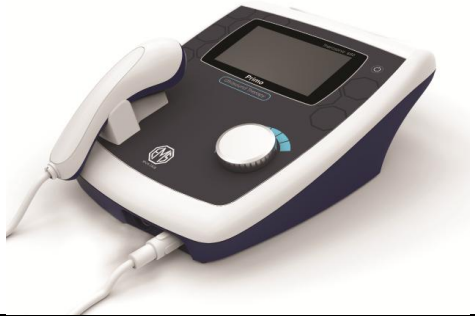
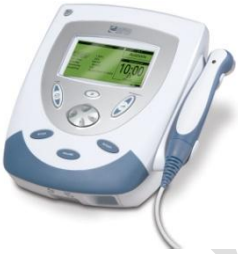
THERAPEUTIC ULTRASOUND

INTRODUCTION

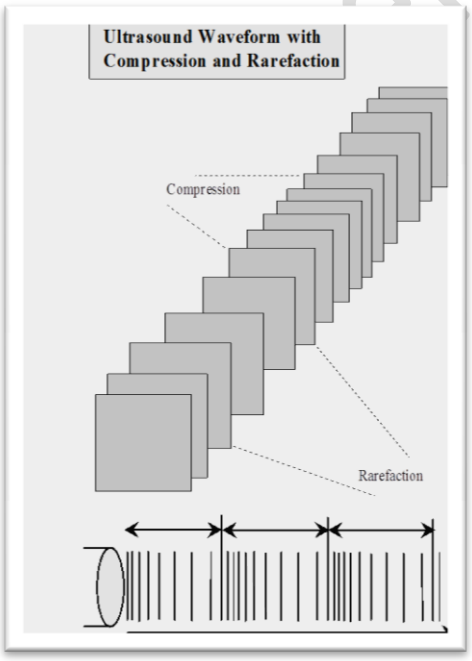
Ultrasound has been a part of clinical practice since sometime back in the 1950's, and remains a popular and evidenced intervention for a range of clinical problems. Shah and Farrow (2012) provide an insight into its current clinical popularity as does the widely cited paper by Pope et al (1995). General (textbook) reviews and explanations can be found in Watson and Young (2008) and Robertson et al (2006) amongst others.

There are myriad therapy ultrasound machines available, from the small, portable devices, through to the multimodal machines which include ultrasound as one of the available options, examples are illustrated below.

		
Dedicated Ultrasound machine (EMS Physio)	Multi modal machine which includes Ultrasound (DJO/Chatanooga)	Portable, Ultrasound device (Ultralieve)

ULTRASOUND ENERGY

Ultrasound (US) is a form of **MECHANICAL** energy, not electrical energy and therefore strictly speaking, not really electrotherapy at all but does fall into the Electro Physical Agents grouping. Mechanical vibration at increasing frequencies is known as sound energy. The normal human sound range is from 16Hz to something approaching 15-20,000 Hz (in children and young adults). Beyond this upper limit, the mechanical vibration is known as **ULTRASOUND**. The frequencies used in therapy are typically between 1.0 and 3.0 MHz (1MHz = 1 million cycles per second).



Sound waves are **LONGITUDINAL** waves consisting of areas of **COMPRESSION** and **RAREFACTION**. Particles of a material, when exposed to a sound wave will oscillate about a fixed point rather than move with the wave itself. As the energy within the sound wave is passed to the material, it will cause oscillation of the particles of that material. Clearly any increase in the molecular vibration in the tissue can result in heat generation, and ultrasound can be used to produce thermal changes in the tissues, though current usage in therapy does not focus on this phenomenon (Williams 1987, Baker et al 2001, ter Haar 1999, Nussbaum 1997, Watson 2000, 2008). In addition to thermal changes, the vibration of the tissues appears to have effects which are generally considered to be non thermal in nature, though, as with other modalities (e.g. Pulsed Shortwave) there must be a thermal component however small. As the US wave passes through a material (the tissues), the

energy levels within the wave will diminish as energy is transferred to the material. The energy absorption and attenuation characteristics of US waves have been documented for different tissues (see absorption section).

ULTRASOUND WAVES :

FREQUENCY - the number of times a particle experiences a complete compression/rarefaction cycle in 1 second. Typically 1 or 3 MHz (though there are devices which operate in the kHz range - see comments on Low Frequency / Longwave Ultrasound at the end of this paper).

WAVELENGTH -the distance between two equivalent points on the waveform in the particular medium. In an 'average tissue' the wavelength @ 1MHz would be 1.5mm and @ 3 MHz would be 0.5 mm.

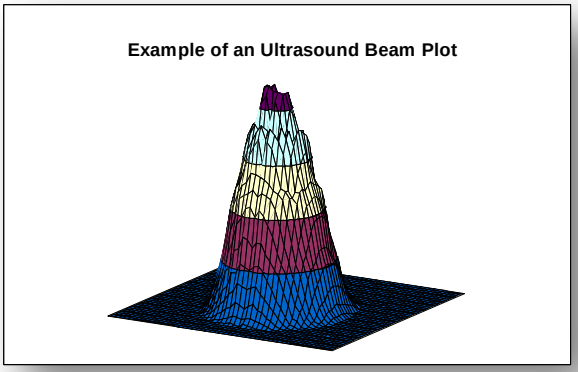
VELOCITY - the velocity at which the wave (disturbance) travels through the medium. In a saline solution, the velocity of US is approximately 1500 m sec^{-1} compared with approximately 350 m sec^{-1} in air (sound waves can travel more rapidly in a more dense medium). The velocity of US in most tissues is thought to be similar to that in saline.

These three factors are related, but are not constant for all types of tissue. Average figures are most commonly used to represent the passage of US in the tissues. Typical US frequencies from therapeutic equipment are 1 and 3 MHz though some machines produce additional frequencies (e.g. 0.75 and 1.5 MHz) and the 'Longwave' ultrasound devices operate at several 10's of kHz (typically 40-50,000Hz – a much lower frequency than 'traditional US' but still beyond human hearing range.

The mathematical representation of the relationship is $\mathbf{V = F.\lambda}$
where **V** = velocity, **F** = frequency and λ is the wavelength.

