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● *Original Contribution*

THE FIRST CLINICAL RESULTS OF "WIDE-FOCUS AND LOW-PRESSURE" ESWL

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Abstract—A clinical study of the concept "wide-focus and low-pressure" extracorporal shock-wave lithotripsy (ESWL) was performed in a scientific cooperation between the Physical Institute of the University of Stuttgart and the Xixin Medical Instruments Co. Ltd. in Wuxian-Suzhou, China. In this cooperation, self-focusing electromagnetic shock-wave generator systems from the University of Stuttgart were integrated into Xixin lithotripters and installed in seven hospitals in China. A total of 297 detailed patient protocols revealed an average of 1532 shock pulses for successful treatment with no necessity for pain medication and auxiliary measures, and a stone-free rate of 86% after a follow-up of 3 months. These results are discussed in terms of the wide-focus low-pressure conditions and the mechanism of binary fragmentation by squeezing. (E-mail: w.eisenmenger@physik.uni-stuttgart.de) © 2002 World Federation for Ultrasound in Medicine & Biology.

Key Words: **ESWL, Extracorporal shock wave lithotripsy, Fragmentation mechanisms, Wide-focus low-pressure ESWL, Self-focusing electromagnetic shock-wave generator, Binary fragmentation by squeezing, Pain, Traumatisation by cavitation.**

INTRODUCTION

Extracorporal shock-wave lithotripsy (ESWL) is accepted world-wide as the most efficient method for the treatment of human kidney stones. The history of the unique development of ESWL is documented in review articles (Coleman and Saunders 1993; Delius 1994, 2000) and textbooks (Chaussy et al. 1997; Eisenberger et al. 1991). Despite increasing perfection in three lithotripter generations, there is little agreement about the question of how further to optimise the physical parameters of the pressure or shock waves with respect to fragmentation results and avoidance of side effects. In lithotripters of the third generation, a narrow focus and a large aperture have been preferred. These allow a high concentration of energy on the stone and a reduced intestinal and skin exposure to the shock wave. In contrast, the principal potentials of a wide focus concept (Eisenmenger 1988) in ESWL have also been discussed. Meanwhile, laboratory studies with self-focusing electromagnetic "wide-focus" shock-wave generators (Brümmer et al. 1992; Staudenraus 1991; Eisenmenger 2001) developed in the Physical Institute of the University of Stuttgart demonstrated interesting physical properties and the high fragmentation rate for artificial stones, in accordance with the mechanism of binary fragmentation by squeezing (Eisenmenger 2001). Thus, the first clinical study was started in 1999 in a scientific cooperation of the Physical Institute of the University of Stuttgart with the Xixin Medical Instruments Co. Ltd. in Wuxian-Suzhou, China. In this cooperation "wide-focus" electromagnetic self-focusing generator systems from the University of Stuttgart were integrated into Xixin lithotripters and tested in China with respect to their clinical properties.

Wide-focus low-pressure ESWL

The principal attributes of the wide-focus low-pressure ESWL are: 1. the wide focus gives a wide error

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margin in stone, and also distributed fragment, targeting; 2. the small aperture in connection with the wide focus allows a high positioning flexibility; 3. there is no need for x-ray fluoroscopy during treatment; 4. ultrasonic localsation by the urologist sitting at the side of the patient allows easy and direct manual targeting and gives more comfort to the patient; 5. in addition, it has been demonstrated earlier *in vitro* that the process of "binary fragmentation by squeezing" (Eisenmenger 2001, 1998) is very efficient and dominant with the large focus width; 6. the high efficiency of the squeezing mechanism also allows low pulse pressures between 10 to 30 MPa (this pressure range, just above the critical breaking strength of about 2 MPa is completely sufficient in ESWL) (Eisenmenger 2001); and 7. consequently, also, the negative pressure mainly causing pain and tissue traumatsation and other side effects by cavitation (Zhong et al. 2001; Carstensen et al. 2000) can be reduced significantly. If this outweighs the more extended shock-wave exposure of the tissue by the wide focus, can only be tested by clinical studies.

