European Journal of Trauma and Emergency Surgery (2020) 46:245–264
https://doi.org/10.1007/s00068-019-01127-z

REVIEW ARTICLE

# Electrical stimulation-based bone fracture treatment, if it works so well why do not more surgeons use it?

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Received: 24 November 2018 / Accepted: 29 March 2019 / Published online: 6 April 2019


## Abstract

**Background** Electrical stimulation (EStim) has been proven to promote bone healing in experimental settings and has been used clinically for many years and yet it has not become a mainstream clinical treatment.

**Methods** To better understand this discrepancy we reviewed 72 animal and 69 clinical studies published between 1978 and 2017, and separately asked 161 orthopedic surgeons worldwide about their awareness, experience, and acceptance of EStim for treating fracture patients.

**Results** Of the 72 animal studies, 77% reported positive outcomes, and the most common model, bone, fracture type, and method of administering EStim were dog, tibia, large bone defects, and DC, respectively. Of the 69 clinical studies, 73% reported positive outcomes, and the most common bone treated, fracture type, and method of administration were tibia, delayed/non-unions, and PEMF, respectively. Of the 161 survey respondents, most (73%) were aware of the positive outcomes reported in the literature, yet only 32% used EStim in their patients. The most common fracture they treated was delayed/non-unions, and the greatest problems with EStim were high costs and inconsistent results.

**Conclusion** Despite their awareness of EStim's pro-fracture healing effects few orthopedic surgeons use it in their patients. Our review of the literature and survey indicate that this is due to confusion in the literature due to the great variation in methods reported, and the inconsistent results associated with this treatment approach. In spite of this surgeons seem to be open to using this treatment if advancements in the technology were able to provide an easy to use, cost-effective method to deliver EStim in their fracture patients.

**Keywords** Bone fracture healing · Electrical stimulation treatment · Literature review · Survey of orthopedic surgeons

## Introduction

The earliest report of using EStim to treat bone fractures in patients appeared in the mid-1800s in which Garrat [1] described using metallic needles placed in non-healing fractures to deliver DC EStim, that resulted in successful healing. Today, in the clinical setting EStim is administered using three different approaches; direct current (DC), pulsed electromagnetic field (PEMF), and capacitive coupled (CC). DC EStim is administered via a surgically implanted EStim power source and electrodes, and is administered at dosages between 10 and 100 µA of current [2]. CC and pulsed PEMF are both administered externally. In CC an alternating voltage is applied to cutaneous electrodes placed on opposite sides of the fracture generating an electrical field of 0.1–20 G [3]. In PEMF alternating currents, in current-carrying coils, on the skin over the fracture site, generate a pulsed electromagnetic field ranging between 3 and 10 V peak-to-peak within the fracture site [4].

In most cases EStim is used as a last resort after other treatments have failed and/or in combination with other treatments in cases of problematic fractures that heal slowly (delayed union) or do not heal at all (non-union) [5].

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Examples include; spinal fusion [6], avascular necrosis [7], internal and external fixation [8], delayed- or non-union fractures [9], osteotomies [10], bone grafts [11], and femoral osteonecrosis [12]. In these cases, EStim has been generally reported to promote bone healing and help resolve these difficult, often chronic, costly, and debilitating fractures.

Several recently published in vitro studies suggest that EStim's pro-healing effect is due to its influence on the behavior and/or function of bone-forming stem cells. Along these lines, we and others have shown that EStim causes bone forming stem cells to migrate [13, 14], proliferate [15, 16], differentiate [17–20], increase mineralization [21], deposit extracellular matrix [22], attach to scaffold materials [23], and increase the expression of several osteogenic genes [19, 20]. Importantly, all these cell behaviors/functions play key roles in fracture healing and/or bone regeneration. In addition to these in vitro findings at the cellular level, in in vivo studies in rat forelimb amputation [24] and large bone defect models [25] we have demonstrated that EStim significantly stimulates new bone, cartilage, and vessel formation and promotes healing and regeneration. In spite of these positive results in preclinical and clinical studies EStim has not become a widespread, universally used clinical treatment.

To better understand this discrepancy between the reported positive results and the relatively low use of EStim in fracture treatment we reviewed the literature and we asked orthopedic surgeons worldwide (in a survey) about their awareness, experience, and acceptance of EStim treatment in their fracture patients. Using this combined approach, we hoped to better understand the discrepancy between the demonstrated success of EStim fracture treatment, and its relatively low use clinically.

## Methods

### Literature review

To identify articles describing the use of EStim in bone healing, both in animal and clinical studies, we searched MEDLINE, Google Scholar, and Web of Science databases for articles describing in vitro and in vivo animal studies and clinical studies published between 1977 and 2017. To maximize the sensitivity of the search and identify the greatest number of studies, we used different combinations of the keywords "electrical stimulation" and "bone healing" and reviewed the reference lists of retrieved publications to identify additional articles we may have missed searching the three databases. We categorized the total number of articles identified into "animal studies", "clinical studies", "cell/organ in vitro", and "reviews/meta analyses" (Table 1). Since the focus of our study was to investigate EStim's effect on fracture healing we reviewed only articles that described fracture healing in animal and clinical studies, and excluded publications focused on in vitro studies, electrical properties of bone, connective tissue, electrical stimulation of nerves and reviews or meta-analyses. The animal studies we identified and reviewed are listed in Table 2 categorized by animal model studied, bone and fracture type, type of EStim treatment used, outcomes, and the listing of the published article, along with the number of occurrences in each category. The clinical studies reviewed are listed in Table 3 under the subtitles; bone and fracture type, number of cases, EStim treatment used, outcomes, complications, and the published article cited along with the total numbers for each of these categories. The total number for each of these categories is summarized in Table 3. The language of the publications reviewed was English.

**Table 1** Total publications identified using different combinations of the keywords "electrical stimulation" and "bone healing"

| Study type | Number of publications |
|---|---|
| Animal studies | 72 |
| Clinical studies | 69 |
| Cell/organ in vitro | 238 |
| Review/meta-analysis | 53 |
| Total | 432 |

### Orthopedic surgeon survey

To determine the level of awareness, experience, and acceptance of EStim-based bone fracture treatment we asked orthopedic surgeons six questions (listed in Figs. 1, 2, 3, 4, 5, 6) using a closed online automated survey method (SurveyMonkey software, Palo Alto, USA). Survey participants were identified from our own network of colleagues and based on their surgical specialty, "Orthopedic Surgeons" in the online professional networking website, LinkedIn [26]. Between May and August 2017, a total of 620 invitations were emailed to orthopedic surgeons worldwide, and their IP addresses were used to record their country of origin and to prevent duplicate entries. No other personal information was collected or stored from the respondents. With this online survey method participants were allowed to review their responses prior to submitting their completed survey. Incomplete surveys were not included in this analysis.

