Ultrasonic Stimulation of Maxillofacial Bone Healing

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ABSTRACT: A substantial part of the maxillofacial surgery practice deals with maxillofacial bone healing. In the past decades, low-intensity ultrasound treatment has been shown to reduce the healing time of fresh fractures of the extremities up to 38%, and to heal delayed and non-unions up to 90% and 83%, respectively. Based on the assumption that the process of bone healing in the bones of the extremities and maxillofacial skeleton is essentially the same, the potential of ultrasound to stimulate maxillofacial bone healing was investigated. Although limited evidence is available to support the susceptibility of maxillofacial bone to the ultrasound signal, ultrasound may be of value in the treatment of delayed unions, in callus maturation after distraction, and in the treatment of osteoradionecrosis.

Key words. Ultrasound, therapy, maxillofacial, bone, healing.

(1) Introduction

Disturbed bone healing is generally considered a serious medical problem because of the resulting impairment of function. Traditionally, bone-healing disturbances have been associated with fractures. These days, however, it may occur as an unwanted side-effect of several therapies, such as osteotomies, bone grafting, bone distraction, and therapeutic irradiation. Insight into the (patho)physiologic mechanisms of bone healing has led to several interventions essentially intended to stimulate the healing process (Einhorn, 1995). Of all the means to influence fracture healing, sound distinguishes itself by being non-invasive and easy to apply. Ultrasound as a treatment modality is traditionally used in the field of physiotherapy to treat soft-tissue disorders by deep-heating of the tissue. This is accomplished by using intensities of 0.5 to 3.0 watts per square centimeter (W cm⁻²). Despite its medical use for more than half a century, the efficacy of ultrasound in the treatment of various musculoskeletal disorders, such as temporomandibular disorders and myofascial pain, still remains to be established (van der Windt et al., 1999). In contrast, the effect of ultrasound on bone healing has become well-established during the past decades. The intensities used in the treatment of fractures are considerably lower than those used in physiotherapy because of the risk of over-heating of bone. Currently, the most widely used device to treat patients with compromised fracture healing is the Sonic Accelerated Fracture Healing System (SAFHS) (Smith and Nephew, Exogen, Memphis, TN, USA) (Fig. 1). This device emits a pulsed soundwave of 1.5 MHz, with an average intensity over space and time of 30 milliwatts per square centimeter (mW cm⁻²).

Since bone healing and regeneration are of particular interest in maxillofacial surgery, it is the aim of this manuscript to review current knowledge of the stimulation of bone healing by means of ultrasound, and to investigate the potential of its application in maxillofacial surgery.

(2) Materials and Methods

This review is based on a MEDLINE search (MEDLINE 1967-2001) with the following key words used as free text, without language restrictions: bone healing, therapeutic, ultrasound, maxillofacial, TMJ, temporomandibular, myofascial. In addition, the register books of Strahlentherapie covering the years 1912-1967 (key words Ultraschall, Knochen, Kiefer, Mund, Schaden), and the textbooks of Cady (1946), Pohlman (1951), Wiedau and Röher (1963), Kolář et al. (1965), Urick (1967), Knoch and Knauth (1977), Wells (1977), Suslick (1988), and Knoch and Klug (1991) were used. The reference lists in the obtained literature were traced for relevant additional publications. Furthermore, information was obtained from the archives of the “Commission de la Défense Nationale”, Academy of Sciences, Paris (France) and from the Internet site of the American Institute of the History of Physics. Publications that could not be traced were not included in this survey.

(3) Review of Current Knowledge

Historical survey

The foundation of ultrasound was laid in 1880, when the brothers Jacques and Pierre Curie (1880) observed that certain crystals generated electricity when subjected to pressure at specific angles. This observed piezo-electric effect can be reversed: If the crystal is subjected to an alternating current at the resonance frequency of the crystal, it expands and contracts at this frequency. Thus, a high-frequency sound wave is emitted. At the beginning of World War I, in France, Paul Langevin (1926) used this principle to perfect a submarine detector. He was also the first to notice biological effects of ultrasound: Fish put within a strong ultrasound field died after a period of violent movements, and investigators experienced pain of considerable severity when thrusting their hands into the water in the tank (Wood and Loomis,
Other experiments confirmed the damaging capabilities of ultrasound involved exposure of the affected area for five to ten minutes. Osteomyelitis of the alveolar bone (Halsscheidt, 1951). However, a case of bone damage involved the practice (Barth and Bülow, 1949). Others reported the same, but a painless dose did not produce bone damage (Barth and Bülow, 1949a). These findings were not in agreement with those reported by Ardan et al. (1954). A slight growth acceleration occurred when a young dog’s leg was exposed to a fast-moving ultrasound transducer (Buchtala, 1949a). A growth acceleration of the heel bone in a child when apophysitis was treated, as well as a growth acceleration after exposure of plant roots to ultrasound, has been observed. In another study, radiographic and histologic changes in bone exposed in water to 1 MHz ultrasound at different intensities have been described (Buchtala, 1949b). Limbs of young dogs and rabbits were treated for five minutes at a time. It was claimed that 1.2 W cm$^{-2}$ for five minutes a day for 4 days was capable of producing bone changes leading to deformation of limbs. Epiphyseal exposed to low-intensity ultrasound responded with an acceleration of growth (i.e., widening of the epiphyseal line). Higher intensities slowed the growth, whereas the highest intensities arrested bone growth. Another observation was that articular cartilage exhibited considerable hypertrophy following ultrasound treatment. The intensities used, however, were not specified.

