Chapter 11

Therapeutic Ultrasounds: Physical Basis and Clinical Assessment

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Abstract

Improving quality in US physiotherapeutical treatments is mandatory in order to get 'evidence-based' clinical results. This implies quality assurance protocols for the equipment, as well as some tentative dosimetrical approaches to predict local heating in joints following US parameter setting and operative modality. Finally, the possibility of 'personalized therapy' with multimodal (by qualitative and quantitative, e.g. based on sonography) assessment is discussed.

Keywords: ultrasound, physiotheraphy, quality, assessment, dosimetry, phantom

1. Introduction

Therapeutic ultrasound (US) is performed in physiotherapy to treat a variety of inflammatory and post-traumatic diseases. Most of their effects depend on the induction of local thermal increases, which elicit local vasodilatation and toxic substances washout; however, specific and quantitative effects are often misconsidered in physiotherapy units. Moreover, despite its widespread use in rehabilitative practice and a large number of studies, low scientific, statistically assessed evidences of therapeutic US effectiveness are available. As a matter of fact, details about the treatment modalities and the way in which the patients' feedback was collected are often missing. The chapter will be focused on the following points:

(1) Physical bases, technical approach and quality assurance of ultrasonic equipment: technological development and wide use of US within the patient's rehabilitation program

led to the need for a thorough understanding of the interaction between ultrasonic waves and biological matter. Scientific evidence of US therapeutic effectiveness in rehabilitation fields requires more attention on the technical specifications of devices used, and the exact parameters applied in the treatment of selected patients in order to avoid standardized US treatments using 'protocols' and non-specific parameter settings.

(2) Towards physiotherapeutic US dosimetry: treatment planning by the assessment of thermal and mechanical effects. Quantitative assessment of thermal and mechanical effects, and their dependence on the US parameters (frequency, emitted power, pulsed or continue waves) and the treatment modalities (fixed field or massage, duration of the treatment) may be quantitatively investigated on joint mimicking phantoms made of muscle-equivalent agar-based material and bone disks. '*In vitro*' temperature increases can be predicted, which are the 'asymptotical values' in the absence of blood perfusion and other heat dissipation mechanisms.

(3) Customized 'in-patient' assessment of clinical effects: clinical, functional and sonographycal evaluation can/should be performed before and at the end of the US therapy using Numeric Rating Scale, Constant Score, DASH questionnaire and sonographic images supporting clinical and functional data.

2. Main body

2.1. Physical bases, technical approach and quality assurance of ultrasonic equipment

Ultrasound (US) is a mechanical non-ionizing radiation, which propagates in a medium transferring energy from one particle to another by molecular oscillation. The longitudinal waves (compression) can propagate in any medium, while the transverse waves are observed only in solids, because of the weak links that are established between atoms and molecules in the tissue fluids. The ultrasonic wave is mainly longitudinal in biological tissues and characterized by alternating compression and rarefaction of the medium in which it propagates, with variations in pressure within it. Related to the pressure amplitude, which describes the degree of compression and rarefaction and thus the strength per unit area to which the material is subjected in unit of Pascal (Pa = N/m^2) and its multiples (e.g. MPa), also the concept of power of an ultrasound beam, i.e. the energy transmitted in the time unit measured in Watt and that of wave intensity, that is the amount of energy flowing in the time unit through a surface of unit area, perpendicular to the direction of wave propagation (measured in W/cm^2) are important. The intensity varies over time both in the case of continuous wave (CW) or pulsed wave (PW): in particular, the presence of a pulsed field introduces a temporal variation, defining a duty cycle (DC) as the ratio between the pulse duration ultrasound (in time units) and the length of the period, calculated as a percentage. Therapies that employ the US can be divided into two groups: 'high power' and 'low power' [1]. The high power applications include HIFU (high-intensity focused ultrasounds) and lithotripsy, while low-power applications include physical therapy, sonophoresis, sonoporation and

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gene therapy. When a US wave proceeds from one medium to another, it is partly reflected and partly transmitted, according to the laws of classical mechanics. Each medium is inherently characterized by a complex quantity, the impedance Z, which synthesizes the acoustic characteristics of the medium and quantifies the resistance that the medium itself opposes the passage of sound waves. The acoustic impedance is defined as the product of the density ρ of the medium (kg/m^3) for the propagation velocity c (m/s)

$$Z = \rho c \tag{1}$$

Its unit of measure is Pa s/m or Rayl, named after the famous British scientist Lord Rayleigh, which is equivalent to kg/m^2 s. Propagating in a medium, the acoustic wave is subject to a progressive loss of energy and, more properly, it causes a decrease in the intensity as a function of distance from the source. This is due both to the absorption, where the mechanical energy of the waves is partially converted into heat, and to the scattering, where the interaction between the wave and any inhomogeneous structure in the medium determines a partial diffusion of energy along directions different from that of direct wave propagation.