ULTRASOUND BEAM, NEAR FIELD, FAR FIELD AND BEAM NON UNIFORMITY

The US beam is not uniform and changes in its nature with distance from the transducer. The US beam nearest the treatment head is called the **NEAR** field, the **INTERFERENCE** field or the **Frenzel zone**. The behaviour of the US in this field is far from regular, with areas of significant interference. The US energy in parts of this field can be many times greater than the output set on the machine (possibly as much as 12 to 15 times greater). The size (length) of the near field can be calculated using r^2/λ where r= the radius of the transducer crystal and λ = the US wavelength according to the frequency being used (0.5mm for 3MHz and 1.5mm for 1.0 MHz).



As an example, a 'crystal' with a diameter of 25mm operating at 1 MHz will have a near field/far field boundary at : **Boundary = $12.5mm^2/1.5mm \approx 10cm$** thus the near field (with greatest interference) extends for approximately 10 cm from the treatment head when using a large treatment head and 1 MHz US. When using higher frequency US, the boundary distance is even greater. Beyond this boundary lies the **Far Field** or the **Fraunhofer zone**. The US beam in this field is more uniform and gently divergent. The 'hot spots' noted in the near field are not significant. For the purposes of therapeutic applications, the far field is effectively out of reach.

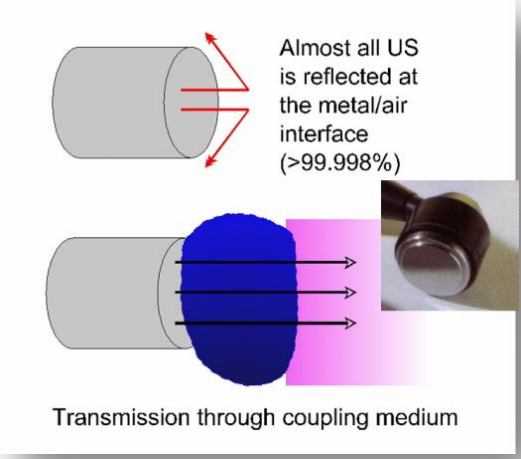
One quality indicator for US applicators (transducers) is a value attributed to the **Beam Nonuniformity Ratio (BNR)**. This gives an indication of this near field interference. It describes numerically the ratio of the intensity peaks to the mean intensity. For most applicators, the BNR would be approximately 4 - 6 (i.e. that the peak

intensity will be 4 or 6 times greater than the mean intensity). It is considered inappropriate to use a device with a BNR value of 8.0 or more. Because of the nature of US, the theoretical best value for the BNR is thought to be around 4.0 though some manufacturers claim to have overcome this limit and effectively reduced the BNR of their generators to 1.0.

Some recent papers (Alvarenga et al 2010; Gutierrez et al 2010; Straub et al, 2008 and Johns et al 2007) have considered some of the inaccuracies associated with current machines and Pye (1996) presents some worrying data with regards the calibration of machines in clinical use in the UK.

ULTRASOUND TRANSMISSION THROUGH THE TISSUES

All materials (tissues) will present an impedance to the passage of sound waves. The specific impedance of a tissue will be determined by its density and elasticity. In order for the maximal transmission of energy from one medium to another, the impedance of the two media needs to be as similar as possible. Clearly in the case of US passing from the generator to the tissues and then through the different tissue types, this can not actually be achieved. ***The greater the difference in impedance at a boundary, the greater the reflection that will occur, and therefore, the smaller the amount of energy that will be transferred***. Examples of impedance values can be found in the literature e.g. Robertson et al 2007, Ward 1986.



The difference in impedance is greatest for the steel/air interface which is the first one that the US has to overcome in order to reach the tissues. To minimise this difference, a suitable coupling medium has to be utilised. If even a small air gap exists between the transducer and the skin the proportion of US that will be reflected approaches 99.998% which means that there will be no effective transmission.

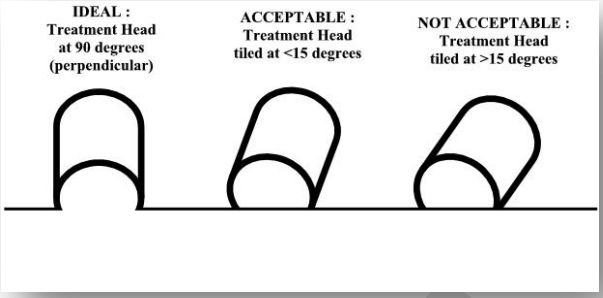
The coupling media used in this context include water, various oils, creams and gels. Ideally, the coupling medium should be fluid so as to fill all available spaces, relatively viscous so that it stays in place, have an impedance appropriate to the media it connects, and should allow transmission of US with minimal absorption, attenuation or disturbance. For a good discussion regarding coupling media, see Casarotto et al 2004, Docker et al 1982, Griffin, 1980, Klucinec et al 2000 and Williams 1987. At the present time the gel based media are preferable to the oils and creams. Water is an effective media and can be used as an alternative but clearly it fails to meet the above criteria in terms of its viscosity. **There is no realistic (clinical) difference between the gels in common clinical use** (Poltawski and Watson 2007). The addition of active agents (e.g. anti-inflammatory drugs) to the gel is widely practiced, but remains incompletely researched. We are currently evaluating this intervention further.

Bacterial Contamination of Ultrasound Treatment Heads and Gel Sources

As a matter of (clinical) interest, the US treatment should be cleaned with an alcohol based swab (not just wiped with tissue) between treatments (Schabrun et al, 2006) to minimise the potential transmission of microbial agents between patients. Spratt et al (2014) sampled ultrasound treatment heads and gel bottles (in the USA) reporting over 50% of gel bottles with contamination, some of which were positive for MRSA. Some 35% of the ultrasound treatment heads tested also demonstrated contamination, though none with MRSA. The authors report that employment of adequate disinfection techniques was effective in significantly reducing these levels (they used Protex, Parker Laboratories).

Ultrasound Application - The Critical Angle

In addition to the reflection that occurs at a boundary due to differences in impedance, there will also be some refraction if the wave does not strike the boundary surface at 90°. Essentially, the direction of the US beam through the second medium will not be the same as its path through the original medium - its pathway is angled. The critical angle for US at the skin interface appears to be about 15°. If the treatment head is at an angle of 15° or more to the plane of the skin surface, the majority of the US beam will travel through the dermal tissues (i.e. parallel to the skin surface) rather than penetrate the tissues as would be expected.



