



Review Article

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Role of Ultra-sonography in Oral & Maxillofacial Surgery

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Abstract

Objective: The purpose of this review is to make the reader aware of the biophysical basis for using ultra-sound. The focus will primarily be on the use of ultrasound in Oral & Maxillofacial surgery.

Methods: Data were gleaned from a literature search of available medical and dental databases including Research gate, Ovid, Pub-med, Medline, Cochrane and non-medical search engines such as Wikipedia and Google.

Result: In the field of Oral & Maxillofacial Surgery, use of ultrasound for therapeutic as well as for diagnostic purposes have been employed for over three decades with modest documentation on its adverse effect. To clearly distinguish the occurrence or absence of mass like lesions in oral & maxillofacial region and to accurately visualize normal and anomalous anatomic structures various imaging modalities like plain radiography, CT, MRI, and US can be used but among these, US imaging is best because it is easy to use, cost-effective and least invasive.

Conclusion: In this present review, we discussed the role and clinical implications of ultrasonography (US) for therapeutic as well as for the diagnosis of various diseases in oral and maxillofacial regions. Today, we are in need of more studies that must emphasis to study the bio-effects of ultrasound in more comprehensive manner and provide reliable method which can be reproducible for better performance of US.

Key words: Ultra-sonography, cavitation, acoustic microstreaming, distraction osteogenesis

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Introduction

A very limited range of sound frequencies can be heard by human ear and it ranges from 20 – 20,000 Hz; beyond the audible range. Sound frequencies which are below the audible range are known as infra-sonic and frequencies above the audible range are known as ultra-sonic^[1]. 'Curie' brothers in the year 1880 revealed the principles and applications of ultrasound (US). Ultrasound imaging was first used in Austria by Dussik brothers and later in 1972; gray scale ultrasonography was introduced by Kossoff and others. Thus, after a long development and upbringing, investigative (diagnostic) ultrasound is now attaining adolescence with a probability for substantial prospective escalation^[2]. Now days investigative and therapeutic US have a very extensive and diverse range of applications in diagnostic medicine. Whenever radiologists examine an underlying pathological condition, US look like a stethoscope^[3]. Originally, in the field of medicine use of US started with its application in therapy rather than diagnosis, utilizing its thermal and unruly effect on animal tissues^[4]. Experimentally, as a promising investigative tool in medicine ultrasound was used in 1940's and now US is definitely the most extensively used soft tissue imaging modality^[5]. Although the most important application of diagnostic ultrasound is in cardiology, gastroenterology,

obstetrics and gynecology, but in recent times it is also achieving significance in the analysis of oral and maxillofacial lesions. When it comes to the diagnosis using US as a diagnostic tool, piezoelectric effect is being used where the application of the electric field across the material causes that material to expand or to contract depending upon the way in which the field is applied, producing longitudinal oscillations in the surrounding medium^[1].

In the field of Oral & Maxillofacial surgery US can be used as a therapeutic, surgical or as a diagnostic tool. Therefore, the purpose of this review is to make the reader aware of the biophysical basis for using ultrasound. The focus will primarily be on the use of ultrasound in Oral & Maxillofacial surgery.

Discussion

Biophysical effects of ultrasound

Biophysical effects of ultrasound can be Therapeutic US have been examined mainly in vitro studies^[6]. Therapeutic results obtained by ultrasonic energy are thought to be due to^[7]

- i. Increased vascular and fluid circulation
- ii. Increase in cell permeability
- iii. Increase in pain threshold and a break in pain cycle

Thermal effects of ultrasound

Ultrasound is competent enough to produce thermal remedial effects^[8]. According to Dyson (1987), for US to be therapeutic in nature, the tissue must reach a temperature of 40°C to 45°C for at least 5 minutes^[9]. When ultrasound are used over non-perfused tissues for the experimental purpose it was found that it could increase the tissue temperature at a rate of 0.868°C/min (1 W/cm², 1 MHz)^[10] but the outcome of these experiments were tricky to interpret as they were performed in non-perfused tissue. In contrast to this, when the temperature of the living tissues is increased it results in increasing blood flow to tissue, which delivers important nutrients and removes waste. Recently, direct in vivo measurement of tissue temperature during ultrasound treatment has resolved the issue of tissue heating. According to the studies of Draper et al, Ashton et al, and Chan et al there is increase in muscle temperature during a 10-minute treatment with either 1-MHz or 3-MHz ultrasound and the results of their studies revealed that treatment with 1-MHz or 3-MHz ultrasound resulted in a time- and dose dependent increase in tissue temperature^[11-14]. The 3-MHz frequency increased tissue temperature at a faster rate than the 1-MHz frequency^[12].

