Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study

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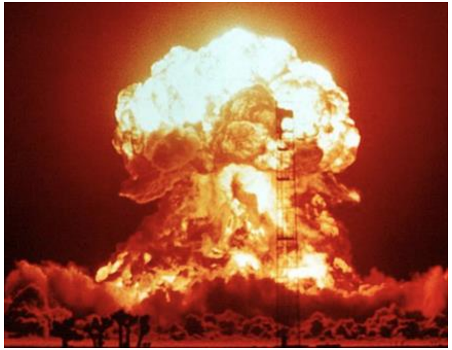

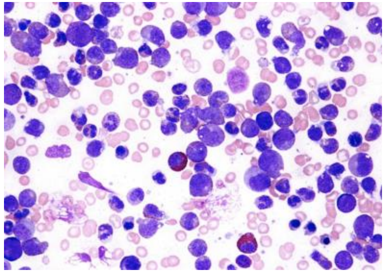

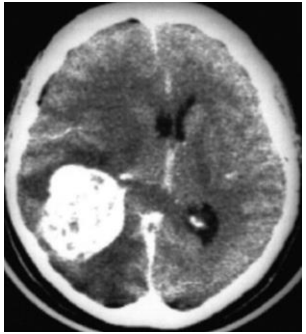

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Learning objectives

By the end of this journal club, participants will:

1. Know how many CT scans are performed in the US.
2. Appreciate the variation and imprecision of radiation dosages.
3. Use epidemiological data to help make decisions regarding radiation stewardship.

Disclaimer

This is a highly complicated topic.

I will not be discussing the physics or nuances of radiation exposure which is beyond the scope of this discussion.

Module Outline

I. **<u>Case</u>**
II. Background
III. Article Overview
IV. Clinical Questions
V. Key Points

Case presentation

20-year-old healthy female patient presents to the emergency department with acute lower abdominal pain and nausea.

On exam, T: 37.6C, BP: 125/80, HR: 92, RR: 14, SpO2: 99% RA, BMI: 19
GI: abdomen soft, tender in the suprapubic region and RLQ.
GU: No CVA tenderness. Normal pelvic exam.

Labs: negative pregnancy test, mild leukocytosis (11.8), no left shift, normal urinalysis.

Imaging: Transvaginal ultrasound negative for tubo-ovarian or uterine pathology.

Case presentation

You consider appendicitis and discuss a CT scan with the patient.

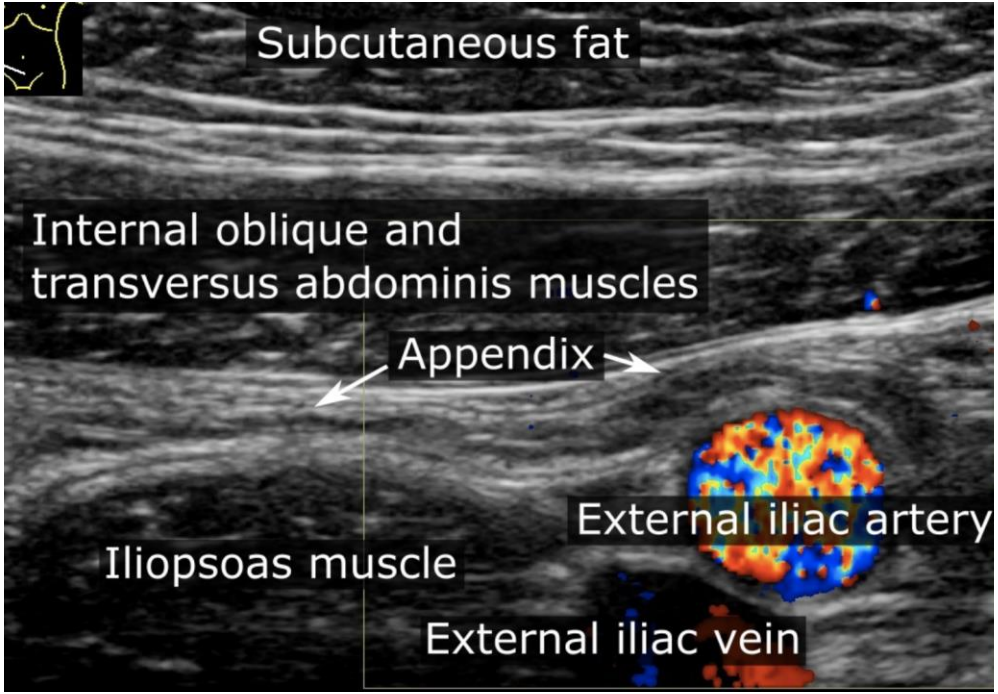
She states she has had 3 CTs in the past and asks you about the risks of radiation exposure relative to her risk of appendicitis.

