4. The role of focal size in extracorporeal shock wave lithotripsy

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Abstract. Shock wave lithotripsy (SWL) has radically changed treatment of stone disease and appears to be the first option for the majority of patients. Since the 1980s technical developments have made modern lithotripsy devices more comfortable, side effects were significantly reduced and fragmentation efficiency was improved. In clinical lithotripsy, the practitioner has control over generator voltage (kV), energy density (mJ/mm²), peak pressure (MPa), rate of shock wave administration, number of shock waves and the type of lithotripter. However, technical improvements in shock wave technology have mainly been made with an eye on providing user convenience and multifunctionality, rather than a mechanistic understanding of stone comminution and side effects, most importantly tissue injury. Although numerous basic research studies have been performed, the parameters determining the extent of renal injury have yet to be fully clarified. This review analyses the impact of focal size and distribution of shock wave fields on the performance of lithotripters and reviews the results of ex-vivo and in-vivo studies concerning this topic.
Introduction

Since 1980, when the first kidney stone patient was treated, extracorporeally generated shock waves (shock wave lithotripsy, SWL) are frequently used in medicine. The indication range expanded from stones in all parts of the body, to orthopaedics, rheumatology, cardiology and urological pain therapy. Numerous new indications will follow in different other medical fields. Extracorporeal shock wave treatment (ESWT) in general is well accepted since it is effective, easy to apply and, usually, without significant side effects. Nevertheless, occasional side effects such as hematoma, petechial bleedings, interactions with cardiac rhythm etc. are reported. The risk of perirenal or intrarenal haematoma is estimated to be between 0.1 % and 0.6 % (detected by ultrasound technology of the eighties) [1,2,3]. Using MRI or CT instead of ultrasound 20 to 25 % haematomas are reported [4,5]. Even though only a few of these require surgical intervention, side effects of shock waves are apparent. An impressive proof for possible shock wave lesions is given by Matlaga et al. [6]. The lesions reported exceeded the nominal focus zone of an unmodified HM3 lithotripter significantly, as seen in Figure 1.

This lithotripter is characterized by a large focal zone and an unfocussed primary wave which is generally associated with electro hydraulic shock wave

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**Figure 1.** Shock wave induced tissue lesion.
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Figure 2. Typical shock wave field of an electro hydraulic generator. The field consists of a focussed field with the focus at F2 and an unfocussed (vagabonding) spherical wave.

generation. The unfocused primary wave is of low intensity; however, it covers large areas of the patient’s body and is not restricted to the nominal (-6dB) focal zone (Figure 2). The general question is how fragmentation can be improved without increasing side effects.

As generally accepted in medicine, the principle statement of Paracelsus (Philippus Theophrastus Bombastus von Hohenheim, 1493-1541) holds true also for shock wave application: "Omnia sunt venena, nihil est sine veneno. Dosis sola facit venenum."

In other words: Shock waves have to be dosed correctly in order to balance efficiency vs. side effects. Not only the total shock wave dose needs to be carefully controlled but also spatial and temporal configurations of shock wave delivery require special care. Side effect may be minimized by appropriate technical improvements.

Goals of generator design

The first rule is: Shock wave energy must be directed towards the region of interest (e.g. stone to be fragmented) and kept away from all other sensitive
tissue areas as far as possible. Since shock waves are generated outside the body, they have to be guided to the target area while passing through different tissue layers without causing significant injury. They are generated in a therapy head with a smaller or larger aperture and are accordingly distributed over a more or less extended coupling area. This allows keeping the energy concentration as well as the shock wave pressure low at skin level. Pain and possible lesions are minimized. While propagating from skin to the target, the energy is concentrated approaching the level of medical efficacy in a well confined volume. There is no way to avoid a slightly increasing risk of lesions simultaneously in that particular target volume. Therefore, the design goal is to shape the effective treatment area as small as appropriate for fragmentation (dimensions of the stones treated) and reduce shock wave energy as much as possible anywhere else. The appropriate measure to shape the shock wave fields accordingly is focussing.

