Do Capacitively Coupled Electric Fields Accelerate Tibial Stress Fracture Healing?

A Randomized Controlled Trial

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Background: Tibial stress fractures increasingly affect athletes and military recruits, with few known effective management options. Electrical stimulation enhances regular fracture healing, but the effect on stress fractures has not been definitively tested.

Hypothesis: Capacitively coupled electric field stimulation will accelerate tibial stress fracture healing.

Study Design: Randomized controlled trial; Level of evidence, 1.

Methods: Twenty men and 24 women with acute posteromedial tibial stress fractures were referred from local clinicians. Subjects were randomly assigned active or placebo capacitively coupled electric field stimulation to be applied for 15 hours per day until healed, given supplemental calcium, and instructed to rest from provocative training. Healing was confirmed when hopping to 10 cm for 30 seconds could be achieved without pain.

Results: No difference in time to healing was detected between treatment and placebo groups. Women in the treatment group healed more slowly than did the men ($P = .05$). Superior treatment compliance was associated with reduced time to healing ($P = .003$). Rest noncompliance was associated with increased time to healing ($P = .05$).

Conclusion: Whole-group analysis did not detect an effect of capacitively coupled electric field stimulation on tibial stress fracture healing; however, greater device use and less weightbearing loading enhanced the effectiveness of the active device. More severe stress fractures healed more quickly with capacitively coupled electric field stimulation.

Clinical Relevance: Although the use of capacitively coupled electric field stimulation for tibial stress fracture healing may not be efficacious for all, it may be indicated for the more severely injured or elite athlete/recruit whose incentive to return to activity may motivate superior compliance.

Keywords: stress fracture; bone stress injury; treatment; novel entities; electric field stimulation; fracture stimulation

Stress fractures are focal structural weaknesses in bone occurring with the repeated application of subfracture threshold forces.[14] Stress fractures typically result from chronic skeletal overloading occurring over a period of time that is inadequate to allow appropriate bone adaptation. They are increasingly common injuries in athletic and military populations and thought to affect more female army recruits than male.[4,20]

With some exceptions, fractures of this nature heal spontaneously if the injury site is relieved for a time from the aggravating loading. The period of time required for healing to occur with rest, however, can be quite prolonged. The most common site of stress fracture is the tibia.[5] A comprehensive review of the literature reveals that a mean of 12 ± 7 weeks rest has been recommended for the resolution of tibial stress fractures. Such a lengthy duration is highly problematic for athletes in critical training or competitive periods, for army recruits engaged in 14-week basic training courses, and for

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individuals simply attempting to maintain a level of fitness for health benefits.

Few treatments to enhance the rate of stress fracture healing have been empirically tested, and of those that have, results have been disappointing or equivocal. For example, the use of a pneumatic leg brace was reported to enhance the rate of healing in a small (N = 18) athlete study[34] but not in a larger (N = 31) controlled study of soldiers with tibial stress fractures.[1]

Electric fields are known to activate the bone formation process in vitro.[22] Furthermore, electric and electromagnetic field stimulation has been shown to facilitate the healing of recalcitrant fractures in humans in vivo.[31-33] The rationale for the current study was based on the assumption that as bone repairs via a similar mechanism regardless of the nature of the fracture, electric field stimulation should similarly promote healing of stress fractures. Some preliminary evidence exists to support such a hypothesis[3]; however, no controlled randomized trial has previously been conducted to appropriately test the theory.

The current study objective, therefore, was to examine the effect of capacitively coupled electric field (CCEF) stimulation versus placebo treatment on the rate of tibial stress fracture healing in men and women via a double-blind, randomized controlled trial. A CCEF device that operates with signal parameters known to stimulate osteoblasts and designed to optimize patient compliance was selected to deliver the intervention stimulation (OrthoPak Bone Growth Stimulator Systems, EBI, formerly Biolectron Inc, Hackensack, NJ; Food and Drug Administration approved for nonunion fracture healing) (Figure 1).

