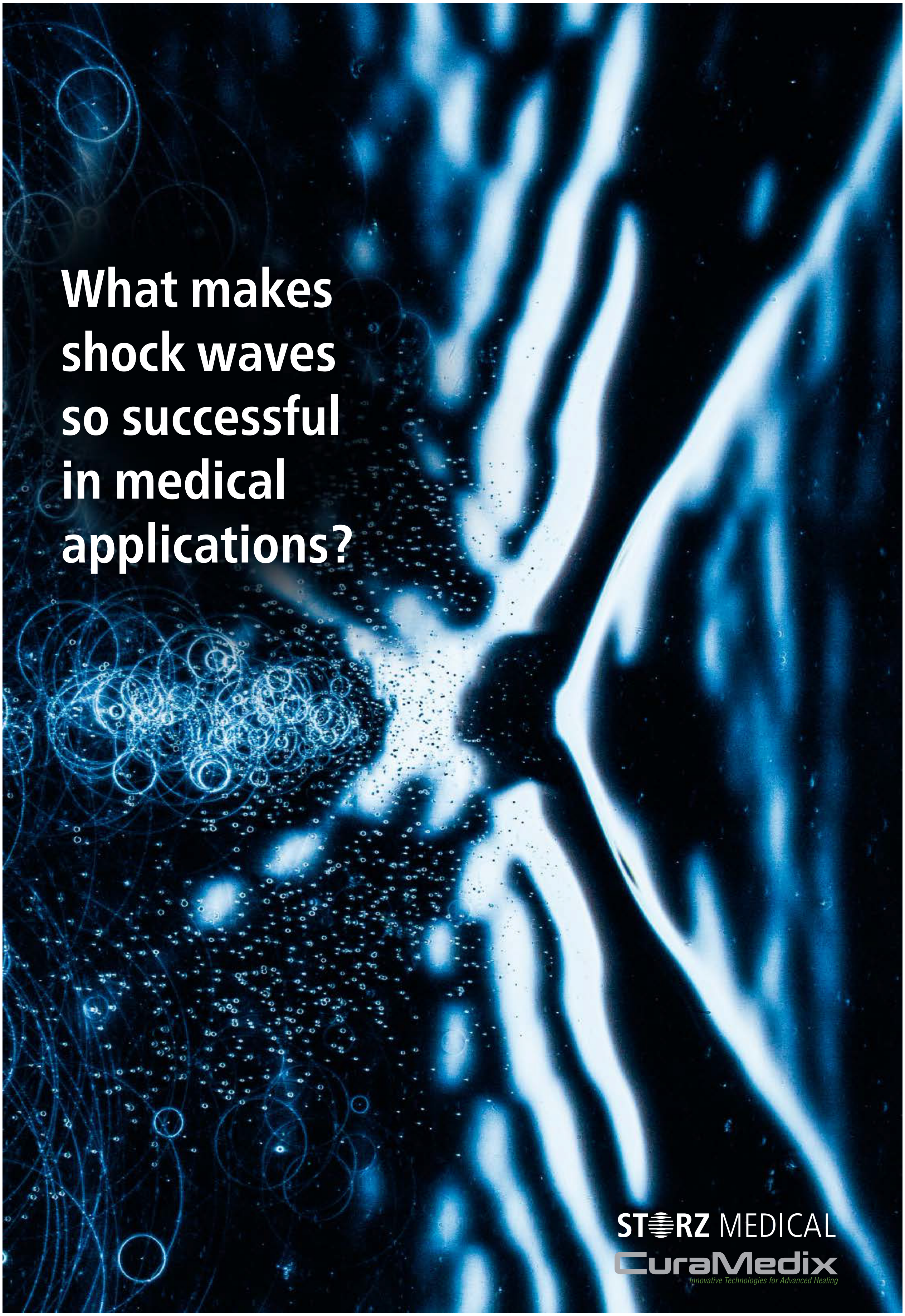
What makes shock waves so successful in medical applications?



