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ORIGINAL ARTICLE

Survival adjusted cancer risks attributable to radiation exposure from cardiac catheterisations in children

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ABSTRACT

Objectives To estimate the risk of developing cancer in relation to the typical radiation doses received from a range of X-ray guided cardiac catheterisations in children, taking variable survival into account.

Methods Radiation doses were estimated for 2749 procedures undertaken at five UK hospitals using Monte Carlo simulations. The lifetime attributable risk (LAR) of cancer incidence was estimated using models developed by the Biological Effects of Ionising Radiation committee, based on both normal life expectancy, and as a function of attained age, from 20 to 80 years, to take reduced life expectancy into account.

Results The radiation-related risks from these procedures are dominated by lung and breast cancer (for females). Assuming normal life expectancy, central LAR estimates for cancer incidence, based on median doses, ranged from <1 in 2000 for atrial septal defect occlusions to as high as 1 in 150 for valve replacements. For a reduced life expectancy of 50 years, estimated risks are lower by a factor of around 7. For conditions with especially poor survival (age 20 years), such as hypoplastic left heart syndrome, estimated cancer risks attributable to radiation were <1 in 20 000.

Conclusions Based on recent UK radiation dose levels, the risk of cancer following cardiac catheterisations is relatively low and strongly modified by survival and the type of procedure. The risk of breast cancer, especially following pulmonary artery angioplasty and valve replacements, is the greatest concern.

INTRODUCTION

Cardiac catheterisations have an established role in the management of acquired and congenital heart conditions. The procedure involves guidance using X-rays, exposure to which is associated with an increased lifetime risk of developing cancer.[1] We have previously reported on the radiation doses from these procedures,[2] concluding that doses have fallen significantly over than last two decades in the UK, despite the introduction of increasingly advanced interventions, including transcatheter valve replacements.[3]

A knowledge of the potential long-term risks following X-ray exposures is essential in the practices of justification and optimisation, as well as communication with patients and parents and obtaining informed consent. Direct epidemiological evaluation of risks from low dose exposures is problematic, due to the requirement of large sample sizes and controlling for confounding factors.[4] Potential risks can also be estimated using models derived from other exposed populations, most notably survivors of the atomic bombings of Hiroshima and Nagasaki. This approach is not limited by sample size, though still involves uncertainties relating to the magnitude of risk per unit dose, the modifying effect of age at exposure, and transfer of risks to non-Japanese populations.

In this study, we estimated the risk of cancer in relation to median organ doses for a range of cardiac catheterisations carried out in the UK. Radiation-induced cancers typically take many years or even decades to develop,[5] including those of organs receiving the largest doses from cardiac catheterisations —that is, the lungs, oesophagus, stomach, and liver. Most risk projections assume normal life expectancy, thus assume the patient will live long enough for tumours to manifest. The survival of children with congenital heart disease (CHD) is variable, however, ranging from around 20% to 90% at 12 years.[6] For many conditions, including isolated pulmonary valve stenosis and atrial septal defect (ASD), survival approaches that of the general population.[7] For other patients, including those with hypoplastic left heart syndrome or those receiving transplanted organs, survival is sufficiently reduced[6 8] that the risk of radiation induced cancer is substantially lower. In this study, we have taken into account the impact of variable survival on cancer risks by calculating risks as a function of attained age, from 20 to 80 years.

METHODOLOGY

The lifetime attributable risk (LAR) of cancer incidence (ie, in excess of background risk) was estimated for 12 procedure types, based on the respective typical radiation dose and age-at-exposure. The median and interquartile range of ages at which each procedure type is undertaken was calculated (table 1) for 4574 cardiac catheterisations carried out since 2002 on patients aged under 22 years, at five UK hospitals, using Siemens Axiom Artis or Artis Zee equipment. Radiation doses were estimated for 2749 procedures falling within the respective interquartile age range for each procedure type. Equivalent doses, in millisieverts (mSv), were estimated for the lungs, bone marrow, stomach, breasts, liver, and thyroid. Doses to other organs, remote from the primary field of irradiation, were sufficiently low for the risks to be considered negligible.

