

Original research

Residential extremely low frequency magnetic fields and skin cancer

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ABSTRACT

Objective Photoinduced radical reactions have a fundamental role in skin cancer induced by ultraviolet radiation, and changes in radical reactions have also been proposed as a mechanism for the putative carcinogenic effects of extremely low frequency (ELF) magnetic fields (MFs). We assessed the association of melanoma and squamous cell carcinoma with residential MF exposure.

Methods All cohort members had lived in buildings with indoor transformer stations (TSs) during the period from 1971 to 2016. MF exposure was assessed based on apartment location. Out of the 225 492 individuals, 8617 (149 291 person-years of follow-up) living in apartments next to TSs were considered as exposed, while individuals living on higher floors of the same buildings were considered as referents. Associations between MF exposure and skin cancers were examined using Cox proportional hazard models.

Results The HR for MF exposure ≥ 6 month was 1.05 (95% CI 0.72 to 1.53) for melanoma and 0.94 (95% CI 0.55 to 1.61) for squamous cell carcinoma. Analysis of the age at the start of residence showed an elevated HR (2.55, 95% CI 1.15 to 5.69) for melanoma among those who lived in the apartments when they were less than 15 years old. This finding was based on seven exposed cases.

Conclusions The results of this study suggested an association between childhood ELF MF exposure and adult melanoma. This is in agreement with previous findings suggesting that the carcinogenic effects of ELF MFs may be associated particularly with childhood exposure.

INTRODUCTION

Extremely low frequency (ELF) magnetic fields (MFs) have been classified as possibly carcinogenic by the International Agency for Research on Cancer.¹ This classification was mainly based on studies indicating increased risk of leukaemia in children living near power lines; meta-analyses published in 2000 were influential in the assessment,^{2 3} but also later research is consistent with increased risk of childhood leukaemia.^{4 5} The risk of adult cancers has been addressed in several studies, with mixed results.^{6 7}

There is no generally accepted biophysical mechanism for explaining a causal link between weak environmental ELF MFs and cancer, but MF effects on chemical reactions involving radical pairs (the radical pair mechanism, RPM) is considered to be

Key messages

What is already known about this subject?

- Extremely low frequency (ELF) magnetic fields (MFs) have been classified as possibly carcinogenic, mainly based on increased risk of childhood leukaemia. The results of studies on adult cancers are inconsistent.
- In our previous study using a unique database of residential buildings with indoor transformer stations, the risk of adult acute lymphocytic leukaemia was particularly associated with childhood exposure.

What are the new findings?

- The overall risks of melanoma or squamous cell carcinoma were not found to be affected by ELF MF exposure, but the study suggested an association between childhood exposure and adult melanoma.

How might this impact on policy or clinical practice in the foreseeable future?

- If further studies validate the finding that carcinogenic effects of ELF MFs are associated particularly with childhood exposure, there might be a need to regulate children's exposure more strictly.
- Improved understanding of the associations between ELF MFs and cancer will be helpful for risk communication.

among the most plausible hypotheses.⁸ The RPM seems to be involved in the avian magnetic compass sense^{9 10} and it could, therefore, potentially explain also other effects of weak MFs. Magnetoreception in birds is believed to operate through magnetosensitive photoinduced radical pairs in cryptochrome flavoproteins. Although all MF effects may not depend on photoinduced radicals,¹¹ recent experiments with living human cells have shown that MFs affect radical pair reactions in flavins excited by blue light.¹² As photoinduced radical reactions have a fundamental role in skin cancer induced by UV radiation, there are good reasons to hypothesise that MF exposure could interact with UV radiation, possibly resulting in cancer-relevant changes in skin biology.

The purpose of the present study was to test the hypothesis that ELF MFs increase the risk of skin cancer. A cohort study was conducted using



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a unique database of residential buildings with indoor transformer stations¹³ providing an opportunity to study possible health effects of ELF MFs using a high-quality study design that includes relatively high exposure levels, avoids biases and minimises potential for confounding.^{13 14} The database has been previously used for studying the association of haematological malignancies and brain tumours with residential ELF MFs.¹⁵

MATERIALS AND METHODS

The previously compiled Database of Finnish Buildings with Indoor Transformer Stations (DaFBITS) formed the basis of this study.¹³ Information from the electricity companies, building control offices and the Population Information System maintained by the Finnish Digital and Population Data Services Agency was used in the creation of the database. The computer-based Population Information System started in 1971, which was selected as the starting year of the study. All individuals who were 18 years of age or older at the end of study (31 December 2016) and had lived in the buildings included in DaFBITS were included in the study.