In spite of this clear and self-evident demand there is an ongoing debate about the appropriate focal size with regard to efficiency and avoidance of side effects. Some of those concerns are due to a diffuse understanding of the term “focus” and the impact of physical parameters of shock wave fields on efficiency and side effects. This article will first discuss the definitions of shock wave field parameters such as pressure, energy, energy flux density and focal dimensions as well as their impact on medical applications. Secondly we will review the scientific literature concerning the biological effects and side effects of shock waves generated from ex vivo and in vivo trials from the last 25 years.

Physical definitions of shock wave parameters

A shock wave field is a spatial and temporal distribution of acoustic energy within a three dimensional space. It is characterized by basic parameters such as peak pressure and temporal behaviour of the pressure at different spatial positions within the field.

To record such a pressure field, a small pressure probe is scanned through the three dimensional space while the temporal pressure curve is recorded in every single position as shown in Fig 3. The spatial position featuring highest peak pressure is usually termed focal spot.

The focal spot exhibits the peak of a mountain like distribution with declining slopes extending rather far beyond the nominal - 6 dB-value as depicted in Fig 4.

The flanks of the mountain may be more or less steep, which is an important quality issue of the shock wave field.
**Figure 3.** Temporal pressure variation of a typical shock wave.

**Figure 4.** Pressure distribution in the vicinity of the focal area.
For two reasons, the focal spot does not define the effective area of shock waves applied. First, the position of the focal spot is defined by the peak pressure in relation to the pressure in the surrounding of that point, independent of the absolute height of the pressure amplitude. It therefore does not qualify the energy content which is needed to show a medical effect. Second, since the effect of shock waves is not restricted to the focal spot but to a certain area around, more information about that area is needed.

The - 6 db focal zone

The quality of energy concentration of a shock wave field is defined by the - 6 dB focal area. That means an area of pressure values being equal or higher than 50 % of the local peak pressure. In case of a peak pressure of 100 MPa (as displayed in Figure 5) 50 %-limit is given by the 50 MPa isobar. Since 50 % is equivalent to - 6 dB, this focus is called the - 6 dB-focus. Selecting another peak pressure of e.g. 40 MPa, the - 6 dB isobar (50 % value) would equal 20 MPa. This example shows no relationship between dimensions of the focal zone and energy content. The - 6 dB-focus does not reflect the shock wave energy contained in the focal area. It, therefore, does not stand for fragmentation efficiency. The - 6 dB-focal size simply defines the “quality” of focussing and is, taken as single measure, no useful parameter to quantify the fragmentation performance of a lithotripter.

The 5 MPa- focal zone

An additional parameter is required to characterize an area of efficient shock wave interaction. This parameter must be closely linked to the energy content of the shock wave field. By definition of the Working Group Technical Developments – Consensus Report of the German Society of Shock Wave Lithotripsy [7], the pressure value of 5 MPa (50 bar) is considered as a limit above which shock waves are assumed to generate some medical effects. Pressure values below 5 MPa are deemed to have no or only minor effects in medical treatments. For the purpose of this paper the precise value does not matter at all as long as there is one fixed value to relate to.

We call this area “treatment zone” of a shock wave generator. Even if a threshold of medical efficiency of shock waves is not precisely known, there is no doubt about that higher shock wave energies create higher effects and/or side effects.

To conclude: The treatment zone, which means the zone where we can expect shock wave effects, is not defined by the focal (- 6 dB) zone. Treatment zones may be significantly larger or smaller than the focal (- 6 dB) zone depending
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Figure 5. - 6 dB-focus and 5MPa-treatment zone.

on the energy level selected. The discrepancy of the two zones is due the fact, that the treatment zone is related to an absolute pressure value (which defines the energy content of a given device) whereas the definition of the - 6 dB-focal zone relates to any actual peak pressure and therefore does not care about absolute energy values at all.

