



## SYSTEMATIC REVIEW

# Effects of pulsed electromagnetic fields on bone fractures: a systematic review update

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### ABSTRACT

**INTRODUCTION:** Fractures are common bone injuries, which have a great burden on global health. Fracture healing is a long-term process that may be influenced by a number of factors. The 10-15% of all bone fractures may be complicated by an impaired healing (*i.e.* delayed union or non-union). The application of weak electromagnetic fields has been proposed to have different effects on bones such as enhancing proliferation – orientation – migration of osteoblast-like cells and supporting osteogenic differentiation in bone marrow-derived mesenchymal stem cells. Despite the amount of evidence on cellular and histological effects, to date the application of pulsed electromagnetic fields has not achieved univocal consensus in daily practice. The purpose of this systematic review update is to research, select, analyze and summarize the most recent scientific evidence regarding the effects of pulsed electromagnetic fields in the treatment of acute bone fractures.

**EVIDENCE ACQUISITION:** A systematic review using the following MeSH terms (Magnetic Field Therapy; Electromagnetic Fields; Bone and Bones; Fractures, Bone; Fractures Healing) and strings {"Magnetic Field Therapy [mh]" OR "Electromagnetic Fields [mh]" OR "magnetotherapy" OR "pulsed electromagnetic field"} and {"Fractures, bone [mh]" OR "Bone and Bones [mh]"} and {"Fractures Healing [mh]"} was conducted on PubMed, Cochrane Library, Epistemonikos and Scopus electronic databases. Only full articles published in English between January 2014 and December 2022 were considered. Eligibility criteria were defined according to the Population, Intervention, Comparison, Outcomes, and Study (PICOS) design framework. Case reports, case series, uncontrolled studies and expert opinions were excluded. All articles were checked for quality and risk of bias.

**EVIDENCE SYNTHESIS:** Three randomized controlled trials were included (197 patients in total). None of the studies found significant effects of pulsed electromagnetic fields on the acute bone healing process. Contradictory results about pain relief emerged. Only one study showed a transitory positive effect of pulsed electromagnetic fields on strength and range of motion recovery in patients with acute bone fracture.

**CONCLUSIONS:** This systematic review update does not support the use of pulsed electromagnetic fields for improving the bone healing process in patients with acute fractures. Controversial evidence was found about the effects of pulsed electromagnetic fields on pain and functional recovery. Considering the scant and heterogenous literature published to date, which represents a limit for our conclusion, further studies with rigorous and high-quality methodology are needed.

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**KEY WORDS:** Bone and bones; Electromagnetic fields; Bone fractures; Fracture healing; Magnetic field therapy; Physical therapy modalities.

## Introduction

Fractures are common bone injuries, representing one of the main causes of disability with a heavy burden on health care system.<sup>1</sup> The global number of new cases of fracture was estimated to be 178 million in 2019.<sup>2</sup> From an epidemiological point of view, lower leg fractures (*i.e.* patella, tibia, fibula and ankle) were the most common and burdensome (incidence rate of 419.9 cases per 100,000 population worldwide) followed by distal (*i.e.* radius, ulna or both) and proximal arm (*i.e.* clavicle, scapula and humerus) ones.<sup>2</sup> Fracture healing is a long-term process that may be influenced by a series of local and systemic factors.<sup>3</sup> It consists of two metabolic phases (*i.e.* anabolic and catabolic), which overlap with three biological stages (*i.e.* inflammatory, endochondral bone formation and coupled remodeling).<sup>4</sup>