DaFBITS contains classification of all apartments of the buildings according to their location in relation to the transformer room, which is always located on the ground floor or basement. There are five ELF MF exposure categories¹³ (online supplemental table 1). This formed the basis of exposure assessment in this study. Persons who had been living for at least 6 months in an apartment located directly above the transformer room or in an apartment sharing a wall with the transformer room (categories 1 and 2 in DaFBITS, respectively) were classified as ‘exposed’. These apartments were located on ground or first floors. Individuals who had resided for at least 6 months in apartments on any other floor than the first or ground floors of the building (category 5 in DaFBITS) were considered as referents. In order to assess possible confounding associated with living on the first or ground floor, disease risk was also estimated for individuals who had lived for at least 6 months in apartments on the first or ground floor but not adjacent to the transformer room (category 4 in DaFBITS). This group is termed ‘first or ground floor residents’ in this study.

Follow-up was started 6 months after an individual had moved into the apartment that defined her/his exposure, and ended on 31 December 2016 (end of the study), emigration from Finland, death or to the date of diagnosis of the outcomes studied, whichever came first. Moving out from the apartment (after

the minimum of 6 months that defined the exposure status) did not generally affect the follow-up. However, if a member of the reference group later moved into an ‘exposed’ or a first or ground floor apartment, she/he was followed as a referent until the move and changed to the relevant group after the move. In cases where the transformer was installed in the building later than the start of residence, follow-up was started 6 months after the installation of transformer. If an individual was younger than 18 years 6 months after the start of residence or the date of the installation of transformer, follow-up started from the 18th birthday.

Overall, the cohort included 225 492 individuals of which 107 732 (47.8%) were men and 117 760 (52.2%) women (table 1). Follow-up of 25 575 individuals ended to death, of 6429 individuals to emigration and of 963 individuals to skin cancer diagnosis. Others were followed to the end of study. In total, 8617 individuals (3.8% of the cohort) were included in the exposed group, 46 169 individuals (20.5%) were first and ground floor residents and 170 706 individuals (75.7%) were referents. The median age of the individuals at the start of the residence ranged from 25.9 years to 26.5 years and the median duration of residence from 2.4 years to 3.0 years in different apartment categories (table 1). The median person-years of follow-up was 15.9 years (IQR from 7.5 years to 25.7 years) for the exposed group, 15.6 years (IQR from 7.2 years to 26.0 years) for the reference group and 15.2 years (IQR from 7.1 years to 24.8 years) for the first or ground floor residents. The total person-years of follow-up were 149 291 for the exposed residents, 2 967 986 for the referents and 777 943 for the first or ground floor residents. Person-years calculated for different age intervals are shown in figure 1.

The study cohort was linked to Finnish Cancer Registry using unique personal identifiers assigned to each Finnish resident. Registration of cases in Finnish Cancer Registry is about 99% complete and the Registry contains population-based data on cancer incidence starting from the year 1953.¹⁶ The outcomes of interest were adult (diagnosis at 18 years of age or older) melanomas (C43) and squamous cell carcinomas (C440–C447 and C449). Basal cell carcinomas were not included, as their registration is not complete in the Finnish Cancer Registry. International Classification of Diseases, 10th revision, codes were used for the classification of disease. International Classification of Diseases for Oncology (3rd edition) coding was used to classify the morphology of the tumours.

Table 1 Characteristics of the study individuals in apartments classified according to their location in relation to the source of extremely low frequency magnetic fields (indoor transformer station).

