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**RESEARCH ARTICLE**

# Pulsed High Intensity Laser Therapy Versus Low Intensity Pulsed Ultrasound in Treatment of Post-menopausal Osteoporosis

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## *Abstract*

**The Purpose** of this study was to compare the effect of pulsed high intensity laser therapy (HLLT) versus low-intensity pulsed ultrasound (LIPUS) on bone mineral density (BMD) in osteoporotic postmenopausal women. **Methods:** This study was conducted on thirty osteoporotic postmenopausal women; age ranged from 51 to 60 years; randomly assigned into two groups. Group (I) consisted of 15 women received HILT, Group (II) consisted of 15 women received LIPUS. Each treatment (pulsed HLLT or LIPUS) was applied trice weekly for eight successive weeks. Bone mineral density of lumbar spine (L1-5) of all participants was measured by Dual X-ray absorptiometry (DXA) before and after the end of eight weeks of treatment. **Result:** Although HLLT or LIPU treatments produced significant increase in BMD in osteoporotic postmenopausal women; there was a highly significant ($P < 0.0001$) increase in the BMD in response to pulsed HILT in comparing of LIPUS. **Conclusion:** pulsed HILT is more effective than LIPUS in treatment of post-menopausal osteoporosis and should be considered as a treatment modality to be used with other therapeutic modalities.



## INTRODUCTION

Osteoporosis is a multifactorial progressive skeletal disorder characterized by reduced bone mass and deterioration of bone architecture, predisposing it to increased fracture risk that exerts a great impact on public health, as they are often associated with increased morbidity, mortality, loss of function and high economic costs (Nikander-Sievänen et al., 2010). Osteoporosis and related fractures represent a serious and global public health problem. It's estimated that 30%-50% of women and 15%-30% of men suffers an osteoporotic fracture in their lifetime. It is a silent "epidemic" that has become a major health hazard in recent years, afflicting over 2000 million people worldwide (Kanis et al., 2008). The International Osteoporosis Foundation (IOF) estimates that 200 million women suffer from osteoporosis across the world (Vondracek and Hansen, 2004).

There are two types of osteoporosis: type I that results from reduction in cumulating estrogens; affects trabecular bone (especially vertebral bone) in female more than male in a ratio of 6:1 and type II (senile osteoporosis) which is

age-related; occurs in cortical and trabecular bones; affects female and male in a ratio of 2:1 (Nolte et al., 2004). Low bone mass is the most important factor for fracture. Several risk factors are well-known to predispose to osteoporosis including estrogen deficiency, negative calcium balance, sedentary life style, immobilization, menopause, amenorrhea, family history of osteoporosis, high alcohol intake, smoking, high caffeine consumption and steroid therapy (Sheng et al., 2001).

Pharmacological and non-pharmacological treatments have been developed to enhance bone mineral density (BMD) as well as to reduce the risk of fractures in patients with osteoporosis. High dietary intake of calcium with sodium fluoride and vitamin D, reduction of excessive protein and phorphorous consumption are indicated as therapeutic options, but the problem still exist regarding abnormal bone architecture and the high incidence of side effects (Ringe et al., 2006). Non-pharmacological treatment is usually based on physical exercise that are specifically designed for patients with osteoporosis and on physical agents that could preserve or enhance BMD (Riggs and Melton, 1995).

Laser is light amplification by stimulated emission of radiation; it alters the cellular functions and affects the mitochondrial respiratory chain through increasing the activity of certain enzymes as cytochrome oxidase and adenosine triphosphatase (Bashardoust-Tajali et al., 2010), increases DNA, collagen and pro-collagen synthesis, increases cell proliferation and alters cells locomotory characteristics (Koutna et al., 2003). Laser accelerates the bone matrix deposition and vascularization, alters the osteoblast and osteoclast cell activities, enhances fracture healing (Khadra et al., 2004) and improves bone regeneration (Saracino et al., 2009). Laser therapy can accelerate bone formation by increasing osteoblastic activity (Boeriu, 2010), vascularization (Garavello-Freitas et al., 2003), organization of collagen fibers, and adenosine tri-phosphates (ATP) levels (Zati and Valent, 2006). HILT works with high peak powers and able to stimulate deep tissues and organs that are difficult to reach by low level lasers (Pires-Oliveira et al., 2008). HILT has been used in treatment of sports lesions, acute osteomuscular diseases (Valent, 2006), degenerative diseases as osteoarthritis (Viliani et al., 2010), low back pain (Conte et al., 2009), knee arthritis (Sabbahi, 2009), carpal tunnel syndrome (Gleiser, 2009), lateral epicondylitis (Kang, et al., 2009).

