Supplementary material for Ardenfors O, et al. Are IMRT treatments in the head and neck region increasing the risk of secondary cancers? Acta Oncol 2014;53:1041–7.

Supplementary Table I. Characteristics of the analysed treatment plans.

Patient	Target site	Applied fields per fraction		Monitor units per fraction	
		IMRT	CRT	IMRT	CRT
1	Base of tongue	7	5	872	251
2	Tonsil	7	5	918	250
3	Hypopharynx	9	4	889	241
4	Tonsil	9	5	1240	255
5	Tonsil	9	5	931	250
6	Tonsil	7	4	738	243
7	Tonsil	9	6	890	255
8	Tongue	9	6	619	258
9	Base of tongue	7	5	952	247
10	Base of tongue	9	6	704	246
Average				875	250

Appendix

Risk models and parameters

Three risk models were used for calculations. The competition model (Equation 1) predicts a bell-shaped dependence and is based on the assumption of a competition between the induction of carcinogenic mutations and cell kill taking into account fractionation effects [1].

$$Risk = \left(\alpha_1 D + \frac{\beta_1 D^2}{n} \right) \exp \left[- \left(\alpha_2 D + \frac{\beta_2 D^2}{n} \right) \right] \quad (1)$$

where α_1 and α_2 are the linear parameters for radiation-induced malignancies and cell kill, respectively, β_1 and β_2 are the corresponding quadratic parameters, D is the total absorbed dose, and n is the number of fractions in which the total dose is delivered.

The linear-exponential (lin-exp) model (Equation 2) is similar to the competition model in Equation 1, but neglects fractionation effects [2].

$$Risk = \alpha_1 D e^{-\alpha_2 D} \quad (2)$$

The third model used is a plateau model (Equation 3) that describes the induction of mutations in a population of precancerous cells leading to a saturation of the risk for higher doses as a result of the balance between malignant cell creation and mutated cell kill [3].

$$Risk = \frac{\alpha_1}{\delta_{org}} \left(1 - e^{-\delta_{org} D} \right) \quad (3)$$

where δ_{org} is an organ-specific parameter of the dose response.

The parameters for the risk models used in the study were derived from radiation protection and from epidemiological data. Thus, the α_1 parameter was estimated from the linear risk coefficients derived from epidemiological studies of populations irradiated with low doses such as the atomic bomb survivors (Equation 4):

$$\alpha_1 = R_C \times DDREF \times w_T \times F_V \quad (4)$$

where $R_C = 0.041 \text{ Gy}^{-1}$ is the average lifetime risk coefficient adjusted for detriments reported by the ICRP for low doses and dose rates [4]. A dose and dose rate effectiveness factor $DDREF = 2$ was chosen according to the recommendations of the ICRP. w_T is the ICRP detriment-adjusted tissue weighting factor which accounts for differences in radiation sensitivity of the tissues [4]. Thus, the values of w_T used in this study were 0.04 for oesophagus, 0.12 for lungs, 0.005 for each parotid gland (ICRP value corresponding to both glands multiplied with 0.5), and 0.06 for the body (ICRP value of remainder multiplied with 0.5). Variations in organ sizes between individuals were accounted for by the use of a volumetric factor, F_V , which assumes that the risk of radiation-induced cancer is related to the number of mutated cells which is proportional to the volume of the irradiated tissue (Equation 5).

$$F_V = \frac{V_i}{\bar{V}} \quad (5)$$

where V_i is the volume of a specific organ for one patient and $\bar{V}$ is the average volume of the organ of interest for all patients. This accounts for interpatient variations in the size of the tissue cell populations irradiated [5–7].

The α_2 parameter was derived with Equation 6 from the total dose, D_{opt} , at which the maximum of the risk curve is achieved [8]:

$$\alpha_2 \approx \frac{1}{D_{opt}} \quad (6)$$

A value $D_{opt} = 5 \text{ Gy}$ has been assumed based on the findings of Dörr and Herrmann [9] regarding the incidence of secondary tumours relative to the absorbed dose.

The β_1 and β_2 parameters in Equation 1 were calculated from α_1 and α_2 respectively assuming $\alpha/\beta = 3 \text{ Gy}$ for all tissues. An organ-specific parameter $\delta_{org} = 2.7 \times \alpha_2$ has been assumed for calculations with Equation 3 to achieve a realistic plateau-shaped risk response. This approach has been based on the relationship between plateau- and linear-exponential risk responses reported by Schneider and Kaser-Hotz [10].

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