## Results

### Literature review

Our initial literature searches identified a total of 432 articles, published between 1977 and 2017 that focused on the use of EStim to promote bone growth, fracture healing, and

**Table 2** Publications between 1977 and 2017 describing animal studies that use EStim to treat bone fractures

| Animal model | Bone affected and/or fracture type | Type of EStim treatment | Outcome | Published article |
|---|---|---|---|---|
| Rabbits | Femur/osteotomy | Type: PEMF<br>Settings: 220–260 G | Improved healing | Aydin and Bezer [46] |
| | Tibia/osteotomy | Type: PEMF | Improved healing (69%) | Barak et al. [47] |
| | Tibia/fracture | Type: PEMF<br>Settings: pulse width 85 μs<br>Duration: 30 min/day | No effect | Buzza et al. [48] |
| | Tibia/osteotomy | Type: PEMF<br>Settings: time-varying field 1.5 Hz<br>Duration: 1 h/day | Improved healing | Fredericks et al. [49] |
| | Lumbar spine/fusion | Type: DC<br>Settings: 20–60 μA | Improved healing | France et al. [50] |
| | Lumbar spine/fusion | Type: CC | Improved healing | Gilotra et al. [51] |
| | Patella–tendon junction/fracture | Type: CC<br>Settings: 15–25 mA | Improved healing | Hu et al. [52] |
| | Mandible/defect | Type: DC<br>Settings: 20 μA<br>Duration: 4 weeks continuous | Improved healing | Kim et al. [53] |
| | Femur/defect | Type: PEMF<br>Settings: 0.8 mT<br>Duration: 4 h/day | Improved healing | Matsumoto et al. [54] |
| | Tibia/fracture | Type: PEMF<br>Settings: 8 mT; 50 Hz<br>Duration: 0.5 h/day | Improved healing | Ottani et al. [55] |
| | Tibia/fracture | Type: DC<br>Settings: 20 μA<br>Duration: 0.5 h/day continuous | Improved healing | Rubinacci et al. [56] |
| | Mandible/defect | Type: DC<br>Settings: 7 μA<br>Duration: 1–2 weeks continuous | No effect | Shafer et al. [57] |
| | Tibia diaphysis/fracture | Type: PEMF<br>Settings: 1.8 G; 1.5 Hz | Improved healing | Shimizu et al. [58] |
| | Femur, tibia/fracture | Type: PEMF<br>Settings: repetitive pulse-72 Hz<br>Duration: 12 h/day continuous | No effect | Smith and Nagel [59] |
| | Tibia/osteotomy | Type: PEMF<br>Settings: asymmetric pulse 1.5 Hz<br>Duration: 20 days continuous | No effect | Taylor et al. [60] |
| | Knee/osteochondral lesion | Type: PEMF<br>Settings: 1.5 mT; 75 Hz<br>Duration: 4 h/day for 40 days | Improved healing | Veronesi et al. [61] |
| | Humerus/fracture | Type: PEMF<br>Settings: 2 G, 25 μs pulses at 10 Hz<br>Duration: 12 h/day × 14 days | Improved healing | Yonemori et al. [62] |
| | Tibia/fracture | Type: DC<br>Settings: 1, 5, 20 μA | Improved healing | Zimmermann et al. [63] |

**Table 2** (continued)

| Animal model | Bone affected and/or fracture type | Type of EStim treatment | Outcome | Published article |
|---|---|---|---|---|
| Dogs | Ulna/fracture | Type: DC<br>Settings: 20 µA<br>Duration: continuous | No effect | Berry et al. [64] |
| | Tibia/fracture | Type: DC<br>Settings: 10–20 µA<br>Duration: continuous | Improved healing (70–80%) | Bins-Ely et al. [65] |
| | Mandible/defect | Type: DC<br>Settings: 20 µA | No effect | Branham et al. [66] |
| | Radius/fracture | Type: DC<br>Settings: 0.1–17 µA | Improved healing | Chakkalakal et al. [67] |
| | Femur/fracture | Type: DC<br>Settings: 50 µA<br>Duration: 6 weeks continuous | Improved healing | Colella et al. [68] |
| | Radius, ulna/fracture | Type: DC<br>Settings: 20 µA<br>Duration: 12 weeks continuous | Improved healing | Connolly et al. [69] |
| | Lumbar spine/fusion | Type: DC<br>Settings: 0.83–10 µA<br>Duration: 6 weeks continuous | Improved healing | Dejardin et al. [70] |
| | Femur/fracture | Type: CC<br>Settings: biphasic waveforms | Improved healing | Doyle [71] |
| | Radius/fracture | Type: DC<br>Settings: 3–5 µA | Improved healing | Fuentes et al. [72] |
| | Tibia/fracture | Type: PEMF<br>Settings: 0–2.4 G<br>Duration: 4 h/day | Improved healing | Inoue et al. [73] |
| | Periodontal/defect | Type: DC<br>Settings: 3–6 nA<br>Duration: continuous | No effect | Jacobs and Norton [74] |
| | Ulna/non-union | Type: DC<br>Settings: 20 µA | Improved healing (22%) | Jacobs et al. [75] |
| | Lumbar spine/fusion | Type: PEMF<br>Settings: 1 G; 1.5 Hz<br>Duration: 0.5–1 h/day | No effect | Kahanovitz et al. [76] |
| | Femur/fracture | Type: DC<br>Settings: 20 µA | No effect | Lindsey et al. [77] |
| | Cranium/osteogenesis | Type: DC<br>Settings: 20 µA | No effect | Moderessi et al. [78] |
| | Mandible/osteogenesis | Type: PEMF<br>Duration: 1 h/day | Improved healing | Ortman et al. [79] |
| | Mandible/non-union | Type: DC | Improved healing | Park et al. [80] |
| | Tibia/non-union | Type: DC<br>Settings: 20 µA | Improved healing | Paterson et al. [81] |
| | Tibia/non-union | Type: DC<br>Settings: 20 µA | Improved healing | Paterson et al. [82] |
| | Tibia/defect | Type: DC<br>Settings: 0.2–20 µA | Improved healing | Paterson et al. [83] |