ULTRASOUND ABSORPTION AND ATTENUATION :

The absorption of US energy follows an exponential pattern - i.e. more energy is absorbed in the superficial tissues than in the deep tissues. In order for energy to have an effect it must be absorbed, and at some point this must be considered in relation to the US dosages applied to achieve certain effects (ter Haar, 1999, Watson, 2008, Watson and Young, 2008).

Because the absorption (penetration) is exponential, there is (in theory) no point at which all the energy has been absorbed, but there is certainly a point at which the US energy levels are not sufficient to produce a therapeutic effect. As the US beam penetrates further into the tissues, a greater proportion of the energy will have been absorbed and therefore there is less energy available to achieve therapeutic effects. The half value depth is often quoted in relation to US and it represents the depth in the tissues at which half the surface energy is available. These will be different for each tissue and also for different US frequencies. The table below gives some indication of typical (or average) half value depths for therapeutic ultrasound. (after Hoogland 1995)

	1 MHz	3 MHz
Muscle	9.0 mm	3.0 mm
Fat	50.0 mm	16.5 mm
Tendon	6.2 mm	2.0 mm

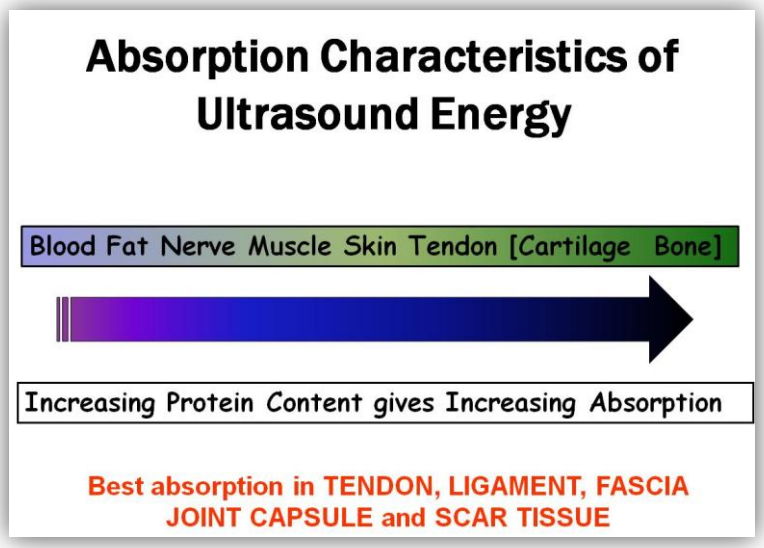
As it is difficult, if not impossible to know the thickness of each of these layers in an individual patient, average half value depths are employed for each frequency

3 MHz 2.0 cm
1 MHz 4.0 cm

These values (after Low & Reed) are not universally accepted (see Ward 1986) and some research (as yet unpublished) suggests that in the clinical environment, they may be significantly lower.

Depth (cm)	3 MHz	1 MHz
2	50%	
4	25%	50%
6		
8		25%

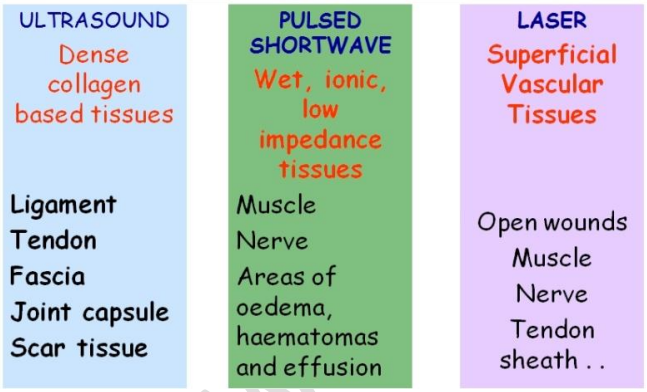
To achieve a particular US intensity at depth, account must be taken of the proportion of energy which has been absorbed by the tissues in the more superficial layers. The table gives an approximate reduction in energy levels with typical tissues at two commonly used frequencies, and more detailed information is found in the dose calculation material and on the web pages (www.electrotherapy.org).



As the penetration (or transmission) of US is not the same in each tissue type, it is clear that some tissues are capable of greater absorption of US than others. Generally, the tissues with the higher protein content will absorb US to a greater extent, thus tissues with high water content and low protein content absorb little of the US energy (e.g. blood and fat) whilst those with a lower water content and a higher protein content will absorb US far more efficiently. Tissues can be ranked according to their relative tissue absorption and this is critical in terms of clinical decision making (Watson, 2008).

Although cartilage and bone are at the upper end of this scale, the problems associated with wave reflection mean that the majority of US energy striking the surface of either of these tissues is likely to be reflected. The best absorbing tissues in terms of clinical practice are those with high collagen content – **LIGAMENT, TENDON, FASCIA, JOINT CAPSULE, SCAR TISSUE** (Watson 2000, 2008, Watson & Young, 2008, ter Haar 1999, Nussbaum 1998, Frizzel & Dunn 1982)

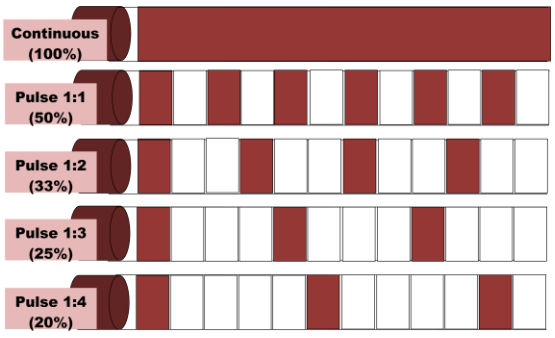
The application of therapeutic US to tissues with a low energy absorption capacity is less likely to be effective than the application of the energy into a more highly absorbing material. Recent evidence of the ineffectiveness of such an intervention can be found in Wilkin et al (2004) and Markert et al (2005) whilst application in tissue that is a better absorber will, as expected, result in a more effective intervention (e.g. Sparrow et al 2005, Leung et al 2004).



The physiological effects of ultrasound are almost identical to those of Pulsed Shortwave and Laser therapy – the key difference however, is that ultrasound energy is preferentially absorbed in different tissue to the other modalities – as summarised in the adjacent diagram.

