TABLE 4
Logistic Regression Analysis of Gamma Radiation Sensitivity in Case Patients and Control Subjects

Chromatid breaks per cell	Case patients (%)	Control subjects (%)	Odds ratio (95% CI)	
			Crude	Adjusted[a]
Dichotomized				
≤ 0.40	3 (5.3)	54 (51.4)	1.00	1.00
> 0.40	54 (94.7)	51 (48.6)	19.05 (5.60–64.76)	17.25 (4.92–60.49)
Trichotomized				
≤ 0.40	3 (5.3)	54 (51.4)	1.00	1.00
0.41–0.52	10 (17.5)	27 (25.7)	6.67 (1.69–26.25)	5.63 (1.37–23.04)
> 0.52	44 (77.2)	24 (22.9)	33.00 (9.32–116.87)	33.79 (8.97–127.32)

CI: confidence interval.
[a] Adjusted for age, gender, ethnicity, and family history.

b/c as a risk factor for cases was 19.05 (95% CI, 5.60–64.76). The OR was 17.25 (95% CI, 4.92–60.49) after adjustment for age, gender, ethnicity, and family history of malignancy (Table 4). When the gamma sensitivity data were trichotomized based on the median and 75th percentile of the control b/c values, the association with risk increased from the low to high b/c values (trend test, $P < 0.0001$). Multivariate analysis with adjustment for age, gender, ethnicity, and family history of malignancy had little impact on these risk estimates (Table 4). Three case patients with MSTs reported previous radiation exposure to the head and neck region, and one patient with BST reported previous irradiation of the feet (two case patients lacked information on radiation exposure history). The number of gamma radiation–induced chromatid breaks per cell was similar among participants with and without a history of radiation exposure (0.59 ± 0.11 and 0.61 ± 0.13, respectively; $P = 0.766$).

Analysis of histologic subgroups revealed that the mean b/c values were 0.62 ± 0.13 for patients with MSTs (median, 0.58; range, 0.40–0.90) and 0.55 ± 0.10 for patients with BSTs (median, 0.55; range, 0.36–0.68) (Fig. 1), both significantly higher than the b/c values of the control subjects ($P < 0.0001$ and $P = 0.007$, respectively). After dividing gamma sensitivity data into high and low values based on the median for the controls (0.40 b/c), the crude OR of b/c as a risk factor was 46.56 for MSTs (95% CI, 6.19–350.34) and 5.29 for BSTs (95% CI, 1.11–25.34) (Table 5). The risk estimates remained significant for MSTs and possessed borderline significance (due to the smaller sample size) for BSTs after adjustment for age, gender, ethnicity, and family history of malignancy. When the data sets were trichotomized based on the distribution of control b/c values, b/c values demonstrated a dose-response relation with risk for both the MST and BST groups

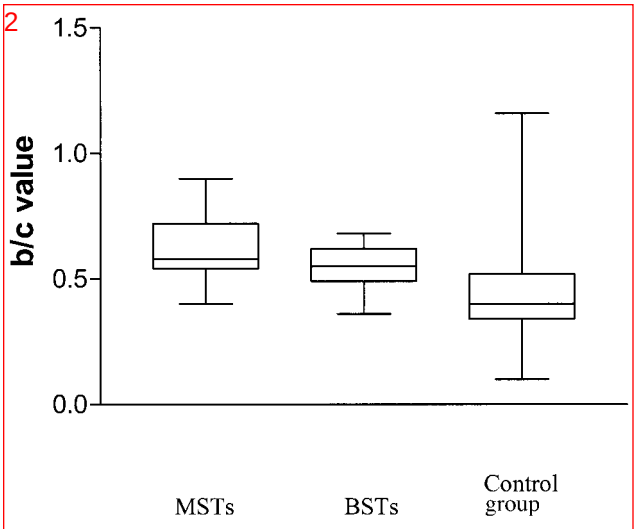

FIGURE 1. Distribution of gamma radiation–induced chromatid breaks per cell (b/c) in patients with malignant (MSTs) and benign salivary gland tumors (BSTs) and control patients (MST group vs. control group, $P < 0.0001$; BST group vs. control group, $P = 0.007$). The outer brackets represent the range values, the box represents the 25th and 75th percentile values, and the middle line represents the median value.

(trend test, $P < 0.0001$ and $P = 0.005$, respectively). Participants with a b/c value > 0.52 had a > 70-fold increased risk of developing MSTs and a > 10-fold risk of developing BSTs (Table 5). Multivariate analysis with adjustment for age, gender, ethnicity, and family history of malignancy had little effect on these risk estimates (Table 5).

DISCUSSION

The current pilot case–control study revealed a significant association between risk for both MSTs and BSTs and gamma radiation sensitivity, as measured by an in vitro assay of induced chromatid breaks. The MST group had an abnormally high number of chromatid breaks, whereas the BST group had an intermediate number of chromatid breaks. When the data sets were divided into tertiles, we found a dose-response relation between gamma radiation sensitivity and risk for both MSTs and BSTs. These results may reflect the underlying efficiency of the individual's DNA damage repair systems.[8] Cells incapable of repairing DNA breaks acquire many chromatid breaks and gaps after exposure to gamma radiation. Therefore, they have a greater risk of histologic abnormalities and, ultimately, malignancies. Therefore, the observed individual variation in gamma sensitivity may contribute to the genetic susceptibility to MSTs and, possibly, to BSTs.

Our findings are consistent with previous reports