**Table 2** (continued)

| Animal model | Bone affected and/or fracture type | Type of EStim treatment | Outcome | Published article |
|---|---|---|---|---|
| | Tibia/fracture | Type: CC<br>Settings: 3–6.3 V; 60 kHz<br>Duration: continuous—28 days | No effect | Pepper et al. [84] |
| | Hip prostheses | Type: CC<br>Settings: 5–6 V; 60 kHz | No effect | Schutzer et al. [85] |
| | Mandible/defect | Type: DC<br>Settings: 20 µA | Improved healing | Shayesteh et al. [86] |
| | Femur/osteotomy | Type: DC<br>Settings: 1.5 V | Improved healing | Shokry [87] |
| | Tibia, femur/fracture | Type: DC<br>Settings: 0–50 µA | Improved healing | Srivastava [88] |
| Rats | Femur/fracture | Type: PEMF<br>Settings: 1.5 mT<br>Duration: 6 h/day | Improved healing | Atalay et al. [89] |
| | Tibia/osteoporosis | Type: CC<br>Settings: low voltage; 60 Hz | Improved healing | Brighton et al. [90] |
| | Tibia/fracture | Type: CC<br>Duration: 20 min/day | Improved healing | Giannunzio et al. [91] |
| | Spine/fusion | Type: PEMF<br>Duration: 18 h/day | Improved healing | Guizzardi et al. [92] |
| | Tibia/osteoporosis | Type: PEMF<br>Settings: 1 G; 5 ms pulse; 15 Hz<br>Duration: 2 h/day | No effect | Jagt et al. [93] |
| | Tibia/osteoporosis | Type: PEMF<br>Settings: 30 mW/cm$^2$; 1.5 MHz | Improved healing | Lirani-Galvao et al. [94] |
| | Tibia/osteoporosis | Type: CC<br>Settings: 10 V peak–peak<br>Duration: 2 h/day | Improved healing | Manjhi et al. [95] |
| | Fibula/osteotomy | Type: CC<br>Settings: 1590 V; 60 Hz | Improved healing | Marino et al. [96] |
| | Spine/injury | Type: CC<br>Settings: 30 mW/cm$^2$ | Improved healing | Medalha et al. [97] |
| | Tibia/fracture | Type: DC<br>Settings: 20 µA<br>Duration: 20 min/day | Improved healing | Nakajima et al. [98] |
| | Femur/fracture | Type: PEMF<br>Settings: 41 Gauss | Improved healing | Puricelli et al. [99] |
| | Tibia/osteoporosis | Type: PEMF<br>Settings: 8 G; 15 Hz<br>Duration: 2 h/day | Improved healing | Shen and Zhao [100] |
| | Spine/bone growth | Type: DC<br>Settings: 0–100 µA | Improved healing | Spadaro [101] |
| | Mandible/defect | Type: PEMF<br>Settings: 1.5–1.8 G; 100 Hz | Improved healing | Takano-Yamamoto et al. [102] |
| | Periodontal/defect | Type: DC<br>Settings: 0–100 µA; 9 kHz<br>Duration: once per day | Improved healing | Tomofuji et al. [103] |

**Table 2** (continued)

| Animal model | Bone affected and/or fracture type | Type of EStim treatment | Outcome | Published article |
|---|---|---|---|---|
| | Mandible/fracture | Type: DC<br>Settings: 9 V<br>Duration: 24 h | Improved healing | Uysal et al. [104] |
| | Cranium/defect | Type: DC<br>Settings: 2 mA; 2 Hz<br>Duration: 15 min; 3 × weeks | Improved healing | Yang et al. [105] |
| | Spine/injury | Type: DC (subcutaneous)<br>Settings: 15 mA; 2 Hz<br>Duration: 0.5 h/day; 3 weeks | Improved healing | Yu et al. [106] |
| | Spine/injury | Type: DC (subcutaneous)<br>Settings: 20–150 mA; 50 Hz<br>Duration: 20 min/day | Improved healing | Zamarioli et al. [107] |
| Sheep | Femur/defect | Type: PEMF<br>Settings: 1.5 mT; 75 Hz<br>Duration: 6 h/day | Improved healing | Benazzo et al. [108] |
| | Tibia/fracture | Type: DC<br>Settings: 7.5 µA<br>Duration: 12 h/day | No effect | Dergin et al. [109] |
| | Spine/injury | Type: DC<br>Settings: low voltage | Improved healing | Flouty et al. [110] |
| | Mandible/defect | Type: DC<br>Settings: 10 µA<br>Duration: 1 mm/day × 10 days | Improved healing | El-Hakim et al. [111] |
| | Tibia/osteotomy | Type: PEMF<br>Settings: 1.6 mT<br>Duration: 24 h/day | No effect | Law et al. [112] |
| | Tibia/fracture | Type: CC<br>Settings: 15 mA; 60 kHz | Improved healing | Mutthini et al. [113] |
| | Lumbar spine/fusion | Type: DC<br>Settings: 40–100 µA | Improved healing | Toth [114] |
| Horse | Metacarpus/defect | Type: PEMF<br>Settings: 28 G; 75 Hz | Improved healing | Cane et al. [115] |
| | Tibia/bone graft | Type: PEMF<br>Settings: asymmetric pulse burst of 30 ms duration repeated at 1.5 Hz | Improved healing | Kold and Hickman [116] |
| | Metatarsal-foot/osteotomy | Type: PEMF<br>Settings: 20 G; 15 Hz<br>Duration: 8 h/day | No effect | Sanders-Shami et al. [117] |

| Total no. of articles | Animal model (no.) | | | | | Type of bone (no.) | | | | | Type of fracture (no.) | | | | | Type of EStim (%) | | | Outcomes (%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Dog | Rat | Rabbit | Sheep | Horse | Tibia | Femur | Spine | Mandible | Other | Delayed-/non-union | Fusion | Osteotomy | Large bone defects | Others | PEMF | DC | CC | Positive | Negative |
| 72 | 25 | 19 | 18 | 7 | 3 | 26 | 13 | 11 | 9 | 16 | 4 | 9 | 3 | 38 | 18 | 35 | 49 | 16 | 77 | 23 |

bone regeneration. Of these 432 publications, 72 reported animal studies, 69 clinical studies, 238 organ or in vitro cell culture studies, and 53 were reviews or meta-analyses (Table 1). A total of 141 publications (animal + clinical studies) were selected and reviewed, the results of which are presented herein.

### Animal studies

A total of 72 animal study articles, that used EStim to treat bone fractures were reviewed. The most commonly used animal model was the dog (25), followed by rabbits (18), rats (19), sheep (7) and horses (3). In these the "bone", and "fracture type" studied varied greatly. The bones were primarily the tibia (26), femur (13), spine (11), mandible, (9) and others (16). Some of the papers reviewed studied more than one bone. The types of fractures/pathologies were large bone defects (38), delayed- and non-unions (4), fusions (9), osteotomies (3), and others (18). The most common method used to administer electrical stimulation in the animal studies was DC EStim (49%), followed by PEMF (35%) and CC and other types, together making up 16% of the reviewed studies.