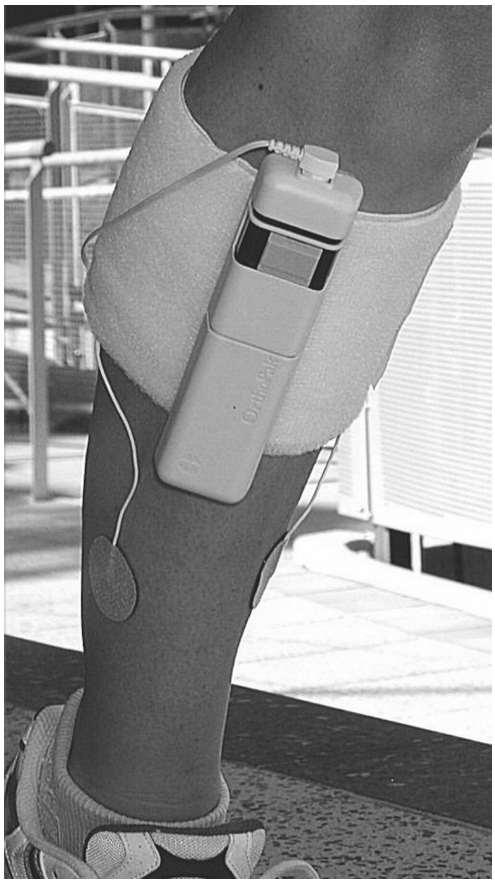

Figure 1. The capacitively coupled electric field stimulator (OrthoPak Bone Growth Stimulator System) in situ for the treatment of midthird to distal third posteromedial tibial stress fracture.

MATERIALS AND METHODS

The study was approved by the US Army Human Subjects Research Review Board, the Stanford University Panel on Human Subjects in Medical Research, the Griffith University Human Research Ethics Committee, and the Australian Defence Human Research Ethics Committee.

Sample Size and Power

Women and men between the ages of 18 and 50 recently diagnosed with 1 or more tibial stress fractures were recruited from a subject pool of referrals from the San Francisco Bay Area (California) and the Gold Coast region (Queensland, Australia) over a period of 7 years. A priori power calculations (based on a predicted effect size of 3 weeks, $s = 4$, $\alpha \leq .05$, and $\beta = .80$) indicated a total of 32 subjects (8 in each of 4 groups) would be required to detect between-group healing differences according to both device status and sex. We chose to recruit additional subjects to avoid potential group shortfalls consequent to blind random allocation, aiming for a total of 40 subjects, 20 men and 20 women. Our figures were derived from the consideration that a healing time difference of 3 weeks would constitute a practically worthwhile effect, based on literature reports of a mean time to tibial stress fracture healing of 12 weeks. Ultimately, power to detect differences between treatment and placebo groups based on our final subject numbers and times to healing was 95.7%, and power to detect differences between male and female responses was 100% for the 95% confidence interval (see Figure 2, CONSORT diagram of subject flow).

Subject Selection

Eligibility for the study was based on the presence of 1 or more acute tibial stress fractures, for which no significant treatment, aside from rest, had been prescribed. Only posteromedial midthird to distal third and proximal medial tibial stress fractures were investigated. Midanterior tibial shaft stress fractures were excluded, being of dissimilar origin to typical tibial stress fractures and particularly prone to delayed union or nonunion.[13] Subjects were excluded from the study if they were pregnant, used a pacemaker, had a metabolic bone disease, or took medication known to influence bone healing.

Clinical Diagnosis

Patients with diagnosed tibial stress fractures were referred to study investigators from local sports medicine clinicians. Study personnel then performed a comprehensive injury assessment to standardized evaluation criteria. The diagnosis of stress fracture was determined according