PULSED ULTRASOUND

Most machines offer the facility for pulsed US output, and for many clinicians, this is a preferable mode of treatment. Until recently, the pulse duration (the time during which the machine is on) was almost exclusively 2ms (2 thousandths of a second) with a variable off period. Some machines now offer a variable on time though whether this is of clinical significance has yet to be determined. Typical pulse ratios are 1:1 and 1:4 though others are available (see dose calculations). In 1:1 mode, the machine offers an output for 2ms followed by 2ms rest. In 1:4 mode, the 2ms output is followed by an 8ms rest period. The adjacent diagram illustrates the effect of varying the pulse ratio.



The effects of pulsed US are well documented and this type of output is preferable especially in the treatment of the more acute lesions. Some machines offer pulse parameters that do not appear to be supported from the literature (e.g. 1:9; 1:20).

Mode	Pulse Ratio	Duty Cycle
Continuous	N/A	100%
Pulsed	1:1	50%
	1:2	33%
	1:3	25%
	1:4	20%
	1:9	10%

Some manufacturers describe their pulsing in terms of a percentage rather than a ratio (1:1 = 50% 1:4 = 20% etc). An equivalence table is provided for convenience. The proportion of time that the machine is ON compared with OFF is a relevant factor in dosage calculations and further details are included in the dose calculation support material.

Pulse Frequency

A point of confusion amongst many therapists is the 'frequency' facility offered on some ultrasound machines. The pulse ratio (duty cycle) is at say 1:4 (20%), but there is an option to alter the pulse frequency (i.e. how many ultrasound pulses are delivered per second). This is achieved by adjusting the DURATION of the pulses. Typically, these are at 2ms, thus on a 1:4 ratio, the machine is ON for 2ms and then OFF for 8ms. It takes 10ms to complete one 'cycle' (ON : OFF), and thus 100 such cycles are completed in a second, so the machine claims to deliver ultrasound at 100Hz. If the pulse duration is increased from 2ms to say 4ms, then on a 1:4 ratio, the machine will be ON for 4ms followed by 16ms OFF, thus taking 20ms to complete a cycle and hence only 50 such cycles being delivered per second and the setting on the machine will be for ultrasound pulsing at 50Hz. There is no evidence that I can find to suggest that one mode of operation has any clinical advantage over another. The 2ms pulse time is 'normal' and is encountered on most machines (which effectively means that 100 pulses of ultrasound energy will be delivered per second.

THERAPEUTIC ULTRASOUND THERMAL AND NON THERMAL EFFECTS OVERVIEW

One of the therapeutic effects for which ultrasound has been used is in relation to tissue healing. It is suggested that the application of US to injured tissues will, amongst other things, speed the rate of healing & enhance the quality of the repair (Watson 2006). The following information is intended to provide a summary of some of the essential research in this field together with some possible mechanisms through which US treatments may achieve these changes. It is not intended to be a complete explanation of these phenomena or a comprehensive review of the current literature. It may, none the less, provide some useful basic information for clinical application. Some of the 'wider' applications for ultrasound therapy (e.g. drug delivery, chemotherapy potentiation) are usefully reviewed in Paliwal and Mitragotri (2008).

The therapeutic effects of US are generally divided into: **THERMAL & NON-THERMAL**.

THERMAL:

In thermal mode, US will be most effective in heating the dense collagenous tissues and will require a relatively high intensity, preferably in continuous mode to achieve this effect.

Many papers have concentrated on the thermal effectiveness of ultrasound, and much as it can be used effectively in this way when an appropriate dose is selected (continuous mode >0.5 W cm^{-2}), the focus of this paper will be on the non thermal effects. Both Nussbaum (1998) and ter Haar (1999) have provided some useful review material with regards the thermal effects of ultrasound. Comparative studies on the thermal effects of ultrasound have been reported by several authors (e.g. Draper et al 1993, 1995a,b, Leonard et al 2004) with some interesting, and potentially useful results. Further work continues in our research centre with a comparison of contact heating and longwave ultrasound (Meakins and Watson, 2006) and comparison of different US regimes combined with US (Aldridge and Watson – in preparation)

It is too simplistic to assume that with a particular treatment application there will either be thermal or non thermal effects. It is almost inevitable that both will occur, but it is furthermore reasonable to argue that the dominant effect will be influenced by treatment parameters, especially the mode of application i.e. pulsed or continuous. Baker et al (2001) have argued the scientific basis for this issue coherently.

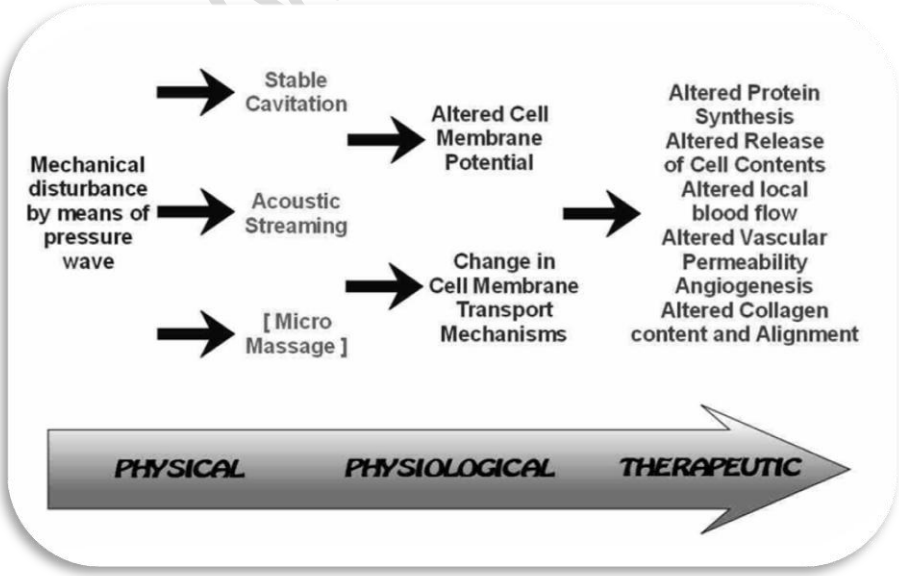
Lehmann (1982) suggests that the desirable effects of therapeutic heat can be produced by US. It can be used to selectively raise the temperature of particular tissues due to its mode of action. Among the more effectively heated tissues are periosteum, collagenous tissues (ligament, tendon & fascia) & fibrotic muscle (Dyson 1981). If the temperature of the damaged tissues is raised to 40-45°C, then a hyperaemia will result, the effect of which will be therapeutic. In addition, temperatures in this range are also thought to help in initiating the resolution of chronic inflammatory states (Dyson & Suckling 1978). Most authorities currently attribute a greater importance to the non-thermal effects of US as a result of several investigative trials in the last 15 years or so.