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Introduction

Shock waves have been an integral part of the spectrum of medical therapies in many specialist fields since as long ago as 1980. The introduction of extracorporeal shock wave lithotripsy (SWL) marked the first time that shock waves were successfully used for the non-invasive fragmentation of kidney stones. A specific property of shock waves proved especially beneficial here, namely the transmission into the human body of sufficient energy to disintegrate the calculus without damaging the tissue anterior to the stone. This obviated the need for an open access route to the kidney stone, thus virtually ruling out potential complications associated with surgery. The procedure rapidly gained acceptance due to its obvious advantages. It can be used for almost all known calculi although it has not become widely established for certain indications (e.g. problems with passage of gallstone fragments from the gallbladder). Despite the substantial amount of energy required to fragment kidney stones, side effects are rare (although not entirely eliminated). They are, as a rule, considerably reduced compared with those of open surgical procedures. Low-impact transmission of energy, and the selective and focused effectiveness at the target structure are, therefore, crucial and highly beneficial properties of shock waves.

Overview of medical applications

Owing to the highly successful use of shock waves to treat a wide range of calculi, it seemed likely this technique could be extended to the fragmentation of calcified deposits in body tissue. However, as calcified deposits in elastic tissue tend to be soft in consistency, they cannot be broken down into small fragments. The surprising outcome of these attempts was improved blood circulation in many cases following shock wave application, resulting in intensified metabolism, induction of healing processes, pain reduction and, indirectly, the breakdown of calcified deposits as well. This stimulating effect of shock waves – combined with their ability to improve blood circulation, stimulate nerves and ease tensed muscles, and to release trigger points and vascular spasms – means that the breadth of applications for shock wave therapy is now regarded as virtually limitless. The number of known indications is continually growing and, due to the properties of shock waves discussed above, these extend well beyond the original application in the field of stone fragmentation.

Today, fields of application as diverse as orthopaedics, cardiology, dermatology, pain therapy, traumatology and neurology are already well established or at a promising stage of evaluation.[4-7, 17-29, 32-34]

How shock waves differ from ultrasound

Like ultrasound, shock waves are mechanical waves generated by compression and subsequent relaxation of matter. Compression of the particles involved propagates as a pressure wave within the medium at the material-dependent sound velocity. Whereas ultrasound is essentially a continuous wave with frequent oscillations chiefly in the megahertz range (Fig. 1), shock waves have a different distinguishing characteristic, namely a single pressure pulse lasting about 1 microsecond followed by a tensile wave with a relieving effect that is of lower amplitude and has a duration of about 4 – 5 microseconds (Fig. 2).

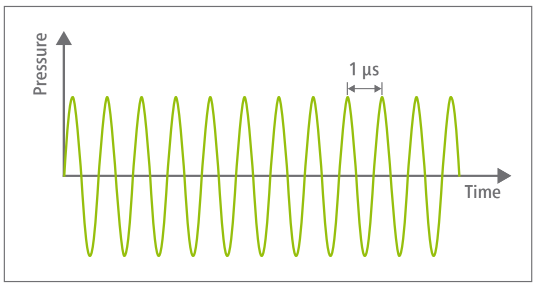

Fig. 1: Ultrasound wave profile over time

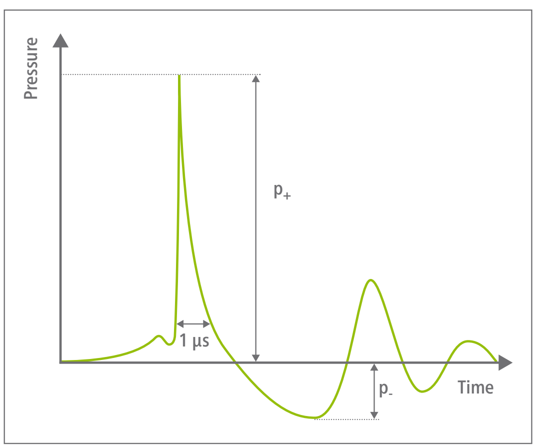

Fig. 2: Shock wave profile over time

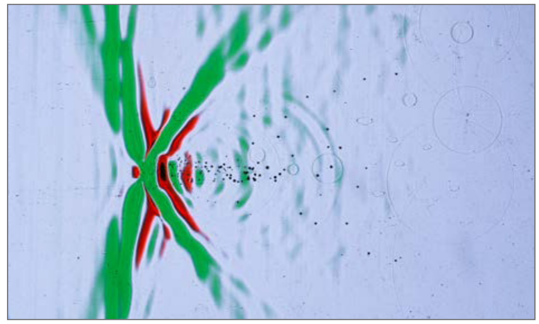

Fig. 3: Shock wave focal zone: the pressure increase is shown in red and the pressure decrease in green. Small cavitation bubbles form during the negative-pressure phase; these grow, then collapse while emitting secondary spherical shock waves.

