Table 4

The association between *XRCC1* and *XPD* genotypes and breast cancer risk according to pack-years smoked

	<5 pack-years			>5 pack-years		
	Cases n (%)	Controls n (%)	OR (95% CI)[a]	Cases n (%)	Controls n (%)	OR (95% CI)[a]
XRCC1-280						
Arg/Arg	37 (82.2)	51 (82.3)	1.0	57 (85.1)	60 (89.6)	1.0
Arg/His+His/His	8 (17.8)	11 (17.7)	0.91 (0.28–2.95)	10 (14.9)	7 (10.4)	1.99 (0.57–7.02)
XRCC1-399						
Arg/Arg	20 (44.4)	35 (57.4)	1.0	25 (37.9)	40 (59.7)	1.0
Arg/Gln	18 (40.0)	22 (36.1)	1.21 (0.46–3.18)	31 (47.0)	21 (31.3)	4.31 (1.66–11.2)
Gln/Gln	7 (15.6)	4 (6.6)	3.99 (0.82–19.4)	10 (15.2)	6 (9.0)	3.55 (0.81–15.6)
Arg/Gln+Gln/Gln	25 (55.6)	26 (42.6)	1.61 (0.64–4.06)	41 (62.1)	27 (40.3)	4.14 (1.66–10.3)
XPD-751						
Lys/Lys	18 (40.0)	20 (32.3)	1.0	22 (32.8)	20 (29.9)	1.0
Lys/Gln	18 (40.0)	31 (50.0)	1.01 (0.37–2.77)	22 (32.8)	38 (56.7)	0.40 (0.14–1.12)
Gln/Gln	9 (20.0)	11 (17.7)	1.59 (0.44–5.74)	23 (34.3)	9 (13.4)	2.77 (0.90–8.59)
Lys/Lys+Lys/Gln	36 (80.0)	51 (82.3)	1.0	44 (65.7)	58 (86.6)	1.0
Gln/Gln	9 (20.0)	11 (17.7)	1.45 (0.46–4.56)	23 (34.3)	9 (13.4)	4.41 (1.62–12.0)

[a]Odds ratios (ORs) and confidence intervals (CIs) adjusted for age, age at menarche, age at first full term pregnancy, number of pregnancies, history of benign breast disease, first degree family history of breast cancer, weist-to-hip ratio and use of alcohol.

breast cancer; the adjusted OR was 10.7 (95% CI 3.62–31.6) compared to those without these genotypes (Table 5). This effect was mainly confined to combination of *XRCC1-399* and *XPD-751* at-risk genotypes (OR 12.1, 95% CI 3.52–41.5). When the combined effect was calculated for the number of at risk alleles (*XRCC1-280 His*, *XRCC1-399 Gln* and *XPD-751 Gln*), a similar increase in the risk was seen; subjects with three at-risk alleles had an OR of 1.72 (95% CI 1.03–2.87; *p* for trend 0.069) among all women, and OR 4.62 (95% CI 1.56–13.7; *p* for trend 0.01) among ever actively smoking women compared to women with no at-risk alleles. Only four cases and one control carried simultaneously four at-risk alleles, and none more than four (of the six).

Discussion

In this study, we examined the role of *XRCC1 Arg280His*, *XRCC1 Arg399Gln* and *XPD Lys751Gln* polymorphisms in relation to breast cancer risk in a Finnish study population. As the products of these genes act in BER and NER pathways, and as some evidence exists on the association of these polymorphisms with smoking-related cancers [13,42,43,52], our special interest was to study the role of these DNA repair enzymes among smoking women. The hypothesis was also supported by a recent finding of an association between the *XPD-751 Gln/Gln* genotype and breast cancer risk in smoking women [44].

The two polymorphisms *Arg280His* and *Arg399Gln* in the coding region of the *XRCC1* gene were recently predicted to be 'possibly damaging' to *XRCC1* function based on the conservation of the sequences in mammalian orthologues [16]. In agreement with this, the frequency of the variant *XRCC1-399 Gln* allele was somewhat higher among the present cases compared to controls, leading to a tendency of increased breast cancer risk. A similar effect has been reported in studies among Korean [28], US radiologic technologists [21], Indian [22], and African-American [29] women. No increased risk was found for white American women [29], in agreement with three other studies performed among American women [30-33]. Moreover, no association was seen in studies among Chinese [35], French [19], Canadian [34], Turkish [36] and Danish [46] women.

In contrast to the *XRCC1 Arg399Gln* polymorphisms, the *Arg280His* polymorphism did not significantly modify breast cancer risk in the present study. Similarly, no association was seen for Indian women [22] or for US radiologic technologists [21]. On the other hand, our findings are in contrast to a French study showing a 1.8-fold (95% CI 1.04–3.08) increase in breast cancer risk for the *XRCC1-280 Arg/His* genotype [19]. One reason for this divergence could be the lack of power; the frequency of the *280His* allele is low (0.08) among Caucasians, including Finns. Consequently, even though having almost twice the size of the French study, the power of our study to detect an OR of 1.5 at a 0.05 significance level was