

Electromagnetic fields and female breast cancer

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Abstract The possibility that long term exposure to relatively weak power frequency electromagnetic fields (EMF) could increase the risk of breast cancer has been investigated during the past decade. The hypothesis is based on the assumption that magnetic field exposures suppress melatonin production and that melatonin is protective against breast cancer. Most epidemiological studies have indicated little or no overall effect of EMF exposure, but some early studies suggested effects among premenopausal women, particularly for estrogen receptor positive breast tumors. The early studies were often limited by small numbers, crude exposure information and lack of information on confounding factors. In more recent occupational studies, again no overall risk increases were reported, but some studies found increased risks in certain subgroups, although with no consistent pattern across studies. A recent very large occupational study with improved exposure assessment and enough statistical power also for subgroup analyses found no indications of increased risks in any subgroups. Most of the recent well-designed residential studies report no increased risks, and similar findings are reported in the majority of studies of bed heating devices. Overall, the weight of the evidence available today does not suggest an increased risk of breast cancer related to EMF exposure.

Key words Breast neoplasm · Estrogen receptor · Exposure assessment · Melatonin

Introduction

It has been hypothesized that long term exposure to extremely low frequency (ELF) magnetic fields in the power frequency range of 50–60 Hz could increase the risk of breast cancer [1]. The hypothesis is based on the assumption that magnetic field exposure affects melatonin production in the same way as light-at-night and that melatonin is protective against breast cancer, possibly by affecting the level of estrogen. Other mechanisms have also been proposed; an oncostatic effect of melatonin on estrogen receptor positive (ER+) breast cancer have been found by Hill and Blask [2], some studies have indicated an effect of melatonin on the immune system [3], and it has been suggested that melatonin acts as a potent antioxidant [4]. In vivo and in vitro experimental research support a protective association between melatonin and breast cancer development [5], whereas the only available prospective epidemiological study found no association between melatonin levels measured in 24 h urine samples and breast cancer risk [6]. The interpretation of retrospective epidemiological studies is hampered by the possibility that the disease itself affects melatonin levels. The evidence of a suppressive effect of ELF magnetic field exposure on melatonin production is contradictory [7]; most of the experimental studies on humans have found no effects on melatonin production when subjects are exposed to ELF fields during sleep in the laboratory (an effect can be clearly demonstrated for exposure to light-at-night using similar study designs), whereas evidence from observational studies in occupational or residential settings

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indicates a lower melatonin production in exposed subjects, however, usually limited to specific subgroups.

The scientific literature on ELF magnetic field exposure and breast cancer risk has been reviewed by several national and international bodies (e.g. IARC [7], NIEHS [8], California EMF Program [9]), and all have reached similar conclusions; the available evidence is inadequate for an assessment of whether ELF magnetic fields can affect breast cancer risk. The most formal of these reviews was conducted by the International Agency for Research on Cancer (IARC) in 2001 [7], and since then additional epidemiological studies have been published that covers the three most common types of exposure sources; occupational exposures, residential exposure, and exposure from electrical bed heating devices.

The review presented here will take the IARC evaluation as a starting point, and focus on the most recent available evidence. At the time of the IARC evaluation a handful of studies were available on each of the three exposure sources: residential, occupational, and exposure from electric blankets. The majority of the studies were case–control studies, although a few cohort studies were also available but usually with very crude exposure information. The epidemiologic evidence indicated little or no overall effect, but some studies suggested an effect among premenopausal women particularly for breast tumors that are rich in estrogen receptors (estrogen receptor positive, ER+), findings that fit the hypothesized biological mechanism [10–13]. However, some of the early studies were not designed to specifically address the hypothesis, and several of the studies had problems with small numbers, crude exposure information and lack of information on confounding factors.