In ultrasound, the mainly periodic oscillations constitute a high-frequency alternating load exerted on the tissue. These oscillations lose part of their energy due to absorption by tissue, and cause an increase in temperature. Accordingly, procedures such as the high-intensity focused ultrasound (HIFU) technique can be used to heat spatially confined tissue regions, resulting in coagulation. Significant tissue heating is, however, not observed in medical applications of shock waves.

Propagation of focused shock waves

Shock waves are acoustic 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 very similar sound transmission properties. These properties are described by the acoustic impedance (Z). As a consequence, shock waves are transmitted to the biological tissue without any significant loss. 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 familiar from the field of optics such as refraction, reflection, scatter and diffraction, causing the waves to deviate from the straight line of propagation. These effects must be taken into consideration when applying shock waves to the human body. This is crucial to ensure that the applied energy is effective in the treatment zone.

For this reason, the first device for kidney stone fragmentation required the patient to be submerged in a water-filled tub. Today's systems involve "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.

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 release of shock wave energy at gas-filled organs would cause damage to the tissue (contraindication).

We also need to assume that 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 considerably 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 shock waves inside the body.

Shock wave parameters / Shock wave measurement / Shock wave pressure

Measurements with pressure sensors are the preferred method of identifying the characteristics of shock waves. 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 generation method used, rise times are very short at around 10 to 100 nanoseconds (ns). The pulse duration is very short, too, at approx. 0.2 to 1 microseconds (µs). Another characteristic of shock waves is the relatively low tensile wave component p-, which is around 10% of the peak pressure p+.

If the p+ peak pressure values measured at various positions in the shock wave field are plotted in a three-dimensional graph (coaxially to the shock wave propagation path and laterally, i.e. vertically, to this direction), the typical pressure distribution obtained is as shown in the chart in Fig. 4. Obviously, the shock wave field does not have clear boundaries, but the shape of a mountain with a peak in the centre and more or less steep slopes. This is referred to as the three-dimensional pressure distribution model. The shape and height of this model may differ, depending on which type of shock wave system is used.

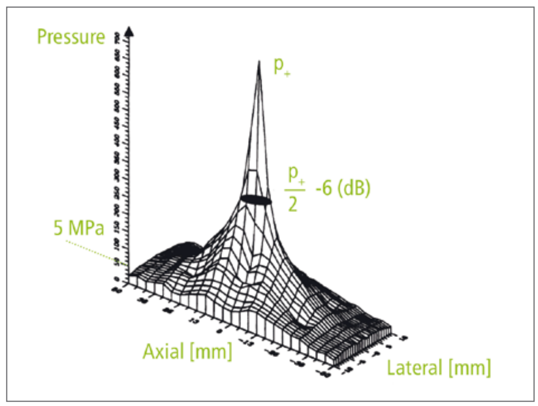

Fig. 4: Typical shock wave pressure distribution shown as a three-dimensional pressure8

Shock wave focus

The shock wave focus is defined as the area within the mountain-like pressure distribution in which the pressure is equal to or higher than 50% of the peak pressure (Figs. 4 and 5). This area is also referred to as the -6dB focal zone or described using the acronym FWHM (full width at half maximum).

