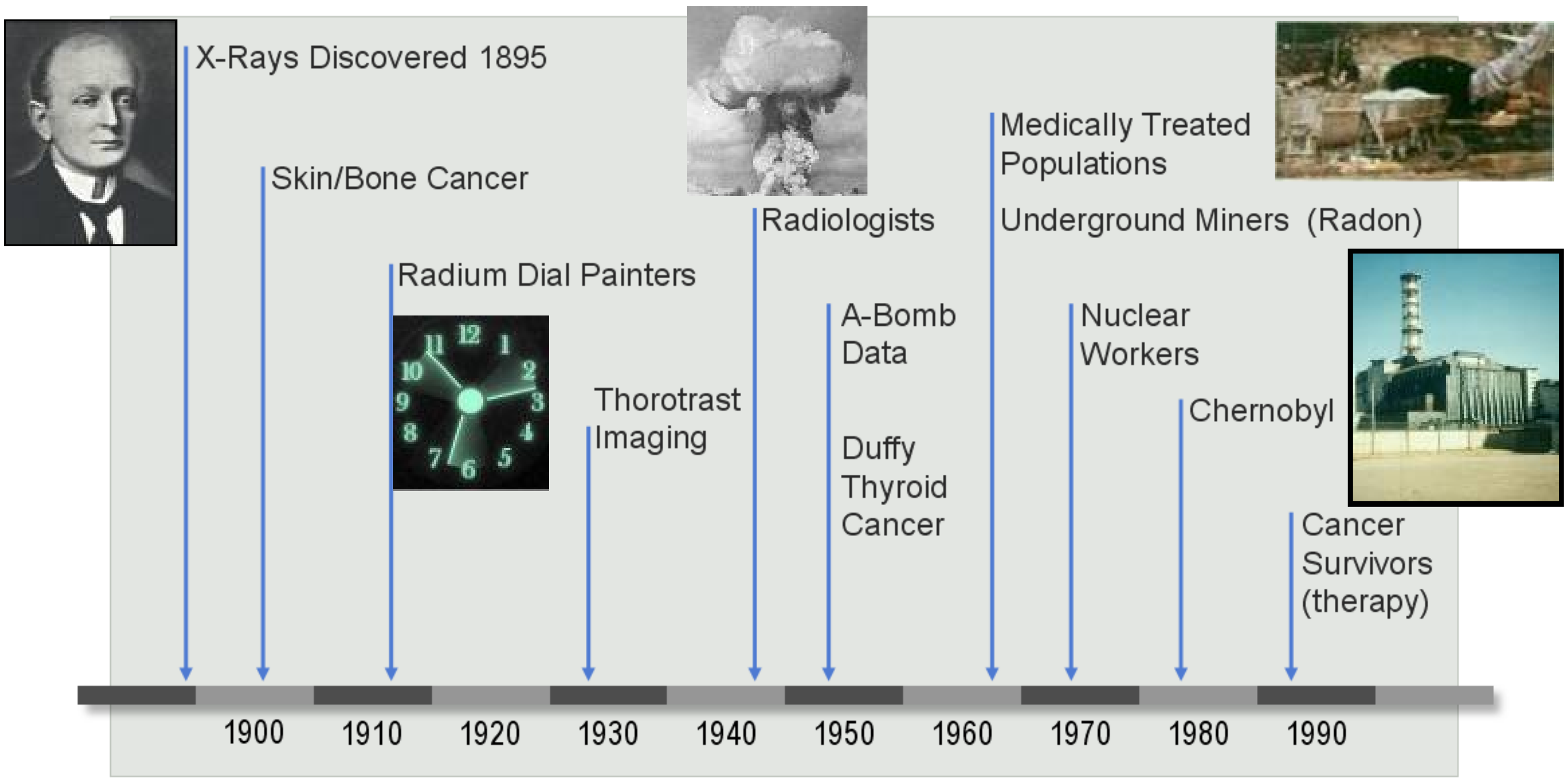
TINEA CAPITIS WITH KERION FORMATION
11-YEAR-OLD BOY WITH 3 YEAR INFECTION

Fig 1.—Five Treatment fields used in the Adamson-Kienbock treatment were positioned with the aid of a "cap" made from steel bands.



Epidemiology is the study of the distribution and causes of disease in humans.

