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RESEARCH ARTICLE

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A novel nonsurgical therapy for peri-implantitis using focused pulsed electromagnetic field: A pilot randomized double-blind controlled clinical trial

Yaniv Mayer DMD[1,2] | **Juan Khoury DMD**[1] | **Jacob Horwitz**[1,2] | **Ofir Ginesin MSc**[1,2] | **Luigi Canullo PhD**[3] | **Eran Gabay PhD**[1,2] | **Hadar Z. Giladi PhD**[1,2]

[1]Department of Periodontology, School of Graduate Dentistry, Rambam Health Care Campus (RHCC), Haifa, Israel

[2]Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

[3]Department of Surgical Sciences (DISC), Division of Prosthodontics and Implant Prosthodontics, University of Genoa, Genova, Italy

Correspondence

Yaniv Mayer, DMD, Department of Periodontology, School of Graduate Dentistry, Rambam Health Care Campus, Haifa, Israel.
Email: yaniv.mayer@technion.ac.il

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Abstract

Pulsed electromagnetic field (PEMF) therapy modulates the immune response and is successfully used in orthopedics to treat osteoarthritis and improve bone regeneration. This may suggest that this treatment may consequently reduce peri-implant soft tissue inflammation and marginal bone loss. To compare clinical, radiographic, and immunological results following nonsurgical treatment for peri-implantitis with or without PEMF therapy. Patients with peri-implantitis were included: pocket probing depth (PPD) between 6 and 8 mm with bleeding on probing (BOP); crestal bone loss between 3 and 5 mm. A novel healing abutment that contained active (test) or inactive (control) PEMF was connected. PEMF was administered via the abutment at exposure ratio of 1/500–1/5000, intensity: 0.05–0.5 mT, frequency: 10–50 kHz for 30 days. Nonsurgical mechanical implant surface debridement was performed. Patients were examined at baseline, 1 and 3 months. Clinical assessment included: plaque index, BOP, PPD, recession, and bone crest level which was radiography measured. Samples of peri-implant crevicular fluid were taken to analyze interleukin-1β (IL-1β). Twenty-three patients (34 implants; 19 control, 15 test) were included. At the follow-up, mean crestal bone loss was lower in the test group at 1 and 3 months (2.48 mm vs. 3.73 mm, $p < 0.05$ and 2.39 vs. 3.37, $p < 0.01$). IL-1β levels were also lower in the test group at 2 weeks (72.86 pg/mL vs. 111.7, $p < 0.05$). Within all the limitation of this preliminary study, the test group improved clinical parameters after a short-term period compared to the control group.

KEYWORDS

nonsurgical therapy, peri-implantitis, pulsed electromagnetic field

1 | INTRODUCTION

As dental implants become the treatment of choice to replace teeth that were lost or are congenitally missing, an ever-greater concern for periimplantitis and its consequences is imminent.

According to the last consensus conference on periodontal and peri-implant diseases, peri-implantitis was defined as a pathological condition around dental implants characterized by inflammation in the peri-implant connective tissue and progressive loss of supporting bone (Schwarz et al., 2018). The prevalence of peri-implantitis is significant, as assessed in several meta-analyses (Rakic et al., 2018; Rokn et al., 2017). A rate of 18.5% was reported at patient and 12.8% reported at implant level (Rakic et al., 2018) while a rate of 27.9% was reported at implant level among university-based patients (Romandini et al., 2021).

Although the etiological factors of periimplantitis and periodontitis are similar (Heitz-Mayfield & Lang, 2010), peri-implantitis exhibits greater tissue and bone destruction (Hiyari et al., 2018). Furthermore, if left untreated, leads to implant loss.

Different factors were indicated to trigger peri-implant disease onset: excess of cement (Staubli et al., 2017), malpositioning (Romandini et al., 2020), implant/abutment misfit, or prosthetic incongruences (Canullo et al., 2020).

Acceptable treatment regimens for this condition are both surgical and nonsurgical. Surgical therapies that have been shown to be efficient include open flap debridement (OFD) coupled with implant surface debridement with or without bone regeneration or resection. However, the predictability of these procedures is yet to be proved (Keeve et al., 2019; Ramanauskaite et al., 2018). Nonsurgical therapies include implant surface debridement using manual or rotatory instruments (Mayer et al., 2020), lasers of various wavelengths (Bach et al., 2000; Sculean et al., 2005), ultrasonic devices and local delivery of antibacterial preparations (Machtei, 2014). All these treatment modalities have shown to have a moderate effect (Lang et al., 2019).

Pulsed electromagnetic field (PEMF) is commonly used to stimulate bone generation throughout various clinical settings including orthopedic surgery. The electromagnetic field is responsible for reducing osteoclastic activity while inducing osteoid formation and neo-vascularization (Midura et al., 2005). It was also reported to have antibacterial properties (Novickij et al., 2018) and increase the rate of osseointegration (Cai et al., 2018). While the exact biological effects of PEMF are not fully understood, researches claim that it affects bone formation by accelerating extracellular matrix (ECM) synthesis (Zhang et al., 2020), endochondral ossification (Aaron & Mc Ciombor, 1996), and inflammatory processes including macrophage polarization to M1/M2 phenotypes and cytokines secretion (Garlet & Giannobile, 2018).

Potential use of PEMFs as modulator of immune responses alone or in combination with pharmacological therapies represents a novel frontier of investigation with interesting clinical perspectives (Nayak et al., 2020). In dentistry, PEMF stimulation may be a useful tool to encourage bone formation, ingrowth of bone on dental implants, which may help decrease time to osseointegration and allow decreasing the time till restoration and loading (Barak et al., 2016).