Regarding the healing time (*i.e.* formation of bony callus with bridging), long bone fractures usually take 6-8 weeks, while 8-10 weeks is the typical healing time for vertebral fractures.<sup>5</sup> Although most part of fractures reach consolidation, it has been estimated that between 10% and 15% of all bone fractures may undergo an impaired healing (rates may vary by the anatomic location of fractures) leading to considerable morbidity and socioeconomic costs.<sup>5,6</sup> A “delayed union” happens when the healing process has slowed down (to date there is no consensus on its standardized definition), while a “non-union” occurs when the healing process has stopped (healing failure by 9 months or a lack of progressive signs of healing by 3 months according to the USA Food and Drug Administration definition).<sup>5</sup> From this perspective, it would be of great importance to decrease the time of fracture consolidation by accelerating the bone healing process thus reducing the incidence of complications.<sup>7</sup>

Few rehabilitation interventions have been suggested in literature to enhance bone regeneration and recovery after fractures, such as the application of weak electromagnetic fields. This type of physical therapy may promote proliferation, orientation and migration of osteoblast-like cells as well as osteogenic differentiation in bone marrow-derived mesenchymal stem cells.<sup>8,9</sup> From a histological point of view, electromagnetic fields could enhance bone cells activity and alveolar bone remodeling.<sup>9</sup> Interestingly, the application of magnetotherapy seems to have a “biological window” for intensity (*e.g.* beyond a certain range of intensity the effects of magnetic fields will decrease and even become inhibitory). Moreover, the direction of magnetic fields may play a role in bone remodeling and healing process.<sup>9</sup>

Despite the amount of evidence on the cellular and histological effects of electromagnetic fields on the bone tissue and the wide use of this treatment in clinical practice, it is currently being debated if magnetotherapy could be a useful tool to enhance the healing process after acute fractures according to the results of a previous systematic review.<sup>10</sup> Probably, this is mainly due to the presence of few studies on this topic with high heterogeneity. Therefore, the purpose of this systematic review update is to analyze the most recent scientific evidence regarding the effects of pulsed electromagnetic fields (which is the most common form of magnetotherapy used for bone growth stimulation in clinics) for the treatment of acute fractures.<sup>10</sup>

## Evidence acquisition

This systematic review update was written according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.<sup>11</sup> Furthermore, it was recorded on the Open Science Framework (OSF) registry (<https://osf.io/m2bea>).

### Eligibility criteria

Eligibility criteria were defined according to the Population, Intervention, Comparison, Outcomes, and Study (PICOS) design framework as follows:<sup>12</sup>

- population: adults ( $\geq 18$  years old) with diagnosis of acute bone fracture documented by radiological examination. No restrictions were applied as to the type or site of fracture. Only studies on humans were included. In vitro and animal studies were excluded;
- intervention: treatment with pulsed electromagnetic fields (alone or associated with standard treatment).
- comparison: placebo alone or associated with standard treatment.
- outcome: primary outcome was to investigate the effects of pulsed electromagnetic fields on bone healing process. Secondary outcomes concerned the evaluation of pain, range of motion and strength;
- study design: randomized controlled trials, non-randomized controlled trials and case-control studies were included. Case reports, case series, uncontrolled studies and expert opinions were excluded.

### Information sources

A systematic search using the following MeSH terms (Magnetic Field Therapy; Electromagnetic Fields; Bone and Bones; Fractures, Bone; Fractures Healing) and strings {"Magnetic Field Therapy [mh]" OR "Electromagnetic

Fields [mh] OR “magnetotherapy” OR “pulsed electromagnetic field”) and (“Fractures, bone [mh]” OR “Bone and Bones [mh]”) and (“Fractures Healing [mh]”)} was conducted on PubMed, Cochrane Library, Epistemonikos and Scopus electronic databases. Only full articles published in English between January 2014 and December 2022 were considered.

### Selection process

Papers were selected by two independent reviewers according to the aforementioned criteria, and by a third independent reviewer with the role of solving conflicts.

