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ORIGINAL STUDY

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IC-Type Electric stimulation for delayed bone healing: monocentric evaluation over eight years of experience

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Electrostimulation is suggested to positively influence bone healing for delayed unions of both fractures and osteotomies. This monocentric series aims to retrospectively assess the outcome of electrostimulation treatment for delayed union after traumatic fractures or knee osteotomy. Patients treated with electrostimulation for delayed union (no bony union on radiographic imaging at 90 days after osteotomy or fracture treatment) over an 8-year period were screened. The delay of treatment, success rate, revision rate and demographic data (age, sex, location of fracture, presence of osteosynthesis materials) were investigated. A questionnaire assessed objective (nicotine abuse, NRS pain assessment, activity levels) and subjective (comfort, usability, cost-effectiveness) aspects. Electrostimulation delivered radiographic healing in 75% of the fracture group and 66% of the osteotomy group. No statistical significant difference (N=136) in success rate was found for age, sex, presence of osteosynthesis material, delay or fracture location. Success rate did differ significantly with pain, activity level and smoking ($p<0.05$). Reflective questions to patients were answered mostly positively. The use of electrostimulation for the delayed union of fractures and knee osteotomies delivers high healing rates avoiding the burden of surgical reintervention. It is generally well received by the patient. No difference in success rate was found between sex, age or fracture location, nor did the delay of therapy onset or presence of osteosynthesis material seem to affect the success rate. Smoking had a negative influence on the efficacy of bone electrostimulation.

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Keywords: Electrostimulation; delayed union; osteotomy.

INTRODUCTION

An important complication of fracture healing includes delayed union, defined in this study as inadequate or absent radiographic healing 3 months after the injury, with an incidence as high as 5 to 10% *(1)*. The etiology of poor bone healing is often multifactorial and includes both patient-dependent as well as external factors *(2,3)*. The impact of a delayed union should not be underestimated as it can lead to a persistent loss of limb functionality, an inability to attain previous professional or sporting tasks, as well as have an economic impact on social healthcare systems *(4)*.

Currently both invasive and non-invasive methods are used as treatment for delayed union.

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Although often severely invasive, revision surgery is considered as the standard of care, involving debridement of the non-healing bone, utilization of different bone grafts and (repeat) osteosynthesis. Other less-invasive treatments such as injections with BMP-analogues, PTH-analogues or PRP are still poorly investigated and are thought to rely on a common mechanism by stimulation of either mesenchymal (stem cells) or preosteoblast cells to differentiate into osteoblastic cells *(5-9)*. Low-intensity pulsed ultrasound (LIPUS) or extracorporeal shockwave therapy (ESWT) are upcoming non-invasive techniques, but scientific evidence is scarce, and often of poor quality with conflicting results *(10-15)*.

Electrostimulation is already used by orthopaedic surgeons for accelerated bone healing, although its usage is not yet widespread *(16)*. The use of electric stimulation to promote tissue healing dates back to 1841, when Reid observed that electric stimulation of denervated muscle delayed the onset and progression of atrophy *(17)*. Since then, studies have shown that due to the intrinsic electromechanical properties of the bone, such as the piezo-electric structures (predominantly collagen fibrils) and streaming potentials, bone healing can arise *(18-20)*. The former consist of a mechanical effect of the crystal matrix, which when compressed generates a negative electric potential. The latter are generated when, due to compression, fluids containing ions rush through small canaliculi and generate a negative electric potential. Rubinacci et al have shown in 1988 that these electronegative potentials stimulate bone growth, whereas electropositive potentials stimulate bone loss *(21)*.

Electric stimulation can be applied in three different methods: direct current (DC), capacitive coupling (CC) and inductive coupling (IC). DC involves local electric stimulation directly into the fracture site, which alters cellular activity and releases VEGF *(22-24)*. CC generates an electric field by opposing skin patches. Bone healing is promoted by multiple induced pathways (VGCCs, calmodulin, prostaglandin and BMPs) *(25-28)*. IC generates a magnetic field, which induces an electric field and generates biological responses similar to CC *(29,30)*. Both IC and CC can be classified as non-invasive and painless. However, since verapamil inhibits CC but not IC, different biological pathways for both methods probably exist *(28)*.

