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# Effects of extremely low frequency magnetic fields on animal cancer and DNA damage: A systematic review and meta-analysis

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ABSTRACT

The objective of this systematic review and meta-analysis was to assess the carcinogenic effects of extremely low frequency magnetic fields (ELF-MF) by analyzing animal and comet assay studies. We have performed a global meta-analysis on all the animal studies on the relation between ELF-MF and cancer incidence and separate meta-analyses on the incidence of cancer, leukemia, lymphoma, breast cancer, brain cancer and DNA damage assessed with the comet assay. Of the 5145 references identified, 71 studies have been included in our systematic review and 22 studies in our meta-analyses. Our global meta-analysis indicated that ELF-MF exposure had no significant impact on the incidence of cancers in rodents (19 studies, OR = 1.10; 95% CI 0.91–1.32). However, our separate meta-analyses showed that ELF-MF increased the odds of developing leukemia in mice (4 studies, OR = 4.45; 95% CI 1.90–10.38) but not in rats. Our systematic review also suggests that ELF-MF can damage DNA in certain cell types like brain cells. Nevertheless, a meta-analysis on three comet assay studies indicated that ELF-MF did not increase DNA damage in neuroblastoma cells (SMD = −0.08; 95% CI -0.18-0.01). Overall, our results suggest that exposure to ELF-MF does not represent a major hazard for mammals and the carcinogenic effects of these magnetic fields could be limited to leukemia.

## 1. Introduction

In 1979, Wertheimer and Leeper (1979) found an association between living near power lines and the occurrence of leukemia in children. They proposed that exposure to extremely low frequency magnetic fields (ELF-MF) from the power lines represents a risk factor for childhood leukemia. Extremely low frequency magnetic fields typically refer to electromagnetic waves with frequencies from 3 to 30 Hz but higher frequencies up to 300 Hz are also often defined as ELF-MF in the medical literature (Karimi et al., 2020). In the context of the present work, ELF-MF will refer to magnetic fields lower than 100 Hz, mostly 50 Hz (utility frequency used in most countries of the world) and 60 Hz (utility frequency used mostly in America). Residential magnetic fields like those emitted by overhead power lines and magnetic fields generated by household electric appliances fall within the range of ELF-MF (Deshayes-Pinçon et al., 2023; Hatch et al., 1998; Malagoli et al., 2023). All residential areas are affected by ELF-MF at least to some degree, which means that virtually all humans are exposed to these electromagnetic waves.

Over the past decades, an abundant scientific literature has examined the relationship between ELF-MF and cancer development but with conflicting results (Carpenter, 2019; Tian et al., 2023). A recent meta-analysis conducted by our team showed that exposure to ELF-MF generated by power lines or electric blankets is associated with a small but significant increase in the odds of developing childhood leukemia (Brabant et al., 2022). However, the conditions under which ELF-MF represent a risk factor for leukemia are still unclear and the carcinogenic effects of ELF-MF are still not well defined. All the studies included in our previous meta-analysis on childhood leukemia were observational studies where variables like the magnetic flux density could not be manipulated. In vitro and animal studies could be relevant to clarify the role of the magnetic flux density. Since most cancers are initiated by damage to the genome of the cells, several in vitro studies have been conducted to examine the genotoxic effects of magnetic fields

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on DNA and chromosomal structure (Ivancsits et al., 2003b; Mihai et al., 2014; Mustafa et al., 2022; Phillips et al., 2009). Moreover, many animal studies have been performed to determine whether ELF-MF exposure can increase the risk of developing cancers in mammals (Boorman et al., 1999; Bua et al., 2018; Campos-Sanchez et al., 2019; Qi et al., 2015). However, there are many conflicting results in this research field. Therefore, we have conducted a systematic review and meta-analysis of studies on the carcinogenic effects of ELF-MF performed with animals and the comet assay to clarify the conditions under which ELF-MF can promote cancer and leukemia development. These conditions could be the magnetic flux density, the duration of exposure to the magnetic field and/or the distance between an animal and the source of the magnetic field. We have taken into account the magnetic flux density in our meta-analyses.

## 2. Materials and methods

This systematic review has been conducted according to guidelines for systematic reviews of preclinical animal studies (Leenaars et al., 2012; Vesterinen et al., 2014). Our manuscript has been written according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 statement (Page et al., 2021). We have used Covidence to upload search results, screen abstracts and full-text articles and resolve disagreements. Our protocol has been pre-registered in Prospero in May 2022 and updated in May 2023 (Registration number: CRD42022321862). The objective of the update of the Prospero protocol was to limit our research to studies that have investigated the impact of ELF-MF on DNA damage assessed with the comet assay, a sensitive and efficient method for detecting DNA damage at the level of individual cells that has frequently been used to study the carcinogenic effects of ELF-MF (Kumaravel et al., 2009; Ostling and Johanson, 1984).

### 2.1. Inclusion and exclusion criteria

The population of our study is limited to animals and cells from animal or human origin. The intervention is defined as exposure to ELF-MF lower than 100 Hz. When studies assessed carcinogenicity in relation to ELF-MF and other agents, only findings based on ELF-MF exposure alone have been considered, because the goal of our systematic review is to focus on the potential carcinogenic effects of ELF-MF alone. The outcomes of the studies included in our systematic review are either the incidence of cancers or DNA damage evaluated with the comet assay. Thus, two types of studies have been included in our systematic review: animal studies that have examined the impact of ELF-MF on the incidence of cancers and comet assay studies that have assessed whether exposure to ELF-MF can damage DNA. The study designs of the articles included in our systematic review are experimental and observational studies. Only peer-reviewed journal articles reporting findings from primary studies published in English or French (because the authors are fluent in English and in French) have been included in our systematic review. We have excluded studies that have assessed DNA damage using techniques other than the comet assay. Meeting abstracts, conference proceedings, editorials and commentaries have been excluded.

### 2.2. Information sources and search strategies

We have systematically searched Medline, Scopus and Embase to find all the studies that have investigated the carcinogenic potential of ELF-MF in animal models and with the comet assay. Therefore, we have created search strategies based on a combination of MeSH and free-text terms associated with the main concepts covered by our systematic review: magnetic fields, cancer, DNA damage and animal models. The search strategies and search terms used in our research are described in Supplementary Tables 1–3. Moreover, we have performed a manual search of the bibliographic references of relevant studies and reviews.

### 2.3. Study selection

In the initial screening stage, two investigators (CB, CD) have independently reviewed the title and abstract of the references to exclude those that are irrelevant to our systematic review. In the second step, the same investigators have independently read the full texts of the articles selected after the initial search stage. Then, they have selected the studies that met the inclusion criteria. All differences of opinion in the selection process have been resolved through discussion and consensus.

### 2.4. Data extraction and data items

Data extraction has been performed by two independent reviewers (CB, CD). Data have been extracted in a standardized Excel sheet pretested on a sample of studies. The data extraction involved the following data: authors, journal name, year of publication, country, objective of the study, sample size, design, type of magnetic field (frequency and magnetic flux density), duration of exposure to the magnetic field, time of the day during which animals were exposed to the magnetic field, outcomes, type of cancer, conclusion, presence of conflicts of interest and funding. In case relevant information was missing from a study, we have contacted the authors.

### 2.5. Methodological quality assessment

The assessment of the methodological quality of the animal studies included in our systematic review has been performed independently by two reviewers (CB, CD) using the SYRCLE's risk of bias tool for animal studies (Hooijmans et al., 2014). Ten items were included in the assessment of the studies and covered selection bias, performance bias, detection bias, attrition bias, reporting bias and other sources of bias. Disagreements between the reviewers have been discussed until a consensus has been reached.

### 2.6. Outcomes

We have performed meta-analyses based on the following outcomes: the incidence of cancers, survival/longevity, body weight (in g) and DNA damage assessed with the comet assay. First, we have performed a global meta-analysis on the incidence of all the cancers that have been reported in all the animal studies that have assessed the impact of ELF-MF. Then, we have conducted secondary meta-analyses on the incidence of cancer but restricted to studies that have performed a complete necropsy of the animals (thus on studies that could assess any cancer after exposure to ELF-MF). Furthermore, we have performed secondary meta-analyses that focused on the incidence of specific cancers: leukemia, lymphoma, breast cancer and brain cancer. Finally, we have conducted meta-analyses on DNA damage with the studies that have used the comet assay.

### 2.7. Data synthesis and statistics

Study results were expressed as standardized mean differences (SMD) for continuous variables and odds ratios (OR) for binary variables with 95% confidence intervals (CI). Crude SMD or OR have been computed from the results that are available in the paper. Since the incidence of rodent hematopoietic neoplasms varies markedly with the species (Frith et al., 1993), we have taken into account the animal model (rats vs mice) in our meta-analyses. We have also considered the magnetic flux density in our meta-analyses and two magnetic field categories have been defined: magnetic fields higher than 0.2 μT and higher than 10 μT. The 0.2 μT threshold is the lowest rounded value that is higher than the ambient magnetic field of the control animals. Sham control rodents from the studies included in our meta-analyses were always exposed to magnetic fields lower than 0.2 μT. The use of magnetic fields higher than 10 μT is particularly relevant for rodents because they

require a greater magnetic field exposure than that required by humans to induce similar current density within the body (Hart, 1992; Xi et al., 1994).

Since experimental settings differed a lot among studies, we have assumed the presence of heterogeneity a priori and used a random-effects model to analyze the data. We have assessed heterogeneity using the $\chi^2$-based Q-Cochrane test and the $I^2$ measure of inconsistency (Higgins et al., 2003). Furthermore, subgroup analyses based on the animal species have been performed. A test of interaction using a mixed-effects model has been performed for all subgroups to determine whether the difference in effect size among subgroups was statistically significant (Brabant et al., 2022).

We have performed sensitivity analyses to evaluate the impact of individual studies on the overall results and the role of methodological quality assessed with the SYRCLE's risk of bias tool for animal studies. To perform the sensitivity analyses evaluating the role of methodological quality, we have excluded the low-quality studies (studies with at least one item with high risk of bias) as recommended by Dr Carlijn Hooijmans (Hooijmans et al., 2014).

The publication bias has been evaluated using a funnel plot and the Egger's regression asymmetry test when there were at least 10 studies per meta-analysis (Higgins et al., 2019). Significance was always set at $P < 0.05$ except when assessing heterogeneity with the Cochran's Q test ($P < 0.10$). We have performed our analyses using Review Manager (version 5.4) and R (metafor package, Viechtbauer, 2010).

## 3. Results

### 3.1. Selected studies and study characteristics

Seventy-one articles have been included in our systematic review (see flowchart on Fig. 1 and Appendix for the studies excluded from our systematic review and reasons of exclusion). The characteristics of the studies included in our systematic review are presented in Tables 1–4. Table 1 presents the characteristics of the animal studies that have assessed the impact of ELF-MF on the incidence of cancer. Table 2 presents the characteristics of the animal studies that have evaluated the effects of in vivo exposure to ELF-MF on DNA. Table 3 presents the characteristics of the in vitro studies that have investigated the impact of in vitro exposure to ELF-MF on DNA. Finally, the characteristics of the human studies in which in vivo exposure to ELF-MF has been examined on DNA are shown in Table 4. Most studies were experimental studies and two studies were observational.