### Data collection process and data items

The principal characteristics of included studies are summarized according to the Cochrane Handbook as follows: author and publication year, study design, participants (total number of participants with gender and age), intervention (type and dose of intervention), comparator (placebo or other intervention), outcomes (primary and secondary outcomes with evaluation tools).<sup>13</sup>

### Study risk of bias assessment

The risk of bias was assessed using the Cochrane risk of bias tools for randomized trials version 2 (RoB 2.0).<sup>14</sup>

## Results

### Study selection

We initially found 692 studies of which 344 were excluded because of duplication. Of the remaining 348 studies, only seven met the inclusion criteria on the base of title and abstract. After reading the full-texts four studies were excluded as they did not meet the eligibility criteria. Therefore, three papers (all reporting about randomized controlled trials) have been selected and analyzed. The total amount of participants included by the three studies selected for this systematic review is of 197 patients. The PRISMA flow diagram of the selection process is reported in Figure 1. Included studies' main features are summa-

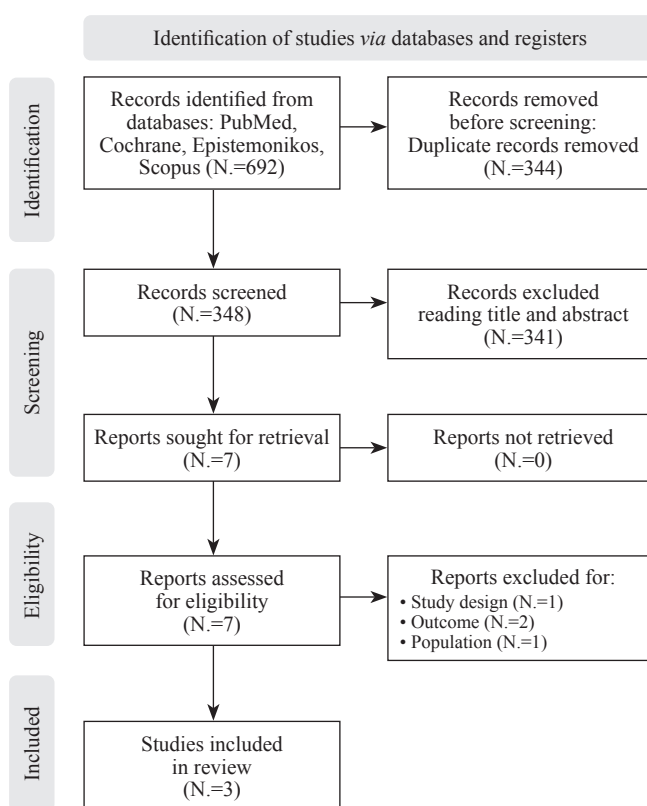


Figure 1.—The PRISMA flow diagram for systematic reviews.

rized in Supplementary Digital Material 1 (Supplementary Table I). Results of the risk of bias assessment were presented in Table I (traffic light plots show the judgment about each bias domain).<sup>15-17</sup>

### Primary outcome

As to bone fracture healing, Martinez-Rondanelli *et al.* reported a not significant faster healing (assessed by means of X-rays and differentiated into three stages: non-union, partial union and union) of femoral diaphysis fractures in patients treated with pulsed electromagnetic fields (intervention group) compared to a placebo device treatment.<sup>15</sup> In particular, at 12 weeks follow-up, fracture union was achieved in 75% (intervention) vs. 58% (placebo group)

TABLE I.—Risk of bias.<sup>15-17</sup>

Study	Randomization process	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall risk of bias
Hannemann <i>et al.</i> (2014) <sup>16</sup>	Low	Low	Low	Low	Low	Low
Mohajerani <i>et al.</i> (2019) <sup>17</sup>	High	Intermediate	Low	Low	Intermediate	High
Martinez-Rondanelli <i>et al.</i> (2014) <sup>15</sup>	Low	Low	Low	Low	Low	low

( $P=0.10$ ) of cases. At 18 weeks follow-up the ratio of fracture union was 94% (intervention) vs. 80% (placebo) ( $P=0.15$ ) as well as it was 94% (intervention) vs. 87% (placebo) ( $P=0.43$ ) at 24 weeks follow-up.<sup>15</sup>