Currently the highest level of evidence on this topic consists of a meta-analysis including 15 randomized control trials (RCT); four after spinal fusion, five of fresh fractures, five of delayed union and one after osteotomy. The majority of these RCTs used PEMF/IC (twelve trials), followed by CC (two) and DC (one) *(31)*. This meta-analysis showed a significant reduction of non-union incidence (RR 0.65; $p<0.01$) and pain (VAS -7.67mm; $p=0.02$). The specific definition of non-union was not mentioned in the meta-analysis.

The aim of this monocentric retrospective study was to present our experience with electrostimulation over an 8-year period. The hypothesis was that electrostimulation for delayed unions has a positive effect on bone healing, greatly decreasing the possible need for revision surgery in the future. The efficacy in promoting bone healing, the occurrence of revision surgery and subjective data such as comfort, pain relief and socio-economic views were monitored.

MATERIALS AND METHODS

Patients who received IC electrostimulation since 2011 over an 8-year period at our department were screened. Electrostimulation was applied with the use of the commercially available Ossatec device (Ossatec Benelux Ltd., Uden, The Netherlands) (Fig. 1). Of the initial 294 patients, 104 patients were excluded due to start of electrostimulation therapy before 90 days of conservative treatment. Additional 54 patients were excluded due to diagnoses not included in this study (e.g. shin splints, stress fracture, arthrodesis, ACL reconstruction tunnels). Due to missing data 21 patients were excluded from the questionnaire analyses. A total of 136 patients were included in the study, 51 patients received electrostimulation after a tibial (n=43) or femoral (n=8) osteotomy (OT) (all procedures were opening wedge with or without graft interposition) and 85 patients had a delayed union after a traumatic fracture (FR), of which 80% was surgically treated (Table I).

Fig. 1. – The Ossatec electrostimulator.

Table I. – Demographics of traumatic fractures.

	Total	Prior Surgery
Clavicula	14	10
Humerus	10	9
Radius	4	4
Ulna	2	1
Carpals	5	3
Femur	23	23
Patella	3	1
Tibia	17	16
Fibula	2	0
Foot	5	1
TOTAL	85	68

Most affected were long bones and the majority was surgically treated.

Data included age, sex, exact location and date of fracture, result of treatment and amount of delay (number of days between date of fracture and start of electrostimulation therapy). Patient reported outcomes (PROMs) such as patient comfort (from 0 to 10, a score of 10 having no complaints during usage), surgical intervention, NRS pain score (from 0 to 10), activity level (from 0 to 10, a score of 10 having the same level of activity as before the fracture/osteotomy) and smoking both before and during the course of this study were noted. A study specific questionnaire was designed to question the current price and reimbursement of this treatment, and whether this treatment would be the first choice should the situation occur agian ("yes"/"no"/" I don't know").

The electrostimulation therapy was prescribed by the orthopaedic surgeon for a period of 6 weeks and was advised to be used at night, resulting in a prescribed usage of at least 8 hours a day. Healing was confirmed by radiographic union with in- or out-hospital radiographic imaging, either X-ray or CT.

Statistical methods

The R-program was used for all statistical analyses *(32)*. The continuous variables were first tested for normality with the Shapiro-Wilk test. In case of non-normality the Wilcoxon rank sum test was used. Level of significance was set at $p = 0.05$.

RESULTS

Of the 136 patients evaluated, 93 were male ($N_{(FR)}=56$, $N_{(OT)}= 37$) and 43 were female ($N_{(FR)}=29$, $N_{(OT)}= 14$) (Table II). There was no significant difference in success between sexes for both the total population ($p_{(BP)} =0.667$) or the two subgroups ($p_{(FR)} =0.575$, $p_{(OT)} =1$). The median ages were 45 years (FR; IQR 29-60) and 54 years (OT; IQR 47-60). No significant difference in success was found with age [$p_{(BP)}=0.509$, $p_{(FR)}=0.200$, $p_{(OT)}=0.911$].