The miniaturized electromagnetic device (MED), The Magdent® is a novel device designed as conventional healing abutment which is screwed into the implant. The Magdent® is made of Ti–6AI–4V and consists of a battery, an electronic device, and a coil that utilizes electromagnetic fields for 1 month. In order to activate the MED for generating the electromagnetic field, an activator is needed. Clinical human studies demonstrated a superior implant stability during the early phase of healing by using Magdent® as compared with standard implants (Barak et al., 2019; Nayak et al., 2020).

Key points

- The study investigates a new method for treating peri-implantitis using pulsed electromagnetic field (PEMF) therapy. It evaluates the clinical, radiographic, and immunological outcomes of nonsurgical peri-implantitis treatments, contrasting the results with and without PEMF therapy.
- Patients with peri-implantitis were treated with either an active or inactive PEMF through a unique abutment for 30 days and received mechanical debridement of the implant surface. Key clinical indicators like plaque index, bone crest level, and IL-1β levels in the peri-implant crevicular fluid were measured at the start, after 1 month, and 3 months.
- Radiographic examination indicated that the bone crest level in the control group remained consistent throughout the study. Conversely, the test group displayed a statistically significant enhancement in bone regeneration as the study progressed.
- Both groups exhibited a reduction in periodontal pocket depth from baseline to 3 months. Notably, the decline in PPD within the test group from baseline to 1 month was more significant than that observed in the control group.
- Examination of pro-inflammatory mediators showed that, by 2 weeks, the test group's average IL-1β level in the peri-implant crevicular fluid was significantly lower than the control group. However, this difference vanished by 1 month due to a rebound effect observed in the test group.

1.1 | Hypothesis

Due to the anti-inflammatory, antiosteoclastic, and pro-osteogenic activity of PEMF, it was hypothesized that this process may improve the outcomes of nonsurgical therapy of peri-implantitis.

The purpose of this pilot randomized, double-blind clinical trial was to compare the results following nonsurgical therapy for periimplantitis using implant surface debridement alone or in combination with PEMF delivered via MED.

2 | MATERIALS AND METHODS

The study was approved by Rambam Health Care Campus Ethics Committee (RMB-0402-19) and registered at ClinicalTrials.gov (Identifier NCT04213144). The study was conducted in the Department of Periodontology, School of Graduate Dentistry, Rambam Health Care Campus, between May 2020 and June 2022. Patients

during supportive periodontal therapy were invited to participate in the study. Patients who were diagnosed with peri-implantitis while fitting the inclusion criteria and signed an informed consent form, were recruited for this prospective, randomized, double-blind sham-controlled study. Inclusion criteria included patients aged 20–85 years, with evidence of peri-implant crestal bone loss greater than 3 mm but not more than 5 mm; presence of bleeding on probing or suppuration; an implant pocket depth of 6–8 mm; implants with an internal hex connection of 3.75 diameter; implant-supported prosthesis that can be removed and later refitted and patients that are willing to adhere to the study schedule and visits. All patients included in the study were under strict periodontal maintenance with no residual pockets at other sites. Exclusion criteria were patients consuming medications that might affect soft and hard tissue healing/health (such as calcium channel blockers, immunosuppressive, and anticonvulsive medications); patients currently taking systemic antibiotics; chronic use of nonsteroidal anti-inflammatory drugs (NSAIDs) on a long-term basis (excluding low dose aspirin); presence of a pacemaker; patients with a periodontal disease and cigarette smoking >10 a day.

2.1 | Study design and outcome variables

This is a prospective, double-blind, randomized, sham-controlled pilot study of a 3-month duration, as shown in the study flow chart (Figure 1). The data are reported according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines. Treatment allocation was by block randomization, with a block size of four. Both patients and evaluators were blind to whether the MED device was active or not.

Baseline (T0) All clinical parameters were evaluated by the same blinded and calibrated examiner (YM);

- Peri-implant pocket depth (PPD) measured from the mucosal margin to the bottom of the probable pocket using a graduated manual periodontal probe (PCP-UNC 15; Hu-Friedy®). Six sites per implant were evaluated (mesiobucal, midbuccal, distobuccal, mesiolingual, midlingual, and distolingual).
- Bleeding on probing (BOP) evaluated dichotomously with either presence/absence of bleeding within 30 s following probing.
- Suppuration on probing (SUP) with either presence/absence of suppuration after probing.
- Recession depth (REC) which was measured from the implant-abutment interface to the gingival margin at the midbuccal aspect using a graduated manual periodontal probe (PCP-UNC 15; Hu-Friedy®). In cases with a mucosal margin coronal to the implant shoulder, it was considered as "0."
- Plaque index (PI) measured on the buccal and lingual surfaces, scoring ranges between 0 (*no plaque*) to 3 (*heavy plaque accumulation*).
- Peri-implant crevicular fluid (PICF) samples were collected for quantification of interleukin-1β (IL-1β) before PPD measurement to avoid blood contamination. The area was isolated with cotton rolls and air-dried. Samples were collected by means of sterile paper points (Absorbent Paper Points; META Biomed). The paper points were placed at the entrance of the crevice and left in place for 30 s at the mesiobuccal, midbuccal, distobuccal, distolingual, midlingual, and mesiolingual sulcus. Papers with blood were not included in the assay. Samples were taken at all time points and were stored at −20°C until assayed. The concentrations of total