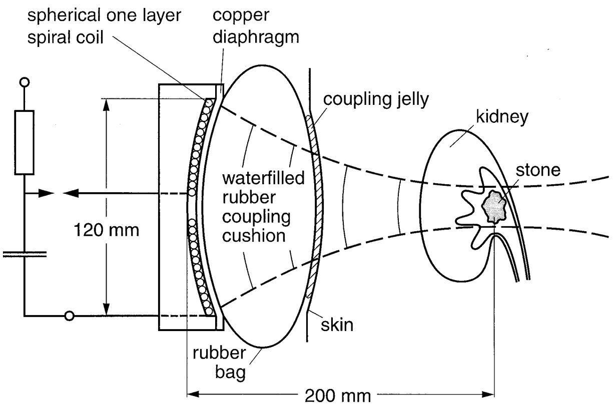

Fig. 1. Electromagnetic wide-focus shock-wave generator (schematic). The discharge current of the capacitor through the spherically shaped solenoid induces an opposed current in the copper diaphragm, leading to repulsion. The resulting self-focused pressure pulse is coupled into the body *via* a water-filled rubber cushion. The aperture of the source is 120 mm with a geometrical focus distance of 200 mm.

MATERIALS AND METHODS

Binary fragmentation by squeezing

The "wide focus" conditions are favourable for the mechanism of binary fragmentation by squeezing (Eisenmenger 2001; 1998). In this mechanism, the part of the wave propagating around the stone boundaries results in a circumferential compression of the stone. This leads to the growth of microcracks and their coalescence to a fracture plane by dynamic fatigue. The fracture surfaces are either parallel or perpendicular to the wave propagation direction. They correspond to the planes of maximum tensile stress amplitudes. The resulting fragments again undergo binary fragmentation by squeezing until a mm size distribution is reached. The mechanism for binary fragmentation was experimentally and theoretically (Eisenmenger 2001) verified for artificial stones.

The wide-focus lithotripter

The wide-focus electromagnetic self-focusing shock-wave generator from the University of Stuttgart (Fig. 1) (Eisenmenger 2001) has an aperture of 120 mm and 200 mm distance of the geometrical focus. In the positive pulse pressure range from 10 to 25 MPa, the –6-dB focal width amounts to 18 mm with a focal length of 180 mm. The –6-dB pulse width is 1.8 μs measured at the focus with 10 MPa positive peak pressure. With the pressure increased to 27.5 MPa, the –6-dB pulse duration is reduced to 1 μs in the focus. Measured laterally displaced from the focus, however, the –6-dB pulse duration is still 1.8 μs. Examples of pressure pulse measurements are shown in Fig. 2a and b. The positive focal peak pressure amplitudes depending on the generator voltage are given in Table 1, together with the negative pressure amplitudes. For the pressure measurements, we used the fiberoptic probe-hydrophone FOPH 300 (Eisenmenger 2001). The shock-wave generator is integrated in the compact Xixin lithotripter in the overcouch arrangement (Fig. 3) with water cushion coupling. The ultrasound (US) B-scanner for localisation and positioning is mounted by 45° inclined to the generator axis. For additional control of the stone targeting, the scanner is mounted on a ring of the generator housing and can be positioned around the generator axis at an arbitrary angle. The pulse-repetition rate of the generator can be adjusted in the range from 0.3 Hz to 2 Hz.

