PRESENTATION OF ACOUSTIC WAVES PROPAGATION AND THEIR EFFECTS THROUGH HUMAN BODY TISSUES

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ABSTRACT

Three types of acoustic waves are mainly used in the medical field, Extracorporeal Shock Waves (ESWs), Pressure Waves (PWs) and Ultrasound (US). Shock waves are acoustic waves that are characterized by high pressure amplitudes and an abrupt increase in pressure that propagates rapidly through a medium. The energy distribution in the treatment area differs from being wide over a large area, or concentrated in a narrow treatment zone, and as such influences the therapeutic and biological effect of the shock wave. Pressure waves are usually generated by the collision of solid bodies with an impact speed of a few metres per second, far below the speed the shock wave travels. There are major differences between PWs and ESWs, concerning not only their physical characteristics and the technique used for generating them, but also the order of the parameters normally used. The simulation effects and therapeutic mechanisms seem to be similar, despite the physical differences and the resulting different application areas (on the surface and in depth respectively). Ultrasound therapy is one of the modalities of physical medicine used for pain management and for increasing blood flow and mobility. Ultrasound and ESWs – PWs differ, despite their acoustic relationship, basically because ESWs – PWs show large pressure amplitudes with direct mechanical effects and US propagates within periodic oscillations within a limited bandwidth, and mainly direct thermal effects. Acoustic waves have direct mechanical and mechanotransduction effects on the cells and ECM increasing porosity, angiogenesis, releasing growth factors, enhancing proteosynthesis and viscoelastisity and inducing histeogenesis and repair processes.

Key words: acoustic waves, shock waves, pressure waves, ultrasound, tissues

Introduction

The effects of acoustic waves on a variety of tissues is under continual investigation. Some of the effects are more widely accepted by the medical community than others; for example the effect of extracorporeal shock-waves for lithotripsy. Here, a brief synopsis is provided of the reported effects of acoustic waves (Extracorporeal Shock Waves, Pressure Waves, Ultrasound) on bone, skin, muscle, and vasculature.

Although it is not fully clarified what the specific universal mechanism is that leads to the clinical benefits of acoustic waves, it is believed to result from direct mechanical effects on the cells to increase porosity [1]; a mechanotransduction type effect from the acoustic differences between cells and the surrounding extracellular matrix, which results in a shear stress on the cell [2, 3]; the violent collapse of cavitation bubbles and their effects on cells [4–8] and on a tissue level due to increased angiogenesis [8, 2]. Whether the effect is direct or indirect the release of growth factors and the up-regulation of cell activity is responsible for the histeogenesis and repair processes.

Extracorporeal Shock Wave Therapy (ESWT)

Extracorporeal shock waves were first used for kidney and ureteral stones fragmentation in 1980 and afterwards, they became the method of choice. More than 10 years later, shock waves were introduced as therapy for a number of orthopaedic pathologies such as bone non-unions, tendinopathies and chronic tissue inflammations.

Shock waves are acoustic waves that are characterized by high pressure amplitudes and an abrupt increase in pressure in comparison with the ambient pressure. As mechanical waves, they can pass through the surface of a body without injury and may act therapeutically in predetermined areas within the body [1].

There occurs pressure disturbance that propagates rapidly through a medium. The wave shows an acute

rise in pressure amplitude (representing the time between 10 and 90% of the total initial rise time) at the wave front of less than 10 nsec (Δt), a low tensile amplitude, a short life-cycle (less than 10 msec), a broad frequency spectrum (16 MHz to 20 MHz) and a variable negative pressure at the end [8] (Fig. 1). At the boundary between two media, a shockwave will be partially reflected, and partially transmitted. Attenuation of the shockwave is dependent on the medium through which the shockwave is travelling. In air, the shockwave weakens quickly. In water, however, attenuation occurs approximately 1000 times less than that which occurs in air [8]. Medically applicable shockwaves are conventionally propagated through a water medium and a coupling gel before penetrating tissue [9].
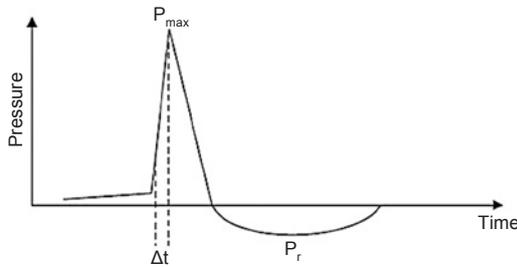
P_{max} – pressure maximum, P_r – negative peak pressure, Δt – pressure rise time