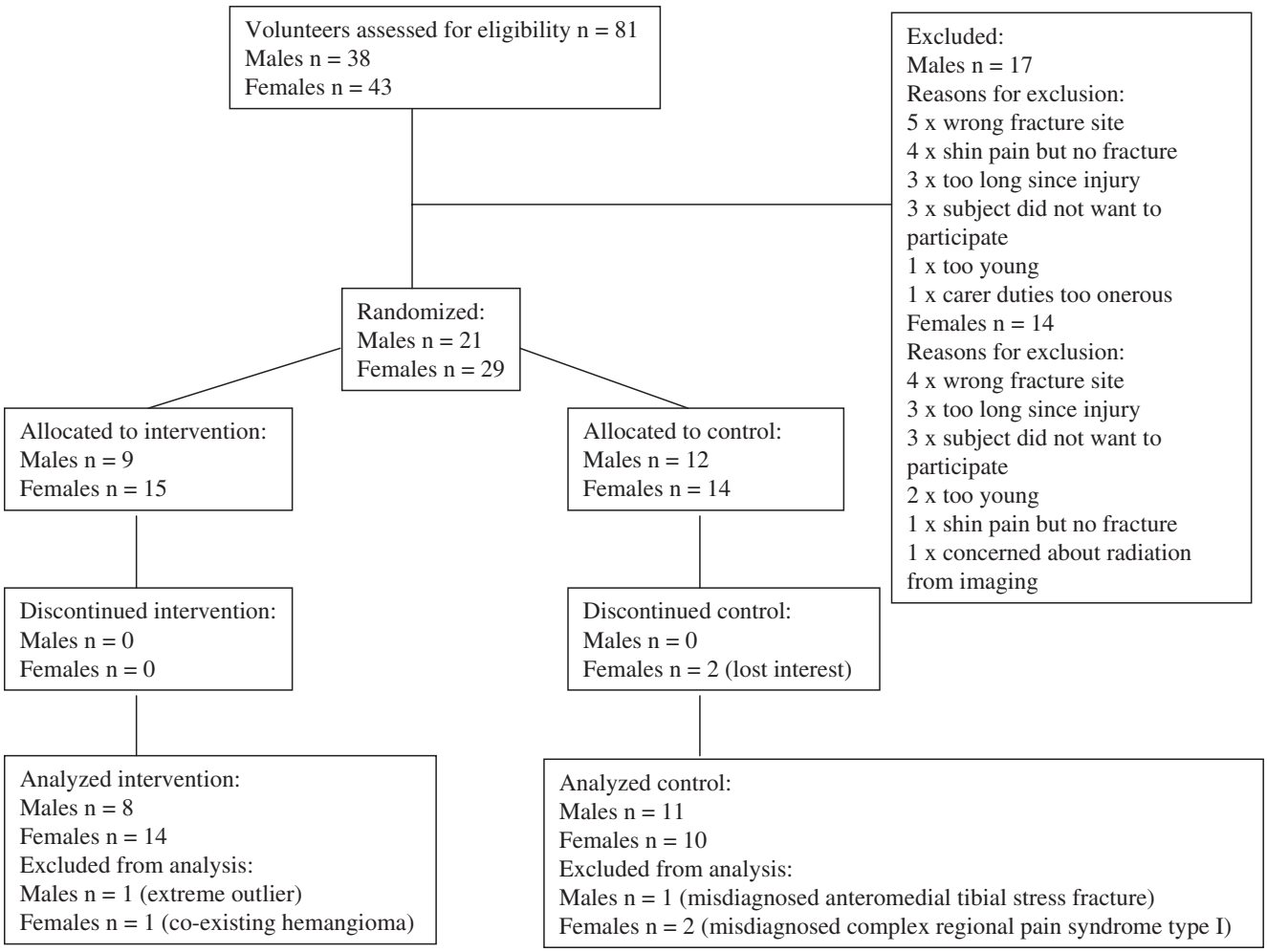

Figure 2. CONSORT diagram of tibial stress fracture subject flow.

to patient history (development of substantial, localized, exercise-related bone pain) and the presence of significant focal tenderness at either of the above described sites that was most pronounced during weightbearing loading. Intensity of signs and symptoms, including tenderness, night pain, pain with percussion, localized bone swelling, spongy texture overlying the injury, and warmth at the site, was recorded on a scale of 1 to 3. A clinical severity score was calculated by the addition of all sign and symptom scores for a possible total of 21.

Diagnostic Imaging

Although eligibility for study enrollment was based exclusively on clinical diagnosis, a comprehensive series of imaging examinations was ordered for each subject to obtain further information regarding injury severity. Plain radiographs have poor diagnostic sensitivity for stress fracture, with detectable changes often lagging 2 to 6 weeks from onset of symptoms. Nevertheless, plain radiographs were obtained to standardize findings and rule out unforeseen pathologic abnormalities. Triple-phase technetium bone scans are highly sensitive to bone stress reactions and are historically the most common imaging modality for stress fractures. Increasingly considered a more specific gold standard for stress fracture diagnosis, MRIs were taken at baseline and follow-up to more precisely observe the location and degree of local swelling. Although not widely used, CT has also been reported for stress fracture imaging and thus was included in the radiological protocol for the purposes of comparison.

Severity of injury was graded on a scale of 0 to 4 for each method of imaging. A radiological severity score was calculated by the addition of imaging scores for each modality for a possible total of 16. The total radiological severity score was stratified into 4 injury grades (grade 1, 1-3; grade 2, 4-6; grade 3, 7-9; grade 4, >10) to approximate the stress fracture grading systems recently reported in the literature.[2,17-19,35] The low-end range of the stratification was emphasized to account for the low sensitivity of plain films and CT and the consequent likely small contribution of those scores to the overall radiological severity score.

All images were blinded and graded independently by musculoskeletal radiologists on separate occasions to evaluate

interreader reliability. A complete description of the radiological analysis will be reported elsewhere.