	Apartment category*			
	1	2	4	5
Number of individuals	7991	626	46 169	170 706
Sex				
Male: N (%)	3879 (48.5)	311 (49.7)	22 245 (48.2)	81 297 (47.6)
Female: N (%)	4112 (51.5)	315 (50.3)	23 924 (51.8)	89 409 (52.4)
Age at the start of residence (years): median (5th–95th percentile)	25.9 (0.4–59.1)	26.1 (0.1–56.7)	26.4 (0.8–60.6)	26.5 (1.1–60.3)
Duration of residence (years): median (5th–95th percentile)	3.2 (0.7–21.0)	3.5 (0.7–21.9)	2.9 (0.7–19.9)	3.0 (0.7–21.3)
First year of study: median (5th–95th percentile)	1995 (1973–2014)	1996 (1978–2013)	1996 (1974–2014)	1996 (1973–2014)

*Apartment categories: 1=apartment located above the transformer room; 2=apartment sharing a wall with the transformer room; 4=apartment located on the same floor as apartment in category 1, 2 or 3; 5=apartment located on any other floor of the building. Note that residents of apartment category 3 (apartment sharing a corner with the transformer room) were excluded from the study. This is a small group of individuals and measurements of exposure level are not available.

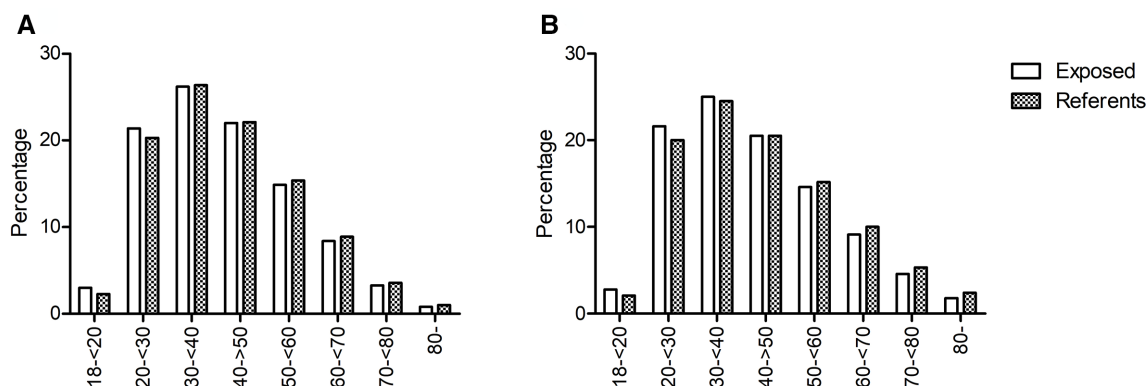


Figure 1 Age distribution of person-years for exposed and reference group males (A) and females (B).

All statistical analyses were carried out using IBM SPSS Statistics V.25. Cox proportional hazard models were used to evaluate the association between residential ELF MF exposure and skin cancers. Time in study (in years) was used as the underlying time scale and results were adjusted for sex, age at the start of residence and birth year. Results are reported as HRs with 95% CIs.

To study dependence of HR on duration of exposure, Cox models were restricted to individuals who had resided in the buildings for ≥ 3 years or ≥ 10 years. Also in these analyses, follow-up started after the specified minimum duration of residence. If this was before the 18th birthday of the individual, follow-up was started from the 18th birthday. To study the effects of childhood exposure, Cox models were run for individuals who had resided in the buildings during the first 2 years of life, at ages from 2 years to <15 years, and at ages ≥ 15 years. Two separate sensitivity analyses were carried out. Residents of apartments sharing a wall with the transformer station were excluded from the exposed group in the first one, and the first or ground floor residents were included in the reference group in the second one.

The analyses were planned a priori. The cut-off points used for duration of residence and age at time of residence were the same that were used in the analysis of haematological malignancies and brain tumours.¹⁵ The minimum duration of residence considered as exposure (≥ 6 months) was higher than the threshold used in the haematological and brain neoplasm analysis (≥ 1 month), as alternative analyses done using longer durations of residence showed stronger associations with haematological and brain neoplasms (unpublished observations).

RESULTS

The truncated age-standardised incidence rate (cases per 100 000 person-years; follow-up started at 18 years of age) of melanoma was 23.9 within the exposed group and 22.1 within the referent group. For squamous cell carcinoma, the rates were 24.8 and 23.5, respectively.