She specifically asks you if other imaging options are available or if it would be reasonable to wait and observe.

You offer to perform an ultrasound with the caveat that sensitivity is very low (<40%), and particularly in equivocal presentations. [1]Hosseini (PMID: 30123787)

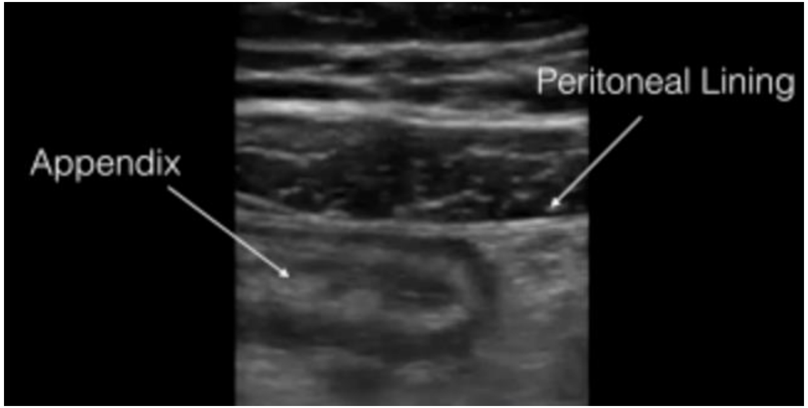
Ultrasound

Normal



https://en.wikipedia.org/wiki/File:Ultrasonography_of_a_normal_appendix,_annotated.jpg

Appendicitis



https://www.acep.org/how-we-serve/sections/emergency-ultrasound/news/april-2015/tips-and-tricks-ultrasound-in-the-diagnosis-of-acute-appendicitis/

Case questions

1. What do we know about the risk of CT radiation exposure?
2. How can we incorporate this risk into decision making?
3. How can we council patients regarding clinical indications for CT scans vs risk

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Background

- Ionizing radiation has long been understood to effect DNA damage capable of causing malignancy.[2,3] Carante (PMID: 25956821), Ballarini (PMID: 15309385)
- The Life Span Study reports increased incidence leukemias, lymphomas and multiple myeloma among ~100,000 atomic bomb survivors (~50mSv).[4] Preston (PMID: 8127953)
- High doses of radiation treatment for lymphoma have been associated with increased risk of secondary malignancies.[5] Toda (PMID: 19591686)
- 80 million CT scans are performed in the U.S. today compared to 3 million in 1980.[6]
- Prior to Pearce study, no comprehensive epidemiological data had been reported on the risk of diagnostic radiation exposure among healthy patients.

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Article specifics

I. Purpose: Assess excess risk of leukemia and brain tumors after CT scans in a cohort of children and young adults.

II. Journal: Lancet 2012; 380: 499–505

III. Study type: Retrospective cohort of the NHS central registry (England, Wales, Scotland)

IV. # Cases: 283,919 CT scans among ~178,000 patients.

V. Data: Incidence of leukemia and brain tumors after CT scan with dose response analysis.

Study cohort

- Patients without previous malignant disease first examined with CT scan between 1985 and 2002 when younger than 22 years of age.
- Scanned at 81 National Health Services (NHS) hospitals.
- Obtained date of birth, sex, CT details, and body parts scanned.

