RISK ESTIMATES FOR MENINGIOMAS AND OTHER LATE EFFECTS AFTER DIAGNOSTIC X-RAY EXPOSURE OF THE SKULL

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This study aims to investigate the contribution of diagnostic exposures to the rising rates of brain tumours and other neoplasms which are observed in several industrial nations. Included are benign tumours in the head and neck region and cataracts which are neglected in usual risk estimates by international and national radiation protection committees. Dose–effect relationships for tumours of the brain, skin, thyroid and other sites of the head region, leukaemia and cataracts are taken from the literature. Risk estimates are derived for paediatric head computed tomographies (CTs) as well as for brain tumours in adults. On the basis of estimates for Germany about the number of head scans, the annual rate of radiation-induced diseases is calculated. About 1000 annual paediatric CT investigations of the skull will lead to about three excess neoplasms in the head region, i.e. the probability of an induced late effect must be suspected in the range of some thousands. Additionally, a relevant increase of cataracts must be considered. The radiation-induced occurrence of meningiomas and other brain tumours most probably contributes to the continuously increasing incidence of these diseases which is observed in several industrial nations, as well as the exposure of the bone marrow by CT to the increase of childhood leukaemia.

INTRODUCTION

The 'effective' dose as a measure for side effects by diagnostic exposures is criticised because it does not evaluate the higher sensitivity of patients in young ages. Because it relates only to cancer induction it does not take into account that the onset of the disease may occur very early in life after exposure in childhood. A further problem is that ionising radiation causes also benign tumours in many tissues. A very important example is the induction of tumours of the central nervous system (CNS) which are mainly of benign type.

BRAIN TUMOURS IN CONSEQUENCE OF SKULL EXPOSURE

With the increasing availability of computed tomography (CT) examinations, CNS tumours have increased, specifically meningiomas, as indicated on the registries of several countries. The investigators usually assume that the higher incidence values are the consequence of improved diagnosis with an advanced imaging technique. But this should have led then to a kind of saturation which was not observed.

The sensitivity of the brain tissues to develop benign and malign tumours after diagnostic X-rays was shown in several case–control studies, four of them from dental exposures (Table 1).

The first one was done in Los Angeles County in women with meningiomas. Persons with four and more panorama films showed a 2.5-fold significant increase. Another US study found a very high effect (relative risk 10.7) after dental X-raying for malign brain tumours which had appeared as a cluster. A Swedish investigation in Uppsala which was done on tumour patients 1987–90 showed a significant increase only in meningiomas, and the more recent findings of a US study relate exclusively to meningiomas.

The last cited study in Table 1 was done in Sweden about causes for meningiomas and other brain tumours and found an effect after X-rays in the head and neck region.

These studies show low level effects in brain, mainly in adults. A dose is, however, not derivable because of the different types of dental and other investigations and the fact, that the dental exposures decreased since the beginning of the regarded period. Therefore, studies with dose-effect findings had to be looked for. These are listed in Table 2.

The A bomb survivors were mainly adults at the time of the bombing. Elevated rates were found for all CNS tumours and the benign tumour categories meningiomas and schwannomas. The effect appeared as proportional to dose and the authors emphasise that it is significant also for low doses of <1 Sv. In order to gain a result for Table 2, it can be derived from their paper that 78 % of meningiomas were intracranial[1]. The number of brain tumours can be estimated by the finding that 88 % of all CNS tumours were intracranial[2].

The other cohorts of Table 2 were exposed in childhood. The children treated for tinea capitis

(fungus disease of the skin) were irradiated at the head to remove the hair. A large cohort of very young patients– babies treated for haemangiomas— was followed up in Sweden.

Table 1. Brain tumours after diagnostic X-ray exposure.

Investigation	Study about	Results (relative risk)
Dental exposures		
Los Angeles[14] 1972–79	Meningiomas	2.5 $p=0.04$
$\geq 4 \times$ Panorama		
Missouri Cluster[15] 1973–82	Malign tumors	10.7 (1.4–81)
Uppsala[16] 1987–90	Meningiomas	2.1 (1.0–4.3)
$\geq 1 \times$ annually	Gliomas	Not elevated
	All tumours	Not sign. elevated
USA[17] 1995–2003	Meningiomas	2.0 (1.0–4.2)
$\geq 6 \times$ Panorama		
X-ray neck/head		
Two Swedish regions[18] 1994–96	Meningiomas	5.0 (1.6–15.8)
	All tumours	1.6 (1.0–2.6)

Case–control studies.