The healing rate was 75% with a delay of 188.5 days (IQR 115-280) and 66% with a delay of 118.5 days (IQR 95-185.25) for the FR- and OT-group respectively. OS was present in 80% and 100% respectively (Table II). Separation of tibial (HTO) and femoral osteotomies (DFO) showed success rates of 70% and 44% respectively. Surgical re-

Table II. – Demographics of study population.

	Fractures	Osteotomies
N	85	51
Age (med – IQR)	45 (29-60)	54 (47-60)
Sex (M)	66%	73%
Succes	75%	66%
Delay (d)	188,5 (115-280)	118,5 (95-185,25)
OS present	80%	100%

Demographics of the two separate population groups. The FR-population has a lower median age and is less dominated by males than the OT-population. The FR-population has a higher treatment delay, but also a higher success rate. In most patients, OS material was still present.

intervention in our hospital occurred in 13% of our patients. No significant differences in success rates were found with the presence of OS ($p_{(BP)}$ =1, $p_{(FR)}$ =0.721) or the time of delay ($p_{(BP)}$=0.881, $p_{(FR)}$=1, $p_{(OT)}$=0.629). There was no significant difference in success rates between both populations (p=0.292).

The FR-population was separated in upper (42%) and lower limb (58%), or long bone fractures (68%) and small bone fractures (32%). No significant difference in success rates was found for fractures in the upper or lower limb (p=0.59) nor for fractures in long or short bones (p=0.38).

Treatment with external electrostimulation was generally reported as comfortable, with a median comfort score of 80% (IQR 70-90). (Table III)

Only a minority of the patients reported nicotine abuse (17%). Pain before treatment was of moderate severity, with a median NRS of 4.5 (IQR 4-5), which decreased to a median NRS of 3 (IQR 2-4) after treatment. The level of activity compared to their normal function before treatment was reported with a median of 60% (IQR 50-70) and increased after treatment to a median of 80% (IQR 70-90).

A significant inverse relationship was found between nicotine abuse and success ($p<0.05$) (Fig. 2), success and difference in pain levels before and after electrostimulation therapy ($p<0.05$) (Fig. 3), and success and difference in activity percentage before and after electrostimulation ($p<0.05$) (Fig. 4).

Table III. – Questionnaire results.

	Fractures (n=64)
Patient comfort x/10, median (IQR)	8 (7-9)
Surgical reintervention	13%
Smoking	17%
Pain x/10, median (IQR) Before After	 4.5 (4-5) 3 (2-4)
Activity x/100, median (IQR) Before After	 60 (50-70) 80 (70-90)
Price justified	66%
Reimbursement needed	58%
First choice	77%

The electrostimulation therapy was generally perceived as comfortable and preferable to other treatment methods. A difference in pain and activity before and after the treatment was noted.

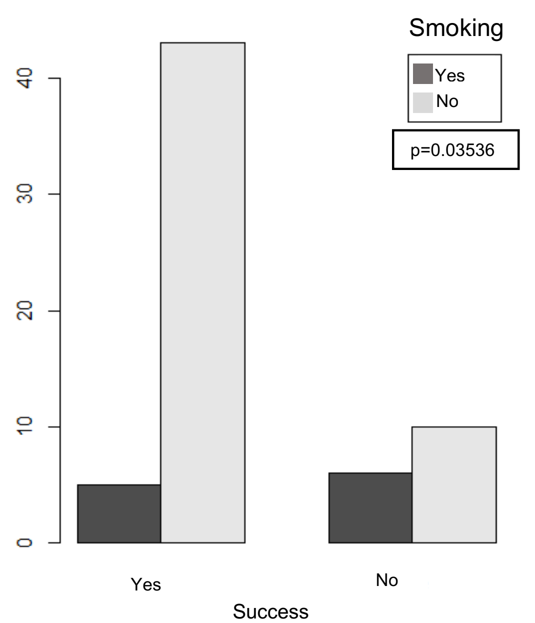

Fig. 2. – Significance of smoking habits and success rate for patients with a fracture (FR-group). A statistical significant relationship was found stratifying the success rate for smoking habits.

