1. Introduction

Electromagnetic fields (EMFs) are composed of magnetic and electric fields that influence each other [1]. There are many EMF subtypes with varying frequency rates, and they can cause either positive or detrimental biological effects. For medical purposes, they can be used in diagnostic modality and be considered as a potential therapeutic option as well. On the other hand, EMFs can penetrate tissues without experiencing intensity decrement [2], pass through the cell membrane, and affect cell responses. Consequently, cells may experience diverse pathophysiological disorders like cancer, thus, elevating one’s concern during the course of using EMFs for therapeutic purposes [3]. However, despite many findings, the carcinogenic role of EMF is still unclear.

Among subtypes of EMFs, low-frequency fields with specific amplitudes and waveforms are referred to as pulsed EMFs (PEMFs) [4]. Being a promising strategy and a type...
of the noninvasive and inexpensive physical approaches, PEMFs have exhibited therapeutic potential for treating various diseases [5]. It has already been shown that they can make changes to cell cycle, apoptosis, cell proliferation, and differentiation. Indeed, they are able to affect and alter the cell function by inducing forced vibration for free ions on the cell membrane surfaces due to an external oscillating field [6]. Irregular gating of ion channels triggered by this situation can certainly disturb the balance of transmembrane proteins and, consequently, disrupt cell function [7]. It has also been proposed that the effect of PEMFs may be propagated and amplified along the whole signal transduction pathway, thereby changing cell behavior [8]. In some studies, it has been reported that PEMFs can modulate both downstream signal transduction pathway and cell surface receptor expression/activation [8, 9]. As a result, homeostatic cell functions such as differentiation, viability, proliferation, interaction with components of extracellular matrix (ECM), and communication with neighboring cells could be restored [10]. In addition, PEMFs could enhance both the neurogenic differentiation of mesenchymal stem cells (MSCs) and osteogenic differentiation. Because EMFs easily permeate through cells [4] and change the electric field of the inner cell membrane, they can induce biological changes. In particular, they

### Table 1: Statistically significant difference cell groups from Figures 1–3.

| Exposure detail | Total | Studies with statistical significant cellular response |
|----------------|-------|-------------------------------------------------------|
| Presence | Absence |
| Human | 14 | 3 (21.43%) | 11 (78.57%) |
| Rat/mouse | 5 | 2 (40%) | 3 (60%) |
| Other species | 0 | 0 | 0 |
| Total cells | 19 | 5 (23.81%) | 14 (76.19%) |

### Table 2: Human cell studies: PEMFs exposure conditions used in in vitro studies.

| No. | Cell line | Frequencies and intensities | Cell response | Result | Year | First author |
|-----|-----------|-----------------------------|---------------|--------|------|--------------|
| 1   | Retinal pigment epithelial (RPE) cells | Frequency of 50 Hz, Intensity of 1 mT | Cell proliferation, cell death, and gene expression | Transcript levels of proangiogenic genes (HIF-1α, VEGFA, VEGFR-2, CTGF, cathespin D TIMP-1, E2F3, MMP-2, and MMP-9) increased | 2019 | Oladnabi et al. [56] |
| 2   | Adipose-derived mesenchymal stem cells (AD-MSCs) | Frequency of 5 Hz, Intensity of 1.1 mT | Cell proliferation | PEMF can be beneficial to tissue-derived stem cell proliferation | 2018 | Daish et al. [16] |
| 3   | Adipose-derived stem cells (ASCs) | Frequency of 50 Hz, Intensity of 1 mT | Cell proliferation, cell differentiation | PEMF could promote cell proliferation and osteogenic differentiation. Bone-related gene expression and protein expression of OPN, OCN, and RUNX-2 increased | 2018 | Yin et al. [17] |
| 4   | Human adipose-derived mesenchymal stromal cells (hAMSC) | Frequencies: 10, 16, 20.6, 23.8, 26, 33, 49.9, 52.3, 75.6, and 90.6 Hz | Cell proliferation, gene expression | PEMF showed significant upregulations of collagen I, alkaline phosphatase, and osteocalcin | 2018 | Poh et al. [18] |
| 5   | H4 glioma cells | Frequency of 7 Hz, Intensity of 30 mT | Cell apoptosis | LPEMF stimulation of H4 glioma cell cultures induced apoptosis in exposed cells. | 2018 | Kaszuba-Zwoinska et al. [38] |
| 6   | Mesenchymal stem cells (hMSCs) | Frequency of 75 Hz, the intensity peak of 1.5 mT | Gene expression | The exposure to PEMFs did not produce any change on notch-related genes | 2017 | Bagheri et al. [20] |
| 7   | Human umbilical vein endothelial cells (HUVECs) | The frequency of 50 Hz, Intensity of 2.25 mT | Cell proliferation, Gene expression | Proteins and mRNA expression levels of Akt, mTOR, and TGF-β1 were elevated | 2017 | Cheng et al. [59] |
| 8   | Human mesenchymal stem cells (MSCs) | Frequency of 15 Hz, Flux densities between 1–4 mT. | Gene expression | Brief and single exposures to low amplitude PEMFs were most effective at stimulating MSC chondrogenesis. | 2017 | Parate et al. [21] |
can induce changes in the Ca\(^{2+}\) efflux and, consequently, modulate various biological effects such as nitric oxide signaling, growth factor secretion, and Mitogen-Activated Protein Kinase (MAPK)/Extracellular Signal-Regulated Kinase (ERK) [11]. It has been hypothesized that the production of second messengers is stimulated by the direct effect of PEMF on phospholipids within the plasma membrane, and subsequently, multiple intracellular signal transduction pathways are initiated [12].

There are many factors affecting the biological responses. To clarify PEMF impacts, studies have reported that signal characteristics play a crucial role in determining the type of biological responses including amplitude and frequency of exposure to the applied PEMF [13]. Indeed, to deliver a therapeutic PEMF, it is necessary to optimize these important parameters [6]. In addition, a large volume of evidence has revealed that some kinds of cells appear exquisitely sensitive to PEMF, while other types appear relatively unresponsive. For instance, undifferentiated PC12 cells are more sensitive to PEMF exposure, while differentiated PC12 cells are more resistant to stress [14]. Consequently, cell properties are of vital importance in establishing a biological response to PEMF in vitro.

Despite a relatively long history of using PEMFs in medicine, little is known about the biological mechanism of such therapies. To develop a reliable working principle of PEMF therapies, it is worth investigating the experimentally observed biological effects caused by these fields alone. Thus, in this study, a meta-analysis was performed using 3249 in vitro experimental observations available in 92 scientific journals (1999-2019) in order to determine the potential effects of PEMF on different cell types of both human and rat/mouse. Our analysis scrutinized the published experiments that had considered the effects of exposure to PEMFs (cytogenetic, gene, and protein expression analysis) on cell types from rats, mice, and humans to gain a more explicit and evidence-based conclusion on the association between PEMFs and cell responses.