The overall effect, in a homogeneous medium, is such that a field of wave initial intensity I_0 after a certain distance z, has an intensity, which decreases exponentially according to the equation:

$$I = I_0 \exp(-2\alpha z) \tag{2}$$

where I_0 is the initial intensity I α and the absorption coefficient of the medium (cm^{-1}).

The energy absorption of ultrasound within the medium (and the biological tissues as well) depends on the frequency of the waves, being the coefficient of attenuation α inversely dependent on the square of the frequency. This is responsible for the fact that most of the tissues crossed by US exhibit an increase in the absorption coefficient of at least three times when the frequency is increased from 1 to 3 MHz (e.g. from 0.14 to 0.42 cm^{-1} in fat, from 1.12 to 3.36 cm^{-1} in tendons, from 0.76 to 2.28 cm^{-1} in muscle).

Lower absorption (and therefore higher penetration) of the ultrasonic wave is observable in water and in fact as tissue rich in water, and therefore the local heating is not significant. On the contrary, the absorption is much higher in the bone tissue and tendons [2]. In general, soft tissues absorb about 10–20% of the emitted power per centimetre, while adult bone completely absorbs the ultrasound beam in short distances. US at the frequency of 1 MHz is mainly absorbed by tissues that are 3–5 cm from the probe, and precisely for this property they are recommended for deeper lesions and in patients with subcutaneous fat [3].

Note that 3 MHz frequency is instead recommended for more superficial lesions, e.g. 1–2 cm deep [3, 4]. All the above parameters contribute to the effects of US in biological tissues, which are normally accounted for as 'thermal' and 'non-thermal' effects.

(i) Thermal effects: When US loose energy and the beam is attenuated due to the absorption and dissipation of the ultrasonic energy, heat is produced by vibration, shock, and friction with the cellular and intercellular structures of the crossed tissues. The temperature increase that occurs in the medium can cause chemical or structural changes in biopolymers.

This phenomenon is influenced by both the characteristics of the ultrasound beam (intensity and frequency), the duration of exposure and the characteristics of the crossed tissues (acoustic impedances). Heating is established quickly; however, a thermal equilibrium due to the heat dissipation due to blood flow is reached in longer times.

The thermal effect is most evident at the interface between tissues and in particular at the interface between fat and muscle and at the level of the periosteum. The periosteum, for its anatomical structure and for the continuity with the bone, absorbs a large amount of energy and is therefore easily heated. The thermal elevation generates, as secondary effects, increase in cellular metabolism and vasodilation; in particular, the latter property is important in the use of therapeutic US in physiotherapy, promoting the wash-out of pro-inflammatory substances and pro-algogenic tissues.

(ii) Non-thermal effects: They include cavitation, which consists in the formation, growth and implosion of gas bubbles within the fluid subjected to an ultrasonic field. In general, the cavitation can be seen as the 'break' of a liquid and the consequent formation inside the same of 'cavities' (bubbles) of the liquid containing dissolved gas or vapour itself. This phenomenon occurs in many situations, for example, in boiling water or in proximity to the propeller in rotation of a ship, and in any case when liquids are subject to high and rapid changes in pressure and can occur in the use of therapeutic US or in Doppler ultrasound [5].

The almost instantaneous variations of density, pressure and temperature of the fluid in which propagates the ultrasonic wave can also produce the so-called shock waves or pressure waves which can also be extremely intense. The ultrasonic irradiation of water leads to the formation of the hydroxyl radical and hydrogen radical, which give as the main final products H_2O_2 (hydrogen peroxide) and H_2.

At the cellular level, the production of radicals induced by exposure to the US can also produce biological effects on DNA; theoretical models and experimental studies have shown that the effects of the US on biopolymers especially relate to the degradation pattern of structures [6].

