EGYPTIAN
DENTAL JOURNAL

VOL. 65, 1173:1185, APRIL, 2019

I.S.S.N 0070-9484

ORAL MEDICINE, X-RAY, ORAL BIOLOGY AND ORAL PATHOLOGY

www.eda-egypt.org • Codex : 43/1904

EFFECT OF COMBINED LOW INTENSITY LASER AND SUPPLEMENTARY MICRONUTRIENTS ON THE HEALING PHASE OF DENTAL IMPLANTS

Tarek Abdel-Hamid Harhash*

ABSTRACT

This study was aimed to assess the effect of low intensity laser (LIL) combined with supplementary micronutrients on the healing phase following endosteal dental implant insertion. Thirty implants were installed in the maxillary premolar regions of thirty male subjects of age ranged from 40-45 years old. Subjects were then randomly divided into three groups (I, II, and III), conventional, drug supplementation, and, laser groups. Following implant insertion, the healing phase of group (I) was left to progress spontaneously without any interference. Group (II) was given drug supplementation regimen for two months (one month before and one month after the implant surgery), while the implant insertion in laser group (III) was followed by low intensity (gallium arsenide diode) laser application with wavelength of 904 nm, an output power of 30 mWatts, and a frequency of 9999 Hz for 3 minutes in three sessions on three alternative days starting from the tenth post-operative day. A six month follow up period was applied radiographically to all subjects of both groups using sequential conventional radiographs. Radiographs were digitized by a professional scanner and bone density was recorded. The results revealed that drug therapy reduced the recommended healing time by 8% while laser therapy reduced the recommended healing time by 33%.

INTRODUCTION

Dental implants are becoming one of the fastest growing dental treatments today. They are used as replacements for single tooth loss, as the support for a bridge either to a natural tooth or to another implant, or to support prostheses (e.g. complete or partial dentures (1). In implant dentistry, a phenomenon called osseointegration has become the accepted standard for success in dental implants. Yet, failure of these devices associated with impaired healing, infection, and overload are well recognized (2). Osseointegration in theory and practice is defined as "continuing structural and functional coexistence, possibly in a symbiotic manner, between differentiated, adequately remodeled, biologic tissues and strictly defined and controlled synthetic

---

* Assist. Professor of Laser Dental Applications, Department of Medical applications of Laser, National Institute for Laser Enhancement Sciences, Cairo University.

components, providing lasting, specific clinical functions without initiating rejection mechanisms" (3). The mechanism of osseointegration is very similar to the primary bone healing. Thus, after surgical trauma, there is an inflammatory process, in which a mediator cascade promotes hematoma as well as circulatory alteration. Following, regeneration is developed and, consequently, the wound is replaced by bone tissue. Subsequently, wound maturation takes place by means of a remodeling mechanism, which is influenced by occlusion pressure (4). When an adequate regeneration occurs, there is a direct contact between the metal surface and bone tissue (osseointegration). Other types of peri-implant response can occur, like the presence of a collagen layer observed between bone and implant surfaces. Fairly prominent, this connective tissue zone consists of both parallel collagen fibers and supporting blood vascular elements, consistent with the anatomical organization of collagenous ligament (5, 6). This tissue response interface is called "fibro-osseous integration" (7). One of the requirements for inducing osseointegration is a stress-free healing period of 3-6 months using a 2-stage surgical procedure (conventional approach) to create a healing environment at the bone-implant interface that would facilitate regeneration and osseointegration rather than fibrous tissue encapsulation (8,9). Unfortunately, the mandibular 3 months and maxillary 6 months no-load healing periods may be inconvenient for certain patients (10, 11), discouraging them from seeking such treatment.

Adequate nutrition is essential for the development and maintenance of the skeleton, that is, bone health. Calcium phosphate, and vitamin D are essential for normal bone structure and function, but several other micronutrients also have essential roles in bone. Trace minerals function in bone metabolism, but their roles in preventing bone loss are not well established. In one study, the administration of several trace elements (copper, fluoride, manganese, and zinc) along with calcium for one year resulted in a smaller loss in lumbar BMD (bone mass density). In another study on hip fractures, clinical outcomes and BMD were improved in patients who were given supplements containing calcium, vitamin A and, vitamin D for an average of 38 days (12).

The effect of low-level laser therapy (LLLT) on wound healing and bone regeneration has become a focus of recent research. LLLT is based on biostimulation of the tissues with monochromatic light. Various biostimulatory effects have been reported on wound healing (13) and collagen synthesis (14). With respect to bone, LLLT has been shown to modulate inflammation (15), accelerate cell proliferation (16) and enhance healing (17). This is why the study was aimed to assess the effect of low intensity laser (LIL) versus supplementary micronutrients and to study the effect of the combination of both modalities on the healing phase following endosteal dental implant insertion.

MATERIAL AND METHODS

Case Selection

The study was performed on thirty selected males of age ranged from 40-45 years that were primarily diagnosed as having partially edentulous areas that require restoration.

Criteria of case selection

Cases were selected based on the following inclusion criteria:

- Selected case must have had at least one missed upper premolar in either side of the upper jaw.
- Cases were free from any acute or chronic systemic disorders.
- Cases were non-smokers.
- Cases were having a good oral hygiene or at least the ability to improve it.
- Cases were free from non-treated generalized progressive periodontitis.

- The neighboring teeth to the receptor site were free from any acute periapical pathology (tooth was non-sensitive to percussion).
- Selected cases did not receive any medications for at least one month before the beginning of the study.
- Cases were having missed tooth or teeth due to previous extractions, trauma, and aplasia but not due to pathologic changes in the receptor site (cysts, tumors, osteomyelitis, etc.).

