BONE REGENERATION

# Therapeutic Low Level Ultrasound and Its Biostimulation Effect on Dental Implant Osseointegration

**Elaf Akram Abdulhameed[1,2], Hamid Hammad Enezei[3,4], Marzuki Omar[2], A.R. Samsudin[1]**

## ABSTRACT

***Background:*** **Marginal bone loss still represents an inevitable risk factor in implant therapy and need a solution. Low power (or level) pulsed ultrasound (LIPUS) holds tremendous potential therapy with great promise as a bone.**

***Aim of this study:*** **To evaluate the effect of LIPUS therapy on bone regeneration and pain relief after surgery following implant insertion.**

***Methods:*** **The study sample is comprised of 14 patients; total of 20 dental implants were installed, who were divided equally into two groups randomly; ultrasound and non-ultrasound. Following maxillary surgery and dental implants insertion, LIPUS treatment was applied 20 min/day to the left or right side for twice a week beginning 2 weeks following dental implant placement for the subsequent 8 weeks after delivered of prosthesis. Control group was treated with sham-LIPUS. Cone Beam CT (CBCT) were obtained immediately after surgery and 6 weeks later. The peri-implant bone regeneration and stability were measured using Resonance Frequency Analysis (RFA) techniquesat at day 0, 3 months and 9 months postoperative. Repeated measure ANOVA with significance level of $p < 0.05$ was used for the evaluation and comparison peri-implant bone regeneration. Postoperation pain was evaluated by means of visual analog scale.**

***Results:*** **With a success rate of 100%, there was an increase in marginal bone level on the buccal bone plate ($p < 0.05$) in the ultrasound group. RFA values were also increased significantly compared to control group with more marginal bone loss in non-ultrasound group, visual analog scale showed more improvement in pain perception issue of ultrasound group with significant decrease in anxiety levels between the day of surgery and the postoperative time points compared with non ultrasound group. For pain and anxiety control in response to LIPUS therapy, patients' questionnaire showed higher pain control and satisfaction in LIPUS group of treatment.**

***Conclusion:*** **LIPUS therapy presents remarkable qualities by increased in bone thickness, implant stability values and post operative complications. These findings may offer new treatment modalities in oral implantology field.**

## KEY WORDS

**dental implant, ultrasound, marginal bone loss, osseointegration**

## INTRODUCTION

Introduction of osseointegration, in 1969, by Professor Per-Ingvar Brånemark, at the Institute of Applied Biotechnology, University of Goteborg[1], opened new avenues in the endosseous dental implant treatment for the partially or fully edentulous patients[2]. Endosseous dental implants may be considered to be the most popular treatment option for partially and fully edentulous patients. It is generally accepted that implant success is primarily dependent upon or achieved by osseointegration, a direct contact between the implant surfaces and living bone[3]. Numerous studies have been published regarding the efforts to increase the quality of osseointegration and shortening the osseointegration time[4,5]. It is generally accepted that implant success is primarily dependent upon or achieved by osseointegration, a direct structural and functional contact between the implant surfaces and living bone[6].

The mechanism behind the effect of LIPUS on bone regeneration might start from the mechanotransduction pathways of LIPUS on bone wound healing which is considered a complex process as numerous cell types respond to this stimulus involving several pathways. Mechanotransduction refers to the processes through which cells sense and response to mechanical stimuli by converting them to biochemical signals that elicit specific cellular responses[7]. Typically the mechanical stimulus gets filtered in the conveying medium before reaching the site of mechanotransduction. Cellular responses to mechanotransduction are variable and give rise to a variety of changes and sensations. From defi-

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1) Sharjah Institute for Medical Research, University of Sharjah
UAE
2) University Science Malaysia (USM)
Malaysia
3) Department of Oral & Maxillofacial Surgery, College of Dentistry, University of Anbar
Ramadi-Iraq
4) Department of Oral & Maxillofacial Surgery, School of Dental Sciences, Universiti Sains Malaysia Health Campus
Kelantan, Malaysia
Correspondence to: Elaf Akram Abdulhameed
(e-mail: elaf.alzubaidi@gmail.com)