### Clinical studies

A total of 69 articles describing clinical studies were reviewed, in which EStim was used to promote bone healing. The main bones treated with EStim in the clinical studies were tibia (25), femur (15), spine (15), radius (11), humerus (7) and others (20). As in the case with the animal study articles some of the clinical papers reported on more than one bone. The most common types of fractures/pathologies were delayed- and non-unions (21), spine fusions (16), arthrodeses (5), osteotomies (4), necrosis (2), large bone defects (2) and others (19). Most of the clinical studies reviewed administered EStim using PEMF (60%), followed by DC (29%), and CC and other methods (11%). The intensity of the magnetic field used in PEMF treatment ranged between 0.3 and 6 mT, while for DC the dosage was 5–40 μA, and for CC treatment the intensity ranged between 3 and 10 V. Half (50%) of the regimens used in the clinical studies consisted of daily stimulation treatments ranging from 0.5 to 16 h/day. Nineteen of the 69 studies (27%) reported complications that included skin irritation and infections, pain [27], dislocation of the device [28], failure of the device [29] and poor patient compliance [30]. Fifty (72%) of the studies reviewed reported no complications. Finally, of the 69 clinical study publications 51 (73%) reported positive and 18 (27%) reported negative outcomes (Table 3).

### Orthopedic surgeon survey

The individual questions and the responses are displayed in six separate graphs (Figs. 1, 2, 3, 4, 5, 6). Of the 620 orthopedic surgeons who were sent emails inviting them to participate in the survey, 161 (26%) from 34 countries responded. Of the 161 respondents, 44% answered that they perform more than 100, (23%) perform 51–100, (22%) perform 11–50, and (11%) perform 0–10 bone surgeries per year (Fig. 1). When asked if they were aware of published clinical studies reporting successful EStim-based fracture treatments, 85 (73%) responded "Yes" and the rest (27%) answered "No" (Fig. 2). Of the 85 respondents who said they were aware of EStim-based fracture treatments, 27 (32%) answered that they had used EStim in their fracture patients while 58 (68%) had not (Fig. 3). Of the 27 surgeons that had used EStim in their patients the pathologies they treated were mainly delayed or non-unions (61%) and large bone defects (16%). The rest, (23%) were spinal fusion, avascular necrosis, calcaneal apophysitis, Charcot foot and ankle reconstructions, loosened hip, knee prosthesis, or other types of fractures (Fig. 4). When asked what they considered to be the major problems associated with using EStim in their fracture patients, 30 (35%) identified "high cost", 24 (28%) answered "inconsistent results", while 8% and 5% responded that EStim devices were "impractical", and "difficult" to use, respectively. Eleven (13%) surgeons responded that they had experienced "other" problems, and nine (11%) replied they had not experienced problems using EStim-based treatments (Fig. 5). Finally, we asked, "If an easy-to-use EStim device to treat bone fractures were available would you use it in your patients?" and 85% answered, "Yes" and the rest answered "No" (Fig. 6).

## Discussion

In his review of more than 100 studies using EStim treatment, published more than 40 years ago Spadaro concludes, "About 95% are positive reports…" and goes on to qualify this assertion saying "…despite an extraordinarily wide selection of experimental techniques and models" [31]. In the present literature review of 141 papers (72 animal and 69 clinical studies), published in the 40 years since then, we also found positive results, and like Spadaro also found a great variation in bone and fracture types, treatment methods, dosages, regimens, etc., reported in the literature. The latter made it difficult to draw well-founded conclusions upon which to develop specific EStim treatment recommendations. One of the primary contributors to this confusion in the literature is the different types, dosages, and regimens used to administer EStim. In the clinical studies we reviewed

**Table 3** Publications between 1977 and 2017 describing clinical studies that use EStim to treat bone fractures

| Bone affected and/or fracture type | No. of cases | Type of EStim treatment | Outcome | Complications | Published article |
|---|---|---|---|---|---|
| Mandible/fracture | 12 | Type: PEMF<br>Duration: 2 h/day × 12 days<br>Settings: pulse duration 200 ns, rise time 8 ns, electromagnetic segment at 50 MHz and down to Hz range | No effect | Infection | Abdelrahim et al. [38] |
| Tibia/non-union | 16 | Type: CC<br>Duration: 7–8 h/day until healed or 30 weeks<br>Settings: 6 V peak-to-peak symmetrical sine wave signal at 63 kHz frequency | Improved healing (68%) | None reported | Abeed et al. [118] |
| Tibia/acute fracture | 106 | Type: PEMF<br>Duration: 10 h/day × 12 weeks | No effect | None reported | Adie et al. [119] |
| Lumbar spine/fusion | 107 | Type: DC | Improved healing | None reported | Andersen et al. [6] |
| Lumbar spine/fusion | 107 | Type: DC | No effect | None reported | Andersen et al. [120] |
| Lumbar spine/fusion | 98 | Type: DC<br>Settings: 40 and 100 μA | No effect | None reported | Andersen et al. [121] |
| Tibia/delayed- and non-union | 44 | Type: PEMF<br>Duration: 3 h/day, maximum 36 weeks | Improved healing (77%) | None reported | Assiotis et al. [122] |
| Tibia/non-union | 9 | Type: PEMF<br>Duration: 12–16 h/day, min 1 h/day × 48 weeks<br>Settings: 1–5 mT peak, 5 ms burst waveform repeated at 15 Hz | No effect | One patient left the study prior to end | Barker et al. [32] |
| Femur/arthrodesis failure | 71 | Type: PEMF | Improved healing (85%) | None reported | Bassett et al. [123] |
| Tibia/fracture | 22 | Type: CC<br>Duration: 15 h/day until healed<br>Settings: sinusoidal wave 3–6 V at 60 kHz and 5–10 mA | No effect | None reported | Beck et al. [124] |
| Metatarsal foot/fracture | 25 | Type: CC<br>Duration: 52 days<br>Setting: amplitude of 3.0–6.3 V and 60 kHz frequency<br>Effective current—5–10 mA | Improved healing (88%) | None reported | Benazzo et al. [125] |
| Femur/intertrochanteric osteotomy | 31 | Type: PEMF<br>Duration: 8 h/day × 3 m<br>Settings: 75 Hz, 1.3 ms impulse width, 2.5 mV amplitude, and 18 Gs magnetic field amplitude | Improved healing | None reported | Borsalino et al. [10] |
| Radius/delayed-and non-union and osteotomy | 21 | Type: PEMF<br>Duration: 10 h/day | Improved (57% non-union healed)<br>Improved (89% osteotomies healed) | None reported | Boyette and Herrera-Soto [126] |