Exposure sources

It is not obvious which aspect of the magnetic field exposure is the most relevant, but the majority of the available studies have focused on estimates of the time weighted average exposure, although other metrics have sometimes been investigated, e.g. rate of change or time above a certain exposure level. Since magnetic fields are imperceptible, information about exposures cannot easily be obtained through self reporting by subjects included in the studies. The investigator has to rely on either direct measurements of the magnetic fields, or the use of proxies based on circumstances or conditions known or thought to entail exposure. Three types of exposure sources can be distinguished; occupational, residential, and exposure from electric bed heating devices. These exposure sources are not directly comparable; occupational exposures may be higher, but more limited in time (e.g. magnetic fields are

elevated only when being close to a specific electric device in use), residential exposure is generally lower than occupational, but is usually experienced during a longer time over the day, whereas level and duration of exposure from electric blankets depend on how long the device is kept on, and which part of the body the critical exposure refer too (low exposure to the head, but high exposure to the rest of the body).

The early occupational studies simply categorized occupational titles into a group of “electrical occupations” and compared the cancer incidence in this group to that in other occupations. Occupations generally considered to be exposed were predominantly held by men; e.g. welders, electricians, linemen, train drivers. Subsequently, systematic measurements were performed in a large number of occupations and job exposure matrices based on these measurements were created. Most of these measurements were, however, performed on men, and in occupations typically held by men. This created a problem in studies of female breast cancer; first, exposure misclassification could be considerable because of differences between men and women holding the same occupation, and second, no information was available about the exposure in typically female occupations leading to a large proportion of women for whom exposure levels were unknown [10]. Some studies instead used exposure estimates in very broad occupational groups [14]. Recently, however, an exposure metric was created based on personal measurements on women, which covers the most commonly held occupations among women [15].

Exposure assessment methods in residential studies have developed considerably over time. Early studies used the so-called wire codes, a crude categorization of exposure based on proximity of the residence to certain electrical installations such as power lines of different voltages [16]. Subsequently, a more sophisticated method to estimate magnetic field exposure from power lines was developed, in which calculations was made of the fields generated by nearby power lines based on detailed information about the configuration of the lines and their historical loads [17]. With the development of new magnetic field meters, measurements of the magnetic fields in the homes were made over 24 h or even longer periods.

Electric bed heating devices such as electric blankets, mattress pads, or water beds generate magnetic fields, and have been the target of several studies of breast cancer risk. The available studies have to a varying degree taken into consideration differences in the habits of use of the appliances; e.g. if the device has been used only to heat the bed or throughout the night, were generally kept on the lowest or highest setting, etc., and the most sophisticated estimates can be found in some of the more recent studies.

Occupational studies

Since the IARC evaluation in 2001 five additional epidemiological studies of occupational EMF exposure have been published in the peer reviewed literature [14, 18–21].

In a Canadian study, all cases of post-menopausal breast cancer were identified at 18 major hospitals in Montreal, and controls were selected among patients with other types of cancers at these hospitals, excluding cancer types possibly related to various occupational exposures [21]. Information about occupational history was collected through interviews, and occupational hygienists assessed the level of ELF magnetic field exposure in four categories; no exposure ($<0.2 \mu\text{T}$), low, medium, and high exposure ($\geq 1.0 \mu\text{T}$). The highest exposure category mainly comprised occupations within the textile industry. An OR of 1.13 (95% CI 0.94–1.35) was found for lifetime exposures, adding up hours of exposure to medium and high levels of ELF magnetic fields. No results were presented for the different exposure categories separately, and therefore dose–response could not be evaluated. Stratified analyses on estrogen receptor status did not change the results. Elevated risks were found in some subgroup analyses; i.e. for progesterone receptor positive breast cancer if exposures occurred before age 35.

In a population based case–control study of breast cancer in North Carolina, exposure was assessed through measurements of the magnetic fields made on a convenience sample of 200 women [14]. The time weighted average exposure was calculated across occupational categories. These categories were, however, very broad, i.e. only six occupational groups were identified, including one with “miscellaneous” occupations. The only groups with elevated fields were industrial workers ($0.54 \mu\text{T}$) and “miscellaneous” occupations ($0.23 \mu\text{T}$). Overall, no associations were found between magnetic field exposure and breast cancer risk. For estrogen receptor positive breast cancer and more than 10 years of exposure an indication of increased risk was found, but with no clear dose–response pattern.