Figure 1. Characteristics of shockwaves

ESW Energy (E)

An important parameter is the energy of the applied shock wave and this may have an effect on the tissue only when succeeding to overpass certain energy thresholds.

The equation for energy generation from a shock wave is $E = A/\rho c \int p(t)dt$, where ρ is the propagation medium density and c is the sound velocity (both acoustical parameters), p(t) is the time curve of the shock wave and A represents the surface, (see also Tab. 3). The acoustical energy of a shock wave pulse is given in millijoules (mJ) and this must be multiplied by the total number of shock wave pulses emitted per treatment (protocol) and thus we shall have the total emitted energy.

Energy flux density (ED)

The energy distribution in the treatment area differs from being wide over a large area, or concentrated in a narrow treatment zone, and as such influences the therapeutic and biological effect of the shock wave.

The energy concentration is obtained by calculating the energy per area (E/A): $E/A = 1/\rho c \int p(t)dt = ED$ (energy flux density), mmJ/mm^2.

Table 1. Categorization of ESWaves due to Energy Flux Density

Energy category	Range of energy density (mJ/mm^2)
Low	< 0.08
Medium	0.08–0.28
High	> 0.6

Shock wave generation makes use of three different principles: electrohydraulic, piezoelectric and electromagnetic. They are focused using spherical arrangements, acoustical lenses or reflectors [1].

Among shock wave generation techniques developed and used until now in clinical applications, electrohydraulic (EH) and electromagnetic (EM) waves have been found to be the most suitable for orthopaedic treatment [8]. The EH device generates a SW by a high-voltage discharge applied across the electrode tips to the first focal point within a water-filled ellipsoid reflector. The EM device generates a SW by inducing a magnetic field in a metal membrane, which is forced away rapidly, and as a result compresses the surrounding fluid medium. The EM acoustic wave is then focused by a lens onto the focal therapeutic point [3].

Piezoelectric systems (PE) have a high accuracy of repetition and are easy to control even in low energy ranges. They can provide focussing on very small spots with pressures of up to 150 MPa (1500 bar). They work using a large number of piezoelectric elements arranged on a spherical shape, which can be displaced in the direction of the centre of the spherical shape by synchronous excitation. Eventually, a convergent spherical wave spreads out and increases its pressure amplitude to therapeutically effective values on its way to the centre [1].

Pressure Waves Therapy (PWT)

In addition to the shock waves described above, also pressure waves with different features are used in medicine. Whereas shock waves typically travel with the propagation speed of the medium (approx. 1500 m/s for soft tissue), pressure waves are usually gener-

Table 2. Physical and technical characteristics and differences of shock and pressure waves

	Shock waves (focused)	Pressure waves (unfocused)	Difference
Focus	Yes	No	
Propagation	Non-linear	Linear	
Steepening	Yes	No	
Rise time	Typically 0.01 µs	Typically 50 µs	Approx. 1:1000
Compression pulse duration	Approx. 0.3 µs	Approx. 200 – 2000 µs	Approx. 1:1000
Positive peak pressure	0–100 MPa	0–10 MPa	10:1 – 100:1
Energy flux density	0–3 mJ/mm^2	0–0.3 mJ/mm^2	Approx. 10:1