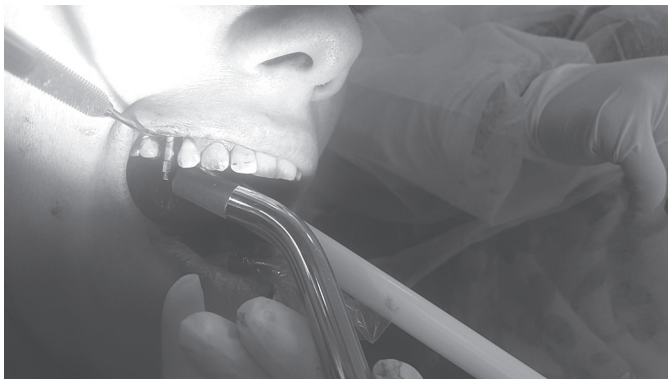

**Figure 1. RFA measurement procedure, the probe close to the smartpeg™ and at bucco-palatal and mesio-distal directions reveals a value of 70 as primary stability on day of implant placement surgery.**

nition of mechanotransduction, LIPUS promotes activation of osteoblast and other necessary cells functions which are considered decisive elements in bone healing by increasing proliferation, migration and differentiation of these cells and change it from inactive phase to active cells. The cellular responses underlying this mechanism are termed mechanotransduction[8]. Dental implant fixture showed the histologic features of the osseointegration upon insertion with functional ankylosis and without any intrusion of connective or fibrous tissues between the implant surface and bone[9]. However, in some situations osseointegration do not take place adequately and at times lead to implant failure. Continuous investigations looking into implant chemical, physical and structural characteristics and the biological response from the surrounding bone are being conducting to identify its causes. Implant success depends upon inseparably on the bone surroundings. Evaluation of the bone surrounding the implant is a common method for observing the implant prognosis[10].

Assessment of changes in marginal bone height is considered an important parameter in evaluating implant success[11]. Excessive marginal bone loss after implant surgery or following prosthesis is seen in the first year. However, in the early phase of osseointegration the process of bone healing is not well understood. One of the etiological factors of marginal bone loss is the disruption of periosteum during flap elevation and placement of implant[12]. Continuous bone resorption affects both function and aesthetic of the implanted teeth. There are several ways to restore and regenerate bone such as advocating bone grafting procedures, usage of growth factors, laser therapy in low levels and therapeutic ultrasound. Low Intensity Pulsed Ultrasound (LIPUS) stimulation is a classical therapeutic modality for bone regeneration. Its efficacy has been widely reported over the years. LIPUS stimulation can be used as a tool to enhance tooth and periodontal regeneration. Besides, enhances bone regeneration based on its angiogenic and osteogenic values both before and after dental implant placement. Current study aimed to evaluate the effect of LIPUS therapy on bone regeneration (bone-implant interface) which is considered the area of interest in our design of the study.

## MATERIALS AND METHODS

This study was approved by the University Human Research and Ethics Committee at the University of Sharjah. The selected age groups were between 20 and 40 years old. All patients were recruited following inclusion and exclusion criteria. Patients in this study were divided into 2 groups; namely Ultrasound and Control, each patient received one or two maximum dental implant. In the first trial group (ultrasound), the ultrasound therapy was applied twice a week for 20 minutes that commenced 2 weeks after stage I implant surgery and continued for 8 weeks using LIPUS machine. The same ultrasound therapy process was repeated 2 weeks after crown installation and continued for another 8 weeks. Clinical data collection composed of measurements of implant stability by RFA values using osstell ISQ and CBCT images taken immediately after the placement of the implant and during follow-up clinical examinations at 3rd and 9th month post-operatively (Figure 2). Total sample size used in this study was comprised of 14 patients; total of 20 dental implants were installed and equally divided into 2 groups, Ultrasound group (n = 7) were subjected to the application of LIPUS and the control group (n = 7) were sham LIPUS used. The dental implant system were used in this study (THOMMEN Medical SPI ELEMENT MC INICELL) bone level type with different diameter was placed to replace the missing teeth for each patient. Radiographic linear measurements of bone thickness (height and width) were taken at 3 different views, (coronal, sagittal and axial) per implant with 4 readings per view. The plat-