In a population based case–control study from Norway [20], information about occupational titles was obtained from the censuses performed every 10th year, and exposure was categorized by an expert panel according to number of hours above background ($0.1 \mu\text{T}$) exposure. The cumulative number of years with exposure was calculated, where occupations with ≥ 24 h per week at exposure levels $>0.1 \mu\text{T}$ was given the weight 3, 4–23 h/week the weight 2, and less than 4 h per week were given the weight 1. Subjects that had changed occupations between censuses were assumed to have had the same occupations during the 5 years surrounding the census. Adjustment was made for age at birth of the first child and education. No association

was found between cumulative occupational magnetic field exposure and breast cancer risk, regardless of age at diagnosis and ER-status.

A cohort study of breast cancer in Norwegian radio and telegraph operators was performed by the same authors [19]. Cumulative exposure was estimated based on ship type (weights between 1 and 3 were given depending on type of ship) and number of years of employment, but no distinction was made between ELF and RF fields. Some indication was found of an increased breast cancer risk in the exposed occupations as compared to the general population, but results were unstable due to a small number of exposed cases. Furthermore, exposure to light-at-night from shift work in the exposed occupations could possibly have confounded the results.

A recent very large Swedish case–control study estimated exposure through a job–exposure matrix based on an extensive magnetic field measurement program among women [18]. The measurements were summarized in several different ways: the arithmetic mean of the geometric means, proportion of time above $0.3 \mu\text{T}$, maximum exposure, and the rate of change. Information about occupation was obtained from the censuses performed every fifth year. The large number of cases (approximately 20,000) allowed statistically stable analyses of all subgroups where previous studies had indicated effects; premenopausal women, ER positive tumors, women with long term exposures, women exposed before age 35. Control of confounding from parity and socioeconomic status was made. Results did not indicate any effects of the exposure, regardless of exposure metric, age at diagnosis, ER-status, or timing of the exposure.

Residential exposure

Four studies of residential magnetic field exposure have been published since the IARC evaluation [20, 22–24]. In a case–control study from Seattle, residential magnetic field exposure was estimated through 48 h bedroom measurements and wire code categorization [22]. Measurements were summarized in several ways: as arithmetic mean, proportion of measurements above $0.2 \mu\text{T}$, and a rate of change metric, and each estimate was categorized into quartiles. As a result, the highest exposure category was set at $0.073 \mu\text{T}$, a quite low level (as a comparison an increased risk of childhood leukemia has been observed at exposures above 0.3 or $0.4 \mu\text{T}$). However, determination of quartiles for the metric “proportion of measurements above $0.2 \mu\text{T}$ ” was based only on subjects with at least one measurement above $0.2 \mu\text{T}$, which means that the highest exposure category using this metric has higher average magnetic field levels. No association was found between

magnetic field exposure and breast cancer risk, regardless of exposure metric used. Analyses based on continuous exposure estimates did not change the results; neither did stratification on age at diagnosis and ER-status.

Another US case–control study investigated female breast cancer on Long Island [24]. Exposure assessment was made through measurements of average bedroom magnetic fields over 24 h and wire codes. Assessment was also made of exposure to ground currents. Exposure was categorized according to quartiles also in this study, and the cut-point for the highest exposure category was 0.17 μT . Analyses was also made of the 90th percentile, but the level of exposure for this group was not reported. No associations were found between any of the exposure estimates and breast cancer risk. Analyses stratified on menopausal status or age at diagnosis did not change the results.

A nested case–control study based on a multiethnic cohort of women in Los Angeles reported no association between any of the indices of magnetic field exposure and breast cancer risk [23]. Exposure was assessed through 7 day night time bedroom measurements and wire codes. The highest exposure cut-point analyzed was $\geq 0.4 \mu\text{T}$, and analyses were also made of the exposure as a continuous variable. Age and ER-status specific analyses did not change the results. A limitation in the study is the low participation rate for the measurement part of the study; less than 50% of cases and controls. Wire codes for the current residence were available for 99% of both cases and controls.

In all three residential studies from the US, analyses were adjusted for confounding from a large number of potential risk factors for breast cancer. The results clearly do not support the hypothesis that magnetic field exposure affects breast cancer risk.