The HR of melanoma was slightly above unity and that of squamous cell carcinoma slightly below, but 95% CIs included 1.00 for both cancers (table 2). The HRs were essentially the same when longer exposure durations (≥ 3 years or ≥ 10 years) were considered; the HR for ≥ 10 years of exposure was 1.06 (0.52–2.16) for melanoma and 1.02 (0.48–2.18) for squamous cell carcinoma. Analysis of the age at the start of residence showed an elevated HR for melanoma among those who lived in the apartments when they were less than 15 years old, and there was a tendency towards higher risk of melanoma from exposures below 2 years of age, in comparison to exposures between

2 years and 15 years of age. Distribution of the melanoma cases according to the age at start of the residence suggested that the excess of melanoma cases associated with childhood exposure is mostly explained by cases among those who lived in the exposed apartments before the age of 10 years (figure 2). All the seven cases observed in persons exposed before the age of 15 years were recorded as non-specified malignant melanoma, so there was no evidence of an association between any specific melanoma type and childhood ELF MF exposure. Because the risk of melanoma is strongly associated with year of birth (showing increasing incidence during the last decades), we checked the year of birth of the seven cases. No evidence for bias was found; the birth years were apparently randomly distributed between 1965 and 1984. The effect of childhood exposure could not be investigated for squamous cell carcinoma as none of the cases, either exposed or referents, had been living in the buildings before the age of 15 years.

No evidence for confounding associated with living on the lowest floors was found; the HR calculated for individuals living in first or ground floor apartments was 1.03 (0.86–1.23) for melanoma and 1.07 (0.85–1.35) for squamous cell carcinoma. Also, the sensitivity analyses produced essentially unchanged HRs: exclusion of the residents of apartments sharing a wall with the transformer room (category 2) from the exposed group

Table 2 HRs and 95% CIs for melanoma and squamous cell carcinoma by exposure to extremely low frequency magnetic fields from indoor transformer stations. HRs were calculated for different age categories according to the age at the start of residence in apartments included in the study

Cancer	Age at the start of residence	Exposed cases	Referent cases	HR* (95% CI)
Melanoma	All ages	29	579	1.05 (0.72 to 1.53)
	≥ 15 years	22	537	0.88 (0.57 to 1.35)
	<15 years	7	42	2.55 (1.15 to 5.69)
	2 years to <15 years	4	27	2.22 (0.78 to 6.37)
	<2 years	3	15	3.17 (0.90 to 11.13)
Squamous cell carcinoma†	All ages	14	341	0.94 (0.55 to 1.61)

*Adjusted for age at the start of residence, sex and birth year.

†All squamous cell carcinoma cases were older than 15 years at the start of the residence.

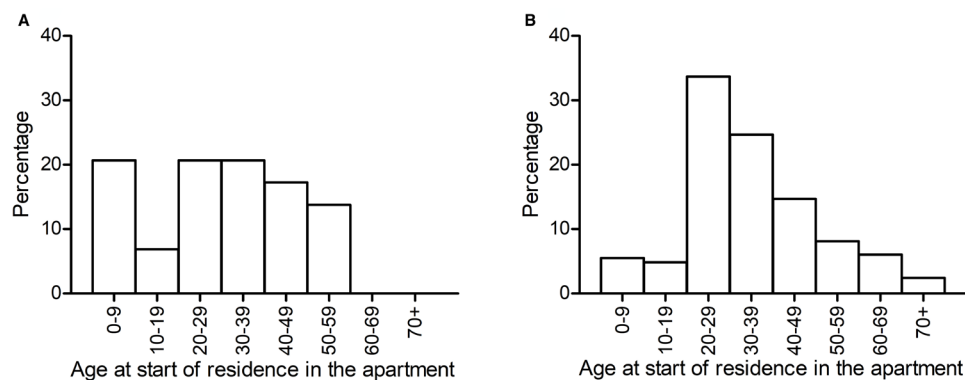


Figure 2 Distribution of the melanoma cases according to the age at the start of residence in the apartment for (A) exposed cases ($n=29$) and (B) referent cases ($n=579$).

resulted in an HR of 1.09 (0.74–1.59) for melanoma and an HR of 0.99 (0.58–1.69) for squamous cell carcinoma; inclusion of the residents of first and ground floor apartments (category 4) to the referent group resulted in an HR of 1.02 (0.69–1.52) for melanoma and an HR of 0.88 (0.50–1.54) for squamous cell carcinoma.