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Table 1 Median kerma area product and patient age and weight (interquartile range) for procedures used in risk estimations

Procedure type	Sample size	Kerma area product (Gy cm²)	Patient age (years)	Patient weight (kg)
ASD occlusion	435	1.7 (0.7–4.6)	6.2 (4.1–10.3)	21.3 (16.5–35.1)
PDA occlusion	890	1.3 (0.7–3.0)	1.8 (1.0–3.9)	10.8 (8.1–15.6)
Pulmonary valvuloplasty	316	1.3 (0.6–3.0)	0.5 (0.1–2.1)	7.1 (4.3–12.2)
Aortic valvuloplasty	165	2.0 (0.7–6.2)	0.9 (0.2–11)	9.2 (4.5–41.4)
PA balloon/stent	351	6.9 (2.9–14.7)	4.2 (1.6–9.8)	15.4 (9.9–27.3)
Coarctation balloon/stent	207	2.9 (1.4–10.6)	3.4 (0.4–12.7)	15.4 (6.2–44.5)
EPS/RFA	716	4.3 (1.5–12)	14.1 (11.7–15.9)	53.8 (41.4–64.0)
Heart biopsy	382	0.8 (0.4–1.9)	12.3 (4.2–15.1)	32.9 (15.5–49.2)
Coronary angiography	675	4.8 (2.4–10.8)	11.7 (6.9–14.9)	37.0 (22.0–52.0)
Valve replacement	38	32.2 (26.2–61.2)	14.8 (11.5–16.9)	45.0 (33.2–56.7)
Pacemaker procedures	246	1.2 (0.4–3.2)	13 (8.9–15.8)	40.8 (25.9–57.5)
Atrial septostomy	153	1.0 (0.3–2.5)	0.1 (0.0–2.9)	5.4 (3.5–15.1)

ASD, atrial septal defect; EPS, electrophysiology study; PA, pulmonary artery; PDA, patent ductus arteriosus; RFA, radiofrequency ablation.

The methodology for dose estimation has been described previously.[2] Briefly, examination-specific organ doses were estimated from dose indicators recorded at the time of each examination (kerma area product (P_{KA}), also known as dose area product), using a dosimetry system based on Monte Carlo simulations (PCXMC V2.0), and incorporating data on projection angles and beam energy obtained from a sample of structured dose reports recorded for clinical examinations. A number of modifications have since been made, including increasing the field size for some procedure types, varying X-ray energy according to patient size and accounting for table attenuation. The overall impact of these changes has been a small reduction in dose estimates.

Median organ doses for each of the 12 procedure types carried out within the interquartile age range were calculated. LAR was estimated in relation to median organ doses using the following equation:

$$\mathrm{LAR}(e,s,D) = \int_{e+L}^{a_{MAX}} \mathrm{ERR}(e,s,D,a) \times m(s,a) \times \frac{S(s,a)}{S(s,e)} \times da$$

Here, the sex (s) specific elevated relative risk (ERR), as a function of age-at-exposure (e), organ dose (D) and attained age (a), was based on models presented by the Biological Effects of Ionizing Radiation (BEIR VII) committee.[9] These are primarily based on data from the cohort study of Japanese atomic bombing survivors, though they also incorporate pooled analyses of data from other cohorts for breast and thyroid cancer. Risks were calculated for each organ, using the respective median equivalent dose and organ specific BEIR VII model.

The LAR is defined as the sum of risks between the age-at-exposure plus a 'latency period' (L, which we set at 5 years for solid cancers and 2 years for leukaemia, based on evidence from the atomic bombing survivors' study[5]), and a maximum age (a_{MAX}), set at 100 years. The ERR model assumes radiation induced cancer occurs in proportion to background rates, m(s, a). UK background rates for 2013 were obtained from Cancer Research UK.[10] The 'survival function' S(s,a)/S(s,e) is the probability of being alive at an attained age of a, conditional on reaching the exposure age e, thus starting at 1.0 and decreasing towards zero. Sex-specific figures for S(s, a), representing normal life expectancy in the UK, for a birth year of 2000, were obtained from the Office for National Statistics (ONS). Given that individuals with CHD may have shorter life expectancies, we performed a further analysis by calculating LAR for attained ages of 20–80 years by varying a_{MAX} and setting the survival function to a constant value of 1.0.