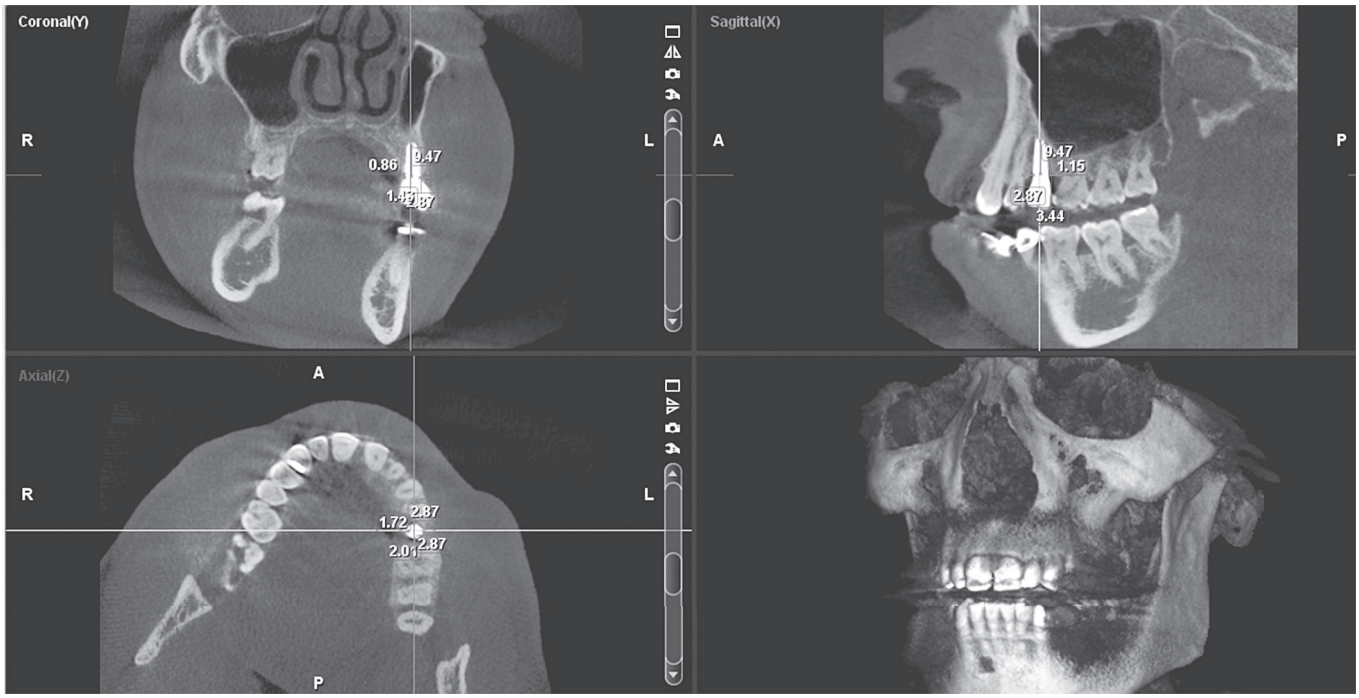


**Figure 2. CBCT image, linear measurements using 3D explorer option of Planmeca Romexis® software at 3 different views (a. coronal, b. sagittal and c. axial) with its standardization**

**Table 1. Comparison of mean difference of marginal bone changes in coronal view within each group (Ultrasound and Control) based on time**

| Comparison | Variable | Ultrasound (n = 7) | | Control (n = 7) | |
|---|---|---|---|---|---|
| | | MD* (95% CI) | p-value | MD* (95% CI) | p-value |
| Day 0-3 Months | CB mm** | 0.19 (0.05,0.57) | 0.023 | -0.51 (-0.13,0.28) | 0.975 |
| | CP mm# | 0.11 (0.09,0.16) | 0.049 | -0.05 (-0.17,0.28) | > 0.95 |
| | AB mm† | 1.20 (0.10,1.38 ) | 0.022 | -1.20 (-1.64,0.95) | 0.091 |
| | AP mm‡ | 0.89 (0.14,1.59) | 0.019 | -0.87 (-2.04,0.74) | 0.861 |
| Day 0-9 Months | CB mm | 0.38 (0.11,1.05) | < 0.001 | -0.58 (-0.40,0.34) | > 0.95 |
| | CP mm | 0.18 (0.33,0.55 ) | 0.035 | -0.40 (-0.47,0.88) | > 0.95 |
| | AB mm | 1.65 (0.25,1.53) | 0.027 | -0.88 (-1.62,1.11) | 0.860 |
| | AP mm | 1.02 (0.09,1.17) | 0.028 | -0.76 (-1.68,0.76) | 0.751 |
| 3 Months -9 Months | CB mm | 0.19 (0.25,0.53) | 0.021 | -0.07 (-0.47,0.26) | > 0.95 |
| | CP mm | 0.07 (0.41,0.57) | 0.033 | -0.35 (-0.39,0.69) | > 0.95 |
| | AB mm | 0.45 (0.23,0.53) | 0.036 | -0.32 (-0.40,0.26) | > 0.95 |
| | AP mm | 0.13 (0.28,0.76) | 0.037 | -0.11 (-0.34,0.68) | > 0.95 |