The results of the methodological quality of the animal studies included in our systematic review are shown in Supplementary Table 4. Overall, many methodological details of the studies covered by our review were missing, especially those related to group allocation, outcome assessment and outcome reporting. As a result, the risk of bias was unclear for many items of several studies. The risk of bias due to blinded group allocation (Item C of Supplementary Table 4) and random outcome assessment (Item F of Supplementary Table 4) was assessed as unclear in each study. Moreover, there were no publicly available

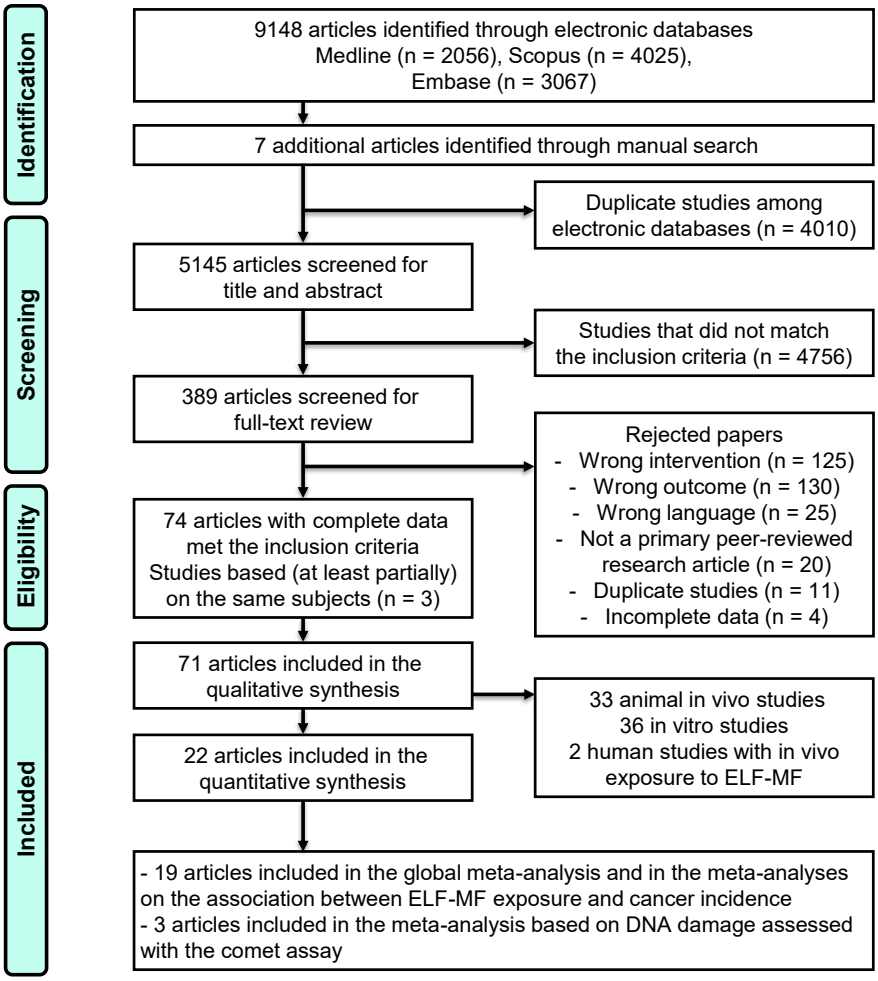


**Fig. 1.** Flowchart of selection of studies for inclusion in the meta-analysis. See Appendix for the studies excluded from our systematic review and the reasons of exclusion.

**Table 1**
Characteristics of the studies included in the systematic review that have assessed the impact of ELF-MF on cancer incidence.

| First author | Animal species, strain, sex | Number of animals | Intervention/ duration of the magnetic field exposure | Experimental groups and magnetic flux density (μT) | Outcomes | Main results | Funding |
|---|---|---|---|---|---|---|---|
| Babbitt et al., 2000 | Female C57BL/ 6J mice | 2660 | Mice were exposed to 60 Hz magnetic fields 18 h per day during their entire life. | Sham-exposure, 1420 μT | Hematopoietic neoplasms (lymphomas and histiocytic sarcomas) | Long-term exposure to 60 Hz magnetic fields had no significant effects on the incidence of hematopoietic neoplasms. | Supported by research contracts with the Electric Power Research Institute, Palo Alto, CA with co-funding from BC-Hydro |
| Baum et al., 1995 | Female Sprague-Dawley rats | 216 (but only 18 rats were only sham-exposed or only exposed to 50 Hz magnetic fields) | Rats were exposed to 50 Hz magnetic fields 24 h per day for 91 days. | Sham-exposure, 100 μT | Breast cancer | Exposure to 50 Hz magnetic fields did not increase the incidence of breast cancer. | Supported by the "Forschungsverbund Elektromagnetische Verträglichkeit Biologischer Systeme" (Braunschweig, Germany) and the "Berufsgenossenschaft der Feinmechanik und Elektrotechnik" (Köln, Germany) |
| Boorman et al., 1999 | Male and female F344/N rats | 1000 | Rats were exposed to 60 Hz magnetic fields 18.5 h per day for 2 years. | Sham-exposure, continuous exposure to 2 μT, 200 μT and 1000 μT, intermittent exposure to 1000 μT (1 h on, 1 h off) | All types of cancers | Long-term exposure to 60 Hz magnetic fields had little or no effect on the development of cancers. | NR |
| Bua et al., 2018 | Male and female Sprague-Dawley rats | 5029 | Rats were exposed to 50 Hz magnetic fields 19 h per day during their entire life (including prenatal life, exposure began on the 12th day of pregnancy). | Sham-exposure, continuous exposure to 2 μT, 20 μT, 100 μT and 1000 μT, intermittent exposure to 1000 μT (30 min on, 30 min off) | All types of cancers | Long-term exposure to 50 Hz magnetic fields had no effect on the development of cancers. | Supported by the Ramazzini Institute (Bologna, Italy), the Regional Agency for Prevention and the Environment, Children with Cancer (UK) and other organizations |
| Campos-Sanchez et al., 2019 | Male and female ETV6-RUNX1 transgenic mice, a model of childhood B-cell acute lymphoblastic leukemia | 61 | Mice were exposed intermittently to 50 Hz magnetic fields (10 min on, 5 min off) 20 h per day, from conception until 3 months of age. Mice were monitored until they were two years old. | Control group, 1500 μT | B-cell acute lymphoblastic leukemia | One mouse exposed to 50 Hz magnetic fields developed B-cell acute lymphoblastic leukemia. None of the control mice developed B-cell acute lymphoblastic leukemia. | Grant sponsor: European Union's 7th Framework Programme |
| Chung et al., 2010 | Female lymphoma-prone AKR mice | 160 | Mice were exposed to 60 Hz magnetic fields 21 h per day from the age of 4–6 weeks to the age of 44–46 weeks. | Sham-exposure, 5 μT, 83.3 μT, 500 μT | Lymphoma | Long-term exposure to 60 Hz magnetic fields had no effect on lymphoma development. | Supported by the Ministry of knowledge Economy |
| Fam and Mikhail, 1996 | Male and female CFW mice | 203 (three generations of mice) | The first generation of mice was continuously exposed to 60 Hz magnetic fields from the age of 8 weeks until death. Mice from the second and third generations were continuously exposed to 60 Hz magnetic fields, from conception (in utero) to | Control group, 25 000 μT | Lymphoma | Long-term exposure to very strong 60 Hz magnetic fields promotes the development of lymphoma in CFW mice. | NR |

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**Table 1** (*continued*)

| First author | Animal species, strain, sex | Number of animals | Intervention/ duration of the magnetic field exposure | Experimental groups and magnetic flux density (μT) | Outcomes | Main results | Funding |
|---|---|---|---|---|---|---|---|
| | | | death. The duration of exposure to the magnetic field varied between 55 and 418 days. | | | | |
| Harris et al., 1998 | Female lymphoma prone Eμ-Pim1 transgenic mice | 685 (with positive controls) | When mice were 6–8 weeks old, they were exposed to 50 Hz magnetic fields 20 h per day for 18 months. | Sham-exposure, continuous exposure to 1 μT, 100 μT and 1000 μT, intermittent exposure to 1000 μT (15 min on, 15 min off) | Lymphoma | Long-term exposure to 50 Hz magnetic fields had no effect on lymphoma development. | Supported by the Electricity Supply Association of Australia and by the National Health and Medical Research Council (Canberra) |
| Kharazi et al., 1999 | Female C57BL/6 mice | 2280 | Beginning at 28–32 days of age, mice were exposed to 60 Hz magnetic fields 18 h per day until their death. | Sham-exposure, 1420 μT | Brain cancer | Long-term exposure to 60 Hz magnetic fields had little or no effect on the development of brain cancer. | Supported by the National Institute of Environmental Health, NIH and research contracts with the Electric Power Research Institute, Palo Alto, CA |
| Mandeville et al., 1997 | Female F344 rats | 335 | Rats were exposed to 60 Hz magnetic fields 20 h per day. Rats were exposed for 104 weeks starting from the prenatal period (2 days before birth) until late adult life. | Sham-exposure, continuous exposure to 2 μT, 20 μT, 200 μT and 2000 μT | All types of cancers | Long-term exposure to 60 Hz magnetic fields had no effect on the development of cancers. | Supported by Health Canada with the collaboration of Hydro Quebec and Ontario Hydro and by a special grant from the Quebec Government and IAF |
| McCormick et al., 1998 | Hemizygous TSG-p53 [C57Bl/ 6TacfBR-(KO) p53] mice | 420 | Mice were exposed to 60 Hz magnetic fields 18.5 h per day for 23 weeks. | Sham-exposure, 1000 μT | Lymphoma | Long-term exposure to 60 Hz magnetic fields had no effect on lymphoma development. | Supported by the National Toxicology Program, National Institute of Environmental Health Sciences, NIH |
| McCormick et al., 1999 | Male and female B6C3F1 Mice | 1000 | Mice were exposed to 60 Hz magnetic fields for 18.5 h per day for 104 weeks. Mice were 6–7 weeks old at the beginning of the study. | Sham-exposure, continuous exposure to 2 μT, 200 μT and 1000 μT, intermittent exposure to 1000 μT (1 h on, 1 h off) | All types of cancers | Long-term exposure to 60 Hz magnetic fields did not promote the development of cancers. | NR |
| Mevissen et al., 1996a | Female Sprague-Dawley rats | 216 (but only 18 rats were only sham-exposed or only exposed to 50 Hz magnetic fields) | Rats were exposed to 50 Hz magnetic fields (24 h per day) for 91 days. | Sham-exposure, 10 μT | Breast cancer | Exposure to 50 Hz magnetic fields for 91 days had no effect on the development of breast cancer. | Supported by the "Forschungsverbund Elektromagnetische Verträglichkeit Biologischer Systeme" (Technical University, Braunschweig, Germany) and the "Berufsgenossenschaft der Feinmechanik und Elektrotechnik" (Köln, Germany) |
| Mevissen et al., 1996b | Female Sprague-Dawley rats | 216 (but only 18 rats were only sham-exposed or only exposed to 50 Hz magnetic fields) | Rats were exposed to 50 Hz magnetic fields (24 h per day) for 91 days. | Sham-exposure, 50 μT | Breast cancer | Exposure to 50 Hz magnetic fields for 91 days had no effect on the development of breast cancer. | Supported by the "Forschungsverbund Elektromagnetische Verträglichkeit Biologischer Systeme" (Technical University, Braunschweig, Germany) and the "Berufsgenossenschaft der Feinmechanik und Elektrotechnik" (Köln, Germany) |