The specificity of the effects stresses the need for accurate quality assessment, by specific acoustic measurements on the clinical equipment.

The performances of the equipment have been investigated, especially on a local basis, by many authors (see Refs. [7–10]), and recommendations have been proposed [11]. For example, the Italian National Institute of Metrological Research (INRIM) settled a protocol [12] for evaluating the ultrasonic power produced by clinical equipment using the Radiation Force Balance (RFB) method. The ultrasonic power is actually determined by the measurement of the force exerted on a target by the sound field generated from an ultrasonic source. The absorbing, connected to the load cell, measures the apparent mass variation due to the ultrasonic field when the source is alternately switched on and off.

2.2. Towards therapeutic US dosimetry: treatment planning by *'in vitro'* parameter evaluation

Most of the therapeutic applications of US induce heating in insonated tissues to obtain some beneficial effect. By increasing temperature a few degrees above the normothermic levels, it

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is possible to induce temporary vasodilation and increase blood inflow in the affected area, performing a sort of 'thermotherapy'. This mechanism has been proposed as the principal one to explain the therapeutic effects obtained in physiotherapy applications: the analgesic effect in the joints and muscles is mediated by vasodilation and by the subsequent wash-out of pro-algogenic substances and pro-inflammatory with local edema reduction. In addition, the increase of tissue temperature promotes a higher extensibility of soft tissue, and a relaxing effect on the muscles; the increase of cell activity and of the local metabolism caused by the heat stimulates the accelerated wound healing and repair of tendon injuries, ligament, muscle, etc.

Even non-thermal effects (cavitation, emulsion, streaming and sonoporation) may play a role in the physiotherapy field: they, in fact, generate a sort of 'micro-massage' in tissues, promote the increase of local blood flow; furthermore, at cellular and intracellular level, US induces an increase of membrane permeability, calcium uptake, protein synthesis, mast cell degranulation, production of growth factors, angiogenesis, increased fibroblast motility and orientation modification of the fibres collagen and shift the type of collagen (type III to type I) in tissue repair [13].

Controindications to the therapeutic US are possibly due to interference with other electronic devices (e.g. cardiac pacemaker) or are related to the possible effects induced from heat and cavitative phenomena.

US can cause damage to eyes, gonads, encephalon and ears, and the presence of growing cartilage remains the most substantial downside.

It is also recommended not to use the US in body regions where there are implants or metallic synthesis; in fact, given the large difference in impedance between these materials and human tissues, areas of friction and heat accumulation can be formed, with unpredictable consequences.

It is also not recommended for any kind of treatment with US in the presence of malignancies, to avoid the spread in a circle of pathogenic cell lines. In order to get the therapeutic effects described above, it is mandatory to know how US may increase local temperature depending on the setting of the main parameters (frequency, power, etc.) and the modality of treatment (CW, PW, etc.). Although in living tissues many biological mechanisms may dissipate heat, preliminary investigations on '*in vitro*' phantoms may help in finding the 'asymptotic' values of the thermal increase locally induced by the US. Many approaches have been proposed in the literature [see 14–16], based on different test materials exhibiting the same mechanical and thermal properties of homogeneous tissues. Also, numerical simulations have been proposed [17].

The use of 'tissue-mimicking phantoms', coupling different tissues (e.g. muscle-equivalent and bone), as the two presented in **Figure 1** to simulate a superficial (A) and a deep (B) joint, respectively, may be useful to evaluate the temperature at different depth depending on the choice of the parameter values of the equipment and the different treatment protocols [18].

A cartoon cylinder filled with homemade agar-based gel, prepared using bi-distilled water (86.5%), glycerine (5.5%), graphite (2%), agar (2.5%) and salicylic acid (traces) was produced.