Repeated measures ANOVA within group analysis was applied followed by pairwise comparison with confidence interval adjustment. Statistically significant at $p < 0.05$

MD* = Mean difference
CB** = Corono-buccal
CP# = Corono-palatal
AB† = Apico-buccal
AP‡ = Apico-palatal

**Table 2. Comparison of mean difference of marginal bone changes in axial view within groups (Ultrasound and Control) based on time**

| Comparison | Variable | Ultrasound (n = 7) | | Control (n = 7) | |
|---|---|---|---|---|---|
| | | MD* (mm) (95% CI) | p-value | MD* (mm) (95% CI) | p-value |
| Day 0-3 Months | AM mm** | 0.11 (0.32,0.46) | 0.025 | -0.53 (-0.08,0.10) | > 0.95 |
| | AD mm# | 0.06 (0.27,0.40) | 0.032 | -0.51 (-0.14,0.13) | > 0.95 |
| | AB mm† | 0.16 (0.50,0.64) | 0.017 | -0.52 (-0.15,0.37) | 0.828 |
| | AP mm‡ | 0.08 (0.19,0.28) | 0.030 | -0.08 (-0.21,0.25) | > 0.95 |
| Day 0-9 Months | AM mm | 0.25 (0.18,0.54) | 0.021 | -0.77 (-0.86,0.37) | 0.845 |
| | AD mm | 0.21 (0.23,0.61) | 0.042 | -0.68 (-0.44,0.24) | > 0.95 |
| | AB mm | 0.38 (0.23,0.99) | <0.001 | -0.58 (-0.03,0.41) | 0.101 |
| | AP mm | 0.18 (0.15,0.33) | 0.043 | -0.45 (-0.37,0.25) | > 0.95 |
| 3 Months-9 Months | AM mm | 0.14 (0.10,0.34) | < 0.001 | -0.24 (-0.84,0.33) | 0.717 |
| | AD mm | 0.15 (0.13,0.45) | 0.022 | -0.17 (-0.35,0.15) | 0.888 |
| | AB mm | 0.22 (0.19,0.43) | < 0.001 | -0.06 (-0.91,0.25) | 0.596 |
| | AP mm | 0.1 (0.11,0.39) | 0.037 | -0.37 (-0.36,0.20) | > 0.95 |

Repeated measures ANOVA within group analysis was applied followed by pairwise comparison with confidence interval adjustment. Statistically significant at $p < 0.05$

MD* = Mean difference
AM** = Axio-mesial
AB† = Axio-buccal
AD# = Axio-distal
AP‡ = Axio-palatal

form of the dental implant represent the reference point, therefore any increase in bone height or width above this line was recorded in positive value and any decrease in bone height or width below the reference line was recorded in negative value (Figure 2). Postoperation pain was evaluated and the preoperative data were collected for each patient participant in this study (collect a medical history and demographic data) and a surgical planning session with a prosthetist. Prior to surgery, the questionnaires were completed 30 minutes before performing the surgery to obtain a complete anamnesis and pain scale data (0 = no pain, 10 = worst pain) by means of visual analog scale used to investigate the positive effect of LIPUS on pain control may be orginate form wound healing around dental implant insertion area. Another step was conducted is the transoperative investigation by mean during the surgical procedure, to obtain data concerning the following parameters: the profile of the patient at the moment of surgery. Finally, postoperative After completing the surgical stage, the patients were followed within 14 days of the procedure; during this period, the sutures were removed. At this stage, the patients were analyzed for changes in daily activities such as (a) chewing, (b) extended mouth opening, (c) communication, (d) sleep, (e) work/school activities, (f) daily routines, (g) social life, and (h) favorite activities. Additionally, each patient was consulted 3 days after the surgical procedure to evaluate the symptoms of swelling, bruising, bleeding, nausea, bad taste/bad breath, and pain. When necessary, these patients were called for an immediate postsurgical evaluation. All patients were analyzed seven days postoperatively to determine the pain scale, the presence of impacted food and the pattern of healing. Additionally, the patients completed the questionnaire on the day of surgery (time zero) and at the seven day follow-up visit time of follow-up during suture removal. Dental implant patient, describes how he feels at the moment by responding to 20 items as follows: 1) absolutely not; 2) slightly; 3) somewhat; or 4) very much. The participants generally describe their psychological state at that moment by responding to 20 questions with one of four answers: a) rarely; b) sometimes; c) frequently; or d) almost always.