### Table 3: Human cell studies: PEMF exposure conditions used in in vitro studies.

| No. | Cell line | Frequencies and intensities | Cell response analysis | Result | Year | First author |
|-----|-----------|-----------------------------|------------------------|--------|------|--------------|
| 9   | MCF-7     | Frequencies of 2122.24, 1970.56, 2072.32, and 2648.64 Hz | Cell viability | There was a significant effect on MCF-7 cells after treatment with PEMF at the resonant frequencies of the genes of RICTOR, PPAR\(\gamma\), and NBN CHEK2 | 2017 | Alcantara et al. [43] |
| 10  | U937 cells (leukemia cell line) | Frequency of 50 Hz, Intensity of 45 mT | Cell viability, protein expression | There were no significant differences in the expression level of calmodulin between control- and only MF-treated samples | 2017 | Wojcik-Piotrowicz et al. [46] |
| 11  | Human bone marrow stromal cells (hBMSCs) | Pulse frequency of 3.8 kHz, Intensity of 3 mT | Enzyme activity, Signal transduction Pathway, Gene expression | PEMF regulated preosteoblast gene expression, and notably, the transforming growth factor-beta (TGF-\(\beta\)) signaling pathway and microRNA 21 (miR21) were the most highly regulated | 2017 | Selvamurugan et al. [25] |
| 25  | Peripheral blood mononuclear cells (PBMCs) | Frequency of 75 Hz, Intensity of 3 mT | Gene expression | LF-PEMF modulated gene expression. | 2017 | Capelli et al. [57] |
| 12  | Human bone marrow mesenchymal stem cells (hBM-MSCs) | Frequency of 60 Hz, Intensity of 10 mT | Protein expression | After exposure to only PEMF, the expression of proteins slightly increased, but there was no significant difference when compared to the nonexposed groups. | 2016 | Choi et al. [26] |
| 13  | Human glioblastoma U87 cell line | Frequencies of 50 Hz and 100 Hz intensities of 10 mT and 5 mT | Cell viability, Cell morphology, Protein expression | A significant increase in the number of cells after 24 h exposure to 50 Hz, 100 G. A dramatic decrease in cells exposed to 100 Hz, 100 G, and 10 Hz, 50 G EMFs compared with controls | 2016 | Akbarnejad et al. [3] |
| 14  | Human glioblastoma cell line (T98G) | Frequency of 75 Hz, Intensity of 2 mT | Cell proliferation, cell apoptosis, miR-421 expression | miR-421 expression significantly increased over the control after PEMF alone. | 2016 | Pasi et al. [39] |
### Table 4: Human cell studies: PEMF exposure conditions used in in vitro studies.

| No. | Cell line                              | Frequencies and intensities | Cell response analysis | Result                                                                 | Year | First author |
|-----|----------------------------------------|-----------------------------|------------------------|------------------------------------------------------------------------|------|--------------|
| 15  | Periodontal ligament stem cells (PDLSCs) | Pulsed burst frequency of 15 Hz, Intensities of 0.6, 1.2, 1.8, 2.4, and 3.0 mT | Cell proliferation, Cell differentiation, Gene expression, Protein expression | No influence on cell proliferation. PEMF appeared to stimulate the earlier onset of osteogenic differentiation of PDLSCs and upregulated the gene expression of Runx2, ALP, and OPN compared with the sham group. | 2016 | Wang et al. [32] |
| 16  | Human mesenchymal stem cells (MSCs)     | Frequency of 50 Hz, Intensity of 0.6 mT | Cell viability | Cell proliferation, Gene expression, Cell morphology, Cell viability, Cell proliferation, Cell apoptosis, Gene expression | PEMFs upregulated genes related to Ca\(^{2+}\) signaling, proliferation, and neurogenic differentiation | 2016 | Lim et al. [11] |
| 17  | Human tendon stem cells (HTSCs)         | Frequency of 10–30 Hz, Intensity of 0.5–1.5 mT | Cell morphology, Cell viability, Cell proliferation, Gene expression | PEMF did not cause any significant changes in proliferation, viability, and morphology. | 2016 | Randelli et al. [33] |
| 18  | Human dental pulp stem cells (hDPSCs)   | Frequency of 50 Hz, Intensity of 1 mT | Cell proliferation, Gene expression | Group treated to PEMF showed significantly greater P75NTR mRNA expression than the control group | 2016 | Hei et al. [34] |
| 19  | HeLa, HEK293, MCF7, and AGS             | Frequency of 75 Hz, Intensity of 2, 4, and 6 mT | Cell proliferation | Cell proliferations of all four different cell lines also showed an increase in PEMF exposure until 4 mT, but not at 6 mT. | 2016 | Cho et al. [44] |
| 20  | Human annulus fibrosus (AF) cells       | Frequency of 3,850 Hz, Intensity of 1.19 mT | Gene expression | PEMF alone had no effect on gene expression. | 2016 | Miller et al. [62] |

### Table 5: Human cell studies: PEMF exposure conditions used in in vitro studies.

| No. | Cell line                              | Frequencies and intensities | Cell response analysis | Result                                                                 | Year | First author |
|-----|----------------------------------------|-----------------------------|------------------------|------------------------------------------------------------------------|------|--------------|
| 21  | Human dermal fibroblasts (HDF), human epidermal keratinocytes (HEK), and human mononuclear cells (HMNC) | Pulse frequency of 1 kHz, intensity of 6.7 A/m | Gene expression | PEMF treatment changed the relative amount of messenger (m) RNA encoding enzymes involved in heme catabolism and removal of reactive oxygen species. | 2015 | Kubat et al. [60] |
| 22  | Acute lymphoblastic leukemia (CEM/C2), B-cell lymphoma (SU-DHL-4), colorectal adenocarcinoma (COLO-320DM), breast adenocarcinoma (MDABM-468), and ductal carcinoma (ZR-75-1) | Frequencies of 15 Hz, 125 Hz, and 625 Hz, Intensity of 5 mT | Cell morphology, cell viability, and cell apoptosis | A PEMF of 125 Hz and 625 Hz for 24 h–48 h increased proliferation activity in the 2 types of cancer cell lines used | 2015 | Loja et al. [48] |
| 23  | Human neuroblastoma SH-SY5Y cells      | Frequency of 75 Hz, Intensity of 2 mT | Enzymatic activity, cell proliferation, cell viability, and cell apoptosis, Basal MnSOD specific activity was higher in PEMF stimulated cells when compared to cells not treated with PEMF | PEMF and the osteogenic differentiation of hBMSCs were increased | 2015 | Osera et al. [42] |
| 24  | Human bone marrow stromal cells (hBMSCs) | Frequency of 200 Hz, Intensity of 0.6, 1 tesla | Cell proliferation, Cell differentiation | The PEMF stimulation could induce osteogenic differentiation, as shown by the expression of osteoblast-specific genes and proteins including alkaline phosphatase and osteocalcin | 2014 | Fu et al. [31] |
| 25  | Human amniotic epithelial cells (AECs)  | Frequency of 50 Hz, Intensity of 1 mT | Cell differentiation, Gene expression, Protein expression | | 2014 | Wang et al. [35] |
2. Material and Methods