Non-thermal effects of ultrasound^[4,15,16]

This effect of ultrasound is achieved at intensities of <0.3-1 Watts/cm². At this intensity waves which are produced apply pressure on the cell walls, attributable to cavitation and micro-streaming.

Cavitation

Effects of the sound waves on the fluid within the cell is known as cavitation and it is occurring due to ultrasonically induced pressure changes in tissue fluids causing expansion and compression in gas filled bubbles., with a resulting increase in flow in the surrounding fluid. Cavitations which are stable are considered advantageous to injured tissues and in contrast to this cavitations which are unstable are considered to cause tissue damage.

Acoustic microstreaming

It is considered as unidirectional movement of fluids along cell membranes as a result of mechanical pressure, within the ultrasound field. It may modify cell membrane structure, function and permeability which have been suggested to encourage tissue repair.

These effects (cavitation and microstreaming) leads to alterations in cell membrane permeability and accordingly the circulation of cellular metabolites leading to edema reduction, pain modulation, and in-

creased capillary density which, in turn, increases local circulation^[9]. According to Arndt-Schulz law, weak stimuli increase physiologic activity and very sturdy stimuli slow down or eliminate activity. Therefore, in the treatment of head and neck lesions one should always use weak intensity for therapeutic ultrasound which should be 0.1-0.6 W/cm² and in no case should the treatment exceed 0.6 W/cm² or a total output of 3 W. The more persistent the tissues condition, the less susceptible, and thus the greater the intensity is obligatory at the lesion in order to initiate a physiological response^[17]. The intensity required at the lesion for acute tissue condition is 0.1-0.3 W/cm² and for persistent is 0.3-0.8 W/cm².

Role of Ultrasound in Bone Healing

Ultrasound is commonly used by physical therapists, but there is no accord concerning the most valuable therapeutic dose for accelerating healing of open or closed wounds^[18]. Byl NN carried out a controlled, single-blind, posttest experimental study to compare differences in wound breaking strength and collagen deposition [hydroxyproline (HoPro)]. In this study Forty-eight incisions were surgically induced in three mini Yucatan pigs. Each incision was randomly assigned to a control or an ultrasound treatment group with the sonated incisions further randomly assigned to 5 or 10 days of ultrasound treatment with either high dose ultrasound (HUS) (1.5 W/cm², continuous mode, 1 MHz, 5 minutes) or low dose ultrasound (LUS) (0.5 W/cm², pulsed mode, 20% duty cycle, 1 MHz, 5 minutes). Using the nonparametric two-sample Wilcoxon test, the breaking strength was found to be significantly higher in the sonated incisions compared with the control incisions

(p 5 0.02), but there were no significant differences in HoPro but Hydroxyproline was significantly higher in the LUS group compared with the HUS group after 5 days of ultrasound.

In bone healing the role of US for therapeutic purpose has a history of more than half a century and Maintz, in 1950 was the first person who published his study regarding the effects of ultrasound on bone healing and concluded that US at high intensities caused thermal damage in bone and lower intensity doses lead to new periosteal bone formation^[19]. Two years after this research, Corradi and Cozzolino, concluded that continuous wave ultrasound at 800 kHz and 1.5 W/cm² enthused new callus formation alongside the fracture line in the radial bones of rabbits^[20].

In context of maxillofacial surgery, a report by Cavaliere^[21] may be considered the first report of the clinical application of ultrasound for enhancing maxillofacial bone healing. He used ultrasound at relatively high intensities (1-2 W/cm²) to 4 patients with mandibular fractures and reported increased calluses and decreased pain with the use of ultrasound therapy and the first in vivo study in this area was published by Fedotov^[22] et al in 1986. They used ultrasound treatment at 0.2 to 0.6 W/cm² in rabbit mandibular fractures and reported a stimulated reparative process at the fracture site.