In 1950, Maintz (1950) published the first study in which the relationship between ultrasound and bone healing was investigated. This study marked a turning point in this research arena, because it focused on the possible stimulatory effects of ultrasound on bone, rather than on its harmful effects. At that time, it was known that callus formation could be accelerated by the induction of a more intensive and longer reactive fracture hyperemia. This was accomplished by, for example, sympathectomies and manual manipulation of the fracture site. The concept that all bone regenerations were accompanied with hyperemia had been stated earlier (Lexer, 1924). Since ultrasound induces tissue-hyperemia, Maintz (1950) decided to investigate the potential of ultrasound to accelerate bone healing. In three-month-old rabbits, a piece of the radius was resected bilaterally. The procedure was not further detailed. The treatment regime involved five ultrasound treatments of the right leg, starting at the third post-operative day. The treatments were done either on a daily basis or every other day. Eight groups were exposed to 0.5, 1.0, 1.5, and 2.5 W cm$^{-2}$ ultrasound energy, for one or five minutes’ duration. Ultrasound of 800 kHz was used. The fractures were examined histologically and radiographically. No effect was observed with the one- and the five-minute ultrasound treatments at 0.5 W cm$^{-2}$. Exposures to ultrasound at higher intensities showed a reduction and arrest of callus formation and a detachment of the epiphysis. The non-treated legs healed without complications. Interestingly, lower doses did cause osteogenesis at a site distant from the fracture site and ultrasound application. Also, the simultaneously exposed ulnar showed subperiosteal osteogenesis. Maintz concluded that periosteal new bone formation could be produced by ultrasonic energy, but only in intact normal bone, and that the required dose was close to the destructive level, so that this new bone formation was often followed by atrophy of bone, with or without fracture. Unfortunately, the study did not show an accelerated healing of bone, but basically confirmed the already-known destructive effect of ultrasound on bone. Later, similar results were reported by Ardan et al. (1954). However, similar treatment regimes did show a positive effect on callus formation in another study which involved bilateral femoral fractures in rabbits (De Nunno, 1952). The fractures on one side were treated daily, during 5 days, for 10 minutes, with 1 MHz ultrasound at 2.0 W cm$^{-2}$. The fracture on the other side served as a control. At post-operative days 4, 6, 8, and 10, animals were killed, and histologic evaluation was performed. The results showed, in contrast to those reported by Maintz, that...
callus formation was more abundant in the ultrasound-treated legs and was observed only during the early phases of healing. The histologic changes seen in callus after 10 days in the non-treated leg were similar to those seen in the ultrasound-treated callus at day 6.

In a controlled study, continuous-wave 800-kHz ultrasound of 1.5 W cm$^{-2}$ was found to stimulate the formation of callus in radial fractures in rabbits (Corradi and Cozzolino, 1952).

Soon after the study by Maintz, it became clear that the intensity of ultrasound had to be decreased if fracture healing and bone growth were to be stimulated (Murolo and Claudio, 1952; Shiro, 1964). Using 0.5 W cm$^{-2}$ ultrasound which was pulsed 1.5 (i.e., period 'on' : period 'off' = 1.5), investigators observed a histologic and radiographic acceleration of ulnar fracture healing in guinea pigs (Murolo and Claudio, 1952).

The treatment regime consisted of a maximum of 25 treatments for two minutes daily. When the ultrasound is administered in short bursts, heat accumulation is limited, and the average amount of administered energy per second is less (Fig. 2). Ultrasound stimulation of bone growth was observed in the proximal end of the tibia in young rabbits (Shiro, 1964). Low-intensity ultrasound (0.2 W cm$^{-2}$), two times for five minutes each, was used. Histologically, osteo-chondroblastic activity was found to be greater than in the non-treated controls.

**Human studies**

An indication that ultrasound could positively influence bone repair processes in humans was found in an early report by Strauß (1948) (Table 1). In his surgical practice, he treated various infectious conditions with ultrasound because of its reported bactericidal action. Ultrasound of 0.8 W cm$^{-2}$ intensity was used, with frequencies of 800 and 2400 kHz. The transducer was applied to the skin in a stroking motion to prevent over heating. Although no data were presented, the author reported an accelerated healing of chronic osteomyelitis due to, for example, gunshot wounds. Another report described the treatment of two cases of osteoradionecrosis, in which ultrasound treatment led to the covering of the non-healing bone with fresh granulation tissue (Halsscheidt et al., 1949). After a period, a sequester formed, exfoliated, and the defects healed. The earliest studies concerning ultrasound treatment of bone disorders can be traced back to the 1950s. In 1953, the treatment of 181 slow- and non-unifying fractures with ultrasound was reported (Hippe and Uhlman, 1953). In 154 cases (85%), healing was obtained by the use of 800 kHz ultrasound of 1 to 1.5 W cm$^{-2}$ for five minutes every two days, with a total of 10-12 treatments. Treatment was applied with the limb and ultrasound transducer under water or with the use of a viscous gel. The ultrasound was administered through a moving or stationary transducer. In the same year, there were similar reports of an increase in callus formation when ultrasound therapy was used (Corradi and Cozzolino, 1953; Corradi and del Moro, 1953). Later, it was reported that the use of ultrasound on mandibular fractures led to less pain and increased callus formation (Cavaliere, 1957). In one case of delayed mandibular union, ultrasound therapy resulted in union (Cavaliere, 1957). One to two W cm$^{-2}$ ultrasound with a frequency of 0.7 to 1 MHz was used, which was administered in pulses of 1 ms. From 10 to 15 treatments of five to 10 minutes' duration were given. The ultrasound transducer was applied to the skin with circular movements. Knoch (1965) reported successfully treating 31 patients with different non-unifying fractures (malleolar, patellar, clavicular, humeral, olecranon, radial, and navicular) with ultrasound.

An 800-kHz ultrasound of 0.3 to 0.8 W cm$^{-2}$ intensity was used for five to eight minutes every other day. After 10-20 sessions, all fractures had united clinically. In another study, the influence of the same ultrasound regime on the healing time of fresh radial and navicular fractures was reported (Knoch, 1965). It was not until the 1980s that ultrasound stimulation of bone healing received more attention and more studies involving human subjects were published. Xavier and Duarte (1983) reported successful application of low-intensity pulsed ultrasound (30 mW cm$^{-2}$) in the treatment of 27 recalcitrant non-unions. In 70% of the cases, complete healing was obtained by daily 20-minute ultrasound exposure of the non-union site. Although these results were very promising, the most compelling evidence that ultrasound accelerates fractures healing was presented in prospective, double-blind, placebo-controlled clinical trials. The first double-blind trial of ultrasound focused on the healing rate of fresh closed or grade I open tibial fractures (Heckman et al., 1994). Ultrasound, based on the sound used by Xavier and Duarte, was administered by the Sonic Accelerated Fracture Healing System (SAFHS) (Smith and Nephew, Exogen, Memphis, TN, USA) (Fig. 1). The ultrasound consists of a 1.5-MHz sine wave, which is administered in bursts of 200 μs, followed by a pause of 800 μs (pulsed 1:4). This is repeated 1000 times per second (repetition rate: 1 kHz). The average intensity over space and time is 30 mW cm$^{-2}$, and the average intensity during the 'on' period is 150 mW cm$^{-2}$. Ultrasound was administered for 20 minutes daily through a non-moving transducer, and led to a 24% reduction in the time for clinical healing to occur (86 ± 5.8 days in the ultrasound treatment group compared with 114 ± 10.4 days in the placebo group, p = 0.01). Based on clinical and radiographic criteria, a 38% decrease in time to overall healing was apparent (96 ± 4.9 days in the ultrasound treatment group compared with 154 ± 13.7 days in the control group, p = 0.0001). Another double-blind trial with SAFHS devices concerned the healing of 61 dorsally angulated fractures of the distal radius. With the same ultrasound treatment protocol, a reduction in time to union of 38% (61 ± 3 days for the treatment
group, compared with 98 ± 5 days for the placebo group, p < 0.0001) was found (Kristiansen et al., 1997). To ensure quality control, these studies excluded patients with conditions that may influence the fracture-healing process. However, in reality, patients present with conditions which may disturb fracture healing, such as diabetes, smoking, and certain medications such as calcium-blockers and steroids. These patients are at a higher risk of developing delayed unions and non-unions. A few studies addressed the influence of ultrasound therapy on medically compromised patients (Cook et al., 1997; Mayr et al., 2000a). When the results of the two aforementioned studies were stratified to patient smoking habits, it became clear that SAFHS ultrasound could overrule the negative effects of nicotine on the fracture-healing process (Cook et al., 1997). Nevertheless, patients who