Radiation Epidemiology Dates Back 100 Years



Epidemiologic Studies of Exposed Human Populations

JAPANESE ATOMIC BOMB SURVIVORS

RADIOTHERAPY - CANCER
- Cervical
- Endometrial
- Childhood
- Breast
- Hodgkin Lymphoma

RADIOTHERAPY - NON-MALIGNANT
- Spondylitis
- Thymus
- Tonsils
- Menstrual Disorders
- Scalp Ringworm
- Mastitis
- Infertility
- Otitis Media
- Ulcer
- Hemangioma

DIAGNOSTIC
- TB - Fluoroscopy
- Pelvimetry
- Scoliosis
- General

RADIONUCLIDES
- Thorotrast
- I - 131
- Uranium
- P - 32
- Ra - 224
- Plutonium

OCCUPATION
- Ra Dial Painters
- Miners (Radon)
- Radiologists
- Technologists
- Nuclear Workers
- Atomic Veterans

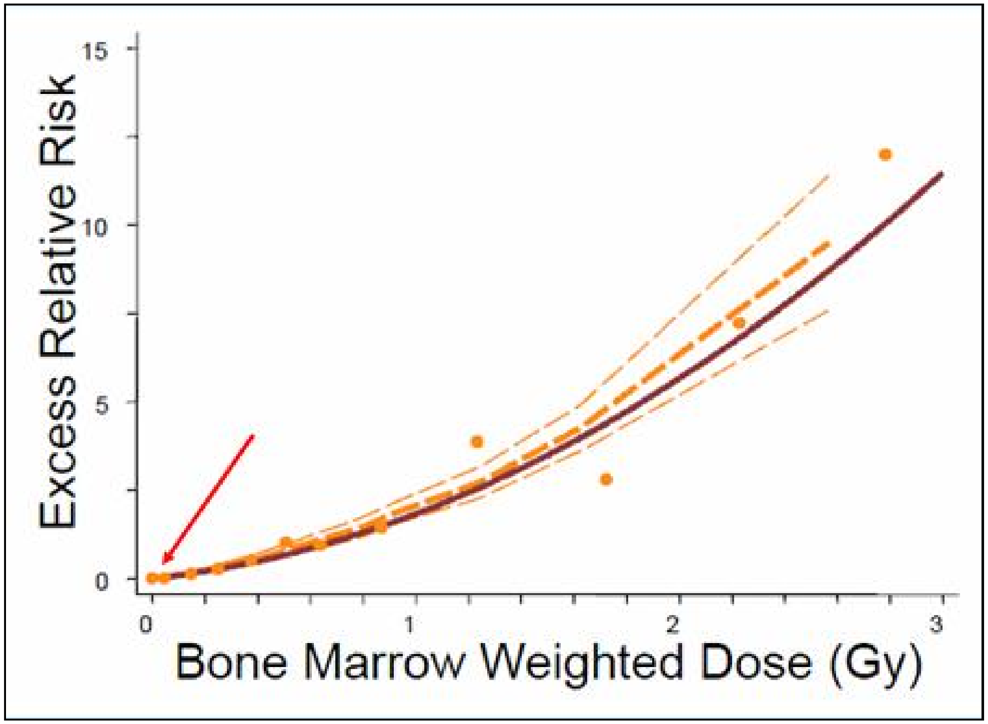
ENVIRONMENT
- Chernobyl
- Weapons Fallout
- Natl Background
- Techa River

For Completion
Leukaemia and Myelodysplastic Disease (MDS)

ñFrom 74 observed leukaemias, they found an ERR Gy^{-1} of 36 é However, they included myelodysplastic syndrome (MDS) with the leukaemias, and the MDS cases had an extremely high relative risk. Without the MDS cases, the estimated risk was no longer statistically significant.ò(UNSCEAR 2013)

Study	ERR/Gy
CT (Pearce 2012)	36.0
Tinea Capitis*	4.4
Childhood Cancer*	0.24
Skin Hemangioma*	1.6
A-Bomb Survivors <20 y (Hsu 2013)	6.5

* UNSCEAR 2008



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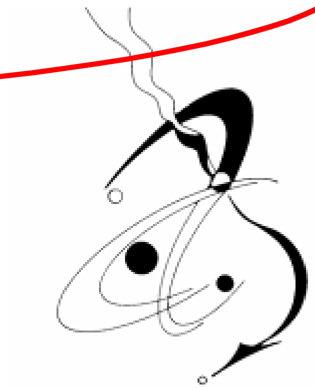


NCRP (Report 171, 2012)
UNSCEAR (Annex B, 2013)

Australian CT Study

(Mathews et al., BMJ 2013)

