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Author
Fabrikant, J.I.

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SOMATIC EFFECTS - CANCER
SALIVARY GLANDS

Jacob I. Fabrikant and Margaret H. Sloan

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Chapter V

Somatic Effects - Cancer

Salivary Glands

Jacob I. Fabrikant, M.D., Ph.D.¹
Biology & Medicine Division
Lawrence Berkeley Laboratory
University of California, Berkeley²

and

Department of Radiology
University of California School of Medicine
San Francisco

and

Margaret H. Sloan, M.D.
Division of Cancer Control and Rehabilitation
National Cancer Institute

¹Professor of Radiology, University of California School of Medicine, San Francisco.

²Mailing Address: Donner Laboratory, University of California, Berkeley, California 94720

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Neoplasms of the salivary glands in man, both benign and malignant, have been reported to occur in excess after irradiation, but the data have been too sparse to provide estimates of radiation risk. The early reports concerned primarily children exposed to therapeutic irradiation of the neck region at high dose rates and atomic-bomb survivors of all age groups; the 1972 BEIR report mentioned salivary-gland tumors only briefly, in connection with other neoplasms of specific types. Since then additional data have been reported from several sources. The 1977 UNSCEAR report summarized briefly the major epidemiologic studies in which salivary-gland tumors have been reported after exposure to ionizing radiation, particularly after radiotherapy for benign disease. From these studies, data are emerging that may provide a preliminary estimate of radiation induction rate in relation to exposure dose.

Tumors of the salivary glands have been observed in experimental rodents exposed to irradiation.

The epidemiologic and experimental literature has not demonstrated the salivary-gland tissue to be more than moderately susceptible to the induction of benign and malignant tumors, and it is so probably only at high doses. However, the recent studies on humans have suggested a much higher susceptibility in man than was previously suspected.
Radiotherapy for Benign Disease

In their early studies of thyroid neoplasia after therapeutic irradiation of the neck and mediastinum for various benign diseases in 1,644 infants and children between 1932 and 1950, Saenger and colleagues observe two excess cases of salivary-gland tumors; comparison was made with 3,777 nonirradiated sibling controls. After a followup period of 10-18 yr, they found two malignant and no benign tumors of the salivary glands in the irradiated population and no salivary-gland tumors in the control siblings. The fields of irradiation included the salivary glands in children irradiated for lymphadenopathy in the tonsils and adenoids, and to a lesser extent for cervical adenitis. Radiation dose estimates were difficult to ascertain, but primarily less than 600 R in air. The authors reported a cumulative incidence rate for salivary-gland tumors of 0.12% in 30,254 patient-yr, or 66.1 cases per 10 patient-yr.

Hempelmann and colleagues have reported four benign salivary-gland tumors and no malignant tumors in 2,872 irradiated patients in the Rochester series of children irradiated between 1930 and 1951 for benign thymus enlargement, with a followup of 20-40 yr until 1971. The control group of 5,055 siblings had two benign and one malignant salivary-gland tumors. The precise estimates of radiation dose are not available, but doses were less than 600 R in air; the cumulative incidence rate for benign and malignant salivary-gland tumors was 0.14% in 47,313 patient-yr, or 84.5 cases per 10 patient-yr in the irradiated patients versus 19.8 cases per 10 person-yr in the control groups. On the basis
of estimates of radiation dose to the thyroid gland, however, the
risk rate would be approximately 5-10 excess salivary-gland tumors
per 10 exposed children per rad over followup period of 20-40 yr.

Janower and Miettiner observed one benign salivary-gland
tumor in 466 thymus-irradiated children treated between 1924 and
1946; two tumors occurred in 3,029 controls. The air dose was less
than 400 R. The incidence rate for salivary-gland tumors was 0.21%
in 14,037 patient-years or 71.2 cases per 10 patient-yr in the
irradiated group, and approximately 0.07% in the controls taken
as a whole.

The initial studies of Albert, Shore, and their colleagues
of 2,215 children treated in New York during 1945-1950 with x-ray
epilation for tinea capitis have now demonstrated three benign and
one malignant salivary-gland neoplasms in exposed patients in a 20-
yr followup to 1973. No salivary-gland tumors were observed in the
control group of 1,413 persons. The cumulative incidence rate for
benign and malignant salivary-gland tumors was 0.18% in approximately
44,300 patient-yr, or some 90.3 cases per 10 patient-yr. On the
basis of radiation dose estimates to the parotid gland of 39 rad
determined by Harley et al., the radiation risk rate for the 20-
yr observation period would be roughly 12 (1-35)* excess salivary
gland tumors (benign and malignant) per 10 exposed children per
rad.