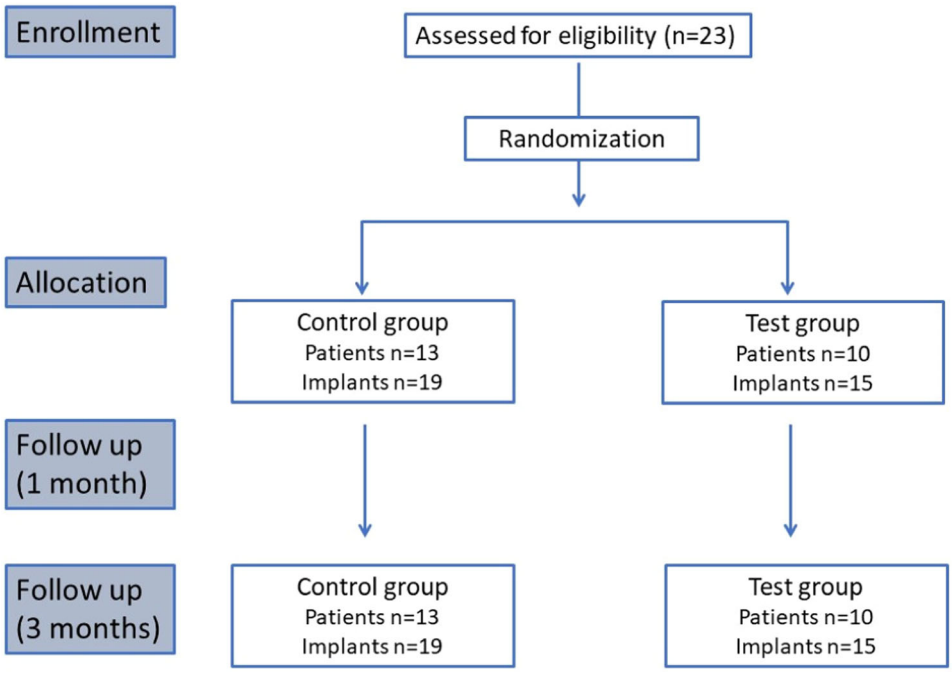

FIGURE 1 Study flow chart.

IL-1β, were determined using commercially available enzyme-linked immunosorbent assay kit (R&D systems).

Following delivery of local anesthesia (Ubistesin Forte; 3 M ESPE) and removal of supra-structure; cemented prosthesis were cut with a straight diamond bur, removing as minimal units as possible while unscrewing the abutments, and the screwed prostheses were unscrewed. All the components which were unscrewed were kept with the patients until the end of the study. Implant surface debridement was performed by a single surgeon (YM) using manual and rotary instruments; a teflon-coated curette and a prophylaxis brush were used to clean the implant surface. MED was connected where the crown and the abutment were removed. If the same patient had multiple implants with peri-implantitis fitting the inclusion criteria, all the implants received the same treatment and were allocated to the same group and were all included in the statistical analysis. To activate the MED, it was inserted into an activator device that uses a magnetic mechanism to initiate the MED's battery. Once the battery was activated, the MED generated a PEMF that was active within a 2 mm radius. The PEMF treatment was administered via the MED for 30 days at an exposure ratio of 1/500–1/5000, an intensity of 0.05–0.5 mT, and a frequency of 10–50 kHz (Figure 2). Sham devices gave outward signs of normal function in the activator but did not generate a PEMF. Patients were instructed to brush the healing abutment as part of their daily oral hygiene. Finally, a radiograph was taken.

Throughout the study, no supplemental antimicrobial treatment (antibiotics or antiseptics) was prescribed.

Radiographic bone level (BL): radiographs were taken using an intraoral sensor Planmeca Intra X-ray unit at 63 kV, 8 mA, 0.064 s, and an XCP-DS FIT Universal Sensor Biteblock (Dentsply). The width of the MED abutment was used to calibrate the radiographs. BL was determined as the distance between the implant shoulder and the first bone to implant contact at the mesial and distal aspects of the implant, using an image analysis software (Planmeca Romexis Version: 3.8.1.R; Planmeca oy). All radiographic measurements were assessed in duplicate by single-blinded and calibrated examiner (JK).

In order to check the intra-observer variance, we used two repeated measurements for each observer. We analysed the difference between measurements by point estimate and 95% CI. For radiographic measurements the results were: for mesial $d = 0.11$ mm (95% CI: 0.033–0.18), $p = 0.006$ and for distal $d = -0.004$ mm (95% CI: −0.083 to 0.075), $p = 0.914$. For ppd measurements $d = -0.250$ mm (95% CI: −0.46 to −0.042), $p = 0.021$. All the differences were relatively small.

FIGURE 2 A cross-sectional view of the miniaturized electromagnetic device (MED) healing abutment (left); An activator device which triggers the battery in the MED (right).

2.1.1 | 2 Weeks (T1)

At 2 weeks PICF samples were taken for IL-1β concentration measurement.

2.1.2 | 1 Month (T2) and 3 months (T3)

At 1 and 3 months, all clinical parameters were measured as well as radiographs of the implants and PICF samples.

After a 3-month period, with an absence of inflammation and shallow PPD (up to 5 mm), screw-retained supra-structures were put back, and patients with cemented supra-structures were sent back to their prosthodontist for new crowns.

2.1.3 | Sample size

Since no data were available for estimating the effect size, a pilot study design was chosen. In total, 23 patients were included in 10 tests and 13 control patients.

2.1.4 | Primary outcome variable

The primary outcome variable was radiographic bone formation.