The clinical protocol

For the clinical study in seven hospitals, a detailed questionnaire (protocol) for each patient was handed to the doctors in charge of the treatment. The protocol covered the patient data, such as weight and height, male or female, the clinical history, the stone position, the number of stones and size, the number and strength (kV, pressure) of the shock waves for the treatment and retreatment, the localisation technique during treatment, the skin or/and intestinal pain sensation with the scale: 0 no pain, 1 first signs of pain, 2 more pain, 3 significant pain, 4 increased pain, 5 strong pain, and the use of anaesthesia. The protocol further asked for the occurrence of complications such as colic, petechiae, haematuria, and perirenal haematoma, as well as the use of auxiliary meaures. The stone-free rate was checked after a follow-up of 1

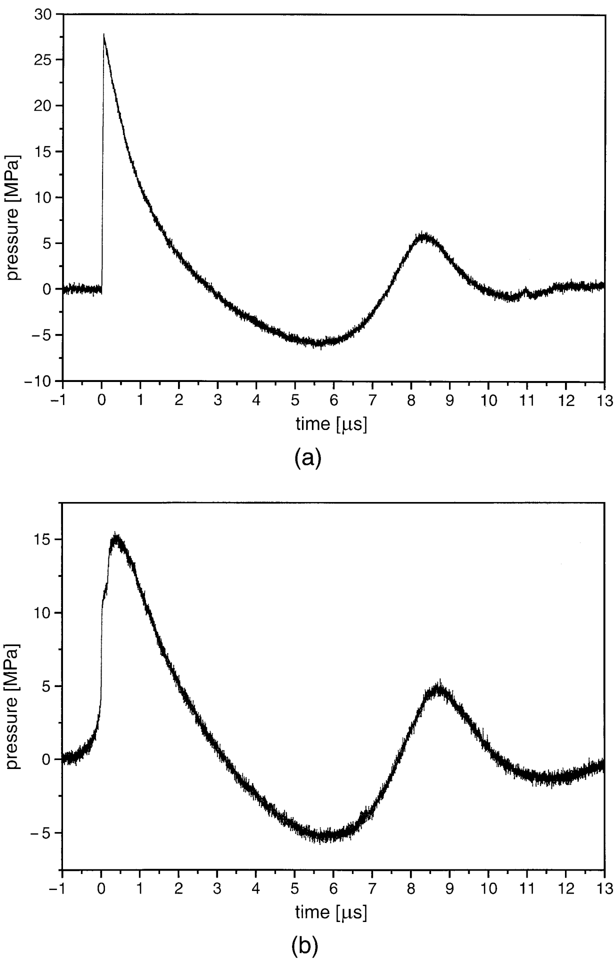

Fig. 2. (a) Example of a shock pulse with positive peak pressure of 27.5 MPa and negative pressure of −6 MPa measured at the geometrical focus with the fiberoptic probe hydrophone FOPH 300. (b) Example of the same pulse as shown in (a) measured in the focal plane, but 9 mm off axis. Corresponding to the −6-dB focal width of 18 mm, the pulse pressure is reduced to 50%, but note that the pulse width is again close to 1.8 μs and the shock-wave front has not developed.

week, 1 month and 3 months. For the stone-disease diagnosis in each case, X rays have been used, as well as for the stone position and stone size. The stone-free rate in the follow-up was determined in part by X rays, but mainly by US. The selection of patients for the

Table 1. Positive and negative focal peak pressures of the self-focusing electromagnetic shock-wave generator

	P^+ MPa	P^- MPa
8 kV	11.6	−4.0
9 kV	17.7	−4.6
10 kV	26.1	−5.6
11 kV	31.3	−6.4
12 kV	33.8	−7.2

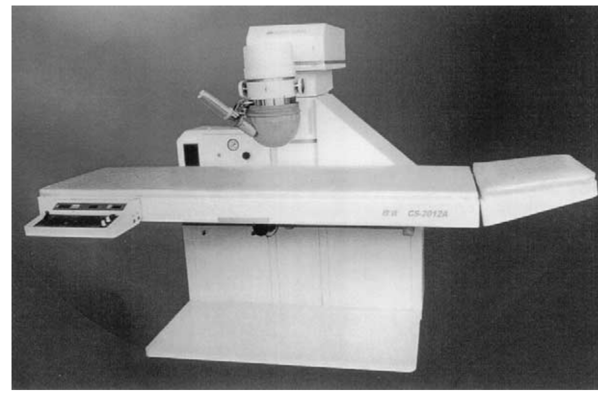

Fig. 3. XiXin lithotripter equipped with the self-focusing shock-wave generator from the University of Stuttgart.

study required only that they be available for checking the stone-free rate in the follow-up intervals of the protocol.