Subject Characteristics

A comprehensive record of relevant physical and behavioral characteristics was collected (age, height, weight, medical history, training patterns, orthopaedic abnormality, menstrual status, etc). Each subject completed a National Cancer Institute Health Habits Food Frequency Questionnaire (Block Dietary Systems, San Francisco, Calif) to determine mean daily calcium consumption in milligrams. Subjects were provided with calcium supplements (TUMS 500 Chewable, 500 mg calcium carbonate, SmithKline Beecham, Pittsburgh, Pa) and instructed to consume 1 supplement per day to ensure adequate calcium availability during the course of the intervention. All subjects were examined by dual-energy x-ray absorptiometry (XR-36 Quickscan Densitometer, software version 2.5.3a, Norland Medical Systems Inc, White Plains, NY) to determine bone mineral density at the whole body, proximal femur, lumbar spine, and forearm. A bone mass score was derived for each subject by calculating the mean *z* score from all regions. Broadband ultrasound attenuation of the nondominant calcaneus was employed to record an additional index of bone quality (QUS-2 Ultrasound Densitometer, Quidel Corporation, San Diego, Calif).

Treatment

Active and inactive (placebo) electric field stimulators (OrthoPak Bone Growth Stimulator Systems) were provided coded and blinded to investigators by the manufacturers. The active device was a small, portable CCEF stimulator that applied a sinusoidal wave of 3 to 6 V at 60 kHz and 5 to 10 mA via 2 adhesive, water-based gel electrodes (Figure 1).

Once the diagnosis was made and baseline data collection complete, each subject was immediately assigned a device with replacement 9-V batteries and electrodes, and the intervention was initiated. The CCEF device manufacturer recommends that patients use the device constantly, unless engaged in water activities. Our subjects were instructed to use the device for 15 hours per day to maximize usage but minimize variability between subjects that was likely to occur as a consequence of a somewhat burdensome protocol. We instructed subjects to replace the battery every morning and to keep the device alarm switched on. The alarm would sound if electrode contact was lost from the skin or battery power was low, an event signaling that the electric field had been interrupted. Electrode contact could be recovered by moistening the electrodes or replacing them. A daily treatment record log was provided for subjects to record actual hours of use and any side effects or exercise activity they undertook. Devices were issued according to sequential serial number, as device status had been randomized in this order. Active and inactive devices looked and ostensibly functioned in the same manner, and all subjects were treated identically.

All subjects received standard stress fracture rehabilitation advice to avoid treatment withholding from the placebo group. Regular rehabilitation primarily consisted of rest from any painful activity. In-saddle stationary cycling and pool running were acceptable training alternatives to repetitive weightbearing training. Crutches were available for subjects unable to perform activities of daily living without pain, but this was never the case. Subjects were issued with acetaminophen to be used as needed (Tylenol Extra Strength Gelcaps, 500 mg, McNeil Consumer Products, Fort Washington, Pa) and asked to avoid nonsteroidal anti-inflammatories. No subject reported use of any form of pain medication during the course of the study.

Subject Monitoring

Participants were contacted by telephone or e-mail every second day for a progress report and asked to rerate any existing signs and symptoms from 1 to 3. Running was not attempted until subjects were pain free with walking, and hopping was not attempted until subjects were pain free with running (50 m).

When a complete absence of pain during hopping on the affected limb for 30 seconds to a height of 10 cm off the ground was reported and confirmed by investigator examination, the subject was considered healed and the intervention ceased. Participants immediately received a follow-up MRI examination and returned their devices and completed treatment logs to investigators. Device use was tested using the manufacturer-provided Physician Test Meter, which detected days of use in 24-hour periods. A functional measure of healing was deliberately chosen as the outcome measure, rather than appearance on follow-up imaging, to standardize the dependent variable to a practical benchmark and reflect usual practice for stress fracture management in the clinical setting. No standardized system of classification to confirm stress fracture healing on MRI was available at the study inception.

Statistical Analysis

Device effect was evaluated via 2-way analysis of variance (ANOVA) to determine if differences existed in time to healing between active and placebo-treated subjects and between men and women. As time to healing from the start of treatment was positively skewed, we also performed a natural log transformation of the data and reran the ANOVA with natural log time to heal from the start of treatment as the dependent variable. To account for variation between subjects in duration of injury before study enrollment, the analysis was run for both the time between date of injury and healing and the time between initiation of intervention and healing. A further analysis was run to examine actual treatment time (time the device was worn) according to the Physician Test Meter. The latter varied from number of days to healing as subjects were instructed to use the device for only 15 hours per day.