2.1.5 | Secondary outcome variable

Secondary outcome variables were PPD, BOP, PI, REC, SUP, and IL-1β.

2.2 | Statistical analyses

Data were analyzed with IBM SPSS statistics software version 28.0. (SPSS Inc.). The significance levels were set at 0.05.

Descriptive analysis was performed providing absolute and relative frequencies for categorical variables and mean, standard deviation, 95% confidence intervals (CI), for continuous variables. Baseline characteristics are presented as means and standard deviations for continuous variables and as frequencies and percentages for categorical variables. Nonparametric Mann–Whitney test and independent *t*-tests were performed to compare the two groups for continuous variables.

3 | RESULTS

Twenty-three subjects (13 females, 10 males) were recruited for the study. The demographic data are shown in Table 1. No significant difference was found between test and control groups at baseline.

Age of the participants ranged from 32 to 80 years, with a mean of 61.7 ± 11.9 years. Two participants were current smokers (<10 cigarettes per day), both were in the test group. Thirty-four implants were included in the study, 21 in the mandible, and 13 in the maxilla. Twenty-four were in the molar region, seven in the premolar region, and three in the anterior region. Seventy-four percent of implants were screw-retained and the remaining 26% cemented. At baseline, the mean of all implants was 3.28 ± 1.55 mm regarding radiographic BL, 5.76 ± 1.16 mm regarding PPD, 0.15 ± 0.53 mm regarding REC, 96.5% BOP, and 1.52 ± 0.8 regarding PI.

TABLE 1 Demographic data at baseline.

	Total	Control	Test
Number of patients	23	13	10
Number of implants	34	19	15
Number of implants per patient			
1 implant	14	9	5
2 implants	7	2	5
3 implants	2	2	0
Age, mean ± SD	61.7 ± 11.9	60.3 ± 11.3	63.6 ± 12.7
Gender			
Female, number (%)	13 (56)	9 (69)	4 (40)
Male, number (%)	10 (43)	4 (31)	6 (60)
Smokers ≤10 cig./day, number (%)	2 (9)	0 (0)	2 (20)
Implant position			
Maxilla, number (%)	13 (39)	7 (37)	6 (40)
Mandible, number (%)	21 (61)	12 (63)	9 (60)
Molar	24	12	12
Premolar	7	4	3
Anterior	3	3	0
Prosthesis			
Screw retained implants (%)	25 (74)	13 (69)	12 (80)
Cemented implants (%)	9 (26)	6 (31)	3 (20)

Radiographic bone loss was measured at baseline, 1, and 3 months (Table 2 and Figure 3). In the control group, the distance from the bone crest to the implant shoulder did not change throughout the study; 3.63 ± 1.55, 3.73 ± 1.65, and 3.75 ± 1.53 at baseline, 1, and 3 months, respectively. The test group showed a decrease in the distance from bone crest to implant shoulder as the study proceeded; 2.84 ± 1.17, 2.48 ± 1.07, and 2.39 ± 1.02 at baseline, 1, and 3 months, respectively, which was statistically significant (Figure 3). Figures 4 and 5 demonstrate the notable improvement of the BL around implants in the test group with the active MED.

Probing depth showed an improvement from baseline to 3 months in both groups. The control group showed an improvement in PPD along the study; 5.89 ± 1.26 mm at baseline, 4.93 ± 1.78 mm at 1 month, and 4.54 ± 1.85 mm at 3 months, significant between baseline, 1 ($p < 0.01$), and 3 months ($p < 0.01$). Similarly, the test group showed an improvement in PPD along the study; 5.58 ± 1.05 mm at baseline, 4.06 ± 1.88 at 1 month and 3.45 ± 1.31 mm at 3 months. In addition, significant reduction in PPD was found between 1 and 3 months in the test group only ($p < 0.05$) (Figure 7). A comparison between control and test groups showed no significant difference at any time point (Table 2).

A subanalysis of the deepest pockets at implant sites revealed that the reduction in PPD of the test group between 1 month and baseline was better than the control group, with a statistical significance ($p < 0.05$) (Table 2 and Figure 6).

Recession was measured at baseline (0.07 ± 0.2 mm in test group and 0.21 ± 0.68 mm in control group), 1 and 3 months (0.26 ± 0.7 mm in test group and 0.15 ± 0.42 mm in control group). No significant changes in recession depth were observed within and between groups. However, the sites with the greatest recession in baseline demonstrated statistically significant greater increase in recession in control group ($p < 0.035$).

Plaque scores and bleeding on probing were measured at baseline, 1, and 3 months. PI was calculated, revealing an improvement in both groups. Bleeding scores decreased in both groups from baseline to 3 months; BOP in 100% and 63% of implants in the control group, and 93% and 33% of implants in the test group (Table 2).

IL-1β was examined in the PICF at baseline, 2 weeks, and after 1 month. At 2 weeks, the test group showed an average level of 72.86 pg/mL of IL-1β while the control group had an average of 111.68 pg/mL. The difference between the groups was statistically significant ($p < 0.05$). At 1 month, a rebound effect was found in the test group with no statistical differences between treatment groups (Figure 7). After 3 months 66% of the implants in test group and 50% in control group no additional treatment was needed, 20% of the implants in test group and 33% implants in control group were extracted. In both group, an additional debridement

TABLE 2 Mean clinical parameters (PPD, REC, PI, BOP) and radiographic measurements (BL) measured at baseline (T0), 1 month (T1) and 3 months (T3).