RESULTS

In Table 2, the main clinical results based on the protocol are presented. For ease of comparison, we used the same form as in the study of Rassweiler et al. (1996), page 600, Table 16. Their study reports clinical results for a narrow focus (diameter 6 mm) lithotripter with a cylindrical electromagnetic generator and parabolic mirror focusing and also on a narrow focus (diameter 4 mm) lithotripter with flat electromagnetic generator and lens focusing. The patient numbers were 287 and 258, respectively.

In our study, the number of patient protocols per hospital ranged from 38 to 55. The total patient number of all 7 hospitals amounted to 94 women and 203 men.

In addition to the criteria of Rassweiler et al. (1996), we included the average positive pulse pressure, as indicated in Table 2. The "average pressure" value has been obtained from the average voltage using a graphic curve interpolation of the data in Table 1. The treatment time per session results from the number of pulses with the relative long time interval of 3 s, which is favourable for the resorption of the remnants of cavitation bubbles. During treatment, localisation by US allows manual position control and correction. The time needed for ultrasonic stone localisation before treatment was about 5 min.

The results show a remarkably small number of 1532 shock waves per session with an acceptable percentage of 33% Re-ESWL (repeated ESWL) and 1.39 sessions per patient. Because there was no standarised treatment procedure, in general, after a start with lower peak pressures, the pressure settings were increased to an

Table 2. Results of the clinical ESWL study in seven hospitals in China with the wide-focus low-pressure lithotripter

	Seven hospitals
Patient data	
n of patients	297
n of stones	398
Stone size (%)	
$<$ 1 cm	41.6
1–2 cm	55.2
$>$ 2 cm	3.2
Stone localisation (%)	
Calyx	32
Pelvis	7
Upper ureter	21.5
Middle ureter	5.5
Lower ureter	30
Bladder	4
Treatment data	
Shockwaves per session	1531.7
Generator voltage (kV)	9.3
Pulse pressure (MPa)	20.8
Treatment time/session (min)	77
Localisation technique (%)	
Ultrasound	86
X ray	0
Combined	14
Time (see comments)	about 5 min
Results	
Re-ESWL (%)	33
Sessions/patient	1.39
Anaesthesia (%)	
IV analgesia/sedation	1
General anaesthesia	0
No anaesthesia	99
Pain (%)	
No intestinal pain, scale no. 0	94.3
First signs of intestinal pain, scale no. 1	5.7
Intestinal pain, scale no. 2,3,4,5	0
No pain at skin, scale no. 0	28.3
First signs of pain at skin, scale no. 1	60.6
More pain at skin, scale no. 2	10.4
Significant pain at skin, scale no. 3	0.7
Pain at skin, scale no. 4,5	0
Auxiliary measures (%)	
Before ESWL	0
Retrograde mobilisation	0
Stent	0
Nephrostomy	0
After ESWL	0
Adjuvant (stent, nephrostomy)	0
Curative (ureteroscopy, PCNL)	0
Complications (%)	
Colic	8
Petechiae	38
Haematuria	85
Perirenal haematoma	0
Stone-free rate (%)	
After 1 week	15.5
After 1 month	51.9
After 3 months	86.2