ated by the collision of solid bodies with an impact speed of a few metres per second, far below the sound velocity [1]. First, a projectile is accelerated, e.g. with compressed air (similarly to an air gun), to a speed of several metres per second and then abruptly slowed down by hitting an impact body. This is the reason why pressure waves are also called Balistic or Pneumatic waves. The elastically suspended impact body is brought into immediate contact with the surface of the patient above the area to be treated, using ultrasound coupling gel, if necessary. When the projectile collides with the impact body, part of its kinetic energy is transferred to the impact body, which also makes a translational movement over a short distance (typically < 1 mm) at a speed of around one metre per second (typically < 1 m/s) until the coupled tissue or the applicator decelerates the movement of the impact body [1]. Then a pressure wave is propagated by transfering the motion of the impact body to the tissue at the point of contact.

There are major differences between Shock and pressure waves, concerning not only their physical characteristics and the technique used for generating them, but also the order of the parameters normally used. The differences between the most important parameters listed in Tab. 2 are approx. 1–3 orders of magnitude.

The simulation effects and therapeutic mechanisms seem to be similar, despite the physical differences and the resulting different application areas (on the surface and in depth, respectively). However, the pressure waves are not able to fragment hard concrements such, as e.g. kidney stones, deeper in the body (> 1 cm). Nevertheless, unfocused pressure waves seem to be well suited for orthopaedic indications near the surface as well as, e.g. trigger point therapy [10].

Tissue effects of ESWT and PWT

Bone tissue

Although it is still being debated by the research community, there is evidence that extracorporeal shockwaves act to increase the volume of laminar bone and the density of trabecular bone (Fig. 2A, B). In one model an uninjured rabbit femur was given a dose of shock wave therapy and after intial short term microdamage, extensive cortical thickening and minor trabecular bone remodelling was observed [11]. ESWT has also been found both to increase repair in non-unions in an animal model (dog radius) [12] and have clinically significant results in the human long bones [13–15]. Another area of potential application for ESWT in osseous tissue is osteonecrosis, specifically of the femoral head [16, 17]. In one of these clinical studies of osteonecrosis of the femoral head, ESWT was found more effective than the current treatments of core decompression and nonvascularized fibular grafting [17].

As with many of the beneficial effects witnessed by ESWT, the mechanism of its altering on osseous tissue is still not fully comprehended. Some of the effects can be espoused from various animal models, *in vitro* models and interpretation of human studies. One mechanism that has been espoused is that microfracture and microdisruption of the vasculature induce angiogenesis [8, 18]. *In vitro* cell models and animal studies revealed the upregulation of osteogenic cell proliferation, the expression of osteogenetic growth factors and differentiation of mesenchymal stem cells [2, 3]. One factor that is gaining increasing support is the idea of angiogenesis resulting from the application of ESWT due to an overexpression of vascular growth factors including εNOS and VEGF [2, 19]. The positive finding for the application of ESWT as a treatment for osteonecrosis is con-
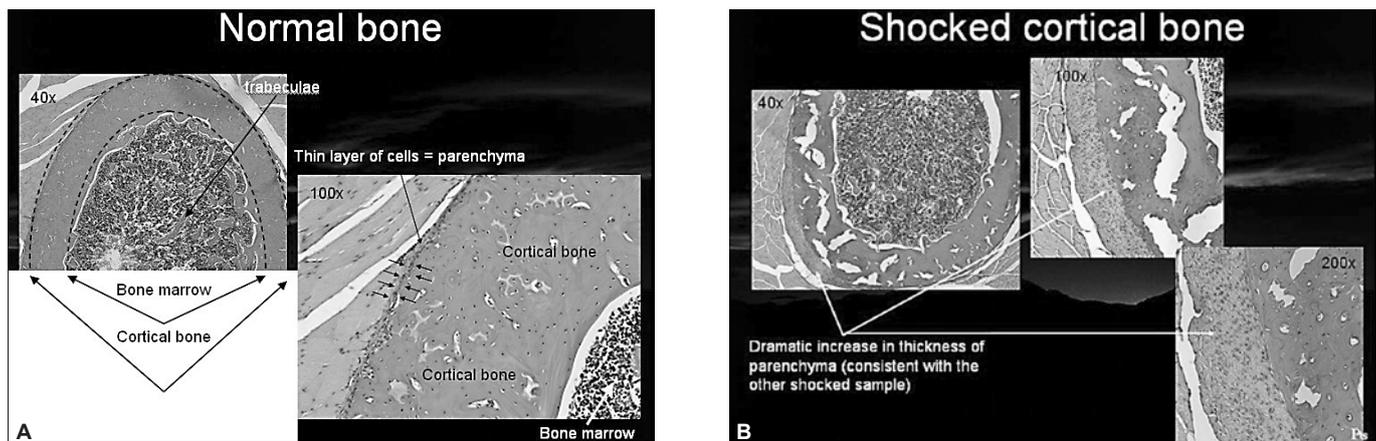
Figure 2 A, B. Osteogenetic response after ESWT, protocol (Tsaklis, preliminary data)