	Baseline (T0)			1-month (T2)			Δ T2-T0	Δ T2-T0		3-months (T3)			Δ T3-T0	Δ T3-T0	
	Test group	Control group	*p* value	Test group	Control group	*p* value	Test group	Control group	*p* value	Test group	Control group	*p* value	Test group	Control group	*p* value
PD	5.58 ± 1.05 (3.83-6.83)	5.89 ± 1.26 (4.3-8.0)	0.656	4.06 ± 1.88 (2.16-9.5)	4.93 ± 1.78 (2.83-8.16)	0.086	1.522	0.887	0.098	3.45 ± 1.31 (1.83-6.9)	4.54 ± 1.85 (2.66-8.66)	0.064	2.128	1.294	0.202
PDd	7.00 ± 0.25	7.16 ± 0.29	0.973	5.27 ± 1.94	6.25 ± 1.94	0.1	1.733	0.88	**0.033***	4.53 ± 1.76	5.18 ± 1.94	0.39	2.466	1.894	0.502
REC	0.07 ± 0.20 (0-0.66)	0.21 ± 0.68 (0-0.5)	0.765	0.23 ± 0.64 (0-0.33)	0.08 ± 0.22 (0-0.66)	0.572	-0.153	0.138	0.412	0.26 ± 0.70 (0-2.5)	0.15 ± 0.42 (0-1.5)	0.882	-0.188	0.036	0.39
RECg	0.13 ± 0.35	0.37 ± 0.95	0.681	0.40 ± 0.82	0.19 ± 0.54	0.52	-0.266	0.201	**0.035***	0.40 ± 0.91	0.41 ± 1.00	0.941	-0.266	-0.21	0.411
BL	2.84 ± 1.17 (0.85-4.2)	3.63 ± 1.55 (0.8-6.05)	0.109	2.48 ± 1.07 (0.8-4.05)	3.73 ± 1.65 (0.5-6.3)	**0.019***	-0.36	0.1	**0.05***	2.39 ± 1.02 (0.65-4.1)	3.75 ± 1.53 (0.15-5.1)	**0.006***	-0.09	0.02	**0.05***
PI	1.73 ± 1.03	1.36 ± 0.76	0.641	0.33 ± 0.48	0.61 ± 0.84	0.842	-1.41	-0.75	0.722	0.53 ± 0.74	0.31 ± 0.58	0.722	-1.21	-0.98	0.855
BOP	93%	100%	NS	40%	72%	NS	53%	28%	NS	33%	63%	NS	60%	37%	

Abbreviations: BL, mean bone level of mesial and distal aspects; BOP, bleeding on probing; NS, nonsignificant; PI, plaque index; PPD, periodontal pocket depth; REC, recession of buccal aspect.
*$p < 0.05$.

was conducted 33% in test group and 16% in the control group.

4 | DISCUSSION

The present study was performed to test the efficacy of PEMF on diseased implants with radiographically evident marginal bone loss. The outcomes reveal the additive effect of active MED abutments and show a significant improvement in PPD when compared to sham abutments at 3 months. Radiographic analysis outcomes exhibit significantly shorter distance from the implant shoulder to bone crest at 1 and 3 months when compared to controls.

To this day, there are no clear guidelines regarding the treatment of peri-implantitis. According to the Consensus report of working group 3 (Renvert et al., 2019) and group 4 (Khoury et al., 2019), the treatment modalities of periimplantitis can be divided into surgical and nonsurgical. Nonsurgical therapy should always be completed before any surgical intervention is attempted, that is to allow an evaluation of its' efficacy (Renvert et al., 2019). Furthermore, to assess the patient's ability and willingness to perform effective oral hygiene measures. Effective plaque control by the patient is paramount for success. On that end, in some cases, the supra-structure might need to be modified or replaced (Khoury et al., 2019; Renvert et al., 2019).

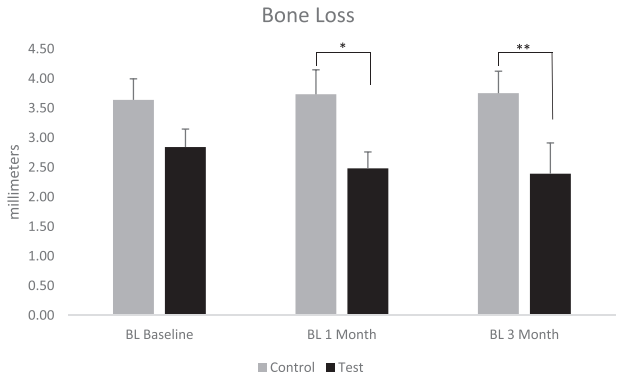

FIGURE 3 The distance from the implant shoulder to bone crest was measured on X-rays using the ImageJ software at baseline (T0), 1 month (T2), and 3 months (T3). *$p < 0.05$, **$p < 0.01$.

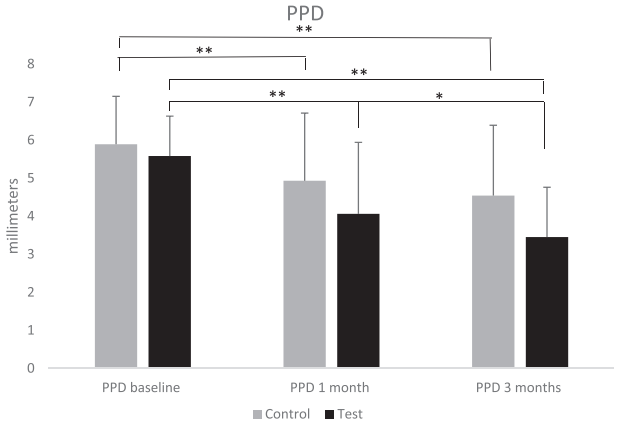

FIGURE 6 Mean of pocket depth measurements at baseline, 1, and 3 months in control and test groups. *$p < 0.05$, **$p < 0.01$.