The ultrasound (US) is a form of mechanical energy which promotes local bone micro-deformations, as the natural mechanical incentive, and which is crucial in stimulating the bone formation (Viliani et al, 2009), (Aynaci et al., 2002). Ultrasound; a potential intervention for osteoporosis; is a high-frequency non-audible acoustic energy that travels in the form of mechanical waves that are relatively focused on beam-typical effective radiating area to exert a local mechanical stimulus (Mayr et al., 2004). Low intensity ultrasound is capable of accelerating the healing of fresh fractures, delayed healing and non-union. Furthermore; therapeutic ultrasound benefits on cases of large bone defects and on spine fusion (Erdogan and Esen, 2009). The beneficial effect of ultrasound on bone healing is due to the piezoelectric phenomenon (Malizos et al., 2006); the stress generated potentials in bone by US application serve as a signal which controls bone remodeling (Hadji-argyrou et al., 1998).

Pulsed-wave ultrasound can alter cell membrane permeability to ions and alter cell membrane electrophysiological properties, causing an immediate decrease in intracellular potassium content in thymocytes, a reversible increase in the intracellular level of calcium in chondrocytes, and an increase in calcium incorporation into differentiating cartilage and bone cell cultures (Warden et al., 2006), which all may be produced by a direct mechanical deformation of the cell membrane, deformation of cell receptors, or indirectly as a consequence of cavitation, micro-streaming, or a combination of these effects (Sigurdsson et al., 1995). Furthermore; US treatment increases the production of prostaglandin E2, an important bone-healing mediator that inhibits mature osteoclasts from resorbing bone and stimulating osteoblasts for bone formation (Doan et al., 1999). Variable techniques are available for bone mineral density assessment. DXA is the most widely used techniques; it's based on X-ray absorption in bone, since the absorption of X-rays is very sensitive to the tissue calcium content (Mazess et al., 1998), (Glüer, 1997).

To our knowledge, and up to recent literatures; no study has been compared the effects of HILT with that of LIPUS on BMD of lumbar vertebrae in postmenopausal women with osteoporosis. So the aim of this study was to compare the effect of HLLT versus LIPUS on BMD in the treatment of osteoporosis in postmenopausal women.

## Material and Methods

**Subjects:**

Thirty sedentary, volunteer postmenopausal women with established osteoporosis were recruited from Kaser El-Aini Hospital and Ain-Shams Hospital, Cairo, Egypt. Their age ranged from 51 to 60 years. Full evaluation of each participant was performed prior to and at the end of the study (including medical history, clinical examination, DXA to diagnose osteoporosis in lumbar vertebrae with no evidence of vertebral compression fractures. All Participants were not under any medications associated with accelerated bone loss (steroids) or any medications affecting bone metabolism (estrogen, calcium, vitamin D), body mass index not exceeding 30 $Kg/m^2$, non-smoker, parity from 1-3