LAR was also estimated using the alternative elevated absolute risk (EAR) BEIR VII models, in which excess cancer risk is assumed to be independent of background rates. Both ERR and EAR models have advantages and disadvantages in terms of closeness of fit to epidemiological data and transferability of risks between populations. To account for this, a weighted sum of the risks estimated using the ERR and EAR methodologies was calculated in linear space. We used the weightings recommended by the BEIR VII committee: a 0.7/0.3 ERR/EAR weighting for leukaemia and oesophageal, stomach, and liver cancers, while for lung cancer, these weightings were reversed. For breast cancer, a purely additive model was used, while risks for thyroid cancer were based entirely on the ERR model. For all sites except leukaemia, calculated risks were reduced by a 'dose and dose rate effectiveness factor' (DDREF) of 1.5, designed to account for the apparently lower risks at low doses (below 200 mSv).[9]

The study received a favourable ethical opinion from the Newcastle and North Tyneside 2 Research Ethics Committee (10/H0907/47), along with Confidentiality Advisory Group approval for using patient identifiable data (ECC 7-04(j)/2010). Local research and development approval was obtained from participating hospitals supplying data.

RESULTS

The organ doses used in risk estimations are shown in the online supplementary materials for this paper. The highest doses were for the lungs (median for whole sample: 7.6 mSv), oesophagus (5.1 mSv), and breasts (4.4 mSv). The LAR of cancer incidence for individual sites, based on typical life expectancy in the UK and median organ doses, are shown in table 2 for each examination type. For example, for every 100 000 males undergoing an ASD occlusion at the representative age of 6.2 years, 9 would develop lung cancer as a result (~1 in 11 000). Equivalent figures based on 25th and 75th percentiles for organ doses are included in the online supplementary materials. Table 3 shows the attributable risk of incidence of all cancers combined, including leukaemia, at attained ages (ie, the age the individual reaches) from 20 to 80 years. More detailed tables with a breakdown by individual sites can be found in the online supplementary materials. The LAR for all cancers is dominated by leukaemia below attained ages of 30 years, with the contribution from cancers of the lung, stomach, oesophagus, and liver rising steeply beyond 40–50 years.

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Table 2 Estimated lifetime attributable risk per 100 000 of incidence of a range of cancers following different cardiac catheterizations