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**Table 1** (*continued*)

| First author | Animal species, strain, sex | Number of animals | Intervention/ duration of the magnetic field exposure | Experimental groups and magnetic flux density (μT) | Outcomes | Main results | Funding |
|---|---|---|---|---|---|---|---|
| Otaka et al., 2002 | C57BL/6J female mice, C3H/HeJ male mice, B6C3F1 offspring | 549 B6C3F1 pups | C57BL/6J female and C3H/HeJ male mice were exposed to 50 Hz magnetic fields. Their B6C3F1 offspring has been examined to study the effect of parental and prenatal magnetic field exposure on cancer incidence. | Sham-exposure, 500 μT, 5000 μT | All types of cancers | Parental/prenatal exposure to 50 Hz magnetic fields did not significantly increase the incidence of cancers. | NR |
| Qi et al., 2015 | Male and female B6C3F1 mice | 148 | C57BL/6NJ female mice mated with C3H/HeNJ male mice and were exposed to 50 Hz magnetic fields for 1 week (12 h per day) and produced B6C3F1 mice. Then, the B6C3F1 mice were continuously exposed to 50 Hz magnetic fields for 15.5 months. | Sham-exposure, 50 μT | All types of cancers | Long-term exposure to 50 Hz magnetic fields increased the incidence of chronic myeloid leukemia. | Supported by the National Natural Science Foundation of China and the Prefectural University of Hiroshima, Hiroshima Tsuchiya General Hospital, Hiroshima |
| Reif et al., 1995 | Dogs (race not mentioned) | 230 | Hospital-based case-control study conducted in the USA. Dogs were exposed to residential 60 Hz magnetic fields. Cases came from a veterinary teaching hospital and had histologically confirmed lymphoma diagnosed between 1987 and 1990. | Dogs exposed to low magnetic fields (<0.2 μT), dogs exposed to high magnetic fields (>0.2 μT) | Canine lymphoma | Residential 60 Hz magnetic fields increased the risk of canine lymphoma. | NR |
| Sommer and Lerchl, 2004 | Female AKR/J mice (strain prone to develop lymphoma) | 480 | Beginning at the age of 4–5 weeks, mice were exposed to 50 Hz magnetic fields 24 h per day for 38 weeks. | Sham-exposure, 1 μT, 100 μT | Thymic lymphoblastic lymphoma | Long-term exposure to 50 Hz magnetic fields had no effect on lymphoma development. | Supported by the "Bundesamt für Strahlenschutz" (Salzgitter, Germany) |
| Sommer and Lerchl, 2006 | Female AKR/J mice (strain prone to develop lymphoma) | 480 | Beginning at the age of 12 weeks, mice were exposed to 50 Hz magnetic fields for 32 weeks, either for 24 h per day or only during nighttime (12 h per day). | Sham-exposure, 1000 μT | Thymic lymphoblastic lymphoma | Long-term exposure to 50 Hz magnetic fields had no effect on lymphoma development. | Supported by the "Bundesamt für Strahlenschutz" (Salzgitter, Germany) |
| Vallejo et al., 2001 | Female OF1 mice | 94 | Mice were exposed to 50 Hz magnetic fields for 14–15 weeks or for 50–52 weeks. | Sham-exposure, 15 μT | Blood leukoproliferative disorders, leukemia | Exposure to 50 Hz magnetic fields increased the incidence of leukemia. | Partially supported by AMYS-UNESA (P.I.E. 134039) |

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**Table 1** (*continued*)

| First author | Animal species, strain, sex | Number of animals | Intervention/ duration of the magnetic field exposure | Experimental groups and magnetic flux density (μT) | Outcomes | Main results | Funding |
|---|---|---|---|---|---|---|---|
| Yasui et al., 1997 | Male and female F344/DuCrj rats | 288 | Beginning at the age of 5 weeks, rats were exposed to 50 Hz magnetic fields until they were 109 weeks old. Average exposure to the magnetic field was 22.6 h per day. | Sham-exposure, 500 μT, 5000 μT | All types of cancers | Long-term exposure to 50 Hz magnetic fields had no effect on the development of cancers. | NR |

All the animal studies included in our systematic review are experimental studies except the case-control study by Reif et al. (1995).

protocols for the studies included in our systematic review. Therefore, all the studies received an unclear risk of bias for the item pertaining to the selective outcome reporting (Item I of Supplementary Table 4).

Two animal studies that have assessed the development of cancer (Otaka et al., 2002; Reif et al., 1995) could not be included in our meta-analyses, because they used methods that differed too much from those used in the other studies included in our systematic review. The results of the studies by Otaka et al. (2002) and Reif et al. (1995) are shown in Table 5. The SYRCLE's risk of bias tool indicated that the study by Otaka et al. (2002) was a low-quality study. The study by Reif et al. (1995) was an observational case-control study performed with dogs and supports an association between residential magnetic fields and canine lymphoma. The article by Reif et al. (1995) has not been evaluated with the SYRCLE's risk of bias tool, because this tool is restricted to experimental studies.

### 3.2. Global meta-analysis

The global meta-analysis based on the cancers reported in all the animal studies that have assessed the effects of ELF-MF on cancer development showed no significant association between magnetic fields above 0.2 μT and the incidence of cancers (OR = 1.10; 95% CI 0.91–1.32; 19 studies; Fig. 2). Heterogeneity between studies was significant (Q (14) = 25.75; p = 0.03; $I^2$ = 46%) in the entire group. The funnel plot suggests that publication bias is likely (Supplementary Fig. 1; Egger's test: p = 0.042). Omission of low-quality studies (Campos-Sanchez et al., 2019; Fam and Mikhail, 1996; Qi et al., 2015; Sommer and Lerchl, 2004; Yasui et al., 1997) from the meta-analysis did not change the results (OR = 1.03; 95% CI 0.88–1.20) but suppressed the publication bias and the Egger's test was no longer significant (p = 0.185).

There was no significant association between ELF-MF and cancer development when the global meta-analysis was restricted to magnetic fields above 10 μT (OR = 1.07; 95% CI 0.89–1.30; 19 studies; Supplementary Fig. 2). Heterogeneity between studies was significant (Q (14) = 26.25; p = 0.02; $I^2$ = 47%) in the entire group. The funnel plot suggests that publication bias is possible (Supplementary Fig. 3; Egger's test: p = 0.062). Omission of low-quality studies (Campos-Sanchez et al., 2019; Fam and Mikhail, 1996; Qi et al., 2015; Sommer and Lerchl, 2004; Yasui et al., 1997) from the meta-analysis did not affect the results (OR = 1.03; 95% CI 0.87–1.21) but suppressed the publication bias (Egger's test: p = 0.182).

### 3.3. Meta-analyses restricted to studies with a complete necropsy

Our meta-analyses based on the six studies that have performed a complete necropsy of the animals after magnetic field exposure indicate that ELF-MF did not increase the incidence of cancer in rodents, compared to non-exposure (Supplementary Figs. 4 and 5). Heterogeneity between studies was not significant. Omission of low-quality studies (Qi et al., 2015; Yasui et al., 1997) from the meta-analyses did not change the results (Supplementary Table 5).

### 3.4. Meta-analyses based on the incidence of leukemia and lymphoma

Our meta-analyses based on seven studies indicate that exposure to ELF-MF did not significantly increase the incidence of leukemia in rodents (Supplementary Figs. 6 and 7). Heterogeneity between studies was significant in the entire group (>0.2 μT: Q (6) = 13.78; p = 0.03; $I^2$ = 56%; >10 μT: Q (6) = 13.32; p = 0.04; $I^2$ = 55%). However, heterogeneity was not significant in mice alone and in rats alone. Compared to non-exposure, exposure to ELF-MF increased the odds of developing leukemia in mice (4 studies, >0.2 μT: OR = 4.45; 95% CI 1.90–10.38; >10 μT: OR = 4.54; 95% CI 1.94–10.60) but not in rats (3 studies, >0.2 μT: OR = 0.92; 95% CI 0.69–1.22; >10 μT: OR = 0.95; 95% CI 0.71–1.27). Omission of low-quality studies from the meta-analyses did not substantially alter the main results (Supplementary Table 5).

Our meta-analyses based on eleven studies indicate that exposure to ELF-MF did not significantly increase the incidence of lymphoma in rodents (Supplementary Figs. 8 and 10). Heterogeneity between studies was significant in the entire group (>0.2 μT: Q (9) = 15.90; p = 0.07; $I^2$ = 43%; >10 μT: Q (9) = 17.35; p = 0.04; $I^2$ = 48%). The funnel plots suggest that publication bias is unlikely (Supplementary Figs. 9 and 11; Egger's tests: p = 0.161 for >0.2 μT; p = 0.166 for >10 μT). Omission of low-quality studies did not importantly alter the results (Supplementary Table 5).

### 3.5. Meta-analyses based on the incidence of breast cancer and brain cancer

Our meta-analyses indicate that exposure to ELF-MF did not increase the odds of breast cancer (nine studies, Supplementary Figs. 12 and 13) and brain cancer (six studies, Supplementary Figs. 14 and 15) in rodents. Heterogeneity between studies was not significant. Omission of low-quality studies did not alter the results (Supplementary Table 5).

### 3.6. Meta-analyses based on survival

Our meta-analyses based on seven studies indicate that exposure to ELF-MF did not alter survival in rodents (Supplementary Figs. 16 and 17), compared to non-exposure. Heterogeneity between studies was not significant. Omission of low-quality studies (Sommer and Lerchl, 2004; Yasui et al., 1997) from the meta-analyses did not alter the results (OR = 1.01; 95% CI 0.83–1.24 for >0.2 μT; OR = 1.00; 95% CI 0.79–1.26 for >10 μT).

**Table 2**
Characteristics of the animal comet assay studies included in the systematic review with in vivo exposure to the magnetic field.