times and led sedentary life style without participation in any exercise training 3 months prior to the study, they had natural menopause at least 1 year before entry into the study with no history of ovariectomy.
All women were given a full explanation of the treatment protocol and a written informed consent form giving agreement to participation and publication of results was signed by the patients and the study was approved by the departmental council and ethics committee of the Faculty of Physical Therapy, Cairo University.
Patients with significant or unstable cardiac, musculoskeletal or psychological problems or medication that could affect or interfere with their performance or affect their safe participation were excluded. Patients with history of cancer, renal diseases, gastrectomy, metabolic bone disease or any condition (such as a neurogenic, myopathic or connective tissue disorder) that could cause secondary osteoporosis were also excluded.
Randomization was performed simply by asking the patient to randomly choose a piece of paper which (A) or (B) letter was written on. (A) Considered a group-I which received pulsed HILT program while (B) considered a group-II which received a LIPUS program. So participants were randomly assigned into one of the two groups; Group-I consisted of 15 women, received pulsed HILT program for ten minutes trice weekly for eight weeks and Group-II consisted of 15 women, received LIPUS program for ten minutes trice weekly for eight weeks.

**Evaluation:**
All participants underwent an identical battery of tests. Initially a screening test including careful history taking and gynecological examination were conducted for each woman before entry in the study. The main evaluated parameter was BMD of lumbar spine (L1-5) in $mg/cm^2$ (evaluated through Dual x-ray Absorptiometry (DXA); Model QDR-1000W, Hologic, Inc., Waltham, MA). Evaluations were performed before the beginning of the study and after the completion of the study (after the end of eight weeks of treatment). The assessors were blinded to the participants' treatment assignments. All subjects' data were collected using standard laboratory procedures. Demographic data including weight in kg, height in m, BMI (weight kg / $height^2$) were all evaluated before the study.

**Treatment:**
All participants in this study received three sessions per week for eight successive weeks. The treatment procedure was explained to all subjects. During the treatment, the position of the participants was the same for both groups (prone lying position with a pillow under the abdomen); Skin was cleaned with alcohol before application of either treatment programs.
**Pulsed HILT program (For group I):**
Participants in group-I received HILT program for 10 minutes (using HILTERAPIA, HIRO 3.0 ® high power pulsed Nd: YAG laser 12W, ASA Italy); Laser was irradiated to the lumbar vertebrae (L1-5) using the following laser parameters: pulsed emission (1064 nm), Very high peak powers (1-3 KW), Elevated energy content (150 - 350 mJ), High levels of fluence (energy density)( 810-1780 $mJ\backslash cm^2$), brief duration (120-150 µs), Low frequency (10-40 Hz), Duty Cycle of about 0.1%. The delivery technique for this group was automatic scanning with total energy of 4000 joule.
HILT was delivered in two different phases, Initial phase and terminal phase. In initial phase, three sub-phases of fast manual scan (every10 cm scanned in about 1.5 second) was performed to lumber region with increasing fluences (710-910-1530 $mJ/cm^2$) and decreasing frequencies (30-20-15Hz) with total energy of 2000 Jules reached lumber region. In Final phase: 3 sub-phases of slow scanning (every 10 cm scanned in about three second) with increasing fluences (710-910-1530 mJ/cm2) and decreasing frequencies (30-20-15Hz) with total energy of 2000 Jules reached lumber region. Scans were longitudinal to the anatomical structure to be treated, ideally following a straight lines path.
**LIPUS program (For group II):**
Participants in group-II) received LIPUS program for 10 minutes (using Enraf Nonius -Sonoplus590 US device, USA); was used to deliver low-intensity pulsed ultrasound therapy. The apparatus provided the following options: I MHz frequency with transducer having an affective radiating area of 5.0 $cm^2$, intensity up to 1.5 W/cm2 in pulsed mode, $3W/cm^2$ in pulsed mode, gel was used as a coupling media.
All subjects received 10 minutes LIPUS application, trice weekly for eight successive weeks of treatment with1MHz frequency and intensity of $0.5W/cm^2$. Ultrasound therapy was applied to the lumbar vertebrae (L1-5) using 5 $cm^2$ ultrasound head surface area.
**Statistical analysis**
Data are presented as mean $\pm$ SD. Changes in BMD within each group before and after the study period were analyzed using paired t-test. Between-groups differences in BMD were analyzed using one way analysis of variance (ANOVA). The level of significance was set at $p < 0.05$.