	Cancer site						
Procedure	**Lung**	**Stomach**	**Liver**	**Oesophagus**	**Breast**	**Thyroid**	**Leukaemia**
Males							
ASD occlusion	9 (4 to 20)	1 (1 to 2)	1 (1 to 2)	3 (0 to 6)	n/a	0.1 (0 to 0.2)	1 (0 to 3)
PDA occlusion	20 (10 to 44)	2 (1 to 3)	2 (2 to 6)	7 (0 to 15)	n/a	0.3 (0.1 to 1.1)	2 (0 to 5)
Pulmonary valvuloplasty	33 (16 to 72)	3 (2 to 6)	4 (3 to 8)	9 (0 to 21)	n/a	0.5 (0.1 to 1.7)	4 (0 to 9)
Aortic valvuloplasty	28 (13 to 61)	2 (1 to 4)	3 (2 to 7)	9 (0 to 19)	n/a	0.3 (0.1 to 1.2)	4 (0 to 9)
PA balloon/stent	54 (26 to 118)	4 (2 to 7)	7 (5 to 16)	14 (0 to 32)	n/a	0.4 (0.1 to 1.6)	5 (0 to 12)
Coarctation balloon/stent	34 (16 to 74)	3 (1 to 5)	4 (3 to 9)	9 (0 to 21)	n/a	0.3 (0.1 to 1.2)	4 (0 to 9)
EPS/RFA	16 (8 to 35)	1 (0 to 1)	1 (1 to 2)	4 (0 to 9)	n/a	0 (0 to 0.1)	2 (0 to 5)
Heart biopsy	3 (2 to 7)	0 (0 to 0)	0 (0 to 1)	1 (0 to 2)	n/a	0 (0 to 0)	1 (0 to 1)
Coronary angiography	17 (8 to 37)	1 (1 to 3)	1 (1 to 3)	5 (0 to 10)	n/a	0.1 (0 to 0.2)	3 (0 to 6)
Valve replacement	113 (54 to 246)	6 (3 to 12)	10 (8 to 24)	26 (1 to 59)	n/a	0.3 (0.1 to 1.2)	13 (1 to 29)
Pacemaker	7 (3 to 16)	1 (0 to 1)	1 (0 to 1)	2 (0 to 4)	n/a	0 (0 to 0.1)	1 (0 to 3)
Atrial septostomy	16 (8 to 35)	1 (1 to 3)	2 (1 to 4)	5 (0 to 12)	n/a	0.3 (0.1 to 0.9)	2 (0 to 5)
Females							
ASD occlusion	26 (18 to 38)	1 (1 to 2)	0 (0 to 1)	2 (0 to 7)	17 (12 to 24)	0.2 (0.1 to 0.9)	1 (0 to 2)
PDA occlusion	54 (37 to 80)	2 (1 to 3)	2 (1 to 4)	4 (0 to 17)	75 (54 to 107)	1.4 (0.4 to 5.1)	2 (0 to 4)
Pulmonary valvuloplasty	58 (39 to 86)	3 (2 to 4)	2 (1 to 4)	5 (0 to 17)	68 (48 to 96)	1.5 (0.4 to 5.6)	2 (0 to 6)
Aortic valvuloplasty	90 (61 to 133)	3 (2 to 5)	2 (1 to 6)	6 (0 to 24)	104 (74 to 147)	1.5 (0.4 to 5.6)	4 (0 to 9)
PA balloon/stent	126 (85 to 185)	4 (3 to 6)	4 (1 to 10)	8 (0 to 32)	183 (132 to 259)	1.8 (0.5 to 6.5)	4 (0 to 9)
Coarctation balloon/stent	103 (69 to 151)	3 (2 to 5)	3 (1 to 7)	6 (0 to 23)	118 (85 to 167)	1.6 (0.4 to 5.9)	4 (0 to 10)
EPS/RFA	33 (22 to 48)	1 (1 to 1)	1 (0 to 1)	2 (0 to 8)	9 (7 to 13)	0.1 (0 to 0.5)	1 (0 to 3)
Heart biopsy	8 (6 to 12)	0 (0 to 0)	0 (0 to 0)	1 (0 to 3)	5 (4 to 8)	0 (0 to 0)	1 (0 to 1)
Coronary angiography	44 (30 to 65)	2 (1 to 3)	1 (0 to 2)	3 (0 to 12)	9 (6 to 12)	0.3 (0.1 to 1.1)	2 (0 to 6)
Valve replacement	311 (210 to 458)	11 (7 to 16)	7 (3 to 19)	20 (0 to 75)	335 (240 to 474)	2.3 (0.6 to 8.4)	14 (1 to 34)
Pacemaker	14 (9 to 20)	0 (0 to 1)	0 (0 to 1)	1 (0 to 3)	6 (4 to 8)	0.1 (0 to 0.5)	1 (0 to 1)
Atrial septostomy	51 (34 to 75)	2 (1 to 3)	1 (0 to 3)	4 (0 to 15)	50 (36 to 71)	1.2 (0.3 to 4.5)	3 (0 to 6)

Figures assume normal life expectancy, based on UK background rates. Figures in parentheses represent 95% confidence intervals based on risk model elevated relative risk and elevated absolute risk coefficients.
ASD, atrial septal defect; EPS, electrophysiology study; PA, pulmonary artery; PDA, patent ductus arteriosus; RFA, radiofrequency ablation.

DISCUSSION

We have estimated the risk of developing cancer for a range of procedure types, based on the typical age at exposure and typical organ doses in UK practice for each procedure. We have also taken potentially reduced survival into account by calculating risk up to attained ages ranging from 20 to 80 years. Table 4 shows a summary of these estimated risks in a form suitable for communication of risks with patients, parents and stakeholders.

Where adjusted for age, dose, and value of DDREF, our estimates of LAR appear to be reasonably similar to those of Beels *et al*,[11] who also applied BEIR VII risk models to organ doses for 49 cardiac catheterisations done in Belgium, estimated from Monte Carlo simulations. LAR for all cancers (incidence) was reported as 0.076% and 0.205% for males and females, respectively (76 and 205 per 100 000). The median effective dose was 6.4 mSv (organ doses were not stated).

