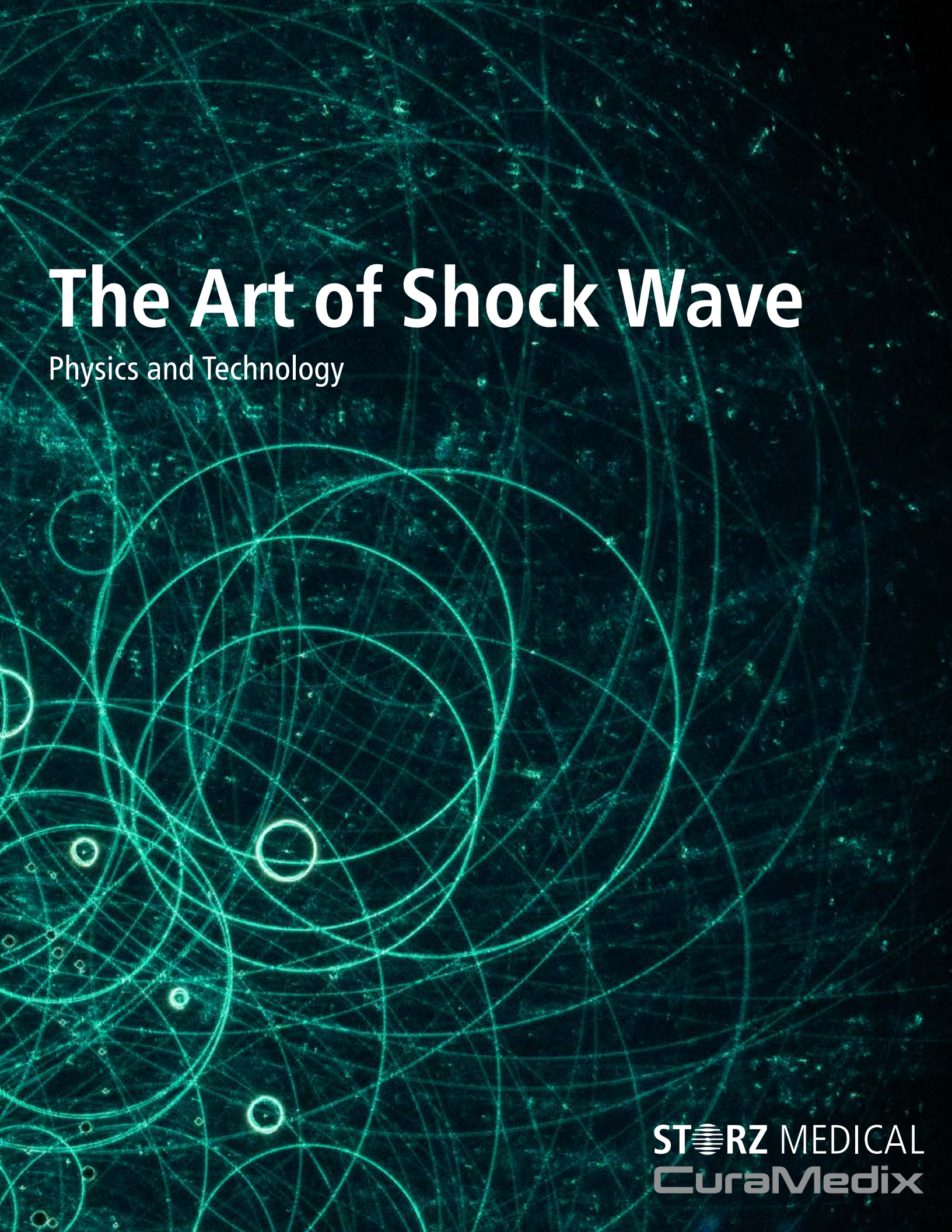

The Art of Shock Wave

Physics and Technology

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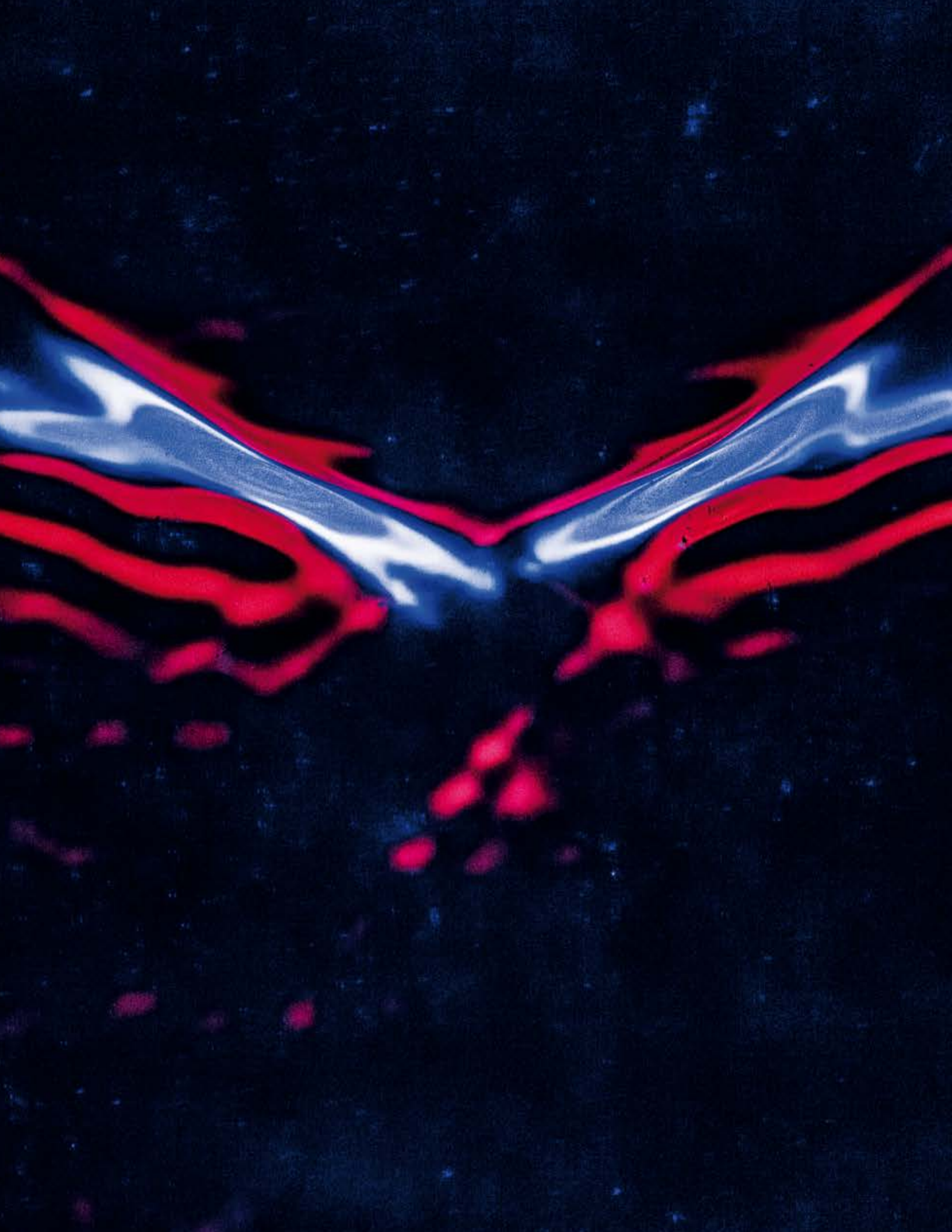


The Art of Shock Wave

Physics and Technology

Introduction

Today, extracorporeally generated shock waves and pressure waves are used in a wide range of medical disciplines.