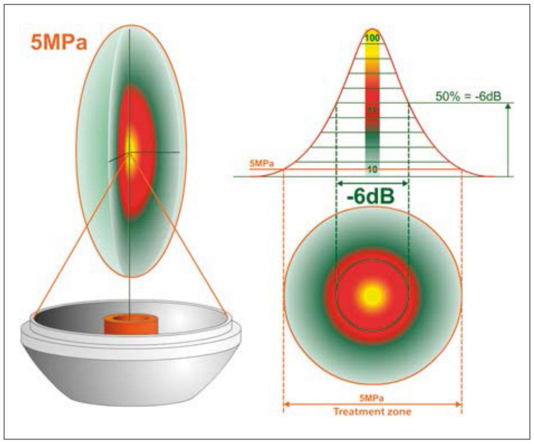

Fig. 5: 5 MPa therapy zone

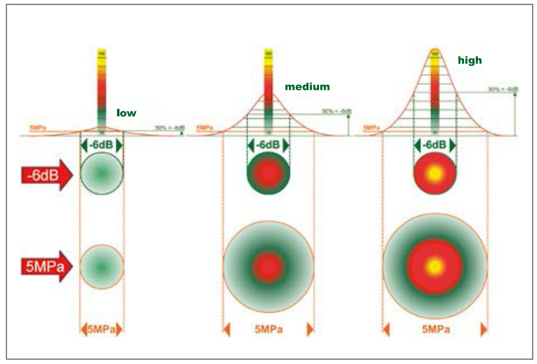

Fig. 6: -6dB focal zone and 5 MPa treatment zone at different energy settings

The area in which the shock wave produces its biological effects can only be gauged when taking into consideration the specific energy level. In other words: 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. This is why an additional parameter has been defined, which is more closely related to the therapeutic effectiveness of shock waves and which is not based on the variable peak pressure, 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 definition 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 therapy zones and their changes with different energy levels are shown in schematic form in Fig. 6. In contrast to the treatment zone, the size of the -6dB focal zone remains nearly 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.

Energy (E)

The shock wave energy is an important parameter5 in medical shock wave application even if, today, greater importance is given to the energy flux density. 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):

$$E = \frac{A}{Z} \int P^2 (t)\, td$$

A distinction is made as to whether integrating the pressure over time only includes the positive pressure (E+) alone or whether it also covers the negative (tensile) components (Etotal). The total energy is usually stated as E (without index). Acoustic energy is obtained by multiplying by the number of pulses.

Energy (E)

The therapeutic effectiveness of shock waves depends on whether the shock wave 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):

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

The energy flux density ED is given in millijoules per square millimetre (mJ/mm2). Here again, a distinction is made between (on the one hand) integration over the positive part of the pressure curve alone and (on the other) inclusion of the negative component. If specified without index (ED), the pressure curve is usually considered to include the negative (tensile) component (total energy flux density).[8-16, 30-31]

Fig. 7: Effect of a focused shock wave on an artificial stone

Momentum

A fact that has received little attention thus far is that shock waves have momentum. As with its energy, a shock wave's momentum is defined in terms of the integration of pressure over time. Unlike a shock wave's energy, however, its momentum is not squared prior to being integrated. Its sign is thus retained and the momentum's vectorial nature means there is both momentum due to the positive pressure component in the shock wave's direction of propagation, and lesser momentum in the backwards direction generated by the negative tensile wave component. The asymmetrical pulse form of the shock wave ensures that both successive momentums cannot compensate for each other, and a reciprocal effect with high pressure and low tension is generated. This is not the case with continuous ultrasound: here the alternating tension and pressure phases largely cancel each other out, so that the resulting momentum is relatively small in magnitude.

$$\text{Momentum } P = A\int p(t)dt$$

$$\text{Momentum density } \frac{P}{A} = \int p(t)dt$$

Shock wave momentum is of crucial importance both for highenergy stone fragmentation and for the low-energy medicobiological stimulating effect.[35]

Mechanism of action for a wide range of medical conditions

Shock waves are employed today in many areas of medicine: for muscular and vascular spasms, for releasing trigger points, for angina pectoris, for pseudarthrosis, for chronic soft-tissue pain, for dermatological skin improvement, for wound healing and for Alzheimer's. If these multidisciplinary applications are considered along with the effect of shock waves on pain memory, the question arises as to the underlying mechanism of action across all these indications.[34]

Since they are mechanical waves, shock waves can in the first instance be expected to give rise only to physical effects suchas pressure and forces – effects that are largely independent of any specific indication. As a second step these parameters may, however, exert an influence on physiological processes by means of interaction with tissue.

