Pulsed Electromagnetic Fields and their Role in Breast Cancer Impedance

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ABSTRACT
As the predicted number of deaths due to cancer is rising, more reliable curative therapies are being pursued. Nanosecond pulsed electromagnetic fields (PEMF) are becoming increasingly researched as a post-surgery pain reliever and cancer therapy alternative. PEMFs are an attractive alternative due to their lack of side effects as well as their quick and efficient delivery. PEMFs do not damage healthy tissue as would be seen with hyperthermia, hypothermia, chemotherapy, and radiation; but can be easily combined with these treatments to further combat diseased cells, tumors, as well as the blood vessels feeding those tumors. Numerous studies have discovered positive results using extremely low frequency PEMFs on not only in vitro and in vivo testing, but also clinical testing. Results have ranged from 3 mT for 60 minutes for three days to 10 mT consistently for 24 hours. The median results have shown PEMFs of 15 mT for 10 minutes a day. Future research is needed to compare the positive results from numerous studies to determine the optimal dosing needed for effective cancer treatment.

Keywords:
breast cancer, pulsed electromagnetic fields, electromagnetic field (EMF), extremely low frequency (ELF), cell viability, vascularity, therapy, oncology, tumor growth, intensity

1 INTRODUCTION
Researchers have been searching for an effective cancer treatment for decades and they may have finally found it in the form of pulsed electromagnetic fields (PEMF). Previous research suggests PEMF use could not only slow/diminish tumor growth, but also possibly strengthen healthy cells [1]. In one study, PEMFs destroyed cancer cells with a single delivery [2].

This review will focus mainly on the role of pulsed electromagnetic fields in breast cancer treatment since previous research suggests breast cancer cells appear more responsive to electromagnetic fields in comparison to other cancer cell types [3] and the optimal uses for future PEMF testing in breast cancer research.

2 BACKGROUND
2.1 Cancer Research
Cancer is the second main cause of death around the world (1 in 6) [4]. This has prompted researchers to investigate cancer treatment alternatives since it is predicted to escalate to 11 million deaths annually by 2030 [5]. Previous cancer research has ranged from vitamin consumption to thermal therapies such as hyperthermia/hypothermia in ablation to electroporation in chemotherapy for increased drug delivery.
Breast cancer is the 5th most common cancer type with more than half a million deaths annually [4] and among the leading causes of deaths amid the female population [6].

2.2 Therapeutic Options

Depending upon the cancer type, differing therapeutic options will be recommended. The options currently available include chemotherapy, immunotherapy, radiation, and surgery [5]. The most common option being surgery in combination with radiation and chemotherapy. Unfortunately, the side effects associated with this treatment option include pain, infection, sores, sickness, swelling, bruising, and exhaustion [5]. Radiation, chemo, and surgery also do not always lead to a curative outcome, but solely a prolongation of life while still allowing for quality life.

When curative options are not feasible, the therapeutic alternative may only be palliative to attempt to improve the quality of life without prolongation. This is often the case with hospice. [4]

Using pulsed electromagnetic fields eliminates the side effects associated with common cancer therapies and could reduce the amount of narcotics consumed thus possibly reducing the probability for addiction [7].

2.3 Pulsed Electromagnetic Fields in Pain Reduction

Pulsed electromagnetic fields (PEMF) were first approved in 1979 for use in bone healing. Since then, its use has branched to include pain reduction, increased blood circulation, cell regeneration, anti-inflammatory responses, and muscle relaxation. [8]

Previous research has been conducted looking at pulsed electromagnetic fields for reduction in pain after surgeries. Using PEMFs increase the amount of nitric oxide that is released into the tissues therefore increasing the anti-inflammatory response and growth factors. Taylor et al conducted a study to attempt to identify the limits that lead to a reduction in post-operative pain as well as the upper and lower bounds of possible dosing. Twenty-six women were tested per group. The women were given a noninvasive disposable dual coil that was placed on top of the surgical dressings and produced a 2 ms 27.12 MHz wave that was repeated every 2 seconds with a peak EMF of 4 µT per breast with a SAR of 40 mW/kg. This was activated either for 5 minutes every 20 minutes or 15 minutes every 2 hours to see if an increase in the pulsed electromagnetic fields would provide an increase in pain reduction compared to 20-minute activations every 4 hours consistent with narcotics timeframe from a previous study [9]. The participants were asked to rate their pain using a visual analog scale before leaving as well as after being discharged. The individual’s pain levels were then based off that initial rating for the future comparisons for each study participant. The surgeries were all performed by the same surgeon with the same techniques, and the patients operating time were not statistically different. A reduction in pain with 15-minute activation every 2 hours was seen. This reduction was lower than previous studies decline in pain while using 20-minute activation every 4 hours. See Figure 1 for the differences between
postoperative rate of pain. The amount of narcotics consumed was not statistically significantly different from the control in this study. The authors believe the lack of pain reduction for 5-minute activation every 20 minutes was due to phosphodiesterase activity taking over and inhibiting cyclic guanosine monophosphate (cGMP) which is used to control inflammation and cell repair. By increasing the rate of the pulsed electromagnetic fields, the production of nitric oxide increased to the point where it inhibits the production of cGMP and blocks the effects of the pulsed electromagnetic fields. Small amounts of pulsed electromagnetic fields enhance the anti-inflammatory signaling while large amounts inhibit it. [7]