The figures for the absolute risk are rather consistent if one considers the increasing sensitivity with lower ages. An exception is meningiomas in the A bomb survivors, but a clear effect is found in the diagnostic studies.

For estimation of the induction rate by head CTs for meningiomas in adults (Table 3), it is assumed that it corresponds at least to the finding in the A bomb survivors of 3.4 per 10 000 as noted in Table 2. The upper limit of the confidence range is multiplied by a factor of 2 because it is considerd that the Japanese collective was exposed to extremely high-energetic gamma rays[3]. In contrast to ICRP, the Relative Biological Effectiveness of this radiation should be regarded as lying remarkably below that of diagnostic X-rays. For brain tumours in adults, to the A bomb survivor data were also referred to. For exposed children in the 0–15 age-band, the mean is used in the tinea capitis studies. For all brain tumours, it is 39.9 and for meningiomas 16.1 per 10 000.

Table 3 shows data for Germany 2007. The number of head CTs in childhood and in adults is only a rough estimate taken from random studies in Germany[4]. The authors wanted to compare the induction rate with the current incidence in order to

Table 2. Dose-effect findings about brain tumours.

Age at exposure	Jap. A bomb survivors[1] All ages	Tinea capitis Israel[19] Children	Tinea capitis USA[20] Children	Haemangioma therapy Sweden[21] 5 months (mean)
Meningiomas	3.4 (0–11) n.s.	19.2	12.8	50.5
All brain tumours	23.9 (7–56)	31.6	48.2	74.0 (9.4–153)

n.s., not significant.
Absolute risk 10^{-4} Sv^{-1} (cases per 10 000 persons exposed by 1 Sv).

Table 3. Estimation of annually induced brain tumours in Germany 2007 by CT investigations in comparison with national incidence data.

	Children 0–14 y: 11.45 million, 97 000 CTs per year		Total population: 82.4 million, 3.41 million CTs per year	
	All brain tumours	Meningiomas	All brain tumours	Meningiomas
Absolute risk 10^{-4} Sv^{-1}	40 (20–60)	18 (8–32)	7.4–48	3.4–22
Induced cases per year	23	9.3	100–1300	46–600
Induced cases in childhood per year	1	0.5		
Induced incidence 10^{-5} per year	0.20	0.08	0.1–1.6	0.06–0.73
Induced incidence in childhood 10^{-5} per year	0.01	0.004		
Incidence Germany 10^{-5} per year	2.75	0.05	8.4	2.1
Relative increase	0.004 in childhood	0.08 in childhood	0.01–0.16	0.03–0.35

Assumed brain dose 60 mSv.

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describe the possible relative increase. The incidence of (benign) brain tumours is, however, not registered in Germany and was therefore derived from several published information in West and East Germany and the USA[4].

Table 4. Leukaemia in childhood in Germany and head CTs.

Absolute risk 10^{-4} Sv^{-1}	Induced cases per 1000 CTs	Induced cases per year	Incidence 10^{-5} y^{-1}
11.4–22.8	0.12–0.24	12–24	0.1–0.2 induced excess

2007 number of children 11.45 million, number of head CTs 97 000 per year, bone marrow dose in the head 107 mSv per CT investigation[8], German incidence 2004 was 4.3 10^{-5} y^{-1}.

The annually radiation-induced cases do not occur immediately, the latencies are long and the excess cases are distributed over the following period. Therefore, a constant exposure by CT in the future was assumed, which will lead to a constant induction rate per year. The amount of excess cases appearing in childhood after exposure in childhood was estimated to be 5 %[4].

The mean CT exposure of the brain is taken from an official estimate of 2–4 mSv effective dose[5], which corresponds to 40–80 mSv brain dose taking the former tissue weighting factor 0.05 of the ICRP.

The results for the relative increase in future projection are as follows (Table 3, last line):

- no observable increase of all brain tumours in children,
- 8 % increase per year of meningiomas in children,

Table 5. Dose-effect data from the literature about neoplasms from irradiation of the skull except brain tumours and leukaemia.