In Tables 1–15, the characteristics of experimental protocols and variables are presented. In this paper, cellular response (presence or absence) in human, mouse, or rat cells is defined as changes due to exposure to PEMFs. We analyzed the reported studies based on the different experimental readouts/endpoints which they used for their studies and the physiological variables they measured. These studies are shown in Figures 1–3, (human cells), Figure 4 (rat/mouse cells), and Figure 5 (other species), separately.

2.1. Collection of Raw Data. An electronic literature search of databases including Web of Sciences and PubMed was conducted for publications in English from 1999 up to 2019. The key terms introduced in the search engines included “pulsed electromagnetic fields” and “cell.” The process of selecting the papers was carried out by reading the titles and abstracts of the studies as well as the full article when necessary. Upon omitting duplicate titles, full-text versions of the selected papers were obtained.

We excluded those experiments that (1) targeted direct animal or human exposure followed by the analysis of individual cells and (2) applied the combination of PEMFs and other effective treatments, e.g., chemotherapy. After screening many research studies, 92 papers with different designs were eligible for meta-analysis.

For data analysis, the cell responses were classified as “presence” (PEMF exposure changed the cell response statistically significantly in comparison to the control group regardless of direction) and “absence” (no significant PEMF effect).

For each included study, the following data were extracted: type of cells, pulse frequency of exposure, exposure flux density, time of exposure, waveform, and assayed cell responses (cells, cell function, and DNA). Bibliographic details of the studies including the first author and year of publication were also retrieved.

2.2. Analysis of Raw Data. According to the above explanations, given that the frequency and intensity of the mentioned exposure differ across studies, achieving different biological responses would not be unexpected. In this respect, we pooled the retrieved experimental data based on used pulse frequencies and flux densities. Our analysis considered the effect of several subgroups of pulse frequency and flux density as follows: (a) \(0.1 < f \leq 10\) Hz, (b) \(10 < f \leq 100\) Hz, (c) \(100 < f \leq 500\) Hz, (d) \(I < 1\) mT, (e) \(1 \leq I < 10\) mT, (f) \(10 \leq I < 100\) mT.
To facilitate conducting the analysis, through which I come. The pooled results were obtained based on cell type, the results obtained from separate studies with a similar outcome, (N) triangle wave, and (O) other waveforms. 

### 2.3. Statistical Analysis

Microsoft Excel was used to organize the data and build a database. Meta-analysis combined the results obtained from separate studies with a similar outcome. The pooled results were obtained based on cell type, frequency, and intensity. A random-effect model was used to facilitate conducting the analysis, through which $I^2$ value was calculated as the indicator of heterogeneity. $I^2$ values greater than 50% could imply significant heterogeneity between the related studies. Also, the random-effect model could account for the above variation between studies, and thus, it achieved more conservative results than a fixed-effect model. Sensitivity analysis was performed to determine the effect of a particular study on the overall effect size. The presence of publication bias was tested using Begg’s and Egger’s regression asymmetry tests [9]. Statistical analyses were conducted using STATA version 14.0. A $p$ value less than 0.05 was considered significant for all tests.

### 3. Results

A number of publications are analyzed in Figure 6, which provides an overview of the years of publication. Cellular response (presence or absence) was observed in human cells (2441 experiments in Figures 1–3), rat or mouse cells (854 experiments in Figure 4), and other species (11 experiments in Figure 5). The results indicated that most of the experiments were carried out on human cells, among which stem cells drew greater experimental attention. Of note, in case the analysis incorporated such parameters as exposure to PEMFs and individual cell types, the potential effects of PEMFs on cell types, such as bone marrow mesenchymal stem cells (BM-MSCs) (based on 559 reported experiments, $p < 0.001$), would become clear. However, based on the reported evidence, no such effect was observed for human adipose-derived mesenchymal stem cells (AD-MSCs) and human osteogenic sarcoma SaOS-2 ($p < 0.001$). As a result, despite the higher susceptibility of cancer cells to PEMFS

| No. | Cell line | Frequencies and intensities | Cell response analysis | Result | Year | First author |
|-----|-----------|-----------------------------|------------------------|--------|------|--------------|
| 34  | Human mesenchymal stem cell osteoblast | Frequencies of 5, 25, 50, 75, 100, and 150 Hz, intensity of 1.1 mT, | Cell differentiation | Levels of human mesenchymal stem cell differentiation changed by PEMF | 2012 | Luo et al. [37] |
| 35  | Stromal cells of human bone marrow (BMSC) | Frequency of 75 Hz, intensity of 1.8-3 mT | Gene expression, cell differentiation | The cells treated with PEMF began differentiation earlier than untreated cells. | 2012 | Esposito et al. [24] |
| 36  | Human breast carcinoma cells (T47D) | Frequencies of 100, 217 Hz intensity of 0.1 mT | Cell proliferation, cell viability, cell morphology, protein expression, and ROS production | PEMF induced a time-dependent decrease in cell growth after 72 h | 2012 | Sadeghipour et al. [49] |
| 37  | Human peripheral blood mononuclear cell (PBMC) | Frequency of 7 Hz flux density of 30 mT | Cell apoptosis | PEMF induced apoptosis in PBMC | 2011 | Kaszuba-Zwoinska et al. [58] |
| 38  | Bone marrow mesenchymal stem cells (BMMSCs) | Frequency of 15 Hz flux density of 1.8 mT | Cell proliferation, Cell apoptosis Protein expression | PEMF treated cells also showed greater MMP-2 expression compared to unstimulated cells. | 2011 | Griffin et al. [27] |
| 39  | Human bone marrow-derived stromal cell (BMSC) Human fetal preosteoblasts (SVHFO) | Frequency of 15 Hz Flux density of 0.1 mT | Cell proliferation, Cell differentiation Protein expression | PEMF treatment increased mRNA levels of bone morphogenetic protein 2, transforming growth factor-beta 1, osteoprotegerin, matrix metalloproteinase-1 and -3, osteocalcin, and bone sialoprotein | 2010 | Jansen et al. [28] |
| 40  | Osteoblast-like cell cultures (MG-63) | Frequency of 75 Hz Flux density of 3 mT | Gene expression | PEMF induced downregulation of genes related to the degradation of extracellular matrix | | | | | |
Table 8: Human cell studies: PEMF exposure conditions used in in vitro studies.