All the study cases were informed about the study and were subjected to thorough diagnostic procedures included detailed medical and dental histories, clinical examination, radiographic examination, laboratory investigations, and study cast formation.

Case Categorization

The previous examinations and diagnostic procedures allowed the selection of thirty males that matched the criteria of case selection. Each case received an implant (***FRIADENT*** GmbH P.O. Box 71 01 11. 68221 Mannheim/Germany) in the place of a missed maxillary premolar. Subjects were then randomly divided into three groups (I, II, and III), in which each group contained ten cases.

Group I (Conventional Group): was left to progress spontaneously without any interference.

Group II (Drug Group): was given drug supplementation regimen for two months in order to cover the recommended daily allowance (RDA). The regimen started one month before the day of surgery and continued for another month after it. The regimen was composed of:

- One daily tablet of ***Centrum*** (***Wyeth*** **Pharmaceuticals**, Lederle Laboratories Division, American Cyanamid Co., Pearl River, NY 10965, USA), a Multivitamin drug with minerals to cover the daily requirements of essential micronutrients.
- Two daily tablets of ***Osteocare*** (***Vitabiotics*** **Ltd**., 1 Apsely Way, London NW2 7HF, UK), a natural dietary supplementation for bone integrity.

Group III (Laser Group): received low intensity laser in sessions during the healing phase that followed implant insertion.

Laser Application

Laser was applied to cases of group III (laser group) in three sessions on three alternative days started from the tenth post-operative day (after removal of the sutures). In each session, laser device (***ORALIA*** Dental Products Ltd., Weiherstraße 20, D-78465 Konstanz-Dettingen/Germany) was pre-adjusted to deliver a laser beam with a wavelength of 904 nm, an output power of 30 mW, and a frequency of 9999 Hz for 3 minutes. Along the pre-adjusted time (3 minutes), each surface (i.e. buccal, occlusal, and palatal surfaces respectively) was allowed to receive the laser beam for one minute. Laser beam was continuously delivered from the tip of the laser applicator and exposing the target surface while the tip was touching the tissues and directed towards the implant site. The applicator tip was moving in a continuous slow circular motion to assure full exposure of the target surface to the beam.

Radiographic Assessment

The evaluation of the osseointegration was radiographically performed through sequential radiographs taken to all cases at predetermined time intervals. The maintenance of the distance between x-ray tube, object, and radiographic film in a fixed position was obtained by fabricating a radiographic template from self-cure acrylic resin on the study cast of the upper dentition. Acrylic was applied on the edentulous area of the cast that represented the area of interest and was allowed to fill it and extend anteriorly and posteriorly to involve the crowns of the adjacent teeth. A periapical film packet was inserted horizontally into the posterior bite block of XCP device (***Rinn*** Corporation, 1212 Abott Drive, Elgin, Illinois, USA) and the bite block was adjusted over the occlusal plane while the film was centering the target area to be imaged and the entire horizontal length of bite block was utilized to position the film in the mid-palatal area.

Radiographic Schedule

Following the surgery, all the subjects were asked to recall according to a predetermined schedule for imaging procedures. A baseline radiograph was taken immediately postoperatively, and then the next images were taken at intervals of fifteen days for the next six months. The outcome of this procedure was thirteen standardized and reproducible images for each subject.

Film processing, image scanning and storing

Each set of films which belonged to the same subject was processed individually to assure that they received the same conditions during image processing. The procedure was applied to all films according to the recommended manufacturer's instructions.

The resultant images were scanned by means of high-resolution PC scanner. Images of each subject were stored in PC within an individual folder belonged to its corresponding subject.

Digital Image processing and Bone Density Determination

Image analysis was performed using ***IDRISI*** Kilimanjaro software (Clark Labs, Clark University, 950 Main Street, Worcester MA 01610-1477, USA) that facilitated image restoration, enhancement, and densiometric measurements. Image restoration allowed for both radiometric and geometric correction of images. Image restoration was followed by image enhancement which allowed for contrast adjustment to all images, in addition, image enhancement facilitated implant edge enhancement. This was followed by subtracting the implant image from the background image (image of the surrounding bone). Finally, the measurements of density were calibrated by quantifying image on 256 gray scales. Zero scale was given to totally black regions, 256th scale for totally white regions, while the values in between represented the variable shades of gray.

IDRISI assessed density of the surrounding bone by dividing it into two zones (fig. 1). The first zone was located just adjacent to implant and represented osseointegration zone (implant-bone interface). The second zone was located just adjacent to first zone and represented the bone surrounding the implant.

Statistical Analysis of Data

All data were collected, tabulated, and statistically analyzed. Descriptive statistics as average, maximum values, minimum values, standard deviation, and mean percentage change were calculated for zones one and two in both groups.

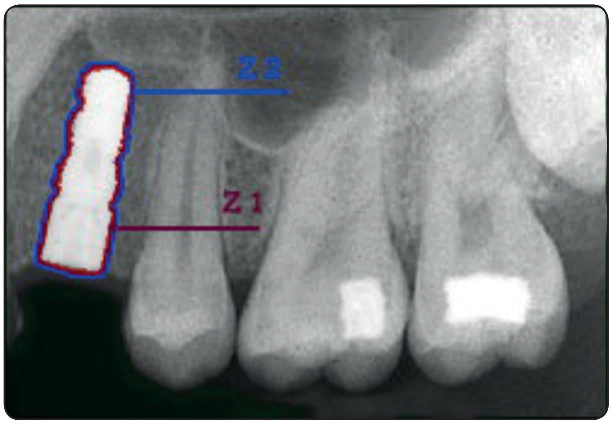

Fig. (1): The two zones of bone density analysis. Z1 represents the 1st zone (the osseointegration zone), while Z2 represents the 2nd zone (zone of the surrounding bone).