In a study performed by Law et al^[27] on low intensity pulsed ultrasound (LIPUS) concluded that if LIPUS is used daily on dentoalveolar tooth root fracture in rat mandible slices it increases healing of dentin, cementum and alveolar bone

Ikai et al^[23] conducted a study on periodontal wound healing and bone repair after creating bone defects intra-orally at the root level of premolar teeth in 4 beagles bilaterally and started low-intensity pulsed ultrasound (LIPU) treatment on one side and evaluated the bone healing using histologic analysis and immune-histochemical studies and concluded that accelerated bone formation was seen at LIPU treated sites.

No grave complications have been reported as regards the clinical use of therapeutic ultrasound. Reported unpleasant effects due to ultra-

sound treatment comprise muscle spasms on the treatment side, mild erythema, and mild swelling.^[24]

Role of Ultrasound in myofascial pain and temporo-mandibular disorders

In the temporomandibular disorders, the therapeutic efficacy of ultrasonography alone is lacking and it is continually used in the amalgamation with electrical stimulation and this effect of US is because of its thermal possessions^[25]. In the study performed by Esposito et al. using pulsed ultrasound at a frequency of 1 MHz, a pulse repetition rate of 120 Hz, and intensity of 0.75 to 2 W/cm² for 3 to 5 min on ^[28] patients suffering from MPDS and were not responding significantly to occlusal splint therapy, concluded that ultrasound is the most reliable therapy in improving muscle symptoms although the role of US in internal derangement was not verified. In the above-mentioned study, the authors discussed that when US is used in such situations, it causes increase in vasodilation and waste removal, accelerates lymph flow, and stimulates metabolism resulting in pain relief^[26].

On the other hand, Griener A et al.^[7] conducted a study on 100 patients who were suffering from TMJ dysfunctions and related symptoms of muscle spasm concluded that when US was used as sole therapy for such disorders it was not effective in alleviating symptoms, but when used as an adjunct to known modalities of therapy like occlusal splint therapy, heat applications, and muscle conditioning exercises.

Role of Ultrasound in Distraction osteogenesis

Distraction osteogenesis (DO), also known as callus distraction, osteo-distraction, and distraction histogenesis, is a bio-logical procedure of forming new bone and covering soft tissue by steady and meticulous traction of the surgically parted bone segments^[28]. It is considered an efficacious technique to achieve bone and soft-tissue mass in people with craniofacial deformities. Successful use of Ultrasound in healing of bone^[18-23] is well established and lately the technique has also been used successfully to increase growth and healing after osteo-distraction.

El-bialy et al.^[29], in their study on distraction osteogenesis on 36 New-Zealand rabbits assessed bone formation using quantitative bone density (QBD), mechanical testing, and histological examination and concluded that with both pulsed and continuous ultrasound bone formation in rapid distraction osteogenesis (3mm/day) can be increased. The authors also stated that in earlier phases of bone healing continuous ultrasound was more effective although in late stages pulsed ultrasound was more effective.

Schortinghuis et al.^[30], in their study on vertically distracted edentulous mandible used US therapy / placebo therapy daily from the very first day and concluded that treatment with ultrasound in severely resorbed mandible does not appear to stimulate bone formation but instead of its therapeutic effect it serves a good way to detect calcified tissue in distraction far earlier than by using serial radiographs.

Role of Ultrasound in Osseointegration

For the state of partially and fully edentulous endosseous dental implants are considered as the most common treatment modality. It is a well-known fact that successful dental implant practice is primarily based upon or attained by osseointegration, which can be defined as a direct contact between the implant and bone surface^[31]. Quality of osseointegration and shortening the time required for osseointegration has always been the important topic of interest among researchers and for this purpose, alteration of the surface or shape of implant has been tried and studies^[32-33] have showed that rougher the implant surface, higher the chances of osseointegration compared to the implants with smooth surfaces.

To improve osseointegration of implants with bone different forms of biophysical stimulations such as low intensity pulsed ultrasounds (LIPU) and pulsed electromagnetic field were used in different studies^[34-35]. Ustun Y et al.^[36], conducted a pilot study on 12 male New-Zealand rabbits to assess the effects of low intensity pulsed ultrasound (20 min/day) on dental implant osseointegration in a rabbit model by means of mechanical-histomorphometric and resonance-frequency analysis (RFA) and gave a conclusion that LIPU may have encouraging effects on osseointegration and stability of implant.

According to the studies^[37-40], LIPU has stimulatory effect on intracellular activity, cytokine release, bone healing process by expression of numerous genes, and it also has direct outcome by increasing the assimilation of calcium ions in cartilage.