| No. | Cell line                                      | Frequencies and intensities                                      | Cell response analysis                  | Result                                                                 | Year  | First author     |
|-----|-----------------------------------------------|----------------------------------------------------------------|----------------------------------------|------------------------------------------------------------------------|-------|------------------|
| 41  | Human osteoblast-like Saos-2 cells            | Frequency of 15 Hz flux density of 2 mT                         | Gene expression                        | PEMF induced increase in RANKL mRNA expression                         | 2010  | Borsje et al. [51]|
| 42  | Bone marrow mesenchymal stem cells (BMMSCs)   | Frequency of 15 Hz flux density of 1.8 mT                       | Cell proliferation, Gene expression    | Exposure of BMMSCs to PEMFs increased cell proliferation              | 2010  | Sun et al. [29]   |
| 43  | Human mesenchymal stem cells (hMSCs)          | Frequency of 7.5 Hz flux density of 0.13 mT                     | Cell proliferation, Cell differentiation, Gene expression | The expressions of osteogenic genes, including Runx2/Cbfa1 and ALP, were modulated by PEMF exposure. | 2009  | Tsai et al. [22] |
| 44  | Human bone marrow mesenchymal stem cells (BMMSC) | Frequency of 15 Hz flux density of 1.8 mT                         | Cell morphology, Cell proliferation, Cell differentiation | PEMF exposure could enhance the BMMSC cell proliferation               | 2009  | Sun et al. [30]   |
| 45  | SaOS-2 osteoblast-like cells                  | Frequency of 15 Hz                                              | Cell viability, Cell proliferation, Cell differentiation | PEMF stimulation did not affect cell number, however, increased ALP activity | 2008  | Martino et al. [7]|
| 46  | Human chondrocyte                             | Frequency of 21.2 MHz                                           | Cell viability                         | PEMF exposure increased cell viability                                | 2007  | Štolfa et al. [66]|
| 47  | Primary human mesenchymal stem cells (MSCs), human chondrocyte | Frequency of 30 Hz, intensity of 35 μT                          | Gene expression                        | PEMF altered the gene expression of a limited number of gene products in human mesenchymal stem cells and human chondrocytes. | 2007  | Walther et al. [23]|
| 48  | Human promyelocytic leukemia HL-60 cells      | Frequency of 0.25 Hz 0.25–4.5 T peak magnetic field strength   | Cell viability signal transduction     | PEMF did not alter the cell viability or content of SAMP               | 2006  | Sontag and Kalka [47]|
| 49  | A human osteosarcoma cell line SaOS-2         | Frequency of 15 Hz, Intensity of 1.6 mT                          | Cell proliferation, Cell differentiation | PEMF reduced proliferation and increased differentiation in SaOS-2 cell line | 2005  | Hannay et al. [52]|
| 50  | MG-63 human osteosarcoma cells                | Frequency of 75 Hz, intensity of 2.3 mT                          | Cell proliferation, Gene expression    | The PEMF increased [3H]-thymidine incorporation                        | 2005  | Mattei et al. [54]|

Table 9: Human cell studies: PEMF exposure conditions used in vitro studies.

| No. | Cell line                                      | Frequencies and intensities                                      | Cell response analysis                  | Result                                                                 | Year  | First author     |
|-----|-----------------------------------------------|----------------------------------------------------------------|----------------------------------------|------------------------------------------------------------------------|-------|------------------|
| 51  | Human astrocytoma cell line U-373 MG          | Frequency of 50 Hz, intensity of 3 mT                            | Cell proliferation                     | PEMF did not cause cell proliferation or cell death                    | 2001  | Pessina et al. [40]|
| 52  | Sympathetic neuronal-like PC6 cells           | Frequency of 2 Hz, intensity of 0.3 mT                           | Cell proliferation, Cell differentiation | Proliferation was unaffected by PEMF                                   | 2001  | Shah et al. [67]  |
| 53  | Human atrophic nonunion cell culture Hyperptrophic nonunion cell culture | Frequency of 15 Hz, intensity of 1.8 mT                          | Cell morphology, Cell proliferation, Cell differentiation               | PEMF resulted in a change in morphologic features of cells.           | 2001  | Guerkov et al. [65]|
| 54  | Human astrocytoma cell line U-373 MG cells    | Frequency of 50 Hz, intensity of 3 mT                            | Cell proliferation, Calcium^2+ concentration | After the cells were exposed to EMFs, the basal [Ca^{2+}] levels increased | 2000  | Aldinucci et al. [41]|
| 55  | TE-85 human osteosarcoma cells                | Frequency of 15 Hz, intensity of 1.8 mT                          | Cell proliferation                    | The cells increase their proliferation when exposed to PEMF            | 1999  | De Mattei et al. [55]|
| 56  | MG63 human osteoblast-like cells              | Frequency of 75 Hz, intensity of 2.3 mT                          | Cell proliferation, Cell differentiation | PEMF caused a reduction in cell proliferation and an increase ALP activity | 1999  | Lohmann et al. [4] |
than that of other cell types, various cancer cells respond differently to PEMF stimulation.

We categorized different experimental techniques as follows: (a) cell structure (cell viability, cell morphology, apoptosis, cell proliferation, and cell differentiation), (b) cell functions (calcium concentration, signal transductions, enzyme activity, membrane potential, and membrane stability), and (c) DNA (gene expression, protein expression, ROS production, chromosome aberration, micronucleus assay, DNA damage, oxidative stress, DNA single-strand breaks, DNA double-strand breaks, and genotoxicity) in Figure 7. Our analysis of the reported results (Figure 8) suggests that most of the experiments used experimental techniques for DNA including gene expression, protein expression, and ROS production for assaying the effect of PEMFs on cells.

We also considered the effects of different pulse frequencies of PEMFs and intensity. To do so, we pooled experimental data based on the frequencies (Figure 9), intensity levels (Figure 10), time of exposure (Figure 11), and waveforms (Figure 12) used in each experiment of the 92 publications. Among subgroups of frequencies, significant effects were observed at 100 Hz < f (p < 0.001). However, at frequencies smaller than or equal to 10 Hz, no statistically significant effects were observed. Among subgroups of intensities, the presence of response as a result of PEMFs was seen significantly in intensities between 1 and 10 mT (p < 0.05) Analysis of different times of exposure in the studies indicated on effectiveness of PEMFs in chronic exposure > 10 days (p < 0.001) and absence of cell response in acute exposure > 24 h (p < 0.001).