The studies by Ait Ali *et al*[12] and Johnson *et al*[13] have the advantage of including all radiation exposures, including CT, allowing cumulative LAR to be calculated, though both appear to have used effective dose and the 'all solid cancers' BEIR VII model, rather than organ doses in their calculations. The former study quotes median LAR estimates of 1 in 382 and 1 in 156 for males and females, respectively (262 and 641 per 100 000) assuming exposure at 1 year.

As with our study, Johnson *et al* have accounted for reduced survival in their risk estimates (Norwood and transplant groups). Their methodology for achieving this was different from ours, in that they replaced the BEIR VII models with the ERR figure (0.035 mSv^{-1}) reported in a recent study of cancer incidence among children undergoing CT scans.[14] Although it is difficult to isolate the impact of this change, it appears to have led to an increase, rather than a decrease, in estimated LAR, which was quoted as 799 and 1677 per 100 000 for the Norwood and transplant groups, respectively, based on respective cumulative effective doses of 28.9 and 63.8 mSv.

There is evidence that radiation induced cancers tend to occur at ages at which they are normally observed in the general population. For example, the number of excess cancers of the lungs, stomach, and liver was close to zero among Japanese atomic bombing survivors below attained ages of around 35 years.[15] The risk of cancers of these organs is only likely to be significant for patients expected to survive well into adulthood. There is some suggestion of relatively early onset of breast cancer among children treated with radiotherapy,[16 17] though early onset cases have been reported in patients treated with chemotherapy/surgery alone.[16] Early onset of leukaemia and thyroid cancer has been observed in populations exposed to radiation, though the doses from cardiac catheterisations to bone marrow and the thyroid are relatively low.

Estimated risks were higher for females than for males, due to both the higher risk per unit dose for many organs, and the important contribution of breast cancer to the risk estimates. There was no suggestion of systematic gender difference in doses. Our dose reconstructions predict relatively high breast doses in the lateral projection. However, this need not be the case; with close collimation, ensuring the anterior chest wall is

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Table 3 Estimated excess risk of cancer incidence, per 100 000, (lung, stomach, liver, thyroid, breast and leukaemia combined) as a function of attained age

