The Chernobyl Catastrophe: Taking Stock of 25 Years of Ecological and Health Damages. International Congress Berlin, April 6-8, 2011

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

S. Pflugbeil[1], C. Pflugbeil[2], I. Schmitz-Feuerhake[1]
[1] German Society of Radiation Protection, Berlin, Germany
[2] Immanuel Hospital, Berlin, Germany

Abstract

Purpose: To investigate the contribution of diagnostic exposures to the rising rates of brain tumors and other neoplasms which are observed in several industrial nations. Included are benign tumors in the head and neck region and cataracts which are neglected in usual risk estimates by international and national radiation protection committees.

Method: Dose-effect relationships for tumors of the brain, skin, thyroid, and other sites of the head region, leukemia, and cataracts are taken from the literature. Risk estimates are derived for pediatric head CTs as well as for brain tumors in adults. On the basis of estimates for Germany about the number of head scans, the annual rate of radiation-induced diseases is calculated.

Results: 1000 annual paediatric CT investigations of the skull will lead to about 3 excess neoplasms in the head region, i.e., the probability of an induced late effect must be suspected in the range of some thousandths. Additionally, a relevant increase of cataracts must be considered.

Conclusions: The radiation-induced occurence of meningiomas and other brain tumors 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 leukemia.

Contact author E-mail: ingesf@uni-bremen.de

INTRODUCTION

The "effective" dose as a measure for side effects by diagnostic exposures is criticized 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 tumors in many tissues. A very important example is the induction of tumors of the central nervous system (CNS) which are mainly of benign type.

BRAIN TUMORS IN CONSEQUENCE OF SKULL EXPOSURE

With the increasing availability of CT exams, CNS tumors 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 advanced imaging techniques. But this should have lead then to a kind of saturation which was not observed.

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

Table 1. Brain tumors after diagnostic X-ray exposure.
Case-control studies

Investigation		Study about	Results (relative risk)
Dental exposures	Los Angeles[1] 1972-1979 ≥ 4 x Panorama	Meningiomas	2.5 P=0.04
	Missouri Cluster[2] 1973-1982	Malign tumors	10.7 (1.4-81)
	Uppsala[3] 1987-1990 ≥ 1 x annually	Meningiomas Gliomas All tumors	2.1 (1.0-4.3) not elevated not sign.elevated
	U.S.A.[4] 1995-2003 ≥ 6 x Panorama	Meningiomas	2.0 (1.0-4.2)
X-ray Neck/Head	2 Swedish regions[5] 1994-1996	Meningiomas All tumors	5.0 (1.6-15.8) 1.6 (1.0-2.6)

The first one was done in Los Angeles County in women with meningiomas. Persons with 4 and more panorama films showed a 2.5 fold significant increase. Another U.S. study found a very high effect (relative risk 10.7) after dental X-raying for malign brain tumors which had appeared as a cluster. A Swedish investigation in Uppsala which was done in tumor patients 1987-90 showed significant increase only for meningiomas, and the more recent findings of an U.S. study relate exclusively to meningiomas.

The last cited study in Table 1 was done in Sweden about causes for meningiomas and other brain tumors 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 we had to look for studies with dose-effect findings. These are listed in Table 2.

The A-bomb survivors were mainly adults at time of the bombing. Elevated rates were found for all CNS-tumors and the benign tumor categories meningiomas and schwannomas. The effect appeared as proportional to dose and the authors emphasize 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 [6]. The number of brain tumors can be estimated by the finding that 88 % of all CNS-tumors were intracranial [10].

Table 2. Dose-effect findings about brain tumors.

Absolute risk 10^{-4} Sv^{-1} (cases per 10,000 persons exposed by 1 Sv)

Age at exposure	Jap.A-bomb survivors[6] *All ages*	Tinea capitis Israel[7] *Children*	Tinea capitis U.S.A.[8] *Children*	Hemangiom therapy Sweden[9] *5 months (mean)*
Meningiomas	3.4 (0-11) n.s.*	19.2	12.8	50.5
All brain tumors	23.9 (7-56)	31.6	48.2	74.0 (9.4-153)

*) not significant

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 hemangiomas – was followed up in Sweden.