NON-THERMAL:

The non-thermal effects of US are now attributed primarily to a combination of **CAVITATION** and **ACOUSTIC STREAMING** (ter Haar 1999, 2008 Baker et al 2001, Williams 1987). There appears to be little by way of convincing evidence to support the notion of **MICROMASSAGE** though it does sound rather appealing.

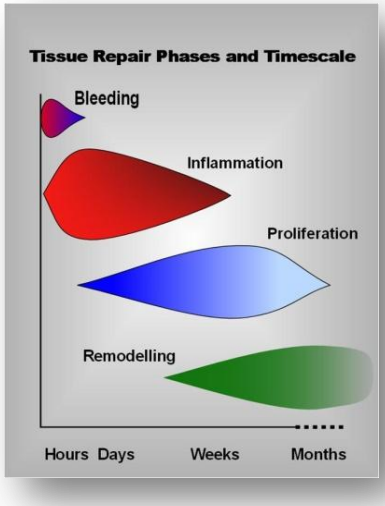
CAVITATION in its simplest sense relates to the formation of gas filled voids within the tissues & body fluids. There are 2 types of cavitation - **STABLE & UNSTABLE** which have very different effects. **STABLE CAVITATION** does seem to occur at therapeutic doses of US. This is the formation & growth of gas bubbles by accumulation of dissolved gas in the medium. They take apx. 1000 cycles to reach their maximum size. The `cavity' acts to enhance the acoustic streaming phenomena (see below) & as such would appear to be beneficial. **UNSTABLE (TRANSIENT) CAVITATION** is the formation of bubbles at the low pressure part of the US cycle. These bubbles then collapse very quickly releasing a large amount of energy which is detrimental to tissue viability. There is no evidence at present to suggest that this phenomenon occurs at therapeutic levels if a good technique is used. There are applications of US that deliberately employ the unstable cavitation effect (**High Intensity Focussed Ultrasound or HIFU**) but it is beyond the remit of this summary.

ACOUSTIC STREAMING is described as a small scale eddying of fluids near a vibrating structure such as cell membranes & the surface of stable cavitation gas bubble (Dyson & Suckling 1978). This phenomenon is known to affect diffusion rates & membrane permeability. Sodium ion permeability is altered resulting in changes in the cell membrane potential. Calcium ion transport is modified which in turn leads to an alteration in the enzyme control mechanisms of various metabolic processes, especially concerning protein synthesis & cellular secretions.



The result of the combined effects of stable cavitation and acoustic streaming is that the cell membrane becomes 'excited' (up regulates), thus increasing the activity levels of the whole cell. The US energy acts as a ***trigger*** for this process, but it is the increased cellular activity which is in effect responsible for the therapeutic benefits of the modality (Watson 2000, 2008, Dinno et al 1989, Leung et al 2004).

MICROMASSAGE is a mechanical effect which appears to have been attributed less importance in recent years. In essence, the sound wave travelling through the medium is claimed to cause molecules to vibrate, possibly enhancing tissue fluid interchange & affecting tissue mobility. There is little, if any hard evidence for this often cited principle.



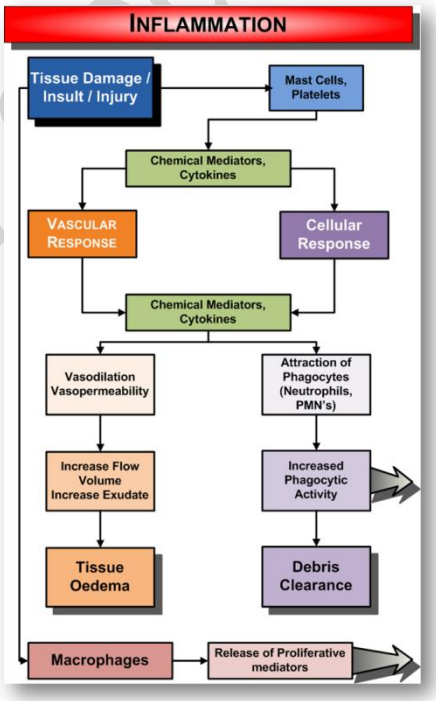
ULTRASOUND APPLICATION IN RELATION TO TISSUE REPAIR

The process of tissue repair is a complex series of cascaded, chemically mediated events that lead to the production of scar tissue that constitutes an effective material to restore the continuity of the damaged tissue. The process is more complex than be described here, but there are several interesting recent papers and reviews including (Wener & Grose 2003, Toumi & Best 2003, Watson 2003, 2006, Hill et al 2003, Neidlinger-Wilke et al 2002, Lorena et al 2002, Latey 2001, Velnar et al 2009, Hauser et al 2013).

The various phases of tissue repair can be usefully represented by the 'blocks' in the figure to the left. The division into Bleeding, Inflammatory, Proliferative and Remodelling phases is almost arbitrary in that from a tissue perspective, this is in fact one continuous series of events, with a change in emphasis with time. Further details, reviews and reference materials can be found in the publications identified above or from the web site at : www.electrotherapy.org.

INFLAMMATION:

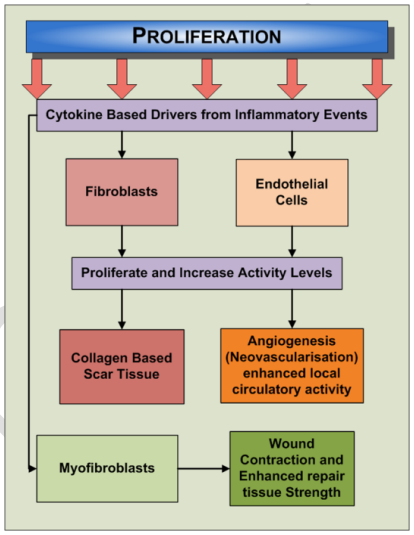
During the inflammatory phase, US has a stimulating effect on the mast cells, platelets, white cells with phagocytic roles and the macrophages (Nussbaum 1997, ter Haar 1999, Fyfe & Cahal 1982, Maxwell 1992, Watson 2008; Li et al 2003). For example, the application of ultrasound induces the degranulation of mast cells, causing the release of arachidonic acid which itself is a precursor for the synthesis of prostaglandins and leukotreine – which act as inflammatory mediators (Mortimer & Dyson 1988, Nussbaum 1997, Leung et al 2004). By increasing the activity of these cells, the overall influence of therapeutic US is certainly pro-inflammatory rather than anti-inflammatory. The benefit of this mode of action is not to 'increase' the inflammatory response as such (though if applied with too greater intensity at this stage, it is a possible outcome (Ciccone et al 1991), but rather to act as an 'inflammatory optimiser' (Watson 2007, 2008). The inflammatory response is essential to the effective repair of tissue, and the more efficiently the process can complete, the more effectively the tissue can progress to the next phase (proliferation). Studies which have tried to demonstrate the anti inflammatory effect of ultrasound have failed to do so (e.g.El Hag et al 1985 Hashish 1986, 1988), and have suggested that US is ineffective. It **is** effective at promoting the normality of the inflammatory events, and as such has a therapeutic value in promoting the overall repair events (ter Haar 99, Watson 2008). A further benefit is that the inflammatory chemically mediated events are associated with stimulation of the next (proliferative) phase, and hence the promotion of the inflammatory phase also acts as a promoter of the proliferative phase.