sistent with the idea of neovascularization; the neogenesis helps supply nutrients to the area where the tissue had died [16, 17].

Skin

ESWT is increasingly being recognized to have a positive effect on the healing of skin wounds, particularly in the case of severe wounds where the prognosis is poor. It has been less rigorously studied than some of the other models but clinical reports on ulcers and other lesions have been published that are promising [20–23]. An animal model that studies the effect of ESWT on a skin flap survival model in rats showed significant increase over the controls [24].

The exact mechanism leading to an improved skin lesion repair is still under investigation but as with most of the tissues, it is believed to result from the increased vascularity and upregulation of cell activity [24]. A second mechanism that is postulated to have an effect, is the antibactericidal effect that has been reported in an *in vitro* study [25].

Muscle tissue

To the best of the author's knowledge, no adverse effects of ESWT on muscle have been reported. On the contrary, ESWT appeared to be promising in treating patients with hypertonia by reducing muscle tone [26, 27].

The mechanism leading to the muscle relaxation is believed to result from the release of nitric oxide (NO), which acts as a muscle relaxant [27]. Direct mechanical effect of the ESWT on the muscle fibers is also proposed; and it is not believed to result from denervation as none was deemed to have taken place [27].

Vasculature

It has been previously stated several times that increased angiogenesis occurs after application of ESWT due to the overexpression of angiongenic growth factors. A second effect that results in increased blood flow is the release of NO which acts as a vasodilator due to the reduction in muscle tone of smooth muscles, [26].

One exciting effect of ESWT is its potential for angiogenesis in ischemic myocardial tissue [28]. Recent reports have shown an increase in blood supply to ischemic cardiac tissue both in an animal model and in a preliminary clinical trial [28, 29].

Ultrasound Therapy (US)

Ultrasound therapy is one of the modalities of physical medicine which is used by specialists for pain management and for increasing blood flow and mobility.

Ultrasound and shock waves differ, despite their acoustic relationship, basically because shock waves show large pressure amplitudes. Another difference is that ultrasound usually consists of periodic oscillations within a limited bandwidth (Fig. 3), whereas shock waves are represented by a single, mainly positive pressure pulse that is followed by comparatively small tensile (negative) wave.

For this reason, steepening effects due to nonlinearities in the propagation medium (water, human tissue) have to be taken into consideration [1].

Ultrasound has a frequency above the range of 20 kHz. The ultrasound generates high-frequency mechanical vibrations created when electrical energy is converted to acoustic energy through mechanical deformation of a piezoelectric crystal located within the transducer.
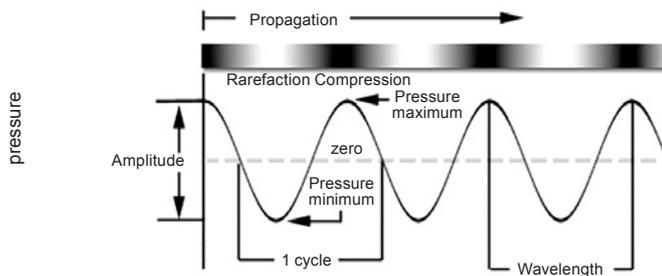
Figure 3. Ultrasound wave characteristics