A potential mechanism of action is outlined below, based on experience gained to date with shock waves.

Effect on tissue

As already mentioned, shock waves can pass through homogeneous soft tissue masses without major changes, absorption or damage. This is, to a certain extent, also the case at high energy levels such as are generated within the focal zone of a shock wave. Why and how shock waves nevertheless interact with tissue is a question that we wish to explore here from a new perspective. Whereas previously the especially high pressure levels (measured in megapascals, MPa) or the very short rise times (expressed in nanoseconds, ns) were the parameters to which the effectiveness of shock waves was attributed, the parameters generally regarded as crucial today are energy (millijoules, mJ) and derived quantities such as energy flux density (mJ/mm2). However, energy itself does not suffice as a measure of an effect; for this purpose it must be converted into work, i.e. the product of a force and its displacement (force x displacement = work = energy), as is taught in physics classes. The crucial factor, therefore, is the manner in which sufficient force is generated from the available shock wave energy – force that can be effective in the desired tissue regions.

It is here that the momentum as a specific property of shock waves comes into its own – a property that has received little attention thus far in relation to medical shock wave applications.[35]

Momentum transfer

The pressure profile of a shock wave shows a strong, short pressure pulse (≈ 1 microsecond) followed by somewhat weaker negative pressure (tensile component ≈ 4 – 5 microseconds). The asymmetrical shape of the pulse gives the shock wave physical momentum that is strongly forward-directed, followed by weaker momentum that is backwards-directed (Fig. 8). This is of great importance for the effect of shock waves on biological tissue.

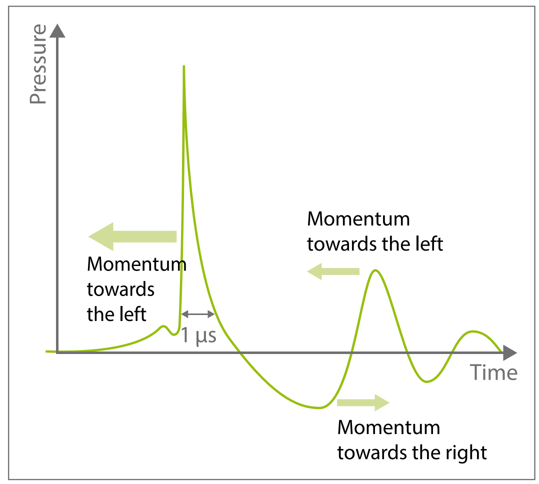

Fig. 8: Pressure profile of a shock wave

At acoustic interfaces, such as those between organs, which bridge different tissue density and/or sound velocities, part of the shock wave is reflected. This means that the momentum of the incident shock wave is split into two components: one whose propagation maintains the previous direction, and one that is reflected backwards in the opposite direction. The change in incident momentum is directly equivalent to the force exerted at the interface. These physical processes were described as long ago as the 17th century in the foundational works of Isaac Newton, who devised the equations $F = ma$ and $F = m\, dv/dt$ in his writings on the principles of mechanics. Momentum transfer, which is related to change in momentum, occurs within a very brief period of exposure: about 1 microsecond (µs), i.e. the duration of a shock wave's positive pressure pulse. On the basis of mass and inertia, the interface – even after the brief application of force – moves somewhat from its rest position until the rate of deflection is slowed down by deformation of the adjacent tissue. These processes occur within the millisecond (ms) range, making them considerably slower than the excitation force of shock waves (µs).

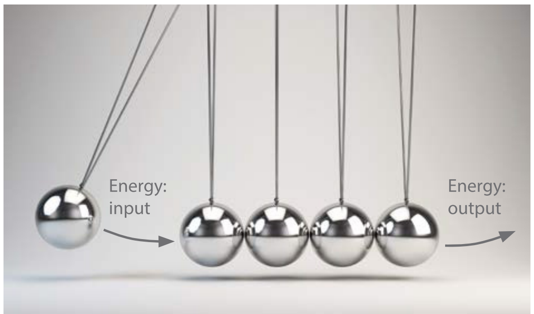

Fig. 9: Newton's cradle – the momentum of the sphere on the left is transferred to those on the right

The underlying mechanical process can be illustrated with reference to a tennis or golf ball which, through a brief strong impact (i.e. being struck by the racket or club) gathers speed and then undergoes free motion until it is slowed down by the frictional drag of air resistance and by other forces.