upper limit between 15 and 25 MPa. As a rule, mostly 1000 shocks have been administered in one session. But note that no anaesthesia was necessary and only three patients needed IV analgesia/sedation. Correspondingly, no intestinal pain was reported for 94.3% of patients, first signs of pain for 5.7% and 0% for the pain scale from 2 to 5. No pain at the skin with 28.3% and first signs of pain with 60% are followed by 10.4% with pain at the skin, 0.7% skin pain scale 3 and 0% for the skin pain scale 4 and 5. Analgesia/sedation was administered 4 days after the first ESWL to one man of age 43 years with a staghorn stone. He had strong colic, but with one Re-ESWL, he was stone-free after 4 weeks. Two women of ages 45 and 56 with lower and upper ureter stones, respectively, received IV analgesia/sedation because they were nervous and afraid of the treatment; only skin pain No. 1 and 2 were reported for them. Auxiliary measures were not necessary and, thus, have not been used. The stone-free rate of 86% after 3 months for all seven hospitals is significantly higher than the results of the clinical study of Rassweiler and colleagues, with 68% and 70%, respectively, for the two narrow-focus lithotripters. The chi-square test resulted in a statistical error probability of $p < 0.0001$ for the 86% and the 70% (68%) stone-free rate.

With all 176 patients of four selected hospitals of our study reporting stone-free rates higher than 90% each, the average of 1330 shock waves, 22% Re-ESWL and 1.24 sessions per patient, the stone-free rate of 97% after 3 months follow-up was even higher. In the study of Rassweiler et al. (1996)), the stone-free rate after 1 year follow-up was 85% and 84%, respectively. It must be noted, however, that the stone-free rate in our study was mainly determined by US and a follow-up of 12 months stone-free rate was not yet possible.

The percentage of minor complications such as colic (8%), petechiae (38%) and haematuria (85%) are also indicated. There was no report of perirenal haematoma.

DISCUSSION

The number of patients as well as the number, the size distribution and localisation of the stones are very similar in our study of the wide-focus low-pressure ESWL treatment and in the study of Rassweiler et al. (1996). With our self-focusing electromagnetic generator, the average shock-wave number was only 1532 per session, which is less than one half of the shock-wave numbers given by Rassweiler and colleagues, with 3288 and 3457, respectively for the two narrow-focus lithotripters. Furthermore, the present results reveal a significantly reduced generator voltage with only 9.3 kV, which is half the voltage in the study of Rassweiler and coworkers. Accordingly, the pulse pressure with 20.8 MPa is remarkably low, which altogether underlines the attributes of the wide focus and the high efficiency of binary fragmentation by squeezing.

The treatment time of 77 min is longer than reported by Rassweiler and colleagues. This is due to the longer time interval of 3 s between succeeding pressure pulses, which allows residual bubbles after cavitation to become progressively resorbed as readily observed in the US image and, thus, reduce their contribution to repeated cavitation at the next pressure pulse. In this first study, the 3-s pulse period has been chosen for reducing pain, traumatisation and uneasiness of the patient to the largest possible extent. The maximal pulse-repetition frequency of this lithotripter, however, is 2 Hz. It has been shown earlier with other lithotripters that there is no loss in fragmentation of artificial stones (Kahmann et al. 1993) up to 1 Hz repetition rate. These authors found that, by increasing the repetition frequency further up to 2 Hz, the fragmentation rate decreases by the factor of 0.5. The same result was recently found by Paterson et al. (2001) and McAteer et al. (2001) with artificial stones *in vitro* and *in vivo*, by implanting artificial stones into the kidney of pigs. These authors report that no attenuation of the pressure pulse amplitude by cavitation residues could be observed, even at 2-Hz pulse frequency. Therefore, they attributed the reduction of the fragmentation rate to a change of the stone surface properties. This, as we think, may be caused by the extremely high density of tiny cavitation bubble residues at the stone surface that, by their collective sound soft properties, shield like a thin air layer the pressure action on the stone and, thus, reduce the fragmentation rate. The authors show excellent pictures of the *in vivo* fragments under 2 Hz and 0.5 Hz pulse frequency after 400 shocks. With 2 Hz, only 2 large fragments and, with 0.5 Hz, about 10 equally sized fragments were observed. This provides evidence that also *in vivo* binary fragmentation by squeezing is dominant. Surprisingly, the authors also found no significant difference of the fragmentation between the *in vivo* and the *in vitro* conditions. This also is consistent with the squeezing mechanism because, by this observation, cavitation as fragmentation mechanism can be excluded. It should be noted that the hydroelectric shock-wave generator used in their experiments had a wide focus of about 15 mm diameter. It has to be tested by further studies under wide-focus and low-pressure conditions if the shock-wave repetition frequency can be increased without increase of pain and traumatisation.