RESULTS

Figures 2, 3, and 4 present the comparisons between the average bone density values of the three groups at the first and the second zones respectively while figures 5, 6, and 7 present the comparisons between the percentage of changes in bone density of the groups at the first and the second zones respectively. There is an overall bone density increase in all groups at both zones along entire follow up period. Laser group attains the highest values, followed by the drug group while conventional group shows the lowest values.

Effect of Therapeutic Modalities on Bone Density

By applying ANOVA test for single factor on the mean bone density values at the first and the second zones of each group separately, the following results were obtained:

Conventional Group

The *calculated F* (15.40 for the 1st zone & 65.81 for the 2nd zone) was greater than *F critical* (2.34) at *0.01* level, which denoted that the increase in bone density per time is highly significant.

Laser Group:

The calculated F (115.96 for the 1st zone & 306.24 for the 2nd zone) was greater than F critical (2.34) at 0.01 level, which denoted that the increase in bone density per time is highly significant.

Effect of Time on Therapeutic Methods

The effect of time on each therapeutic modality was studied using t-test (two-sample assuming unequal variance) at a significance level 0.01 as time is the main parameter for evaluating the progression in bone density under the effect of each therapeutic method. The test was applied on each group between the baseline and each successive interval separately. This would reflect the progression in bone density along the entire follow up.

Non-laser groups (I and II)

The first zone of both groups (***conventional*** and ***drug*** groups) provided a significant difference that started from the 4th interval and continued to occur in the next intervals with the same level of significance up to the last one. Similar results were obtained in the second zone of the same group.

Laser group (III)

The first zone of laser group provided a significant difference that started from the 2nd interval and continued to occur in the next intervals with the same level of significance up to the last one. Similar results were obtained in the second zone of the same group. The difference in the results between both groups came to the favor of laser, in which its effect appeared to be a main factor in the early occurrence of the significant increase in bone density.

Comparative Analytical Studies

These studies were aiming to identify the effect of laser modality on bone density of osseointegration zone by comparing it to those of the conventional modality. In this context, a student t-test (two-sample assuming equal variance) was applied at a significance level 0.05, in which *t Critical* (two-tail) was always 2.1.

Effect of drug:

By comparing the t-test results of drug group with those of conventional group, the findings showed that drug didn't provide any significant effect along the entire follow up period when compared to conventional therapy owing to the insignificant increase in bone density along the follow up.

Effect of laser:

By comparing the t-test results of laser group with those of conventional group, the findings showed that laser produced a sustained significant effect on bone density. The effect started at the 2nd interval and extended along the rest of the intervals up to the end of the follow up.

Differential comparison between laser and drug:

By applying t-test between drug and laser, a significant difference was recorded at the 7th, 9th, and 10th intervals respectively. This denoted the individual effect of each therapeutic method on bone density. Drug produced a cumulative effect on bone density until its withdrawal after a month from operation, and then, its effect showed a gradual recession. During this recession, drug produced a non-symmetrical behavior on bone density. Such a behavior was similar to that of conventional therapy. The only difference is that drug provided slightly higher values of bone density while keeping the same behavior.

On the other hand, as laser biostimulates cells that present only in the proliferative phase or cells that are in a state of stress (adding to its variable actions on wounded area) thus, it produced an actual significant, sustained, and regular improvement on osseointegration.

By comparing drug with laser, the significance was recorded at the 7th, 9th, and 10th intervals respectively. This was explained by the asymmetry in the effect of drug on bone density compared to the symmetrical laser effect.

Efficiency of laser modality

Zone one: Evaluation of the efficiency of laser as a therapeutic method using the highest bone density value in conventional group as a reference (table 1) led to the determination of the rate by which drug as well as laser could accelerate osseointegration. This was performed by considering the highest bone density value in the conventional group (133.7) as a reference number as it also represents the last value at the end of the follow up period. With taking in consideration that the six months period is a recommended healing period by many authors after which implant could be exposed and loaded safely. An appropriate number to the determined reference number could be seen at the eleventh interval in drug group (after five and a half months) which means that drug succeeded in reducing the recommended healing time by 8% compared to the conventional method.

TABLE (1) Tracing the most appropriate bone density values in different groups in relation to the end value in conventional group at the first zone.

Intervals	Conventional	Laser	Drug
0	66.63	63.81	69.54
1	67.78	75.62	72.91
2	71.63	87.56	80.63
3	78.38	99.04	87.14
4	91.93	110.1	101.4
5	94.26	116.3	103.3
6	103.7	124.6	111.8
7	106.4	130.4	114.5
8	117.1	135.3	125.7
9	119.7	140.8	124.6
10	125.2	144.6	128.9
11	130.5	147.1	133.2
12	133.7	149.4	134.3

An appropriate number to the determined reference number could be seen at the eighth interval in laser group (after four months) which means that laser succeeded in reducing the recommended healing time by 33% compared to the conventional method.

Zone two: While the effect of the drug is similar to that at the first zone, the effect of laser at the second zone was weaker than that at the first zone (table 2). This could be explained by the greater effect of laser at sites that show inflammation, regeneration, cellular activity, and healing, in which the first zone is the zone of interaction after surgical wounding and implant insertion while the second zone is a relatively more stable zone.

TABLE (2) Tracing the highest average bone density value of conventional group versus laser group at the second zone.