Hannemann *et al.* found no significant difference in timing of scaphoid fractures union (assessed by means of CT scan and differentiated into three stages: non-union, partial union and union) between patients treated with pulsed electromagnetic fields (intervention) and those treated with placebo (sham pulsed electromagnetic fields) over a follow-up period of 6 ( $P=0.23$ ), 12 ( $P=0.51$ ), 24 ( $P=0.74$ ) and 52 ( $P=1.00$ ) weeks.<sup>16</sup>

Mohajerani *et al.* observed no significant difference ( $P>0.05$ ) as to the mean bone density between patients with mandibular fracture who underwent closed reduction treated with pulsed electromagnetic fields group (intervention) and those who received no additional treatment (control) over a 4-week follow-up period.<sup>17</sup> However, the percentage of changes in bone density of the two groups revealed that the intervention group had a significant increase in bone density at 4 weeks post-surgery compared with the control group ( $P<0.05$ ).<sup>17</sup>

### Secondary outcomes

#### Pain

As to pain, Martinez-Rondanelli *et al.* did not find any effects on this parameter in their paper.<sup>15</sup> Hannemann *et al.* described no significant difference regarding pain after a longitudinal compression of the scaphoid bone between patients treated with pulsed electromagnetic fields and those treated with placebo (sham pulsed electromagnetic fields) over a follow-up period of 6 ( $P=0.80$ ), 9 ( $P=1.00$ ), 12 ( $P=0.67$ ), 24 ( $P=0.47$ ) and 52 ( $P=1.00$ ) weeks.<sup>16</sup> Mohajerani *et al.* observed a significant difference in pain intensity between patients treated with pulsed electromagnetic fields and those who received no additional treatment at 7 and 14 days of follow-up ( $P<0.05$ ).<sup>17</sup>

#### Range of motion and strength

Considering range of motion and strength, Martinez-Rondanelli *et al.* reported no data in their paper.<sup>15</sup> Hannemann and collaborators found a significant difference for the wrist movement (percentage of wrist movement on the fractured arm compared with the non-fractured side) between patients treated with pulsed electromagnetic fields and those treated with placebo (sham treatment) at 24 weeks of follow-up ( $P=0.04$ ). Conversely, no significant difference regarding wrist range of motion was found between

groups over a follow-up period of 6 ( $P=0.30$ ), 9 ( $P=0.34$ ), 12 ( $P=0.54$ ) and 52 ( $P=0.44$ ) weeks.<sup>16</sup> Similarly, they reported a significant difference as to grip strength (percentage of grip strength on the fractured compared with that of non-fractured side) and those treated with placebo at 12 weeks of follow-up ( $P=0.03$ ). On the other hand, no significant difference as to grip strength was found between groups over a follow-up period of 6 ( $P=0.16$ ), 9 ( $P=0.21$ ), 24 ( $P=0.37$ ) and 52 ( $P=0.33$ ) weeks.<sup>16</sup> Mohajerani *et al.* observed a significant difference as to the maximum amount of mouth opening between patients treated with pulsed electromagnetic fields and those who received no additional treatment over a follow-up period of 28 days ( $P<0.01$ ).<sup>17</sup>

### Discussion

This systematic review update mainly aimed to research, analyze and summarize the most recent scientific evidence on the effects of pulsed electromagnetic fields in the treatment of acute bone fractures, published on Cochrane, Epistemonikos, PubMed and Scopus databases. We decided to search the literature from 2014 to 2022 to update the results of a previous, well-conducted, systematic review on the same topic published by Hannemann *et al.*, which focused on studies published between 1980 and 2013.<sup>10</sup> Hannemann *et al.* selected 16 randomized controlled trials comparing pulsed electromagnetic fields (three articles) or low-intensity pulsed ultrasound (13 articles) bone growth stimulation with placebo for the treatment of acute bone fractures.<sup>18-20</sup> Another reason for our focus on the recent literature regards the technological progress of medical devices. In our view it would be not appropriate to consider very old studies (*e.g.* since 1966) with ancient devices for magnetotherapy together with modern ones.