In our study, the localisation technique during treatment used predominantly US. In general, localisation by US requires higher skill and experience of the urologist; yet, with the wide focus, it is less difficult to hit the stone and the fragments. Also, the wide focus results in a more homogeneous fragmentation. Middle and lower ureter stones, despite being compacted under prestress of the ureter and/or the bladder entrance, could be fragmented without difficulty. Also, bladder stones of large size (> 3 cm) were treated successfully under the condition of a sufficiently liquid-filled bladder. In some cases, Chinese antipyrotic medicine and medicine to dilatate the ureter for an easy passage of the fragments was administered.

Re-ESWL was predominantly limited to a second session, as indicated by the Re-ESWL of 33% and the number of sessions per patient of 1.39. In Rassweiler et al. (1996), Re-ESWL only of 28% and 27% is reported but the number of sessions per patient were 1.41 and 1.39, respectively. This indicates a higher percentage of three sessions as compared to our study. It should be noted that the four selected hospitals in our study with an average stone-free rate of 97% for all patients after a follow-up of 3 months reported a Re-ESWL of only 22% with 1.24 sessions per patient and a shock-wave number of only 1330. These data confirm that, in our study, the retreatment was limited to only a second session.

In Rassweiler and colleagues' study, 80% and 77%, respectively, of IV analgesia/sedation and 6% general anaesthesia were reported. In contrast, the treatment in our study was almost free of pain (see Table 2) and, therefore, no anaesthesia or analgesia/sedation (only three cases) and also no acupuncture were used. This is in accord with the moderate negative pressure level of –5 MPa. This value, together with the positive pulse pressure of 20.8 MPa for 9.3 kV, results by interpolation from Table 1. In the negative pressure range of −5 MPa and with a pulse period of 3 s, cavitation is less strong (Zhong et al. 2001; Carstensen et al. 2000) and causes no pain. Because the fragmentation with the wide focus, together with the mechanism of binary fragmentation by squeezing (Eisenmenger 2001; 1998), leads to a more homogeneous and small fragment-particle size distribution, it appears plausible that auxiliary measures are not required. It should be noted that all seven hospitals had the staff and the instrumentation for the auxiliary measures available, if needed. It should be noted, however, that the patients drink enough special medical liquid or tea as readily available and most popular in China before and after the treatment. The presence of liquid in the urinary tract is favourable for the US localisation of the stones, the fragmentation process by squeezing and for the removal of the stone fragments on the natural way. For comparison, Rassweiler et al. (1996) report auxiliary measures with 31% and 33% before ESWL and 7% and 9% after ESWL, with the two narrow-focus lithotripters, respectively.

The observation of only minor complications is also in accord with the reduced cavitation. Petechiae and pain at the skin apparently can be avoided by bubble-free application of the US coupling gel (Eisenmenger 2001). There was no report of perirenal haematoma, again in accord with the moderate negative pressure level and reduced cavitation.

CONCLUSION

Our first clinical study of ESWL under wide-focus and low-pressure conditions indicates that this concept in connection with binary fragmentation by squeezing has the potential of high fragmentation efficacy at significantly reduced shock-wave numbers, as well as a treatment that does not require pain medication or auxiliary measures. The governmental clinical approval in China for the Xixin lithotripter equipped with the self-focusing electromagnetic shock-wave generator was given on October 31, 2000.

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