Intervals	Conventional	Laser	Drug
0	29.76	28.23	30.20
1	30.04	33.55	31.65
2	31.99	38.51	34.91
3	35.60	43.54	38.61
4	42.02	48.41	45.69
5	46.11	54.28	50.51
6	47.38	58.08	51.23
7	54.23	64.99	58.34
8	61.73	69.03	65.32
9	61.80	76.50	64.61
10	66.32	80.82	68.28
11	71.20	88.09	72.65
12	73.83	95.87	74.14

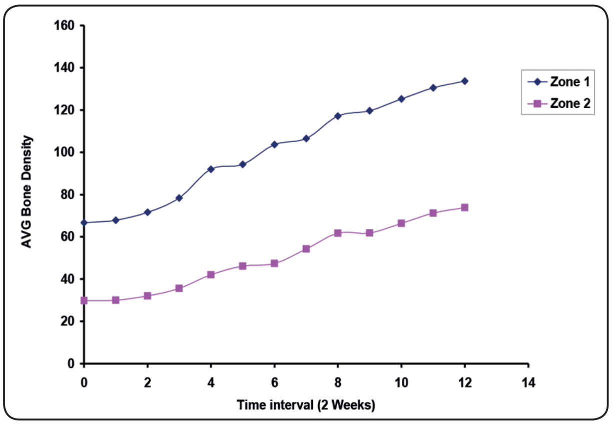

Fig. (2): Comparison between the mean bone density values at the first and second zones of Conventional group at different time intervals.

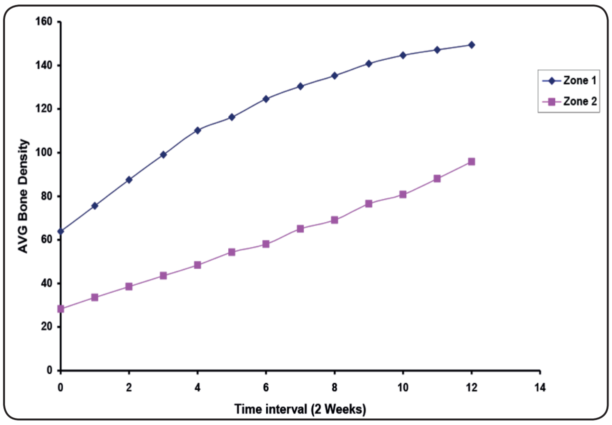

Fig. (3): Comparison between the mean bone density values at the first and second zones of Drug group at different time intervals.

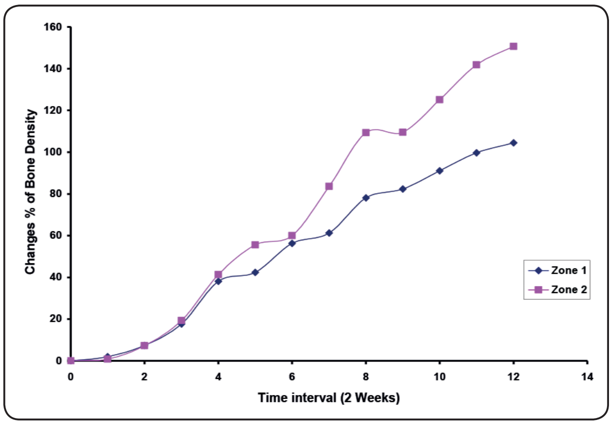

Fig. (4): Comparison between the mean bone density values at the first and second zones of Laser group at different time intervals.

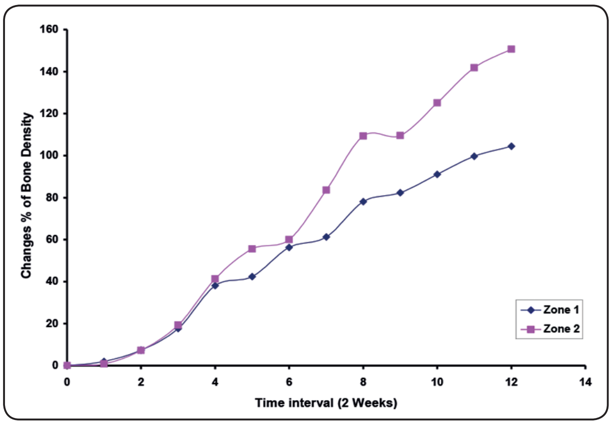

Fig. (5): Comparison between the changes percentage of bone density at the first and second zones of Conventional group at different time intervals.

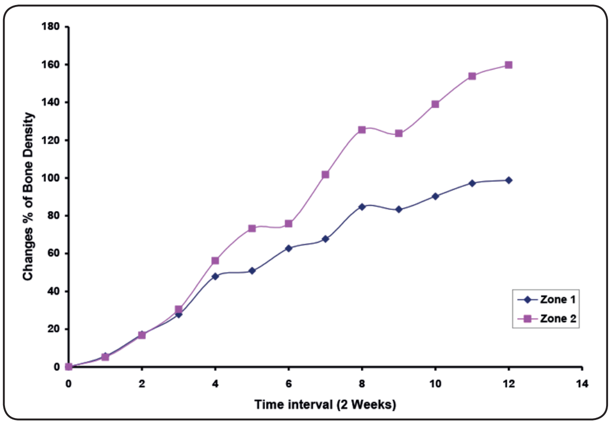

Fig. (6): Comparison between the changes percentage of bone density at the first and second zones of Drug group at different time intervals.