## Result

Thirty osteoporotic, post-menopausal women were participated in this study. They underwent initial pre-study evaluation, allocated to either (I) or (II) group, received the group-specified treatment program according to group allocation, and finally underwent final evaluation. (Fig.1)

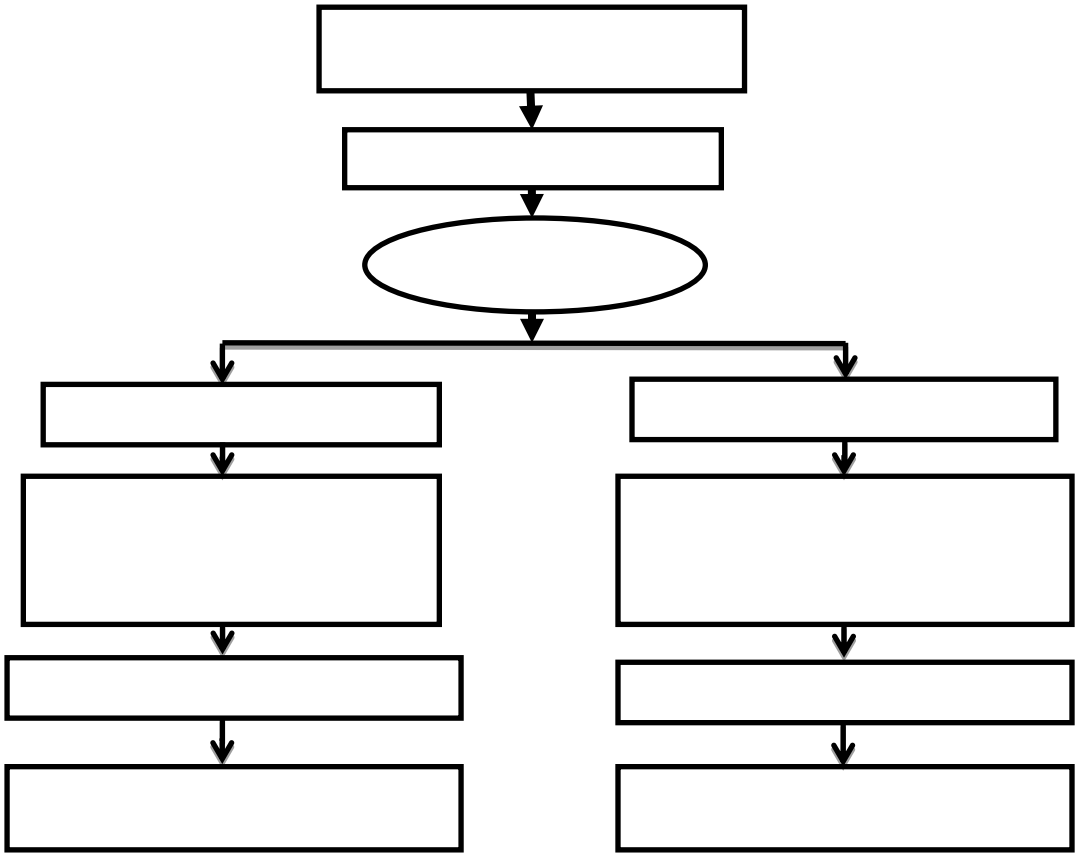

**Fig 1: Patient's flow chart.**

**Patients' characteristics**

The general characteristics of the two groups before treatments (Age, body weight, height, body mass index "BMI") are shown in table (1) as mean (M) ± standard deviation (SD). As evident from the table there were no statistically significant differences between the two groups.