The non-invasive procedure dates back to the 1960s when the idea emerged to generate shock waves extracorporeally and then transmit them into the body to disintegrate kidney stones and gallstones without damage to surrounding tissue passed by the acoustic waves on their way to the target area.

The first successful stone fragmentation in a human body[1,2,3] was performed by Professor Christian Chaussy, M.D., in Munich in February 1980. In the years since, the level of clinical evidence supporting the use of shock waves has significantly increased across a growing number of medical disciplines and applications such as the treatment of pseudarthrosis[4,5] or the dissolution of calcific deposits in the shoulder or at tendon insertions[7] with more than six million patient treated annually and growing.

Shock waves were first used on a human patient in early 1980 for the fragmentation of a kidney stone.

Focused shock waves vs radial pressure waves

Today, both focused shock waves and radial pressure waves are used successfully in the practice of medicine.

Focused shock waves and radial pressure waves differ not only with regard to their platform or method of generation, but also in terms of the physical parameters, penetration depths, and theraputic levels inside the body/tissue. Planar shock waves, also referred to as defocused shock waves, are based on a unique platform of focused shock wave. They propagate similarly to radial pressure waves with very little pain or discomfort and clinically have been shown to be as effective as focused shock waves.

The following summary provides important background information on the physical principles and technology of focused shock wave and radial pressure wave application and on the differences between them.

Focused shock waves

What are shock waves?

Focused shock waves are sound waves. They occur in the atmosphere during explosive events, for example during detonations or lightning strikes, or when airplanes break through the sound barrier. Shock waves are acoustic pulses characterized by high positive pressure amplitudes and a steep pressure increase compared to the ambient pressure. They are capable of temporarily transmitting energy from the point of generation to remote regions and can cause window panes to shatter.

Shock waves propagate explosively and may cause window panes to shatter at great distances.

Shock waves vs ultrasound

Although focused shock waves are similar to ultrasound, there are major differences. Focused shock waves have substantially higher pressure amplitudes, which means that steepening effects resulting from non-linearities in the propagation medium (water, human tissue) have to be taken into consideration. Another difference is that most ultrasound waves are periodic oscillations with narrow bandwidth (Fig. 1) whereas focused shock waves are characterized by a single, mostly positive pressure pulse followed by a comparatively small tensile wave component (negative pres-sure pulse) (Fig. 2). Such a pulse contains frequencies that may range from a few kilohertz to over 10 megahertz.[1,8,9]

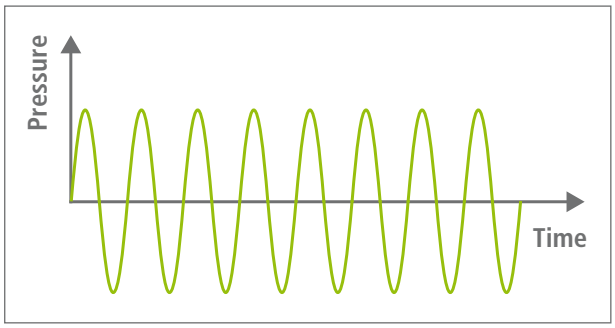


Fig. 1: Typical ultrasound signal

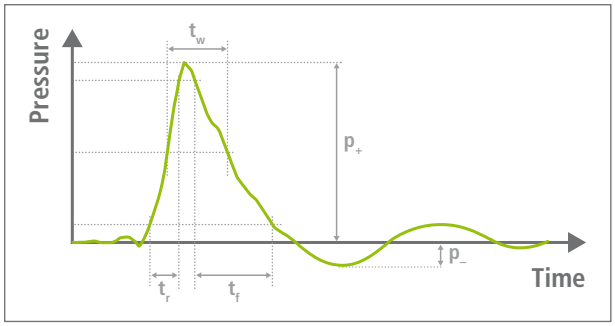


Fig. 2: Typical shock wave profile

Focused shock waves and radical pressure waves are acoustic pressure wave pulses, ultrasound waves are continuous oscillations.

Generation of focused shock waves

Focused shock waves can be generated by means of electro-hydraulic, electromagnetic, or piezoelectric platforms and/or shock wave generators (Fig. 3. Electrohydraulic systems produce shock waves directly at the source (also referred to as Spark-Gap). Piezoelectric and electromagnetic platforms on the other hand create focused shock waves as a result of wave steepening and superposition, which means that the wave only forms in the focal zone.

Focused shock waves produced with different types of technology platforms and generators have different sized focal zones which play a key role in medical applications. Focused shock waves generated with the piezoelectric principle or platform feature the smallest focus, while those produced with an electrohydraulic source have the largest focus. Subject to the technology platform utilized, the dosage requirements for a specific treatment will vary.[1,9]

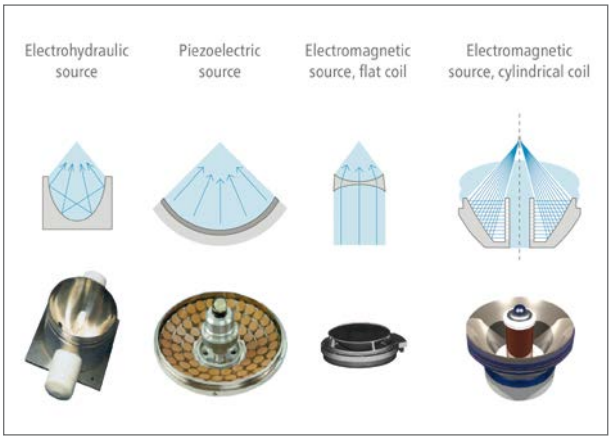


Fig. 3: Shock wave sources used in medicine[8]

Example: Electromagnetic focused shock wave generation

The method of electromagnetic shock wave generation is based on the physical principle of electromagnetic induction. As and example, this principle is also used in loudspeakers. Electromagnetic focused shock wave platforms and generators enable precise and gentle dosing of the applied acoustic wave energy, both axially (in depth) and laterally. Ideally, a cylindrical coil is used, focusing the shock waves by means of a rotation paraboloid. Due to the comparatively large aperture of the focused shock wave source relative to the focus size, the acoustic energy can be introduced into the body over a large coupling area, causing only minor discomfort to the patient. Most of the acoustic energy is only released in the relatively small focal zone inside the body (Fig. 4).