Opposite results were found in a Norwegian nested case–control study based on a population living close to power lines [20]. Exposure was assessed through calculations of the magnetic fields generated by the power lines. Ever being exposed to magnetic fields $\geq 0.05 \mu\text{T}$ was associated with an increased risk of breast cancer, with similar results for both pre- and post-menopausal breast cancer. The lack of a dose–response pattern, and lower risk estimates for residential and occupational exposure combined than for residential exposure alone detract from the credibility of the findings.

Electric bed heating devices

At the time of the IARC evaluation, the majority of studies of electric blankets and other bed heating devices reported no association with breast cancer [7]. Despite this, three

additional studies on this issue have been published [22, 25, 26]. The study from Seattle described above included also analyses of bed warming devices, with exposure estimated both as ever use, and according to hours of use per year disregarding periods when the electric blanket was used only to warm the bed [22]. No association was found between use of electric bed warming devices and breast cancer risk.

The study from Long Island also estimated exposure to electric bed heating devices [25], adding even more detailed information about conditions surrounding the use in order to identify situations when the device would cycle on and off more often, thereby generating higher magnetic fields, e.g. if the window was open or whether the heat in the room was off. None of the analyses indicated any association with breast cancer risk. Stratification was made according to age and ER-status with similar results.

A study of breast cancer in African-American women found an increased risk related to use of an electric bedding device, with an increasing risk with numbers of years of use [26]. Using an electric bedding device for more than 10 years was associated with an almost fivefold risk increase. The results were similar when stratified on menopausal status and ER-status. A limitation in the study is the small proportion of eligible cases that participated in the study. The cancer registry used for case identification had an 80% complete case ascertainment, and of 670 cases eligible for the study, only 304 finally participated.

Discussion

Since the IARC evaluation in 2001 [7], a dozen additional studies have been published examining the potential effects of exposure to different sources of power frequency magnetic fields and breast cancer risk. The overall results from studies of occupational exposures did not indicate any effects, but some of the studies found increased risks in certain subgroups. This was also the general picture at the time of the IARC evaluation. The subgroups where effects were indicated were, however, not the same in all studies, and chance is perhaps a more plausible explanation for the findings in these subgroup analyses. A very large case–control study with a sufficient number of cases also for subgroup analyses did not find any indications of increased risks in any of the subgroups previously suggested [18]. There is still a possibility that non-differential exposure misclassification might have diluted moderately increased risks, even if attempts have been made to improve exposure assessment. This is something, however, that would have affected all of the occupational studies to a varying degree, but less so in later studies with improved exposure assessment methods. The results from these later studies do

not, however, support the assumption that non-differential exposure misclassification can explain the lack of association.

Results from three well designed studies of residential exposure with extensive magnetic field measurements taken in the homes of cases and controls likewise did not indicate any increased risks [22–24]. An exception is a Norwegian study, where effects were seen at quite low exposure levels ($\geq 0.05 \mu\text{T}$) [20]. It is difficult to find any reason why the three US residential studies would not observe any effect, should the finding in the Norwegian study be real, especially when considering the thorough exposure assessment performed in the US studies, including several different exposure parameters and methods.

Most of the studies of electric bed heating devices do not indicate increased risks; one early study found an increased breast cancer risk [27, 28], whereas all subsequent studies except one report no associations [7]. The two studies reported after the IARC evaluation that found no association with breast cancer risk had a detailed assessment of the exposure, including information about how the device was used, duration of use, and other details. The latest study where an increased breast cancer risk was reported was based on a population of African-American women, and the authors speculate that this group might be more sensitive to electromagnetic field exposure, in an effort to explain the lack of consistency between their results and most previous studies [26]. However, African-American women were also included in the residential study by London et al. [23], where no association between magnetic field exposure and breast cancer risk was found in any of the ethnic groups investigated.

Exposure misclassification is still a concern in studies of magnetic field exposure and cancer risk, especially since it is unknown which aspect of the exposure would be biologically relevant, should an effect exist. However, considering the results of the latest well designed studies performed specifically to test the hypothesis that ELF magnetic field exposure increase breast cancer risk, one must conclude that the weight of the evidence available today suggests that power frequency magnetic field exposure most likely is not a risk factor for breast cancer development.

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