**Table 3** (continued)

| Bone affected and/or fracture type | No. of cases | Type of EStim treatment | Outcome | Complications | Published article |
|---|---|---|---|---|---|
| Tibia/non-union | 57 | Type: DC<br>Settings: 10–20 μA | Improved healing (70% healed) | Eight patients did not receive adequate electricity—due to device failure | Brighton [29] |
| Tibia/non-union | 20 | Type: CC<br>Settings: 60 kHz, 5 V peak-to-peak | No effect | 11 patients started with DC withdrew prior to end of study | Brighton and Pollack [33] |
| Tibia/non-union | 271 | Type: DC and CC | No effect | Risk factors | Brighton et al. [9] |
| Sesamoid-foot/delayed union | 1 | Type: PEMF<br>Duration: 7–8 h/day × 52 weeks | Improved healing | None reported | Bronner et al. [127] |
| Femur, Tibia, radius, humerus/arthrodesis | 24 | Type: PEMF<br>Duration: 8 h/day<br>Settings: 75 Hz, 3.0 ± 0.5 mV | No effect | None reported | Capanna et al. [128] |
| Tibia/pseudoarthroses | 22 | Type: PEMF<br>Duration: 8 h/day, average 5–6 ms<br>Settings: 75 Hz, 10–20 A/cm, 180–220 V | Improved healing (90%) | Infection (three cases), protrusion of material (nine cases),<br>Screw break (three cases) | Cebrián et al. [37] |
| Tibia/fracture | 33 | Type: PEMF<br>Duration: 12–15/day, until healed<br>Settings: 0.8 mT, 50 Hz | Improved healing (85%) | Infection | Colson et al. [39] |
| Tibia/fracture | 37 | Type: DC | Improved healing (100%) | None reported | Cundy and Paterson [81] |
| Tibia/non-union | 17 | Type: PEMF<br>Duration: 20 h/day, 4–8 weeks<br>Settings: 150–300 Gs | No effect | None reported | De Haas et al. [129] |
| Hind foot/fusion | 13 | Type: DC | Improved healing (92%) | None reported | Donley and Ward [130] |
| Humerus, tibia, femur/non-union and osteotomy | 52 | Type: PEMF<br>Duration: 2–12 m | Improved healing (82%) | None reported | Dunn and Rush [131] |
| Cervical spine/fusion | 122 | Type: PEMF<br>Duration: 4 h/day × 3 m | Improved healing (83%) | None reported | Foley et al. [132] |
| Tibia/fracture | 41 | Type: DC interferential currents | No effect | Sepsis (six cases) | Fourie and Bowerbank [133] |
| Tibia, hip, radius/delayed- and non-union | 12 | Type: PEMF<br>Duration: 12 h/day × 3 m min | No effect | None reported | Freedman [134] |
| Knee/osteoarthritis | 139 | Type: CC<br>Duration: 6–14 h/day | Improved healing | None reported | Garland et al. [135] |
| Lumbar spine/fusion | 85 | Type: CC<br>Duration: 24 h/day until healed or 9 m<br>Setting: 60 kHz, current density 5 μA root mean square/$cm^2$, 12 mV root mean square/cm | Improved healing (84%) | None reported | Goodwin et al. [136] |
| Tibia/non-union | 45 | Type: PEMF<br>Duration: 12 h/day, 6–12 weeks<br>Settings: 0.008 Weber/$m^2$ | Improved healing (35% healed in 10 weeks and 85% in 4 ms) | Poor compliance | Gupta et al. [30] |

**Table 3** (continued)

| Bone affected and/or fracture type | No. of cases | Type of EStim treatment | Outcome | Complications | Published article |
|---|---|---|---|---|---|
| Foot joint/arthropathy | 11 | Type: PEMF (combined)<br>Duration: 0.5 h/day | Improved healing | None reported | Hanft et al. [137] |
| Hand/acute fracture | 53 | Type: PEMF<br>Duration: continuous for 52 weeks<br>Settings: pulse amplitude 50 mV<br>Pulse width 5 μs; burst width 5 ms<br>Burst refractory period 62 ms<br>Repeat repetition rate 15 Hz | No effect | None reported | Hannemann et al. [138] |
| Hand/acute fracture | 102 | Type: PEMF<br>Duration: continuous max 52 weeks<br>Settings: pulse amplitude 50 mV<br>Pulse width 5 μs; burst width 5 ms<br>Burst refractory period 62 ms<br>Repeat repetition rate 15 Hz | No effect | None reported | Hannemann et al. [139] |
| Metatarsal-foot/delayed- and non-union | 9 | Type: PEMF<br>Duration: 8–10 h/day × 3 m<br>Settings: 0–20 Gs, 4.5 ms pulse bursts duration repeated at 15 Hz | Improved healing (100%) | None reported | Holmes [140] |
| Tibia/non-union | 30 | Type: PEMF<br>Duration: 8 h/day<br>Settings: 1–15 mV, 5 ms bursts of asymmetrical 15 Hz pulses | Improved healing (83%) | None reported | Ito and Shirai [141] |
| Radius/fracture | 18 | Type: DC (pulsed)<br>Settings: 2 Hz, 30 μA | Improved healing | None reported | Itoh et al. [142] |
| Lumbar spine/fusion | 17 | Type: DC and PEMF | No effect | Infection | Jenis et al. [143] |
| Tibia/fracture | 24 | Type: pulsed DC<br>Duration: 6 m<br>Settings: 1 Hz, 40 μA | Improved healing (30%) | Skin reaction and infection | Jorgensen [144] |
| Tibia/fracture | 3 | Type: DC<br>Duration: 30–60 min 3–4 × day<br>Settings: pulse width 300 μs, 1–2 Hz < 20 mA | Improved healing (66%) | None reported | Kahn [145] |
| Lumbar spine/fusion | 31 | Type: DC | Improved healing (78%) | None reported | Kane [146] |
| Spine/fusion | 65 | Type: DC | Improved healing (96%) | None reported | Kucharzyk [147] |
| Radius/colles' fracture | 30 | Type: PEMF<br>Duration: 30 m/day, 5 days/week × 2 weeks<br>Settings: 6 mT, 25 Hz | Improved healing | None reported | Lazovic [148] |
| Lumbar spine/fusion | 104 | Type: PEMF (combined)<br>Duration: 30 m/day × 9 m | Improved healing (64%) | None reported | Linovitz [149] |