Role of Ultrasound imaging in fine-needle aspiration biopsy

To clearly distinguish the occurrence or absence of mass like lesions in oral & maxillofacial region and to accurately visualize normal and anomalous anatomic structures ultrasound images using B mode can be used. In this mode, the probe of ultrasound is in direct contact with overlying skin areas at different angles. Thus, salivary gland and lymph node associated disease can readily be identified and diagnosed using ultrasound and it is also a very practical tool for FNA biopsy (FNAB)^[41]. FNAB is a precise, quick and cost-effective diagnostic method for diseases in oral and maxillofacial region, and to make FNAB more accurate and safe different imaging modalities like US, CT and MRI can be of assistance. Of these modalities, US imaging is best because it is easy to use, cost-effective and least invasive⁴¹. According to the report by Al-khafaji et al.^[42] on parotid masses, ultrasound guided FNAB has 82% sensitivity and 86% specificity.

In another report published by Mukhi PU and Mahindra UR^[43] on ultrasonographic diagnosis and management of acute superficial facial space infections in 26 subjects concluded that Clinical specificity (69.23%) was found to be poorer than ultrasound specificity (100 %), both clinical and ultrasound showed the same percentage of sensitivity (92.30%).

Role of Ultrasound in hemostasis and vascular occlusion

A number of researchers have confirmed that high intensity focused ultrasound (HIFU) can coagulate blood vessels by combination of tissue disruption, release of coagulation initiation factors and platelet activation resulting in arrest of blood flow in that particular vessel. For this purpose highly focused ultrasound are used with intensity in range of 400-6500 W/cm². This property of ultrasound to selectively occlude the blood vessel can be used in management of cancer where it is necessary to cut-off feeder vessels supplying tumour to prevent tumour spillage^[44].

Sonoporation

Sonoporation is also known as cellular sonication. This technique is used for the delivery of therapeutic agents like proteins, anti-inflammatory and chemo-therapeutic agents and genetic material into the cell, in a cell disruption process called transfection. In this procedure permeability of cell plasma membrane is modified. It employs the acoustic cavitation of micro-bubbles to augment delivery of these large molecules. Therefore, it can be said that this technique has a promising role in drug delivery and gene therapy^[45-46].

Results

In the field of Oral & Maxillofacial Surgery, use of ultrasound for therapeutic as well as for diagnostic purposes have been employed for over three decades with modest documentation on its adverse effect. To clearly distinguish the occurrence or absence of mass like lesions in oral & maxillofacial region and to accurately visualize normal and anomalous anatomic structures various imaging modalities like plain

radiography, CT, MRI, and US can be used but among these, US imaging is best because it is easy to use, cost-effective and least invasive^[4]. Although to study the bio-effects of ultrasound in more comprehensive manner and to better understand its effect on the tissues we need more prospective studies.

Conclusion

In this present review, we discussed the role and clinical implications of ultrasonography (US) for therapeutic as well as for the diagnosis of various diseases in oral and maxillofacial regions. For noninvasive detection of soft tissue-related diseases in oral and maxillofacial regions US is easy to use and at power levels US are capable of producing heat and other biologic effects. Thus, by altering the power levels of US one can attain reasonable amount of palliation either alone or in combination with other available treatment. At present, scientific literature has very less clinical evidence related to therapeutic utility of US, therefore it would be impulsive to abandon the use of US for therapeutic purposes. Today, we are in need of more studies that must emphasize to study the bio-effects of ultrasound in more comprehensive manner and provide reliable method which can be reproducible for better performance of US. The ongoing advancements in this field may assure exciting developments in the coming years.