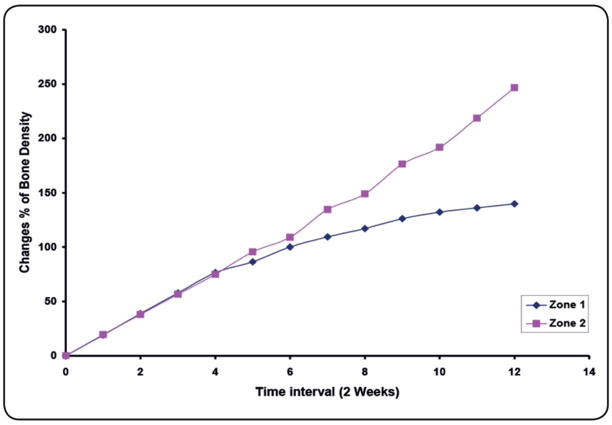

Fig. (7): Comparison between the changes percentage of bone density at the first and second zones of Laser group at different time intervals.

DISCUSSION

Implant losses can arbitrarily be divided into early, when osseointegration fails to occur, and late, when the achieved osseointegration is lost after a period of function. Early failure refers to an implant that fails to osseointegrate before second-stage surgery or uncovering of the implant. Late failure refers to loss of osseointegration or mechanical failure of an implant after second-stage surgery. (4)

Because osseointegration is essentially a wound healing process, factors that interfere with healing may contribute to implant failure. Hence, conditions shown to adversely affect wound healing may decrease the potential for successful osseointegration (18).

Various strategies to improve osseointegration have been specifically focused on the implant surface characteristics such as surface morphology, surface roughness, and chemical composition (19).

The maxillary premolar region was used in this study as a standard site for implant insertion as this region is known to have a relatively lower bone quality and a higher failure rate compared to anterior region (20). It was suggested that selecting maxillary premolar region would provide an additional challenge against the attempts to improve and/or accelerate osseointegration by the studied methods.

Systemic host factors play an important role in implant osseointegration. Age is an important determinant of bone mass density (BMD) (21). Most implant patients tend to be older, as there is more likelihood of tooth loss with increasing age (22). The mineral composition, the collagen and the morphogenetic protein content of the bone change with time. Conformation of the bone and fracture healing tend to be delayed and failure rates may be increased (4). At Approximately age 40, BMD begins to diminish gradually in both sexes, but bone loss increases greatly in women after age 50 or the time of menopause (21).

Osseointegrated implants act similarly to ankylosed teeth and, therefore, lack the ability of natural teeth to compensate for skeletal bone changes in growth. While this may be acceptable in adult patients, it is a significant factor to consider in adolescent or younger patients who are still growing as the placement of implants too early in life may lead to the submerging of an implant into the jaw, loss of support for the implant, relocation of the implant, and/or potential for interference with normal growth of the jaws. (23, 24).

The current study was performed on male groups ranged from 40 to 45 years old as this range was far from the active growth. In addition, this range provided a comparatively normal healing away from the delayed healing that might have occurred in the older age groups. Males were preferably used in this study instead of females to exclude any impact of female hormonal variations on the healing status. Thorough medical and dental histories, clinical examinations, radiographic evaluation, and laboratory investigations were applied on each subject before the study in order to exclude any systemic manifestations that could interfere with healing (4, 22). Also, subjects with habits as smoking (25, 26) and/or parafunctions (clenching and bruxism) (27, 28) were excluded from the study.

The effect of low-level laser therapy (LLLT) on wound healing and bone regeneration has become a focus of recent research. LLLT is based on biostimulation of the tissues with monochromatic light. Various biostimulatory effects have been reported on wound healing (13) and collagen synthesis (14). With respect to bone, LLLT has been shown to modulate inflammation (15), accelerate cell proliferation (16) and enhance healing.(17) In addition, Laser mediated vasodilatation enhances the transport of nutrients and oxygen to the damaged cells and facilitates repair and removal of cellular debris. (31, 32) LLLT is also improves the entire lymphatic response is beneficially (33).

In animal model studies, LLLT proved that it could significantly improve osseointegration with much higher removal torque needed to remove implants rather than in usual osseointegration (34). It also increases the activity in bone cells (resorption and formation) around the site of the repair without changing the bone structure (35), and significantly increase bone-to-implant contact by increasing the weight percentages of calcium and phosphorus that suggest faster bone maturation (36).

In cellular model, Khadra et al., proved that LLLT enhanced the attachment and proliferation of cells derived from human mandibular bone, cultured on titanium implant material. The results indicated that LLLT modulates the activity of cells and tissues surrounding an implant. The authors concluded that the introduction of laser therapy for implant treatment seems feasible and may be of therapeutic benefit in accelerating healing as it enhances the functional attachment of titanium implants to bone and promotes bone healing and mineralization in vitro (17).

In an *in vivo* study on female subjects, Radwan(37) proved that LILT significantly enhanced bone density around delayed immediate titanium implants.

A wide variation exists in recommendations for the optimal energy for different conditions; the usual ranges are from 0.5 to 10 J/cm^2. Generally, a laser wavelength of 600 to 984 nm is used in physical medicine, and a laser wavelength of 632.8 nm helium neon and 904 nm GaAs are most frequently used in wound healing (30). Therefore, GaAs laser with a wavelength of 904 nm (***Ora-laser* 1030**) was chosen for this study. Laser was applied to cases of group III in three sessions on three alternative days started from the next day to operation. In each session, laser device was pre-adjusted to deliver a laser beam with an output power of 30 mW, and a frequency of 9999 Hz. in a continuous mode for 3 minutes, one minute for each surface (i.e. buccal, occlusal, and palatal surfaces respectively). Along the pre-adjusted time (3 minutes), laser beam was continuously delivered from the tip of the laser applicator and exposing the target surface while the tip was touching the tissues. The applicator tip was directed towards the tissue and was moving in a continuous slow circular motion to assure full exposure of the target surface to the beam. By calculations, the energy received by each surface within one minute of laser application equals to 6.4 J/cm^2.