**Table 3** (continued)

| Bone affected and/or fracture type | No. of cases | Type of EStim treatment | Outcome | Complications | Published article |
|---|---|---|---|---|---|
| Humerus neck/fracture | 21 | Type: PEMF<br>Duration: 30 m/day × 10 days<br>Settings: 35 Hz, max pulse 300 W | No effect | None reported | Livesley [150] |
| Radius/non-union | 10 | Type: PEMF<br>Duration: 104 days<br>Settings: 2.5 Gs | Improved healing (66%) | None reported | Madronero et al. [151] |
| Tibia/osteotomy | 18 | Type: PEMF<br>Duration: 8 h/day × 57 days<br>Settings: pulse duration 1.3 ms, 75 Hz, 3.0 ± 0.5 mV | Improved healing | Thrombophlebitis (three cases) | Mammi et al. [152] |
| Lumbar spine/fusion | 42 | Type: PEMF<br>Duration: 4 h/day | Improved healing (97%) | None reported | Marks [153] |
| Femur/fracture | 32 | Type: PEMF<br>Duration: 1 h/day × 8 weeks<br>Settings: 5–105 Hz, 0.5–2.0 mT | Improved healing (94%) | None reported | Martinez-Rondanelli et al. [154] |
| Femur head/osteonecrosis | 66 | Type: PEMF<br>Duration: 8 h/day × 3–7 m<br>Settings: 75 Hz, 1.3 ms pulse, 2 ± 0.5 mV | Improved healing (94%) | None reported | Massari et al. [155] |
| Mandible/fracture | 40 | Type: DC<br>Duration: 10–14 days<br>Settings: 10–20 μA | Improved healing | None reported | Masureik and Eriksson [156] |
| Lumbar spine/fusion | 122 | Type: DC<br>Duration: 24 weeks min<br>Settings: 20 μA | Improved healing (76%) | Infection (four cases) | Meril [40] |
| Tibia/delayed- and non-union | 57 | Type: PEMF | Improved healing (75%) | None reported | Meskens [157] |
| Tibia/congenital pseudarthrosis | 27 | Type: DC<br>Duration: 6 m<br>Settings: 20 μA | Improved healing (74%) | Infection (two cases) | Paterson and Simonis [158] |
| Humerus, ulna, radius, femur, tibia/non-union | 93 | Type: PEMF<br>Duration: 13 weeks<br>Settings: pulse amplitude 50 mV<br>Pulse width 5 s at 15 Hz | Improved healing (74%) | None reported | Punt et al. [159] |
| Ankle/cystic osteochondral defect | 68 | Type: PEMF<br>Duration: 4 h/day × 60 days<br>Settings: 1.5 mT at 75 Hz | No effect | Temporary foot paresthesia × 2<br>Wound drainage × 2 | Reilingh et al. [160] |
| Lumbosacral spine/fusion | 53 | Type: DC<br>Duration: 20.5 m<br>Settings: 10 μA/cathode | Improved healing (96%) | None reported | Rogozinski and Rogozinski [161] |
| Foot, ankle arthrodesis/delayed union | 19 | Type: PEMF<br>Duration: 5–27 m | Improved healing (77%) | None reported | Saltzman et al. [162] |

**Table 3** (continued)

| Bone affected and/or fracture type | No. of cases | Type of EStim treatment | Outcome | Complications | Published article |
|---|---|---|---|---|---|
| Tibia, femur/non-union | 10 | Type: CC<br>Duration: 6 m<br>Setting: 5–10 V peak-to-peak sine, 60 kHz | Improved healing (60%) | Electrode allergic skin reaction (two cases) | Scott and King [163] |
| Tibia/delayed union | 20 | Type: PEMF<br>Duration: 12 h/day × 12 weeks<br>Settings: 200 μs with 25 μs interval, 5 T/s | Improved healing | None reported | Sharrad [28] |
| Humerus, ulna, radius, femur, tibia/non-union | 53 | Type: PEMF<br>Duration: 12–16 h/day × 3 m<br>Settings: 5 ms bursts, 15 Hz, 11.5 mV | Improved healing (71%) | Plate/screw loosening (eight cases) | Sharrad et al. [8] |
| Humerus, ulna, radius, femur, tibia/non-union | 31 | Type: PEMF<br>Duration: 8 h/day × 5 m | Improved healing (77%) | None reported | Shi et al. [164] |
| Lumbar spine/fusion | 13 | Type: PEMF<br>Duration: 8–10 h/day × 4 m<br>Settings: 0–0.0003 T, 50 ms pulse repetition rate | Improved healing (76%) | None reported | Simmons [165] |
| Lumbar spine/fusion | 100 | Type: PEMF<br>Duration: 2 h/day × 90 day min | Improved healing (67%) | None reported | Simmons et al. [166] |
| Metatarsal-foot/non-union | 5 | Type: PEMF<br>Duration: 10 h/day × 24 weeks max | Improved healing | None reported | Streit et al. [167] |
| Femur head/avascular necrosis | 20 | Type: CC<br>Duration: 24 h/day × 6 m | No effect | None reported | Steinberg et al. [168] |
| Lumbar spine/fusion | 143 | Type: DC<br>Duration: 24 weeks<br>Settings: 20 μA | Improved healing (91.5%) | Pain | Tejano et al. [27] |
| Ankle/cystic osteochondral defect | 68 | Type: PEMF<br>Duration: 4 h/day × 60 days<br>Settings: 1.5 mT at 75 Hz | Improved healing | None reported | van Bergen et al. [169] |
| Radius/fracture | 15 | Type: PEMF<br>Duration: 8 weeks<br>Settings: 0.00004 T at 1–1000 Hz | Improved healing | None reported | Wahlstrom and Knutsson [170] |
| Cervical spine/arthrodesis | 16 | Type: DC<br>Duration: 26 weeks min; settings: 12 μA | Improved healing (93%) | Infection (one case)<br>Local discomfort (four cases) | Welch et al. [171] |

| Total no. of articles | Type of bone (no.) | | | | | | Type of fracture (no.) | | | | | | | Type of EStim (%) | | | Compli-cations (%) | | Outcomes (%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Tibia | Femur | Spine | Radius | Humerus | Others | Delayed-/non-union | Fusion | Arthrode-sis | Osteotomy | Necrosis | Bone defect | Others | PEMF | DC | CC | Yes | No | Positive | Negative |
| 69 | 25 | 15 | 15 | 11 | 7 | 20 | 21 | 16 | 5 | 4 | 2 | 2 | 19 | 60 | 29 | 11 | 27 | 73 | 73 | 27 |