<table>
<thead>
<tr>
<th>Year, Author</th>
<th>Indication</th>
<th>Study Design</th>
<th>No. of Patients</th>
<th>Ultrasound Intensitya</th>
<th>b</th>
<th>Observed Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>1948, Strauß</td>
<td>Osteomyelitis</td>
<td>O</td>
<td>1</td>
<td>800 (cw)b</td>
<td>Healed</td>
<td></td>
</tr>
<tr>
<td>1949, Halsscheidt et al.</td>
<td>Osteoradionecrosis</td>
<td>O(CS)</td>
<td>2</td>
<td>600-1300 (cw)</td>
<td>Healed</td>
<td></td>
</tr>
<tr>
<td>1953, Corradi and del Moro</td>
<td>Lunate necrosis</td>
<td>O(CS)</td>
<td>3</td>
<td>Unknown</td>
<td>Less pain, improved function</td>
<td></td>
</tr>
<tr>
<td>1953, Corradi and Cozzolino</td>
<td>Slow-uniting fractures</td>
<td>O(CS)</td>
<td>6</td>
<td>Unknown</td>
<td>Healed</td>
<td></td>
</tr>
<tr>
<td>1953, Hippe and Uhlein</td>
<td>Non-unions</td>
<td>O(CS)</td>
<td>181</td>
<td>1000-1500 (cw)</td>
<td>85% healed</td>
<td></td>
</tr>
<tr>
<td>1957, Cavaliere</td>
<td>Mandibular fractures (3 fresh and 1 delayed union)</td>
<td>O(CS)</td>
<td>4</td>
<td>1000-2000 (p)</td>
<td>Less pain, more callus</td>
<td></td>
</tr>
<tr>
<td>1965, Knoch</td>
<td>Slow-uniting fractures</td>
<td>O(CS)</td>
<td>31</td>
<td>300-800 (cw)</td>
<td>100% healed</td>
<td></td>
</tr>
<tr>
<td>1965, Knoch</td>
<td>Fresh radial fractures</td>
<td>O(CC)</td>
<td>200</td>
<td>300 (cw)</td>
<td>41% reduction in disability time</td>
<td></td>
</tr>
<tr>
<td>1965, Knoch</td>
<td>Fresh navicular fractures</td>
<td>O(CC)</td>
<td>28</td>
<td>300 (cw)</td>
<td>60% reduction in disability time</td>
<td></td>
</tr>
<tr>
<td>1983, Xavier and Duarte</td>
<td>Non-unions</td>
<td>O(CS)</td>
<td>27</td>
<td>30;150 (p)</td>
<td>70% healed</td>
<td></td>
</tr>
<tr>
<td>1992, Harris</td>
<td>Mandibular osteoradionecrosis</td>
<td>O</td>
<td>24</td>
<td>1000 (p)</td>
<td>48% spared surgery</td>
<td></td>
</tr>
<tr>
<td>1994, Heckman et al.</td>
<td>Fresh tibial fractures</td>
<td>DBRCT</td>
<td>67</td>
<td>30;150 (p)</td>
<td>38% reduction in healing time</td>
<td></td>
</tr>
<tr>
<td>1997, Kristiansen et al.</td>
<td>Fresh distal radial fractures</td>
<td>DBRCT</td>
<td>61</td>
<td>30;150 (p)</td>
<td>38% reduction in healing time</td>
<td></td>
</tr>
<tr>
<td>1997, Cook et al.</td>
<td>Fresh radial fractures</td>
<td>DBRCT</td>
<td>67</td>
<td>30;150 (p)</td>
<td>41% reduction in healing time in smokers</td>
<td></td>
</tr>
<tr>
<td>1997, Cook et al.</td>
<td>Fresh distal radial fractures</td>
<td>DBRCT</td>
<td>61</td>
<td>30;150 (p)</td>
<td>51% reduction in healing time in smokers</td>
<td></td>
</tr>
<tr>
<td>1998, Nolte et al.</td>
<td>Osteotomies of lower extremity</td>
<td>DBRCT</td>
<td>20</td>
<td>30;150 (p)</td>
<td>24% reduction in healing time</td>
<td></td>
</tr>
<tr>
<td>1999, Emami et al.</td>
<td>Fresh tibial fractures</td>
<td>DBRCT</td>
<td>30</td>
<td>30;150 (p)</td>
<td>No effect on healing rate</td>
<td></td>
</tr>
<tr>
<td>1999, Sato et al.</td>
<td>Leg distraction</td>
<td>O</td>
<td>1</td>
<td>30;150 (p)</td>
<td>Increased bone mineral density</td>
<td></td>
</tr>
<tr>
<td>2000a, Mayr et al.</td>
<td>Delayed unions</td>
<td>O(CS)</td>
<td>26</td>
<td>30;150 (p)</td>
<td>85% healed</td>
<td></td>
</tr>
<tr>
<td>2000b, Mayr et al.</td>
<td>Non-unions</td>
<td>O(CS)</td>
<td>16</td>
<td>30;150 (p)</td>
<td>94% healed</td>
<td></td>
</tr>
<tr>
<td>2000, Fujioka et al.</td>
<td>Hamate non-union</td>
<td>O</td>
<td>1</td>
<td>30;150 (p)</td>
<td>Healed</td>
<td></td>
</tr>
<tr>
<td>2001a, Nolte et al</td>
<td>Non-unions</td>
<td>O(CS)</td>
<td>29</td>
<td>30;150 (p)</td>
<td>86% healed</td>
<td></td>
</tr>
</tbody>
</table>

a When continuous-wave (cw) ultrasound was used, the average intensity over space and time is given (I_{SATA}). When pulsed (p) ultrasound was used, both the I_{SATA} and the average intensity of the 'on' period (I_{SAPA}) are given.