As the forces generated are only of extremely short duration (1 microsecond), data on movement obtained using test specimens can be used to calculate forces of several hundred newtons (N) and accelerations of 10,000 g, i.e. ten thousand times as strong as gravitational acceleration.

The outcome is local extension and distortion of the affected interface for the duration of a few milliseconds. Whereas a pulse lasting about 1 microsecond (µs) is too short to stimulate most physiological processes, the duration of the mechanical distortion of the interface is orders of magnitude greater (ms).

It is these very durations within which cell membranes can be electrically and mechanically stimulated and their pores open to exchange various ions. In particular, nerve cells can be stimulated to transmit action potentials via brief mechanical pulses (ms). It is this property that considerably distinguishes shock waves from ultrasound; the latter exhibits similar effects only when it is pulsed, and even thento a far lesser extent. The mechanism of momentum transfer by means of focused shock waves has a further advantage, namely that the short duration (i.e. a microsecond) of the original pulse, which corresponds to a spatial pulse length in tissue of around 1.5 mm, allows focusing on a target only a few millimetres in extent (see Fig. 5, focal size). The physiologically effective longer pulses of about one millisecond are not focusable when working within the human body, the pulse length being one thousand times greater at around 1.5 m. The focusing of the primary shock wave thus creates scope for carrying out specific treatment at deeper tissue layers, using the required energy densities and medically effective pulse shapes. The surrounding tissue serves as a medium for transmitting shock waves, but the lower energy densities outside the focal area mean the tissue is protected.

Shock waves thus have a number of special properties that enable therapeutically effective forces to be exerted on localized tissue regions, and that enable the mechanism of mechanotransduction to take effect.

Mechanotransduction

There is a mechanism known as mechanotransduction via which, as already described, mechanical forces generated by focused shock waves are exerted at acoustic interfaces. The crucial factor is the possibility of influencing cell membranes and specifically activating ion exchange by means of extension.

It can be assumed that momentum transfer at interfaces directly results in the release of various suothers) via the mechanism of mechanotransduction. To a large extent, it is nerve cells in particular that can be stimulated by weak shock wave momentum to transmit action potentials.

By contrast, as a general rule ultrasound is not observed to stimulate nerve cells. The difference is also evidenced in the fact that ultrasound is perceived not as a brief pulse, whereas shock waves are definitely sensed as brief sensory events or even as pulse-like pain.

The possibility of stimulating nerve cells with weak shock waves can therefore be postulated as being a key mechanism in the therapeutic effect of shock waves, especially given the lasting pain relief achieved.

Considering the wide range of indications other than lithotripsy, it can be concluded that enhanced blood circulation in the treated body regions occurs as a direct result of shock wave therapy. If the problem is chiefly one of chronic induration and spasming of muscle fibres (trigger points) and vessels, shock wave therapy can not only alleviate these in the short term but also eliminate them permanently. It would appear obvious that not only should acute nerve stimulation be considered here, but the influence on pain memory as well. During the chronification phase, sensory signals (along afferent pathways) are permanently associated with motor signals (along efferent pathways), thus forming a feedback loop (autonomic reflex arc) that is retained as a pain memory. The reflex is now a conditioned, pathological reflex that makes muscular or vascular spasming persist, although the original cause – an impact or other injury – has abated. Stimulation with shock waves to induce forced triggering of action potentials then removes the link between sensory input (along afferent pathways) and motor output (along efferent pathways).[34] This hyperstimulation is used to selectively treat the tissue affected by activating the relevant nerve fibres, and to mitigate the tonic effect of the efferent signals. This can release spasms and initiate metabolic processes that promote healing.