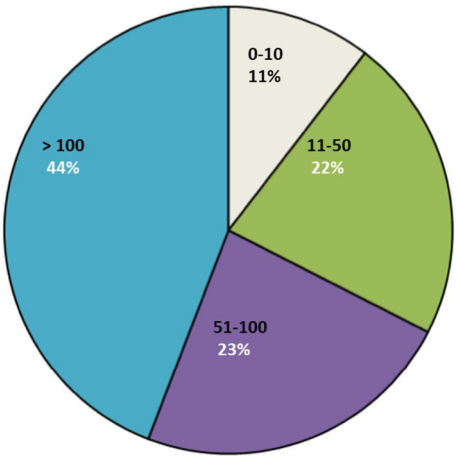


**Fig. 1** How many bone surgeries do you perform per year?

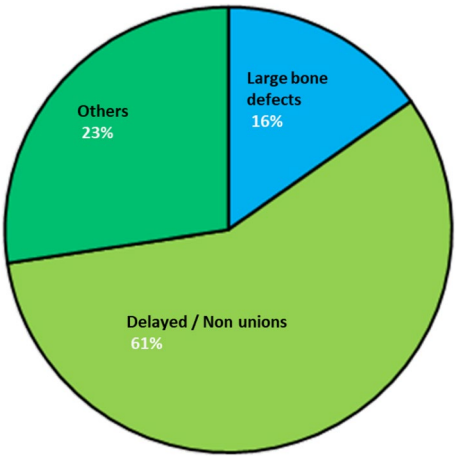


**Fig. 4** In what type of bone fractures have you used an electrical stimulation device?

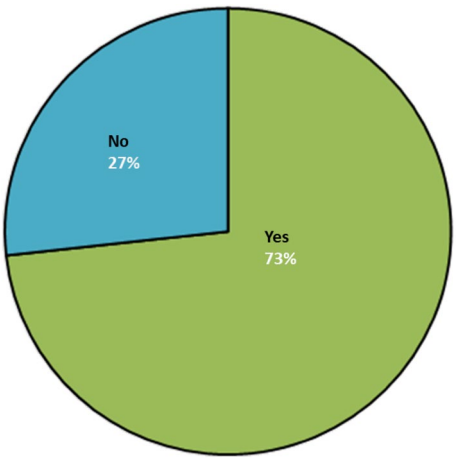


**Fig. 2** Did you know that electrical stimulation has been proven to accelerate bone healing in many clinical studies?

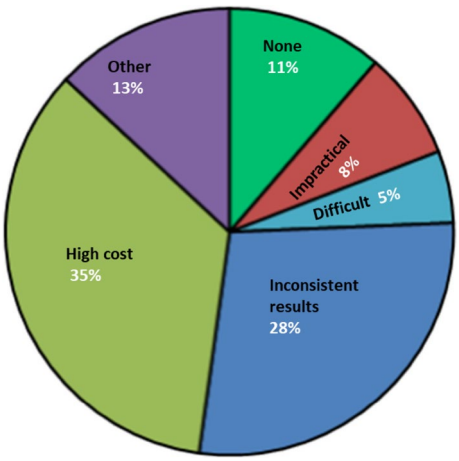


**Fig. 5** What problem(s) do you see in current devices?

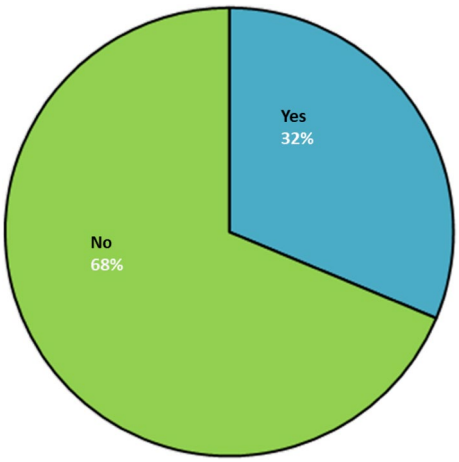


**Fig. 3** Have you ever used an electrical stimulation device to treat bone fractures in your patients?

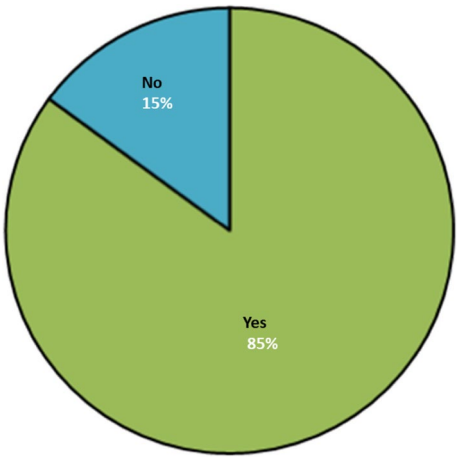


**Fig. 6** If an easy-to-use electrical stimulation device to treat bone fractures were available, would you use it in your patients?

that the most commonly used method of administering EStim was PEMF while in the animal studies DC was the predominant treatment method. This preference in patients is most likely due to the fact that PEMF is administered using an external noninvasive device, whereas DC treatment requires that the EStim device be surgically implanted. While being noninvasive is a major benefit of PEMF for clinical use, patient non-compliance, associated with its use, is a major problem and is cited as one of the primary reasons for inconsistent results when using PEMF [28–30].

Another source of confusion is the dosages and regimens used. The most commonly used dosage for administering PEMF ranged between 0.3 and 6 mT, while for DC the intensity was 5–40 μA, and for CC treatment the intensity ranged between 3 and 10 V. Half of the regimens used in the clinical studies consisted of daily EStim treatments ranging from 0.5 to 16 h/day, delivered either continuously or in interrupted intervals, the latter being for periods of 1–6 h/day. The dosages, regimens, and exposure times in the animal studies also varied widely. This great variation makes it difficult to combine the results of these studies into one or a few treatment recommendations. Another reason why it is difficult to combine the results of the different studies is because of the many different bones and fracture types studied. Of all the different bones and fracture types reported in the clinical articles by far the most common bone was the tibia and the most studied fracture types were delayed- and non-unions. In fact, this was confirmed in our survey in which orthopedic surgeons that use EStim mostly used it to treat delayed- and non-unions in their patients (Fig. 4). Again, this variation in bone and fracture types described in the literature would make it difficult to compare healing rates between, say a mandible and a tibia, or between non-unions and osteotomies, which makes it difficult to draw meaningful conclusions.

Poor fracture healing is often associated with both a lack of healing and mal-position of bone fragments. In these cases, surgeons prefer operative intervention to EStim because of the ability to restore alignment as well as facilitate fracture healing. Revision fixation and osteotomies, to correct alignment, are fraught with high rates of delayed bone healing and persistent non-unions. While EStim does not improve the position of bone fragments, it still can play an adjunctive role in the treatment of non-unions [34].