The figures for the absolute risk are rather consistent if one considers the inreasing sensitivity with lower ages. An exception are 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) we assume 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 we consider that the Japanese collective was exposed by extremely high-energetic gamma rays[11]. 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 tumors in adults we also refer to the A-bomb survivor data. For exposed children in the 0-15 age-band we use the mean in the tinea capitis studies. For all brain tumors 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[12]. We wanted to compare the induction rate with the current incidence in order to describe the possible relative increase. The incidence of (benign) brain tumors is, however, not registered in Germany and was therefore derived from several published informations in West and East Germany and the U.S.[12].

The annually radiation-induced cases do not occur immediately, the latencies are long and the excess cases are distributed over the following period. Therefore, we assumed a constant exposure by CT in the future which will lead to a constant induction rate per year. The amount of excess cases appearing in childhood after exposure in childhood was estimated by us to be 5 %[12].

The mean CT exposure of the brain is taken from an official estimate of 2-4 mSv effective dose[13], 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 tumors in children
- 8 % increase per year of meningiomas in children
- 1-16 % increase per year of all brain tumors in the whole population
- 3-35 % increase per year of meningiomas in the whole population

Table 3. Estimation of annually induced brain tumors in Germany 2007 by CT-investigations in comparison to national incidence data.

Assumed brain dose 60 mSv

	Children 0-14 years 11.45 million 97,000 CTs per year		Total population 82.4 million 3.41 million CTs per year	
	All brain tumors	***Meningiomas***	***All brain tumors***	***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**

LEUKEMIA AFTER SKULL EXPOSURE

After ICRP, up to 30 % of the bone marrow of children is situated in the skull. The leukemia risk in dependency of age at exposure was calculated by the BEIR committee(14) using data of the A-bomb survivors. As a reference, we take their estimate for children at the age of 5 which is 6.5 $10^{-4}Sv^{-1}y^{-1}$ and lasts for 10 years. Therefore, we get an absolute risk of 65 $10^{-4}Sv^{-1}$. For an upper limit we multiply again with 2 on regard of the lower effectiveness of the A-bomb radiation. Because the skull of the 5 year-old contains only 17.5 % of the bone marrow we receive risk figures for skull exposure of 11.4-22.8 (Table 4).

The German incidence of childhood leukemia 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(15). 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.

Table 4. Leukemia in childhood in Germany and Head CTs.
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[16]
German incidence 2004 was 4.3 $10^{-5}y^{-1}$

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

OTHER TUMORS IN THE HEAD AND NECK REGION

Table 5 shows dose-effect data from the literature for other tumors in the head and neck region. Table 6 contains the estimated risk figures for them. Tissue doses are taken from the literature[16,26,27]. Together with the brain tumors (0.2 per 1000 CTs) and leukemia (0.15 per 1000 CTs) we derive a number of about 3 radiation-induced tumor cases after 1000 head CTs applied in childhood.

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[28].

At present, dose-effect data are still rare. The Swedish hemangioma patients showed a very high effect of 8,360 $10^{-4}Sv^{-1}$ with a mean dose of the eye lens of 0.36 Sv[29]. 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 $10^{-4}Sv^{-1}$[30]. Because there is no standardisation of diagnosis and agreement up to now about the state of lens opacity which should be noted as “cataract” we have to wait for further research in this field.

CONCLUSIONS

- 1000 annual pediatric CT investigations of the skull will lead to about 3 excess neoplasms in the head region. Additionally, a relevant increase of cataracts must be considered.
- The radiation-induced occurence of meningiomas and other brain tumors 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 leukemia.