b Abbreviations: cw, continuous wave; p, pulsed; I_{SATA} = space average time average intensity; I_{SAPA} = space average peak average intensity; O, observational; O(CS), observational case series; O(CC), observational case control; RCT, randomized clinical trial; DBRCT, double-blind randomized clinical trial.
TABLE 2
Data from the Worldwide Prescription Use of the SAFHS Device in the Treatment of Fresh Fractures, Delayed Unions*, and Non-unions (completed cases as of June 15, 2000)

<table>
<thead>
<tr>
<th>Fracture Age (Range)</th>
<th>Healed/Treated</th>
<th>Heal Rate (%)</th>
<th>Heal Time (days)</th>
<th>Fracture Age (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fresh fracture (0-90 days)</td>
<td>4761/5058</td>
<td>94</td>
<td>112</td>
<td>39</td>
</tr>
<tr>
<td>Delayed union (91-255 days)</td>
<td>2852/3173</td>
<td>90</td>
<td>120</td>
<td>149</td>
</tr>
<tr>
<td>Non-union (&gt; = 256 days)</td>
<td>1283/1546</td>
<td>83</td>
<td>136</td>
<td>692</td>
</tr>
</tbody>
</table>

* A delayed union is defined as no clinical or radiographic healing observed between 91 and 255 days. A non-union is defined as no clinical or radiological healing for more than 256 days. The fractures were located at different sites in the extremities (humerus, radius, ulna, scaphoid, femur, tibia, fibula, and metatarsus).

smoke during therapy have lower healing rates than those who have never smoked (Mayr et al., 2000a). This means that ultrasound therapy not only accelerates fracture healing, but also helps to ensure undisturbed fracture healing.

In disturbed fracture healing (delayed union, non-union), ultrasound can produce healing at a high success rate (Nolte et al., 2001b). Furthermore, the worldwide prescription use registry of the SAFHS device shows that ultrasound is of value in the non-operative treatment of fresh fractures, delayed unions, and non-unions located at various sites (Exogen Inc., 2000) (Table 2). It should be noted that the positive effects of SAFHS ultrasound are not always evident. During a 75-day course of SAFHS ultrasound of Tibial fractures fixed with a locked intramedullary nail, there were no differences in the healing rates between the placebo and the treatment groups (Emami et al., 1999). In contrast, a longer period of ultrasound treatment of Tibial fractures which were treated by closed reduction and cast immobilization resulted in a 38% reduction in healing time (Heckman et al., 1994). This illustrates that ultrasound does not always work in all orthopedic conditions (Rubin et al., 2001).

(4) Insight into the Mechanism of Ultrasound

The basis of the biological effect of ultrasound is an altered, albeit unknown, cell response. Despite the complexity of the fracture-healing process (Einhorn, 1998) and the complexity of the interaction of ultrasound with living tissue, many effects of ultrasound on living cells and tissues are known. These effects provide insights into the biological effects of ultrasound. It seems that the biological effect of ultrasound on bone is the result of a combination of physical and piezo-electric effects leading to cellular responses in which the cell membrane plays an important role (Fig. 3).

PHYSICAL EFFECTS

When ultrasound traverses through a tissue, vibrating forces are applied on every tissue component, such as intra- and extra-cellular fluids and cell membranes. For example, 1.5 MHz, 150 mW cm$^{-2}$ ultrasound displaces particles in the tissue over a distance of 4.6 nm (i.e., some 30 diameters of the hydrogen ion), with a peak velocity of 4.6 cm s$^{-1}$ and a peak acceleration of 410.000 m s$^{-2}$. The peak pressure applied to the medium equals 70 kPa (Wells, 1969). The direction of particle displacement is reversed 1.5 million times per second, according to the frequency. Because of these fast vibrations, ultrasound treatment is described in terms of 'internal tissue massage' or 'micromassage'. The physical effects of these motions can be grouped into those which are predominantly thermal in origin and those which are predominantly non-thermal (Dyson, 1982). When an ultrasound wave traverses through tissue, the wave energy is absorbed and can result in heating. This process of energy loss (attenuation) is related to the density of the tissue (ter Haar, 1987), making bone sensitive to heat. In physiotherapy, this selective tissue heating is considered beneficial in the treatment of soft-tissue disorders (with intensities of 0.5 - 3.0 W cm$^{-2}$ and a moving transducer). The observed thermal effects include an increased blood flow, increased extensibility of collagenous tissues, decreased pain, and decreased muscle spasm (Dyson, 1987). However, thermal effects are not considered to play a role in the ultrasound treatment of bone, because the intensities currently used are low. For example, the pulsed ultrasound of 30 mW cm$^{-2}$ (SAFHS device) is considered incapable of heating bone (Ziskin, 1989). This suggests that non-thermal mechanisms must account for the observed effects on the bone-healing process. Non-thermal effects that could explain some observed effects include stable cavitation, microstreaming, acoustical streaming, and direct mechanical effects on the cell membrane.

Stable cavitation is the formation of very small gas- or vapor-filled bubbles in fluids as a result of ultrasonically induced pressure changes. Cavities may be present in aerated media or may develop through the process of rectified diffusion. The bubbles

![Figure 3](https://example.com/figure3.png)

**Figure 3.** The basis of biophysical stimulation of bone healing according to Wolff's Law is depicted in a simplified scheme. In the case of injury, bone-stimulating signals through physiologic loading are absent. Ultrasound and electric/electromagnetic stimulation provide a substitute for these signals.
grow and may oscillate in the sound field, increasing and decreasing in volume. This motion gives rise to a localized liquid flow in the fluid around the vibrating bubble, called microstreaming, which in turn may alter cellular processes (Dyson, 1982). Cavitation may occur in living tissue, even when it is subjected to ultrasound of low intensities. There is evidence that 0.75 MHz ultrasound at peak intensities of 240 mW cm\(^{-2}\) and higher can produce bubbles greater than 10 \(\mu\)m in guinea pigs’ hind legs (ter Haar et al., 1982). For the SAFHS device, it has been calculated (data from manual, SAFH 2000\(^{2}\) system) that peak intensities of 350 mW cm\(^{-2}\) are present in the ultrasound field, which may increase further due to reflections at the bone surface. Consequently, cavitation may play a role in the treatment of fractures when the SAFHS ultrasound field is used. Cavitation is probably likely to produce cellular change, because certain cellular effects could not be observed under elevated ambient pressure which prevents the process of cavitation. It has been reported that collagen synthesis by human fibroblasts was stimulated by five minutes’ exposure to 3 MHz ultrasound at a space-time peak intensity of 0.5 W cm\(^{-2}\) and at ambient pressure, but not at a positive pressure of 2 atmospheres (Webster et al., 1978). However, the extent to which cavitation plays a role in vivo is not well-understood and still needs to be determined (Frizzell, 1988).