Fig. 4: Shock wave generation

Focused shock waves generated with an electromagnetic source cause minimal pain and can be precisely targeted dosed.

Propagation of focused shock waves (acoustic pressure waves)

Focused shock waves are acoustic pressure waves. They require a medium such as water or air for propagation. In general, medically used shock waves are generated in water outside the body and then transmitted to the biological tissue. As tissue mainly consists of water, it has similar sound transmission properties. These properties are described by the acoustic impedance (Z). As a consequence, transmission of the acoustic pressure waves to the body tissue takes place without any significant loss. The acoustic impedance is defined as follows:

$Z = \rho c$

where ρ= density and c = sound velocity

Acoustic interfaces at which the acoustic properties – i.e. density (ρ) and sound velocity (c) – change, give rise to phenomena such as refraction, reflection, scatter and diffraction, which cause the waves to deviate from the straight line of propagation. These effects must be taken into consideration when applying focused shock waves to the human body. The clinical outcome depends upon getting the correct amount of applied energy (dosage) to the target tissue (treatment zone.)

Shock waves, similarly to light, are reflected and refracted at acoustic interfaces. The greater the difference between the acoustic impedances of two media, the stronger this effect will be.

For this reason, the first device for kidney stone fragmentation required the patient to be submerged in a water-filled

tub. Today's devices work with so-called "dry" coupling, which means that the water bath is connected to the body via a flexible coupling membrane. Trapped air in between is eliminated with coupling gel or a thin water film.

> Trapped air or air bubbles between the shock wave source and the body significantly diminish the effectiveness of shock waves.

In addition to this, it is important that no gas-filled organs (lungs) or large bone structures are located on the shock wave propagation path. They would act as obstacles to the transmission of shock waves to the target area and thus inhibit the desired therapeutic effect. Moreover, the premature release of acoustic energy would cause damage to pulmonary tissue (contraindication).

Different types of soft tissue (skin, fat, muscles, tendons, etc.) have inhomogeneous acoustic properties and that they do have interfaces. However, the differences in the acoustic properties are significantly less pronounced than at the interfaces between water and air. In addition to absorption and reflection, refraction effects occur here which may lead to difficult-to-control deviations from the straight line of propagation of acoustic pressure waves inside the body.

Shock wave parameters/Shock wave measurement/Shock wave pressure

Measurements with pressure sensors are the preferred method to identify the characteristics of focused shock waves.[9] Shock waves used in medicine (Fig. 2) typically have p_+ peak pressures of about 10 to 100 megapascals (MPa), which is equivalent to about 100 to 1000 times the atmospheric pressure.

Depending on the shock wave platform or generator used, t_r rise times are very short at around 10 to 100 nanoseconds (ns). The t_w pulse duration is approx. 0.2 to 0.5 microseconds (µs) (and thus much shorter than that of the medical pressure waves described below; see Fig. 13). Another characteristic of focused shock waves is the relatively low p_- tensile wave component, which is around 10% of the p_+ peak pressure.

If the p_+ peak pressure values measured at various positions in the acoustic pressure wave field are plotted in a three-dimensional graph (coaxially to the focused shock wave propagation path and laterally, i.e. vertically, to this direction), the typical pressure distribution is as shown in the chart in Fig. 5. Obviously, the shock wave field does not have clear boundaries, but the shape of a mountain with a peak in the center and more or less steep slopes. This is referred to as three-dimensional pressure distribution model. The shape and height of this 3D pressure distribution model may differ, depending on which type of shock wave system is used.

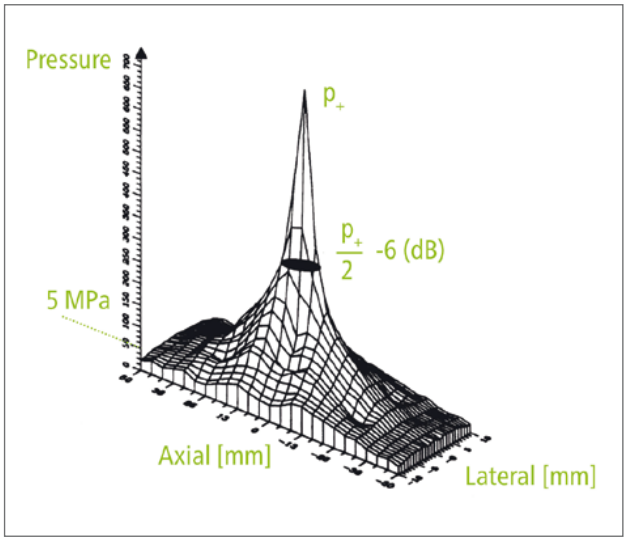
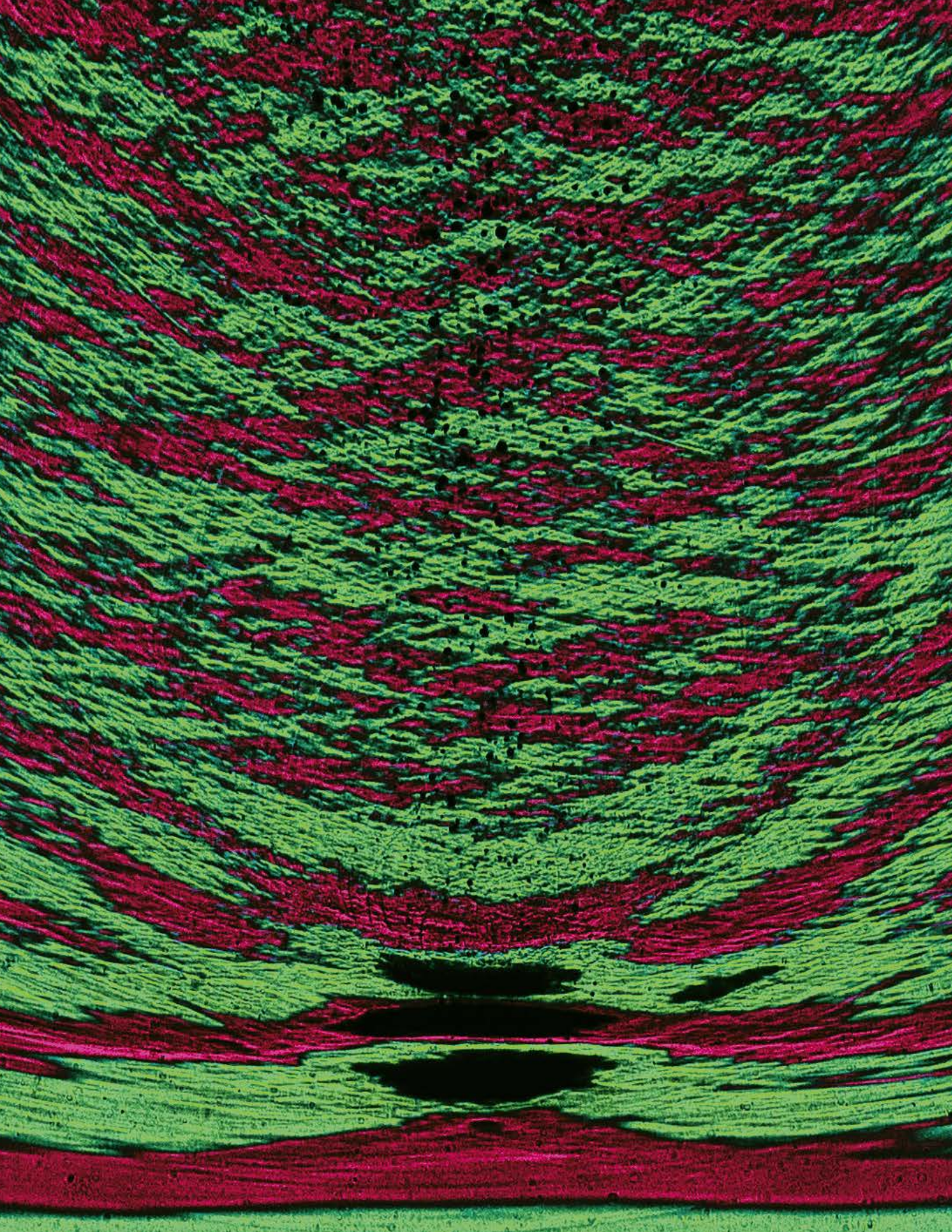