Reference

- Venkataraman SS, Aravind RJ, Kavin T. The role of diagnostic ultrasound as a new diagnostic aid in oral and maxillofacial surgery. *J Pharm Bioallied Sci.* 2012 Aug; 4 (Suppl 2): S121–S124.
- Vincent LM. Ultrasound of soft tissue abnormalities of the extremities. *Radiol Clin North Am.* 1988; 26:131–44.
- Whaites E. *Essentials of dental radiography and radiology.* 3rd ed. Philadelphia: Elsevier Publications; 2003. p. 191–208.
- Koneru J, Alaparathi R, Yalamanchali S, Reddy RS. Therapeutic ultrasound - The healing sound and its applications in oral diseases: The review of literature. *Journal of Orofacial Sciences*, June 2012; Vol. 4: Issue 1.
- El Bialy T. Therapeutic ultrasound applications in craniofacial growth, healing and tissue engineering. *Rejuvenation Res* 2007; 10:367–72.
- Speed CA. Therapeutic ultrasound in soft tissue lesions. *Rheumatology (Oxford)* 2001; 40:1331–6.
- Grieder A, Vinton PW, Cinotti WR, Kangur TT. An evaluation of ultrasonic therapy for temporomandibular joint dysfunction. *Oral Surg Oral Med Oral Pathol* 1971; 31:25–31.
- Kitchen SS, Partridge CJ. A review of therapeutic ultrasound. *Physiotherapy.* 1990; 76:593–600.
- Dyson M. Mechanisms involved in therapeutic ultrasound. *Physiotherapy.* 1987; 73:116–120.
- Williams R. Production and transmission of ultrasound. *Physiotherapy.* 1987; 73:113–116.
- Draper DO, Schulthies S, Sorvisto P, Hautala AM. Temperature changes in deep muscles of humans during ice and ultrasound therapies: an in vivo study. *J Orthop Sports Phys Ther.* 1995; 21:153–157.
- Draper DO, Castel JC, Castel D. Rate of temperature increase in human muscle during 1-MHz and 3-MHz continuous ultrasound. *J Orthop Sports Phys Ther.* 1995; 22:142–150.
- Ashton DF, Draper DO, Myrer JW. Temperature rise in human muscle during ultrasound treatments using Flex-All as a coupling agent. *J Athl Train.* 1998; 33:136–140.
- Chan AK, Myrer JW, Measom G, Draper DO. Temperature changes in human patellar tendon in response to therapeutic ultrasound. *J Athl Train.* 1998; 33:130–135.
- Baker KG, Robertson VJ, Duck FA. A review of therapeutic ultrasound: Biophysical effects. *Phys Ther* 2001; 81:1351–8.
- Tim Watson. Therapeutic Ultrasound. www.electrotherapy.org web pages 2010;1–14.
- Tim Watson. Ultrasound Dose Calculations. www.electrotherapy.org web pages 2010;1–5.
- Byl NN, McKenzie A, Wong T, Judith West RN, Hunt TK. Incisional Wound Healing: A Controlled Study of Low and High Dose ultrasound. *Journal of Orthopaedic & Sports Physical Therapy.* 1993; 18(5): 619–28
- Ter Haar G. Therapeutic applications of ultrasound. *Prog Biophys Mol Biol* 2007; 93:111–29.
- Schortinghuis J, Stegenga B, Raghoobar GM, de Bont LG. Ultrasound stimulation of maxillofacial bone healing. *Crit Rev Oral Biol Med* 2003; 14:63–74.
- Cavaliere R. Role of ultrasound in healing of rabbit mandibular fracture. *Riv Ital Stomatol* 1957; 12:1397–1406.
- Fedotov SN, Minin EA, Borisov IN. Effect of local cooling and ultrasound on the reparative processes following mandibular fracture [in Russian]. *Stomatologiya (Mosk)* 1986; 65:4–6.
- Ikai H, Tamura T, Watanabe T, et al. Low-intensity pulsed ultrasound accelerates periodontal wound healing after flap surgery. *J Periodontol Res* 2008; 43:212–216.
- Kokubu T, Matsui N, Fujioka H, Tsunoda M, Mizuno K. Low intensity pulsed ultrasound exposure increases prostaglandin E2 production via the induction of cyclooxygenase-2 mRNA in mouse osteoblasts. *Biochem Biophys Res Commun* 1999; 256:284–287.
- Mohl ND, Ohrbach RK, Crow HC, Gross AJ. Devices for the diagnosis and treatment of temporomandibular disorders. Part III: Thermography, ultrasound, electrical stimulation, and electromyographic biofeedback. *J Prosthet Dent* 1990; 63:472–7.
- Esposito CJ, Veal SJ, Farman AG. Alleviation of myofascial pain with ultrasonic therapy. *J Prosthet Dentistry* 1984; 51:106–8.
- Law A, Sadeghi H, Sloan A.J, El-Bialy TH. Effect of therapeutic ultrasound on dentoalveolar fracture in organ culture. iadr.confex.com/iadr/2011/sandiego/.../abstract_149263.htm.
- Cope JB, Samchukov ML, Cherkashin AM. Mandibular distraction osteogenesis: a historic perspective and future directions. *Am J Orthod Dentofac Orthop* 1999; 115:448–60.
- El-Bialy TH, Elgazzar RF, Megahed EE, Royston TJ. Effects of ultrasound modes on mandibular osteodistraction. *J Dent Res* 2008; 87:953–7.
- Schortinghuis J, Bronckers AL, Gravendeel J, Stegenga B, Raghoobar G.M. The effect of ultrasound on osteogenesis in the vertically distracted edentulous mandible. A double-blind trial. *Int J Oral Maxillofac Surg* 2008; 37:1014–21.
- Brånemark PI, Zarb G, Albrektsson T. Tissue-integrated prosthesis. In: Brånemark PI, ed. *Osseointegration in clinical dentistry.* Chicago, IL: Quintessence Publishing Co. 1985:11–76.
- Buser D, Schenk RK, Steinmann S, Fiorellini JP, Fox CH, Stich H. Influence of surface characteristics on bone integration of titanium implants. A histomorphometric study in miniature pigs. *J Biomed Mater Res* 1991; 25:889–902.
- Ericsson I, Johansson CB, Bystedt H, Norton MR. A histomorphometric evaluation of bone-to-implant contact on machine-prepared and roughened titanium dental implants. A pilot study in the dog. *Clin Oral Implan Res* 1994; 5:202–206.
- Fini M, Giavaresi G, Setti S, Martini L, Torricelli P, Giordano R. Current trends in the enhancement of biomaterial osteointegration: Biophysical stimulation. *Biomaterials* 2004; 27:681–690.
- Tanzer M, Kantor S, Bobyn JD. Enhancement of bone growth into porous intramedullary implants using non-invasive low intensity ultrasound. *J Orthop Res* 2001; 19:195–199.
- Ustun Y, Erdogan O, Kurkcu M, Akova T, Damlar I. Effects of low-intensity pulsed ultrasound on dental implant osseointegration: A preliminary report. *Eur J Dent* 2008; 2:254–262.

