

# **Quantification of the range of motion of kidney and ureteric stones during shockwave lithotripsy in conscious patients.**

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## **Abstract**

Effective shockwave lithotripsy requires accurate targeting of the stone throughout the course of treatment. Stone movement secondary to respiratory movement can make this more difficult. In vitro work has shown that stone motion outside the focal region reduces the efficacy of stone fragmentation; however, there is little clinical data on the degree of stone movement in patients during treatment. To investigate this, X-ray fluoroscopic images of kidney and ureteric stones at the upper and lower limits of the normal respiratory cycle were acquired during SWL of 54 conscious patients, and stone excursion was calculated from these images. In addition, respiration rate and patient perceived pain were recorded during the course of the treatment. It was found that stone motion secondary to respiration was  $7.7 \pm 2.9$  mm for kidney stones and  $3.6 \pm 2.1$  mm for ureteric stones—less than has been reported in studies with anaesthetised patients. There was no significant change of motion over the course of a treatment although pain was found to increase. These data suggest that stone motion in conscious patients is less than in anaesthetised patients. Further it suggests that lithotripters with focal regions of 8 mm or greater should not suffer from a marked drop in fragmentation efficiency due to stone motion.

## **Introduction**

Shockwave lithotripsy (SWL) is the most commonly performed treatment for nephrolithiasis in the UK and US [1,2]. Effective stone fragmentation is dependent on accurate positioning of the stone in three dimensions—particularly in the plane normal to the acoustic beam—and on maintaining the stone position during the course of treatment. After initial targeting, SWL is delivered at a regular rate (1-2Hz). Most patients receive a full course of up to 4000 shocks because currently there are no established endpoints for treatment. SW delivery is stopped at regular intervals during the treatment to confirm targeting, typically every 500 SWs at our centre. Excessive stone movement during lithotripsy will reduce the number of incident shocks resulting in reduced stone comminution rates; for example, motion exceeding 10 mm has been demonstrated to reduce fragmentation efficacy in vitro on a lithotripter with a nominal 4.5 mm focal zone width [3]. Further, if a large fraction of the shock waves do not interact with the stone then this will result in more shock waves being delivered to the patient which would suggest a greater potential for collateral tissue damage [4].

Previous imaging studies have reported superior-inferior displacement of the kidney due to respiration ranging from 5 to 50 mm [5,6,7,8]. Many factors might influence this range of movement, including anaesthesia, pain, respiratory pathology and body habitus, all of which affect respiratory patterns. Although it has been proposed that anaesthesia might reduce respiratory movement and improve stone targeting [9], respiratory motion during anaesthesia has also been reported to be greater than in conscious subjects [10]. A recent study in anaesthetised patients suggests that stone movement due to respiration is ~15mm and may result in 40% of shock waves missing the stone [11]. However, to our knowledge there is no data on stone motion of non-anaesthetised patients undergoing SWL. Given that one of the main attractions of lithotripsy as a treatment modality is that it can be performed on conscious patients and in an outpatient setting, quantifying stone motion would provide insight into whether targeting is of greater concern in these patients. In addition, improved understanding of stone motion during SWL will be necessary to develop stone tracking and triggered firing systems to maximise comminution efficacy and minimise renal parenchymal damage.

## **Patients and methods**

Between January and February 2013, 54 patients (39 men, 15 women, mean age 52.9 years) undergoing elective outpatient lithotripsy for ureteric or renal stones were evaluated. All lithotripsy treatments were performed on a Storz Modulith SLX-F2 fixed-site lithotripter at the Churchill Hospital, Oxford, UK as

described previously [11]. All patients were treated in a supine position using fluoroscopic guidance only. Patients needing ultrasound targeting or treatment in the prone position were excluded. All patients received the same pre-procedure analgesia, antiemetic, and prophylactic antibiotics a few minutes before treatment (pethidine 100mg, intramuscularly, diclofenac 75mg per rectum, prochlorperazine 12.5mg intramuscularly, ciprofloxacin 100mg orally). All patients were fully conscious throughout their treatment and were offered audio-visual distraction to reduce pain perception [11]. The operator aimed to deliver 4000 shocks in each treatment in total but reduced this if the patient could not tolerate the treatment or if the stone was adequately fragmented. Stones were visualised at regular intervals to ensure alignment of stone. Follow-up data (radiographs) were available for 29 patients (15 renal stones and 14 ureteral stones), and were graded in a blinded fashion to assign outcomes as no change, remaining calculus but reduced in size, or stone free.

During lithotripsy stone movement was evaluated at four time-points (0 (baseline), 500, 1500 and 3000 shocks) by recording fluoroscopic images taken at the limits of stone excursion due to respiratory motion. Respiratory rate (determined by measuring the number of breaths taken in a 15 second period) and verbal pain score (0-none to 10-worst possible) were also recorded at each time-point. For each image the outline of the stone was drawn manually. Paired fluoroscopic images were overlaid and the distance between the centroids of the two outlines and the distance of the outlines from the nominal focal point were calculated using ImageJ software (Figure 1). Fluoroscopy images of a coin taken in the plane of the focal zone were used to calibrate the pixel size of the images.

The stone position data was used to estimate the acoustic energy delivered to the stone due to motion. Because only images at the extrema of respiration were captured it was necessary for a model of respiratory motion to be employed to determine the stone location at all times. The equation proposed by Lujan et al.[12] was used

$$z(t) = z_0 - b \cos^{2n} \left( \frac{\pi t}{\tau} \right) \quad (1)$$

where  $z(t)$  is the position of stone at time  $t$ ,  $z_0$  the position at expiration,  $b$  the amplitude of motion (that is,  $z_0 - b$  the position at inspiration),  $\tau$  the period of motion, and  $n$  the degree of asymmetry. The degree of asymmetry accounts for the longer time period spent in expiration than inspiration and a value of  $n=3$ , as suggested by Lujan et al, was used in the modeling here.