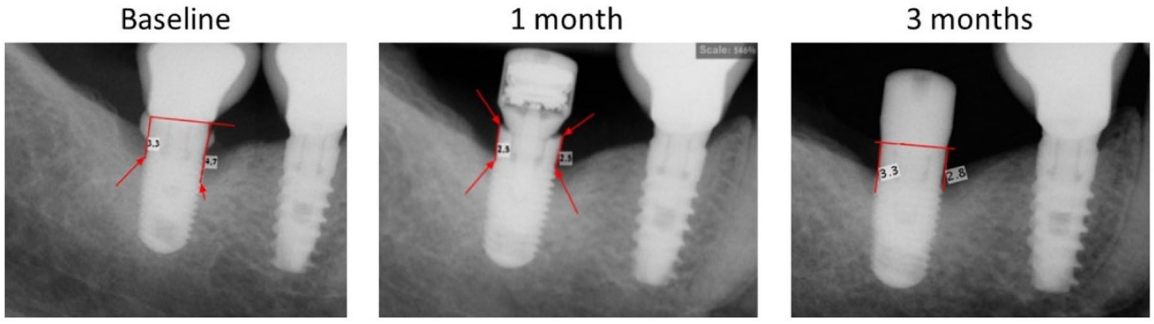

FIGURE 4 The distance from the implant shoulder to bone crest in a patient from the test group. 1, measurements taken at baseline; 2, measurements taken at 1 month; 3, measurement taken at 3 months.

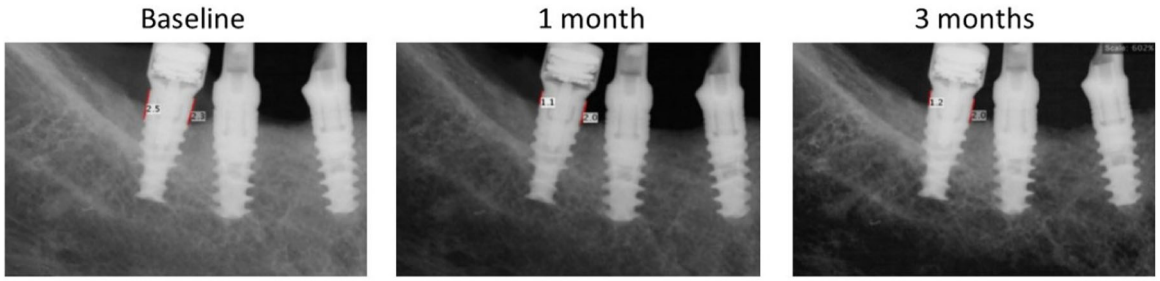

FIGURE 5 The distance from the implant shoulder to bone crest in a patient from the test group. 1, measurements taken at baseline; 2, measurements taken at 1 month; 3, measurement taken at 3 months.

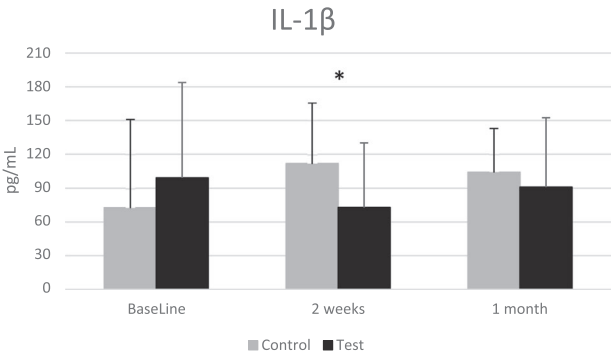

FIGURE 7 Levels of IL-1 at baseline (T0), 2 weeks (T1), and 1 month (T2). *$p < 0.05$. IL-1, interleukin-1.

Mechanical debridement alone usually provides clinical improvements in reduced bleeding tendency (20%–50%) and in some cases pocket reduction (≤1 mm) (Renvert et al., 2019). Our study reveals similar results where the control group which had mechanical debridement with sham MED, showed a delta of 1.3 mm improvement in PPD from 0 to 3 months, in addition to a reduced bleeding tendency. In general, mechanical debridement of implants with peri-implantitis may result in some improvement in the bleeding tendency but with limited effect on pocket reduction (Wang et al., 2019).

Power-driven air-polishing devices, antiseptics, antibiotics, Er:YAG lasers, metal curettes, and ultrasonic curettes with plastic sleeves can be used to clean the affected implants as an adjunct to debridement. Antiseptics have shown an additional benefit to PPD reduction of about 0.5 mm (Levin et al., 2015), furthermore exhibiting lesser sites with BOP (Levin et al., 2015; Machtei et al., 2012). A combination of mechanical debridement and systemic antibiotics reduced PPD (5.34 ± 1.29 mm vs. 3.69 ± 0.70 mm ($p < 0.001$) between baseline and 12 months), and achieved radiographic bone fill (a decrease from 1.87 ± 1.10 mm at baseline to 1.60 ± 1.19 mm at the 12-month follow-up [$p = 0.057$]), yet fails to resolve BOP (Nart et al., 2020). Adjunctive local antibiotics (minocycline, doxycycline) (Büchter et al., 2004; Renvert et al., 2008) with nonsurgical treatment may have additional positive benefits on PD but mainly on BOP. Laser-assisted therapy may result in short-term improvements primarily for BOP. There is insufficient evidence to support that any particular nonsurgical treatment for peri-implantitis shows better performance than debridement alone (Faggion et al., 2014). The additional use of adjunctive therapies provides only minimal clinical improvements in bleeding tendency and pocket reduction (Renvert et al., 2019). Predictable complete resolution of infection is challenging, and advanced lesions may still warrant surgical treatment (Renvert et al., 2011).

