



## Electromagnetic irradiation may be a new approach to therapy for peri-implantitis

Zhensheng Cao<sup>a</sup>, Yijia Chen<sup>a</sup>, Yuxue Chen<sup>a</sup>, Qing Zhao<sup>a</sup>, Xiaomei Xu<sup>b</sup>, Yangxi Chen<sup>a,\*</sup>

<sup>a</sup> Department of Orthodontics, West China Hospital of Stomatology, State Key Laboratory of Oral Diseases, Sichuan University, Chengdu 610041, Sichuan, PR China

<sup>b</sup> Department of Orthodontics, Stomatological Hospital of Luzhou Medical College, Luzhou 646000, Sichuan, PR China

### ARTICLE INFO

#### Article history:

Received 1 March 2011

Accepted 9 December 2011

### ABSTRACT

Peri-implantitis can lead to bone destruction around a dental implant through inflammation and immune reactions caused by bacteria adhering to the surface of the implant abutment. Electromagnetic irradiation can inhibit bacterial growth, increase bone formation, decrease bone resorption and reduce the inflammatory response. Our hypothesis is that electromagnetic irradiation may be a new treatment approach for peri-implantitis and may simultaneously maintain bone mass around the dental implant. The results would be more significant when combined with other agents, because the effect of some antibiotics and anti-inflammatory drugs is strengthened by electromagnetic irradiation. This non-invasive therapy is expected to be conducted in a convenient manner, and even by patients at home, thereby facilitating the prevention and treatment of peri-implantitis.

© 2011 Elsevier Ltd. All rights reserved.

### Background

Dental implants have been employed successfully in the oral rehabilitation of edentulous patients. However, peri-implantitis is still the major reason implant failure [1]. Peri-implantitis is associated with a biofilm of oral microorganisms, predominantly anaerobic Gram-negative bacilli, which infect the gingival crevice and cause gingival inflammation.

Host-mediated immune responses to these microorganisms and gingival inflammation lead to the destruction of peri-implant tissues. The proinflammatory molecules such as interleukin-1 and tumor necrosis factor- $\alpha$ , and cytokine networks play essential roles in this process. Antigen-stimulated lymphocytes (B and T cells) also seem to be important. A final cascade of events leads to osteoclastogenesis and subsequent bone loss via receptor activator of nuclear factor- $\kappa$ B ligand (RANKL)/RANK/osteoprotegerin (OPG) molecular triad, which is the critical modulator in bone metabolism [2]. Thus the main goal of treatment of peri-implant disease is to control infection and prevent bone loss. However, present non-surgical therapy was not found to be effective. Minor beneficial effects of laser therapy on peri-implantitis have been shown, but this approach needs to be further evaluated [3]. Prevention is still the most important approach.

### Antibiotic characteristics of electromagnetic irradiation

As pathogenic bacteria cause a wide range of human infections and multidrug-resistant bacteria rise rapidly because of the extensive use of antibiotics, many physical means, including electromagnetic irradiation, are investigated for their potential use for inhibiting bacteria. There is evidence that electromagnetic irradiation of extremely high frequency and low intensity causes antibacterial effects on *Escherichia coli* and other bacteria [4]. These effects are dependent on the frequency and intensity of the electromagnetic irradiation, irradiation duration, composition of growth media, and membrane properties in the bacteria. Although the underlying mechanism is not clear, the sharp resonance influence of extremely high frequency electromagnetic irradiation on bacterial membrane and on genome or DNA and other types of biological macromolecules, as well as on structure and properties of water, is likely to be involved. It was suggested that, in bacteria, all or some of the degrees of freedom of certain biological structures take part in coherent self sustained oscillations, which are fed with metabolic energy. If an external electromagnetic field is applied at the same frequency, synchronization can take place, resulting in possible macromolecular conformational transitions followed by changes in cell function. Besides, electromagnetic irradiation can also reinforce the reciprocal reaction of organisms against the chemical agents such as inhibitors of bacterial transport systems and antibiotics that react with cells predominantly via their membranes [5,6]. Although present studies of the bacterial effects of extremely high frequency electromagnetic fields are limited to a few bacteria and the mechanisms need to be further investigated; electromagnetic irradiation is a promising therapeutic approach to

\* Corresponding author. Tel.: +86 028 85502207.