A follow up period extended for six months came in accordance to Brånemark et al., (8) who advised a stress-free healing period of 3-6 months using a 2-stage surgical procedure (conventional approach) to create a healing environment at the bone-implant interface that would facilitate regeneration and osseointegration rather than fibrous tissue encapsulation. This also comes in accordance to Krennmair et al., (38) who concluded that the six-month healing period for the maxillary implants provides excellent results.

Baseline radiographs were taken immediately postoperatively(39). Recalls for follow up radiographs were made at intervals of two weeks for the six-month period to allow for an accurate and a homogenous monitoring of any changes in bone density along the follow up period. The relatively low radiation parameters (70 kVp and 8 mA for 0.30 sec. using long cone and ultra-speed periapical films) allowed for such a frequent radiographing.

Image analysis using ***IDRISI*** Kilimanjaro software facilitated monitoring the changes in bone density at two zones around implant images. The first zone represented the osseointegration zone and it was located just adjacent to the implant borders. The second zone was located just adjacent to first zone and represented bone around the implant. (37)

In the current study, an insignificant difference in bone density between all groups at both zones (zones 1 & 2) continued through the first two weeks. Later on, LLLT started to produce a striking increase in the values of bone density in laser group, compared with the slow, delayed, and non-homogenous increase in bone density in conventional as well as drug groups.

Laser group showed a significant increase in bone density values in the first zone starting from the 2nd interval (the end of the first month) and up to the last interval. Laser group showed a significant increase in bone density values in the second zone starting from the 2nd interval (the end of the first month) and up to the last interval.

Conventional and drug groups showed a significant increase in bone density values in both zones starting from the 4th interval (the end of the second month) and up to the last interval. These findings go in agreement with Dörtbudak et al.,(40) Dörtbudak et al.,(4) and Nicola et al., (35) who concluded that LLLT increases the activity in bone cells at early phases of bone healing around the repair site without changing the bone structure.

Radiographic evaluation of osseointegration zone (the first zone) revealed early, sustained and homogenous increase in bone density in laser group, a finding that was not observed in non-laser groups (I, II). These findings go in agreement with Radwan(37) who found that LLLT has accelerated bone formation around dental implants and this was evident from the first month of the follow up-periods.

Moreover, the observed increase in the osteoblastic activity in the first six weeks of laser therapy go in accordance with Ozawa et al., (42) and Guzzardella et al.,(43) who observed an early significant increase in alkaline phosphatase activity after laser application, as well as early significant stimulated cellular proliferation and osteocalcin gene expression thereafter. Furthermore, laser irradiation at earlier stages significantly stimulated a greater number and larger area of bone nodules.

The magnitude of the biostimulatory laser effect depends on the physiologic state of the cell at the moment of irradiation. This explains the high bone density values within laser group along the follow up period compared to those of the non-laser groups. It also explains the relatively higher change percentage of bone density in laser group. Many authors reported that during wound healing, laser biostimulates cells that present only in the proliferative phase or cells that are in a state of stress. Such effects occur due to the enhancement of the metabolic and enzymatic processes as a result of laser therapy, thereby affecting the electrophysiological properties of tissues (44, 45).

The early significant increase in bone density in laser group (the end of the first month) compared to non-laser groups (the end of the second month) is supported by the results of Motomma et al.,(46) and Maegawa, et al., (47) who observed that there is an effect of LLLT on osseous tissue in promoting healing of bony wounds at the initial phase and an activity of accelerating osteogenesis. These findings are explained by Nicola et al., (35) who demonstrated the positive effect of LLLT on the stimulation of bone with latent promotion of bone remodulation at injury sites without changes in bone architecture, increased bone volume and increased osteoblast surface through increased formation of bone with higher apposition rates.

The effect of laser was evaluated by statistically comparing the records of laser versus conventional group at different follow up intervals. The results showed a significant difference to the favor of laser. The significance started from the 2nd interval (the first month) and continued up to the last one. These findings go in agreement with Radwan (37) who reported that bone regeneration in her lased group was superior to the non-lased one. These results are explained by the studies of Ueda and Shimizu (16), Nicola et al. (35), and Khadra et al. (36), who found that LILT accelerates cell proliferation, increases the activity of bone cells around the repair site without changing the bone structure, and processes faster bone maturation.

The results showed no significant difference between drug and conventional groups along the follow up period, although the mean bone density values of different intervals were higher to the favor of drug.

The highest bone density value reached at the osseointegration zone of the conventional group (133.7) was used as a reference number in measuring the efficiency of different therapeutic methods. This value was the last value reached at the end of the six-month follow up period recommended by many authors to assure load-free healing phase after witch the implant could be exposed and loaded safely. The resultant calculations revealed that drug therapy reduced the recommended healing time by 8% and laser therapy reduced the recommended healing time by 33%.

Although the density in the second zone was less than its correspondence in the osseointegration zone, yet the density of the second zone in the laser group (III) shows a significant increase than non-laser groups (I, II), i.e. laser therapy provided faster osseous tissue formation and enhanced bone vascularization (42, 48).

The correlation between the statistical analyses of radiographic bone density in the two bone zones that surrounded the implants assured that laser accelerated healing and osteogenesis when compared to non-laser therapies throughout the entire study period, the findings go in accordance with the results of Salah El-Din and Dahaba (49), Salah El-Din et al (50), and Radwan (37), who found an increase in the percentage of bone density in their laser groups compared to non-laser groups.

The results of the current clinical study denoted that low intensity laser therapy provides an easy as well as efficient method for accelerating bone healing and improving osseointegration. The combined LIL application with supplementary micronutrients administration provided the best method for accelerating the healing and improving the quality of osseointegration around endosteal dental implants.