Fig. 5: Typical shock wave pressure distribution shown as a three-dimensional pressure plot[8]

Shock wave focus and focal area

The shock wave focus and focal area is defined as the area within the pressure distribution model in which the pressure is equal to or higher than 50% of the peak pressure (Figs. 5 and 6). This area is also referred to as -6dB focal zone or described using the acronym FWHM (Full Width at Half Maximum).



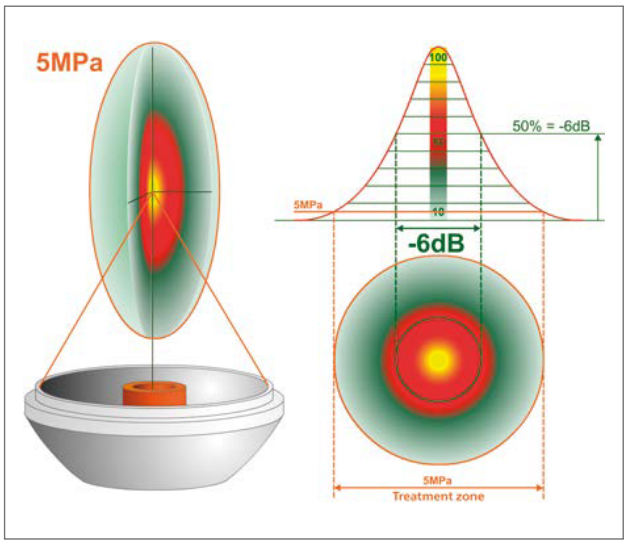


Fig. 6: Pressure distribution and focal zone[8]

5 MPa treatment zone

The area in which the shock wave produces biological effects can only be defined when taking into consideration the specific energy level. The shock wave treatment area inside the body is not identical with the size of the -6dB focal zone. It can be larger or smaller. Thus, an additional parameter has been defined, which is more closely related to the therapeutic effectiveness of shock waves and is not based on relative values (relationship to the peak pressure in the center), but on an absolute quantity, namely the 5 MPa pressure (50 bar). Consequently, the 5 MPa focus has been defined as the spatial zone in which the shock wave pressure is higher than or equal to 5 MPa. This parameter is based on the assumption that a certain pressure limit exists below which shock waves have no or only minimal therapeutic effectiveness.

The 5 MPa value is not supported by scientific evidence. However, the above definition also reflects changes in the treatment zone resulting from changes in the selected energy level. Different therapeutic zones and their changes with different energy levels are shown in schematic form in Fig. 7. Contrary to the treatment zone, the -6dB focal zone basically remains the same even if the energy settings change.

The focal zone is the area of maximum energy intensity. Its size is basically independent of the selected energy level. By contrast, the size of the treatment zone depends on the selected energy level and is generally larger than the focal zone.

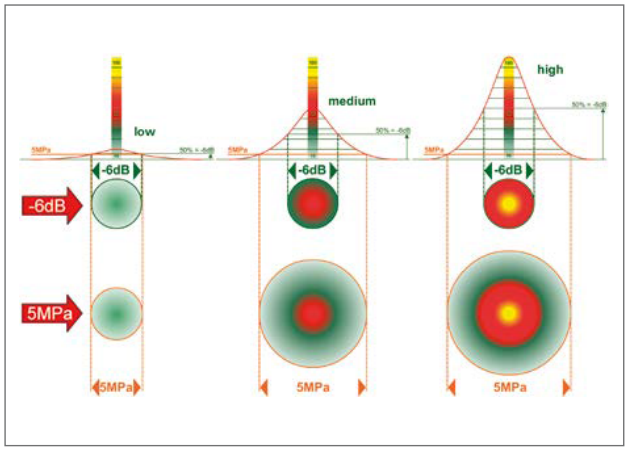


Fig. 7: -6dB focal zone and 5 MPa treatment zone at different energy settings

Energy (E)

The acoustic pressure energy is an important parameter[5] in clinical applications. It can be assumed that shock waves only have an effect on tissue when certain energy thresholds are exceeded. The energy is determined by integration from the time curve of the pressure wave p(t). It is proportional to the surface area (A) and inversely proportional to the acoustic impedance (Z):

$$E = \frac{A}{Z} \int p^2(t)dt$$

A distinction is made as to whether integrating the pressure over time only includes the positive pressure components (E_+) alone or whether it also covers the negative (tensile) components (E_{total}). The total energy is usually given with E (without index). The acoustic energy of a shock wave pulse is given in

millijoules (mJ). As a rule, several hundred or thousand shock wave pulses are applied per treatment session. This means that the total amount of energy applied is calculated by multiplication by the number of pulses.[1,9]

Energy flux density (ED)

The therapeutic effectiveness of shock waves depends on whether the acoustic energy is distributed over a large area or focused on a locally confined treatment zone (focal zone). A measure of the energy concentration is obtained by calculating the energy per area (E/A):

$$\textbf{ED (Energy flux density)} = \frac{E}{A} = \frac{1}{Z}\int p^2(t)dt$$

The energy flux density ED is given in millijoules per square millimetre (mJ/mm^2). Here again, one distinguishes between integration over the positive part of the pressure curve alone on the one hand and inclusion of the negative component on the other hand. If specified without index (ED), the pressure curve is usually considered to include the negative (tensile) component (total energy flux density).