Shock wave energy

The energy (E) of the applied shock wave is an important parameter for practical applications. It can be assumed that the shock wave only has an effect on the tissue if certain energy thresholds are exceeded. In addition to the time curve of the shock wave p(t) (see Figure 3), the surface A, in which the pressure can be measured, is also decisive. Using the acoustical parameters of the propagation medium density (ρ) and sound velocity (c) yields the following equation for energy:

\[ E = \frac{A}{\rho c} \int p^2(t) dt. \]

A distinction is made as to whether integrating the pressure over time only records the positive pressure components (E+) or the negative (tensile)
components \( (E_{\text{total}}) \) as well. The total energy is usually given with \( E \) (without index). The acoustical energy of a shock wave pulse is given in millijoules (mJ). As a rule, several hundreds or thousands of shock wave pulses are emitted per treatment, so that the total emitted energy is yielded by multiplication with the number of pulses.

**Energy flux density (ED)**

As previously mentioned the therapeutic effect of shock waves is affected by whether the shock wave energy is distributed over a large area or concentrated on a narrow treatment zone. A measure of the energy concentration is obtained by calculating the energy per area \( (E/A) \):

\[
E/A = \frac{1}{\rho c} \int p^2(t) \, dt = ED \text{ (energy flux density)}.
\]

The energy flux density \( ED \) is given in millijoules per square millimetre \( (\text{mJ/mm}^2) \). In the case of energy flux density, one also distinguishes between integration over the positive part of the pressure curve or the negative part as well [7]. Without index \( ED \), the pressure curve is usually considered including the negative (tensile) components.

The above parameters are usually sufficient to characterise a shock wave field for medical applications. Shock wave devices that work with different generation principles can differ in relation to the listed parameters. The “quality” of the shock waves used in the treatment zone should be independent of the generation principle, however. In other words: The measurement of the above parameters in the treatment zone does not allow any fundamental conclusions to be drawn about the type of generation. “Electro-hydraulically generated shock waves are not better or worse than piezo-electrically generated shock waves”, although secondary parameters such as repeat accuracy, dose ability, energy range, operating costs for expendables etc. may differ.

Note that the above parameters are usually measured in water. Due to the inhomogenities in living tissue, however, deviations from the straight propagation of shock waves lead to a spatial expansion of the focal zones. With increasing depth in the body, the peak pressure as well as \( ED \) values may be significantly reduced by realistic anatomical conditions[8].

**What should a shock wave field for lithotripsy look like?**

Knowing about the basic shock wave parameters pressure, energy, energy flux density we may ask the question which parameter determines stone fragmentation, which causes lesions? Is it one and the same parameter or are they different? How should a shock wave field be designed to perform best
with respect to fragmentation without causing significant tissue lesions? Is there a chance to adjust different parameters independently to reach optimum performance? Is there a preferred parameter setting or a preferred focal size to be selected? Those questions are vigorously debated amongst medical users of lithotripsy devices.

Historically seen kilovolt (kV) settings were used to characterize the power of the applied shock waves when the first lithotripter HM3 was introduced into the market. This parameter relates only to the electrical loading conditions of the specific capacitors of an HM3 lithotripter. Therefore “kV” neither qualifies shock wave fields in general, nor different lithotripter devices. This is the reason, why it is not listed as a basic shock wave parameter although it was often used and published in early literature. The medical community, however, is used to simplify the complexity of shock wave fields by taking only one single parameter to characterize the shock wave field used for clinical applications. If not “kV”, what then? There was a tendency to use the peak pressure value p, alternatively, the parameter energy is taken (which has no relevance without selection of the area of measurement) or the ED value. Although describing separate features of the real shock wave field none of the above mentioned parameters (pressure p, energy E, energy flux density ED, focal zones etc.) taken alone, predicts fragmentation efficiency and/or generation of tissue lesions.