Acoustic streaming is caused by absorption of kinetic energy of the ultrasonic field in a fluid due to absorption or scattering. This causes a motion of the fluid which is referred as ‘a sonic wind’. This motion, at least in theory, may facilitate the movement of intra- and extracellular ions and metabolites.

Ultrasound is capable of producing changes within the cell membrane (Dinno et al., 1989). This is illustrated by ultrasound’s capacity to alter cell membrane permeability to ions and to alter cell membrane electrophysiological properties. Ultrasound can cause an immediate decrease in intracellular potassium content in thymocytes (Chapman et al., 1980), a reversible increase in the intracellular level of calcium in chondrocytes (Parvizi et al., 1997), and an increase in calcium incorporation into differentiating cartilage and bone cell cultures (Ryaby et al., 1989). In addition to these changes in membrane permeability, ultrasound is also capable of changing the electrophysiological properties of cell membranes. This was found in frog skin, which resembles human skin. Following exposure of frog skin (bathed in amphibian sodium chloride Ringer’s solution) to 1 MHz continuous-wave ultrasound at 60-480 mW cm\(^{-2}\), a 5 to 50% intensity-dependent decrease in transepidermal potential and resistance was measured in open-circuit conditions. In short-circuit conditions, an intensity-dependent decrease of 20 to 220% in total ionic conductance was found (Dinno et al., 1989). This suggests that ultrasound reduces the electromotive force of the sodium-potassium ATP-ase pump. Because no effect was observed in a de-gassed solution, cavitation seemed to be involved in producing these effects.

Depending on the cell type, the result of changes in intracellular calcium ions can be synthesis, secretion, or motility changes, all of which could promote healing (Dyson, 1987). With respect to bone healing, there are also indications that ultrasound influences the adenylate cyclase cascade in the cell membranes of osteoblasts (Ryaby et al., 1992), a finding which is similar to that observed following an application of static mechanical load (Ryaby et al., 1990). The changes in the cell membrane may be the most important mechanism by which the ultrasound signal influences cellular changes and responses. It is not clear if these changes are brought about by a direct mechanical deformation of the cell membrane, deformation of cell receptors, or indirectly as a consequence of cavitation, microstreaming, or a combination of these or other effects.

### Piezo-electric effects

It has been argued that the beneficial effect of ultrasound on bone healing is due to the piezo-electric phenomenon (Duarte, 1983; Klug, 1983; Zorlu et al., 1998). Bone is piezo-electric, which means that electric potentials are produced in bone when it is subjected to mechanical stress (Fukada and Yasuda, 1957). Since Wolff’s law (Wolff, 1992) 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 (Bassett, 1962). Much research has been conducted to help us gain insight into the nature of these stress-generated potentials, and this eventually has led to the development of successful therapies to stimulate fracture healing with electromagnetic and electric fields (Uhl, 1989; Ryaby, 1998). It has been stated that this biological intervention serves as a surrogate for the regulatory signals that normally arise as a result of functional loading of the skeleton, but which are absent following bone injury (Hadjiargyrou et al., 1998) (Fig. 3). Ultrasound is a biological intervention that is capable of generating piezo-electric effects in bone (Behari and Singh, 1981), and increasing electric potentials in bone (Klug, 1983). Using 1.27-MHz ultrasound with a very low intensity of 0.0083 W cm\(^{-2}\) on bone, Behari and Singh (1981) measured an electric potential of 64 \(\mu\)V at the ultrasound frequency in vivo. In a 21-day-old rabbit tibial fracture, there is an increase in callus potential of 0.9 mV during application of 880-kHz low-intensity ultrasound of 0.01 W cm\(^{-2}\) (Klug, 1983). A major problem with the theory that locally developed potential differences are responsible for cellular change is that the potentials generated by ultrasound are very small compared with potential changes generated by muscle activity. In rabbits, the potential difference generated at a bone surface by bone deformation (2.2 mV) was considerably less than the electric potential difference measured on the bone surface which was generated by muscle activity (100 mV) (McDonald and Houston, 1990). So, it may be concluded that the extent to which ultrasonic induced potentials exert an effect still remains to be determined.

### Ultrasound and the process of bone healing

The physical and piezo-electric mechanisms through which ultrasound may exert an effect are not limited to one single process during healing. The acceleration of fracture repair seems to be the result of the stimulation of different steps in the fracture-healing process.

In the combined results of in vitro studies utilizing cell lineages associated with inflammation and other studies concerning the ultrasound effects on inflammation, the influence of ultrasound on the inflammatory, reparative, and remodeling phases of the fracture-healing process has been described in detail (Warden et al., 2000). In the inflammatory phase, ultrasound is capable of increasing mast cell degranulation (Fyfe and Chahl, 1980), augmenting leukocyte adhesion to endothelium (Maxwell et al., 1994), stimulating collagen production by fibroblasts (Doan et al., 1999; Reher et al., 1999), and increasing the release of the macrophage fibroblast (Young and Dyson, 1990b) and vascular endothelial growth factors (Reher et al., 1999). Thus, applying ultrasound to a fresh fracture may result in an earlier resolution of the inflammatory phase and earlier commencement of the reparative phase. This may explain why
the restoration of mechanical strength in animals following fracture is accelerated by a factor of 1.4 to 1.6 when ultrasound is used (Pilla et al., 1990; Wang et al., 1994; Yang et al., 1996). It also may explain why the period of aggrecan gene expression seems to occur earlier in the fracture-healing process following ultrasound treatment. In bilateral rat femur fractures, aggrecan gene expression was significantly higher on day 7 post-fracture and lower on day 21 as compared with that on the non-treated side. In these animals, ultrasound of 0.5 MHz, 50 mW cm⁻², pulsed 1:4, and a repetition rate 1 kHz for 15 min daily was used (Yang et al., 1996). However, there are indications that ultrasound directly stimulates chondrocytes to increase aggrecan gene expression (Wu et al., 1996).