**Table 1. The mean and SD of the age, height, weight, and BMI of the two groups (pre- study).**

| Character | Study group (I) | Study group (II) | P-Value |
|---|---|---|---|
| | Mean ± SD | Mean ± SD | |
| **Age (Ys)** | 54 ± 3.2 | 55 ± 2.9 | 0.413** |
| **Weight (Kg)** | 75.55 ± 4.16 | 75.75 ± 3.71 | 0.873 ** |
| **Height (m)** | 1.65 ± 3.44 | 1.65 ± 3.74 | 0.896 ** |
| **BMI (kg/m$^2$)** | 27.79 ± 1.14 | 27.83 ± 1.18 | 0.919 ** |

**Level of significance at P<0.05. * = significant ** = non-significant**

Paired T- test was performed to examine and compare BMD within each group. Results revealed that in group (I); there was highly significant increase in BMD (P<0.0001), where in group (II); there was significant increase in BMD. (P-value < 0.05) (Tab. 2 and Fig. 2).
Unpaired T-test was performed to examine and compare BMD between groups. Results revealed that pre-study; there was non-significant difference in the BMD mean value between both groups. Post-Study; there was significant difference in the BMD mean value between both groups, but in favor of group (I). (Tab. 2, Fig. 3).

**Table II. Within and between groups comparison of BMD (mg/cm$^2$) (T & P values).**

| | HILT; group (I) | LIPU; group (II) | T- Value | P-Value |
|---|---|---|---|---|
| | Mean ± SD | Mean ± SD | | |
| **Pre-Treatment** | -3.28 ± 0.39 | -3.61 ± -0.75 | 1.50 | 0.144 ** |
| **Post-Treatment** | -0.30 ± 1.54 | -2.91 ± 0.68 | 6.00 | P<0.05* |
| **T-Value** | -7.51 | -2.24 | | |
| **P-Value** | P<0.0001* | 0.042 * | | |