| First author | Animal species, strain, sex | Cell type | Number of animals | Intervention/duration of the magnetic field exposure | Experimental groups and magnetic flux density (μT) | Comet assay parameters | Main results | Funding |
|---|---|---|---|---|---|---|---|---|
| Lai and Singh, 1997a | Male Sprague-Dawley rats | Brain cells | 72 | Rats were exposed to 60 Hz magnetic fields for 2 h. | Sham-exposure, 100 μT, 250 μT and 500 μT | DNA migration length (in μm) | Dose-dependent increase in DNA damage | Supported by the National Institute of Environmental Health Sciences |
| Lai and Singh, 1997b | Male Sprague-Dawley rats | Brain cells | Unclear | Rats were exposed to 60 Hz magnetic fields for 2 h, with or without free radical scavengers (melatonin or N-tert-butyl-α-phenylnitrone). | Sham-exposure, 500 μT | DNA migration length (in μm) | DNA damage. The free radical scavengers blocked the magnetic-field-induced DNA damage | Supported by the National Institute of Environmental Health Sciences |
| Lai and Singh, 2004 | Male Sprague-Dawley rats | Brain cells | 158 | Rats were exposed to 60 Hz magnetic fields for 24 h or 48 h, with or without Trolox (vitamin E analog) or 7-nitroindazole (nitric oxide synthase inhibitor). | Sham-exposure, 10 μT | DNA migration length (in μm) | DNA damage. Trolox or 7-nitroindazole blocked the magnetic-field-induced DNA damage | Supported by the National Institute of Environmental Health Sciences |
| Mariucci et al., 2010 | Male CD1 mice | Brain cells (cerebral cortex-striatum, hippocampus and cerebellum) | 99 | Mice were exposed to 50 Hz magnetic fields for 1 or 7 days (15 h per day) and sacrificed either at the end of the exposure or after 24 h to evaluate DNA damage. | Sham-exposure, 1000 μT | Tail moment, tail intensity (% DNA in the comet tail) | DNA damage (reversible) | Supported by the University of Perugia and by the "Fondazione Cassa di Risparmio di Perugia" |
| McNamee et al., 2002 | Immature (10-day-old) ICR mice | brain cells (cerebellum) | 120 | Mice were exposed to 60 Hz magnetic fields for 2 h. | Sham-exposure, 1000 μT | Tail ratio, tail moment, comet length and tail length | DNA damage detected by tail ratio but not with other measures | NR |
| McNamee et al., 2005 | Male Sprague-Dawley rats, male ICR mice, immature ICR mice | Brain cells | 252 | Rodents were exposed to 60 Hz magnetic fields for 2 h. | Sham-exposure, 100 μT, 1000 μT and 2000 μT | Tail ratio, tail moment, comet length and tail length | No effects | NR |
| Rageh et al., 2012 | Newborn rats (strain not mentioned) | Brain cells | 20 | Rats were exposed continuously to 50 Hz magnetic fields 24 h per day for 30 days. | Sham-exposure, 500 μT | Tail moment | DNA damage | NR |
| Singh and Lai, 1998 | Male Sprague-Dawley rats | Brain cells | 64 | Rats were exposed to 60 Hz magnetic fields for 2 h. | Sham-exposure, 500 μT | DNA migration length (in μm) | DNA damage | Supported by grants from the National Institute of Environmental Health Sciences |
| Svedenstal et al., 1999a | Male CBA/Ca mice | Brain cells | 74 | The mice were housed under 220 kV transmission lines (50 Hz magnetic field) for 11, 20 or 32 days. | The control mice were placed 200 m or 500 m away from the lines, where the magnetic flux density was ~0.06 or ~0.02 μT, respectively. The exposed mice were exposed to ~8 μT magnetic fields | DNA migration length, ratio of tail/head | DNA damage after 32 days of magnetic field exposure | Supported by the Swedish Electrical Utilities R & D Company |
| Svedenstal et al., 1999b | Male CBA/Ca mice | Brain cells | 37 | Mice were exposed to 50 Hz magnetic fields for 2 h, 5 days or 14 days. | Sham-exposure, 500 μT | DNA migration length, ratio of tail/head | DNA damage after 14 days of magnetic field exposure | NR |
| Udroiu et al., 2015 | Young CD-1 Swiss outbred mice | Epididymal sperm | 103 | Pups were exposed to 50 Hz magnetic fields 24 h per day from day 12 post conception until weaning, for a total of 30 days. | Sham-exposure, 65 μT | Tail intensity, percentage of sperm with damaged DNA | No DNA damage in the comet assay | Supported by the "Istituto nazionale per l'assicurazione contro gli infortuni sul lavoro" |
| Villarini et al., 2013 | Adult male CD1 mice | Brain cells | 96 | Mice were exposed to 50 Hz magnetic fields for 7 days (15 h per day) and sacrificed either at the end of the exposure or after 24 h to evaluate DNA damage. | Sham-exposure, 100 μT, 200 μT, 1000 μT and 2000 μT | Tail intensity (% DNA in the comet tail) | Dose-dependent increase in DNA damage (reversible) | Supported by the University of Perugia and by the "Fondazione Cassa di Risparmio di Perugia" |

**Table 3**
Characteristics of the comet assay studies included in the systematic review with in vitro exposure to the magnetic field.

| First author | Cell origin, cell type | Intervention/duration of the magnetic field exposure | Experimental groups and magnetic flux density (μT) | Comet assay parameters | Main results | Funding |
|---|---|---|---|---|---|---|
| Ahuja et al., 1999 | Human, peripheral leukocytes | Cells were exposed to 50 Hz magnetic fields for 1 h. | Unexposed control cells, 2000 μT, 3000 μT, 5000 μT, 7000 μT, 10 000 μT | Tail length | DNA damage | NR |
| Buldak et al., 2012 | Mouse, AT478 squamous cell carcinoma cells | Cells were exposed to 50 Hz magnetic fields for 16 min. | Sham-exposure, 1000 μT | Tail moment | DNA damage | Grant sponsor: Medical University of Silesia in Katowice |
| Burdak-Rothkamm et al., 2009 | Human, VH25 human skin fibroblasts | Cells were intermittently exposed (5 min on, 10 min off) to 50 Hz magnetic fields for 15 h. | Sham-exposure, 50 μT, 100 μT, 500 μT, 1000 μT | Tail moment, % DNA in tail | No effects | Supported by the EMF Biological Research Trust |
| Duan et al., 2015 | Mouse, mouse spermatocyte-derived cell line (GC-2) | Cells were exposed to 50 Hz magnetic fields for 24 h. | Sham-exposure, 1000 μT, 2000 μT, 3000 μT | % DNA in tail, tail length | Dose-dependent increase in DNA damage | Supported by the National Basic Research Program of China, the National Natural Science Foundation of China and the Natural Science Foundation from Chongqing science and technology commission |
| Fairbairn and O'Neill, 1994 | Human, Raji cells | Cells were exposed to 50 Hz magnetic fields for 1 h or 24 h. | Sham-exposure, 5000 μT | Ratio of the height of the comet divided by the length of the comet in the direction of electrophoresis | No effects | NR |
| Hao et al., 2011 | Human, K562 cells (ATCC, CCL-243) | Cells were exposed continuously to a uniform static 50 Hz magnetic field for 12 h. | Sham-exposure, 8800 μT | Olive tail moment | No effects | Supported by the National Natural Science Foundation of China, the National Basic Research Priority Program of China and the Fundamental Research for the Central Universities |
| Huang et al., 2022 | Human, primary human gingival fibroblasts (HGFs) from healthy donors | Cells were exposed to 10 Hz pulsed magnetic fields for 24 h. | Unexposed control cells, 1000 μT | Olive tail moment, tail DNA percentage | DNA damage in some samples, no effects in other samples | Supported by the Key medical disciplines of Hangzhou and other grants |
| Ivancsits et al., 2002 | Human, human diploid fibroblasts from two healthy donors | Cells were exposed to 50 Hz magnetic fields for 24 h. To study dose-response effects, the magnetic flux density varied between 20 and 2000 μT and an intermittent exposure was used (5 min on/10 min off). | Sham-exposure, 20 μT, 50 μT, 70 μT, 100 μT, 250 μT, 500 μT, 750 μT, 1000 μT, 2000 μT | Tail factor (%) | Intermittent exposure to 50 Hz magnetic fields caused an increase in DNA damage | Supported by the European Union under the program "Quality of Life and Management of Living Resources", Key Action 4 "Environment and Health": QLK4-CT-1999-01574 |
| Ivancsits et al., 2003a | Human, human diploid fibroblasts from healthy donors | Cells were intermittently exposed to 50 Hz magnetic fields (5 min on/10 min off). Exposure duration varied between 1 and 24 h in 1-h steps. | Sham-exposure, 1000 μT | Tail factor (%) | DNA damage with a maximal response after 15–19 h of magnetic field exposure | Supported by the European Union under the program "Quality of Life and Management of Living Resources", Key Action 4 "Environment and Health": QLK4-CT-1999-01574 |
| Ivancsits et al., 2003b | Human, human diploid fibroblasts from healthy donors | Cells were intermittently exposed to 50 Hz magnetic fields (5 min on/10 min off) for 15 h. | Sham-exposure, 20 μT, 35 μT, 50 μT, 70 μT, 100 μT and 1000 μT | Tail factor (%) | Dose-dependent increase in DNA damage | Supported by the European Union under the program "Quality of Life and Management of Living Resources", Key Action 4 "Environment and Health": QLK4-CT-01574 |
| Ivancsits et al., 2005 | Human, rat, 6 types of cells: human diploid fibroblasts, human melanocytes, rat granulosa cells, human lymphocytes, human | Cells were intermittently exposed to 50 Hz magnetic fields (5 min on/10 min off) for 15 h. Time-dependent effects were | Sham-exposure, 1000 μT | Tail factor (%) | DNA damage in human fibroblasts, human melanocytes and rat granulosa cells. No effects in human lymphocytes, human | Supported by the European Union under the program "Quality of Life and Management of Living Resources", Key Action 4 "Environment |

(*continued on next page*)

**Table 3** (*continued*)

| First author | Cell origin, cell type | Intervention/duration of the magnetic field exposure | Experimental groups and magnetic flux density (μT) | Comet assay parameters | Main results | Funding |
|---|---|---|---|---|---|---|
| | monocytes, human skeletal muscle cells | studied at a magnetic flux density of 1000 μT. Exposure duration varied between 1 and 24 h in 1-h steps. | | | monocytes and human skeletal muscle cells | and Health": QLK4-CT-1999-01574 |
| Jajte et al., 2001 | Rat, rat lymphocytes | Cells were exposed to 50 Hz magnetic fields for 3 h. | Sham-exposure, 7000 μT | Percentage of damaged cells | No effects | NR |
| Jin et al., 2014 | Human, mouse, NIH3T3 mouse fibroblast cells, WI-38 human lung fibroblast cells, L132 human lung epithelial cells, MCF10A human mammary gland epithelial cells | Cells were exposed for 4 or 16 h to 60 Hz magnetic fields. | Sham-exposure, 1000 μT | Olive tail moment | No effects | Supported by the Power Generation & Electricity Delivery of the Korea Institute of Energy Technology, Evaluation and Planning, the Korean Ministry of Trade, Industry & Energy and the Ewha Global Top 5 Grant 2012 of Ewha Womans University |
| Kim et al., 2012 | Human, IMR90 (human lung fibroblast) and HeLa cells (human cervical carcinoma) | Cells were exposed to 60 Hz magnetic fields for 30 min. | Sham-exposure, 7000 μT | Description of the comet tail length (no tail, short dragging tail or long dragging tail) | DNA damage | Supported by the Korean Research Institute for Chemical Technology, the Ministry of Knowledge Economy, Korea and the Korean Research Foundation |
| Luceri et al., 2005 | Human, peripheral human lymphocytes | Cells were exposed to 50 Hz magnetic fields for 18 h. | Sham-exposure, 1 μT, 10 μT, 100 μT | DNA breaks, DNA base oxidation | No effects | Supported by the Italian Ministry for Productive Activities |
| Luukkonen et al., 2011 | Human, SH-SY5Y neuroblastoma cells | Cells were exposed to 50 Hz magnetic fields for 24 h. | Sham-exposure, 100 μT | Olive tail moment | No effects | Supported by the Finnish Ministry of Education and the University of Eastern Finland |
| Luukkonen et al., 2017 | Human, SH-SY5Y neuroblastoma cells | Cells were exposed to 50 Hz magnetic fields for 24 h. | Sham-exposure, 100 μT | Olive tail moment | No effects | Supported by strategic funding of the University of Eastern Finland |
| Mihai et al., 2014 | Monkey, Vero cells | Cells were exposed to 100 Hz magnetic fields, continuously or intermittently (1 s on, 3 s off), for 45 min. | Sham-exposure, 5600 μT | Tail length, % tail DNA, tail moment and Olive tail moment | DNA damage | Supported by the Sectoral Operational Programme for Human Resources Development |
| Moretti et al., 2005 | Human, Jurkat cells (human lymphoblastoid T-cells) | Cells were exposed to 50 Hz magnetic fields for 1 h. | Sham-exposure, 1000 μT | Tail intensity (percentage of fluorescence migrated in the comet tail) | No effects | Supported by the Ministry of Labour and Social Policies |
| Mustafa et al., 2021 | Mouse, murine FDC-P1 hematopoietic cells | Cells were exposed for different durations (15 min, 2 h, 12 h and 24 h) to 50 Hz magnetic fields. | Sham-exposure, 200 μT | Olive tail moment | No effects | Supported by the University of Eastern Finland's Doctoral School, the Environmental Physics, Health and Biology doctoral program and by the Academy of Finland |
| Mustafa et al., 2022 | Human, SH-SY5Y neuroblastoma cells | Cells were exposed to 50 Hz magnetic fields for 24 h. | Sham-exposure, 100 μT | Olive tail moment | No effects | Supported by the Academy of Finland and the UEF Doctoral Programme in Environmental Physics, Health and Biology |
| Nakayama et al., 2016 | Mouse, macrophage RAW264 cells | Cells were exposed to 50 Hz magnetic fields for 24 h. | Sham-exposure, 500 μT | Olive tail moment | No effects | Supported by the Grant-In-Aid from MEXT and a scholarship (Weaving Science Web beyond Particle-Matter Hierarchy) from Tohoku University |
| Nikolova et al., 2005 | Mouse, mouse embryonic stem cells (embryonic stem cell-derived neural progenitor cells) | Cells were exposed to 50 Hz magnetic fields intermittently (5 min on, 30 min off) for 6 or 48 h. | Sham-exposure, 2000 μT | Tail factor (%) | No effects | Supported by the VERUM Foundation, the FCI ("Fonds der Chemischen Industrie") and the EU project QLK4-CT-1999-01574 (REFLEX) |