	Attained age (years)						
Procedure type	**20**	**30**	**40**	**50**	**60**	**70**	**80**
Males							
ASD occlusion	1 (0 to 2)	1 (0 to 2)	1 (0 to 3)	2 (0 to 5)	4 (1 to 9)	9 (3 to 19)	16 (6 to 35)
PDA occlusion	2 (0 to 4)	2 (0 to 4)	3 (0 to 6)	4 (1 to 10)	9 (3 to 21)	19 (7 to 42)	35 (13 to 78)
Pulmonary valvuloplasty	3 (0 to 8)	4 (0 to 9)	5 (1 to 11)	8 (2 to 18)	16 (5 to 35)	31 (11 to 69)	57 (22 to 126)
Aortic valvuloplasty	3 (0 to 8)	4 (0 to 9)	5 (1 to 11)	7 (2 to 16)	14 (4 to 31)	27 (9 to 60)	49 (18 to 109)
PA balloon/stent	4 (0 to 8)	4 (1 to 10)	6 (1 to 14)	11 (3 to 24)	23 (7 to 51)	48 (17 to 106)	90 (35 to 198)
Coarctation repair	3 (0 to 7)	4 (0 to 8)	5 (1 to 10)	8 (2 to 17)	16 (5 to 35)	32 (11 to 70)	58 (22 to 128)
EPS/RFA	0 (0 to 1)	1 (0 to 2)	2 (0 to 3)	3 (1 to 6)	6 (2 to 14)	14 (5 to 30)	26 (9 to 56)
Heart biopsy	0 (0 to 0)	0 (0 to 1)	0 (0 to 1)	1 (0 to 2)	2 (0 to 3)	3 (1 to 7)	6 (2 to 12)
Coronary angiography	1 (0 to 2)	1 (0 to 3)	2 (0 to 5)	4 (1 to 8)	8 (2 to 17)	16 (5 to 35)	29 (11 to 64)
Valve replacement	2 (0 to 5)	5 (1 to 12)	9 (2 to 21)	19 (5 to 43)	45 (14 to 99)	96 (34 to 212)	182 (70 to 400)
Pacemaker	0 (0 to 1)	1 (0 to 1)	1 (0 to 2)	2 (0 to 3)	3 (1 to 7)	7 (2 to 15)	12 (4 to 27)
Atrial septostomy	2 (0 to 4)	2 (0 to 5)	3 (0 to 6)	4 (1 to 10)	8 (2 to 18)	16 (5 to 36)	29 (11 to 64)
Females							
ASD occlusion	1 (0 to 1)	1 (0 to 2)	3 (1 to 5)	7 (4 to 11)	14 (9 to 22)	26 (17 to 41)	43 (28 to 68)
PDA occlusion	2 (0 to 4)	4 (2 to 7)	9 (5 to 16)	23 (15 to 36)	47 (31 to 73)	82 (54 to 128)	130 (86 to 202)
Pulmonary valvuloplasty	2 (0 to 5)	4 (2 to 8)	9 (5 to 16)	22 (14 to 36)	45 (29 to 72)	80 (52 to 125)	127 (83 to 200)
Aortic valvuloplasty	3 (1 to 8)	6 (2 to 12)	14 (8 to 24)	33 (21 to 53)	68 (45 to 107)	121 (80 to 189)	193 (127 to 301)
PA balloon/stent	3 (1 to 7)	8 (4 to 14)	21 (13 to 34)	53 (35 to 82)	110 (74 to 168)	193 (130 to 295)	305 (204 to 467)
Coarctation repair	3 (1 to 7)	6 (3 to 12)	15 (8 to 26)	37 (23 to 59)	77 (51 to 119)	137 (90 to 211)	218 (144 to 337)
EPS/RFA	0 (0 to 1)	1 (0 to 2)	2 (1 to 3)	5 (3 to 8)	12 (7 to 19)	24 (15 to 38)	42 (26 to 67)
Heart biopsy	0 (0 to 0)	0 (0 to 1)	1 (0 to 1)	2 (1 to 3)	4 (3 to 7)	8 (5 to 13)	14 (9 to 22)
Coronary angiography	1 (0 to 2)	1 (0 to 3)	3 (1 to 5)	6 (3 to 11)	15 (9 to 25)	31 (18 to 51)	54 (33 to 89)
Valve replacement	2 (0 to 5)	12 (6 to 22)	38 (23 to 61)	101 (66 to 157)	219 (145 to 336)	396 (262 to 610)	638 (421 to 987)
Pacemaker	0 (0 to 0)	0 (0 to 1)	1 (1 to 2)	3 (2 to 4)	6 (4 to 9)	11 (7 to 18)	19 (12 to 31)
Atrial septostomy	2 (0 to 5)	4 (1 to 8)	8 (4 to 14)	17 (10 to 29)	36 (23 to 57)	64 (41 to 101)	102 (66 to 162)

Figures in parentheses represent 95% confidence intervals for risk model elevated relative risk and elevated absolute risk coefficients.
ASD, atrial septal defect; EPS, electrophysiology study; PA, pulmonary artery; PDA, patent ductus arteriosus; RFA, radiofrequency ablation.

Table 4 Estimated lifetime risk of radiation induced cancer incidence (all sites combined, risks rounded to the nearest hundred) presented in the form 1 in x, for both normal and reduced life expectancy

	Normal life expectancy		Survival to 50 years	
Procedure	**Males 1 in:**	**Females 1 in:**	**Males 1 in:**	**Females 1 in:**
ASD occlusion	6600	2100	50 000	14 300
PDA occlusion	3000	700	25 000	4300
Pulmonary valvuloplasty	1900	700	12 500	4500
Aortic valvuloplasty	2200	500	14 300	3000
PA balloon/stent	1200	300	9100	1900
Coarctation balloon/stent	1800	400	12 500	2700
EPS/RFA	4200	2100	33 000	20 000
Heart biopsy	20 000	6700	100 000	50 000
Coronary angiography	3700	1600	25 000	16 700
Valve replacement	600	150	5300	1000
Pacemaker procedure	8300	4500	50 000	33 000
Atrial septostomy	3800	900	25 000	5900

Figures are based on typical organ doses in UK practice, based on kerma area product levels given in table 1.
ASD, atrial septal defect; EPS, electrophysiology study; PA, pulmonary artery; PDA, patent ductus arteriosus; RFA, radiofrequency ablation.

entirely excluded from the primary radiation field, breast doses, and associated risks, can be reduced by around 80%. Lung dose may also be reduced through the use of lung 'shuttering' techniques. These practices should be especially encouraged for pulmonary artery angioplasty and pulmonary valve replacement —both relatively high dose procedures carried out on patients with potentially good survival.