The present study was inspired from orthopedics where the use of PEMF has shown promising results in the quantity of new woven bone tissue, and improved repair within fibula fractures (Androjna et al., 2014), and fibular osteotomies (Midura et al., 2005) in rat models. Dental implants inserted into femurs of rabbit models, and the effect of PEMF was checked. The bone contact ratios of the PEMF-treated femurs were significantly larger than those of the control groups without the PEMF, in addition, a significantly greater amount of bone had formed around the implant of the 2-week treated femurs than the 1-week treated femurs, yet no significant difference was observed between the 2-week and 4-week treated femurs (Matsumoto et al., 2000). Regarding human dental studies, MED-abutment implants demonstrated a superior stability during the early phase of healing as compared with standard healing abutment implants and reduction of proinflammatory cytokines (Barak et al., 2019; Nayak et al., 2020). Both studies were done at implant placement and checked the effect MED on early phase of healing and implant stability. Barak and colleagues' paper revealed that resonance frequency analysis of at 30 days postimplantation demonstrated significantly increased stability in MED as compared with the control 73.5 ± 3.2 versus 66.7 ± 4.8 in mandibular implants and 74 ± 1.7 versus 65 ± 2.3 in maxillary implants (Barak et al., 2019). Nayak and colleagues found that MED-activated abutments resulted in an overall 13% increase of implant stability, while the control group showed an overall decrease of 2% ($p = 0.008$) (Nayak et al., 2020), in addition to a lower TNF-α concentration at 1 month.

According to the Magdent® manufacturer, the PEMF is active for 1 month, meaning there is an additive ongoing effect in addition to the initial debridement. This can be compared to slow-release antiseptic or antibiotic devices, which last for approximately 7–10 days in the periodontal pocket (Machtei et al., 2012; Soskolne et al., 1998). PPD reductions around implants are shown to be generally moderate with the use of antibiotics slow-release device (Renvert et al., 2006). On the other hand, the improvement in PPD with antiseptic slow-release device around implants was shown to be 2.21 mm after several applications (0, 2, 4, 6, 8, 12, and 18 weeks) (Machtei et al., 2012). These results are similar to ours. Nonetheless, our application of the MED abutment was done once without further intervention, that is, less cooperation needed.

As metal instruments were found to cause major damage to implant surfaces (Louropoulou et al., 2012), caution was taken while debriding the implant surface and the peri-implant tissue, that is, granulation tissue. While ultrasonic-driven devices were used to clean the granulation tissue as well as for the flushing effect of the debris in the periodontal pocket, a teflon-coated curette and a prophylaxis brush were used to clean the implant surface to minimize the alteration of the implant surface (Matarasso et al., 1996) and to maintain surface integrity for reosteointegration (Louropoulou et al., 2012).

It was found that PEMF enhanced cell proliferation, adhesion, and the osteogenic commitment of mesenchymal stem cells, even in inflammatory conditions (Ferroni et al., 2018). Their evidence indicated that PEMFs enhanced anti-inflammatory cytokine-IL-10 expression and reduced the expression of the proinflammatory cytokine IL-1 (Ferroni et al., 2018). A recent

clinical study showed that post-implantation cytokines levels (TNF-α and IL1-β) were lower in the PEMF-treated group (Nayak et al., 2020).

Regarding the cytokine profile of the PICF; according to a meta-analysis, IL-1β is the most studied cytokine. IL-1β controls the degradation of ECM during inflammation and wound healing. It was concluded that IL-1β can be used as additional criteria for a more robust diagnosis of peri-implant infection (Faot et al., 2015). The assessment of proinflammatory cytokines (mainly IL-1β) in the PICF was shown to be of beneficial value to differentiate between peri-implant health and disease (Schwarz et al., 2017). As low IL-1β levels characterize healthy peri-implant conditions, it is suggested to be used as a biochemical marker for the early diagnosis of peri-implant disease (Casado et al., 2013).

After 2 weeks of treatment, the levels of IL-1β in the PICF around MED-abutment implants was significantly lower when compared with sham MED. Other time points (T0 and T2) did not reach significant levels. Previous meta-analysis found that other nonsurgical treatments reduce the IL-1β levels including adjunctive use of lasers and antimicrobials agents (Moaven et al., 2022). These results are in a line with a recent previously published in vitro study that used MED which indicated that PEMFs heightened anti-inflammatory cytokine, such as IL-10 expression, and lessened the expression of the proinflammatory cytokine IL-1β (Casado et al., 2013). The reduction in IL-1β in test group for short period of time can be explained due to the short lifespan of the battery and the limited cleaning protocol. It appears that the reduction of IL-1β could be related to the reduction in biofilm caused by PEMF, as suggested by the study conducted by Faveri et al. (2020) using checkerboard DNA–DNA hybridization. The study demonstrated that after 96 h of PEMF exposure, there were antimicrobial effects on the bacterial species.