To determine if severity of injury affected time to healing, a number of severity indices were also compared with outcome measures. Two-way ANOVA was used to compare time to healing using device status and clinical severity score as factors. Time to healing was also compared via 2-way ANOVA using

TABLE 1
Characteristics of Stress Fracture Subjects Treated With Active and Placebo Electric Field Stimulation (Means ± SDs)

	Men (n = 19)		Women (n = 24)	
Characteristic	Active (n = 8)	Placebo (n = 11)	Active (n = 14)	Placebo (n = 10)
Age, y	28.33 ± 7.68	26.09 ± 7.99	27.79 ± 7.93	23.90 ± 6.23
Height, cm	178.17 ± 5.43	178.60 ± 7.24	164.69 ± 4.90	166.05 ± 6.95
Weight, kg	78.25 ± 8.35	80.54 ± 7.53	61.04 ± 9.61	57.41 ± 4.68
Body mass index, kg/cm^2	24.65 ± 2.40	25.26 ± 2.03	22.56 ± 3.79	20.83 ± 1.41
Daily calcium intake, mg	1543.30 ± 759.30[a]	1432.10 ± 811.20[a]	1013.2 ± 437.60	881.0 ± 207.6
Percentage fat	18.40 ± 5.69	15.71 ± 6.59	33.76 ± 7.49	25.10 ± 5.06[b]
Percentage lean mass	78.26 ± 5.30	80.51 ± 6.23	62.65 ± 7.20	70.37 ± 5.01[c]
Broadband ultrasound attenuation, dB/MHz	102.63 ± 14.06	114.16 ± 21.21	91.95 ± 16.29	93.75 ± 15.84
Bone mineral density composite (mean z score)	0.73 ± 1.20	0.88 ± 1.00	0.55 ± 1.2	–0.26 ± 0.60

[a]Men > women, $P = .02$.
[b]Women active > placebo, $P = .02$.
[c]Women active < placebo, $P = .03$.

device status and radiological severity score as factors. Finally, time to healing according to tibial stress fracture injury grade (1-4) was compared via 1-way ANOVA for the whole group and using a split-file analysis for device status.

The effect of subject compliance with investigator instructions on treatment time was similarly examined via 2-way ANOVA. One model examined actual hours of device use (from the Physician Test Meter) per number of real treatment days, that is, treatment compliance versus device status. Device use compliance was examined more closely by way of a t test comparison of subjects who complied >70% with those who complied <70%, using Physician Test Monitor hours to healing as the dependent variable. Further, a split-file (according to device status) correlation analysis of days to healing from the start of treatment versus device use compliance was performed. A second compliance model used a rating assigned to the level of weightbearing activity during the intervention (derived from number and intensity of exercise bouts recorded in the subject log), that is, rest compliance versus device status.

Correlation analyses were performed to observe the nature of specific relationships between time to healing and variables such as injury severity or delay to treatment start.

RESULTS

A total of 50 tibial stress fracture treatments were initiated, of which 44 (20 men and 24 women) were completed. Twenty-three of the randomly allocated devices were active (9 to men, 14 to women), and 21 were placebo (11 to men, 10 to women). Subjects excluded from the final analyses included 4 patients with misdiagnoses (1 anterior tibial stress fracture, 1 hemangioma, 2 cases of complex regional pain syndrome type I), 2 subjects released for failure to initiate the protocol, and 1 extreme outlier (see Figure 2).

All statistical analyses satisfied the Levene test for homogeneity of variance for between-group comparisons.

Subject characteristics are summarized in Table 1. Subjects were primarily involved in running and running-related activities (Table 2). Treatment versus placebo group comparisons revealed no subject characteristic differences with the exception of percentage fat (active > placebo, $P = .02$) and percentage lean mass (active < placebo, $P = .03$). Within sex, there were no differences between treatment and placebo groups with the same body composition exceptions. Women allocated an active device had significantly greater percentage body fat ($P = .02$) and less lean mass ($P = .03$) than did women issued a placebo device. Between-sex group comparisons revealed predictable differences in height, weight, body mass index, percentage fat, percentage lean mass, and broadband ultrasound attenuation, with men being significantly taller and heavier with lower percentage fat than were women. Men consumed more calcium than did women (1391.7 ± 689.1 mg vs 958.1 ± 359.9 mg, $P = .02$).