*Numbers in parentheses are 90% confidence limits.
Modan and colleagues have reported the results of their detailed observations on 10,902 children in Israel treated with scalp x irradiation for tinea capitis during the 11-yr period 1949-1960. They found four malignant and three benign tumors of the salivary (parotid) glands during the 15-yr followup to 1973 in the irradiated population; one benign tumor occurred in the two control series. On the basis of phantom calculations of the mean thyroid dose in the irradiated children, a parotid-gland dose of approximately 39 rad might be estimated from the measurements of Harley et al. in the New York series. These values would yield cumulative radiation risk estimates for benign and malignant salivary-gland (parotid-gland) tumors of at least 16 excess cases per 10 children exposed per rad for the 15-yr followup period.

Atomic-Bomb Survivors, Hiroshima and Nagasaki

The original report by Belsky and colleagues on salivary-gland tumors in Japanese atomic-bomb survivors for the period 1957-1970 has now been extended to 1975. In the life span study, the cases of salivary-gland tumors reported were those indexed in several different tumor registries in both cities from 1957 to 1970 and from the ABCC-JNIH Adult Health Study index of cases. The case incidence data from Hiroshima and Nagasaki were combined. The gamma and neutron radiation estimates were added in these studies. Of 1,433 exposed persons examined in a 12-yr period (16,172 patient-yr), there was a significant excess of two cases of malignant salivary-gland tumors observed versus 0.12 expected and an excess of
one case of benign tumor observed versus 0.28 expected in the over-300-rad kerma group (observed/expected = 18.2). Assuming a mean kerma of 400-500 rads, the radiation risk estimate was approximately three (one to eight) excess salivary-gland tumors per 10 persons per rad over the 12-yr followup period, 1957-1970. No excess of salivary-gland tumors was observed in the below-300-rad kerma group (observed/expected = 0.02).

Takeichi and associates have now observed 17 benign and malignant salivary-gland tumors (1.7 expected) over a 25-yr period (1945-1971) in the atomic-bomb survivors in Hiroshima and nearby Kure within 5,000 m at the time of the bombing, as determined from records of hospital pathology departments. Standardized incidence rates for benign and malignant salivary-gland tumors were calculated as 1.8 cases per 10 exposed persons per year and 0.7 case per 10 unexposed persons per year. The incidence rates decreased with increasing distance from the hypocenter, from 3.8 cases per 10 exposed persons per year at 0-1,500 m to 1.3 cases per 10 exposed persons per year at 1,501-5,000 m. For malignant cancers alone, the standardized incidence was 2.2 cases per 10 exposed persons per year at 0-1,500 m; 0.7 case per 10 exposed persons per year, 1,500 m and beyond, and 0.1 case per 10 unirradiated persons per year. Thus, the incidence of all benign and malignant salivary-gland tumors was some 5.4 times greater among the high-dose survivors than in the unexposed group; in the low-dose survivors, the incidence was only some 1.9 times greater than in the unirradiated population. This increased incidence of tumors with
increasing proximity to the hypocenter was statistically significant 
\((p < 0.001)\). The radiation risk rate for salivary-gland tumors in 
survivors exposed in the region less than 1,500 m from the hypocenter 
(assuming total air doses of 32 rads at 1,500 m and 135 rads farther 
in) would be approximately 21 (9-41) excess tumors per 10 persons 
exposed per year, and possibly only one-third of that in survivors 
exposed at 1,500-5,000 m. The life span study dosimetry exposure 
determinations would permit a very rough estimation of radiation 
risk: perhaps no more than one or two excess salivary-gland tumors 
per 10 exposed persons per rad over the 19-yr followup period.

**Conclusions**

Since the 1972 BEIR report, additional radiation-induced 
benign and malignant salivary-gland tumors have been reported 
in significant excess in irradiated children and in Japanese 
atomic-bomb survivors. The numbers in each group are small, 
the latent period for both benign and malignant tumors is rela-
tively long, and the diagnosis has occurred after 13-25 yr. The 
induction rate for both benign and malignant tumors is low, per-
haps no more than 10 excess cases per 10 exposed children per 
rad over a 20-yr period of followup; the rate would be expected 
to increase over a longer period of observation. Exposure in 
adult life might result in a decreased risk, perhaps only one-
third or less of that after childhood exposure. No conclusions 
can yet be reached about the relationship of age at the time of 
irradiation to the incidence of tumors; in the childhood studies,
the age range was relatively narrow. Neither can conclusions be reached on sex ratios; in the childhood studies, the patients were predominantly male. Finally, as in the case of thyroid tumors, salivary-gland tumors are both benign and malignant, and the present evidence from clinical studies of salivary-gland tumors indicates that patients with radiation-induced tumors of the salivary glands should be expected to have a high survival rate in association with modern diagnosis and management.
REFERENCES


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