Employed at an appropriate treatment dose, with optimal treatment parameters (intensity, pulsing and time), the benefit of US is to make as efficient as possible to earliest repair phase, and thus have a promotional effect on the whole healing cascade. For tissues in which there is an inflammatory reaction, but in which there is no 'repair' to be achieved, the benefit of ultrasound is to promote the normal resolution of the inflammatory events, and hence resolve the 'problem' This will of course be most effectively achieved in the tissues that preferentially absorb ultrasound – i.e. the dense collagenous tissues.

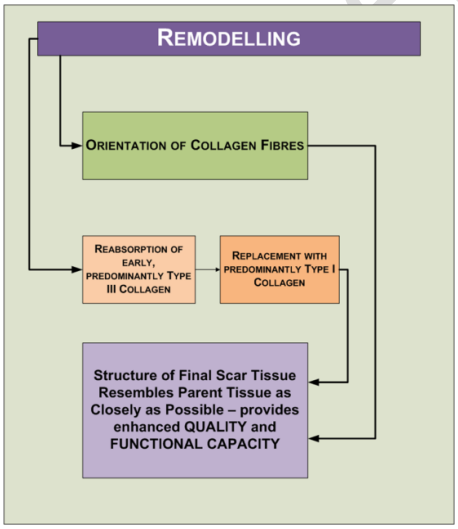
PROLFERATION:

During the proliferative phase (scar production) US also has a stimulative effect (cellular up regulation), though the primary active targets are now the fibroblasts, endothelial cells and myofibroblasts (Ramirez et al 1997, Mortimer and Dyson 1988, Young & Dyson 1990, Young & Dyson 1990b, Nussbaum 1997, 1998, Dyson & Smalley 1983, Maxwell 1992, Watson and Young 2008, Watson 2007, 2008, Ng 2011). These are all cells that are normally active during scar production and US is therefore pro-proliferative in the same way that it is pro-inflammatory – it does not change the normal proliferative phase, but maximises its efficiency – producing the required scar tissue in an optimal fashion. Harvey et al (1975) demonstrated that low dose pulsed ultrasound increases protein synthesis and several research groups have demonstrated enhanced fibroplasia and collagen synthesis (Enwemeka et al 1989, 1990, Turner et al 1989, Huys et al 1993, Ramirez et al 1997, Warden et al 2006, Zhang et al 2004). Recent work has identified the critical role of numerous growth factors in relation to tissue repair, and some accumulating evidence has identified that therapeutic US has a positive role to play in this context (e.g. Leung et al, 2006; Lovric et al 2013; Li et al, 2002; McBrier et al 2007; Reher et al 1999; Tsai et al 2006) and also with heat shock proteins (Nussbaum and Locke 2007)



REMODELLING:

During the remodelling phase of repair, the somewhat generic scar that is produced in the initial stages is refined such that it adopts functional characteristics of the tissue that it is repairing. A scar in ligament will not 'become' ligament, but will behave more like a ligamentous tissue. This is achieved by a number of processes, but mainly related to the orientation of the collagen fibres in the developing scar (Culav et al 1999, Gomez et al 1991, Watson, 2003) and also to the change in collagen type, from predominantly Type III collagen to a more dominant Type I collagen. The remodelling process is certainly not a short duration phase – research has shown that it can last for a year or more – yet it is an essential component of quality repair (El Batouty et al 1986, ter Haar 1987)



The application of therapeutic ultrasound can influence the remodelling of the scar tissue in that it appears to be capable of enhancing the appropriate orientation of the newly formed collagen fibres and also to the collagen profile change from mainly Type III to a more dominant Type I construction, thus increasing tensile strength and enhancing scar mobility (Nussbaum 1998, Wang 1998). Ultrasound applied to tissues enhances the functional capacity of the scar tissues (Nussbaum 1998, Huys et al 1993, Tsai et al 2006, 2011, Yeung et al 2006). The role of ultrasound in this phase may also have the capacity to influence collagen fibre orientation as demonstrated in an elegant study by Byl et al (1996), though their conclusions were quite reasonably somewhat tentative.

The application of ultrasound during the inflammatory, proliferative and repair phases is not of value because it changes the normal sequence of events, but because it has the capacity to stimulate or enhance these normal events and thus increase the efficiency of the repair phases (ter Haar 99, Watson 2007, 2008, Watson & Young, 2008). It would appear that if a tissue is repairing in a compromised or inhibited fashion, the application of therapeutic ultrasound at an appropriate dose will enhance this activity. If the tissue is healing 'normally', the application will, it would appear, speed the process and thus enable the tissue to reach its endpoint faster than would otherwise be the case. The effective application of ultrasound to achieve these aims is dose dependent.

OTHER APPLICATIONS :

There are a growing number of 'other applications' for ultrasound energy ranging from tumour ablation – using ***High Intensity Focussed Ultrasound (or HIFU)*** though to stimulated related of encapsulated systemic drugs. HIFU is beyond the scope of this review which is mainly concerned with 'standard' therapy ultrasound.