The risk estimates presented in tables 2 and 3 are based on median organ doses for each procedure type. Considerable variation in dose is seen, however, from one procedure to the next, or between different centres, depending on equipment and technique preferences.[2] Risk estimates based on 25th percentiles of organ doses (shown in the online supplementary materials) were around 40% lower than those based on median doses, while those based on 75th percentiles are around 80% higher. The presented risk estimates are based on median ages at which each procedure is done. The BEIR VII models used in our LAR estimates assume risks fall with increasing age-at-exposure (figure 1). Where procedures are commonly done at other ages, we have provided further risk estimates, for all sites combined, in the online supplementary materials, based on representative median doses. A further table of LAR estimates is provided for exposure ages of 0–20 years, based on median organ doses for the whole cohort.

There are several sources of uncertainty in risk estimates derived using the modelling approach. The uncertainty in the

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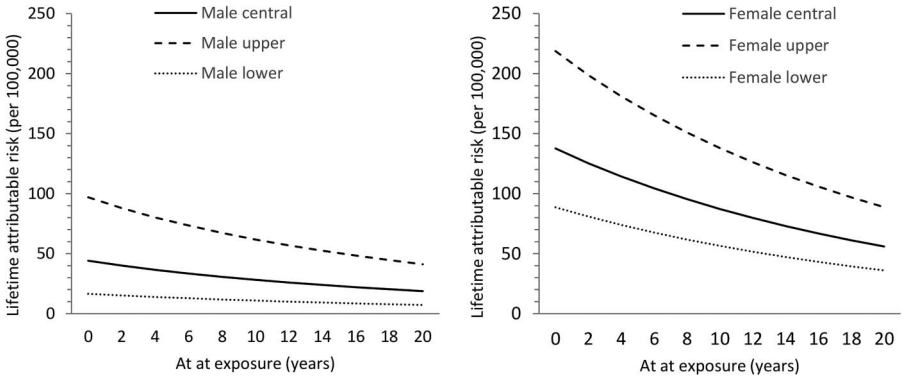


Figure 1 Lifetime attributable risk for all cancers combined as a function of age-at-exposure. Upper and lower bounds are based on 95% confidence intervals of elevated relative risk (ERR) and elevated absolute risk (EAR) risk model coefficients. Risks based on average dose for all procedures combined.

value of ERR and EAR risk coefficients is reflected in 95% confidence intervals incorporated into these estimates. A linear relationship between radiation dose and excess risk is assumed, with no threshold dose below which there is no risk. This approach is the basis for radiation protection standards in the UK. There is currently insufficient evidence to confirm or refute alternative proposals. The decision to use BEIR VII risk models, as opposed to others developed by the International Commission on Radiological Protection (ICRP)[18] or the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR)[4] was arbitrary. Although all are based on the same underlying data, the modifying effect of age-at-exposure varies between models. In the ICRP approach, lung cancer ERR increases with increasing age-at-exposure, in contrast to the BEIR VII model. A sensitivity analysis was carried out by removing the age-adjustment term from the risk models for lung cancer—meaning the risks do not vary with age-at-exposure. This resulted in an average reduction in LAR, for all sites combined, by 37% for males and 26% for females, assuming normal life expectancy.

The decision to apply either multiplicative or additive methodologies, or the weighting of both in the combined approach, also lacks common consensus.[19] ICRP 103 risk estimates utilise equal ERR/EAR weightings for liver and stomach cancer and a purely additive model for leukaemia.[18] For the current study we used the weightings recommended by the BEIR VII committee[9] and the online risk calculation tool RadRat[20] of 0.7/0.3 for all three sites. Risk estimates based on relative risk transport are also affected by regional variation in background rates. The estimates presented in this study are based on UK-wide background rates and may differ from those obtained using rates specific to the region of residence of individual patients.