When EStim is used as an adjunct to other treatment attempts, as a last resort it can require prolonged and costly interventions. While the clinical studies we reviewed did not provide information about costs associated with EStim treatments, information available online from companies who sell clinical EStim devices indicate that the current unit cost of most EStim devices, regardless of the company (OL1000 Bone Growth Stimulator, Orthopak, EBI Bone Healing System, Physio-Stim Lite, or Exogen), is about US $3000. Additional costs to treat delayed unions is approximately $24,892, that includes $20,575 for surgery and recovery + $4317 outpatient costs. These figures are quoted from a report published by EXOGEN [35].

Added to this, failure rates in these treatments is relatively high (17–64%) and when present can lead to additional costs [36]. Finally, the costs associated with using EStim devices are usually not reimbursed, thus further reducing the incentive to use this treatment option. While comparing the costs of EStim to other treatments used in problematic fractures is beyond the scope of this paper, from the responses we received in our survey it is clear that high costs is an important factor for surgeons in their decision whether or not to use EStim. Of the drawbacks associated with using EStim, the greatest number of surgeons surveyed cited high costs as being the main problem with using EStim in their fracture patients (Fig. 5).

The second most cited problem with EStim was inconsistent results. While the questions in our survey did not ask about the specific cause of the inconsistent results associated with using EStim, from our literature review we were able to identify some possible causes. In the clinical papers a few different device-related problems were cited that could cause "inconsistent results". These included "damaged" or "disconnected" implanted stimulators, misplacement of hardware, and migration of the EStim device's electrode leads that can occur due to muscle movement or insufficient flexibility of the muscles [9, 28, 37]. Eight and five percentage of surgeons surveyed indicated that the problems they encounter using EStim were associated to the devices used to administer the treatment, choosing "impractical", and "difficult to use", respectively, to describe their experience. In a white paper generated by industry that compares costs associated with the use of five different EStim bone stimulators the authors write that using these devices the "probability of failure" ranges between 17 and 64% [36]. While the exact causes of failure are not specified in this paper these high failure rates could certainly cause inconsistent results.

Of the 69 clinical studies we reviewed, 19 reported complications experienced during treatment with EStim. In these 19 studies, the most common type of complication experienced was skin irritation and infections, when using the externally applied PEMF device, and infections at the fracture line when using the implanted DC device [24–27]. Other types of complications experienced with EStim treatment were pain [27], dislocation of the device [28], failure of the device [29] and poor patient compliance [30]. The above-mentioned complications and particularly patient non-compliance could be other causes of the inconsistent results surgeons cited in our survey. Existing external PEMF units are cumbersome and require many hours of treatment per day over months, which interferes with activities of daily living, causing decrease compliance. If a patient does not (or

is not able to) utilize the PEMF EStim device in the manner prescribed then the beneficial effects are diminished. Smaller units are available and only require 30-min treatments, however, they require very precise fitting to encompass the fracture site within the small field which also decreases the effectively applied dose and clinical efficacy. Although 73% of clinical studies demonstrate a benefit to EStim, the magnitude and consistency of the effect are less than reported in animal studies. Patient compliance is much lower in clinical studies than in animal studies. We believe that problems with compliance account for the large gap in the results reported in the clinical versus animal studies.

In a study we reviewed, Simmons et al. compared PEMF (where patient compliance is required) to DC EStim (where compliance is not an issue since the device is implanted), and found that spinal fusion rates in the former were lower than in the latter [41], attributing this difference to patient non-compliance. In another study non-compliance was cited as a possible reason for EStim-treated patients having the same spinal fusion rates as non-treated controls [42]. The above problems, "high cost", "inconsistent results", and "impractical/difficult to use" go a long way toward answering our original question, why EStim-based fracture treatments have not gained more acceptance in the orthopedic community.

When comparing EStim to other adjunct treatments used to treat delayed healing or non-unions, Ebrahim et al. compared EStim with low intensity-pulsed ultrasound and found no significant difference [43]. Kertzman et al. used radial extracorporeal shock wave therapy to treat fracture non-unions of superficial bones and found that 70% of tibia non-unions healed within 6 months suggesting that this approach is on par with EStim [44]. Similarly, in a recent study by Putnam et al. non-unions in 26 patients using surgical volar plate fixation and cancellous grafting, they found 82% healed by 12 weeks [45]. With this, one can reasonably assume that rates of success with these different procedures are similar to those reported with EStim.

The present study had several drawbacks, the greatest being difficulty making sense of the large variation in the methods reported in the different studies we reviewed. In both the animal and clinical studies, the bones and fracture types studied, the EStim method/dosages/regimens, and the methods used to report outcomes differed greatly. This made it difficult to combine these various parameters into well-founded treatment recommendations. Another weakness in this study was positive publication bias. All the articles we reviewed were published, and since studies that found EStim to be effective are more likely to be written up, submitted, and accepted for publication, our review did not include unpublished studies with negative results. Another shortfall is related to the questions we used in our survey. We did not test these questions for validity or reproducibility prior to sending them out. Had this been done perhaps we could have improved the quality of the answers we received. Finally, in the survey we could have included more specific questions that might have provided answers to other important questions such as the specific causes of the problem's respondents encountered with EStim treatment. While it would have been nice to get more information with more detailed questions, we decided to have few and simple questions thinking that this would help maximize the response rate in this first study.

## Conclusion

Most of the orthopedic surgeons we surveyed were aware of EStim and its positive outcomes in fracture treatment. These positive outcomes were confirmed in the literature we reviewed, in which both preclinical animal and clinical studies reported positive overall outcomes using EStim to treat bone fractures. Despite the awareness and positive impression our respondents had about EStim only a fraction actually use it in their fracture patients. The reason for this discrepancy could be problems such as, confusion in the literature, due to the great variation in methods reported, and the inconsistent results associated with this treatment approach. On the positive side, when asked "If an easy-to-use electrical stimulation device to treat bone fractures were available, would you use it in your patients?", 85% of the surgeons surveyed responded "Yes". This suggests that despite the problems, given an easy-to-use method for administering EStim, surgeons are open to using this treatment approach. An improved delivery system for EStim could overcome the compliance problem, markedly increase the clinical efficacy and make EStim an accepted form of treatment of non-unions and acute fractures associated with poor healing.

**Funding** This study was supported in part by the Friedrichsheim Foundation (Stiftung Friedrichsheim) based in Frankfurt/Main, Germany, and the Chinese Scholarship Council (CSC).

### Compliance with ethical standards

**Conflict of interest** The authors have no conflicts of interest to declare.

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