TABLE 2
Primary Sport/Activity of Tibial Stress Fracture Subjects According to Sex

Sport/Activity	Men (n = 19)	Women (n = 24)
Distance running	10	14
Sprinting	1	4
Aerobics		4
Triathlon	2	1
Team sport (football, netball, ultimate Frisbee)	4	
Boxing	2	1

A summary of injury severity ratings and compliance scores is presented in Table 3. There were no differences in severity of injury between treatment and placebo groups, whether assessed clinically or radiologically. There were no detectable differences in treatment compliance (number of hours per day of device use) between treatment and placebo groups or in degree of compliance with the instruction to rest from weightbearing activities during treatment. Similarly, no between-sex differences existed in any compliance or injury severity variable.

A summary of healing data is presented in Table 4. There was no main effect of device status on time to healing from

TABLE 3
Comparison Between Treatment and Placebo Group Injury Severities and Compliance Scores According to Sex[a]

	Men (n = 19)			Women (n = 24)		
	Active	Placebo	Total	Active	Placebo	Total
Clinical injury severity (pain) score	11.1 ± 4.8	12.8 ± 3.0	12 ± 3.9	13.3 ± 3.2	13.9 ± 2.5	13.5 ± 2.9
Radiological injury severity score	4.9 ± 1.6	5.5 ± 2.4	5.2 ± 2.0	4.3 ± 1.8	6.1 ± 2.9	4.9 ± 2.3
Delay to begin intervention, d	34 ± 22.8	18 ± 16.2	25 ± 20.6	33 ± 29.6	27 ± 19.3	31 ± 25.3
Device use compliance, physician test meter hours/treatment days	13.5 ± 5.8	16.9 ± 5.2	15.3 ± 5.6	14 ± 4.9	15.7 ± 3.2	14.7 ± 4.3
Rest compliance, degree of continued weightbearing activity	1.1 ± 0.9	1.2 ± 0.4	1.1 ± 0.7	1.0 ± 0.7	1.3 ± 0.9	1.1 ± 0.8

[a]Data are means ± SDs.

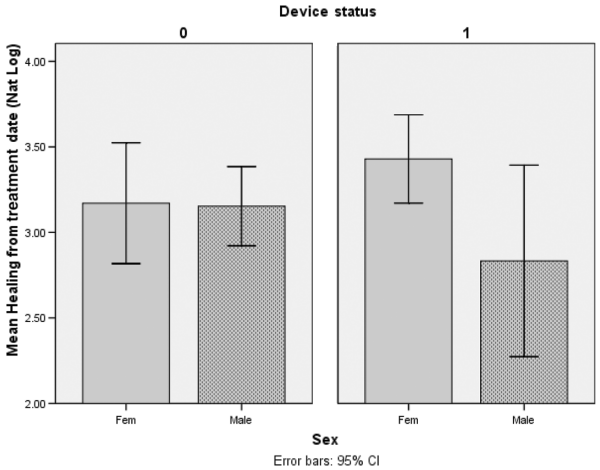

Figure 3. Mean natural log time to heal from start of treatment for male and female tibial stress fracture subjects in placebo (0) and treatment (1) groups. A sex difference in time to healing is evident in the treatment ($P < .05$) but not placebo group. CI, confidence interval; Fem, female.

the start of treatment (treatment group, 29 days; placebo group, 25.9 days); however, overall, women healed more slowly (31 days) than did men (23 days; $P = .05$). Analysis of the log transformed data revealed an interaction effect, such that the sex difference was only evident in the treatment group (Figure 3).

In the analyses of (1) treatment compliance (actual hours of device use per number of real treatment days) and (2) rest compliance (amount of weightbearing activity during treatment), 2 main effects were revealed. Increased hours of device use per day were associated with greater reduction in time to healing in the treatment group than in the placebo group ($F = 57.533$, $P = .003$). The split-file correlation analysis similarly indicated a significant inverse relationship between time to healing and device use compliance for subjects allocated an active device ($r = –3.55$, $P = .05$) but no relationship for placebo-allocated subjects ($r = –0.009$, $P = .972$). Subjects who complied more than 70% (used the OrthoPak for >12.25 h/d) healed significantly faster than did those who complied less than 70% ($t = 2.739$, $P = .009$; 95% confidence interval, 2.07-13.797). Greater engagement in weightbearing activities during treatment (rest noncompliance) increased the time to healing from the start of treatment for subjects using the active device in comparison with placebo users ($F = 2.583$, $P = .05$).