As for the current systematic review update we selected three articles (all reporting about randomized controlled trials) out of the 692 ones initially identified. With regard to our primary outcome, none of the studies considered by this systematic review found significant effects of pulsed electromagnetic fields on the acute bone fracture healing process.<sup>15-17</sup> This may appear in contrast with the findings reported by Hannemann *et al.* in their previous systematic review and meta-analysis: they suggested that pulsed electromagnetic fields or low-intensity pulsed ultrasound may be beneficial in the treatment of acute fractures considering the time for radiological and clinical union, while they underlined the existence of insufficient evidence to conclude that those two modalities of physical therapy, applied to acute fractures, could reduce the incidence of

non-unions.<sup>10</sup> In particular, Hannemann *et al.* pointed out that pulsed electromagnetic fields and low-intensity pulsed ultrasound may significantly shorten time to radiological union for acute (upper limb and managed non-operatively) fractures and accelerate the time to clinical union for acute diaphyseal fractures.<sup>10</sup> However, these observations come from the analysis of a mixed evidence about pulsed electromagnetic fields and low-intensity pulsed ultrasound, with a greater number of studies on the latter topic (three studies *vs.* 13 studies, respectively). If we focus only on the three studies about the effects of pulsed electromagnetic fields for managing acute bone fractures included in the review by Hannemann *et al.*, only one placebo-controlled trial reported a significantly faster healing of intracapsular femoral neck fracture in patients actively treated.<sup>18</sup> Overall, our findings are in line with the main body of current literature about the use of pulsed electromagnetic fields for treating acute bone fracture, which assigns no additional value to this therapeutic approach as its influence on fracture healing process.<sup>10, 19, 20</sup> However, we have to consider the limited number of publications on this topic with a consequent risk of publication bias as well as their heterogeneity, such as to the type of fracture (*i.e.* femoral neck and diaphysis, scaphoid, mandibula and tibia) and intervention. Therefore, as previously concluded by Hannemann *et al.*, the potential effects of pulsed electromagnetic fields on acute bone fracture healing is far from being clarified.<sup>10</sup>

For our secondary outcome regarding pain, we found contradictory results.<sup>16, 17</sup> In the previous review, Hannemann *et al.* identified two studies reporting about pain. One study showed a significant lower level of pain in patients with intracapsular femoral neck fracture treated by means of pulsed electromagnetic fields at 1, 2 and 3 months of follow-up,<sup>18</sup> while another one found a significant decrease in pain after 6 weeks of follow-up (but not at 4, 9, 12, 24 and 52 weeks) in patients with scaphoid fracture treated by means of pulsed electromagnetic fields.<sup>20</sup> Even if scant, the majority of (currently and previously) revised literature on the use of pulsed electromagnetic fields for treating acute fractures reports some positive effects on pain.<sup>16-18, 20</sup> This appears in line with the analgesic effect of pulsed electromagnetic fields observed in other bone diseases (*i.e.* osteoarthritis and musculoskeletal pain).<sup>21, 22</sup> Another relevant secondary outcome is about the motion and strength recovery after acute fractures. Only one study of those selected by this review dealt with strength, describing a positive effect only at 24 weeks of follow-up in patients with scaphoid fracture treated by

magnetotherapy.<sup>16</sup> In the same study, a positive effect on range of motion was identified in the study group at 12 weeks of follow-up.<sup>16</sup> This is not in line with the literature previously revised by Hannemann *et al.*, that reported no significant effects on the strength and motion after the treatment with pulsed electromagnetic fields.<sup>20</sup> The range of motion was also investigated in another study included in our review, showing significant improvements in the maximum amount of mouth opening in patients with mandibular fracture treated by means of pulsed electromagnetic fields.<sup>17</sup>

In our opinion, the effect of pulsed electromagnetic fields on functional recovery after acute fractures remains controversial, considering that functional recovery is mainly related to type and amount of physiotherapy (not detailed in the most of papers) as magnetotherapy plays a role of adjuvant treatment.