DISCUSSION

This study addressed possible increased risks of skin cancer in adults exposed to residential ELF MFs. The overall risks of melanoma or squamous cell carcinoma were not found to be affected by MF exposure. However, the analysis focusing on age at the time of exposure suggested that MF exposure during childhood (below the age of 15 years, particularly during the first 10 years of life) is associated with increased risk of melanoma. This finding is based on seven exposed cases. The association of squamous cell carcinoma with childhood MF exposure could not be assessed because of the lack of cases who had resided in the study apartments before the age of 15 years.

This study had several strengths. Assessing ELF MF exposure based on apartment location (without contacting the residents) enabled elimination of selection bias. This approach to exposure assessment has been validated in several studies both in Finland^{14,17} and elsewhere.^{18–21} According to these studies, residents of apartments above transformer stations are exposed to ELF MFs that are clearly higher than the average residential background level. A further advantage of the study was that outcome data were obtained from a reliable nationwide register with nearly complete registration of melanoma and squamous cell carcinoma cases. Furthermore, the study design allowed long follow-up of the cohort members.

A disadvantage resulting from our approach was that we had no information about exposure to ELF MFs' sources other than transformer stations. Other residential sources are not likely to be important compared with transformer stations,¹⁵ and occupational exposure is not relevant, as the increased risk of melanoma was confined to childhood exposure. Exposures in schools and kindergartens are not likely to be essentially higher than the levels in normal residences.²² Because of the study design (see strengths in the previous paragraph), no MF measurements in individual apartments were available. Dose response with respect to magnetic flux density could, therefore, not be addressed.

As the study subjects were not contacted, information about other personal exposures—most importantly UV radiation—was not available. This limitation was at least partly overcome by the study design; selecting both exposed and referent individuals from the same buildings minimised differences in potential

environmental confounders, but it also favoured similar distributions of all potential confounding factors, including lifestyle-related factors (eg, sunbathing), which are associated with socioeconomic status. Some residual confounding might be associated with living at the lowest floors of the buildings (where all 'exposed' apartments are), since slightly higher apartment prices on higher floors may cause differences in social status. We were able to test this possibility by assessing skin cancer risk among such first or ground floor residents who did not live next to a transformer station. No evidence of confounding was found. Another limitation of the study was low number of cases, particularly in the analysis focusing on childhood exposure. Because of the low numbers, the association between melanoma risk and childhood MF exposure might be a chance finding. However, it should be noted that this finding did not result from data dredging; the analysis was planned a priori, because previous observations^{15,23} suggested that childhood exposure may be particularly important.

Studies on possible carcinogenicity of ELF MFs have focused mainly on haematological neoplasms,^{7,24,25} brain tumours^{24–26} and breast cancer.^{25,27,28} Only a few previous studies have addressed risk of skin cancers in relation to ELF MF exposure. Tynes *et al*²⁹ reported an OR of 1.87 with a 95% CI of 1.23 to 2.83 for malignant melanoma among persons who had been exposed to residential ELF MFs with a time-weighted average magnetic flux density ≥ 0.2 μ T. An elevated OR (1.85; 95% CI 1.22 to 2.81) was also observed in the lower exposure category (0.05–0.20 μ T). In the study by Verkasalo *et al*³⁰ on adult cancers in relation to residential MF exposure, the relative risk (RR) of malignant melanoma was slightly elevated in all cumulative exposure categories (0.20–0.39 μ T years, 0.40–0.99 μ T years, 1.00–1.99 μ T years and ≥ 2.0 μ T years). However, the magnitude of the increase was low (RR: 1.08 per 1 μ T year increase in exposure; 95% CI 0.94 to 1.23), and the highest RR occurred in an intermediate exposure category. No increase was observed in non-melanoma skin cancers. These two studies did not address skin cancer risk above time-weighted average magnetic flux density of 0.4 μ T, which is the exposure level that seems to be associated with increased risk of childhood leukaemia.² The advantage of our approach was that exposure levels exceeding 0.4 μ T are common in apartments next to transformer stations (see online supplemental table 1 for data of MF levels measured in apartments above transformer stations). Elliot *et al*²⁸ reported no increase in malignant melanoma in five residential exposure categories up to ≥ 1.0 μ T. Use of cancer controls was an important limitation of this case-control study.