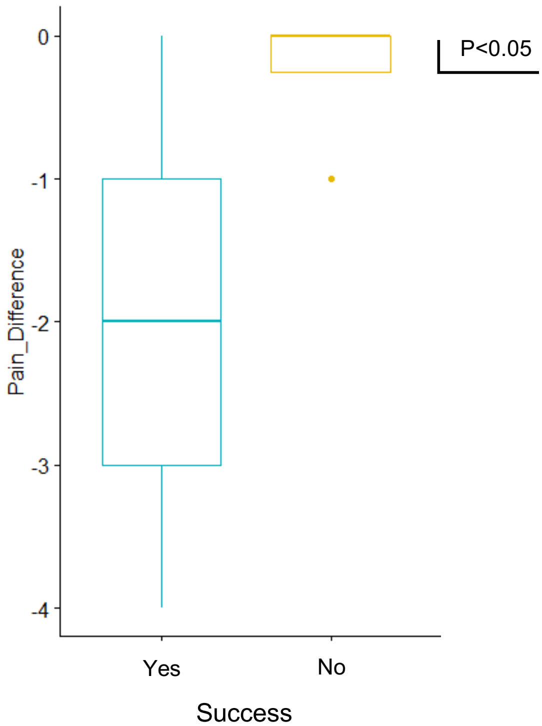

Fig. 3. – Significance of pain sensation and success rate for patients with a fracture (FR group).
A statistical significant relationship was found for the correlation of success and pain sensation.

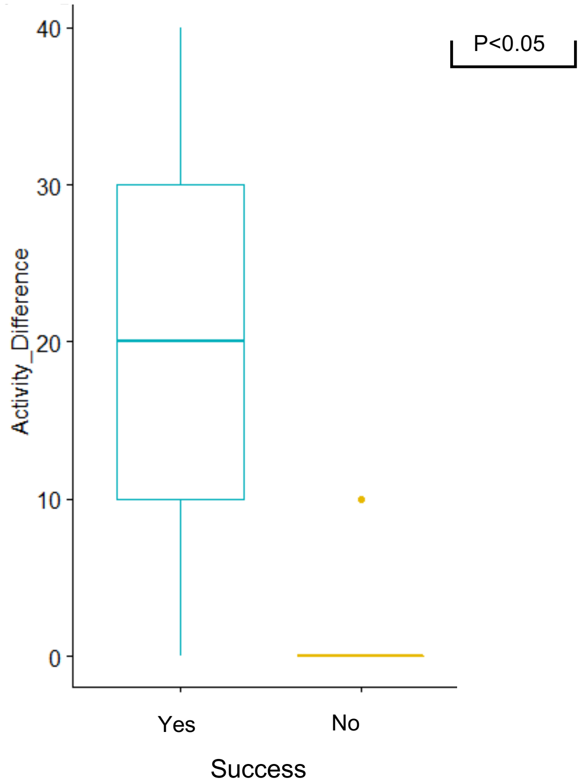

Fig. 4. – Significance of level of activity and success rate for patients with a fracture (FR group).
A statistical significant relationship was found for the correlation of success and level of activity.

A total of 42 patients (66%) answered the treatment was worth the equipment price and 77% would choose electrostimulation as a treatment option for a delayed union (n=49) should this situation reoccur. In contrast, only 37 patients (58%) approved the statement that this treatment should be reimbursed by the government (n=37; 58%).

DISCUSSION

This study evaluated the outcome of IC electrostimulation as a non-invasive treatment for delayed union in fractures and knee osteotomies. Our results show electrostimulation can be universally applied to both groups resulting in improved radiographic healing rates with significant pain reduction, increase in function and without the need for surgical (re)intervention. Active smoking habits detrimentally affected the success rates.

Our results show that the use of electrostimulation (IC) does seem to be a viable, non-invasive treatment option for delayed unions after fractures or knee osteotomies with success rates of respectively 75% and 66%. Although femoral osteotomies showed a far lower success rate compared to tibial osteotomies, the number of these cases was too small to draw significant conclusions. These results are in line with the current literature: a meta-analysis reported a 61% success percentage for delayed unions treated with electrostimulation compared to a 30% success percentage for the control group (conservative treatment according to injury (immobilization/ stress-free movement/…)), although it is important to take into consideration this result was not found to be statistically significant and an exact definition of delayed union was not mentioned *(31)*. Treatment intensity ranged between 8 and 14 hours a day and median ages ranged between 35 and 46 years old, mostly composed by males (70-80%). Only one prospective study concerning osteotomies was included in the meta-analysis and noted a 44% success percentage for electrostimulation, compared to a 16% success percentage for the control group. However, electrostimulation was randomly applied after tibial osteotomy surgery and not after confirmation of delayed union, as is the case in this study. This difference in timepoint of application could explain the difference in success rates (66%) in our population.