The cells exposed to PEMFs in vitro experiments, which reported results (cellular response, either presence, or absence Table 1) under different exposure conditions, are as follows: (a) classification of experimental techniques in Figure 8, (b) frequency of PEMFs in Figure 13, (c) intensity levels in Figure 14, (d) time of exposure in Figure 15, and (e) waveform in Figure 16. It should be noted that our statistical test only reports the presence or absence of cellular responses in the literature, and it is not concerned with the increased or reduced effect of the mentioned responses.

### 4. Publication Bias and Sensitivity Analysis

The results of Egger’s and Begg’s test demonstrated no publication bias in the meta-analysis of cellular response (presence or absence) in human cells, rat or mouse cells, and other species according to different frequencies and intensity.
Table 1: Rat/mouse cells: cellular response (presence or absence) for cultured rat/mouse cells.

| No. | Cell line                                      | Frequency and intensity | Cell response analysis                                      | Result                                                                 | Year  | Authors          |
|-----|------------------------------------------------|-------------------------|-------------------------------------------------------------|----------------------------------------------------------------------|-------|------------------|
| 64  | RAW264.7 cells                                 | Frequency of 15 Hz, intensities of 0.5, 1, 2, and 3 mT | Cell apoptosis, gene expression                              | Gene expression of RANK, NFATc1, TRAP, CTST, BAX, and BAX/BCL was significantly decreased by 0.5 mT PEMF, but increased by 3 mT PEMF resulted in elongated and fibroblast-like shapes in GC-1 spg cells. PEMF increased the total p53 protein level in GC-2 spd cells. | 2017  | Wang et al. [79] |
| 65  | Spermatogonia germ cell line, (GC-1), spermatocyte cell line (GC-2) | Frequencies of 2, 50, and 120 Hz, intensity of 2.5 mT | Cell proliferation, cell morphology, cellular oxidative stress, protein expression, cell viability | Exposure to PEMF resulted in a significant increase in the proportion of apoptotic cells Stimulation of nucleus pulposus cells with LF-PEMFs did not appear to affect cell morphology or nucleus pulposus cell IL-1β and TNF-α expression levels. The level of intracellular Ca²⁺ after PEMF treatment was significantly higher. | 2017  | Solek et al. [83] |
| 66  | Adipose-derived stem cells (ADSCs) isolated    | Frequency of 7 Hz, flux density of 30 mT | Cell apoptosis                                               | Increase of proliferation, no influence on the apoptosis the phosphorylation level of extracellular, signal-regulated kinase (ERK) was significantly increased, while p38 MAPK and c-Jun N-terminal kinase (JNK) pathways were not affected. PEMFs significantly promoted the activity of ALP in the BMSCs and mRNA expression of osteogenic proteins | 2017  | Baranowska et al. [69] |
| 67  | Primary rat nucleus pulposus cells             | Frequency of 2 Hz, intensities of 0.5, 1.0, 2.0, and 3.0 A/m | Cell morphology, cell viability, protein expression          | Increase of proliferation, no influence on the apoptosis the phosphorylation level of extracellular, signal-regulated kinase (ERK) was significantly increased, while p38 MAPK and c-Jun N-terminal kinase (JNK) pathways were not affected. PEMFs significantly promoted the activity of ALP in the BMSCs and mRNA expression of osteogenic proteins | 2017  | Zou et al. [84] |
| 68  | Mouse osteosarcoma cell line (LM8 cells)       | Frequency of 200 Hz, flux density of 5 mT | Ca²⁺ concentration, cell apoptosis                           | Increase of proliferation, no influence on the apoptosis the phosphorylation level of extracellular, signal-regulated kinase (ERK) was significantly increased, while p38 MAPK and c-Jun N-terminal kinase (JNK) pathways were not affected. PEMFs significantly promoted the activity of ALP in the BMSCs and mRNA expression of osteogenic proteins | 2017  | Muramatsu et al. [85] |
| 69  | C2C12 myoblasts                                | Frequency of 100 Hz, flux density of 1 mT | Cell proliferation, cell apoptosis, signal transduction, pathway, protein expression | The level of intracellular Ca²⁺ after PEMF treatment was significantly higher. | 2017  | Xue et al. [96] |
| 70  | Bone marrow stem cells (BMSCs)                 | Frequency of 20 Hz, flux density of 2 mT | Gene expression, cell differentiation                       | PEMF increases the proliferation of MSC cells. | 2015  | Lu et al. [74] |

Table 2: Rat/mouse cells: cellular response (presence or absence) for cultured rat/mouse cells.

| No. | Cell line                                      | Frequency and intensity | Cell response analysis                                      | Result                                                                 | Year  | Authors          |
|-----|------------------------------------------------|-------------------------|-------------------------------------------------------------|----------------------------------------------------------------------|-------|------------------|
| 71  | Rat bone marrow-derived stem cells             | Frequency of 75 Hz, intensities of 1, 2, or 5 mT | Cell proliferation                                           | PEMF stimulation did not cause significant changes in rat BMSC proliferation | 2015  | Wang et al. [75] |
| 72  | The murine MN9D dopaminergic cell line         | Frequency of 5 Hz       | Cell morphology                                             | PEMF signals increased cell body width                                | 2014  | Lekhrjaj et al. [68] |
| 73  | Primary culture osteoblastic cells             | Intensities of 0.06 and 0.2 mT | Cell proliferation, cell viability, protein expression       | Control group had a higher cell proliferation than 0.06 and 0.2 mT PEMF groups | 2013  | Emes et al. [86] |
| 74  | RAW 264.7 macrophage-like cells (murine)       | Frequencies of 5.1 Hz, 7.8 Hz, 10.8 Hz, 15.6 Hz, 20.8 Hz, 23.4 Hz, or 30 Hz, intensity of 4 mT | Cell proliferation, Gene expression                           | Cells exposed to PEMF demonstrated changes in the downregulation of NFkB | 2013  | Ross and Harrison [80] |
| 75  | PC12 and NR8383 rat alveolar macrophages       | Frequency of 0.172 Hz, intensity of 700 mT | Cell proliferation, Gene expression                           | PEMF induced activation of ERK1/2 in PC12 cells                      | 2013  | Tada-Aki et al. [81] |
| 76  | Rat brain cortical neurons, PC12, U87MG cells  | Frequency of 75 Hz, intensity of 1.5 mT | Cell proliferation, Gene expression                           | PEMF treatment induced an upregulation of A3ARs, A2ARs                | 2012  | Vincenzi et al. [82] |
| 77  | C3H10T1/2 cells iCALs                          | Frequency of 1000 Hz    | Cell differentiation, Gene expression, Protein expression   | PEMF stimulation augmented osteopontin and osteocalcin expression      | 2012  | Teven et al. [72] |
| 78  | Mesenchymal stem cells (MSCs)                  | Frequency of 50 Hz, intensity of 10 mT | Cell viability, cell proliferation                           | PEMF increases the proliferation of MSC cells.                        | 2012  | Li et al. [76] |
levels ($p$ values for Begg’s test and Egger’s test for all categories were >0.05). To evaluate the effect of each single study on the pooled effect size, we removed each study, one by one. We found no significant effects of any individual study on the combined effect sizes in different meta-analysis presentation.
### Table 15: Other species cell studies.