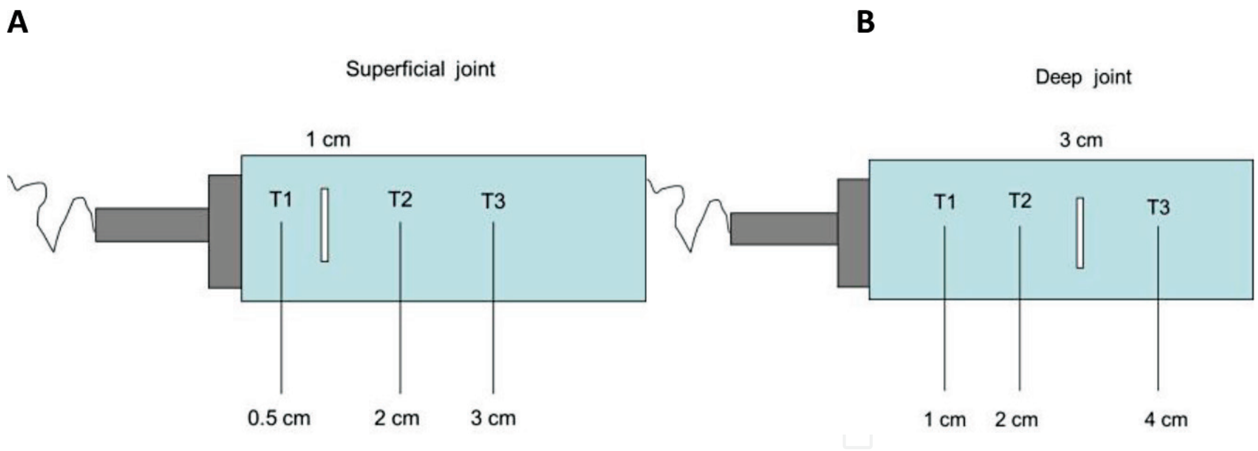

Figure 1. Scheme of the phantoms mimicking a superficial (A) and a deep (B) joint indicating the position of the bone insert and of the temperature probes.

The phantom contains at one end a bovine bone disk 2 (±1) mm thick inserted at 3 (±0.5) cm depth (simulating a 'deep joint') and at the other end a bovine bone disk 1 (±0.5) mm thick inserted at 1 (±0.5) cm (simulating a 'superficial joint') (see **Figure 1A** and **B**). The two disks were always fixed approximately in the centre of the phantom, and their diameter was always smaller than one-half of the phantom diameter. Deep and superficial 'joints' were treated at 1 and 3 MHz, respectively, using the equipment Enraf Nonius SonoPlus. Thermal probes, inserted at different depth, perform temperature measurements before, during and after sonications lasting 5 min and performed using the most diffused clinical treatment modalities (e.g. selecting 'continuous' (CW) or 'pulsed' (PW) wave on the apparatus and keeping fixed or massaging the probe on the phantom surface). Such massaging is performed by small circular movements where the probe is freely and randomly moved on the phantom cross section. The temperature increases detected into the phantoms are different in superficial and deep joints, and mainly depends on the operating mode (CW or PW) and on the fixed or massage modality selected for the probe application. The (min-max) temperature increases detected at different positions (see **Figure 1**) and with different modalities are given in **Table 1**.

3 MHz		
T1	T2	T3
CW: (5–10)	CW: (10–12.5)	CW: (5–15)
PW: (0–2.5)	PW: (0–2.5)	PW: (2.5–5)
1 MHz		
T1	T2	T3
CW: (5–7.5)	CW: (5–7.5)	CW: (2.5–5)
PW: (0–2.5)	PW: (0–2.5)	PW: (0–2.5)

Table 1. (Min-max) temperature increase (in °C).

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PW modality is always safer, while CW can induce temperature peaks (hot-spots) at different depth inside the joint.

The local characteristics of the thermal field are not easily predictable based only on wave attenuation, because the bone insertions influence the temperature distribution. In Ref. [18] also the mechanical effects may be detected by inserting contrast agents (e.g. nanobubbles [19]), which can be exploded when the US pressures exceed some threshold values, but no significant differences could be detected in the nanobubbles diameter distribution before and after US sonication. As a consequence, very accurate and anatomically based experimental and numerical models are required to predict the thermal field inside any particular joint or non-homogeneous body region. The starting points should be joints which most benefit from physiotherapeutic US [20, 21], and in particular, shoulders, which often suffer from muscle-skeleton diseases treated with US [22]. On any specific pathologies, such specifically those affecting the shoulders, the previous investigations on phantoms may be useful to perform some 'treatment planning' based on the different anatomical and functional features [23], as shown in **Table 2**.