E-mail address: [hxchenyangxi@hotmail.com](mailto:hxchenyangxi@hotmail.com) (Y. Chen).

preventing bacterial infection, and for a wide range of bone disorders [7].

### Effect of electromagnetic irradiation on bone remodeling and implant osseointegration

Electromagnetic irradiation can enhance differentiation of mesenchymal stem cells responsible for the increase in extracellular matrix synthesis and bone maturation, and enhanced proliferation of bone marrow mesenchymal stem cells. Electromagnetic irradiation can also increase mineralization in osteoblast-like cell cultures, potentially during transcription, cell proliferation and differentiation. Chang found that osteoclastogenesis can be inhibited by electromagnetic stimulation, attributed to a concomitant decrease in local factor production, including Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin 1 $\beta$  (IL-1 $\beta$ ), and interleukin 6 (IL-6) [8]. Chang also showed how the electromagnetic field induced up-regulation of OPG while RANKL mRNA expression was down-regulated, resulting in an increased OPG/RANKL ratio which is the key axis in bone remodeling [9]. Researchers have also examined the effect of applying a pulsed electromagnetic field on bone formation around a dental implant, finding that bone-healing and peri-implant bone formation are accelerated under conditions of proper magnetic intensity, duration per day, and length of treatment [10]. The electromagnetic field can decrease inflammatory response. Albeit general, the inflammation sometimes is a severe threat to the host, e.g., peri-implantitis is currently implicated as the main reason for implant failure. Myriad agents and therapies have been carried out in attempts at preventing or decreasing the inflammatory response. Recently, low-intensity, extremely high-frequency electromagnetic radiation, showed anti-inflammatory effects, which is frequency and power dependent and which may be enhanced when combined with other anti-inflammatory drugs such as diclofenac [11]. Arachidonic acid metabolites and histamine are likely to be involved in the process. The electromagnetic field can increase the content of lipid messengers in phospholipids of cellular membranes involved in inflammatory and immune reactions, facilitating the realization of its anti-inflammatory effects [12].

### Hypothesis

Peri-implantitis can cause bone destruction around the implant through the inflammation and immune reaction caused by bacteria adhering to the surface of the implant abutment. Electromagnetic irradiation can inhibit the bacteria, increase bone formation, decrease bone resorption, and reduce the inflammatory response. Thus, our hypothesis is that the application of electromagnetic irradiation may be a new treatment approach for peri-implantitis and for maintaining bone mass around the dental implant. The effect would be more significant when combined with other agents, as the effect of some antibiotic and anti-inflammatory drugs is strengthened with electromagnetic irradiation. Therapeutic efficacy is probably dependent on the intensity, frequency of exposure and duration of the electromagnetic irradiation.

### Evaluation of the hypothesis

This hypothesis is based on the following three points: (1) The primary etiologic factor of peri-implantitis are pathogenic bacteria, which may be inhibited by electromagnetic irradiation. (2) Bone loss around the implant, which will lead to loosening and eventual failure of the implant, is the hallmark of peri-implantitis. Electromagnetic irradiation can increase bone formation and decrease bone resorption, resulting in positive bone remodeling. Furthermore, reports have also showed that electromagnetic fields can