| No. | Cell line (Human) | Number of experiments | Cell line (human) | Number of experiments | Cell response | p-value | Presence rate (%95CI) |
|-----|-------------------|-----------------------|-------------------|-----------------------|--------------|---------|-----------------------|
| No. | Cell line Frequency and intensity | Cell response analysis | Result | Year | Authors |
| 91 | Intervertebral discs (IVDs) from bovine caudal spines | Pulse frequency of 3850 Hz | Protein expression, signal pathway | Overall p65 expression was increased, and P38 expression was not influenced. | 2019 | Tang et al. [99] |
| 92 | Rabbit adipose-derived mesenchymal stem cells (AD-MSCs) | Frequencies of 25 Hz and 50 Hz, intensity of 1.6 mT | Cell proliferation, Gene expression | PEMF did not cause any significant increase in SOX9 mRNA productions | 2016 | Kavand et al. [100] |

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**Figure 1:** Human cells (stem cells): cellular response (presence or absence) for cultured human cells (3249 in vitro exposures) pooling data from 92 peer-reviewed scientific articles published in 1999-2019. Statistical significant cell groups are highlighted. Heterogeneity results: \( I^2 = 92.03 \), p-value < 0.001.

**Figure 2:** Human cells (cancer cells): cellular response (presence or absence) for cultured human cells (3249 in vitro exposures) pooling data from 92 peer-reviewed scientific articles published in 1999-2019. Statistical significant cell groups are highlighted. Heterogeneity results: \( I^2 = 92.03 \), p-value < 0.001.
5. Discussion

This study scrutinized the related scientifical literature for the association between PEMFs and cell responses in vitro. Realizing that there were distinctions between cell types in terms of apoptosis, rate of proliferation and age, and other characteristics and that PEMFs parameters can be characterized in terms of frequency, intensity, time of exposure, and waveform, we investigated if there were distinct properties of positive and negative findings associated with these characteristics. The results showed that there was no significant difference between the presence and absence of the cell response to PEMF stimulation in human cells, rat/mouse cells, and other species (Figure 17 for each row ($p > 0.05$)). However, several aspects of our results are notable, which are given below.

Our findings demonstrated that in in vitro studies, nearly 50% of human cells (Figure 17) would undergo changes due to PEMFs, whereas fewer number of cells in rats/mice (44.61%) and other species (18.18%) were influenced by PEMFs. Thus, a large number of experiments on cells in rats/mice and other species pointed out the absence of any effect caused by PEMFs. Among the studies conducted on human cells, most of them were performed on stem cells. According to the results, it seems that the type of stem cell plays as an effective factor in intracellular processes affected by PEMFs. Especially, in the field of bone tissue engineering in which mesenchymal stem cells are activated by EMF, this finding would be considerable.

Another significant finding of our study was among osteoblast-like cells, MG-63 human osteosarcoma cells seemed to be very sensitive to PEMFs (86.1%). The studies have shown that these fields could alter activity through changes in local factor production [4]. However, in human osteogenic sarcoma SaOS-2, the absence of cell response to PEMFs alone was greater in degree than the presence of cell response (75%). PEMFs appeared to have little effect on the phenotype and number of SaOS-2 cells [7].

The potential effects of PEMFs on tendon cells showed that these fields (87.74%), focusing on the potential applicability of this cell source for regenerative medicine purpose, could be effective in the treatment of tendon disorders. In fact, these fields could influence the proliferation, release of anti-inflammatory cytokines, tendon-specific marker expression, and angiogenic factor in healthy human TCs culture models [15].

Analysis of the results of other related studies concerning the effect of PEMFs on the cells of blood cancers like leukemia and lymphoma in human (and on basophilic leukemia cells in rats/mice) showed that these cells were not affected.

| Cell line (human) | Number of experiments | Cellular response | Presence | Absence | $p$-value | Presence rate (%95CI) |
|-------------------|-----------------------|-------------------|----------|---------|-----------|-----------------------|
| Retinal pigment epithelial (RPE) [57] | 12 | 10 (83.3%) | 2 (16.7%) | 0.038 |
| Peripheral blood mononuclear cells (PBMCs) [58, 59] | 21 | 12 (57.14%) | 9 (42.86%) | 0.514 |
| Umbilical vein endothelial cells (HUVECs) [60] | 13 | 4 (30.8%) | 9 (69.2%) | 0.177 |
| Human dermal fibroblasts (HDF) [61] | 25 | 15 (60%) | 10 (40%) | 0.321 |
| Human epidermal keratinoocyte (HEK) [61] | 25 | 9 (36%) | 16 (64%) | 0.167 |
| Human mononuclear cells (HMNC) [61] | 25 | 15 (60%) | 10 (40%) | 0.321 |
| Tendon cells (hTCs) [16, 62] | 118 | 13 (11.02%) | 105 (88.98%) | <0.001 |
| Annulus fibrosus (AF) cells [63] | 15 | 0 (0%) | 15 (100%) | 0.012 |
| Nucleus pulposus (NP) cells [63] | 18 | 0 (0%) | 18 (100%) | 0.618 |
| Human normal osteoblast cells (NHOOC) [56] | 16 | 9 (56.25%) | 7 (48.75%) | 0.083 |
| Disc cells [64, 65] | 15 | 11 (73.33%) | 4 (26.64%) | 0.067 |
| Atrophic nonunion cell culture [66] | 13 | 3 (23.08%) | 10 (76.92%) | 0.206 |
| Hypertrophic nonunion cell culture [66] | 13 | 3 (23.08%) | 10 (76.92%) | 0.206 |
| Human chondrocyte [24, 67] | 15 | 10 (66.7%) | 5 (33.3%) | 0.198 |
| MCF10 [46] | 3 | 0 (0%) | 3 (100%) | 0.140 |
| Sympathetic neuronal-like PC6 cells [68] | 4 | 0 (0%) | 4 (100%) | 0.105 |
| Total | 351 | 114 (32.48%) | 237 (67.52%) | 0.001 |

Heterogeneity results: $I^2 = 92.03$, $p$-value < 0.001.