- Data Linkages study of 680,000 children (0-19 y) who received CT scans and 10,000,000 with no record of such exposures.
- Excesses reported for practically all cancers:

  - Digestive organs
  - Melanoma
  - Soft tissue
  - Female genital
  - Urinary tract
  - Brain
    - after brain CT scan
    - after other CT scan
  - Thyroid
  - Leukaemia (myeloid)
  - Hodgkin's lymphoma

But not for:

- Breast Cancer
- Lymphoid Leukaemia

unscear.org

UNSCEAR

United Nations Scientific Committee
on the Effects of Atomic Radiation

Effects of radiation exposure of children

Fred A. Mettler Jr. MD, MPH (UNITED STATES OF AMERICA)

Briefing of Fourth Committee of the United Nations General Assembly
25 October 2013

UNEP

UNSCEAR 2013 – Implausible Risks

- **Reverse causation** (cancers were caused by the medical conditions prompting the CT scans rather than by the CT dose) -- as a potential bias could not be examined since no documentation was available on the indications for the CT scans.

- The risk estimate for ñall cancers, excluding brain cancer after brain CTòrisk (ERR Sv^{-1}) was **statistically incompatible** with the data at comparable ages from the Japanese LSS study on atomic bombing survivors:

27 (95% CI: 17, 37) vs. 3 (95% CI: 2, 6).

UNSCEAR 2013 – Latency Too Short

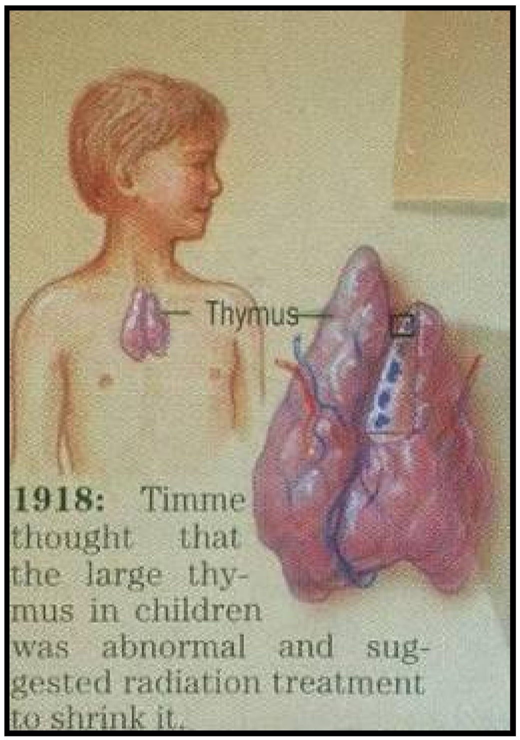
- **One Year Minimum Latency**. Focusing on cancers that occurred at least one (rather than 5 or 10) year after the initial CT scan amplified the potential for reverse causation and is biologically implausible.

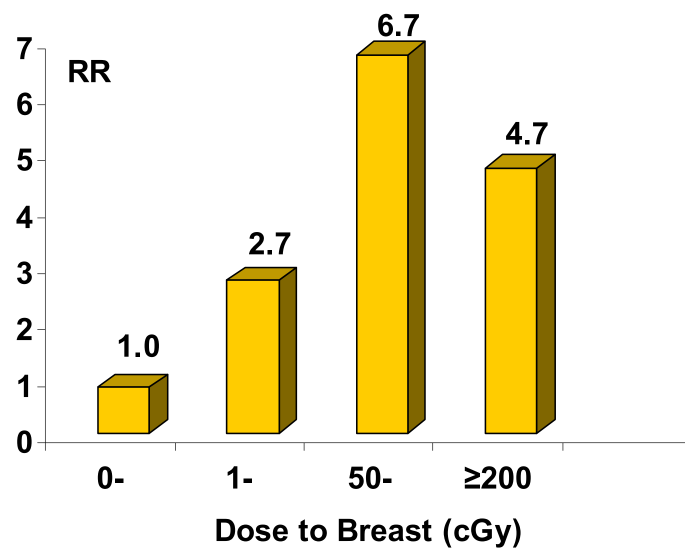
- The finding of generally stronger associations if they included years 1-4 after the CT scan than if they included only later years reinforces this concern.