REFFERENCES

1. McKinney, R.V. (ed) (1991): Dental and Oral Implantology. In: Endosteal Dental Implants. St. Louis, Mosby Inc. pp.3.
2. Ratner, B.D. (2001): Replacing and Renewing: Synthetic Materials, Biomimetics, and Tissue Engineering in Implant Dentistry. Journal of Dental Education; 65(12): 1340-1347.
3. Brånemark, R., Brånemark, P-I., Rydevik, B., and Myers, R.R. (2001): Osseointegration in skeletal reconstruction and rehabilitation: A review. J Rehabil Res Dev; 38: 175-181.
4. Santos, M. C. L. G., Campos, M. I. G., and Line, S. R. P. (2002): Early dental implant failure: A review of the literature. Braz J Oral Sci; 1(3): 103-111.
5. McKinney, R.V., Koth, D.L. (1982): The single crystal sapphire endosteal dental implant: Material characteristics and 18-month experimental animal trials. J Prosthet Dent; 47: 69-84.

6. McKinney, R.V., Steflik, D.E., Koth, and D.L., et al. (1987): Histological results from a comparative endosteal dental implant study. J Dent Res; 66(special issue): 186.
7. Weiss, C.M. (1986): Tissue integration dental endosseous implants: Description and comparative analysis of the fibro-osseous integration and osseous integration systems. J Oral Implantol; 12:169-214.
8. Brånemark, P-I., Hansson, B. O., Adell, R., et al. (1977): Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. Scand J Plast Reconstr Surg; 16: 1-132.
9. Alberktsson, T., Bergman, B., Folmer, T., et al. (1988): A multicenter report of osseointegrated oral implants. J Prosthet Dent; 60: 75-84.
10. Balshi, T. J., Wolfinger, G. J. (1997): Immediate loading of Brånemark implants in edentulous mandibles: A preliminary report. Implant Dentistry; 6: 83-88.
11. Tarnow, D. P., Emtiaz, S., Classi, A. (1997): Immediate loading of threaded implants at stage 1 surgery in edentulous arches: Ten consecutive case reports with 1- to 5- year data. Int J Oral Maxillofac Implants; 12: 319-324.
12. Anderson, J.J.B. (2012): Overview of Relationships between Diet and Bone in Anderson, J.J.B., Garner, S. C., and Klemmer, P.J., (eds): Diet, Nutrients, and Bone Health. CRC Press, Taylor& Francis Group Co. pp 3-16.
13. Trelles, M.A., Mayayo, E. (1987): Bone fracture consolidates faster with low-power laser. Lasers Surg Med; 7: 36–45.
14. Ghamsari, S.M., Yamada, H., Acorda, J.A., Taguchi, K., Abe, N. (1995): Histopathological effects of low level laser therapy on secondary wound healing of teat wound in dairy cattle. Laser Ther; 7: 81–8.
15. Lizarelli, R.F.Z., Lamano-Carvalho, T.L., Brentegani, L.G. (1999): Histometrical evaluation of the healing of the dental alveolus in rats after irradiation with a low-powered GaAlAs laser. SPIE; 3593: 49–55.
16. Ueda, Y., Shimizu, N. (2003): Effects of pulse frequency of low-level laser therapy (LLLT) on bone nodule formation in rat calvarial cells. J Clin Laser Med Surg; 21: 271–7.
17. Khadra, M., Lyngstadaas, S. P., Hans, R., Haanæs, H. R., Mustafa, K. (2005): Effect of laser therapy on attachment, proliferation and differentiation of human osteoblast-like cells cultured on titanium implant material. Biomaterials; 26: 3503–3509.
18. Elsubeihi, E.S., Zarb, G.A. (2002): Implant Prosthodontics in Medically Challenged Patients: The University of Toronto Experience. J Can Dent Assoc; 68(2): 103-8.
19. Giavaresi, G., Ambrosio, L., Battiston, G.A., Umberto Casellato, U., Gerbasi, R., Milena Finia, M., Aldini, N.N., Martini, L., Lia Rimondini, L., Roberto Giardino, R. (2004): Histomorphometric, ultrastructural and microhardness evaluation of the osseointegration of a nanostructured titanium oxide coating by metal-organic chemical vapour deposition: an in vivo study. Biomaterials; 25: 5583–5591.
20. Esposito, M., Hirsch, J-M., Lekholm, U., Thomsen, P. (1998): Biological factors contributing to failures of osseointegrated oral implants. (II) Etiopathogenesis. Eur J Oral Sci; 106: 721-764.
21. Anderson, J.J.B. (2014): Nutrition for Bone Health in Mahan, L.K., Escott-Stump, S., and Raymond, J.L., (eds): Krause's Food & the Nutrition Care Process - Middle Eastern Edition. Philadelphia, WB Saunders Co. pp 611-632.
22. Wood, M.R., Vermilyea, S.G. (2004): A review of selected dental literature on evidence-based treatment planning for dental implants: Report of the Committee on Research in Fixed Prosthodontics of the Academy of Fixed Prosthodontics. J Prosthet Dent; 92: 447-62.
23. Beikler, T., Flemmig, T.F. (2003): IMPLANTS IN THE MEDICALLY COMPROMISED PATIENT. Crit Rev Oral Biol Med; 14(4): 305-316.
24. Bryant, S.R. (1988): The effects of age, jaw site, and bone condition on oral implant outcomes. Int J Prosthodont; 11: 470-90.
25. Misch, C.E. (1996): Early bone loss etiology and its effect on treatment planning. Dent Today; 15: 44-51.
26. Wilson, T.G. Jr., Nunn, M. (1999): The relationship between the interleukin-1 periodontal genotype and implant loss. Initial data. J Periodontol; 70: 724-9.
27. Quirynen, M., Naert, I., van Steenberghe, D. (1992): Fixture design and overload influence marginal bone loss and fixture success in the Brånemark system. Clin Oral Implants Res; 3: 104-11.
28. Rangert, B., Krogh, P.H., Langer, B., van Roekel, N. (1995): Bending overload and implant fracture: a retrospective clinical analysis. Int J Oral Maxillofac Implants; 10: 326-34.
29. Schortinghuis, J., Stegenga, B., Raghoebar, G.M., de Bont, L.G.M. (2003): Ultrasound Stimulation of Maxillofacial Bone Healing. Crit Rev Oral Biol Med; 14(1): 63-74.