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

Effect	Collective; Age at exposure	Number of persons	Mean follow-up years	Cases obs./ expected	Dose Sv	Absolute risk $10^{-4}Sv^{-1}$
Pituary gland tumors	Japanese A-bomb survivors[6] All ages	80,160	24.8		0.11	4.4
Salivary gland tumors	Japanese A-bomb survivors[17] All ages	60,057	35.4			19.9
malignant	Tinea capitis 1-15 y.[18,19]	10,834	11; 21.5	16/4	0.39	52
& benign	Tinea capitis 1-15 y.[8,19]	2,224	39	6/2	0.39	46*)
Other tumors of the head	Japanese A-bomb survivors[20] Oral cavity and pharynx only malignant		24.8			5.7
Malignant	Tinea capitis 1-15 y.[8]	2,224	39	13/1	0.05	899
& benign	Tinea capitis[21]	10,834	40			396**)
thyroid tumors	Hemangioma therapy Mean age 5 y.[22]	14,350	34		1.07	28.6**)
Parathyroid adenomas	Hemangioma therapy Mean age 5 y[23]	28,000	34	43/20.5	0.20	40.3
	Therapy cervical spine Mean age 48.9 y.[24]	8,144	22.2	22/10.5	1.0	14.1
Skin cancer	Tinea capitis[25] 1-15 y.	2,224	39	3.6	4.8	240

*) not significant **) only malignant tumors investigated

Table 6. Estimate of radiation-induced neoplasms (morbidity) from exposure by pediatric CTs of the head in Germany except brain tumors and leukemia.

97,000 CTs assumed in 2007

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

REFERENCES

1. Preston-Martin, S. and White, S.C. Brain and salivary gland tumors related to prior dental radiography: implications for current practice. J. Am. Dental Ass. 120, 151-158 (1990).
2. Neuberger, J.S., Brownson, R.C., Morantz, R.A. and Chin, T.D. Association of brain cancer with dental x-rays and occupation in Missouri. Cancer Detect. Prev. 15, 31-34 (1991).
3. Rodvall, Y., Ahlbom, A., Pershagen, G., Nylander, M. and Spännare, B. Dental radiography after age 25 years, amalgam fillings and tumours of the central nervous system. Oral Oncol. 34, 265-269 (1998).
4. Longstreth, W.T. Jr., Phillips, L.E, Drangsholt, M., Koepsell, T.D., Custer, B.S., Gehrels, J.A. and van Belle, G. Dental X-rays and the risk of intracranial meningioma: a population-based case-control study. Cancer 100, 1026-1034 (2004).
5. Hardell, L., Hansson Mild, K.H., Pahlson, A. and Hallquist, A. Ionizing radiation, cellular telephones and the risk for brain tumours. Eur. J. Cancer Prev. 10, 523-529 (2001).
6. Preston, D.L., Ron, E., Yonehara, S., Kobuke, T., Fujii, H., Kishikawa, M., Tokunaga, M., Tokuoka, S. and Mabuchi, K. Tumors of the nervous system and pituary gland associated with atomic bomb radiation exposure. J. Natl. Cancer Inst. 94, 1555-1563 (2002).
7. Sadetzki, S., Chetrit, A., Freedmann, L., Stovall, M., Modan, B. and Novikov, I. Long-term follow-up for brain tumor development after childhood exposure to ionizing radiation for Tinea capitis. Radiat. Res. 163, 424-432 (2005).
8. Shore, R.E., Moseson, M., Harley, N. and Pasternack, B.S. Tumors and other diseases following childhood x-ray treatment for ringworm of the scalp (Tinea Capitis). Health Phys. 85, 404-408 (2003).
9. Karlsson, P., Holmberg, E., Lundell, M., Mattsson, A., Holm, L.E. and Wallgren, A. Intracranial tumors after exposure to ionizing radiation during infancy: a pooled analysis of two Swedish cohorts of 28,008 infants with skin hemangioma. Radiat. Res. 150, 357-364 (1998).
10. Yonehara, S., Brenner, A.V., Kishikawa, M., Inskip, P.D., Preston, D.L., Ron, E., Mabuchi, K. and Tokuoka, S. Clinical and epidemiologic characteristics of first primary tumors of the central nervous system and related organs among atomic bomb survivors in Hiroshima and Nagasaki, 1958-1995. Cancer 101, 1644-1654 (2004).
11. Straume, T. High-energy gamma rays in Hiroshima and Nagasaki: implications for risk and w_R. Health Phys. 69, 954-956 (1995).
12. Schmitz-Feuerhake, I., Pflugbeil, S. and Pflugbeil, C. Röntgenrisiko: Radiation risks from diagnostic radiology: meningiomas and other late effects after exposure of the skull (In German). Gesundheitswesen 72, 246-254 (2010).

13. Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit. Umweltradioaktivität und Strahlenbelastung im Jahr 2007. Unterrichtung durch die Bundesregierung. www.bmu.de/files/pdfs/allgemein/application/pdf/parlamentsbericht07.pdf
14. BEIR V: Committee on the Biological Effects of Ionizing Radiations, Health Effects of Exposure to Low Levels of Ionizing Radiation. Washington D.C.: Nat. Academy Press; 1990.
15. Spix, C., Eletr, D., Blettner, M. and Kaatsch, P. Temporal trends in the incidence rate of childhood cancer in Germany 1987-2004. Int. J. Cancer 122, 1859-1867 (2008).
16. Nickoloff, E. Current adult and pediatric CT doses. Pediatr. Radiol. 32, 250-260 (2002).
17. Land, C.E., Saku, T., Hayashi, Y., Takahara, O., Matsuura, H., Tokuoka, S., Tokunaga, M. and Mabuchi, K. Incidence of salivary gland tumors among atomic bomb survivors, 1950-1987. Evaluation of radiation-related risk. Radiat. Res. 146, 28-36 (1996).
18. Modan, B., Chetrit, A., Alfandary, E., Tamir, A., Lusky, A., Wolf, M. and Shpilberg, O. Increased risk of salivary gland tumors after low-dose irradiation. Laryngoscope 108, 1095-1097 (1998).
19. Harley, N.H., Albert, R.E., Shore, R.E. and Pasternack, B.S. Follow-up study of patients treated by x-ray epilation for tinea capitis. Estimation of the dose to the thyroid and pituitary glands and other structures of the head and neck. Phys. Med. Biol. 21, 631-642 (1976).
20. BEIR VII PHASE 2: Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation, Health Risks from Exposure to Low Levels of Ionizing Radiation. Washington D.C.: Nat. Academies Press; 2006 www.nap.edu.
21. Sadetzki, S., Chetrit, A., Lubina, A., Stovall, M. and Novikov, I. Risk of thyroid cancer after childhood exposure to ionizing radiation for tinea capitis. J. Clin. Endocrinol. Metab. 91, 4798-4804 (2006).
22. Lundell, M., Hakulinen, T. and Holm, L.E. Thyroid cancer after radiotherapy for skin hemangioma in infancy. Radiat. Res. 140, 334-339 (1994).
23. Holmberg, E., Wallgren, A., Holm, L.-E., Lundell, M. and Karlsson, P. Dose-response relationship for parathyroid adenoma after exposure to ionizing radiation in infancy. Radiat. Res. 158, 418-423 (2002).
24. Rasmuson, T., Damber, L., Johansson, L., Johansson, R. and Larsson, L.G. Increased incidence of parathyroid adenomas following x-ray treatment of benign diseases in the cervical spine in adult patients. Clin. Endocrinol. 57, 731-734 (2002).
25. Shore, R.E., Moseson, M., Xue, X., Tse, Y., Harley, N. and Pasternack, B.S. Skin cancer after x-ray treatment for scalp ringworm. Radiat. Res. 157, 410-418 (2002).
26. Brenner, D.J., Elliston, C.D., Hall, E.J. and Berdon, W.E. Estimated risks of radiation induced fatal cancer from pediatric CT. AJR 176, 289-296 (2001).
27. Huda, W. Effective doses to adult and pediatric patients. Pediatr. Radiol. 32, 272-279 (2002).
28. Worgul, B.V., Kundiev, Y., Likhtarev, I., Sergienko, N., Wegener, A. and Medvedovsky, C.P. Use of subjective and nonsubjective methodologies to evaluate lens radiation damage in exposed populations - an overview. Radiat. Environ. Biophys. 35, 137-144 (1996).
29. Hall, P., Granath, F., Lundell, M., Olsson, K. and Holm, L.E. Lenticular opacities in individuals exposed to ionizing radiation in therapy. Radiat. Res. 152, 190-195 (1999).
30. Fedirko, P.A. and Buzunov, V.A. Risk assessment of eye diseases development in Chernobyl clean-up workers in remote period after the catastrophe. International Journal of Radiation Medicine (Kiev) 5, 211-216 (2003).