accelerate osseointegration around the dental implant. (3) Gingival inflammation around the implant is an important step in the pathology of peri-implantitis as some cytokines that regulate bone remodeling are released during inflammation. Electromagnetic radiation has significant anti-inflammatory activity, which can be enhanced when combined with non-steroidal anti-inflammatory drugs. Apart from the effect mentioned above, the electromagnetic field also influences other tissue. However, long-term practice and clinical employment of electromagnetic field in the Russian Federation and Eastern European countries has shown that electromagnetic therapy, as a rule, has no side effects and remote adverse consequences. It is non-invasive, possesses a variety of medical effects, and augments other methods (medicinal, surgical, physiotherapeutic); strengthening their efficacy, and removing side effects [13]. Although a variety of treatment methods have been spawned, the dental implant has been, and remains at risk for peri-implantitis from its inception. More effective and more convenient treatment modalities for peri-implantitis are needed for the amelioration of this situation in the field of implant dentistry. Because of its effect on key pathological steps of peri-implantitis, electromagnetic irradiation may be applied as therapy for peri-implantitis. The influence of electromagnetic radiation intensity, frequency and duration of exposure, are areas for future scientific investigation. Electromagnetic fields can be produced by portable devices and influence tissues non-invasively. Future devices for the treatment of peri-implantitis may be designed for domestic use, facilitating an acceptance rating by the general public, similar to that of current preventive devices like dental floss. Thus, treatment and prevention of peri-implantitis may be rendered more feasible, resulting in greater long term success for dental implants.

### Conflict of interest statement

None declared.

### Acknowledgements

This study is supported in part by the National Nature Science Foundation of China (Grant Nos. 30801316/c170804 and 30801206/c161201), and we wish to express our sincere gratitude to Dr. Gerald Volière for his encouragement and critical reading of the manuscript.

### References

- [1] Heitz-Mayfield IJ. Peri-implant diseases: diagnosis and risk indicators. *J Clin Periodontol* 2008;35(Suppl. 8):292–304.
- [2] Fransson C et al. Severity and pattern of peri-implantitis-associated bone loss. *J Clin Periodontol* 2010;37(5):442–8.
- [3] Renvert S, Roos-Jansaker AM, Claffey N. Non-surgical treatment of peri-implant mucositis and peri-implantitis: a literature review. *J Clin Periodontol* 2008;35(Suppl. 8):305–15.
- [4] Torgomyan H, Trchounian A. Low-intensity electromagnetic irradiation of 70.6 and 73 GHz frequencies enhances the effects of disulfide bonds reducer on *Escherichia coli* growth and affects the bacterial surface oxidation-reduction state. *Biochem Biophys Res Commun* 2011;414(1):265–9.
- [5] Torgomyan H, Tadevosyan H, Trchounian A. Extremely high frequency electromagnetic irradiation in combination with antibiotics enhances antibacterial effects on *Escherichia coli*. *Curr Microbiol* 2010;62(3):962–7.
- [6] Tadevosyan H, Kalantaryan V, Trchounian A. Extremely high frequency electromagnetic radiation enforces bacterial effects of inhibitors and antibiotics. *Cell Biochem Biophys* 2008;51(2–3):97–103.
- [7] Griffin XL, Warner F, Costa M. The role of electromagnetic stimulation in the management of established non-union of long bone fractures: what is the evidence? *2008;39(4):419–29*
- [8] Chang K et al. Pulsed electromagnetic field stimulation of bone marrow cells derived from ovariectomized rats affects osteoclast formation and local factor production. *Bioelectromagnetics* 2004;25(2):134–41.
- [9] Chang WH. Effect of pulse-burst electromagnetic field stimulation on osteoblast cell activities. *Bioelectromagnetics* 2004;25(6):457–65.

- [10] Grana DR, Marcos HJ, Kokubu GA. Pulsed electromagnetic fields as adjuvant therapy in bone healing and peri-implant bone formation: an experimental study in rats. *Acta Odontol Latinoam* 2008;21(1):77–83.
- [11] Gapeyev AB, Mikhailik NK, Chemeris NK. Anti-inflammatory effects of low-intensity extremely high-frequency electromagnetic radiation: frequency and power dependence. *Bioelectromagnetics* 2008;29(3):197–206.
- [12] Gapeyev AB, Kulagina TP, Aripovsky AV, Chemeris NK. The role of fatty acids in anti-inflammatory effects of low-intensity extremely high-frequency electromagnetic radiation. *Bioelectromagnetics* 2011;32(5):388–95.
- [13] Pakhomov AG, Murthy PR. Low-intensity millimeter waves as a novel therapeutic modality. *IEEE transactions on plasma science* 2000;28(1):34–40.