Although no main effects of clinical or radiological injury severity on time to healing could be detected, a direct comparison of time to healing according to radiological injury grade (1-4, described above) revealed significant between-group differences ($F = 4.79$, $P = .007$). When a split-file analysis was run according to device status, time to healing differed between subjects of different injury grades only if they were allocated a placebo device ($F = 11.08$, $P = .001$). That is, there were no differences between healing times of subjects with bone scan severity grades of >2 versus ≤2 in the treatment group (23.5 ± 16.3 days vs 31.2 ± 22.0 days). However, there was a significant difference in healing time for the same comparison of subjects allocated a placebo device (48.0 ± 36.8 days vs 24.4 ± 8.7 days; $P = .01$). These figures indicate that grades 3 and 4 tibial stress fractures treated with an active device healed 24.5 days faster than did those allocated a placebo device. It is important to note that these analyses are not sufficiently powered to make definitive conclusions owing to the small number of subjects classified >2 in bone scan severity grade.

Correlation analyses revealed no significant relationships between time to healing and variables such as injury severity or delay to treatment start. One exception was a split-file analysis for device status that reconfirmed a significant positive relationship between radiological injury severity and time to healing from the date of injury for subjects issued placebo devices (Pearson $r = 0.456$, $P = .03$). Appearance of follow-up MRI did not consistently reflect clinical healing. The use of CCEF stimulation bore no relationship to the appearance of posttreatment MRI.

DISCUSSION

Our goal was to examine the effect of CCEF stimulation on the rate of stress fracture healing with a level of study design rigor not previously reported. We standardized stress fracture site and included both male and female subjects in a double-blind, randomized controlled trial.

Primary between-group comparisons detected no differences in rate of healing between treatment and placebo

TABLE 4
Whole-Group and Sex-Specific Tibial Stress Fracture Healing Times According to Device Status[a]

	All Subjects (N = 43)		Men (n = 19)			Women (n = 24)		
	Active (n = 22)	Placebo (n = 21)	Active (n = 8)	Placebo (n = 11)	Total	Active (n = 14)	Placebo (n = 10)	Total
Time to healing from start of treatment, d	29.0 ± 15.8	25.9 ± 13.5	20.6 ± 13.9	24.7 ± 9.0	23 ± 11.1	33.8 ± 15.3	27.1 ± 17.6	31.0 ± 16.2[b]
Time to healing from injury date, d	60.7 ± 31.5	48.1 ± 24.3	52 ± 30.8	42 ± 23.8	47 ± 27.0	67 ± 31.8	55 ± 24.4	61 ± 28.9
Actual stimulation time, 24-hour periods	15.2 ± 9.4	16.2 ± 7.7	10 ± 6.2	15 ± 5.9	13 ± 6.0	19 ± 9.7	17 ± 9.9	18 ± 9.6[c]

[a]Data are means ± SDs.
[b]Women > men, $P = .04$.
[c]Women > men, $P = .05$.

groups but indicated that men healed a mean of 8 days faster than did women from the initiation of treatment. The sex difference was small (2.4 days) in the placebo group but significant in the treatment group, wherein men healed a mean of 13.2 days faster than did the women, suggesting a sex-CCEF interaction effect existed. The observation that women but not men in the treatment group had greater percentage body fat and less lean mass than did the placebo group coincides with the sex-specific treatment effect. It is unclear how body composition might modify the effect of CCEF stimulation on stress fracture healing, as factors influencing and influenced by fat and lean mass were not measured. The observation of the significantly greater daily calcium consumption (433.6 mg) of male subjects versus female subjects may be of relevance to the sex-specific treatment response.

Close scrutiny of the data suggests that an effect of electric field stimulation on stress fracture healing did exist. For example, increased hours of device use per day reduced time to healing in the treatment group but not in the placebo group. The fact that the more severe tibial stress fractures treated with an active device healed substantially faster (24.5 days) than did similar grade fractures treated with placebo is additionally suggestive of a treatment effect. To prospectively test the hypothesis that tibial stress fracture injury grade influences the efficacy of CCEF stimulation, future investigations must recruit adequate numbers of each stress fracture grade (1-4) to maximize statistical power for cross-grade comparisons.

Electrical stimulation has been used sporadically by clinicians for more than a century.[25,27] More recently, electric and electromagnetic fields have been shown to effect responses from bone cells in culture.[7,8,15,22,30] Clinical effects, such as the stimulation of bone graft, spine fusion, osteotomy, and nonunion healing,[9,11,21,26,32] and the prevention of disuse osteopenia[6,29] have also been reported.