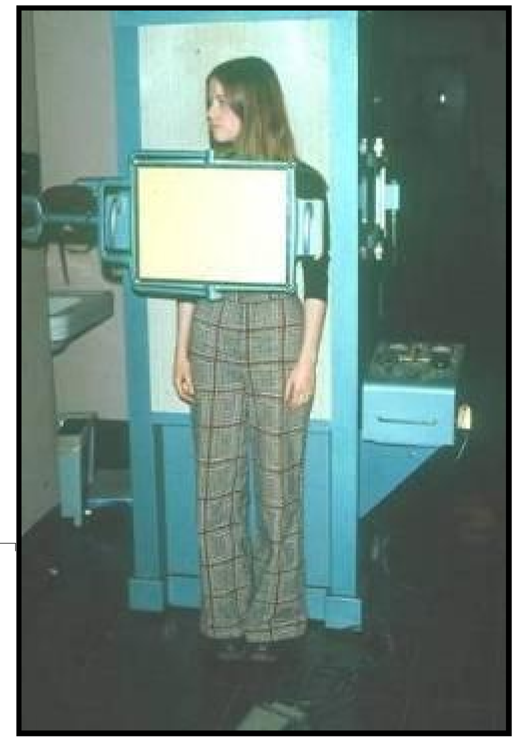
- The **implausibly early risk** that declined with time suggests the possibility of óreverse causationô

UNSCEAR 2013 - Inconsistent Cancers

- Implausible CT and tumour associations included radiation excesses seen for melanoma and Hodgkinôs lymphoma, neither of which is known to be associated with radiation, but not for breast cancer, a radiosensitive site.







Inconsistent Age at Exposure Effect

- No clear excess of leukaemia seen for those exposed before age ten but it appeared for those exposed at later ages

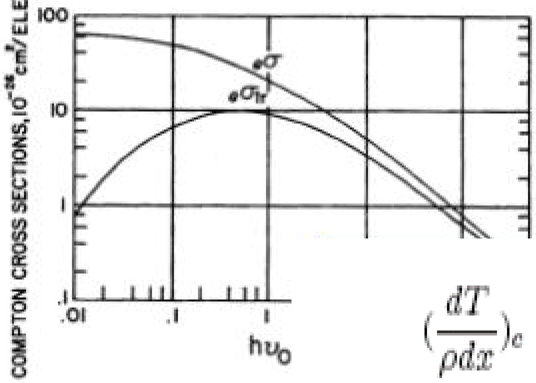
Age at exam	RR
0-	0.95
5-	1.04
10-	1.26*
15-19	1.36*

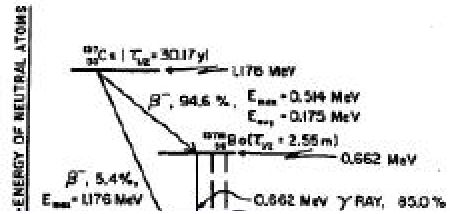
- unlike other studies of radiogenic childhood leukaemia, which tend to show the greatest leukaemia risk for exposure at early ages.

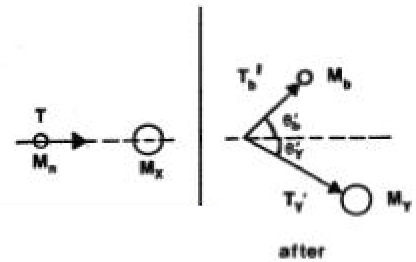
UNSCEAR

Dosimetry & Medical Physics Issues

$${}_e\sigma_{tr} = 2\pi r_0^2\left[\frac{2(1+\alpha)^2}{\alpha^2(1+2\alpha)} - \frac{1+3\alpha}{(1+2\alpha)^2} - \frac{(1+\alpha)(2\alpha^2-2\alpha-1)}{\alpha^2(1+2\alpha)^2} - \frac{4\alpha^2}{3(1+2\alpha)^3} - \left(\frac{1+\alpha}{\alpha^3} - \frac{1}{2\alpha} - \frac{1}{2\alpha^3}\right) ln(1+2\alpha)\right]$$