Figure 3: Human cells (other normal cells): cellular response (presence or absence) for cultured human cells (3249 in vitro exposures) pooling data from 92 peer-reviewed scientific articles published in 1999-2019. Statistical significant cell groups are highlighted. Heterogeneity results: $I^2 = 92.03$, $p$ value < 0.001.
### Cell line (rat/mouse)

| Cell line (rat/mouse) | Number of experiments | Cellular response | p-value | Presence rate (95% CI) |
|-----------------------|-----------------------|-------------------|---------|-----------------------|
| MN9D dopaminergic [69] | 1                     | 1 (100%)          | 0 (0%)  | -                     |
| Adipose-derived stem cells (ADSCs) [70] | 1                     | 1 (100%)          | 0 (0%)  | -                     |
| Tendon stem and progenitor cells (TDSPCs) [71] | 6                     | 0 (0%)            | 6 (100%) | 0.081                 |
| C3H10TF1/2 mesenchymal cells [72, 73] | 70                    | 47 (67.14%)       | 23 (32.86%) | 0.005                 |
| Bone marrow-derived mesenchymal stem cells [74] | 15                    | 10 (66.7%)        | 5 (33.3%) | 0.206                 |
| bone marrow stem cells (BMSCs) [75, 76] | 66                    | 28 (42.42%)       | 38 (57.58%) | 0.220                 |
| Immortalized calvarial cells (iCALs) [73] | 6                     | 3 (50%)           | 3 (50%)  | 0.980                 |
| Mesenchymal stem cells (MSCs) [77] | 10                    | 2 (20%)           | 8 (80%)  | 0.080                 |
| Neural stem cells (NSCs) [78] | 48                    | 18 (37.5%)        | 30 (62.5%) | 0.087                 |
| RAW264.7 [79-81] | 69                    | 34 (49.28%)       | 35 (50.72%) | 0.904                 |
| Alveolar macrophages (NR8383) [82] | 2                     | 0 (0%)            | 2 (100%) | 0.299                 |
| Oligodendrocyte precursor cells (OPCs) [5] | 38                    | 32 (84.21%)       | 6 (15.79%) | <0.001                |
| Pheochromocytoma cells (PC12) [48, 82, 83] | 20                    | 6 (30%)           | 14 (70%) | 0.082                 |
| Brain Cortical Neurons [83] | 6                     | 2 (33.3%)         | 4 (63.7%) | 0.423                 |
| U87MG (glioblastoma) [83] | 6                     | 2 (33.3%)         | 4 (63.7%) | 0.423                 |
| Spermatogonia germ cell line, (GC-1) [84] | 57                    | 25 (43.86%)       | 32 (56.14%) | 0.355                 |
| Spermatocyte cell line, (GC-2) [84] | 57                    | 11 (19.3%)        | 46 (80.7%) | <0.001                |
| Nucleus pulposus cells [85] | 16                    | 0 (0%)            | 16 (100%) | 0.015                 |
| Osteosarcoma cell line (LM8 cells) [86] | 6                     | 2 (33.3%)         | 4 (66.7%) | 0.423                 |
| Primary culture osteoblastic cells [87-89] | 67                    | 24 (35.8%)        | 43 (64.2%) | 0.022                 |
| Osteogenic cell line (UMR106-01 BSP) [90] | 11                    | 5 (45.45%)        | 6 (54.55%) | 0.763                 |
| Osteoblast-like cells [91] | 28                    | 11 (39.29%)       | 17 (60.71%) | 0.261                 |
| MC3T3-E1 [88, 92-96] | 175                   | 77 (44%)          | 98 (56%)  | 0.113                 |
| MLO-Y4 osteocyte-like cells [96] | 15                    | 9 (60%)           | 6 (40%)  | 0.442                 |
| ROS 17/2.8 osteosarcoma cells [96] | 5                     | 0 (0%)            | 5 (100%)  | 0.105                 |
| C2C12 myoblasts [97] | 22                    | 8 (36.36%)        | 14 (63.64%) | 0.207                 |
| Basophilic leukemia cells (RBL-2H3) [98, 99] | 22                    | 14 (63.63%)       | 8 (36.36%) | 0.670                 |
| Fibroblast cell lines [96] | 9                     | 8 (88.9%)         | 1 (11.11%) | 0.050                 |
| Total | 854                   | 381 (44.61%)      | 473 (55.39%) | 0.006                 |

Heterogeneity results: $I^2 = 56.25$, p-value < 0.001

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### Cell line (Other species)

| Cell line (Other species) | Number of experiments | Cellular response | p-value |
|---------------------------|-----------------------|-------------------|---------|
| Intervertebral discs (IVDs) [100] | 3                     | 2 (66.67%)        | 1 (33.33%) | 0.571 |
| Adipose derived mesenchymal stem cells (AD-MSCs) [101] | 8                     | 0 (0%)            | 8 (100%)  | 0.052 |
| Total | 11                    | 2 (18.18%)        | 9 (81.82%) | 0.182 |

Heterogeneity results: $I^2 = 70.90$, p-value = 0.064
to PEMFs. Thus, it seems that these fields alone are not an effective treatment for blood cancers. Further investigations are required to examine the responsiveness of different types of blood cancer cells to PEMFs. Evaluation of different experimental techniques used in the studies showed that most of the experiments were carried out on the expression of genes and proteins, because PEMFs could verifiably promote bone fracture healing and enhance the maturation of osteoblastic cells. Also, most of studies have examined the effect of osteogenic differentiation of these fields on mRNA level.

| Published year | Number of publications | Number of experiments | Cellular response Presence | Absence | p-value | Presence rate (%95CI) |
|---------------|-----------------------|-----------------------|---------------------------|---------|---------|----------------------|
| 1999          | 2                     | 48                    | 26 (54.17%)               | 22 (48.53%) | 0.564   |
| 2000          | 1                     | 5                     | 1 (20%)                   | 4 (80%)  | 0.215   |
| 2001          | 3                     | 33                    | 6 (18.18%)                | 27 (81.82%) | 0.001   |
| 2002          | 1                     | 15                    | 9 (60%)                   | 6 (40%)  | 0.442   |
| 2003          | 1                     | 20                    | 9 (45%)                   | 11 (55%) | 0.655   |
| 2004          | 1                     | 28                    | 11 (39.29%)               | 17 (60.71%) | 0.261   |
| 2005          | 2                     | 54                    | 11 (20.37%)               | 43 (79.63%) | <0.001 |
| 2006          | 3                     | 57                    | 24 (42.11%)               | 33 (57.89%) | 0.235   |
| 2007          | 3                     | 62                    | 23 (37.1%)                | 39 (62.9%) | 0.045   |
| 2008          | 2                     | 21                    | 10 (47.62%)               | 11 (52.38%) | 0.827   |
| 2009          | 3                     | 126                   | 46 (36.51%)               | 80 (63.49%) | 0.003   |
| 2010          | 6                     | 711                   | 566 (79.61%)              | 145 (20.39%) | <0.001 |
| 2011          | 3                     | 62                    | 9 (14.52%)                | 53 (85.48%) | <0.001 |
| 2012          | 7                     | 204                   | 70 (34.31%)               | 134 (65.69%) | <0.001 |
| 2013          | 9                     | 145                   | 54 (37.24%)               | 91 (62.76%) | 0.002   |
| 2014          | 4                     | 104                   | 34 (32.69%)               | 82 (70.69%) | 0.001   |
| 2015          | 5                     | 217                   | 86 (39.63%)               | 131 (60.37%) | 0.002   |
| 2016          | 11                    | 276                   | 81 (29.34%)               | 195 (70.65%) | <0.001 |
| 2017          | 12                    | 538                   | 325 (60.75%)              | 210 (39.25%) | <0.001 |
| 2018          | 6                     | 375                   | 101 (26.93%)              | 274 (73.07%) | <0.001 |
| 2019          | 7                     | 196                   | 101 (51.53%)              | 95 (48.47%) | 0.668   |
| Total         | 92                    | 3306                  | 1603 (48.48%)             | 1703 (51.51%) | 0.019   |