While the exact mechanism of how PEMF affects biofilm and reduces inflammation is not yet fully understood, there is growing evidence suggesting that PEMF therapy can be beneficial in reducing inflammation and promoting tissue repair. Our research had several limitations. This is a feasibility study with strict inclusion and exclusion criteria were done in order to prevent masking of different factors, and therefore the groups are relatively small. Furthermore, all patients included in the study were under strict periodontal maintenance with no residual pockets at other sites. It is important to note that the MED abutments can be screwed to standard implant connections with an internal hex solely, a factor that should be taken into consideration in future studies. Finally, the follow-up time was relatively short of only 3 months, that is, a longer follow-up period should be taken into consideration. Based on our pilot study and the power analysis, we have determined that it will be need a total sample size of 40 patients (20 in each group) to detect a difference of 0.9 in radiographic measurements between the groups, with a standard deviation of 0.76, using an independent t-test with a significance level of 5% and power of 90%.

5 | CONCLUSION

To the best of our knowledge, this is the first study that examined the effects of focused continues PEMF in treatment of peri-implantitis. Within all the limitations of this preliminary study, the test group improved clinical parameters, radiographic BL, and cytokine level after a short-term period compared to the control group. This implies, however, that a larger RCT study longer period of time is required to determine the effectiveness of this treatment.

AUTHOR CONTRIBUTIONS

Yaniv Mayer conceived the ideas, performed the treatment, collected the data, and led the writing. Juan Khoury collected the data, analyzed the data, and led the writing. Jacob Horwitz analyzed the data. Ofir Ginesin analyzed the data. Luigi Canullo analyzed the data. Eran Gabay analyzed the data. Hadar Z. Giladi analyzed and interpreted the data, and critically revised the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

ETHICS STATEMENT

The study was approved by the institutional ethical committee (Approval ID: RMB-0352-20) and registered at ClinicalTrials.gov (Identifier NCT04640857). The study was conducted according to the principles outlined in the Declaration of Helsinki and Ethical Conduct for Research with Human Beings. Informed consents were obtained from all the subjects who participated in this study. The clinical trial is reported in accordance with Consolidated Standards of Reporting (CONSORT) guidelines.

OPEN RESEARCH BADGES

This article has earned a Preregistered Research Designs badge for having a preregistered research design, available at https://clinicaltrials.gov/study/NCT04213144.

ORCID

Yaniv Mayer http://orcid.org/0000-0001-5500-7961

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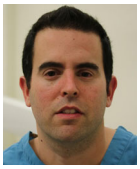
AUTHOR BIOGRAPHIES

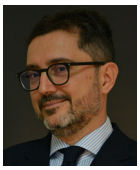
Yaniv Mayer is a clinical assistant professor in the Technion's Faculty of Medicine and a specialist in periodontics, past president of the Israeli society of periodontics and the director of clinical research and innovation in the department of periodontology in Rambam Health Care Campus, Haifa, Israel. Dr. Mayer acquired his dental education at the Hebrew University Hadassah School of Dental Medicine in Jerusalem and specialized in periodontics at Rambam's School of Graduate Dentistry. Dr. Mayer practices both basic and clinical research. His research is primary focused on utilizing new technologies, bone regeneration, and perio-systemic interactions.

Juan Khoury is a resident at the Department of Periodontology in Rambam Health Care Campus in Haifa, Israel. she is a graduate of the Hebrew University Faculty of Dental Medicine. Dr. Khoury is actively involved in both basic and clinical research in periodontology and implantology.

Jacob Horwitz is the chief of continuing education and periodontist at the Department Periodontology in Rambam Health Care Campus. He is a graduate of the Hebrew University Faculty of Dental Medicine and received specialty training at the Hebrew University Faculty of Dental Medicine, Department of Periodontology. His research interests focus on dental implants, 3D imaging and planning of dental implants, radiographic imaging, and monitoring of periodontal disease.



Ofir Ginesin is a specialist in periodontics and a senior physician in the Department of periodontology in Rambam Health Care Campus. He graduated from the Faculty of Dentistry of the Hebrew University and Hadassah and specialized in periodontal diseases and implants in the Periodontology Department of the Rambam Medical Center in Haifa. Engages in basic and clinical research within the Periodontology Department and the Bone Research Laboratory at the Rambam Research Institute.



Luigi Canullo is an assistant professor at the University of Genova (Italy). Graduated *cum laude* in Dentistry and Dental Prosthesis at the University of Rome "La Sapienza" in 1994. PhD at the University of Bonn (Germany). National and international speaker on surgical and prosthetic aspects of implant dentistry. Active member of the Italian Academy for Osseointegration (IAO) and European Academy of Osseointegration (EAO). Visiting Professor at the University of Bern (Switzerland).

Eran Gabay is a specialist in periodontics, deputy head of the department of periodontology, School of Graduate Dentistry, Rambam Health Care Campus, and the Technion Faculty of Medicine. Dr. Gabay specialized in periodontics at the School of Postgraduate Dentistry at Rambam Healthcare Campus in Haifa. Dr. Gabay acquired his dental education at the Hebrew University Hadassah School of Dental Medicine in Jerusalem and completed both a DMD

degree and a PhD degree. Dr. Gabay practice both clinical and basic science research, in the fields of periodontology and dental implantology.

Hadar Z. Giladi is a periodontal surgeon and researcher in the field of bone regeneration, and the Head of the Department of Periodontology at Rambam Health Care Campus. Head of the Laboratory for Bone Repair in the School of Graduate Dentistry at Rambam Health Care Campus, and a member of the Clinical Research Institute at Rambam (CRIR) where she performs her research.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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