## STATISTICAL ANALYSIS

Statistical analyses were performed using statistical software PASW® Statistics 20.0 (SPSS Inc, Chicago, IL, USA). Normality of the data was examined through Kolmogorov- Smirnov test and the results showed that the data was normally distributed. Thus, the data were expressed as mean and standard deviation (mean and SD). Repeated measures ANOVA was used for the evaluation and comparison within the same group and between two different groups of study based on time. Data showed no extreme values in each group. Mean differences were evaluated. Repeated measures ANOVA was robust to slight non normality and small sample size but not to extreme values[13]. A p-value of less than 0.05 was considered statistically significant. A descriptive

statistical analysis were conducted also to analysis the questionnaires designed in this study for the demographic, medical history and installed implant data both transoperatively and postoperatively.

## RESULTS

All patients completed the 9 months follow up examination and all the dental implants achieved primary stability at the day of dental implant placement. After a period of 2 months of dental implant placement the final dental prosthesis was provided to each patient. At 2 months post-operative, gingival overgrowth and peri-coronal bone overgrowth were observed above the cover screw and healing cap post-operatively in the ultrasound group. No gingival overgrowth or peri-coronal bone overgrowth was observed in the control group and the gingiva around the cover screw and healing cap remain normal in size and color. In the CBCT images obtained at day 0, there was adequate availability of bone height and width at the platform of dental implant for both groups. At 3 months post-operative, there was an increase in buccal plate thickness of 0.2-0.3 mm in the ultrasound group compared to control group. At 9 months post-operative, there was marginal bone loss around dental implant in the control group and maintained bone height and width in the ultrasound group. In the coronal view, there was an overgrowth of the bone width at corono-buccal and corono-palatal and less reduction of the bone height at apico-buccal and apicopalatal in the ultrasound group but the bony tissue overgrowth was more pronounced at the buccal bone plate at 3 months and 9 months rather than at the palatal bone plate. In the control group, the marginal bone loss was more in height and width compared to ultrasound group.

In the sagittal view, there was an overgrowth of the bone width at sagitto-mesial and sagitto-distal aspects of dental implants and less reduction of the bone height at apico-mesial and apico-distal in the ultrasound group but the bony tissue overgrowth was more pronounced at the mesial bone plate at 3 months and 9 months. In the control group, there was a reduction in the bone width and height from day 0 to 9 months. In the axial view, the bony tissue overgrowth was revealed the axio-buccal than axio-palatal, axio-mesial and axio-distal bone plate at 3 months and 9 months in the ultrasound group while in the control group there was marginal bone loss in all aspects of dental implant. In the coronal view, within the ultrasound group there was statistically significant increase in the buccal and palatal bones thickness (height and width) from day 0 to 3 months, day 0 and 9 months and from 3 months to 9 months as p-value was less than 0.05, but it was more pronounced at the buccal bone plate, While in the control group there was no statistically significant increase in bone thickness and there was marginal bone loss at all aspects of dental implant (Table 1). In the sagittal view, within the ultrasound group there was statistically significant increase in the mesial and distal bones thickness (height and width) from day 0 to month 3, day 0 and month 9 and from month 3 to month 9 as p-value was less than 0.05, While in the control group there was no statistically significant increase in bone thickness and there was marginal bone loss at all aspects of dental implant.