The absence of significant differences in success rates between age, sex and fracture location suggest that electrostimulation can be used universally in all age groups, sexes and locations with equal positive results.

An important variable to take into consideration is the presence of osteosynthesis material. Electrostimulation as treatment for delayed unions after surgical treatment cannot be justified if the presence of osteosynthesis material has a negative impact on the success rate. This would imply that the standard of care, namely invasive revision surgery with removal of the osteosynthesis material and bone grafting, should be performed before the application of electrostimulation. As our results did not show any interaction between success and the presence of osteosynthesis material, we can conclude that electrostimulation (IC) can be used even when metallic material is still present.

Delayed union can be defined as the absence of radiographic progression of healing upon clinical examination within an average anticipated time. For a given fracture, this healing time varies with location and configuration as well as the specific bone. If healing is not present after 3 consecutive months, the condition is often arbitrarily defined as a delayed union. Some authors propose a definition of 4 months *(33,34)*, while others propose one of 3 months *(35,36)*. As more than 90% of patients show progressive bone healing 3 months postoperative after a tibial open-wedge procedure *(37)*, this timepoint was chosen as a cut-off in our study.

Statistical investigation showed that the delay of electrostimulation therapy in our study did not have a significant impact on the rate of success ($p_{(BP)}$ =0.88, $p_{(FR)}$ =1, $p_{(OT)}$ =0.63). These results are in concordance with the findings of Shi et al. (2013) who evaluated early treatment of electrostimulation of long bones *(38)*. Compared to fractures, successfully treated osteotomy patients did show less delay than unsuccessfully treated osteotomy patients, but this was not found to be statistically significant.

The use of nicotine on the success rate tested significant. It is thus of utmost importance, with the additional detrimental effects of active smoking habits on bone healing, to prohibit a patient from smoking before starting the electrostimulation therapy or planning an osteotomy to achieve optimal results *(39)*.

Our results showed a significant reduction in pain and increase in patient reported activity levels after electrostimulation. Although these finding are linked with fracture healing, 30% of patients with persistent delayed union reported a reduction of pain.

Currently no evidence can confirm pain relief of IC electrostimulation for treatment of delayed unions. The results of this study seem to indicate IC electrostimulation can help for pain relief. This is in line with a meta-analysis investigating pain relief after CC electrostimulation, although it must be noted the physiological changes invoked by CC and IC are different and thus the same results cannot be guaranteed *(40)*.

A significant limitation of this study is the absence of a control group. To correctly analyze our results we compared them to the existing literature. However, readers should exercise caution interpreting the results due to this shortcoming.

Although not all patients experienced benefit from the electrostimulation therapy, even patients without bone healing would prefer to try this non-invasive option compared to invasive revision surgery (77%).

CONCLUSION

Our study confirms the results of prior publications that electrostimulation has a beneficial effect on the healing of delayed unions, whether after initial fracture treatment or osteotomies, and can thus lower the incidence of revision surgery. In addition, our results suggest the therapy can be used for all sexes, age groups and fracture locations, with positive effects regarding pain sensations and levels of activity, but suffers detrimentally from active smoking habits.

Abbreviations: BMP (Bone Morphogenetic Protein), PTH (Para Thyroid Hormone), PRP (Platelet Rich Plasma), TGFbeta (Transforming Growth Factor beta), LIPUS (Low-Intensity Pulsed Ultrasound), ESWT (Extracoporeal Shock Wave Therapy), DC (Direct Current), IC (Inductive Coupling), CC (Capacitive Coupling), PEMF (Pulsed Electromagnetic Field), VGCC (Voltage Gated Calcium Channel), FR (Fracture), OT (Osteotomy), BP (Both Populations), HTO (High Tibial Osteotomy), DFO (Distal Femoral Osteotomy)

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