Therapeutic ultrasound has a frequency range of 0.75 MHz (referred to as lower frequency) up to 3 MHz (referred to as higher frequency), with most machines set at a frequency of 1 MHz or 3 MHz. Using Low-frequency ultrasound, waves have greater depth of penetration but are less focused. Ultrasound at a frequency of 1 MHz is absorbed primarily by tissues at a depth of 3–5 cm [30] and is therefore recommended for deeper injuries and in patients with more subcutaneous fat. A frequency of 3 MHz is recommended for more superficial lesions at depths of 1–2 cm [30, 31].

Tissues can be characterized by their acoustic impedance, the product of their density and the speed at which sound will travel through them [32, 33] (Table 3).

US stimuli effect

When using US therapy, two phenomena can occur on the underlying tissues. These are:, the tissue heating and the cavitation phenomenon. During the ultrasound therapy, it is possible to create tissue lesions through tissue heating due to ultrasound absorption, especially when the application is prolonged in the same area and the US wave has a constant emission mode [6]. This phenomenon can be avoided when we constantly move the US transducer head in the treatment area, or/and use intermittent emission mode [5].

The acoustic cavitation phenomenon which occurs during the US emission, refers to the activity of bubbles or micro-bubbles of gas undergoing movement due to an acoustic field, into the tissue [7]. Every living medium contains certain amount of dissolved gas present in the form of bubble micronuclei. Under the effect of an ultrasound field, the nuclei expand through a physical phenomenon known as rectified diffusion to reach a critical size known as the Blake threshold. Cavitation phenomena become even more accentuated as acoustic intensity increases. Bubbles expand up to their resonant size, and then implode violently. The energy accumulated by the bubbles is simultaneously released in the form of a shock wave, with intense heat (generally from 1.000 K to 20.000 K, or 726.85°C to 19.726°C) and microjets that can introduce speeds of 100 m/s up to 250 m/s through the water medium. All this leads to the creation of free radicals and mechanical destruction of surrounding tissue.

Thus, there are two types of cavitation: *stable cavitation* where the walls of the bubbles are oscillating at the frequency of the ultrasound field without too great a consequence for the surrounding cells and can appear at very low pressure levels as soon as bubbles are present in the medium. Stable (regular) cavitation is considered to be beneficial to injured tissue. The other form is the *transient cavitation* where bubbles expand up to their resonant size, and then implode violently and cause tissue damage, [4].

Table 3. Acoustic impedance of different tissues in relation to density and sound propagation. Modified from Wolbarst [33]

Material	Density ρ (kgm^{-3})	Speed c (ms^{-1})	Characteristic impedance Z (kgm^{-2}s^{-1}) × 10^6	Absorption coefficient α (dB cm^{-1}) at 1 MHz
Water	1000	1480	1.5	0.0022
Blood	1060	1570	1.62	(0.15)
Bone	1380–1810	4080	3.75-7.38	(14.2–25.2)
Brain	1030	1558	1.55–1.66	(0.75)
Fat	920	1450	1.35	(0.63)
Kidney	1040	1560	1.62	–
Liver	1060	1570	1.64–1.68	(1.2)
Lung	400	650	0.26	(40)
Muscle	1070	1584	1.65–1.74	(0.96–1.4)
Spleen	1060	1566	1.65–1.67	–

Table 4. The biological and resultant effects of therapeutic ultrasound

Type of effect	Result
Thermal	Increase in tissue extensibility
	Increase in blood flow
	Modulation of pain
	Mild inflammatory response
	Reduction in joint stiffness
	Reduction of muscle spasm
Non-thermal	Cavitation
	Acoustic microstreaming
	In combination may result in stimulation of fibroblast activity, increase in protein synthesis increased blood flow, tissue regeneration and bone healing

The stimulation effects of US on specific tissues such as the skin, bone, muscle and vascular, are dependent on the phenomena of heating and cavitation described above.