To date, only 1 study has investigated the effects of electric field stimulation on stress fractures.[3] Of 25 stress fractures treated with CCEF stimulation (3.0-6.3 V, 60 kHz) for a mean time of 7.4 weeks (navicular, 8.6 weeks), 88% healed, 8% improved, and 4% did not heal. As the mean time between stress fracture symptom onset and beginning treatment was 21 weeks (navicular, approximately 32 weeks), time to healing with the addition of electric field stimulation appeared to be a substantial improvement (13 and 24 weeks, respectively) on healing without stimulation. Although the results were encouraging, the study controlled for neither a placebo effect nor stress fracture type or prior healing.

Although all create potentially effective electric fields in tissue, CCEF stimulation has distinct advantages over direct current or pulsed electromagnetic field (PEMF) stimulation of bone. Direct current stimulation (24-hour stimulation) is an invasive approach, necessitating surgery. Pulsed electromagnetic field (recommended 3-10 h/d) generates an electromagnetic field from a rigid, unwieldy coil, using a heavy power supply requiring daily recharging. A CCEF device, by contrast, is small and light weight (4 oz), using a 9-V battery and small, flexible gel electrodes. Capacitively coupled electric field stimulation has been shown to stimulate significantly more DNA production from bone cells than does PEMF.[12] The difference in effect is likely owing to different mechanisms of action, PEMF being reliant on the activation of finite intracellular stores of calcium, whereas CCEF stimulation can use the infinite amount of calcium available in the extracellular space.[12]

Current opinion is that mechanical loads on the skeleton are transduced to bone cells by strain-induced fluid flow within the bone tissue. Membrane shear stress, a tangential force generated by fluid flow, is known to stimulate the reorganization of the cytoskeleton and increase expression of cyclooxygenase-2 after inositol-triphosphate–mediated intracellular calcium release,[16,28] with a similar increase in activated calmodulin that is observed with CCEF stimulation.[10,12] Streaming potentials, detectable from the surface of loaded bone, are measurable evidence of fluid flow across bone cortices. It is conceivable that electric field stimulation of bone achieves its effect by way of fluid flow electroosmosis, an electrokinetic relative of streaming potentials. That is, flow of the electrolytic bone fluid may arise as a consequence of the application of an electric field to bone. That low-intensity pulsed ultrasound stimulation appears to accelerate the healing of frank fractures and complex tibial fractures[23,24] suggests an ability of sound waves to also perturb bone fluid. We hypothesized that the passive application of an electric field to bone would force

fluid to flow through the interstitial spaces and channels, stimulating osteogenesis and, ultimately, stress fracture healing. It is possible that both electrochemical and mechanical mechanisms are involved in the transduction of the osteogenic signal. It is unknown if low-intensity pulsed ultrasound stimulates stress fracture healing. The short treatment time of 20 minutes per day suggests it may be an appealing possible alternative to CCEF stimulation.

The lack of a generalized effect of the CCEF device to accelerate healing in our cohort may have arisen from an intrinsic threshold rate of stress fracture healing below which extrinsic stimuli fail to promote further effect. It is noteworthy that previous reports of the time required for tibial stress fracture healing of 12 ± 7 weeks (84 days) grossly exceed the mean time taken for our study subjects to heal (roughly 27 days from treatment initiation or 55 days from injury), regardless of device allocation. A priori power calculations based on finding a between-group difference in a healing time of 3 weeks may have constrained the sensitivity of our statistical analysis. It is possible that the close monitoring of subjects, the constant encouragement to minimize weightbearing training during treatment, the provision of calcium supplements, and the discouragement from ingesting nonsteroidal anti-inflammatories optimized rate of healing for all subjects. Under such conditions, subtle differences in healing rates become very difficult to detect and are arguably clinically insignificant. This would likely not be the case for more exceptional fractures (frank, nonunions, and pseudarthroses) for which healing times are more prolonged, and significant CCEF stimulation efficacy has been reported. Our findings generate the hypothesis that more severe tibial stress fractures may derive considerable benefit from CCEF stimulation, a premise that remains to be tested with larger subject numbers.

CONCLUSION

On the basis of primary between-group comparisons, we cannot conclude that treatment with CCEF stimulation accelerated tibial stress fracture healing in our sample. There is compelling evidence, however, that CCEF stimulation accelerated healing in the more severe cases and that greater compliance and reduced weightbearing activity during healing promoted efficacy.

Our analysis likely reflects the real-life efficacy of CCEF stimulation on the healing of relatively minor tibial stress fractures of the average individual. It is possible, however, that the higher stakes associated with healing for elite or more severely injured athletes or recruits may inspire superior treatment compliance and justify the use of CCEF stimulation when even minor reductions in days to healing could mean the difference between an ability or inability to compete in a once-in-a-lifetime event.

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