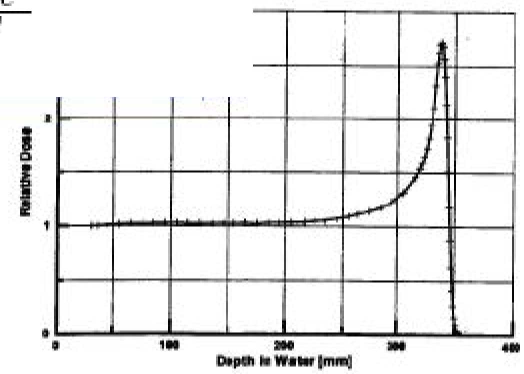


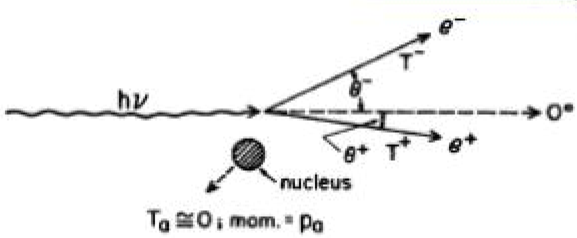
$$\left(\frac{dT}{\rho dx}\right)_c = 0.3071\frac{Zz^2}{A\beta^2}[13.8373 + \ln(\frac{\beta^2}{1-\beta^2}) - \beta^2 - \ln I]$$

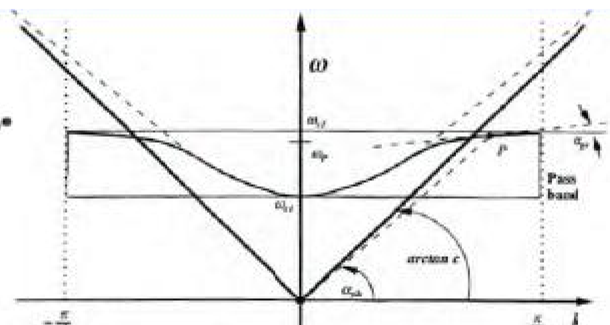
$$-\frac{2\sqrt{M_a M_b T T_b'} cos\theta_b'}{M_Y}$$

$$\frac{d\sigma}{d\Omega} = \frac{r_0^2}{2}[\frac{1+}{[1+\alpha(1}$$

$$f = \frac{qB}{2\pi M} = \frac{qB}{2\pi M_0}\sqrt{1-\beta^2} = f_0\frac{M_0c^2}{E}$$







$$d({}_a\kappa) = \frac{\sigma_0 Z^2 P}{h\nu - 2m_0c^2}dT^+$$

$$\vec{\nabla}\bullet\mathbf{E} = \frac{\rho}{\varepsilon_0}, \qquad \vec{\nabla}\times\mathbf{E} = \frac{\partial\mathbf{B}}{\partial t},$$

$$\vec{\nabla}\bullet\mathbf{B} = 0, \qquad c^2\,\vec{\nabla}\times\mathbf{B} = \frac{\mathbf{j}}{\varepsilon_0} + \frac{\partial\mathbf{E}}{\partial t},$$

$$\left(\frac{dT}{\rho dx}\right)_c = 0.3071\frac{Zz^2}{A\beta^2}[13.8373 + \ln(\frac{\beta^2}{1-\beta^2}) - \beta^2 - \ln I]$$