### Limitations of the study

The main limitation of this review is given by the restricted number of studies found and analyzed. This is a consequence of the lack of high quality in the methodology of the studies published on this issue (which is probably also due to a publication bias) despite the large use of pulsed electromagnetic fields in daily clinical rehabilitation practice. In addition, the large heterogeneity of selected studies regarding the type of fracture, treatment protocols and evaluated outcomes further limits our conclusions. Lastly, we did not perform metanalysis, given the scant amount of data.

### Conclusions

This systematic review update does not support the use of pulsed electromagnetic fields for improving bone healing process in patients with acute fracture. Controversial evidence was found about the effects of pulsed electromagnetic fields on pain and functional recovery. Considering the scant and heterogenous literature published to date, which represents a limit for our conclusion, further studies with high quality methodology are needed.

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#### Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

#### Authors' contributions

Alessandro Picelli: conceptualization (lead); methodology (lead); data curation (lead); investigation (lead); writing – original draft (lead); writing – review and editing (lead). Rita Di Censo: conceptualization (lead); methodology (lead); writing – original draft (lead); writing – review and editing (lead). Sofia Tomasello: conceptualization (equal); investigation (equal). Dalila Scaturro: conceptualization (equal); methodology (equal); writing – review and editing (equal). Giulia Letizia Mauro: conceptualization (equal); methodology (equal); writing – review and editing (equal). Nicola Smania: writing – review and editing (equal). Mirko Filippetti: conceptualization (lead); methodology (equal); writing – review and editing (lead). All authors read and approved the final version of the manuscript.

#### History

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SUPPLEMENTARY DIGITAL MATERIAL 1

Supplementary Table I.—Characteristics of the studies included in this systematic review.

Study	Study design	N. of patients (age and gender)	Fracture type	Intervention	Comparator	Primary outcome	Secondary outcomes	Follow-up period
Martinez-Rondanell <i>et al.</i> (2014)	RCT	64 (18-59 years, 52 M, 12 F)	Femoral diaphysis fracture surgically treated within the first 10 days from trauma	Electromagnetic devices were designed for the study with Helmholtz coil: 1 h/day for 8 weeks (5-105 Hz, 0.5-2.0 mT)	Placebo device	Radiographic consolidation (evaluated by femur X-ray)		6, 12, 18 and 24 weeks after the fracture
Hannemann <i>et al.</i> (2014)	RCT	102 (18-77 years, 78 M, 24 F)	Scaphoid fracture treated with immobilization	PEMF bone growth stimulator (Ossatec, Uden, the Netherlands): 24 hours/day for 6 weeks (15 Hz, 50 mV, pulse width 5 $\mu$ s, burst width 5 ms, burst refractory period 62 ms)	Placebo device	Radiographic consolidation (evaluated by Multiplanar reconstructed CT scans)	Grip strength (JAMAR dynamometer, Sammons Preston Rolyan, Bolingbrook, IL, USA), ROM (handheld goniometer), clinical union of scaphoid fracture (evaluated by anatomical snuff box tenderness and pain with longitudinal compression)	6, 9, 11, 24, 52 weeks after diagnosis of the fracture
Mohajerani <i>et al.</i> (2019)	RCT	32 (19-51 years, 24 M, 8 F)	Mandibular fracture treated with closed reduction	Portable PEMF device: 6 h post-surgery, 3 h/die for 6 days after surgery, next 1.5 h/die for other 6 days (1 mT intensity and 40 Hz frequency)	Placebo device	Computerized bone density (evaluated by direct digital panoramic machine)	Pain (VAS), ROM (maximum amount of mouth opening determined by measuring the distance between upper and lower anterior teeth with a Vernier caliper)	7, 14, and 28 d post-surgery