**Level of significance at P<0.05. * = significant ** = non-significant**

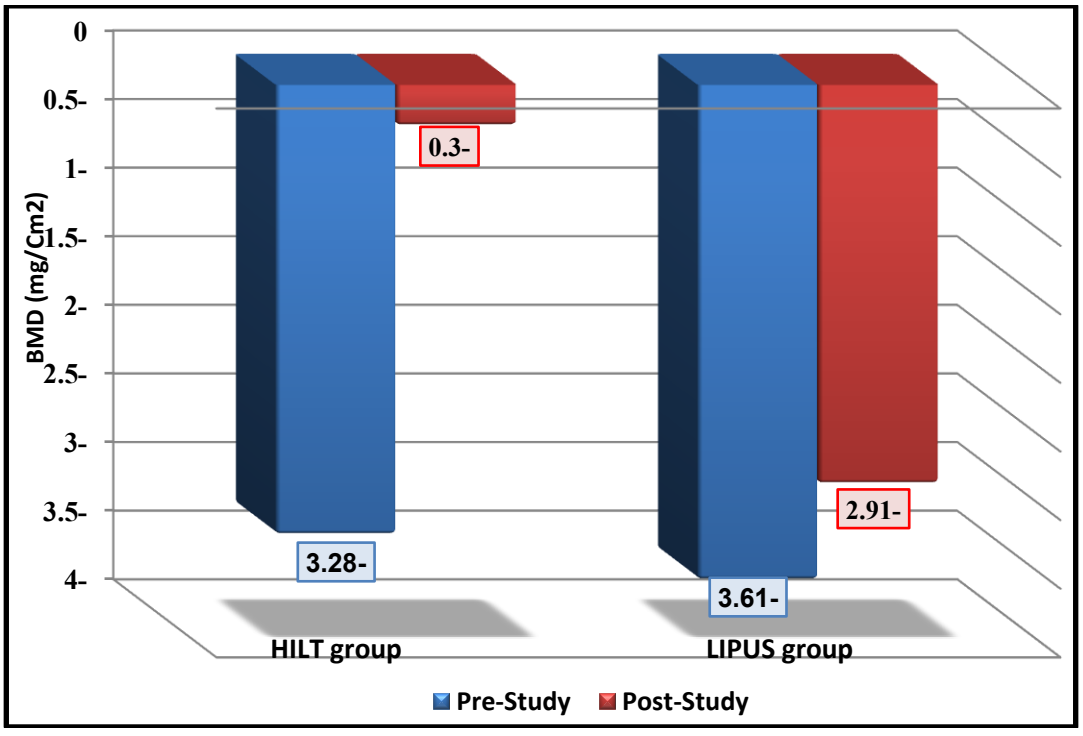


**Fig 2: Within groups comparison of BMD (mg/cm$^2$) (Pre and Post- Study)**

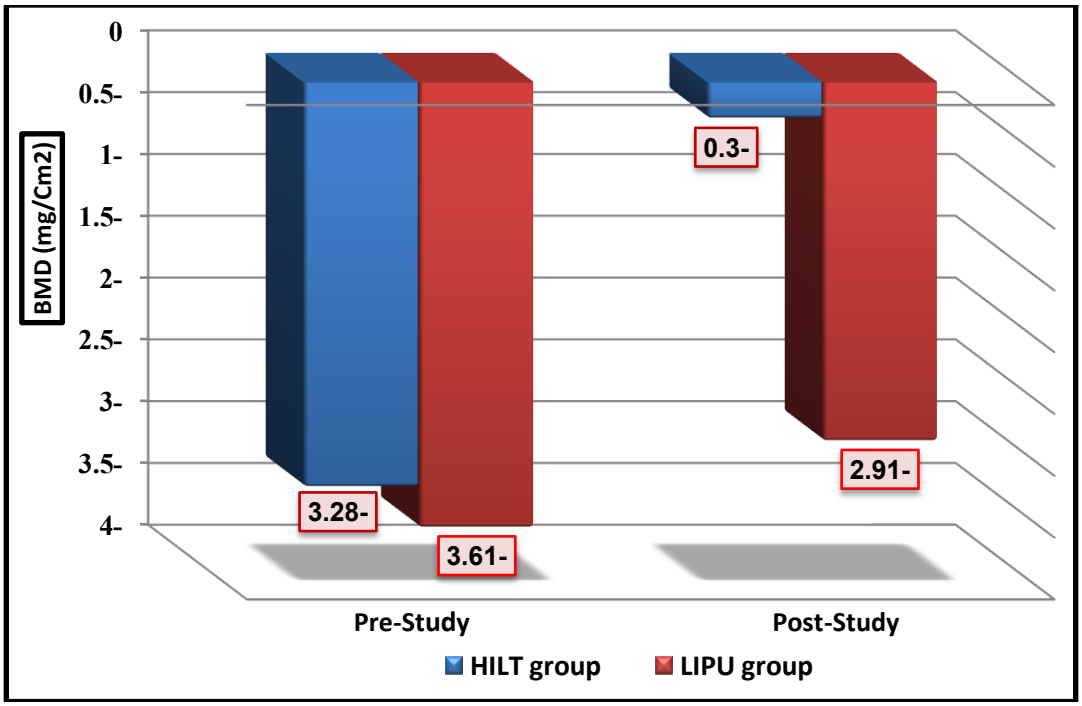


**Fig 3. Between groups comparison of BMD (mg/cm$^2$) (Pre and Post- Study)**

## Discussion

This study was designed to determine the effectiveness of pulsed high intensity laser therapy (HILT) versus low intensity pulsed ultrasound (LIPUS) in the treatment of osteoporosis. At the end of the treatment program, the obtained results showed that although both pulsed HILT and LIPU were effective in improving BMD in post-menopausal women with osteoporosis; but pulsed HILT was more effective than LIPUS.

The application of HILT in physiotherapy is quite recent. It is due to the development of instruments which allow the control of photothermal and photomechanical processes to obtain therapeutic effects without tissue damage. In particular, pulsed Nd: YAG laser has proved its versatility and efficacy in the treatment of many different musculoskeletal diseases and it is believed to have anti-inflammatory, anti-edema, analgesic and also reparative effects. The interaction between tissue and laser radiation alters the mechanics of cell micro-environment, thus acting on the cells as a mechanical stress (Monici et al., 2008).