30. Demir, H., Yaray, S., Kirnap, M., Yaray, K. (2004): Comparison of the effects of laser and ultrasound treatments on experimental wound healing in rats. JRRD; 41(5): 721-728

31. Silveira LB, et al. (2002): In vivo study on mast cells behavior following low-intensity visible and near infrared laser radiation. Laser Surg Med. Abstract issue. Abstract 304.

32. Trelles, M.A., et al. (2000): LLLT in vivo effects on mast cells. Department of Tissue Pathology, University Hospital, Tarragona, Spain. Abstract from the 7th International Congress of European Medical Laser Association, Dubrovnik, Croatia, June 2000.

33. Stadler, I., et al. (2000): In vitro effects of low level laser irradiation at 660 nm on peripheral blood lymphocytes. Lasers Surg Med; 27(3): 255-61

34. Blay, A., Blay, C. C., Groth, E. B., et al. (2002): Effects of visible NIR low intensity laser on implant Osseo integration in vivo. Laser Med Surg; Abstract issue, 11.

35. Nicola, R.A., Jorgetti, V., Rigau, J., Pacheco, M.T., dos Reis L.M., Zangaro, R.A. (2003): Effect of low-power GaAlAs laser (660 nm) on bone structure and cell activity: an experimental animal study. Lasers Med Sci; 18(2): 89-94.

36. Khadra, M., Kassem, N., Haanæs, H.R., Ellingsen, J.E., Lyngstadaas, S.P. (2004): Enhancement of bone formation in rat calvarial bone defects using low-level laser therapy. Oral Surg Oral Med Oral Pathol Oral Endod; 97: 693-700.

37. Radwan, D., A. (2005): A clinical study on the effect of diode laser therapy on the osseointegration of delayed immediate implants. A thesis of doctor’s degree in oral surgery, Cairo University.

38. Krennmair, G., Schmidinger, S., Waldenberger, O. (2002): Single-Tooth Replacement with the Frialit-2 System: A prospective Clinical Analysis of 146 Implants. Int J Oral Maxillofac Implants; 17(1): 78-85.

39. Gomez-Roman, G., Kruppenbacher, M., Schulte, W. (2001): Immediate Post Extraction Implant Placement with Root-Analog Stepped Implants: Surgical Procedure and Statistical Outcome after 6 Years. Int J Oral Maxillofac Implants; 16(4): 503-512.

40. Dörtbudak, O., Hass, R., Mallath-Pokorny, G. (2000): Biostimulation of bone marrow cells with a diode soft laser. Clin Oral Implants Res; 11(6): 540-5.

41. Dörtbudak, O., Haas, R., Mailath-Pokorny, G. (2002): Effect of low-power laser irradiation on bony implant sites. Clin Oral Implants Res 13(3): 288-292.

42. Ozawa, Y., Shimizu, N., Mishima, H., Kariya, G., Yamaguchi, M., Takiguchi, H., Iwasawa, T., Abiko, Y. (1995): Stimulatory effects of low-power laser irradiation on bone formation in vitro. In Altshuler, G.B., Blankenau, R.J., Wifdor, H. A. (eds): Advanced laser Dentistry. SPIE; 1984, pp 281- 288.

43. Guzzardella, G.A., Torricelli, P., Nicoli-Aldini, N., Giardino, R. (2003): Osseointegration of endosseous ceramic implants after postoperative low-power laser stimulation: an in vivo comparative study. Clin Oral Implants Res. 14: 226-232.

44. Karu, T.I. (2003): Low-Power Laser Therapy. In: Biomedical Photonics Handbook. Boca Raton, CRC Press. pp 48-1--48-25.

45. Walker, D.M., Rumpf, S., Baxter, D.G., Lowe, S.A. (2000): Effect of low intensity laser irradiation (660 mm) on the radiation-impaired wound healing model in murine skin. Lasers Surg Med; 26:41-47.

46. Motomma, K., Nakashima, M., Ihara, A., Atsmi K. (1986): Effect of argon-dye laser on fracture healing. Journal of Japan society of laser medicine; 6(3): 171-174.

47. Maegawa, Y., Itoh, T., Hosokawa, T., Yaegashi, K., Nishi, M. (2000): Effects of Near-Infrared Low-Level Laser Irradiation on Microcirculation. Lasers in surgery and medicine; 27: 427-437.

48. Gable, P., Tunér, J. (2003): Bone Stimulation by Low Level Laser - A Theoretical Model for the Effects. Clinixperience; Vol. 2003(67).

49. Salah El-Din, M., Dahaba, M.M. (2001): Effect of diode laser therapy on healing of persistent periradicular lesions in endodontically treated teeth. Egy Dent J; 47: 299-309.

50. Salah El-Din, M., Marzouk, A., Dahaba, M.M. (2004): The effect of low energy laser on endo-perio and periapical lesions. Egy Dent J; 50: 103-112.