Many experimental studies have been conducted to explore the possible causal relationship between ELF MFs and cancer.^{1,31} The main interest has been to explain the epidemiological association with childhood leukaemia, and there has been no special interest in skin cancer. Nevertheless, a few studies have used induction of skin tumours as an experimental model to study the role of MFs in carcinogenesis. These studies have provided some evidence that ELF MF exposure may enhance the development of skin tumours induced by UV radiation,³² while evidence for promotion of chemically induced skin tumours is weaker.^{33–35} MF effects on skin biology are supported also by findings showing MF-induced alterations in skin ornithine decarboxylase activity and polyamine levels,³⁶ formation of epidermal cysts³² and suppression of UV-induced apoptosis.³⁷ All these studies have employed magnetic flux densities of 100 μ T or higher, so they do not directly support epidemiological findings suggesting that human cancer risk is affected by ~ 0.4 μ T MFs.

Although the study was inspired by the reported effects of MFs on photoinduced radical reactions, it is not straightforward to interpret the findings as support to the hypothesis that residential MF enhances skin cancer by affecting UV-induced radical reactions. Exposure to solar UV radiation occurs outdoors, so the UV-induced radical reactions cannot be directly affected by the MFs present in residences; the lifetimes of radical pairs (whose recombination can be affected by MFs) are of the order of microseconds.⁹ It is nevertheless of interest to discuss the possible involvement of the RPMs, as it is currently the most plausible mechanism for explaining biological effects of weak MFs. Avian magnetoreception is believed to be based on light-induced radical pairs in cryptochrome proteins,^{9,10} but sensitivity to MFs has also been shown in other flavin-containing proteins.^{12,38} Radical pairs in these (and possibly other) molecules can be induced by visible light, which is also present indoors; this opens the possibility that MF exposure at home affects multiple biological processes in the skin, possibly interfering with repair of earlier UV-induced damage. Furthermore, MFs may also affect light-independent radical reactions.¹¹ It is, therefore, possible that MF exposure at home could affect the repair of earlier UV-induced damage. It has been proposed that the primary MF effect (through the RPM) could lead to disruption of the interlinked circadian clock system, DNA damage responses and reactive oxygen species-related cellular processes due to the role of cryptochromes in the regulation of this system.⁸ However, it is still a major challenge to explain how a ~ 0.4 μ T, 50 Hz, MF could affect biological processes in the presence of the much stronger (~ 50 μ T) static geomagnetic field.^{8,39}

The observed association of childhood MF exposure with adult melanoma may be important. Previous studies have suggested that childhood MF exposure is associated with haematological malignancies in adults.^{15,23} Together with the reported association with childhood leukaemia, these findings suggest that early childhood may be a time window for the carcinogenic effects of MFs. With regard to melanoma, it is of interest that UV exposure in childhood is believed to be particularly important for development of melanoma during later life stages.⁴⁰ It is therefore tempting to speculate that childhood MF exposure could enhance the effect of childhood UV exposure. Based on the mouse skin tumour study by Kumlin *et al.*,³² we proposed the hypothesis that repeated long-term interaction of MFs and UV radiation was necessary for the observed effects of MF exposure on UV-induced tumours.³¹ The experimental model used by Kumlin *et al.*³² involved repeated exposures to UV radiation and continuous MF exposure when the animals were not under the UV lamps—this corresponds roughly to exposure of a child

who is repeatedly exposed to UV radiation outdoors and to MFs at home.

CONCLUSIONS

The results of the present study provide some further evidence that ELF MFs of the order of 1 μ T or below may influence carcinogenesis, but the mechanistic explanation is still uncertain. However, the finding suggesting an association between childhood MF exposure and adult melanoma is based on only seven exposed cases. If this is a true signal, it strengthens previous findings suggesting that the carcinogenic effects of ELF MFs may be associated particularly with childhood exposure.

Contributors MWK, JJ and PR designed the study, acquired funding and analysed the data. PR acquired the data. MWK and JJ drafted the manuscript. All authors critically reviewed the draft for important intellectual content and agreed to be accountable for all aspects of the work in ensuring that questions related to accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Patient consent for publication Not applicable.

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