In the axial view, within the ultrasound group there was statistically significant increase in the buccal, palatal, mesial and distal bones thickness (height and width) from day 0 to 3 months, day 0 and 9 months and from 3 months to month 9 as p-value was less than 0.05, While in the control group there was no statistically significant increase in bone thickness (Table 2). For both groups (Ultrasound and Control) there was an increase in the mean RFA values but it was more significant in the ultrasound group compared to the control group and those RFA values were statistically significant p-value was $< 0.05$ from day 0 to 9 months and from 3 months to 9 months. Questionnaires results were completed within 30 minutes before performing the surgery, during, and three weeks after surgical session of implant insertion procedure. LIPUS group showed high scores of satisfections including pain control and anxiety compared it to non LIPUS group. Therefore, this step should be based on adequate analgesia and management of patient anxiety, as these strategies result in a reduction in their pain experience and anxiety levels during rehabilitation treatment.

## DISCUSSION

Marginal bone loss is considered to be an inevitable risk factor in implant therapy. The reduction in height and width of marginal bone level affects the success rate of implant treatment in terms of aesthetic and function. The majority of marginal bone loss occurs in the first year after implant placement[14]. Thus, the clinical crown-to-implant ratio rises with time to become more unfavorable as years go by. However, the etiology of long-term marginal bone loss or late implant failure seems to be of different origin and prone to peri-implantitis or occlusal overload[15]. It is important to consider multiple factors together in assessing implant failure rates as interactive effects may be observed in the establishment and maintenance of osseointegration. Thus, in the present study, attempts were made to control the relevant confounding variables (patient gender and age, implant location, implant diameter and neck design, insertion torque, insertion depth, and crown-to-implant ratios). In this study project we tried to measure the marginal bone level around the implant and its stability both at the time of implant placement and at time of loading. For this reason we chose the 3 and 9 months intervals to examine the marginal bone level and implant stability after soft and hard tissue maturation and early bone remodeling. Ultrasound is the generation of sound waves with a frequency above the limit of human audibility of 20 kHz that transfers mechanical energy into the tissues; it is used extensively in sports medicine and physiotherapy. Therapeutic ultrasound can induce angiogenic and bone morphogenetic factors and bone formation *in vitro*. Clinical findings of the present study demonstrate wide acceptance of patients toward post-operative ultrasound therapy. Kamath *et al*. (2015)[16] in his study on the effect of LIPUS on healing of femur fracture revealed that there was more significant callous formation at the early stage of femur fracture in the LIPUS group compared to control group. Therefore, even in other parts of the body like femur there are good results when LIPUS is applied. In view of the increasing use of high-intensity and low frequency ultrasonic technology, in medicine and in surgery, better understanding of the benefits or side effects of US application is significant in order to establish appropriate clinical studies maints comfortable patients' status along with LIPUS therapy/dental implant. Nevertheless, therapeutic LIPUS is proposed to deliver energy to deep tissue sites through ultrasonic waves, to produce increases in tissue temperature or non-thermal physiologic changes. Ebadi *et al*. (2011)[17] explained that ultrasonic energy causes soft tissue molecules to vibrate from exposure to the acoustic wave. This increased molecular motion generates frictional heat, thus increasing tissue temperature. Referred to as ultrasound's "thermal effects", this heating is proposed to increase collagen extensibility, increase nerve conduction velocity, alter local vascular perfusion, increase enzymatic activity, alter contractile activity of skeletal muscle, and increase nociceptive threshold[18]. However, in our study, the intensity of LIPUS used 30mW/cm2 and the duration of application was only for 20 minutes and this treatment was commenced 2 weeks after the acute inflammatory phase has subsided. CBCT images showed adequate availability of bone height and width at the dental implant platform for both groups. In this study, results obtained using CBCT were reliable for linear measurements of bone thickness in height and width for both ultrasound treated group and control group. At 3 months, there was an increase of buccal bone plate width of 19% in the ultrasound group compared to control group . At 9 months, there was a mean marginal bone loss of 58% in width of the buccal bone plate around dental implant platform in the control compared to 45% increase in the mean buccal bone width in the ultrasound group. The justification of using LIPUS in this study is to accelerate the bone wound healing processes within the region of interest (ROI) which is the region replacing missing teeth r following trauma to the bone as implant placement surgery is considered to be traumatic procedure even though the surgery is minimally invasive to bone. Our aim in this study is to mimic what happened in natural tissue repair by inducing, triggering and provocating of the cells related to bone formation by encouragement of mechanotransduction pathways involved in cell responses[19-21]. These responses include integrin/mitogen-activated protein kinase (MAPK) and other kinases signaling pathways, gap-junctional intercellular communication, up-regulation and clustering of integrins, involvement of the most important protein Cx43)[22]. Based on time intensity and period of exposure of cells to waves of ultrasound, LIPUS can recruit mesenchymal stem cells from neighboring tissues and other sites in the body in attractive processes (chemotactic) with other biomedical pro-inflammatory mediators (growth factors) which are considered necessary in bone wound healing processes and triggers it from inactive phase to the active form[20]. In our study, The marginal bone level was assessed and measured at three different views (coronal, sagittal and axial) in which four points were located and measured per implant (apico-buccal and apico-palatal, sagitto-mesial and sagitto-distal aspects, axio-buccal than axio-palatal, axio-mesial and axio-distal respectively and at three different time interval post-operatively at day 0, 3 months and 9 months. The results of this study showed an increase in buccal bone width from 1.43 mm at day 0 to 2.51 mm at 9 months