The obtained results agreed with previous study reported that laser therapy improves bone repair process manifested in increased bone formation, as well as COX-2 and Cbfa-1 immunoexpression, angiogenesis and collagen deposition in osteoporotic rats (Bossini et al., 2011). The significant increase in BMD in response to laser stimulation can be attributed to improved bone repair secondary to stimulation of the newly formed bone, fibro-vascularization and angiogenesis in osteoporotic bones (Bossini et al., 2012).

Also; this study results came in consistence with Stein et al., who showed that LLLT, has stimulatory effects on osteoblast-like cells, increasing its viability (Stein et al., 2008), DNA and RNA synthesis, bone nodule formation (Stein et al., 2005), as well as alkaline phosphatase activity and expressions of osteopontin and collagen type-I

mRNA (Liu et al., 2007). Application of laser therapy has the ability to accelerate the process of fracture repair by increasing callus volume and BMD, especially in the early stages of bone remodeling, LLLT also have a positive effect on osteogenesis in osteopenic rats, increasing bone strength, calcium content and BMD of the treated femoral area (Renno et al., 2007). Moreover; Diniz et al., demonstrated that the association of bisphosphonate and LLLT is able to increase trabecular bone volume in vertebrae of osteopenic rats in an additive manner (Diniz et al., 2009).

Application of laser therapy are not only helpful in enhancing bone formation and decreasing bone resorption in the osteoporotic ovariectomized rats (Saad et al., 2010), but also; it has positive effects on bone fracture healing (Ninomiya et al., 2003), Laser therapy has the ability to stimulate the attachment and proliferation of the human osteoblasts like cells cultured on titanium implant material indicating that laser therapy can modulate the activity of cells surrounding implant material (Khandra et al., 2005).

The obtained results also agreed with a study assessed the effect of Laser Photo biomodulation on the repair of surgical defects on the femur of rats filled with lyophilized bovine bone. The results showed that there was histological evidence of improved collagen fiber deposition at early stages of the healing; increased amount of well-organized bone trabeculae at the end of the experimental period on irradiated animals (Márquez Martínez et al., 2008).

Results of the present study showed that there was significant improvement in BMD of osteoporotic post-menopausal women in response to LIPUS program. Another form of mechanical stimulation on bone, LIPUS was approved by the Food and Drug Administration (FDA) to promote bone repair (Lind and Bunger, 2001), was utilized by Duarte to accelerate fracture consolidation (Duarte, 1983), has been shown to accelerate bone nodule formation and enhance alkaline phosphatase activity in human osteoblast lineage, and increase trabecular spongiosa of femurs in ovariectomized rats (Wu et al., 2009).

These results were supported by a study showed that osteogenesis is stimulated by ultrasound can be found in vitro studies, osteoblasts can be stimulated to increase collagen production (Rutten et al., 2008). Although restricted to the outer bone cortex; alternate doses of US have beneficial effects on intact bone (Warden et al., 2001), (Carvalho and Cliquet, 2004). Furthermore; in clinical randomized trials, it has been shown that LIPUS can considerably reduce the time to fracture repair (Busse et al., 2002), therapeutic ultrasound can be used to facilitate fracture repair (Wardenm et al., 2006).

These results agreed with previous study reported that ultrasound can cause an immediate decrease in intracellular potassium content in thymocytes a reversible increase in the intracellular level of calciumin chondrocytes, and an increase in calcium incorporation into differentiating cartilage and bone cell cultures (Duncan and Turner, 1995). The beneficial effect of ultrasound on bone healing is due to the piezoelectric phenomenon (Sheng et al., 2001). Bone is piezo-electric, which means that electric potentials are produced in bone when it is subjected to mechanical stress. Since Wolff's law basically states that bone remodels according to functional demands, it is assumed that the stress generated potentials in bone serve as a signal which controls bone remodeling (Hadjiargyrou et al., 1998).

According to the results of this study, it can be concluded that although treatment of osteoporosis in post-menopausal women with either HILT or LIPUS yielded beneficial improvements in BMD, but it is clear that HILT is more effective than LIPUS for the management of osteoporosis in improving BMD in post-menopausal women.

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