Apart from the inflammatory phase, ultrasound seems to influence the reparative phase as well. This stage is characterized by a union through the formation of a primary or provisional callus which stabilizes the fracture fragments. This primary callus is formed through the process of chondrogenesis and osteogenesis. There is evidence that ultrasound directly stimulates both processes. In the process of chondrogenesis, ultrasound stimulates chondrocyte proliferation (Wiltink et al., 1995) and chondrogenesis-associated gene expression (Wu et al., 1996; Yang et al., 1996). Also, ultrasound is capable of increasing the intracellular concentration of the second messenger, calcium, in chondrocytes (Parvizi et al., 1997). Evidence that osteogenesis is stimulated by ultrasound can be found in in vitro studies. Osteoblasts can be stimulated to increase collagen production (Reher et al., 1997; Doan et al., 1999), and increase the production of prostaglandin E₂, an important bone-healing mediator (Kokubo et al., 1999).

Following union, the secondary or definite callus is formed by cartilage replacement by bone through the process of endochondral ossification. The influence of ultrasound on this process has been investigated in in vitro growing bone. Ultrasound can stimulate this process in vitro in neonatal mouse tibial epiphyses (Elmer and Fleischer, 1974) and in fetal mouse metatarsal rudiments (Wiltink et al., 1995; Nolte et al., 2001b). In 17-day-old fetal mouse metatarsal rudiments, the influence of pulsed ultrasound at 30 mW cm⁻² on the process of endochondral ossification was measured. The increase in length of the calcified diaphysis during 7 days of culture was higher in the ultrasound-treated rudiments as compared with the untreated controls. The total length was not affected by ultrasound (Nolte et al., 2001b). These results are in accordance with those of another study, which indicated that DNA synthesis, but not the total length, in neonatal mouse tibial epiphyses was increased after exposure to 1.8 W cm⁻² ultrasound (Elmer and Fleischer, 1974). In a similar study which investigated the effects of different intensities of ultrasound on endochondral ossification on fetal mouse metatarsal rudiments, histology revealed a significantly increased length of the proliferative zone, whereas the length of the hypertrophic cartilage zone was unaltered. This suggested that the proliferation of cartilage cells is stimulated without influence on cell differentiation (Wiltink et al., 1995).

Although the above indicates that ultrasound stimulates endochondral ossification, there are also indications that ultrasound stimulates intramembranous ossification. This is illustrated by the use of SAFHS ultrasound (Kristiansen et al., 1997) to accelerate healing of radial fractures, which are believed to heal primarily by intramembranous ossification. This finding is of interest, because maxillofacial bone healing can involve both intramembranous and endochondral bone-healing processes.

In summary, ultrasound stimulation of bone healing may be mediated through cavitation, piezo-electric phenomena, and effects on the cell membrane. This stimulation appears to be multilevel, involving different cell types in and during the healing process.

(5) The Potential of Ultrasound to Stimulate Maxillofacial Bone Healing

Stimulation of maxillofacial bone healing by ultrasound may be possible if the maxillofacial bone is susceptible to the ultrasound signal. In the literature, only limited evidence is available that supports the susceptibility of this bone to ultrasound signals. Evidence that the cells of the mandibular bone respond to ultrasound was reported in an in vitro study which showed that human mandibular osteoblasts could be stimulated by ultrasound to proliferate and produce angiogenesis-related cytokines (Doan et al., 1999). In mandibular fractures in rabbits, eight days of ultrasound treatment (five minutes each day, 0.2 to 0.6 W cm⁻²) stimulated fracture consolidation, as compared with those in non-treated controls (Férotov et al., 1986). In a paper concerning the treatment of four mandibular fractures in humans, ultrasound treatment appeared to decrease pain and promote callus formation (Cavaliere, 1957). Another study found that osteoradionecrosis of the mandible could be treated with some success with 3 MHz ultrasound at 1.0 W cm⁻² (Harris, 1992). In several fields of maxillofacial surgery, ultrasound may be applied to benefit bone healing. These will be discussed below.

TRAUMATOLOGY

Normalization of occlusion and function are the most important aims in the treatment of maxillofacial fractures. Although rigid fixation has largely replaced intermaxillary fixation in the treatment of many fractures of the maxillofacial bones, there may still be many circumstances that make closed reduction preferable to open reduction and rigid fixation (Baker et al., 1997). Prolonged intermaxillary fixation has adverse effects on the masticatory system and poses additional problems such as difficulties in the maintenance of nutritional status due to difficulties with eating. Therefore, the period of intermaxillary fixation should be limited. Therapeutic ultrasound has been shown to reduce the time to union in fracture healing by 38% in the tibia, which consists of predominantly cortical bone (Heckman et al., 1994), and by 38% in the radius, which consists of predominantly cancellous bone (Kristiansen et al., 1997). If these results would be obtained in fractures of the cortical bone of the mandible and the cancellous bone of the maxilla, ultrasound might be helpful in reducing post-operative intermaxillary fixation in fresh fractures. However, when multiple fractures are present, ultrasound treatment of all fractures may not be practical.

Apart from possible benefits of ultrasound treatment in fresh maxillofacial fractures, ultrasound may be helpful in the treatment of compromised maxillofacial fractures. Ultrasound is indicated for the treatment of fractures in the extremities that do not heal with conservative treatment. In the treatment of various delayed unions (defined as failure of healing of a fracture between 3 and 9 months post-fracture) and non-unions (defined as failure of healing after more than 9 months), ultrasound treatment resulted in an overall success rate of 88% (Mayr et al., 2000a). Although delayed unions of the facial skeleton are relatively uncommon (1-2%) and non-unions are rare (Bochlogyros, 1985), their occurrence can increase up to 43% and 12%, respectively, during war time (Chambers and
Scully, 1987). In the management of fractures of the edentulous mandible, non-union may be as high as 20% (Bruce and Strachan, 1976). Also, when endosseous implants are inserted into an atrophic mandible, fracture may occur during or after surgery, resulting in non-union (Raghoebar et al., 2000).

In these cases, ultrasound treatment may offer a non-invasive treatment alternative. This may especially be of value in medically compromised patients for whom surgery is not preferred.