Effect	Collective; age at exposure	Number of persons	Mean follow-up years	Cases obs./ expected	Dose Sv	Absolute risk 10^{-4} Sv^{-1}
Pituitary gland tumours	Japanese A bomb survivors[1] All ages	80 160	24.8		0.11	4.4
Salivary gland tumours	Japanese A bomb survivors[22] All ages	60 057	35.4			19.9
Malignant & benign	Tinea capitis 1–15 y[23, 24]	10 834	11; 21.5	16/4	0.39	52
	Tinea capitis 1–15 y[20, 24]	2224	39	6/2	0.39	46[a]
Other tumours of the head	Japanese A bomb survivors[25] Oral cavity and pharynx only malignant		24.8			5.7
Malignant & benign thyroid tumours	Tinea capitis 1–15 y[20]	2224	39	13/1	0.05	899
	Tinea capitis[26]	10 834	40			396[b]
	Hemangioma therapy Mean age 5 y[27]	14 350	34		1.07	28.6[b]
Parathyroid adenomas	Hemangioma therapy Mean age 5 y[28]	28 000	34	43/20.5	0.20	40.3
	Therapy cervical spine Mean age 48.9 y[29]	8144	22.2	22/10.5	1.0	14.1
Skin cancer	Tinea capitis[30] 1–15 y	2224	39	3.6	4.8	240

[a]Not significant.
[b]Only malignant tumours investigated.

- 1–16 % increase per year of all brain tumours in the whole population and
- 3–35 % increase per year of meningiomas in the whole population.

LEUKAEMIA AFTER SKULL EXPOSURE

After ICRP, up to 30 % of the bone marrow of children is situated in the skull. The leukaemia risk in dependency of age at exposure was calculated by the BEIR committee[6] using data of the A bomb survivors. As a reference, their estimate for children at the age of five which is $6.5 \ 10^{-4} Sv^{-1} \ y^{-1}$ and lasts for 10 y was taken. Therefore, an absolute risk of $65 \ 10^{-4} Sv^{-1}$ is got. For an upper limit, it is multiplied again with two with regard to the lower effectiveness of the A bomb radiation. Because the skull of the 5 y-old contains only 17.5 % of the bone marrow risk figures for skull exposure of 11.4–22.8 are received (Table 4).

The German incidence of childhood leukaemia is 4.3 cases in 100 000 per year. Between 1980 and 2004, an annual increase of 0.06 cases per 100 000 and year is observed[7]. The derived radiation-induced excess by head CTs is higher: 0.1–0.2 (Table 4), but this may not contradict to the reality because it is a projection to the future.

OTHER TUMOURS IN THE HEAD AND NECK REGION

Table 5 shows dose-effect data from the literature for other tumours in the head and neck region. Table 6 contains the estimated risk figures for them. Tissue

Table 6. Estimate of radiation-induced neoplasms (morbidity) from exposure by paediatric CTs of the head in Germany except brain tumours and leukaemia.

Effect	Tissue dose (mSv)	Number of cases per 1000 CTs	Annual number Germany
Pituitary gland tumours	80	0.04	3.4
Salivary gland tumours	60	0.31	30
Other tumours in the head region	60	0.03	3.3
Thyroid tumours	6	0.54	52
Parathyroid adenomas	6	0.03	2.3
Skin cancer	80	1.92	186
Sum		2.87	277

97 000 CTs assumed in 2007.

doses are taken from the literature[8–10]. Together with the brain tumours (0.2 per 1000 CTs) and leukaemia (0.15 per 1000 CTs), a number of about three radiation-induced tumour cases after 1000 head CTs applied in childhood is derived.

CATARACTS

Cataracts were formerly thought to occur only after high exposures of several Sv. Recent experience in populations living in contaminated regions (e.g. Chernobyl) and in pilots lead to the opinion that they may also represent stochastic effects[11].

At present, dose-effect data are still rare. The Swedish haemangioma patients showed a very high effect of $8360 \ 10^{-4} Sv^{-1}$ with a mean dose of the eye lens of 0.36 Sv[12]. This is certainly due to the high sensitivity in very young ages. 'Liquidators' of Chernobyl—mainly young men who managed the shielding of the reactor radiation—showed a much lower effect of $25 \ 10^{-4} Sv^{-1}$[13]. Because there is no standardisation of diagnosis and agreement up to now about the state of lens opacity which should be noted as 'cataract' for further research in this field has to be awaited.

CONCLUSIONS

- 1000 annual paediatric CT investigations of the skull will lead to about three excess neoplasms in the head region. Additionally, a relevant increase of cataracts must be considered.
- The radiation-induced occurrence of meningiomas and other brain tumours most probably contributes to the continuously increasing incidence of these diseases which is observed in several industrial nations, as well as the exposure of the bone marrow by CT to the increase of childhood leukaemia.

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