This process requires the nerve fibres to be stimulated to the point of numbness, but not destroyed. A fuller explanation is provided in the publication titled "A neural model for chronic pain and pain relief by extracorporeal shock wave treatment".[34]

Whereas shock wave therapy is applied routinely for numerous indications, its use for treating neurological pathologies is still in its infancy. Since experience shows that non-destructive stimulation of nerve cells by shock waves forms the basis for healing processes, it is appropriate to stimulate these cells at locations where they are of particular importance. Conditions affecting the brain, such as Alzheimer's, are attributable to functional loss of nerve cells.

Direct transcranial pulse stimulation (TPS®) using shock waves can be used to specifically treat localized regions of the brain.[36] The result is that metabolic processes are activated and "trained" at the synaptic contact sites of nerves, so that sustained reduction of their threshold levels is achieved via frequent stimulation pulses.

The idea underlying transcranial pulse stimulation is that repetitive, weak shock wave momentum reactivates nerve cells that have reduced function, and that (in what is a continuing learning process) previous mental capabilities are reconstituted, at least in part.

Fig. 10: Specific treatment of cerebral regions using TPS®

References

1. Wess, O.: Physikalische Grundlagen der extrakorporalen Stoswellentherapie. Journal für Mineralstoffwechsel, 11(4), 7 – 18, 2004.
2. Chaussy, C. et al.: Extracorporeally induced destruction of kidney stones by shock waves. The Lancet, 316(8207), 1265 – 1268, 1980.
3. Chaussy, C. et al.: First clinical experiences with extracorporeally induced destruction of kidney stones by shock waves. The Journal of Urology, 127(3), 417 – 420, 1982.
4. Valchanov, V. et al.: High energy shock waves in the treatment of delayed and nonunion of fractures. International Orthopaedics, 15(3), 181 – 184, 1991.
5. Schaden, W. et al.: Extracorporeal shock wave therapy (ESWT) in 37 patients with non-union or delayed osseus union in diaphyseal fractures. In: Chaussy, C. et al. (eds.): High Energy Shock Waves in Medicine, Georg Thieme Verlag, Stuttgart, 1997.
6. Loew, M. et al.: Die Wirkung extrakorporaler Stosswellen auf die Tendinosis calcarea der Schulter. Urologe (A), 34(1), 49 – 53, 1995.
7. Dahmen, G. P. et al.: Die Extrakorporale Stosswellentherapie in der Orthopädie – Empfehlungen zu Indikationen und Techniken. In: Chaussy, C. et al. (eds.): Die Stosswelle – Forschung und Klinik. Attempto Verlag, Tübingen, 1995.
8. Wess, O.: Physics and technology of shock wave and pressure wave therapy. ISMST Newsletter 2(1), 2 – 12, 2006.
9. Wess, O. et al.: Working group technical developments – consensus report. In: Chaussy, C. et al. (eds.): High Energy Shock Waves in Medicine. Georg Thieme Verlag, Stuttgart, 1997.
10. Church, C.: A theoretical study of cavitation generated by an extracorporeal shock wave lithotripter. The Journal of the Acoustical Society of America, 86(1), 215 – 227, 1989.
11. Church, C.: The risk of exposure to diagnostic ultrasound in postnatal subjects. Journal of Ultrasound in Medicine, 27(4), 565 – 592, 2008.
12. Delius, M. et al.: Biological effects of shock waves: in vivo effect of high energy pulses on rabbit bone. Ultrasound in medicine and biology, 21(9), 1219 – 1225, 1995.
13. Forssman, B. et al.: Stosswellen in der Medizin, Medizin in unserer Zeit. 4: 10, 1980.
14. Crum, L. A.: Cavitation on microjets as a contributary mechanism for renal calculi disintegration in ESWL. The Journal of Urology, 140(6), 1587 – 1590, 1988.
15. Coleman, A. J. et al.: Acoustic cavitation generated by an extracorporeal shockwave lithotripter. Ultrasound in medicine and biology, 13(2), 69 – 76, 1987.
16. Byron, C. R. et al.: Effects of radial shock waves on membrane permeability and viability of chondrocytes and structure of articular cartilage in equine cartilage explants. American Journal of Veterinary Research, 66(10), 1757 – 1763, 2005.
17. Kisch, T. et al.: Repetitive shock wave therapy improves muscular microcirculation. Journal of Surgical Research, 201(2), 440 – 445, 2016.
18. Goertz, O. et al.: Short-term effects of extracorporeal shock waves on microcirculation. Journal of Surgical Research, 194(1), 304 – 311, 2015.
19. Maier, M. et al.: Substance P and prostaglandin E2 release after shock wave application to the rabbit femur. Clinical Orthopaedics and Related Research, (406), 237 – 245, 2003.
20. Klonschinski, T. et al.: Application of local anesthesia inhibits effects of low-energy extracorporeal shock wave treatment (ESWT) on nociceptors. Pain Medicine, 12(10), 1532 – 1537, 2011.