In particular, the statement “energy breaks the stone, energy flux density creates lesions” is nonsense or at least misleading. Accordingly, the feature of a big focal spot with large energy content does not guarantee a superb fragmentation and simultaneous reduction of side effects. The complex interactions of these parameters with stones and tissue material require a deeper look inside and a final proof by experimental and clinical validation. There is no doubt that fragmentation requires a certain amount of physical energy. The question is how the energy should be packed, in a large focus with low pressure (equivalent with low energy flux density) or, in a small focus, with high pressure (equivalent with high energy flux density). There is also no doubt that the energy has to hit the stone and not to pass it in a distance without affecting the stone. So, very large focal zones, significantly larger than the cross area of the stone, will expose the tissue to shock wave energy but will not contribute to fragmentation. A small focus, on the other hand, concentrates the energy to a small area and delivers shock wave energy just to this restricted zone. With respect to a given cross section of a stone, energy and energy flux density cannot be adjusted independently from each other. Obviously, this follows from the above described formulas.

Once the shock wave has passed tissue in front of the target stone and has been concentrated in the treatment area, there is no evidence to assume that
fragmentation and generation of tissue lesions can be varied independently by a tricky parameter selection. In other words, whenever the shock wave energy applied is high enough for stone fragmentation, there is also a certain risk to generate tissue lesions even if they may be considered minor.

**What does it mean with respect to lithotripsy?**

The spatial dimensions of the treatment zone will significantly change with the selected energy settings as shown in Figure 6. The area of efficient stone fragmentation is not a fixed quantity but will be significantly larger at high energy settings compared to low settings. Depending on the shock wave generator the -6 dB-focus may stay almost unchanged or may even become smaller with higher energy settings if the peak pressure is increased. Figure 6 depicts the case of unchanged -6 dB-focus with different energy settings.

![Image of Figure 6](image)

**Figure 6.** Low, medium and high energy settings and corresponding decreasing treatment (5 MPa) areas. Note that the -6 dB-focus remains unchanged although, obviously, the disposed shock wave energy is significantly reduced.

**Ideal, conventional and optimized focal sizes**

Ideally, shock wave energy should only be disposed to the target stone or the region of interest as a small spherical focus and nowhere else. This would
optimize efficacy and completely avoid side effects. The technical approach would require wave fronts shaped as full spheres concentrating at the centre. Obviously, due to anatomical and technical reasons, the shock waves cannot access the human body from a full sphere enclosing the patient. Bony structures and gas-filled organs such as lung tissue provide only limited access windows to reach the target area. Therefore a small spherical focus is unrealistic for all human applications.

Shock wave energy is weakly concentrated in a relatively large area. As a consequence, pressures amplitudes are either far below optimum values required for fragmentation or, if adjusted to optimum fragmentation, generate excessive strain to surrounding tissue.

Conventional shock wave systems such as the HM3 feature a significant larger focal zone of up to lateral 16 mm and longitudinal 100 mm. Due to the limited apertures angles in the range of 50° - 65° (aperture app. 12 – 20 cm, focal depth of app. 13 – 15 cm) energy concentration is limited by diffraction. Figure 7 shows a schematical view of a shock wave field of a typical electro hydraulic generator.

A realistic limit is to utilize shock wave applicators with large apertures angles up to approximately 90°. A large aperture provides a good compromise with respect to large area coupling with low energy density and accordingly minimized tissue load and optimal concentration of energy on the treatment area.

Figure 7. Shock wave field distribution of an electro hydraulic generator (schematic) in humans. Beside several organs such as liver, pancreas, which may be covered by the large focal zone, also heart and lung tissue may be affected by the unfocussed wave.
A specially designed electromagnetic shock wave source featuring a cylindrical generator and a parabolic reflector with a diameter of 30 cm is shown in Figure 8. Unlike usual electro hydraulic systems an unfocused vagabonding wave is avoided by design.