Materials and Methods

NHS central registry utilized to obtain cancer incidence, mortality, and loss to follow up. Data followed until first cancer dx, death or loss to follow up.

Excluded patients who developed leukemia within 2 years and brain tumor within 5 years of CT scan to reduce inclusion of patients who were scanned due concern for cancer.

Calculated radiation dose exposure based on age, sex, examination type, year of scan and typical machine settings obtained by UK wide surveys.[7,8]

Combined this data with hybrid computational human phantoms to estimate absorbed doses to the brain and red bone marrow.[9] Lee (PMID: 20019401)

Statistical analysis: Poisson relative risk fitted by maximum likelihood.

	Male patients		Female patients	
	Brain dose (mGy)	Red bone marrow dose (mGy)	Brain dose (mGy)	Red bone marrow dose (mGy)
Age at brain CT				
0 years	28	8	28	8
5 years	28	9	28	9
10 years	35	6	35	6
15 years	43	4	44	6
20 years	35	2	42	2
Age at chest CT				
0 years	0·4	4	0·4	4
5 years	0·3	3	0·3	3
10 years	0·3	3	0·3	3
15 years	0·2	4	0·3	4
20 years	0·2	4	0·3	4
Age at abdominal CT				
0 years	0·2	3	0·2	3
5 years	0·1	2	0·1	2
10 years	0·1	3	0·1	3
15 years	0·0	3	0·0	3
20 years	0·0	3	0·0	4
Age at extremity CT				
0 years	0·0	1	0·0	1
5 years	0·0	0·2	0·0	0·2
10 years	0·0	0·1	0·0	0·1
15 years	0·0	0·0	0·0	0·0
20 years	0·0	0·0	0·0	0·0

Table 1: **Estimated radiation doses to the brain and red bone marrow from one CT scan, by scan type, sex, and age at scan, as used in this study for scans after 2001**

Estimated Radiation Dosages

- 1 mSv ~ the average accumulated background radiation dose to an individual for 1 year.
- 1 mSv = dose produced by exposure to 1 mGy
- Dosages before 2001 were generally 2-3x higher.
- Authors calculated organ specific dosages regardless of CT targeted organ.

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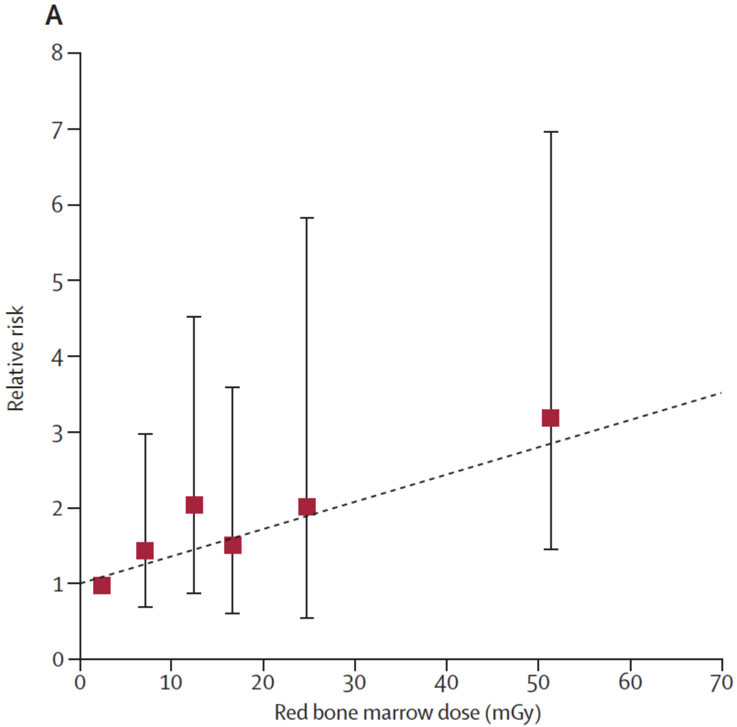
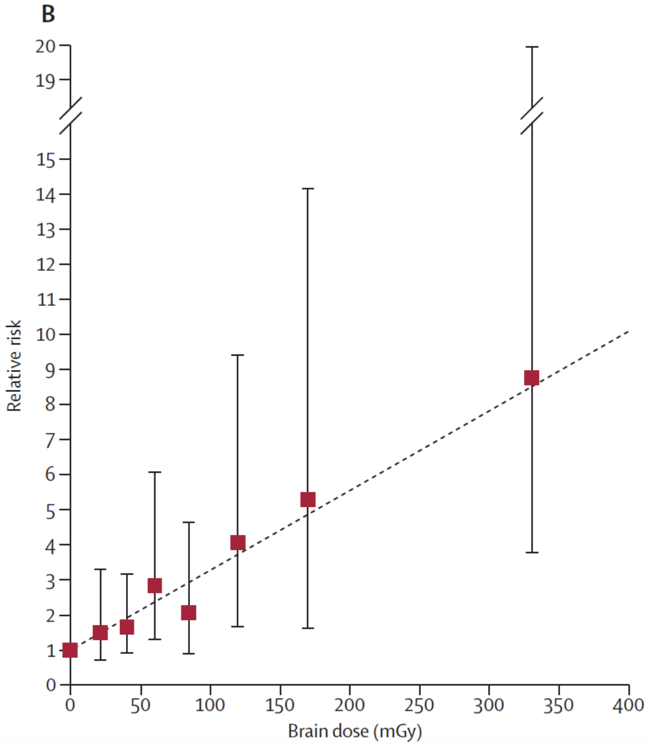
Results