21. Nishida, T. et al.: Extracorporeal cardiac shock wave therapy markedly ameliorates ischemia-induced myocardial dysfunction in pigs in vivo. Circulation, 110(19), 3055 – 3061, 2004.

22. Mariotto, S. et al.: Extracorporeal shock waves: From lithotripsy to anti-inflamatory action by NO production. Nitric Oxide, 12(2), 89 – 96, 2005.

23. Horn, C. et al.: The effect of antibacterial acting extracorporeal shockwaves on bacterial cell integrity. Medical Science Monitor, 15(12), 364 – 369, 2009.

24. Chao, Y.-H. et al.: Effects of shock waves on tenocyte proliferation and extracellular matrix metabolism. Ultrasound in medicine and biology, 34(5), 841 – 852, 2008.

25. Christ, Ch. et al.: Improvement in skin elasticity in the treatment of cellulite and connective tissue weakness by means of extracorporeal pulse activation therapy. Aesthetic Surgery Journal, 28(5), 538 – 544, 2008.

26. Gollwitzer, H. et al.: Radial extracorporeal shock wave therapy (rESWT) induces new bone formation in vivo: results of an animal study in rabbits. Ultrasound in medicine and biology, 39(1), 126 – 133, 2013.

27. Schuh, C. M. et al.: In vitro extracorporeal shock wave treatment enhances stemness and preserve multipotency of rat and human adipose-derived stem cells. Cytotherapy, 16(12), 1666 – 1678, 2014.

28. Raabe, O. et al.: Effect of extracorporeal shock wave on proliferation and differentiation of equine adipose tissuederived mesenchymal stem cells in vitro. American Journal of Stem Cells, 2(1), 62 – 73, 2013.

29. Auersperg, V. et al.: DIGEST-Leitlinien zur Extrakorporalen Stosswellentherapie, www.digest-ev.de, 2012.

30. 30. Cleveland, R. O. et al.: Acoustic field of a ballistic shock wave therapy device. Ultrasound in medicine and biology, 33(8), 1327 – 1335, 2007.

31. Uberle, F. et al.: Ballistic pain therapy devices: measurement of pressure pulse parameters. Biomedical Engineering/ Biomedizinische Technik, 57 (SI-1 Track-H), 700 – 703, 2012.

32. Grecco, M. V. et al.: One-year treatment follow-up of plantar fasciitis: radial shockwaves vs. conventional physiotherapy. Clinics, 68(8),1089 –1095, 2013.

33. Gleitz, M.: Die Bedeutung der Trigger-Stoßwellentherapie in der Behandlung pseudoradikularer Cervicobrachialgien. Abstracts 53. Jahrestagung der Vereinigung Süddeutscher Orthopäden e.V., 2005.

34. Wess, O.: A neural model for chronic pain and pain relief by extracorporeal shock wave treatment. Urological Research, 2008; 36(6), 327 – 334, 2008.

35. Wess, O. et al.: Fragmentation of brittle material by shock wave lithotripsy. Momentum transfer and inertia: a novel view on fragmentation mechanisms. Urolithiasis, doi: 10.1007/s00240-018-1102-6

36. Beisteiner, R. et al.: Transcranial Pulse Stimulation with Ultrasound in Alzheimer's Disease—A New Navigated Focal Brain Therapy. Advanced Science, 7(3):1902583, 2019. doi: 10.1002/advs.201902583