LIPUS (Low Intensity Pulsed Ultrasound) for Fracture Repair – there is a wealth of research information in this area (summarised on the www.electrotherapy.org web pages if you want the detail). The NICE guidelines (Jan 2013) are supportive of this clinical application. Essentially, the application of very low dose ultrasound over a fracture (whether healing normally or delayed or non union) can be of significant benefit. The main clinical issue is that the effective 'dose' is actually lower than most therapy machines can deliver – which is frustrating! Higher intensity ultrasound over a fracture can initiate a strong pain response – which is useful when it comes to using the modality to locate potential stress fractures (see below). A useful recent review (fully detailed on the web pages) can be found at Zura et al (2015)

The LIPUS ultrasound field is starting to expand - working on the principle that if it is so effective for fracture healing, then it might also be effective for soft tissue lesions and other musculoskeletal problems. Much of this work is still in development, though results and publications are anticipated (reviewed in Khanna et al, 2009). Examples of additional bone related papers include El Bialy et al (2002) who evaluated its effects during distraction osteogenesis.

Low Frequency (Longwave) Ultrasound : There is a range of experimental, lab and clinical evidence with regards the specific use of ultrasound in the kHz range of frequencies (over the 20kHz hearing upper limit, but below the MHz frequencies more commonly employed in therapy. Ahmadi et al (2012) have usefully reviewed both bioeffects and safety issues at this frequency range. A separate Low Frequency (Longwave) Ultrasound information page and pdf download are available from the web pages (www.electrotherapy.org) for those interested in this field.

Therapy Ultrasound as a Diagnostic Tool for Stress Fractures : The use of therapy ultrasound machines as a means to 'diagnose' whether there is a stress fracture is a technique what has been employed sporadically for many years. Some claim (anecdotally) that it is very effective whilst others dismiss the technique. Essentially, a 'strong' ultrasound application (typically 1MHz; 1.0 W cm^{-2}; continuous) is applied over the suspect area. If there is a stress fracture (or other significant bony injury) it is common for a sharp pain to be felt by the patient. It can be a useful technique when working without immediate access to XRay, MRI or other higher level imaging technology. The research reports covering this technique are mixed. The more recent papers include Papalada et al (2012) who suggest that the technique is reproducible and reliable whilst Khatri et al (2008) suggest that the technique is not as accurate as MRI - no argument - it is not claimed to be - but that does not make it invalid as a quick, cost effective and easily accessible assessment for the therapist. Other papers include Devereaux et al (1084) and Delacerda (1981).

Ultrasound Therapy for Wound Healing : There have been a range of research papers over the years which have set out to evaluate the benefits (or otherwise) of ultrasound therapy as a means to stimulate healing in **chronic wounds** (typically venous ulcers and pressure sores). Whilst some research has not demonstrated significant clinical benefit, others have clearly done so, and therefore, as with other wound based

electrophysical agent applications, it is likely to be a dose dependent response. Cullum et al (2010) contributed a Cochrane review on this topic, though only 8 trials were included (I have over 400 papers the in one way or another consider ultrasound and wound healing). Of the 6 papers which employed MHz ultrasound, 5 demonstrated significant benefit, though as these trials employed small samples, it was suggested that the evidence was not sufficiently strong to constitute support for the therapy (in Cochrane terms). A quick search of the literature will identify numerous papers, which a swift review of the Cullum et al paper will give you rapid access to some useful leads as will the slightly older, but none the less useful Uhlemann et al (2003) publication which considers both MHz and kHz versions of the modality. Ennis et al (2005) provide a useful RCT based publication demonstrating beneficial outcomes. Low frequency (longwave) ultrasound (including MIST Therapy where the ultrasound is delivered through a saline 'mist') is being increasingly employed as an evidenced wound debridement treatment (e.g. Bell et al, 2008; Stanisic et al, 2005) whilst Serena et al (2009) and Harris et al (2014) identify its potential benefit in relation to wound bacterial counts. An example of a recent, well constructed trial for ultrasonic treatment of pressure ulcers can be found in Polak et al (2014).

The use of ***US at trigger points*** has been used clinically for some time and is well supported from the anecdotal evidence. A study by Srbely et al (2007) raises some interesting points and demonstrates a measurable benefit. Other studies in this area include Sarrafzadeh et al (2012); Unalan et al (2011); Draper et al (2010); Aguilera et al (2009); Majlesi and Unalan (2004); Manca et al (2014). More recently Morishita et al (2014) have demonstrated some interesting effects of ultrasound (to trapezius), stretch and pain effects, which may link to trigger point applications.

A recent review and meta analysis (Zeng et al, 2014) evaluated continuous and pulsed ultrasound applications in **knee osteoarthritis (OA) management**. It was shown that pulsed ultrasound is more effective in terms of pain management and functional improvement compared with control conditions. The use of continuous ultrasound was effective only in terms of pain management.

There is an increasing body of evidence which supports the use of Ultrasound in **chronic sinusitis and rhinosinusitis**. This has been usefully reviewed in Bartley et al (2014) and detailed clinical trials can be found in Ansari et al (2014); Young et al (2010); Naghdi et al (2008); Ansari et al (2007). Doses applied in these trials were typically at 1MHz; 0.5-1.0W cm^{-2}; pulsed mode; 15-18 minutes; 3 x weekly; 10 sessions with significant clinical benefit.

'STATUS' Ultrasound : Enraf (www.enraf-nonius.com) have recently introduced a 'new' method of delivering traditional ultrasound therapy which employs a stationary treatment applicator which is held in place using a vacuum system. There is currently limited clinical research with regards any different effect - none are expected - the advantage being that (a) it is safe and (b) the therapist does not need to deliver the treatment in the classic way - they can affix the applicator and proceed with other jobs. The STATUS application employs 'traditional' ultrasound (as described in this paper) - it is sometimes confused with LIPUS (see above) given that the application is made with a stationary treatment applicator. This is not a LIPUS treatment.

Home based Ultrasound : there is an increasing availability of home based ultrasound treatment options. The (potential) advantage is that the therapist need not use clinic time to deliver the treatment, and secondly, if ultrasound is at its most effective when delivered daily, it becomes a realistic option. The disadvantage of most of these portable, handheld devices is that (currently) they rarely offer a choice of treatment dose, thus reducing their value. Some new systems are becoming available on which there are dose selection options, making them potentially useful (e.g. www.ultralieve.com). It is anticipated that is will be a treatment option which increases in popularity and value in the near future.