(*continued on next page*)

**Table 3** (*continued*)

| First author | Cell origin, cell type | Intervention/duration of the magnetic field exposure | Experimental groups and magnetic flux density (μT) | Comet assay parameters | Main results | Funding |
|---|---|---|---|---|---|---|
| Scarfi et al., 2005 | Human, human diploid fibroblasts | Cells were intermittently exposed to 50 Hz magnetic fields (5 min on/10 min off) for 15 or 24 h. | Sham-exposure, 1000 μT | Tail factor, tail DNA percentage, tail moment, comet moment | No effects | Supported by the Commission of the European Communities |
| Stronati et al., 2004 | Human, human leukocytes | Cells were exposed to 50 Hz magnetic fields for 2 h. | Sham-exposure, 1000 μT | Tail moment | No effects | Partially supported by the Ministry of Environment |
| Sun et al., 2018 | Mouse, wild-type and Atm-deficient mouse embryonic fibroblasts | Cells were exposed to 50 Hz magnetic fields for 1 or 24 h. | Sham-exposure, 2000 μT | Olive tail moment, % tail DNA | No effects | Supported by the Ministry of Science and Technology and the National Natural Science Foundation of China |
| Sun et al., 2021 | Human, 2BS cells isolated from human fetal lung fibroblasts | Cells were exposed intermittently to 10 Hz pulsed magnetic fields (1 day on/1 day off) for 2 weeks. | Unexposed control cells, 1000 μT | Olive tail moment | Nonsignificant increase in DNA damage (but significant with γH2AX technology) | Supported by the Medical Science and Technology Project of Zhejiang Province and other grants |
| Testa et al., 2004 | Human, human peripheral lymphocytes | Cells were exposed to 50 Hz magnetic fields for 48 h. | Sham-exposure, 1000 μT | Tail moment, % tail DNA | No effects | Supported by the Ministry of the Environment |
| Villarini et al., 2006 | Human, human peripheral leukocytes | Cells were exposed to 50 Hz magnetic fields for different time periods (30, 60 or 120 min). | Sham-exposure, 3000 μT | Tail moment | No effects | NR |
| Villarini et al., 2017 | Human, SH-SY5Y and SK-N-BE-2 human neuroblastoma cells | Cells were exposed to 50 Hz magnetic fields. Exposure was continuous for 1 h or intermittent (15 min on, 15 min off) for 5 h. | Sham-exposure, 10 μT, 100 μT, 1000 μT | Tail intensity | No effects | Supported by the "Fondazione Cassa di Risparmio di Perugia" and the University of Perugia |
| Wang et al., 2019 | Human, human ventricular cardiomyocyte cell line AC16 cells (human ventricular cardiomyocytes) | Cells were exposed to 50 Hz magnetic fields, continuously for 1 h or intermittently (15 min on/15 min off) for 75 min. | Sham-exposure, 100 μT | Tail DNA %, tail length, tail moment and comet length | No effects | Supported by the National Natural Science Foundation of China and The Science and Technology Project of the State Grid Corporation of China |
| Wolf et al., 2005 | Human, rat, human promyelocytic leukemia HL-60 cells, Rat-1 fibroblasts (immortalized cells), WI-38 diploid fibroblasts derived from embryonic human lung | Cells were exposed to 50 Hz magnetic fields for 24–72 h, with or without the antioxidant α-tocopherol. | Unexposed control cells, 500 μT, 750 μT, 1000 μT | Tail moment | Dose-dependent increase in DNA damage (results of unexposed control cells not shown). The magnetic-field-induced DNA damage was prevented by α-tocopherol | Supported by COFIN, ISPESL (Istituto Superiore per la Prevenzione e la Sicurezza del Lavoro) and UCSC |
| Yin et al., 2016 | Rat, primary cultured hippocampal neurons from newborn Sprague-Dawley-rats (both genders) | Cells were exposed to 50 Hz magnetic fields for 90 min. | Sham-exposure, 8000 μT | Tail DNA %, tail moment | DNA damage | Supported by the National Natural Science Foundation of China and the Special Research Fund for National Public Industry |
| Yuan et al., 2020 | Human, human nephroblastoma cell line G401, human lung cancer cell line A549 | Cells were exposed to 50 Hz magnetic fields 2 h daily for 3 consecutive days, with or without incubation with the free radical scavenger N-acetyl-cysteine. | Sham-exposure, 5100 μT | % tail DNA | DNA damage. N-acetyl-cysteine blocked most of the magnetic-field induced DNA damage | Supported by the National Natural Science Foundation of China and the Natural Science Foundation of Zhejiang Province |
| Zhu et al., 2016 | Human, human lens epithelial cells, SRA01/04 | Cells were exposed to 50 Hz magnetic fields for 2, 6, 12, 24 or 48 h. | Sham-exposure, 400 μT | Tail length, tail moment | No effects | Supported by the Ministry of Science and Technology and the Natural Science Foundation of China |
| Zmyslony et al., 2000 | Rat, rat lymphocytes | Cells were exposed to 50 Hz magnetic fields for 3 h. | Sham-exposure, 7000 μT | Percentage of damaged cells | No effects | NR |

**Table 4**
Characteristics of the human comet assay studies included in the systematic review with in vivo exposure to the magnetic field.

| First author | Study design | Cell type | Number of subjects | Intervention/duration of the magnetic field exposure | Experimental groups and magnetic flux density (μT) | Comet assay parameters | Main results | Funding |
|---|---|---|---|---|---|---|---|---|
| Albert et al., 2009 | Experimental study | Peripheral human leukocytes | 30 | Healthy human volunteers received a 4-h whole-body exposure to 60 Hz magnetic fields. | Sham-exposed control subjects vs subjects exposed to 200 μT | Tail length, tail moment, % DNA in tail | No effects | Supported by the Canadian Institute of Health Research and the Natural Sciences Engineering Research Council |
| Bagheri Hosseinabadi et al., 2019 | Cross-sectional study | Peripheral human lymphocytes | 238 | Chronic exposure at a thermal power plant to ELF-MF. Participants were all the employees working in different sections of the thermal power plant. | Unexposed group vs exposed group. The exposed group worked full time at the power plant and had at least two years of work experience | Tail length, tail DNA percent, tail moment, tail factor (%) and damage index | DNA damage | Supported by Shahroud University of Medical Sciences |

**Table 5**
Results of the animal studies that have assessed the development of cancer after atypical protocols of exposure to the magnetic field.

| First author | Animal species, strain, sex | Number of animals | Intervention/duration of the magnetic field exposure | Experimental groups and magnetic flux density (μT) | Outcomes | Main results |
|---|---|---|---|---|---|---|
| Otaka et al., 2002 | C57BL/6J female mice, C3H/HeJ male mice, B6C3F1 offspring | 549 B6C3F1 pups | C57BL/6J female and C3H/HeJ male mice were exposed 50 Hz magnetic fields. Their B6C3F1 offspring has been examined to study the effect of parental and prenatal magnetic field exposure on cancer incidence. | Sham-exposure, 500 μT, 5000 μT | All types of cancers | Parental/prenatal exposure to 50 Hz magnetic fields did not significantly increase the incidence of cancers. |
| Reif et al., 1995 | Dogs (race not mentioned) | 230 | Hospital-based case-control study conducted in the USA. Dogs were exposed to residential 60 Hz magnetic fields. Cases came from a veterinary teaching hospital and had histologically confirmed lymphoma diagnosed between 1987 and 1990. | Dogs exposed to low magnetic fields (<0.2 μT), dogs exposed to high magnetic fields (>0.2 μT) | Canine lymphoma | Residential 60 Hz magnetic fields increased the risk of canine lymphoma. |