Different intensities of pulsed ultrasound have distinct biological effects on bone mineralization in the process of bone fracture repair, even across a narrow range (e.g. 30–120 mW/cm^2), [32]. During high-intensity focused US administering on or near the skeletal system care should be taken because thermal damage can cause osteocyte damage and necrosis, characterized by pyknotic cells and empty lacunae not just at the bone surface, but more deeply within the bone [32].

The stimulating effect on bone tissue gives evidence that low intensity (30 mW/cm^2), but not high-intensity (120 mW/cm^2), pulsed ultrasound may accelerate the formation of the molecular packing of collagen fibers conducive to mineralization. There is an increased Cyclooxygenase COX-2 mRNA expression and PGE2 production by osteoblasts in an ultrasound, intensity-dependent manner. This high dose of Prostaglandin E2 (PGE2) induced by high-intensity ultrasound may be detrimental to the physiological cross-link formation required for initiation of the mineralization process [32].

Concerning the skin tissue wounds, ultrasound seems to interact with one or more components of inflammation, and earlier resolution of inflammation [34]. In vitro founded an accelerated fibrinolysis and a stimulation of macrophage-derived fibroblast mitogenic factors. This also leads to a heightened fibroblast recruitment and an accelerated angiogenesis, followed by an increased matrix synthesis. The collagen fibrils are more dense and the tissue shows increased tensile strength [31].

The stimulation effect on the vasculature tissue points that the ultrasound can be effective during the early inflammatory phase, after a wound. In the later phase of repair the ultrasound treatment does not appear to have any further significant effect on angiogenesis. In this early phase, the macrophage, which are present in large numbers in the wound bed and contain factors which stimulate angiogenesis, are a possible target of the US. Ultrasound at a low frequency, i.e. 0.75 MHz, can cause a greater effect on angiogenesis than higher frequency, i.e. 3.0 MHz, which suggests that there may be a nonthermal component of the ultrasound involved in the stimulatory process [35].

The intramuscular effect of the US is associated mainly with the heating phenomenon and the resultant increase of blood supply, proteosynthesis and viscoelastisity of the tissue.

Research has established that both 1 and 3 MHz continuous ultrasound can produce subcutaneous tissue temperature increases of 4°C or greater when the appropriate ultrasound treatment parameters are selected, including a treatment area no greater than 2 times the effective radiating area (ERA) of the ultrasound applicator, [36].

Further research showed that pulsed ultrasound (3 MHz, 1.0 W/cm^2, 50% duty cycle, for 10 minutes) produced similar intramuscular temperature increases to continuous ultrasound (3 MHz, 0.5 W/cm^2, for 10 minutes) at a depth of 2 cm in the human gastrocnemius, assuming that pulsing ultrasound precludes the development of a heating response in human tissue, as well [37].

Conclusions

Acoustic wave therapy includes extracorporeal shock waves, pressure waves and Ultrasound waves. There are distinct differences between these three types of waves. These mainly refer to the technical way each type of wave is produced, as well as the physical-mechanical characteristics of each modality. The extracorporeal shock waves and the pressure waves show typically the same mechanical characteristics, concerning the way the wave propagates with big differences in the amplitude – energy flux and focussing in the treatment area. Thus, the ESW, are more intense and focused than the pressure waves, with more mechanical energy released and consequent biological effects. On the other hand, the mechanical characteristics of the periodical

oscillations of the ultrasounds make them differ from the other two types of waves and the dominant phenomenon here is the production of heating energy. All three types of waves appear to influence and propagate a biological response from different tissues in the body. This depends of the protocol (parameters of intensity – time – energy flux, etc.), the anatomical location and the nature of the tissue itself. Eventually, acoustic waves comprise a very useful therapeutic modality with the reservation that the therapist must be familiarized and well educated on their use and consequent effects.

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