THERAPEUTIC ULTRASOUND : CONTRAINDICATIONS AND PRECAUTIONS

CONTRAINDICATIONS :

- Do not expose either the embryo or foetus to therapeutic levels of ultrasound by treating over the uterus during pregnancy
- Malignancy (history of malignancy is NOT a contraindication – DO NOT treat over tissue that is, or considered to be malignant)
- Tissues in which bleeding is occurring or could reasonably be expected (usually within 4-6 hours of injury but may be longer in some instances and for some patients)
- Significant vascular abnormalities including deep vein thrombosis, emboli and severe arteriosclerosis / atherosclerosis (if increase in local blood flow demanded by the treatment can not reasonably be delivered)
- Patients with Haemophilia not covered by factor replacement
- Application over :
    - The eye
    - The stellate ganglion
    - The cardiac area in advanced heart disease & where pacemakers in situ
    - The gonads
    - Active epiphyses in children (Ok to use US in children – critical question is whether the applied energy would reach the epiphysis whilst it is active)

[There is additional information on these topics and explanation of contraindication position on the FAQ page at electrotherapy.org]

PRECAUTIONS :

- Always use the lowest intensity which produces a therapeutic response
- Ensure that the applicator is moved throughout the treatment (speed and direction not an issue)
- [not necessary with LIPUS applications or the newly advocated STATUS application]
- Ensure that the patient is aware of the nature of the treatment and its expected outcome
- If a thermal dose is intended, ensure that any contraindications that apply have been considered
- Caution is advised in the vicinity of a cardiac pacemaker or other implanted electronic device
- Continuous ultrasound is considered unwise over metal implants

HAZARDS :

Reversible blood cell stasis can occur in small blood vessels if a standing wave is produced while treating over a reflector such as an air/soft tissue interface, soft tissue/bone or soft tissue/metal interface whilst using a stationary applicator. This having been said, I can identify no evidence that this occurs at 'normal' therapeutic levels and with a moving head application method. Treatment with a stationary treatment head is considered bad practice in the normal therapy environment (LIPUS excepted).

TREATMENT RECORD :

The operator should note :
Machine (if more than one available)
Machine settings – : frequency, intensity, time, pulse parameters
Area treated (size and location)
Any immediate or untoward effects

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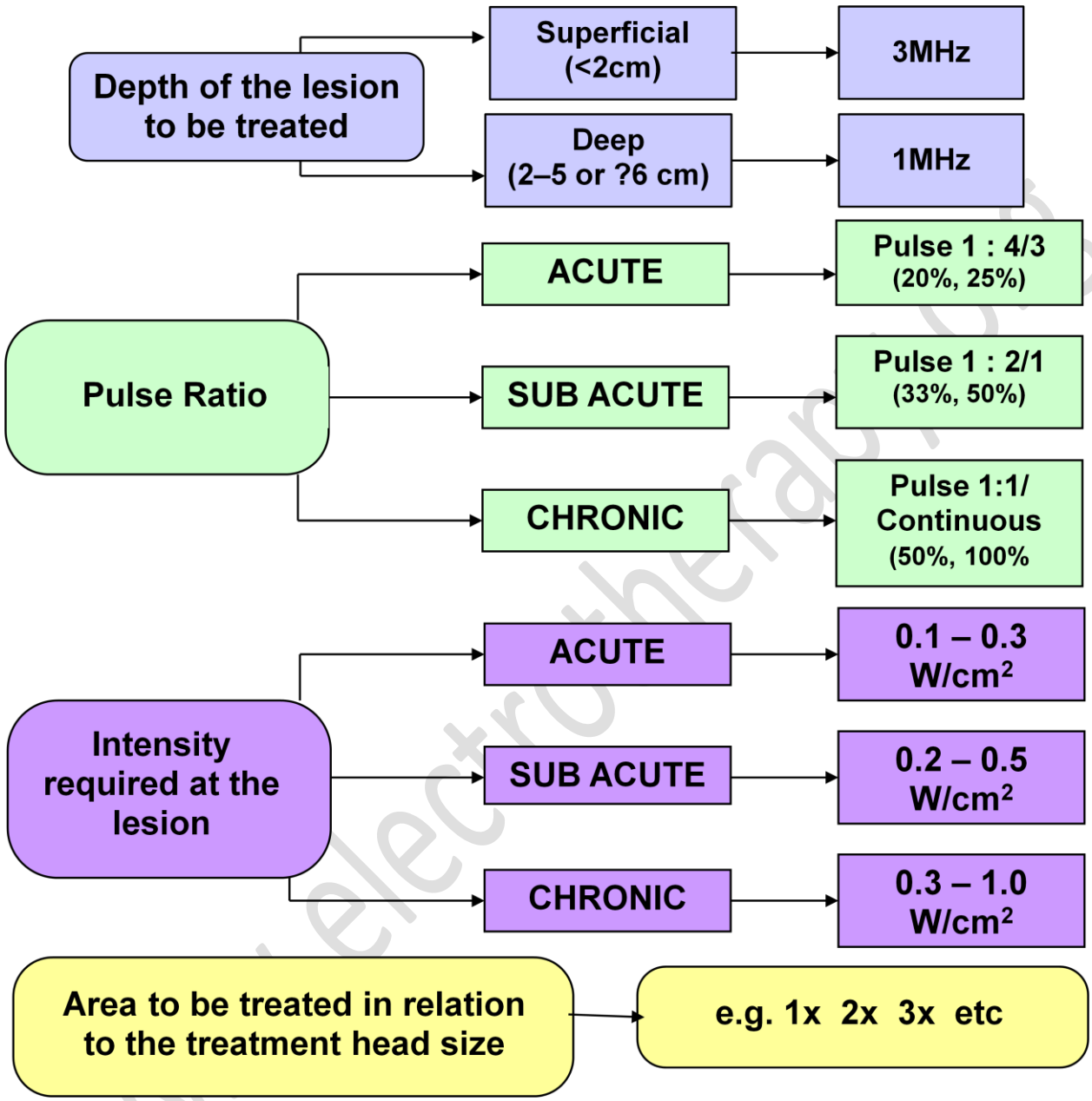
Ultrasound Dose Calculation Summary Chart



Ultrasound treatment : aim for **1 minutes worth of ultrasound per treatment head area**

Therefore longer if **PULSED** and longer for **LARGER TREATMENT AREAS**

Treatment time = 1 x (no of times treatment head fits onto tissue to treat) x (pulse factor)

The **PULSE FACTOR** in the calculation can be achieved by adding the two elements of the pulse ratio e.g. pulse 1:1, adds to 2, multiply x 2. Pulse 1:4. Adds to 5. Multiply x 5

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