The first focused shock wave systems were equipped with an electrohydraulic shock wave generator. Unlike today, the energy levels were not given in mJ/mm^2, but were specified as voltage values (kV). The following table lists typical voltage values (OssaTron) and their mJ/mm^2 equivalents.

Energy level specification			
Voltage (kV)	14	24	28
Energy flux density (mJ/mm^2)	0.18	0.30	0.40

Physical effects of focused shock waves

Direct effects on interfaces

The characteristics of shock waves and ultrasound waves are different. Ultrasound exerts a high-frequency alternating load on the tissue in the frequency range of several megahertz, which leads to heating, tissue tears and cavitation at high amplitudes.[10,11] The effect of focused shock waves is determined, among other factors, by a forward-directed dynamic effect (in the direction of acoustic pressure wave propagation), which causes a pulse to be transmitted to the interface. This dynamic effect can be increased to such an extent that even kidney stones can be destroyed.[2,3] In general, these dynamic effects occur at interfaces characterized by discontinuities in the acoustic impedance, but hardly ever in homogeneous media (tissue, water).[12] As a result, shock waves are the ideal means for creating effects in deep tissue without interfering with the tissue located along the propagation path.

Fig. 8: Effect of a focused shock wave on an artificial stone

However, even less distinct interfaces within soft tissue structures experience a minor dynamic effect from the application of focused shock waves. Depending on the acoustic pressure wave intensity (Fig. 9), mechanical destruction of cells, membranes and bone tra-beculae[12], for example, as well as cellular stimulation through reversible deformation of the cell membrane[13] may occur. The results that can be achieved in this manner are the destruction of brittle structures (kidney stones) on the one hand and the irritation and stimulation of tissue structures with consequential healing processes on the other hand. This phenomenon is evident in orthopaedic applications. Focusing shock waves allows the desired effect to be confined to the target area, so that side effects outside the treatment zone can be reduced or even completely avoided.

Shock wave focusing enables targeted treatment of a confined area.

In most cases, shock wave treatment results in increased blood circulation and enhanced metabolic activity, leading to the onset of the healing process.

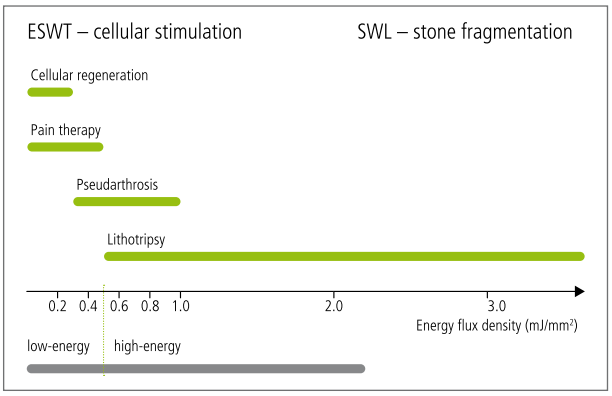


Fig. 9: Typical fields of application of shock waves in medicine and relative energy levels

Indirect effects – cavitation

In addition to the direct dynamic effect of shock waves on interfaces, a phenomenon referred to as cavitation[10] occurs in specific media such as water and, to a certain extent, tissue.

Cavitation bubbles occur directly after the pressure/tension alternating load of the shock waves has passed the medium. The majority of the bubbles grow for about 100 microseconds after the waves have passed and then violently collapse while emitting secondary spherical shock waves. When close to interfaces, cavitation bubbles can no longer collapse without being disturbed. The medium flowing back into the bubble (water, body fluid) can no longer flow unhindered. Therefore, the bubble collapses asymmetrically while developing a microjet.[14] This microjet is directed at the interface at a velocity of several hundred meters per second (Fig. 10).

The microjets contain a high amount of energy and penetration power so that they can erode the hard interfaces of stones. As the acoustic pressure waves pass through medium, gas dissolved in the blood or tissue is released and forms bubbles. This phenomenon is referred to as soft cavitation. The cavitation bubbles formed in this manner may tear open blood vessels and cells. This causes micro-bleeding or membrane perforation. Cavitation is not limited to the focal zone alone, but it is especially pronounced there.[1,9,15]

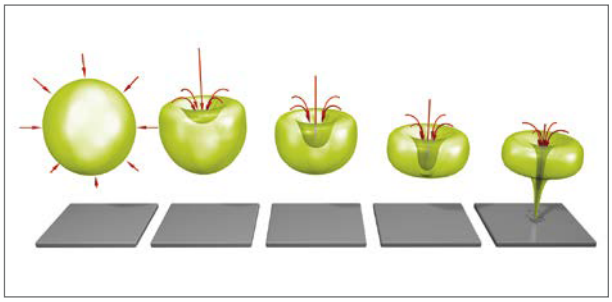


Fig. 10: Microjet formation by cavitation bubble collapse[1,9]

Biological effects of shock waves

Shock waves also induce a variety of biological reactions resulting from the shear and pressure forces they produce. This mechanism of action is referred to as mechanotransduction. The following effects have been investigated and confirmed in scientific studies:

- Increase in cell permeability[16]
- Stimulation of microcirculation (blood, lymph)[17,18]
- Release of substance P[19]
- Reduction of non-myelinated nerve fibers[20]
- Release of nitric oxide (NO), which leads to vasodilation, increased metabolic activity and angiogenesis and has an anti-inflammatory effect[21,22]
- Antibacterial effect[23]
- Release of growth hormones (blood vessels, epithelium, bones, collagen, etc.)[21,24,25,26]
- Stimulation of stem cells[27,28]

Targeted application of focused shock waves

The targeted application of shock waves requires that the focal zone of the shock wave system be directed at the treatment area within the body. When treating stones (lithotripsy), bones and specific tissue structures, X-ray or ultrasound systems can be used for this purpose. In the treatment of musculosckeletal pain, biofeedback and effective communication with the patient are necessary to identify the points of maximum pain and helps to localize both superficial and deep sited treatment points.

Radial pressure waves

What are radial pressure waves?

In addition to focused shock waves, modern medicine also uses radial pressure waves. Physicist Sir Isaac Newton established his famous law of "action and reaction" as early as in 1687. The method of action of a ballistic pressure wave system is based exactly on the linear impulse-momentum principle deduced from Newton's law. Mechanical energy in the form of an acoustic pressure wave is transmitted to the body tissue and, consequently, to the painful area by means of specially shaped transmitters. Introduced in the late 1990s, ballistically generated radial pressure waves are a lower-cost alternative to shock waves, especially in the treatment of musculoskeletal disorders.