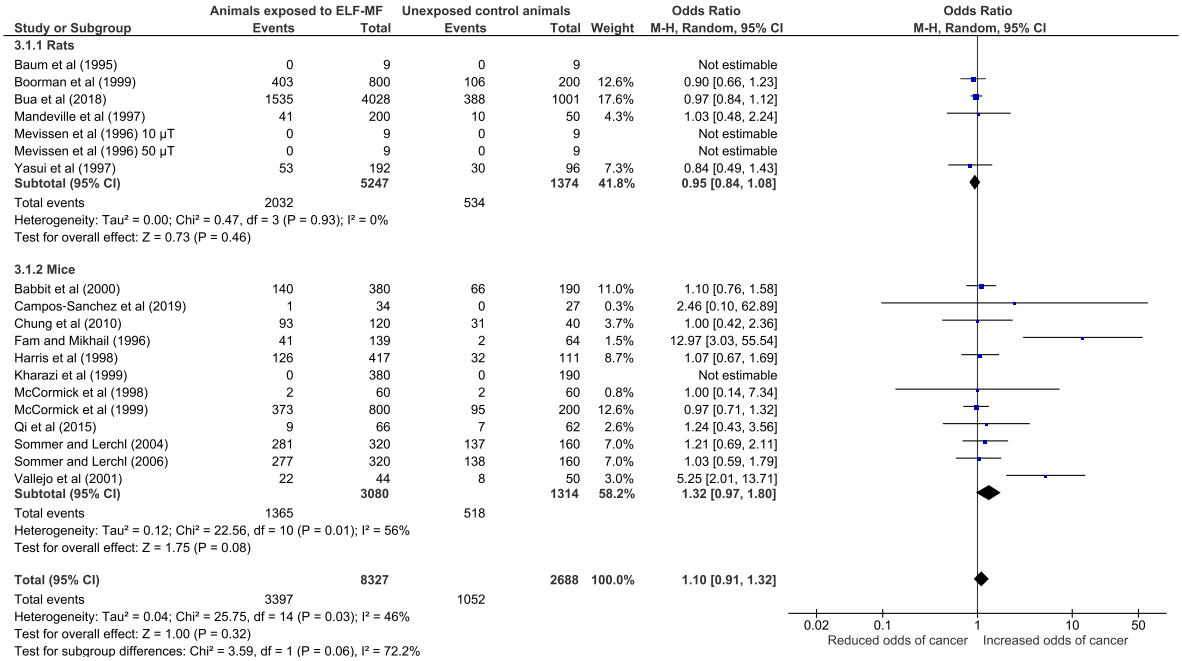


**Fig. 2.** Association between exposure to ELF-MF higher than 0.2 μT and the development of cancers in rodents. "Events" represent the number of animals with cancer that had been reported in the animal studies included in the global meta-analysis. Leukemia incidence is the outcome of the studies by Campos-Sanchez et al. (2019) and Vallejo et al. (2001). Lymphoma incidence is the outcome of the studies by Babbitt et al. (2000), Chung et al. (2010), Fam and Mikhail (1996), Harris et al. (1998), McCormick et al. (1998) and Sommer and Lerchl (2004, 2006). The incidence of breast cancer is the outcome of the studies by Baum et al. (1995) and Mevissen et al. (1996a, 1996b). The incidence of brain cancer is the outcome of the study by Kharazi et al. (1999). Cancer incidence (each type of cancer) is the outcome of the studies by Boorman et al. (1999), Bua et al. (2018), Mandeville et al. (1997), Yasui et al. (1997), McCormick et al. (1999) and Qi et al. (2015). The OR for the studies by Baum et al. (1995), Kharazi et al. (1999) and Mevissen et al. (1996a, 1996b) were not estimable, because the incidence of the cancers reported by the authors of these articles was zero.

### 3.7. Meta-analyses based on mean body weight

Several studies that have examined the effects of ELF-MF on the mean body weight of animals have presented their data on weights in figures without estimates of the standard deviation. As a result, the data of these studies could not be extracted to be included in our meta-analyses. Only three studies with the necessary data (means and SD) were sufficiently similar to perform a meta-analysis on the relation between ELF-MF and mean body weight. These three studies all used the same magnetic flux density of 1000 μT. Continuous or intermittent exposure to high ELF-MF (1000 μT) for one year had no significant effect on mean body weight in mice and in rats (Supplementary Figs. 18 and 19). Heterogeneity between studies was not significant. There were no low-quality studies in this meta-analysis.

### 3.8. Qualitative synthesis of the comet assay studies

Table 6 presents the results of all the studies included in our systematic review that have used the comet assay. Results have been classified based on the cell type and the method of exposure to the magnetic field (in vivo vs in vitro).

As shown in Table 6, eleven studies out of twelve have reported a significant increase in DNA damage in brain cells of rats and mice exposed in vivo or in vitro to ELF-MF. Table 6 indicates that in vivo exposure to 50 Hz or 60 Hz magnetic fields for 24 h or more causes DNA damage in brain cells of rodents. One study (Yin et al., 2016) has examined the effects of ELF-MF on DNA of brain cells in vitro. Yin and colleagues (2016) have found that in vitro exposure to high 50 Hz magnetic fields (8000 μT) caused DNA damage in cultured hippocampal neurons from newborn rats.

Mixed results have been found in other cells after exposure to ELF-MF. Most studies indicate that exposure to ELF-MF does not affect DNA in peripheral leukocytes or lymphocytes from human or rat origin (Table 6). The study by Bagheri Hosseinabadi et al. (2019) showed that long-term occupational exposure to ELF-MF increased DNA damage in power plant workers but it was an observational cross-sectional study. Some studies found that exposure to ELF-MF damages DNA in human fibroblasts (Ivancsits et al., 2002, 2003a, 2003b, 2005) but other studies do not support these findings (Scarfi et al., 2005; Burdak-Rothkamm et al., 2009). DNA damage after ELF-MF exposure has mostly been found in cancer cell lines such as HeLa cells (Kim et al., 2012), G401 cells, A549 cells (Yuan et al., 2020) and AT478 cells (Buldak et al., 2012). Nevertheless, exposure to 50 Hz magnetic fields at 100–1000 μT for 1–24 h did not increase DNA damage in neuroblastoma cells (Luukkonen et al., 2011, 2017; Mustafa et al., 2022; Villarini et al., 2017). Mihai and colleagues (2014) have found that exposure to 100 Hz magnetic fields increased DNA damage in Vero cells. DNA damage has also been shown in GC-2 cells exposed to 50 Hz magnetic fields for 24 h (Duan et al., 2015).

### 3.9. Meta-analysis based on DNA damage assessed with the comet assay

We could only perform a meta-analysis with three comet assay studies because the other studies included in our systematic review were not sufficiently similar to be meaningfully pooled and/or important information was missing from the articles. Three studies included in our systematic review (Luukkonen et al., 2011, 2017; Mustafa et al., 2022) have investigated the effects of in vitro exposure to 50 Hz magnetic fields (100 μT) for 24 h on DNA in human SH-SY5Y neuroblastoma cells. Exposure to 50 Hz magnetic fields at 100 μT for 24 h did not cause DNA damage expressed as Olive tail moment in neuroblastoma cells (Supplementary Fig. 20). Heterogeneity between studies was not significant.

## 4. Discussion

Our global meta-analysis and other meta-analyses indicate that exposure to extremely low frequency magnetic fields (ELF-MF) had no significant effect on the incidence of cancer (when all cancer types are combined), lymphoma, breast cancer and brain cancer in rodents. However, our results suggest that ELF-MF could increase the odds of developing leukemia in mice but not in rats. Finally, our systematic review suggests that exposure to ELF-MF can increase DNA damage in certain cell types, especially brain cells of mice and rats.

The results of our global meta-analysis do not support the carcinogenic effects of 50/60 Hz magnetic fields. Our other meta-analyses show that ELF-MF exposure did not significantly affect the odds of lymphoma, breast cancer and brain cancer but increased the incidence of leukemia in mice (Supplementary Figs. 6 and 7). The discrepancy between the non-significant OR of the global meta-analysis in mice (OR = 1.32 for >0.2 μT; Fig. 2) and the significant OR for leukemia in mice (OR = 4.45 for >0.2 μT; Supplementary Fig. 6) results from the fact that the global meta-analysis takes into account leukemia but also the other cancers whose incidences are not increased after ELF-MF exposure. Since our other meta-analyses show that 50/60 Hz magnetic fields did not significantly alter survival and body weight in rodents (Supplementary Figs. 16–19), our results taken as a whole suggest that these magnetic fields do not represent a major hazard for mammals.

Our meta-analyses based on the studies that had performed a complete necropsy of the rodents show that ELF-MF exposure had no significant effect on the incidence of cancer in mice and rats when all cancer types were assessed and combined in the statistical analysis (Supplementary Figs. 4 and 5). Nevertheless, it is important to keep in mind that ELF-MF have been reported to possess both carcinogenic effects and anti-tumor effects (Lai, 2019; Yuan et al., 2018). ELF-MF applied alone can inhibit the development of cancer (Koh et al., 2008). Since the meta-analyses shown in Supplementary Figs. 4 and 5 include each type of cancer, these meta-analyses actually mean that the net effect of ELF-MF (thus the combination of carcinogenic and anti-tumor effects) on the development of all cancers analyzed together is negligible. Nevertheless, it is also important to analyze the effects of ELF-MF on specific cancers because exposure to ELF-MF could have promoted the development of certain cancers and inhibited the development of other cancers (Lai, 2019; Yuan et al., 2018).

Our meta-analyses indicate that exposure to ELF-MF increased the odds of developing leukemia in mice but not in rats (Supplementary Figs. 6 and 7). Nonetheless, these results must be interpreted with caution. There were two low-quality studies in the meta-analysis on magnetic fields and leukemia in mice (Campos-Sanchez et al., 2019; Qi et al., 2015). After omitting the studies of lower quality, the OR for the association between ELF-MF and leukemia in mice was 4.58 (95% CI 1.83–11.49) when mice were exposed to magnetic fields above 10 μT but the association was no longer significant in the analysis based on magnetic fields above 0.2 μT (OR = 3.72; 95% CI 0.87–15.94). These results are in line with our previous meta-analysis showing that only magnetic fields higher than 0.4 μT caused a significant increase in the odds of developing childhood leukemia (OR = 1.37; 95% CI 1.05–1.80) (Brabant et al., 2022). However, the confidence interval (CI) of the OR between magnetic fields higher than 10 μT and leukemia is large after omitting the lower-quality studies (OR = 4.58; 95% CI 1.83–11.49). Consequently, it is difficult to draw a definite conclusion on the magnitude of the association between ELF-MF exposure and leukemia in mice based on the current data. More studies are needed. In the future, high quality studies with a valid sham-control group should be conducted to determine whether the increased incidence of leukemia found in mice chronically exposed to ELF-MF detected in the present meta-analysis can be replicated. It is noteworthy that almost all the mice that developed leukemia in our meta-analyses were females (Supplementary Figs. 6 and 7). Twenty-six mice out of twenty-seven were females among the mice exposed to magnetic fields suffering