- 74 cases of leukemia of 178,604
  - Excess relative risk (ERR) per mGy: 0.036, 95% CI: 0.005 – 0.120; $p = 0.0097$
- 135 brain tumors of 176,587 patients
  - ERR per mGy: 0.023, 95% CI: 0.010 – 0.049; $p < 0.0001$.

Leukemia RR



Brain tumor RR



- Wide ranging and overlapping confidence intervals (CI)
- CI’s cross 1 for dose <50 mGy.
- There is signal of dose response

Discussion

- 2-3 head CT's in the early 2000's (~60mSv to brain) could almost triple the relative risk of brain tumors.
  - Dose response for leukemia in atomic bomb survivors was similar after 15 years since exposure (0.045/mSv compared to 0.036/mSv).
- 5-10 CT's in early 2000's (~50mSv to bone marrow) could triple the relative risk of leukemia.
- Important to note these risks are very low compared to the general population lifetime risk of cancer which is 1 in 3.

Limitations

Underestimating risk:

1. Follow up was only from 1985-2002. *what will these numbers look like in 20-40 years?

2. Only studied 2 types of cancer, but ionizing radiation is associated with malignancy in many organ systems

3. CT scans in the US have increased from 3 to 80 million over 40 years.

Overestimating risk:

1. Radiation dosages significantly higher in the early 2000's.

Generalizability concerns:

1. Only pediatric patients studied who have more years to accumulate DNA damage.

2. Brain and bone marrow in pediatric patients are exquisitely radiosensitive.

3. Dosages widely vary in the United States depending on clinical setting.

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Clinical Question/Key points

How should we proceed in our patient with questionable appendicitis?

- There is a small but statistically significant risk of radiation exposure for developing cancer which exhibits a dose response relationship.
- Lifetime risk of cancer is 1 in 3.
- If a CT scan is clinically justified, then the benefits of CT outweigh the risks.
- Radiation exposure is highly variable and requires further study and efforts at standardization and minimization.

References

PMIDs are embedded in the earlier slides. Also

[6]https://www.health.harvard.edu/cancer/radiation-risk-from-medical-imaging.

[7]National Radiological Protection Board. Survey of CT practice in the UK. Chilton, UK: National Radiological Protection Board, 1991.

[8]Shrimpton P, Hillier M, Lewis M, Dunn M. Doses from computed tomography (CT) examinations in the UK-2003 (NRPB-W67). Chilton, UK: National Radiological Protection Board, 2005.