An increased aperture angle significantly modifies the shock wave field and focal energy distribution. Not only shock wave transmission from outer skin to inner target zones is performed with essentially less tissue lesions but energy concentration and consequently fragmentation efficiency can be strongly enhanced simultaneously. The beneficial influence of larger apertures is due to basic physics laws and the character of waves in general.

Figure 8. Design of a cylinder/parabol-configuration with the extreme aperture angle of 84° and a wide source diameter of 30 cm (focal depth 16.5 cm).
The influence of respiratory movement

The above mentioned arguments are valid in general but request precise targeting in order to always guide the shock wave energy on to the target stones. Realistic treatment conditions however, often may not guaranty permanent targeting within a millimetre range. The patient may move a few millimetres without notice or regular respiratory movements may shift the stone in an oscillatory manner. This may be controlled by positioning the target stone exactly into the reversal point of expiration, since the stone stays longest in this spatial position and enables highest hit rate. Nevertheless, there is a chance to miss target stones with a significant number of shocks. This is true for any available shock wave device in the market. We should realize however, that there are always tissue areas within the focal area exposed to missing shock waves. Also in front of the stone there is unavoidably tissue area within the shock wave pass even during perfect hits of the shock waves. It is just one of the beneficial features of shock wave lithotripsy that predominantly brittle materials such as mineral stones are affected by shock wave forces whereas elastic material such as soft tissue is passed with little or almost no lesion.

Dual focus design

In spite of these considerations it is speculated, that shock wave energy scattered over a larger area may be still efficient even in cases of coarse...
targeting. One may expect a higher hit rate with a larger focus. Each single hit, however, may be less effective due to lower energy flux density and thus lower energy deposited by individual shots on the target stones. For compensation of the lower effect of each single shot consequently energy levels may be increased. So we end up with the original dilemma described above: Increased energy levels for increased fragmentation will also increase risk of tissue lesions in an extended treatment area simultaneously.

Due to the conflicting expectations of the market Storz Medical designed a special shock wave generator with switchable focal zones in order to follow the specific market requests. The medical rationale how to use different focal zones may be developed according to the above statements: A wider focus for larger and relatively soft stones, for multiple and separated stones whereas the smaller focus may be utilized for treatments of smaller and harder stones,

![Figure 10](image)

**Figure 10.** Different focal sizes (small with high energy flux density and large, with low energy flux density) may be appropriate for selected applications such as extended kidney stones or impacted ureteric stones.
particularly for hard and impacted ureteric stones. Without going into technical
details how different focal zones may be generated by the same generator
configuration, especially with unchanged geometry of the focussing mirror, it
is important to mention, that the wide aperture of the system is unchanged. It
means that the energy is widely distributed over the large coupling area in both
focus configurations. Only the degree of energy concentration is matched to
the different focus geometries.

Beyond all theoretical and conceptual considerations an experimental
confirmation is requested with respect to induced tissue lesion within the focal
zone, particular in a target kidney when the energy levels are adjusted to equal
fragmentation power. In other words: It needs to be confirmed that for equal
stone comminution the level of tissue lesions do not differ significantly. It is
clear that outside the focal or treatment area, large aperture systems expose the
tissue less compared to small aperture systems.

Biological effects from ex vivo, in vivo and clinical trials

Although numerous basic research studies have been performed, the
parameters determining the biological effects and side effects (i.e. the renal
injury) have yet to be fully clarified. Expertise on the biological effects of
SWL on renal tissue is mostly derived from animal studies. Currently, the pig
is felt to be the most appropriate for SWL bioeffect in vivo studies, as porcine
kidneys mimic human kidneys both in size and morphology [9]. However,
animal trials for testing SWL-induced renal injury have several disadvantages.
The interindividual variance in the animals is largely due to unpredictable
artifacts such as shock wave attenuation (absorption, reflection) from the
intracorporeal path and respiratory movement of the kidney. Furthermore, the
number of experiments is limited because of high costs and administrative
barriers (ethics committee). To overcome these limitations, ex vivo kidney