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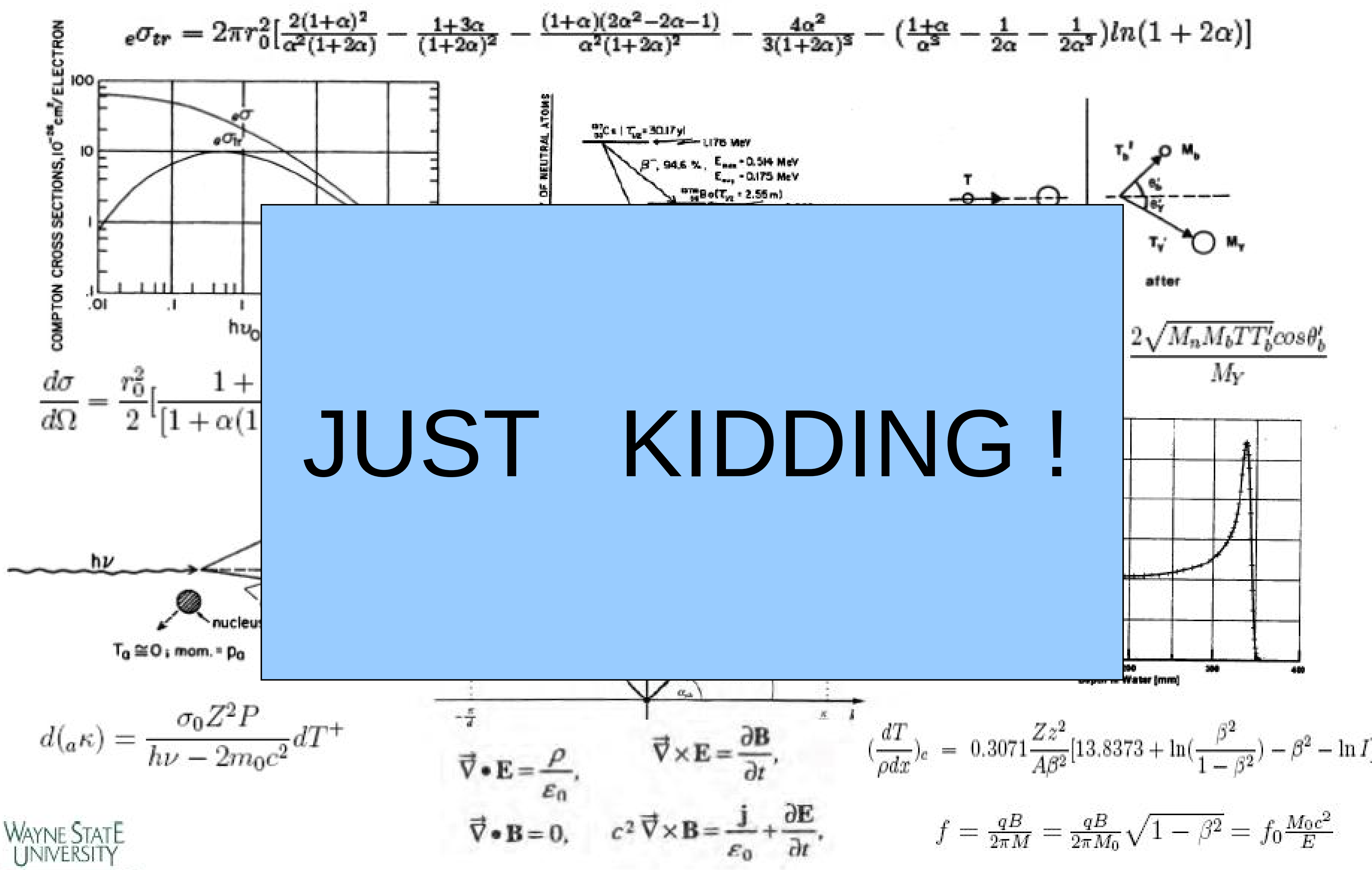
Thanks to Mike Joiner

Dosimetry & Medical Physics Issues



Dosimetry – Challenging

- Individual dose determinations were not made and a somewhat arbitrary year (2001) was chosen as the demarcation of the high exposures of years past (conventional CT) and the lower exposures currently used (helical CT).
- The scan time for pediatric patients with a conventional CT scanner could be from 10-35 minutes in the 1990s in comparison with a scan time of 50-60 seconds with a helical CT scanner.

Missed Examinations

- For children examined during the early years of CT imaging, there is the likelihood that any **movement** during an examination, which for conventional CT scanners could take up to 35 minutes, would result in a blurred image and prompt a repeat examination.
- Evidence of repeat CT examinations were not available from the electronic databases.
- Missing CT exposures included those due to unrecorded repeat CT scans (e.g. because of patient movement) and those occurring outside the age or time ranges of the study.
- Missing doses would tend to inflate the estimates of risk per unit dose.

Conclusions

- Current studies do not provide evidence that low doses are causally associated with cancers in children. **Association is not causation**!
- **Reverse causation** is the likely reason for the associations, i.e. the condition caused the CT exams.
- The **inconsistencies** with previous studies in terms of age at exposure, latency, tumour sites, and radiation risks per Gy “give one pause”.
- **No individual dosimetry** was done, doses from conventional and helical scanners are different, blurred exams and repeats not recorded.
- Unless the reasons for the examination can be determined in **future studies**, the results will likely be similarly ambiguous.

شكراً

Thank You

Informative References

Critique of Both Studies

UNSCEAR 2013: EFFECTS OF RADIATION EXPOSURE OF CHILDREN

Critique of UK Study

NCRP Report 171 (2012): UNCERTAINTIES IN THE ESTIMATION OF RADIATION RISKS

Critique of Australian Study

Walsh L, Shore R, Auvinen A, Jung T, Wakeford R. BMJ 4 June 2013 (http://www.bmj.com/content/346/bmj.f2360/rr/648506)

Boice J. Health Physics News July 2013.

Example of Reverse Causation

Dickman PW, Holm LE, Lundell G, Boice JD Jr, Hall P. Thyroid cancer risk after thyroid examination with 131I: A population-based cohort study in Sweden. Int J Cancer 106(4):580–587; 2003.