As previous research has shown, pulsed electromagnetic fields can decrease postoperative pain, but further research needs to be done to determine the optimal range of pulsed signals to get the greatest pain and narcotics reduction without increasing the production of nitric oxide to the blocking point.

PEMFs are also used in combination with other cancer treatments such as chemotherapy as a therapeutic alternative without additional painful side effects since electromagnetic fields can impede cell division and thus possibly result in cell destruction [3]. PEMF in cancer research has shown promising results for the future of cancer therapy as anticancer agents [10] [1] [3] [2] [7] [5] [11].

Numerous studies have been investigating the optimal PEMF dosing for the most effective cancer treatment options. The plethora of test methods are discussed in the following review section.

3 REVIEW

This review consists of both in vivo, in vitro, and clinical studies dealing with pulsed electromagnetic field use with cancer.

3.1 Test Methods

3.1.1 Electromagnetic field intensity vs pulse frequency

Extremely low frequency nanosecond pulsing of electromagnetic fields are the future for drug-free cancer treatments. Extremely low frequencies were chosen to limit the thermal aspects often associated with energy delivery. Numerous studies have been conducted to determine the parameters around the optimal PEMF dosing without the addition of heat that could damage healthy cells and tissues. The following sections will outline that testing and discuss the consistent conclusions.
3.1.1.1 Exposure parameters on tumor growth

Differing test methods were used to determine if specific pulsed electromagnetic fields would inhibit breast cancer cell growth while leaving normal cells intact as a form of selective killing. Wu et al. tested 50 pulses of 20 kV/cm, 300 pulses of 25 kV/cm, and 100 pulses of 30 kV/cm and chose pulsing of 100 ns with 30 kV/cm for 1 minute for three consecutive days with an operating voltage between 12 and 15 kV and an operating current of 100 mA. This ended up delivering approximately 240 pulses for each day for a total of 720 pulses of 30 kV/cm. The results of this testing showed inhibited tumor growth and no metastasis detected via MRI imaging. The PEMF treated tumors almost stopped growing during the first week of treatment and then slowly started to grow again after 10 days. Showing only an inhibition in tumor growth instead of destruction. After the tumors started to grow again, they were still 79% smaller than the control tumors that did not receive PEMF treatment. [11]

Cameron et al. tested increasing duration with a steady intensity as well as an increasing intensity with a steady duration. All PEMFs produced approximately 120 pulses per second using a “complex magnetic field generating device” from Bio-Dynamics. The first group had three increasing durations from 3 minutes to 10 minutes as well as 40 minutes at a steady intensity of 10 mT. The second group had three increasing intensities from 10 mT to 15 mT and 20 mT all at a steady duration of 10 minutes. The results showed that increasing duration did not result in tumor growth retardation in comparison to the control group; however, increasing intensity did result in a statistically significant difference when compared to the control group which thus resulted in smaller tumors see Figure 2. [10]

![Figure 2](image-url)
3.1.1.2 Exposure parameters on vascularity

Since tumor growth directly relies upon a blood supply. By preventing the supply of blood, the tumors become starved of both oxygen and nutrients which leads to cell death. Studies were conducted to determine if introducing pulsed electromagnetic fields would reduce the vascularization of the tumors and would thus reduce the growth of that tumor via necrosis.

Wu et al. tested the number of blood vessels around the treated tumors after pulsing of 100 ns with 30 kV/cm for 1 minute for three consecutive days with an operating voltage between 12 and 15 kV and an operating current of 100 mA. The number of blood vessels subjected to the PEMFs decreased to 50% (day 7) and 65% (day 14) while the number of blood vessels around the control tumors steadily increased (Figure 3). Immunohistochemistry revealed that angiogenesis was also suppressed in the treated tumors, specifically the following blood vessel growth markers: VEGF, VEGFR, and CD34. [11]

Cameron et al. tested the exposures in Table 1 on mammary tumor vascularization with 120 pulses per second using the Bio-Dynamics device. The results of this testing showed that using an intensity of 15 mT for 10 minutes is a safe and effective therapy to not destroy all blood vessels but give the lowest percentage of tumor vascularization. Not using any EMF (control group) produced the largest percentage of tumor vascularization. [10]

3.1.1.3 Exposure parameters on cell survival

Cell viability assays are utilized to determine cell proliferation (ratio of treated cell absorption divided by control cell absorption) and is often combined with a fluorescent assay to determine percentage of cell death.