Heterogeneity results: $I^2 = 36.12, p-value = 0.049$.

**Figure 6:** Overview of the published year: cellular response (presence or absence) for cultured human, rat/mouse, and other species cells (3249 in vitro exposures) pooling data from 92 peer-reviewed scientific articles. Heterogeneity results: $I^2 = 36.12, p-value = 0.049$.

| Technique | Different methods | Number of experiments | Cellular response Presence | Absence | p-value | Presence rate (95%CI) |
|-----------|-------------------|----------------------|---------------------------|---------|---------|----------------------|
| Cells     | Cell viability, cell morphology, apoptosis, cell proliferation, cell differentiation | 1131 | 402 (35.64%) | 729 (46.63%) | <0.001 |
| Cell Functions | Calcium concentration, signal transductions, enzyme activity, membrane potential, membrane stability | 245 | 94 (38.37%) | 151 (61.63%) | <0.001 |
| DNA       | Gene expression, protein expression, ROS production, chromosome aberration, micronucleus assay, DNA damage, oxidative stress, DNA single-strand breaks, DNA double-strand breaks, genotoxicity | 1930 | 1107 (57.36%) | 823 (42.64%) | <0.001 |
| Total     |                    | 3306 | 1603 (48.48%) | 1703 (51.52%) | 0.137 |

Heterogeneity results: $I^2 = 98.49, p-value < 0.001$.

**Figure 7:** Different experimental techniques: cellular response (presence or absence) for cultured human, rat/mouse, and other species cells (3249 in vitro experiments) pooling data from 92 peer-reviewed scientific articles. Heterogeneity results: $I^2 = 98.49, p-value < 0.001$.
frequencies higher than 100 Hz and intensities between 1 and 10 mT seemed to be more effective in establishing a cellular response. In addition, the analysis of times of exposure showed that in chronic exposure to PEMF more than 10 days may observe the effect of these fields (presence: 57.66%, absence: 42.34%; p < 0.01), while acute exposure more than 24 h may cause to less effect (presence: 17.87%, absence: 82.13%, p < 0.01).

Figure 8: Classification of experimental techniques observed from 3306 experiments from 92 peer-reviewed scientific publications (1999-2019). Cells exposed to PEMFs in vitro experiments that reported results (cellular response (presence or absence)) for different exposure conditions (frequency and intensity). These experimental techniques are classified as (i) cells (cell proliferation, cell differentiation, cell viability, cell morphology, and apoptosis), (ii) cell functions (enzyme activity, calcium concentration, signal transductions, membrane potential, and membrane stability), and (iii) DNA (chromosome aberration, micronucleus assay, DNA damage, oxidative stress, DNA single-strand breaks, DNA double-strand breaks, genotoxicity, gene expression, protein expression, and ROS production).

Figure 9: Different frequency levels: cellular response (presence or absence) for cultured human, rat/mouse, and other species cells (3249 in vitro experiments) pooling data from 92 peer-reviewed scientific articles published in 1999-2019. Please note that frequency values were not given in 85 experiments/exposures. Heterogeneity results: $I^2 = 96.7$, p-value < 0.001.

Figure 10: Different intensity levels: cellular response (presence or absence) for cultured human, rat/mouse, and other species cells (3249 in vitro experiments) pooling data from 92 peer-reviewed scientific articles published in 1999-2019. Please note that intensity values were not given in 624 experiments/exposures. Heterogeneity results: $I^2 = 92.36$, p-value < 0.001.
It is worth noting that we may be able to find optimal parameters of PEMF in future studies in the effective ranges obtained from the present study to achieve the most effective response, depending on the desired effect.

Basically, in vitro studies use cells to investigate the interaction mechanisms better by breaking down the complexity of a whole organism into a controllable system. Indeed, each cell with a model system of its own could be suitable for a...
Figure 14: Intensity observed from 3306 experiments from 92 peer-reviewed scientific publications (1999-2019). Cells exposed to PEMFs in vitro experiments that reported results (cellular response (presence or absence)) for different exposure conditions. Intensity values are shown in mT.

Figure 15: Time of exposure observed from 3306 experiments from 92 peer-reviewed scientific publications (1999-2019). Cells exposed to PEMFs in vitro experiments that reported results (cellular response (presence or absence)) for different exposure conditions.

Figure 16: Waveforms observed from 3306 experiments from 92 peer-reviewed scientific publications (1999-2019). Cells exposed to PEMFs in vitro experiments that reported results (cellular response (presence or absence)) for different exposure conditions.

Figure 17: Cellular response (presence or absence) for cultured human, rat/mouse, and other species cells (3249 in vitro exposures) pooling data from 92 peer-reviewed scientific articles published in 1999-2019. Heterogeneity results: $I^2 = 88.92$, $p$-value < 0.001.
specific biological aspect. Therefore, although it cannot be expected that humans respond to PEMFs, studies of simple biological systems can advance our understanding about which systems in the body are more susceptible to PEMFs. Therefore, conducting an analysis similar to the present meta-analysis could be useful as a reference for many epidemiological studies or in vivo experiments using the whole organism animal models.

6. Conclusion

To the best of our knowledge, no other meta-analysis has investigated the effects of PEMF on cell responses in vitro. The findings of this study provided us insight into which cell types could be more responsive to PEMFs. Additionally, we determined the range of frequencies and intensities which PEMFs appeared more effective. Future research would need to explore the effects of other variables on cell response in vitro and to investigate the effectiveness of PEMFs in vivo.

Data Availability

Access to data is restricted due to ethical concerns.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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