37. Chapman I, Macnally NA, Tucker S. Ultrasound-induced changes in the rates of influx and efflux of potassium ions in rat thymocytes in vitro. *Ultrasound Med Biol* 1980; 6:47-58.
38. Li JK, Chang WH, Lin JC, Ruaan RC, Liu HC, Sun JS. Cytokine release from osteoblasts in response to ultrasound stimulation. *Biomaterials* 2003; 24:2379-2385.
39. Rubin C, Bolander M, Ryabi JP, Hadjiargyrou M. The use of low-intensity ultrasound to accelerate the healing of fractures. *J Bone Joint Surg Am* 2001; 83:259-270.
40. Yang KH, Parvizi J, Wang SJ, Lewallen DG, Kinnick RR, Greenleaf JF, Bolander ME. Exposure to low-intensity ultrasound increases aggrecan gene expression in a rat femur fracture model. *J Orthop Res* 1996; 14:802-809.
41. Sato NW, Kodama M, Kou Matsuo, Yamamoto M, Oda M, Ishikawa A et al. Advanced Clinical Usefulness of Ultrasonography for Diseases in Oral and Maxillofacial Regions. *International Journal of Dentistry* Volume 2010, Article ID 639382, 1-10.
42. B. M. Al-Khafaji, B. R. Nestok, and R. L. Katz, "Fine-needle aspiration of 154 parotid masses with histologic correlation. Ten-year experience at the University of Texas M.D. Anderson Cancer Center," *Cancer*, vol. 84, no. 3, pp. 153-159, 1998.
43. Mukhi PU, Mahindra UR. The use of ultrasonography in diagnosis and management of superficial fascial space infections. *Indian Journal of Dental Research*, 23(3), 2012; 313-319.
44. Ter Haar G. Therapeutic applications of ultrasound. *Prog Biophys Mol Biol* 2007; 93:111-29.
45. Pitt WG, Hussein GA, Staples BJ. Ultrasonic Drug Delivery – A General Review. *Expert Opin Drug Deliv* 2004; 1:37-56.
46. Maeda H, Tominaga K, Iwanaga K, Nagao F, Habu M, Tsujisawa T, et al. Targeted drug delivery system for oral cancer therapy using sonoporation. *J Oral Pathol Med* 2009; 38:572-9.