**Table 6**
Comet assay results classified by cell type and method of exposure to the magnetic field.

| First author | Cell origin and cell type | Main intervention/duration of the magnetic field exposure | Experimental groups and magnetic flux density (μT) | Comet assay parameters | Main results |
|---|---|---|---|---|---|
| **Brain cells from animals exposed in vivo to magnetic fields** | | | | | |
| Lai and Singh, 1997a | Brain cells from male Sprague-Dawley rats | Rats were exposed to 60 Hz magnetic fields for 2 h. | Sham-exposure, 100 μT, 250 μT and 500 μT | DNA migration length (in μm) | Dose-dependent increase in DNA damage |
| Lai and Singh, 1997b | Brain cells from male Sprague-Dawley rats | Rats were exposed to 60 Hz magnetic fields for 2 h, with or without free radical scavengers (melatonin or N-tert-butyl-α-phenylnitrone). | Sham-exposure, 500 μT | DNA migration length (in μm) | DNA damage. The free radical scavengers blocked the magnetic-field-induced DNA damage |
| Singh and Lai, 1998 | Brain cells from male Sprague-Dawley rats | Rats were exposed to 60 Hz magnetic fields for 2 h. | Sham-exposure, 500 μT | DNA migration length (in μm) | DNA damage |
| Lai and Singh, 2004 | Brain cells from male Sprague-Dawley rats | Rats were exposed to 60 Hz magnetic fields for 24 h or 48 h, with or without Trolox (vitamin E analog) or 7-nitroindazole (nitric oxide synthase inhibitor). | Sham-exposure, 10 μT | DNA migration length (in μm) | DNA damage. Trolox or 7-nitroindazole blocked the magnetic-field-induced DNA damage |
| Rageh et al., 2012 | Brain cells from newborn rats (strain not mentioned) | Rats were exposed continuously to 50 Hz magnetic fields 24 h per day for 30 days. | Sham-exposure, 500 μT | Tail moment | DNA damage |
| McNamee et al., 2002 | Brain cells (cerebellum) form 10-day-old ICR mice | Mice were exposed to 60 Hz magnetic fields for 2 h. | Sham-exposure, 1000 μT | Tail ratio, tail moment, comet length and tail length | DNA damage detected by tail ratio but not with other measures |
| McNamee et al., 2005 | Brain cells from male Sprague-Dawley rats, male ICR mice and immature ICR mice | Rodents were exposed to 60 Hz magnetic fields for 2 h. | Sham-exposure, 100 μT, 1000 μT and 2000 μT | Tail ratio, tail moment, comet length and tail length | No effects |
| Mariucci et al., 2010 | Brain cells (cerebral cortex-striatum, hippocampus and cerebellum) from male CD1 mice | Mice were exposed to 50 Hz magnetic fields for 1 or 7 days (15 h per day) and sacrificed either at the end of the exposure or after 24 h to evaluate DNA damage. | Sham-exposure, 1000 μT | Tail moment, tail intensity (% DNA in the comet tail) | DNA damage (reversible) |
| Villarini et al., 2013 | Brain cells from adult male CD1 mice | Mice were exposed to 50 Hz magnetic fields for 7 days (15 h per day) and sacrificed either at the end of the exposure or after 24 h to evaluate DNA damage. | Sham-exposure, 100 μT, 200 μT, 1000 μT and 2000 μT | Tail intensity (% DNA in the comet tail) | Dose-dependent increase in DNA damage (reversible) |
| Svedenstal et al., 1999a | Male CBA/Ca mice | The mice were housed under 220 kV transmission lines (50 Hz magnetic field) for 11, 20 or 32 days. | The control mice were placed 200 m or 500 m away from the lines, where the magnetic flux density was ~0.06 or ~0.02 μT, respectively. The exposed mice were exposed to ~8 μT magnetic fields | DNA migration length, ratio of tail/head | DNA damage after 32 days of magnetic field exposure |
| Svedenstal et al., 1999b | Male CBA/Ca mice | Mice were exposed to 50 Hz magnetic fields for 2 h, 5 days or 14 days. | Sham-exposure, 500 μT | DNA migration length, ratio of tail/head | DNA damage after 14 days of magnetic field exposure |
| **Brain cells exposed in vitro to magnetic fields** | | | | | |
| Yin et al., 2016 | Rat, primary cultured hippocampal neurons from newborn Sprague-Dawley rats (both genders) | Cells were exposed to 50 Hz magnetic fields for 90 min. | Sham-exposure, 8000 μT | Tail DNA %, tail moment | DNA damage |
| **Germ cells from animals exposed in vivo to magnetic fields** | | | | | |
| Udroiu et al., 2015 | Epididymal sperm from young CD-1 Swiss outbred mice | Pups were exposed to 50 Hz magnetic fields 24 h per day from day 12 post conception until weaning, for a total of 30 days. | Sham-exposure, 65 μT | Tail intensity, percentage of sperm with damaged DNA | No DNA damage in the comet assay |
| **White blood cells from humans exposed in vivo to magnetic fields** | | | | | |
| Albert et al., 2009 | Peripheral human leukocytes | Healthy human volunteers received a 4-h whole-body exposure to 60 Hz magnetic fields. | Sham-exposed control subjects vs subjects exposed to 200 μT | Tail length, tail moment, % DNA in tail | No effects |
| Bagheri Hosseinabadi et al., 2019 | Peripheral human lymphocytes | Chronic exposure at a thermal power plant to ELF-MF. Participants were all the employees working in different sections of the thermal power plant. | Unexposed group vs exposed group. The exposed group worked full time at the power plant and had at least two years of work experience | Tail length, tail DNA percent, tail moment, tail factor (%) and damage index | DNA damage (but cross-sectional study) |
| **White blood cells exposed in vitro to magnetic fields** | | | | | |
| Jajte et al., 2001 | Rat lymphocytes | Cells were exposed to 50 Hz magnetic fields for 3 h. | Sham-exposure, 7000 μT | Percentage of damaged cells | No effects |
| Zmyslony et al., 2000 | Rat lymphocytes | Cells were exposed to 50 Hz magnetic fields for 3 h. | Sham-exposure, 7000 μT | Percentage of damaged cells | No effects |

(*continued on next page*)

**Table 6** (*continued*)

| First author | Cell origin and cell type | Main intervention/duration of the magnetic field exposure | Experimental groups and magnetic flux density (μT) | Comet assay parameters | Main results |
|---|---|---|---|---|---|
| Ivancsits et al., 2005 | Human lymphocytes | Cells were intermittently exposed to 50 Hz magnetic fields (5 min on/10 min off) for 15 h. Time-dependent effects were studied at a magnetic flux density of 1000 μT. Exposure duration varied between 1 and 24 h in 1-h steps. | Sham-exposure, 1000 μT | Tail factor (%) | No effects |
| Luceri et al., 2005 | Human peripheral lymphocytes | Cells were exposed to 50 Hz magnetic fields for 18 h. | Sham-exposure, 1 μT, 10 μT, 100 μT | DNA breaks, DNA base oxidation | No effects |
| Testa et al., 2004 | Human peripheral lymphocytes | Cells were exposed to 50 Hz magnetic fields for 48 h. | Sham-exposure, 1000 μT | Tail moment, % tail DNA | No effects |
| Stronati et al., 2004 | Human leukocytes | Cells were exposed to 50 Hz magnetic fields for 2 h | Sham-exposure, 1000 μT | Tail moment | No effects |
| Ahuja et al., 1999 | Human peripheral leukocytes | Cells were exposed to 50 Hz magnetic fields for 1 h. | Unexposed control cells, 2000 μT, 3000 μT, 5000 μT, 7000 μT, 10 000 μT | Tail length | DNA damage |
| Villarini et al., 2006 | Human peripheral leukocytes | Cells were exposed to 50 Hz magnetic fields for different time periods (30, 60 or 120 min). | Sham-exposure, 3000 μT | Tail moment | No effects |
| Moretti et al., 2005 | Human, Jurkat cells (human lymphoblastoid T-cells) | Cells were exposed to 50 Hz magnetic fields for 1 h. | Sham-exposure, 1000 μT | Tail intensity (percentage of fluorescence migrated in the comet tail) | No effects |
| **Fibroblasts exposed in vitro to magnetic fields** | | | | | |
| Ivancsits et al., 2002 | Human diploid fibroblasts from two healthy donors | Cells were exposed to 50 Hz magnetic fields for 24 h. | Sham-exposure, 20 μT, 50 μT, 70 μT, 100 μT, 250 μT, 500 μT, 750 μT, 1000 μT, 2000 μT | Tail factor (%) | DNA damage (intermittent exposure) |
| Ivancsits et al., 2003a | Human diploid fibroblasts from healthy donors | Cells were intermittently exposed to 50 Hz magnetic fields (5 min on/10 min off). Exposure duration varied between 1 and 24 h in 1-h steps. | Sham-exposure, 1000 μT | Tail factor (%) | DNA damage (maximal response after 15–19 h of exposure) |
| Ivancsits et al., 2003b | Human diploid fibroblasts from healthy donors | Cells were intermittently exposed to 50 Hz magnetic fields (5 min on/10 min off) for 15 h. | Sham-exposure, 20 μT, 35 μT, 50 μT, 70 μT, 100 μT and 1000 μT | Tail factor (%) | DNA damage (dose-dependent) |
| Ivancsits et al., 2005 | Human diploid fibroblasts | Cells were intermittently exposed to 50 Hz magnetic fields (5 min on/10 min off) for 15 h. Time-dependent effects were studied at a magnetic flux density of 1000 μT. Exposure duration varied between 1 and 24 h in 1-h steps. | Sham-exposure, 1000 μT | Tail factor (%) | DNA damage |
| Scarfi et al., 2005 | Human diploid fibroblasts | Cells were intermittently exposed to 50 Hz magnetic fields (5 min on/10 min off) for 15 or 24 h. | Sham-exposure, 1000 μT | Tail factor, tail DNA percentage, tail moment, comet moment | No effects |
| Burdak-Rothkamm et al., 2009 | Human VH25 skin fibroblasts | Cells were intermittently exposed (5 min on, 10 min off) to 50 Hz magnetic fields for 15 h. | Sham-exposure, 50 μT, 100 μT, 500 μT, 1000 μT | Tail moment, % DNA in tail | No effects |
| Huang et al., 2022 | Human, primary human gingival fibroblasts (HGFs) from healthy donors | Cells were exposed to 10 Hz pulsed magnetic fields for 24 h. | Unexposed control cells, 1000 μT | Olive tail moment, tail DNA percentage | DNA damage in some samples, no effects in other samples |
| Kim et al., 2012 | Human, IMR90 (human lung fibroblast) | Cells were exposed to 60 Hz magnetic fields for 30 min. | Sham-exposure, 7000 μT | Description of the comet tail length (no tail, short dragging tail or long dragging tail) | DNA damage |
| Jin et al., 2014 | WI-38 human lung fibroblasts, NIH3T3 mouse fibroblasts | Cells were exposed for 4 or 16 h to 60 Hz magnetic fields. | Sham-exposure, 1000 μT | Olive tail moment | No effects |
| Sun et al., 2021 | Human, 2BS cells isolated from human fetal lung fibroblasts | Cells were exposed intermittently to 10 Hz pulsed magnetic fields (1 day on/1 day off) for 2 weeks. | Unexposed control cells, 1000 μT | Olive tail moment | Nonsignificant increase in DNA damage (but significant with γH2AX technology) |
| Wolf et al., 2005 | WI-38 diploid fibroblasts derived from embryonic human lung, Rat-1 fibroblasts (immortalized cells) | Cells were exposed to 50 Hz magnetic fields for 24–72 h, with or without the antioxidant α-tocopherol. | Unexposed control cells, 500 μT, 750 μT, 1000 μT | Tail moment | Dose-dependent increase in DNA damage (results of unexposed control cells not shown). The magnetic-field-induced DNA damage was prevented by α-tocopherol |
| Sun et al., 2018 | Mouse, wild-type and Atm-deficient mouse embryonic fibroblasts | Cells were exposed to 50 Hz magnetic fields for 1 or 24 h. | Sham-exposure, 2000 μT | Olive tail moment, % tail DNA | No effects |