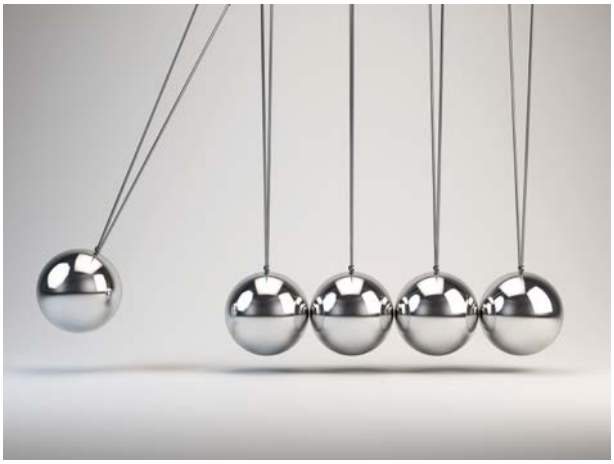


Fig. 11: Newton's cradle

Radial shock waves, also referred to as "radial pressure waves," have been clinically proven for many indications with treatment results similar to focused shock waves.[29]

Radial shock wave treatment is based on the law of "action and reaction" established by physicist Sir Isaac Newton in 1687.

In physical terms, however, focused shock waves and radial pressure waves are different. The pulse length of radial pressure waves is much longer than that of focused shock waves. Radial pressure waves have wavelengths of between 0.15 and 1.5 m. By contrast, the wavelength of a focused shock waves is only about 1.5 mm. This explains why focused shock waves, unlike pressure waves, can be focused.[30]

In practice, radial pressure waves are commonly referred to as radial shock waves.

Extracorporeal Pulse Activation Technology (EPAT) refers to our proprietary acoustic pressure wave (shock wave) technology platforms and device portfolio to better differentiate and explain different modes of action.

The term EPAT is used to differentiate our proprietary technology platforms and unique device portfolio as well as to avoid the generic reference to shock waves.

Although there are significant differences between device manufacturers and technology platforms, in global/ international markets, the technology is commonly referred to as Extracorporeal Shock Wave Therapy (ESWT), Radial Shock Wave Therapy (RSWT), Extracorporeal Shock Wave Lithotripsy (ESWL), Low-Intensity Shock Wave Treatment (LIESWT), Extracorporeal Cardiac Shock Wave Therapy (ECSWT), Acoustc Wave Therapy (AWT) subject to the area of medicine.

Generation of radial pressure waves

Radial pressure waves are generated by the collision of solid bodies (Fig. 12). First of all, a projectile is accelerated, e.g. with com-pressed air (similar to an air gun), to a speed of several meters per second (approx. 5 to 25 m/s, far below the sound velocity in water of about 1500 m/s) and then abruptly slowed down by hitting an impact body (transmitter). The elastically suspended impact body is brought into direct contact with the patient's skin above the area to be treated, preferably using ultrasound coupling gel. When the projectile strikes the impact body, some of its kinetic energy is transmitted to the impact body. The impact body then performs a translational movement over a short distance (typically < 1 mm) at slower speed (typically < 1 m/s) until the coupled tissue or the handpiece decelerates the impact body movement. The motion of the impact body is transmitted to the tissue at the point of contact, from where it propagates divergently in the form of a "radial" pressure wave.

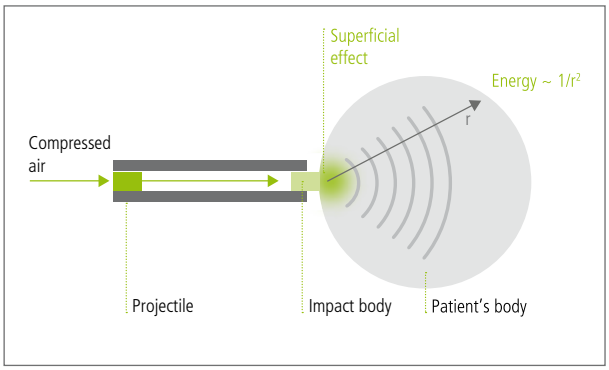


Fig. 12: Formation of pneumatically generated ballistic acoustic pressure waves and their super-ficial effects

The time duration of the pressure pulse (Fig. 13) is determined by the translational movement of the impact body and is typically about 0.2 to 5 milliseconds (ms) in tissue. This means that the radial pressure wave pulses applied to the tissue are longer by a factor of 1000 than those of focused shock waves. Typical peak pressures of radial pressure waves are about 0.1 to 1 MPa, i.e. significantly lower – by a factor of 100 – than those of focused shock waves.[1,9]

The collision of the projectile with the impact body also generates a higher-frequency acoustic wave (solid-borne sound) in the impact body. Owing to the great difference between the

two acoustic impedances (metal, water), only a minimal portion (about 10%) of this oscillation energy is transmitted to the tissue or water. The energy contained in the high-frequency acoustic oscillation is significantly smaller than the energy of the low-frequency pressure pulse described above.[31]