Clinical diagnosis	**US parameters selected (intensity (W/cm²); frequency (MHz); modalities; duration (minute)**
Impingements and tendonitis BBLC	1.5; 3; pulsed (DC 25%); massage; 10
Frozen shoulder	1.5; 1; continuos; massage; 5
Rotator cuff tendinopathy	1.5; 1; pulsed (DC 25%); massage; 10
Suvraspinal tendonitis and bursitis SAD	1.5; 3; pulsed (DC 25%); massage; 10
Impingement syndrome	1.5; 3; pulsed (DC 25%); massage; 10
Tendonitis BBLC	1.5; 1; pulsed (DC 25%); massage; 10
Tendonitis BBLC and rotator cuff	1.5; 3; pulsed (DC 25%); massage; 10

Table 2. 'Treatment planning' based on the different anatomical and functional features in shoulders.

3. 'Customized' 'in-patient' assessment of clinical effects

Very often physiotherapeutic US is applied by using 'protocols' which sets the same treatment parameters values (e.g. duration and treatment modalities) for all patients and all kind of diseases [22, 24]. In everyday clinical practice, it is uncommon to give a definite and quantitative clinical evaluation of the therapeutic results. Whenever it is done, the effectiveness of the US treatment is often evaluated only by using clinical tests and pain scores such as VAS or NRS, which give a subjective rather than quantitative and objective measure. It is therefore necessary, in order to obtain an objective assessment of the US treatment effectiveness, a multimodal evaluation of patients, including clinical, functional and pain scores, and also including a sonographic quantitative investigation of the local phlogosis before and after the treatment and of the final edema resolution. In a pilotal study [23] performed at the Department of Physical Therapy and Rehabilitation Medicine at Turin University from May to September 2015, 10 patients with shoulder pain and functional limitation, due to biceps brachii long head muscle or rotator cuff tendonitis, bursitis, intra-articular effusion, without indication for surgical treatment were enrolled. After a preliminary physiatric evaluation, each patient underwent the US and other successive rehabilitative treatments. The US therapeutic protocol is based on 10 sessions in consecutive days for an overall period of 2 weeks. US treatments were then designed and performed by selecting the specific US parameters values and the treatment modalities for each patient in consideration of their specific clinical, functional and sonographic findings. A preliminary sonographic study was performed in order to quantify edema, phlogosis or effusion. Relevant images were saved and transferred on PC for further elaboration. As far as the other US parameter values are concerned, a careful evaluation of the estimated depth of the lesion suggested the choice of the frequency of 1 MHz for deep and of 3 MHz for more superficial treatment sites. Moreover, depending on the expected therapeutic increase in temperature at the lesion, the 'continuous' modality was selected to induce more heat deposition (for a shorter time) while the 'pulsed' modality, with a Duty Cycle (i.e. the US emitting time related to the total time length of the cycle) selected at 25% was preferred for longer time (10 min) treatments. A multimodal assessment (clinical, functional and sonographic) of the actual pathology was performed before the US treatment, recording shoulder pain, ROM, strength, functional parameters and sonographic imaging. Pain was estimated using the Numeric Rating Scale (NRS), Constant Score and DASH scale were used for shoulder's function evaluation [25, 26]. The same procedure for result assessment was followed at the end of the US treatment. The sonographic examination was performed following a standardized procedure for the shoulder imaging named muskuloskeletal ultrasonographic exam (MSUS) which satisfactorily detects the main findings of the phlogosis process [27]. MSUS exam was performed before the US treatment session and at the end of the last US session by a rehabilitation medical specialist, using an Edge Ultrasound System (Sonosite, USA) connected to a 7.5 MHz frequency probe. To each alteration, a semi-quantitative score from 0 to 3 was given (0: no alterations; 1, 2, 3: low, mid and high inflammatory alterations). Single scores were added to give a total value (total score), indicating the global index of phlogosis of the shoulder in each patient [28]. All patients enrolled in the study showed a significant reduction of shoulder pain and functional limitations with NRS and DASH scores significantly improved. Sonographic imaging supports clinical data, showing a considerable reduction of bursa or tendon's area of phlogosis. The previous experience obtained in monitoring temperatures in a realistic model (phantom) heated with US with different modalities have been useful in defining more precisely which values of the US parameters and which treatment modalities would be optimal to induce the expected thermal effects for each specific patient.

4. Conclusions

Paying attention to the equipment efficiency, the '*in vitro*' and '*in vivo*' investigations of the thermal field induced by any specific US probe working at different modalities and to the specific characteristics of the joint to be treated, US physiotherapy may dramatically improve its quality and possibly show evidences of effectiveness which are nowadays lacking.

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