Filipovic et al. tested breast cancer cell exposure to 50 Hz frequencies of 10 mT for both 24 and 72 hours. The results of this testing showed that cell death was more prevalent with a shortened amount of time in the presence of EMF. Breast cancer cells had around 50% cell viability after 24 hours and around

![Figure 3: Blood vessel number on day 1, 7, and 14. Figure taken from [11].](image)

<table>
<thead>
<tr>
<th>Group number</th>
<th>EMF exposure condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Control (0 mT) sham exposure</td>
</tr>
<tr>
<td>2.</td>
<td>10 mT 3 minutes per day</td>
</tr>
<tr>
<td>3.</td>
<td>10 mT 10 minutes per day</td>
</tr>
<tr>
<td>4.</td>
<td>10 mT 40 minutes per day</td>
</tr>
<tr>
<td>5.</td>
<td>10 mT 40 minutes twice per day</td>
</tr>
<tr>
<td>6.</td>
<td>15 mT 10 minutes per day</td>
</tr>
<tr>
<td>7.</td>
<td>20 mT 10 minutes per day</td>
</tr>
<tr>
<td>8.</td>
<td>20 mT 10 minutes twice per day</td>
</tr>
</tbody>
</table>

There were 20 mice in group 1, all other groups had 10 mice.
80% cell viability after 72 hours. [3]

Wu et al. determined cell apoptosis via H&E staining to calculate the amount of cytoplasm since having less cytoplasm is a gauge for apoptosis. The tumors treated with 50 pulses of 30 kV/cm at 100 ns for 1 minute had reduced amounts of cytoplasm compared to the control up until 6 hours post treatment. [11]

Crocetti et al. tested 2 mT, 3 mT, or 5 mT PEMFs (6 ms intervals) at 20 Hz for 60 minutes a day for 3 days. The 3 mT group was additionally tested for a duration of 30 minutes, as well as 90 minutes. Differences in cell death between duration can be seen in Figure 4 and differences in cell death between exposure can be seen in Figure 5. Using 50 Hz was also tried with no cellular effects. The results of this testing showed that the 3 mT test parameters exhibited the best results for cancer cell deaths. The results also revealed that exposure to the same 3 mT test parameters helped normal cell survival. The 60-minute test parameters showed the most breast cancer cell deaths while not harming the normal cells. [1]

![Figure 4: Percentage of dead cells in each duration group. Figure taken from [1].](image4)

Cameron et al. also evaluated the survival rate of the mice after 20 days. The control group dropped to 65% with the test group mice resting at 93% (for exposure to 20 mT for 10 minutes). [10]

### 3.2 Clinical Studies

Vadala et al. specify two known clinical studies, but one focused on individuals with advanced hepatocellular carcinomas and is not discussed in this review.

![Figure 5: Percentage of dead cells in each exposure group. MCF7 (breast cancer cells) MCF10 (normal cells). Figure taken from [1].](image5)
The other study was by Barbault et al. and examined specific frequencies that specifically affect tumors. Twenty-eight individuals with 14 different types of cancer were tested using 1524 frequencies that went up to 114,000 Hz at increments of 100 Hz. The radiofrequency output of the PEMF device was adjusted to 100 mW. The individuals administered the PEMFs themselves for one hour three times a day and the cancers became stable anywhere between 4 months to 3 years suggesting the use of amplitude-modulated EMFs as anticancer therapy. [12] [5]

4 CONTRADICTING RESULTS

Among the journal articles reviewed only one did not have positive results. Loja et al. examined five cancer cell types including breast exposed to 5 mT PEMFs of 15 Hz with 2 ms pulses, 125 Hz with 0.5 ms pulses, and 625 Hz with 0.1 ms pulses for 20 minutes. Measurements were taken 24 and 48 hours after exposure and cell morphology was inspected after 1, 2, and 5 days. The results showed an increase in cell proliferation in two of the five cancer types (colorectal and ductal). The other three exhibited zero changes in cell proliferation. Cell morphology also exhibited zero changes in all five cancer types. [13]

5 CONCLUSION

In conclusion, since using pulsed electromagnetic fields does not damage healthy tissues that would otherwise be damaged using hyperthermia and/or chemotherapy, it is an excellent alternative to reducing tumor growth as well as safely and effectively reducing the percentage of tumor vascularization. There are no side effects with using pulsed electromagnetic fields vs. a plethora of side effects with conventional cancer therapies making nanosecond pulsing a great method for combinational cancer therapy or for tumor and side effect reduction prior to surgery. Future research is needed to compare the positive results from numerous studies to determine the optimal dosing needed for effective cancer treatment.

6 REFERENCES