which revealed the buccal bone plate width increased by 45% while, the palatal bone width was also increased by 22% at 9 months.

Results of the control group showed increased loss of bone height from 1.20 mm at 3 months to 0.88 mm at 9 months at the apico-buccal aspect of the dental implant and increased MBL in width from 1.43mm at day 0 to 0.85 mm at 9 months as compared with LIPUS treated group. It reveals that LIPUS has positive effect on the healing of bone and the loss of marginal bone in the control group was contributed to no using US therapy. For control of pain, The vast majority of the installed implants were pain control beside the success level; therefore, the implants were installed at the bone level by surgical invasive procedure. Before and after completing the surgical implant insertion, mandatory using suitable protocol for control infections and pain: antibiotic and effective pain killer (analgesic, anti-inflammatory) before surgery followed postoperatively suitable agents must be used as prophylaxis[24].

The results of the LIPUS treated group showed higher values of RFA (75.45) at 9 months as compared with the value of RFA (55.54) at 9 months in the control group. This finding is in agreement with previous finding[25]. Alterations in the ISQ values in the early and the late phase of osseointegration periods have been compared between the groups in terms of implant stability. Our results further indicated that increased bone thickness with good fixture stability and no marginal bone loss was seen in US group indicated the activities of osteogenesis in the ROI

## CONCLUSION

The clinical results shown in this study confirmed that LIPUS have powerful therapeutic potential to promote an environment conductive to neovascularization and osteogenesis in bone regeneration. These findings may offer new treatment modalities in oral implantology field.