**Reconstructive Surgery**

Although most studies concerning the successful clinical application of ultrasound on bone describe bone discontinuities which were accidental in nature (i.e., fresh fractures, delayed and non-uniors), the positive influence of ultrasound in the healing of non-accidental bone discontinuities has been described as well. These include osteotomies (Nolte et al., 1998) and osteodistraction (Sato et al., 1999). This indicates that ultrasound can influence bone-healing processes in general, both accidental and intentional in nature. In the reconstruction of maxillofacial bone, different techniques such as osteotomies, bone grafting, and osteodistraction may be used to optimize treatment.

In fibula osteotomies in rabbits, low-intensity ultrasound treatment for 20 minutes a day was capable of increasing the strength of the fibulas. From days 17 to 28, all ultrasound-treated osteotomies were as strong as intact bones, whereas the ultimate strength of the control osteotomies attained intact values only by day 28 (Pilla et al., 1990). In the case of fresh human osteotomies of the lower extremities (femur, tibia, fibula), preliminary results of a double-blind trial indicate a 24% shortening of clinical and radiological time to consolidation, with the SAFHS device (Nolte et al., 1998). In the case of osteotomies that progress to delayed union or non-union, ultrasound treatment resulted in healing in 88% and 89%, respectively (Mayr et al., 2000a). If these results would be applicable to osteotomies of the facial bones, ultrasound would benefit both fresh and compromised consolidation.

Although no specific studies concerning the influence of ultrasound on the healing of bone grafts have been published, some information is available indicating a 91% healing rate of ultrasound treatment for delayed unions after surgical intervention involving bone grafts (Mayr et al., 2000a).

Although the osteodistraction technique as a pre-implantological procedure has the advantage that it limits the need for bone grafting, poor callus formation can be observed during the distraction phase. Moreover, after distraction, a substantial consolidation time has to occur to ensure that enough bone has formed to provide implant stability. This means that the distraction devices must remain in situ during this time. Ultrasound may have the potential to present a solution to these shortcomings. In the field of distraction osteogenesis, ultrasound-stimulated callus formation has been described in rabbits (Shimazaki et al., 2000), sheep (Mayr et al., 1999, 2001), and in the human leg (Sato et al., 1999). In rabbits, ultrasound therapy 20 minutes a day after distraction of the right tibia resulted in a more mature callus, as measured by radiography, bone mineral density, and mechanical testing. In a situation of poor callus formation, i.e., at a faster rate of distraction (1.5 mm/12 hrs instead of 0.5 mm/12 hrs), and no post-operative waiting time before active distraction (instead of seven days), ultrasound therapy was capable of achieving bone maturation. The control group showed only immature bone regeneration (Shimazaki et al., 2000). In distracted sheep metatarsus, the influence of SAFHS ultrasound on callus maturation was studied (Mayr et al., 1999).

Daily application of low-intensity ultrasound for 20 minutes resulted in an increased bone mineral content, increased stiffness, and homogeneity of the regenerated tissue in the treatment group as compared with the control group. Radiographically, an accelerated maturation of the regenerated tissue was found in the ultrasound-stimulated group (Mayr et al., 2001). In humans, ultrasound stimulation of callus formation during distraction was reported in a 22-year-old woman who was treated for short stature by means of nine-centimeter bilateral leg lengthening (Sato et al., 1999). During distraction at a rate of 1 mm/day, poor callus formation was observed at one month. Shortening of the bone gap, increasing the distraction frequency, and lowering the daily distance did not improve callus formation in the following six months. In the eighth month, it was decided to use ultrasound in an attempt to stimulate the callus formation. It was administrated for 20 minutes daily until pin removal. The bone mineral content, as determined by dual-energy x-ray absorptiometry, showed a marked increase after commencement of ultrasound treatment (from 0.003 g/day to 0.016 g/day). During the consolidation phase, bone mineral density increased up to 0.052 g/day, and healing progressed uneventfully. In summary, the above reports indicate that ultrasound treatment can stimulate callus maturation, even in compromised situations. If this would apply to the facial bones, ultrasound might have a beneficial effect in shortening consolidation time and in ensuring callus maturation.

**Oncology**

In maxillofacial surgery, therapeutic success often depends on the successful healing of bone under different, sometimes challenging, circumstances. This is illustrated by mandibular osteoradionecrosis, where the healing tendency is severely compromised. In head and neck oncology, the current curative treatment modalities include surgery and radiotherapy. In advanced cases, a combination of these treatments is necessary. The dose of radiotherapy is limited by its toxicity to normal tissues. Because bone is particularly sensitive to radiotherapy dosages, osteoradionecrosis is seen regularly, despite the elimination of dental focal infections prior to radiotherapy. When osteoradionecrosis occurs, removal of necrotic bone under antibiotic treatment is indicated. Also, treatment can be supported by hyperbaric oxygen, which is of value in establishing revascularization (Grim et al., 1990; Thorn et al., 1997).

Very little information is available concerning the treatment of osteoradionecrosis by means of ultrasound. In 1949, the treatment of ‘x-ray burns’, most likely osteoradionecrosis, was reported (Halscheidt et al., 1949). In two cases, exposure to ultrasound led to the covering of the non-healing bone with fresh granulation tissue. After a while, a sequester was formed and removed, and the defects healed. In these cases, ultrasound with an intensity of, at the most, 1.3 W cm$^{-2}$ was used. Another study examined the conservative management of osteoradionecrosis of the mandible with ultrasound therapy (Harris, 1992). This study was based on ultrasound’s capability to promote neovascularity and neocellularity in ischemic tissues (Young and Dyson, 1990a). Of 24 patients with osteoradionecrosis, 19 received long-term antibiotic therapy with local surgery for at least a year prior to ultrasound therapy. According to the treatment protocol, retained roots and infected teeth were first removed under antibiotic coverage. Subsequently, ultrasound was applied with the transducer stroked for 10-15 minutes daily onto the skin overlying the ischemic mandible (3 MHz, 1 W cm$^{-2}$, pulsed 1:4), for 40 days. When healing was progressive, but not complete,
other fields not necessarily limited to maxillofacial surgery may be accomplished by, for example, hyperbaric oxygen treatment (Thorn et al., 1997). If blood flow can be re-established or increased, cell delivery and tissue oxygenation will improve, and so should healing. It seems that ultrasound can heal osteoradionecrotic bone by countering the negative effects of hypocellularity, hypoxia, and hypovascularity. In ulnar osteotomies in dogs, a ten-day period of low-intensity ultrasound increased blood flow at the osteotomy site, during and after treatment, and increased the amount of callus (Rawool et al., 1998). This suggests that oxygen delivery could be improved through a direct dilatory effect on the vessels. Ultrasound can also stimulate the production of angiogenesis-related cytokines (interleukin-8, fibroblast growth factor, and vascular endothelial growth factor) in human mandibular osteoblasts (Reher et al., 1998), which indicates that it can promote the formation of vessels.