tissue models were developed by Köhrmann et al. [10] and Bergsdorf et al.
have proven easy to handle, are low-costs and have the potential of providing
large series of experiments under standardized conditions and therefore reduce
animal trials. However, the ex vivo findings are not directly transferable to the
conditions of clinical lithotripsy and the experimental setting does not reflect
the clinical usage of SWL, as the kidneys are isolated and denerved (no
influence on the vegetative innervations of the vessels), respiratory movements
are excluded, and interfering tissue (muscle, fat) is extracted. This
disadvantage may also be regarded as an advantage, as the model excludes
these unpredictable influences.
We used the ex vivo model as described and evaluated by Köhrmann et al. [10]. Our ex vivo study confirms the histological results of in vivo studies that revealed vascular and parenchymal injury at and near the focus, with veins and arteries showing varying degrees of damage [9,12-14]. The tubular injury induced by SWL involves disruption of the tubular epithelium and the associated basement membrane. Our ex vivo study also confirms in vivo findings showing that the numbers of shock waves intensifies renal injury. Delius and colleagues [15] first reported this correlation. Several other groups [16-17] have confirmed these findings, while others observed no quantitative differences in renal injury when different amounts of shock waves were applied [10,19-21]. However, the direct comparison of these results may include systematic errors, as a large variety of lithotripters was used the different animal models (rat, rabbit, dog, pig). A recent in vivo study performed by Willis et al. [9] confirms that the number of shock waves influences renal injury. Most recently, Connors et al. [12] could show in vivo that a lower number of shock waves decreases lesion size and functional changes dramatically. They concluded that shock wave number should be reduced to the lowest number that fractures kidney stones in order to minimize renal injury and functional impairment.

Delius and associates [15] have reported the influence of the shock wave rate on renal injury. Generator voltage (kV) may be another important factor [12,20,22,23]. These groups discovered that the renal injury increased along with generator voltage. Generator voltage mainly determines the peak pressure in the focal zone, although all other physical parameters of the shock wave (i.e. negative pressure, shock wave energy, intensity), are also affected. Thus, it is unclear which physical parameter is responsible for the vascular injury. Interestingly, Bergsdorf et al. [11] were able to show in a similar ex vivo model compared to the one used by us, that the energy density of the applied shock wave had a direct influence on the grade of renal vascular lesion. Their findings also correlate to the grading of renal tissue lesion in a canine model [20].

To our knowledge, there are no reports available on systems used to investigate the influence of focal diameter and positive peak pressure on SWL-induced renal injury. Our preliminary ex vivo results show that the extent of renal injury is not influenced by positive peak pressure and focal size.

The exact mechanism that triggers shock wave-induced renal injury is as yet unknown. Two different mechanisms have been proposed: shear stress due to shock front distortion [24] and the cavitation that is induced inside blood vessels, in particular, by the expansion of intraluminal bubbles [25,26]. Shock waves produce cavitation bubbles that collapse with great force. These bubbles have been shown to pit metal foils and lyse isolated cells [27]. In vitro studies also indicate that the expansion of cavitation bubbles can cause model vessels
to rupture [25,26]. In this context, Evan et al. [28] have shown, that shock wave renal injury is reduced when cavitation/intraluminal bubble expansion is suppressed. These findings support the idea that cavitation plays a prominent role in shock wave-induced renal injury. Williams et al. [29] suggested that each cavitation bubble could increase its volume and destruction-potential. This is induced by the following shock waves hitting the already existing bubble (cavitation nucleus). This may explain in part the correlation of renal injury and number of shock waves administered.

Summary

Shock wave lithotripsy remains the safest available treatment modality for urinary calculi. Although shock wave energies may induce tissue damage, acute adverse effects are rare and may depend on individual risk profile but also on lithotripsy principles and different treatment protocols. There is an ongoing controversy on long-term complications of SWL and future studies hopefully will add information on this topic.

References