It should be noted that the estimated risks presented here are specifically those related to radiation exposure and do not represent the overall risk of cancer in this group per se. Our risk estimates are based on the assumption that background cancer rates among people with CHD are the same as the general population. A number of studies have suggested relatively high cancer rates in this group, however,[21 22] especially among those undergoing transplantation.[23] Our risks based on ERR models may, therefore, be underestimates, although the relative contribution of radiation exposure and genetic factors to observed cancer rates among CHD patients is currently unclear. Increasing background rates by 50% results in an increase in LAR for all sites of 25% and 14% for males and females, respectively. Conversely, the risk of lung cancer is influenced by smoking rates, which tend to be relatively low[24] among adults with CHD. In this respect, our risk estimates for radiation induced lung cancer may be overly pessimistic.

It is generally assumed that low doses (<200 mSv) or dose rates (<0.1 mGy/min) result in a decreased risk, per unit dose, compared to higher doses—hence the practice of reduction in estimated LAR by a 'DDREF'. The value of DDREF used in this study (1.5) was equal to that used by the BEIR VII committee.[9] Models presented in ICRP 103[18] utilise a DDREF of 2.0, which if adopted here, would lead to a reduction in LAR by 25%. However, recent studies of cancer mortality in nuclear workers[25 26] and following CT scans[14 27] do not suggest a reduction in risk for low or protracted exposures, implying a DDREF of no more than 1.0. Adopting a DDREF of 1.0 would lead to an increase in estimated LAR by 33%.

Information on the latency period between exposure and cancer development, which we set at 5 and 2 years for solid cancers and leukaemia, respectively, is limited. The impact of changes to the latency period for solid cancers is negligible as the contribution to LAR from early years following exposure is small. Leukaemia LAR estimates are more sensitive, however, falling by around 25% when the latency period is doubled to 4 years.

Finally, risk estimation must also take into account the uncertainty in dose estimates. The combined uncertainty due to variation in beam angle, X-ray energy, and field size from expected values was estimated at around ±30%. This does not include inherent uncertainty due to differences in organ shape and density between the somewhat crude representation of the human body (phantom) used in Monte Carlo simulations, and real patients. The alternative methodology of using physical measurements in tissue equivalent mannequins also involves a number of anatomical approximations and it is not possible to claim any one approach provides more accurate dose estimates than the other. Breast dose errors are potentially large (up to +200% and −90%) due to the difficulty in determining breast inclusion within the primary field in the lateral projection. We have assumed the thyroid is entirely excluded from the primary beam, thus receiving a dose only from scattered radiation. If the primary field includes the thyroid, the dose, and the associated risk of cancer, increases by a factor ranging from 5 to 20 depending on patient size (frontal projection).

CONCLUSION

The risk of cancer associated with radiation exposures from cardiac catheterisations is relatively low, considering the diagnostic and therapeutic value of these procedures. For the most common procedures, assuming normal life expectancy, the attributable risk of cancer was below 50 per 100 000 (0.05% or 1 in 2000) for males and 200 per 100 000 (0.2%, or 1 in 500) for females. For those patients with reduced life expectancy,

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radiation related risks may be especially low. The risk of breast cancer, especially following pulmonary artery angioplasty and valve replacements, is the greatest concern.

Key messages

What is already known on this subject?

- The radiation exposure from cardiac catheterisations is associated with an increased lifetime cancer risk. Most previous assessments assume normal life expectancy and are based on risks for all cancers combined.

What might this study add?

- The study provides information on site-specific risks based on individual organ doses, and takes into account potentially reduced survival among people with congenital heart disease.
- Excluding valve replacements and biopsies, the average lifetime risk is 1 in 3600 for males and 1 in 1400 for females.
- For children with reduced survival chances, risks may be reduced by a factor of 7 or more.

How might this impact on clinical practice?

- At current UK dose levels, the benefit from these procedures far outweighs the risk of radiation induced cancer.
- Risks are strongly related to survival as most diseases will not manifest until middle age.
- Care should be taken to avoid exposure of the breasts in the lateral projection, where possible.

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