When ultrasound is compared with the other forms of treatment, such as surgical intervention or hyperbaric oxygen treatment, adjunct ultrasound treatment of osteoradionecrotic bone seems to be more patient-friendly and economically viable (Harris, 1992).

OTHER POTENTIALS
Apart from traumatology, reconstructive surgery, and oncology, other fields not necessarily limited to maxillofacial surgery may benefit from ultrasound’s potential. A recent study indicated that cartilage repair can be improved by means of SAFHS low-intensity ultrasound (Cook et al., 2001). In rabbits, osteochondral defects of the patella healed earlier and with fewer degenerative changes at follow-up when treated with ultrasound. Furthermore, it was found that doubling the treatment time to 40 minutes per day increased the histologic quality of the repair cartilage. This finding could be of value in the treatment of cartilage defects in other joints, such as the temporomandibular joint.

Endosseous implants are widely used in maxillofacial surgery to support crowns, bridges, overdentures, and facial prostheses. These implants are mostly made of titanium, and bone forms directly against the implant. This process of osseointegration takes a substantial amount of time.

In implant dentistry, it has been stated that implants require, for successful osseointegration, a healing period of at least three months in the mandible and six months in the maxilla (Adell et al., 1981, 1985). In dogs, it was found that low-intensity ultrasound could stimulate bone growth in small porous titanium cylinders (Tanzer et al., 1996). The cylinders were made of 187- to 250-micrometer-diameter sintered titanium beads and had a pore size of 100 to 350 micrometers. In 12 dogs, 22 pairs of these cylinders were placed in holes drilled in the lateral femoral cortex, bilaterally. Ultrasound (SAFHS) was applied daily to one leg. In each dog, one femur served as a control, and the other was subjected to daily ultrasound stimulation for two, three, or four weeks. Overall, the ultrasound-stimulated implants demonstrated an 18% increase in bone ingrowth as compared with the contralateral controls. Ultrasound had its greatest effect in the first three weeks of stimulation. At two and three weeks, the ultrasound-stimulated implants showed 21 and 16% more ingrowth than their respective contralateral controls. This study indicates that the amount of bone formation in contact with the surface of the titanium implant can be increased by means of ultrasound. If these results could be obtained in humans, more bone would be formed against endosseous implants. As a consequence, the osseointegration period could be facilitated by ultrasound therapy. In the case of poor bone quality and/or quantity and in irradiated, resorbed, and atrophic bone, ultrasound might help in ensuring osseointegration when implants are inserted. However, at the present time, this has not been established.

Finally, some investigators have attempted to treat periodontitis with ultrasound (Pohlman, 1951). The ultrasound was applied extra-oraly, on the skin overlying the alveolar bone. Others did not recommend ultrasound treatment of periodontitis, because the disease itself was poorly understood at that time (Halling and Leidholdt, 1949). However, today, the process of periodontitis and associated bone loss is less obscure, and it may be noted that ultrasound treatment might contribute to stimulating bone healing around periodontal defects.

(6) General Discussion

ULTRASOUND IN THE PRESENCE OF SURGICAL METALLIC IMPLANTS
The widespread use of surgical metallic implants in maxillofacial surgery, such as osteosynthesis material, distraction devices, and endosseous implants, makes it necessary to investigate the influence of ultrasound on the tissues near these devices. Theoretically, the ultrasound is reflected by metallic implants, which may lead to a more than double increase of ultrasound intensity in front of the implant. This may cause a rise in temperature inside the body, possibly leading to destructive effects. However, this does not appear to occur in vivo. In two similar studies that investigated the influence of 2.0 W cm$^{-2}$ ultrasound on surgical metal implants, ultrasound caused no extra rise in temperature in front of the metal (Lehman et al., 1958) and was not associated with evidence of burns or delayed healing of bone or soft tissue.
The effects of the influence of ultrasound on the internal fixation of osteosynthesis plates has also been studied. Ultrasound did not affect the internal fixation of osteosynthesis plates (Skoubo-Kristensen and Sommer, 1982). In dogs, three-hole AO plates were fixed on femura and humera by means of tight-fitting cortical screws. Low-dose (0.5W cm\(^{-2}\)) and high-dose (3.0 W cm\(^{-2}\)) 1 MHz ultrasound was administered to the legs five minutes daily for 14 consecutive days. Screw torque measurements on insertion and at removal four weeks post-operatively were not influenced to a significant degree by the ultrasound treatment.

In humans, it has been reported that fractures that were stabilized with metallic implants, such as marrow-nails, Kirschner wires, or wire, responded with rapid callus formation when exposed to ultrasound (Knoch, 1965). In humans, no harmful effects were observed when the lower ultrasound intensities of the SAFHS device were used in the presence of metallic surgical implants (Emami et al., 1999; Mayr et al., 2000a). Thus, the presence of metallic implants does not appear to be a contraindication for ultrasound treatment.

**SAFETY**

The head region contains delicate tissues, such as the tissues of the senses and the brain. Therefore, care should be taken when ultrasound is applied to this region. Reported adverse effects in the maxillofacial region following the treatment of soft-tissue and temporomandibular disorders were associated with the use of high intensities of ultrasound in the order of magnitude of several W cm\(^{-2}\). Hemorrhages in the masticatory muscles, dizziness, nausea, and headaches have been reported (Hallscheidt et al., 1949; Hildebrand, 1950). Also, life-threatening complications occurred after the treatment of acute inflammations associated with impacted third molars and peri-mandibular abscesses (Hallscheidt et al., 1949). However, the low intensity currently used to stimulate bone healing has not been shown to cause any harmful side-effects.

(7) **Conclusion**

Although ultrasound treatment has been used since 1938, the ultrasound stimulation of both fresh and compromised fracture healing of the long bones has become well-established only in the past few decades. The question remains, however, whether ultrasound can stimulate bone healing in the maxillofacial skeleton in healthy individuals. In the treatment of mandibular osteoradionecrosis, ultrasound has showed beneficial effects. Although limited evidence is available to support the susceptibility of maxillofacial bone to the ultrasound signal, ultrasound may be of value in the treatment of delayed unions, in callus maturation after distraction, and in the treatment of osteoradionecrosis. Given the successes in the stimulation of bone healing in other parts of the body, it seems that additional research in this field may lead to promising results which will determine the feasibility and potential of ultrasound treatment in maxillofacial surgery.

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