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## RFEFERENCES

1) Jayesh, R. S. & Dhinakarsamy, V. Osseointegration. Journal of pharmacy & bioallied sciences 2015; 7: 226-232.
2) Kishore, K., Anne, G., Mohan, T., Kumar, K., Dev, J., Rakesh, R. & Devi, N. Evaluation Of Crestal Bone Loss Around Two Different Implant Systems Supporting A Mandibular Overdenture-A Clinical Study. Indian Journal of Dental Sciences 2014; 6: 001-004.
3) Brånemark PI, Zarb G, Albreksson T. Tissue-integrated prosthesis. In: Brånemark PI, ed. Osseointegration in clinical dentistry. Chicago, Il: Quintessence Publishing Co., 1985:11-76.
4) Barzelai S, Sharabani-Yosef O, Holbova R, Castel D, Walden R, Engelberg S, Scheinowitz M. Low-intensity ultrasound induces angiogenesis in rat-limb ischemia. Ultrasound Med Biol 2006; 32:139-145.
5) Wang SJ, Lewallen DG, Bolander ME, Chao EY, Ilstrup DM, Greenleaf JF. Low intensity ultrasound treatment increases strength in a rat femoral fracture model. J Orthop Res 1994; 12:40-47.
6) Albrektsson, T., Hansson, H. & Ivarsson, B. Interface analysis of titanium and zirconium bone implants. Biomaterials 1985; 6: 97-101.
7) Gardinier, J. D., Majumdar, S., Duncan, R. L. & Wang, L. Cyclic hydraulic pressure and fluid flow differentially modulate cytoskeleton re-organization in MC3T3 osteoblasts. Cellular and molecular bioengineering 2009; 2: 133-143.
8) Katiyar, A., Duncan, R. L. & Sarkar, K. Ultrasound stimulation increases proliferation of MC3T3-E1 preosteoblast-like cells. Journal of therapeutic ultrasound 2014; 2: 1182-1181.
9) Parithimarkalaignan, S. & Padmanabhan, T. V. Osseointegration: an update. J Indian Prosthodont Soc 2013; 13: 2-6.
10) Ibrahim, N., Parsa, A., Hassan, B., van der Stelt, P. & Wismeijer, D. Diagnostic imaging of trabecular bone microstructure for oral implants: a literature review. Dentomaxillofac Radiol 2013; 42: 20120075.
11) Nandal, S., Ghalaut, P. & Shekhawat, H. A radiological evaluation of marginal bone around dental implants: An in-vivo study. Natl J Maxillofac Surg 2014; 5: 126-137.
12) Al-Juboori, M. J., Ab Rahman, S., Hassan, A., Bin Ismail, I. H. & Tawfiq, O. F. What is the effect of initial implant position on the crestal bone level in flap and flapless technique during healing period? J Periodontal Implant Sci 2013; 43: 153-159.
13) Rogness, N. Applying and Interpreting Statistics, A Comprehensive Guide. Journal of the American Statistical Association 2002; 97: 926-927.
14) Wennström, J. L., Ekestubbe, A., Gröndahl, K., Karlsson, S. & Lindhe, J. Implant-supported single-tooth restorations: a 5-year prospective study. Journal of clinical periodontology 2005; 32: 567-574.
15) Sakka, S., Baroudi, K. & Nassani, M. Z. Factors associated with early and late failure of dental implants. Journal of investigative and clinical dentistry 2012; 3: 258-261.
16) Kamath, J. B., Jayasheelan, N., Reddy, B., Muhammed, S. & Savur, A. The effect of low-intensity pulsed ultrasound therapy on fracture healing. Muller Journal of Medical Sciences and Research 2015; 6: 49-53.
17) Ebadi, S., Ansari, N. N., Henschke, N., Naghdi, S. & van Tulder, M. W. The effect of continuous ultrasound on chronic low back pain: protocol of a randomized controlled trial. BMC musculoskeletal disorders 2011; 12: 1112-1159.
18) Allen, R. J. Physical agents used in the management of chronic pain by physical therapists. Physical medicine and rehabilitation clinics of North America 2006; 17: 315-345.
19) Enezei HH, Ahmad A, Khamis MF, Ab Rahman R, Abdul NH and Mutum SS. Eff ects of local delivery of vascular endothelial growth factor on biological performance of the composite biomaterial used to accelerate bridging of critical-sized mandibular bone defect in rabbit model. J Med Bioeng 2015; 4: 93-99,
20) Enezei HH, Azlina A, Khamis MF, Rahman RA, Abdul Razak NH, Mutum SS, Samsudin AR. Effect of Local Implantation of Composite Biomaterial Loaded with Vascular Endothelial Growth Factor in Healing of Critical-Sized Mandibular Defect-A Pilot Study. J Dent Oral Disord Ther. 2014; 2 :1-5.
21) Enezei HH , Ahmad A, Khamis MF, Alshehadat S, Abdul Razak NH , Abbas SK, Ali Al Qabbani A and Alam MK. Enhanced Osteogenic and Angiogenic-Related Gene Expression of Human Dental Stem Cells on Biphasic Calcium Phosphate Scaffold Treated with Vascular Endothelial Growth Factor: Part I. J Hard Tissue Biol (Accepted), 26 (4); 2017 (in press).
22) Enezei HH and Al Qabbani. A. Antiresorber Bone Coupled with IGF-1 Supplementation in Maxillofacial Bone Cell Line Culture, Regeneration Mediated by Cx43 mRNA Expression. International Medical Journal. (In review).
23) Ganzorig K, Kuroda S, Maeda Y, Mansjur K, Sato M, Nagata K and Tanaka E. Low-intensity pulsed ultrasound enhances bone formation around miniscrew implants. Arch Oral Biol 60(6): 902-910, 2015
24) Enezei HH, Alam MK. Survival Analysis for the Use of Two Types of Antibiotics in the Remedy of Mandibular Third Molar Deep Abscess. International Medical Journal. 2015 Oct 1;22(5):430-432.
25) Nedir R, Bischof M, Szmukler?Moncler S, Bernard JP and Samson J. Predicting osseointegration by means of implant primary stability. Clin Oral Implants Res 15: 520-528, 2004