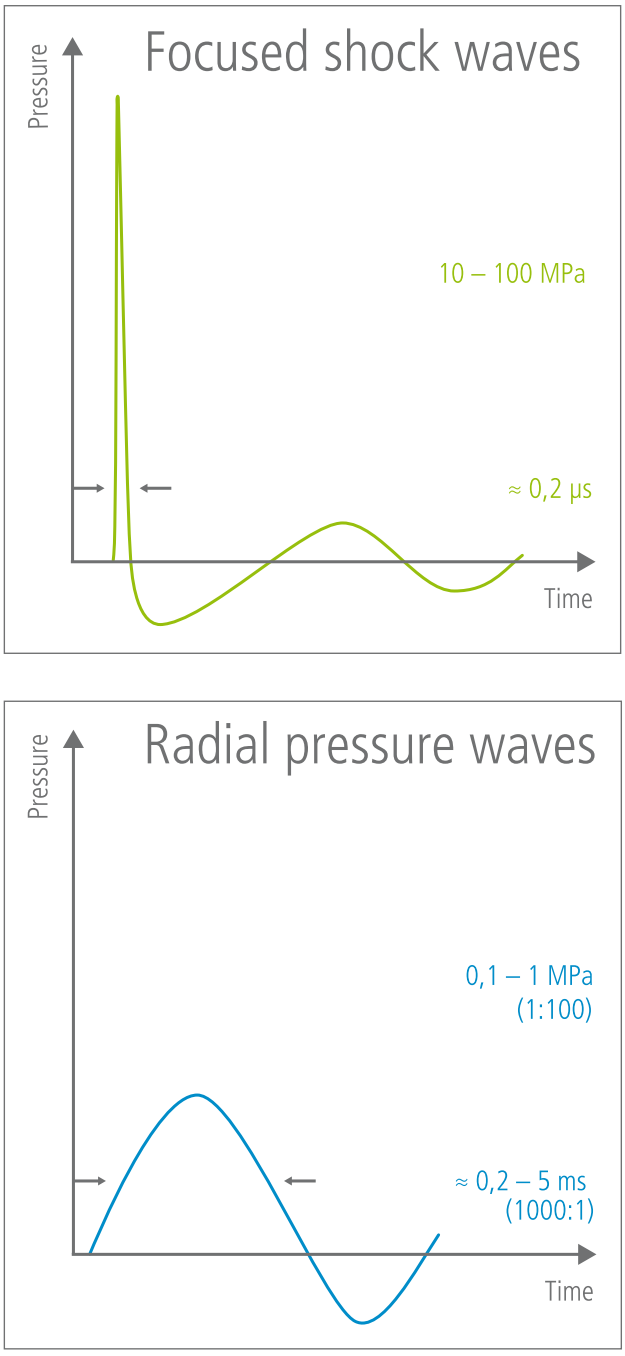


Fig. 13: Typical parameters of focused shock waves and radial pressure waves

Propagation of radial pressure waves

Radial pressure waves as described here originate from the application point of the impact body and travel radially into the adja-cent tissue.[30] The energy density of the induced pressure wave rapidly drops with increasing distance from the application point (by a proportion of $1/r^2$). This means that the strongest effect is at the application point of the impact body, that is at the skin surface (Fig. 14).

The therapeutic effectiveness of radial acoustic pressure waves reaches a depth of 3 to 6 cm, but it is strongest at the skin surface.

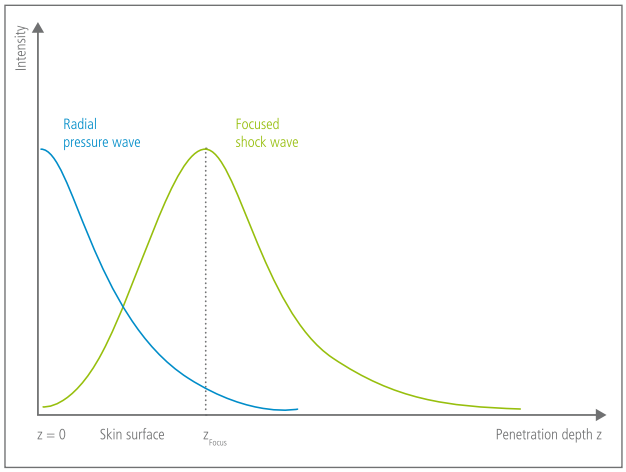


Fig. 14: Differences in intensity of focused shock waves and radial pressure waves in the human body

Radial pressure wave parameters/ Radial pressure wave measurement

Due to the significantly longer pulse duration and low pressure amplitude of radial acoustic pressure waves compared to focused shock waves, pressure measurements in water as commonly performed for shock waves would not provide conclusive results. More accurate information can be obtained by measuring the excursion of the impact body (Fig. 15) and the force transmitted to a viscoelastic tissue phantom. However, since these parameters strongly depend on the type of impact body (transmitter) used,

the intensity parameter commonly quoted is the pressure that drives and accelerates the projectile.

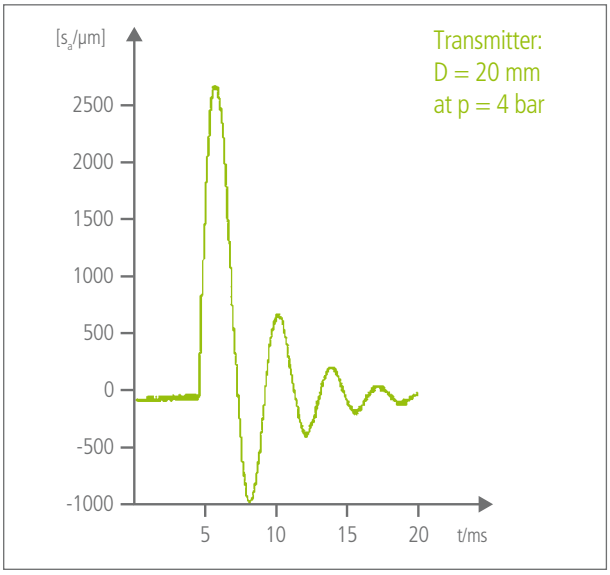


Fig. 15: Excursion of a D20S transmitter in air at a 4 bar driving pressure

Physical and biological effects of pressure waves

Radial pressure waves generate oscillations in tissue which lead to improved microcirculation and increased metabolic activity.[32]

Focused shock waves vs radial pressure waves

Focused shock waves and radial pressure waves differ not only with regard to their physical properties and mode of generation, but also in terms of the magnitude of the standard parameters used and the therapeutic tissue penetration depths achieved. The main differences are summarized in Fig. 16.

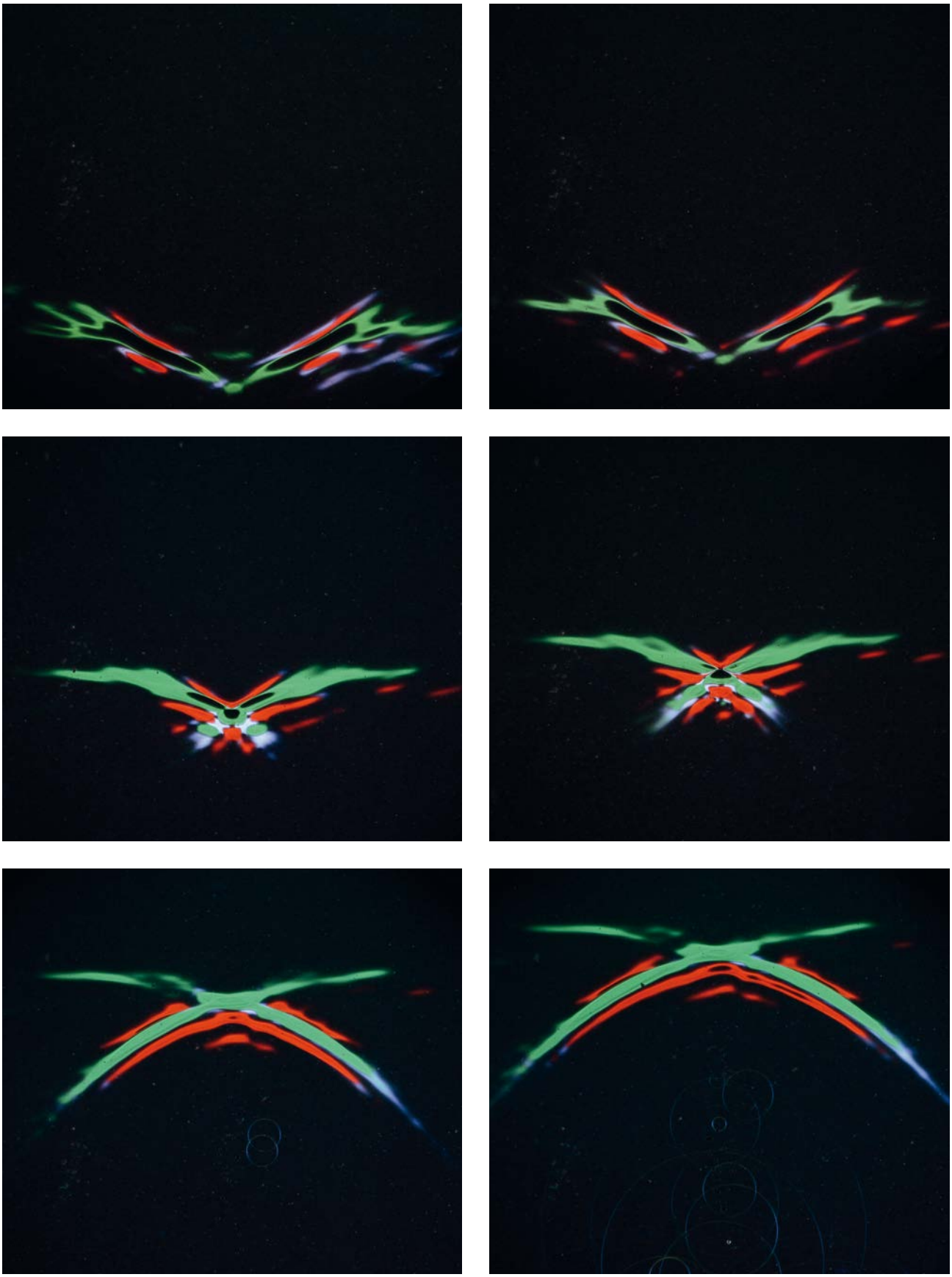
Interestingly, despite the physical differences and the resulting different application areas (superficial or deep target areas), the stimulation effects and therapeutic mechanisms seem to present certain similarities. Radial pressure waves are ideal for the treatment of superficial pain, for example.