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**Table 6** (*continued*)

| First author | Cell origin and cell type | Main intervention/duration of the magnetic field exposure | Experimental groups and magnetic flux density (μT) | Comet assay parameters | Main results |
|---|---|---|---|---|---|
| **Neuroblastoma cells exposed in vitro to magnetic fields** | | | | | |
| Luukkonen et al., 2011 | Human SH-SY5Y neuroblastoma cells | Cells were exposed to 50 Hz magnetic fields for 24 h. | Sham-exposure, 100 μT | Olive tail moment | No effects |
| Luukkonen et al., 2017 | Human SH-SY5Y neuroblastoma cells | Cells were exposed to 50 Hz magnetic fields for 24 h. | Sham-exposure, 100 μT | Olive tail moment | No effects |
| Mustafa et al., 2022 | Human SH-SY5Y neuroblastoma cells | Cells were exposed to 50 Hz magnetic fields for 24 h. | Sham-exposure, 100 μT | Olive tail moment | No effects |
| Villarini et al., 2017 | Human SH-SY5Y and SK-N-BE-2 neuroblastoma cells | Cells were exposed to 50 Hz magnetic fields. Exposure was continuous for 1 h or intermittent (15 min on, 15 min off) for 5 h. | Sham-exposure, 10 μT, 100 μT, 1000 μT | Tail intensity | No effects |
| **Other cells from human origin exposed in vitro to magnetic fields** | | | | | |
| Kim et al., 2012 | Human, HeLa cells | Cells were exposed to 60 Hz magnetic fields for 30 min. | Sham-exposure, 7000 μT | Description of the comet tail length (no tail, short dragging tail or long dragging tail) | DNA damage |
| Wolf et al., 2005 | Human promyelocytic leukemia HL-60 cells | Cells were exposed to 50 Hz magnetic fields for 24–72 h, with or without the antioxidant α-tocopherol | Unexposed control cells, 500 μT, 750 μT, 1000 μT | Tail moment | Dose-dependent increase in DNA damage (results of unexposed control cells not shown). The magnetic-field-induced DNA damage was prevented by α-tocopherol |
| Yuan et al., 2020 | Human nephroblastoma cell line G401, human lung cancer cell line A549 | Cells were exposed to 50 Hz magnetic fields 2 h daily for 3 consecutive days, with or without incubation with the free radical scavenger N-acetyl-cysteine. | Sham-exposure, 5100 μT | % tail DNA | DNA damage. N-acetyl-cysteine blocked most of the magnetic-field induced DNA damage |
| Fairbairn and O'Neill, 1994 | Human, Raji cells | Cells were exposed to 50 Hz magnetic fields for 1 h or 24 h. | Sham-exposure, 5000 μT | Ratio of the height of the comet divided by the length of the comet in the direction of electrophoresis | No effects |
| Hao et al., 2011 | Human, K562 cells (ATCC, CCL-243) | Cells were exposed continuously to a uniform static 50 Hz magnetic field for 12 h. | Sham-exposure, 8800 μT | Olive tail moment | No effects |
| Jin et al., 2014 | Human, L132 human lung epithelial cells, MCF10A human mammary gland epithelial cells | Cells were exposed for 4 or 16 h to 60 Hz magnetic fields. | Sham-exposure, 1000 μT | Olive tail moment | No effects |
| Wang et al., 2019 | Human ventricular cardiomyocyte cell line AC16 cells (human ventricular cardiomyocytes) | Cells were exposed to 50 Hz magnetic fields, continuously for 1 h or intermittently (15 min on/15 min off) for 75 min. | Sham-exposure, 100 μT | Tail DNA %, tail length, tail moment and comet length | No effects |
| Zhu et al., 2016 | Human lens epithelial cells, SRA01/04 | Cells were exposed to 50 Hz magnetic fields for 2, 6, 12, 24 or 48 h. | Sham-exposure, 400 μT | Tail length, tail moment | No effects |
| **Cells from monkey origin exposed in vitro to magnetic fields** | | | | | |
| Mihai et al., 2014 | Vero cells (kidney epithelial cells extracted from an African green monkey) | Cells were exposed to 100 Hz magnetic fields, continuously or intermittently (1 s on, 3 s off), for 45 min. | Sham-exposure, 5600 μT | Tail length, % tail DNA, tail moment and Olive tail moment | DNA damage |
| **Other cells from mouse origin exposed in vitro to magnetic fields** | | | | | |
| Buldak et al., 2012 | Mouse, AT478 squamous cell carcinoma cells | Cells were exposed to 50 Hz magnetic fields for 16 min. | Sham-exposure, 1000 μT | Tail moment | DNA damage |
| Duan et al., 2015 | Mouse spermatocyte-derived cell line (GC-2) | Cells were exposed to 50 Hz magnetic fields for 24 h. | Sham-exposure, 1000 μT, 2000 μT, 3000 μT | % DNA in tail, tail length | Dose-dependent increase in DNA damage |
| Mustafa et al., 2021 | Mouse, murine FDC-P1 hematopoietic cells | Cells were exposed for different durations (15 min, 2 h, 12 h and 24 h) to 50 Hz magnetic fields. | Sham-exposure, 200 μT | Olive tail moment | No effects |
| Nakayama et al., 2016 | Mouse, macrophage RAW264 cells | Cells were exposed to 50 Hz magnetic fields for 24 h. | Sham-exposure, 500 μT | Olive tail moment | No effects |
| Nikolova et al., 2005 | Mouse embryonic stem cells (embryonic stem cell-derived neural progenitor cells) | Cells were exposed to 50 Hz magnetic fields intermittently (5 min on, 30 min off) for 6 or 48 h. | Sham-exposure, 2000 μT | Tail factor (%) | No effects |

from leukemia. Eight mice out of eight were females among the mice suffering from leukemia that were not exposed to magnetic fields. It is possible that the gender of the mice could play a role and both female and male mice should be examined in the future studies on the impact of ELF-MF on leukemia incidence.

It is difficult to explain why ELF-MF exposure significantly increased the odds of developing leukemia in mice but not in rats in the present work. All the rats examined in our meta-analyses on leukemia were F344 rats. It is possible that the strain of rats plays a role. Bua and colleagues (2018) have assessed the effects of 50 Hz magnetic fields on leukemia and lymphoma in Sprague-Dawley rats but the incidence of lymphoma and leukemia has not been reported separately in this study. In the future, it could be useful to conduct large high quality studies with different rat strains to further examine the impact of ELF-MF on leukemia incidence.

Table 6 suggests that exposure to ELF-MF can increase DNA damage in brain cells of rats and mice. However, our meta-analyses indicate that ELF-MF exposure does not increase the odds of brain cancer in these rodents (Supplementary Figs. 14 and 15). DNA damage after ELF-MF exposure has also been found in cancer cell lines like HeLa cells (Kim et al., 2012), G401 and A549 cells (Yuan et al., 2020) and AT478 cells (Buldak et al., 2012). Furthermore, DNA damage has been shown in Vero cells (Mihai et al., 2014) and GC-2 cells (Duan et al., 2015) exposed to ELF-MF (Table 6). Some authors have argued in the past that there was no evidence to claim that ELF-MF could damage the genetic material of mammalian cells (Vijayalaxmi and Obe, 2005). However, our systematic review that also covers recent studies suggests that ELF-MF exposure can damage DNA in certain cell types and the evidence is particularly strong in brain cells. Most comet assay studies show that in vivo or in vitro exposure to ELF-MF increases DNA damage in brain cells of rodents (Table 6). Nevertheless, these comet assay results must be interpreted cautiously because they do not provide an overall assessment of the carcinogenic effects of ELF-MF. It is important to determine whether the carcinogenic effects of these magnetic fields found in brain cells can be replicated with other techniques (Schmitz et al., 2004). Unfortunately, most studies that have investigated the genotoxic effects of ELF-MF in brain cells have used the comet assay. Schmidt and colleagues have used autoradiographic methods to study the impact of 50 Hz magnetic fields on DNA in different brain regions in mice (Schmitz et al., 2004; Korr et al., 2014). They have found increased DNA damage in epithelial cells of the choroid plexus in mice exposed to high 50 Hz magnetic fields (1.5 mT examined in Schmitz et al., 2004) but lower magnetic fields (0.1 mT and 1 mT) had no effects (Korr et al., 2014). Furthermore, in vivo exposure to 50 Hz magnetic fields can cause oxidative stress in the hippocampus and striatum of mice (Cui et al., 2012). Oxidative stress can cause DNA damage (Lai, 2019). However, the impact of 50/60 Hz magnetic fields on brain cells is still unclear. In the future, more studies using methods other than the comet assay should be performed to further examine whether exposure to ELF-MF can damage DNA in brain cells. The mechanism through which ELF-MF could damage DNA is also unclear. It is generally accepted that ELF-MF are unable to transfer sufficient levels of energy to cells that can cause direct genotoxic effects. Thus, the effects of these magnetic fields on DNA are likely indirect and secondary to other biochemical changes in the cells (Phillips et al., 2009). One hypothesis is that ELF-MF damage DNA through the formation of free radicals inside the cells, possibly via the Fenton reaction (see Lai, 2019 for a complete review on this topic).

A strength of this work is the comprehensive nature of our systematic review that covers most of the carcinogenic effects of ELF-MF assessed in different animal species and in cells from animal and human origin. We have conducted the first meta-analysis that investigates the impact of ELF-MF on the incidence of cancer in rodents. Furthermore, our meta-analysis takes into account the different types of cancer (leukemia, brain cancer and breast cancer, see Carpenter, 2019) that have been identified in epidemiological studies as possible targets of magnetic field action. We have also analyzed the publication bias in detail in a global meta-analysis that includes all the experimental animal studies on ELF-MF and cancer. Finally, we have performed the first systematic review following the PRISMA guidelines about the effects of ELF-MF on DNA based on all the comet assay studies. Several reviews about the carcinogenic potential of ELF-MF have been published in the past (Boorman et al., 2000; McCann et al., 2000; Phillips et al., 2009; Tian et al., 2023; Vijayalaxmi and Obe, 2005) but none of these articles are systematic reviews referring to pre-registered protocols. It is noteworthy that a meta-analysis has been performed by Vijayalaxmi and Prihoda (2009) on the genetic damage associated with exposure to low frequency magnetic fields (from 16 Hz to 4400 Hz). Nonetheless, these authors have used a methodology and a statistical approach that differed a lot from the present work and cell types have not been differentiated in their analyses. As a result, it is very difficult to meaningfully compare their results with those reported in our systematic review.

A limitation of the present work is that we could only include three articles in the meta-analysis based on comet assay studies (see Supplementary Fig. 20). The other studies included in our systematic review that have assessed DNA damage using the comet assay were not sufficiently similar to be meaningfully pooled. Furthermore, important information necessary to perform meta-analyses was missing from certain articles and we could not obtain this information despite our efforts to contact the authors of these articles. A wide variety of comet assay indices have been defined in the scientific literature and used to investigate the carcinogenic potential of 50/60 Hz magnetic fields. As a result, it was sometimes not possible to perform meta-analyses on studies that used similar magnetic field exposure protocols only because different comet assay indices have been used in these studies to evaluate DNA damage.

In conclusion, our meta-analyses indicate that exposure to ELF-MF does not increase the incidence of lymphoma, brain cancer and breast cancer in rodents and has no significant impact on their survival. Nonetheless, our other meta-analyses suggest that ELF-MF can increase the odds of developing leukemia in mice but not in rats. Since our previous meta-analysis also found a small increased risk of leukemia in children exposed to ELF-MF above 0.4 μT (Brabant et al., 2022), our findings suggest that the carcinogenic effects of these magnetic fields seem to be limited to leukemia, a blood cancer with a very low incidence in children (Orkin et al., 2009). Our systematic review also suggests that ELF-MF can damage DNA of certain cell types, especially brain cells in mice and in rats. However, this DNA damage does not necessarily translate into cancer development, because our meta-analyses did not find an increased risk of brain cancer in rodents after ELF-MF exposure. While further research is needed to clarify the relationship between ELF-MF and leukemia, our results suggest that exposure to ELF-MF at 50/60 Hz does not represent a major hazard for mammals.

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## CRediT authorship contribution statement

**Christian Brabant:** Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Germain Honvo:** Writing – review & editing, Methodology, Conceptualization. **Céline Demonceau:** Writing – review & editing, Validation, Conceptualization. **Ezio Tirelli:** Writing – review & editing, Validation, Conceptualization. **François Léonard:** Writing – review & editing, Validation, Conceptualization. **Olivier Bruyère:** Writing – original draft, Supervision, Methodology, Funding acquisition, Conceptualization.

## Declaration of competing interest

Our work was supported by a grant obtained by the University of Liège from the Belgian BioElectroMagnetics Group (BBEMG). There is no other commercial affiliation or consultant role of an author that could be construed as a conflict of interest.

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## Appendix A. Supplementary data

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