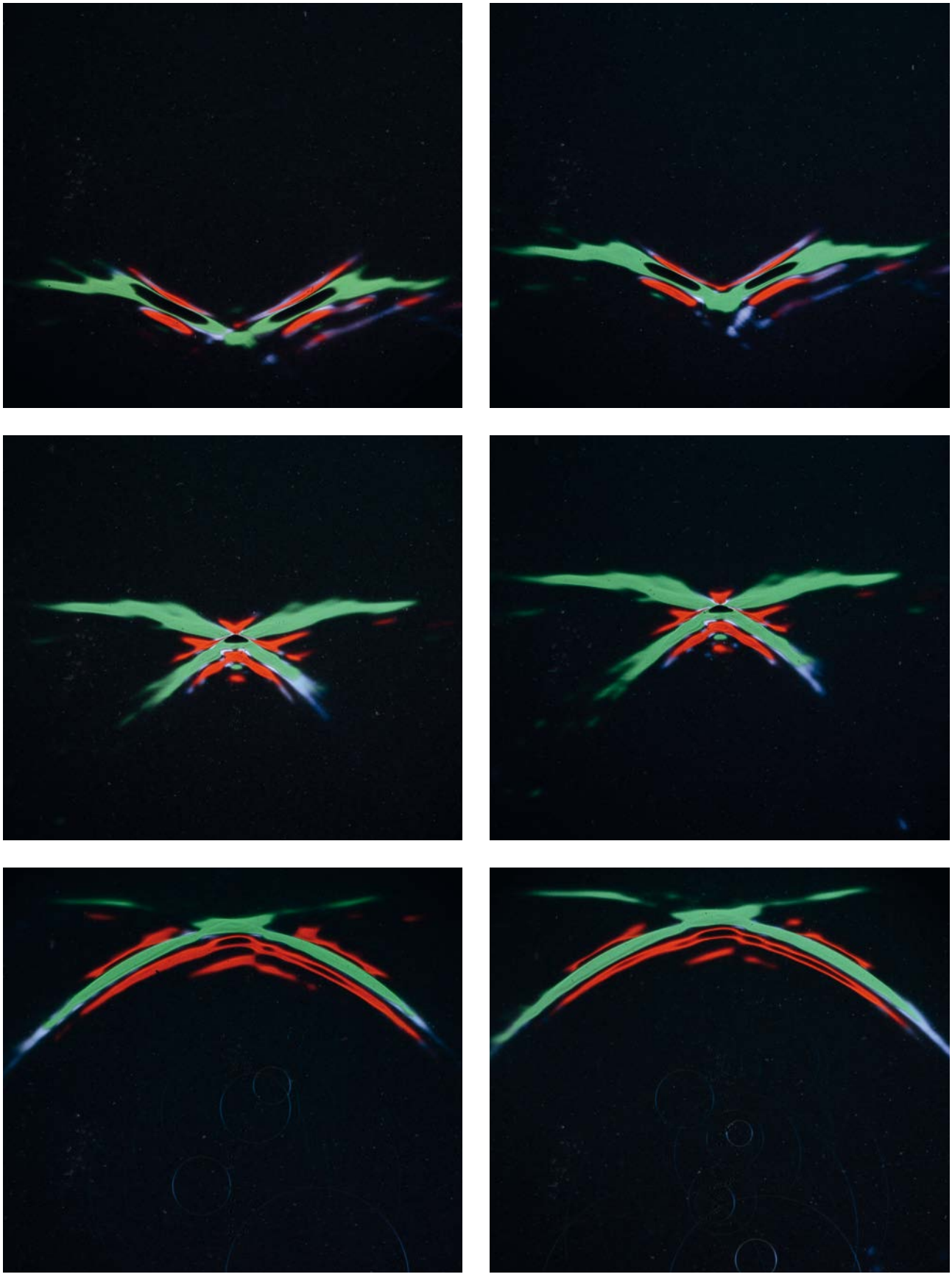
In the treatment of myofascial pain syndromes, radial pressure waves are indispensable for smoothing muscles and/or fascia before or after focused shock wave application. Local painful spots, chronic enthesopathies and deep trigger points are ideally treated with focused shock waves.[33] "Planar," or defocused shock waves, are preferably used in the treatment of trigger points, wound healing and aesthetic indications.[34]

Focused shock waves		**Radial pressure waves**
10 – 100 MPa	**Pressure**	0.1 – 1 MPa
≈ 0.2 µs	**Pulse duration**	≈ 0.2 – 5 ms
0.5 – 2 mNs	**Impact**	100 – 200 mNs
20 – 35 mJ	**Energy**	150 – 200 mJ
100 – 150 MPa/mm	**Pressure gradient**	0.1 – 0.5 kPa/mm
Focused	**Pressure field**	Radial, divergent
Large, up to 200 mm	**Penetration depth**	Small, superficial, up to 50 mm
Cells	**Effects**	Tissue

Fig. 16: Main differences between focused shock waves and radial pressure waves

Propagation of focused shock waves





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