The incident energy on the stone throughout its motion was calculated using a bespoke computer simulation written in Matlab (The Mathworks, Natick, MA) which carried out the following operations. A

pressure map in the focal region was assumed to follow a Gaussian profile with a  $1/e$  radius of 3.6 mm which corresponds to the manufacturer specified 6 mm diameter of the precise focus. A normalised energy flux density map was then created by squaring the pressure map, this step assumes no significant change in waveform shape across the focal region [13]. The outline of each stone was imported from fluoroscopic images and converted into an image mask for the energy flux density map. Figure 2 shows an example image of the energy flux density map with the stone mask overlaid at three different locations: inspiration, expiration and the mid-point. The stone was translated, by assuming it moved in a straight line between the location of inspiration and expiration, according to Eq. 1. The energy delivered to the stone was calculated at each location by integrating the energy flux density over the projected area of the stone. The energy was then normalised to the energy that would be incident on the stone if it were located exactly at the focus of the lithotripter. From the simulations the following quantities were calculated over an entire respiratory cycle: the average energy delivered to the stone, the mean distance of the stone from the lithotripter focus and the minimum distance of the stone from the focus.

Statistics. Overall effects on motion of the stones were tested using generalized linear modeling. Treatment outcomes were also assessed using generalized linear modeling for the 29 patients for whom follow-up data were available. Repeated measures MANOVA was used to assess data on a within-subject basis and 2-way ANOVA was used to evaluate data by shock-wave number and location in kidney or ureter. Correlations were tested using the conventional least-squares method. All statistics were calculated using JMP (SAS, Inc., Cary, NC, USA), and significance was assumed when  $P < 0.05$ .

## Results

Of the 54 stones that were analysed 37 (69%) were kidney stones and 17 (31%) were ureteric stones. The mean kidney stone size was 8.53mm (range 4-23mm) and the mean ureteric stone size was 8.05mm (range 3-22mm). In four cases the lithotripsy was concluded before 3000 SWs had been delivered and so fluoroscopic image data sets were incomplete.

Figure 3 shows the total motion (distance between inspiration and expiration) of kidney and ureteric stones at the four time points. The mean kidney stone motion was  $7.7 \pm 2.9$ mm (range 2.2-14.7mm) and was greater than the motion of ureteric stones  $3.6 \pm 2.1$ mm (range 0.5-7.8mm). Using a full model, or using only a 2-way ANOVA with SW-number, motion differed between renal and ureteral stones,  $P < 0.0001$ . The stone motion did not change over the course of treatment (by repeated measures  $P = 0.56$ ).

Figure 4 shows pain and respiratory rate at the four time points. Pain was found to increase at 500 and 1000 shock waves but without a significant further increase at 3000 shock waves. By repeated measures, pain increased on average with every patient,  $P < 0.0001$ . There was no effect of stone location (renal vs ureteral,  $P = 0.73$ ). Respiratory rate did not change significantly with the number of shock waves ( $P = 0.96$ ) nor with stone location ( $P = 0.38$ ). These data indicate that even though pain increased during the treatment it did not have a measurable effect on motion or respiration.

Figure 5 shows a scatter plot of the mean distance of the stone from the focus (as calculated by the Matlab programme) against the straight-line distance between inspiration-to-expiration distance. The correlation of these two measures is significant ( $P < 0.0001$ ), with no effect of location ( $P = 0.53$ ). The outliers in the scatter plot do not represent specific patients, so it appears that this relationship is independent of subject; similarly, repeated measures analysis of the distance to the focus showed no significant variation within subjects ( $P = 0.60$ ). However, the overall slope of the scatter plot is relatively shallow, as motion in the stone due to respiration has a minor effect on the total distance that the SW travels.

Figure 6 shows a scatter plot of the energy delivered to a stone and the average distance between the stone and the geometric focus of the lithotripter for all the measurements. It can be seen that the two are well correlated ( $P < 0.0001$ ) and that for more than 50% of the energy to be delivered to a stone, the stone should have an average distance from the focus of less than 4 mm – which is similar to the 3 mm radius of the focal zone.

For the 29 patients where follow-up data was available, in 48% of the cases no change in the stone was apparent by radiograph, in 28% the stone showed visible diminution of stone size, and in 24% of the cases the patient was deemed to be stone-free. Full model analysis of outcome showed no correlation with any measured parameters ( $P = 0.45$ ); specifically, there was no correlation between outcome and any measure of stone motion in the patients.

## **Discussion and Conclusions**

To our knowledge, this is the first study to measure stone movement due to respiration in conscious patients undergoing lithotripsy. This study found that mean stone movement was 7.7 mm for kidney stones and 3.6 mm for ureteric stones. This degree of movement is consistent with data from MRI of kidney

movement during conscious respiration [8] but less than the approximately 15mm of stone movement previously reported in anaesthetised patients undergoing lithotripsy [10]. This suggests that the range of motion may be less in conscious patients than those that are anaesthetised, although we acknowledge this comparison is across patient groups from different countries. However, in the study in anaesthetised patients one patient was performed under sedation and had the least amount of respiratory related motion (10mm) but at a higher respiratory rate [10] which is consistent with the hypothesis that patients that are more conscious have less respiratory motion.

Analysis of stone motion suggested that just measuring the distance between expiration and inspiration is not a robust measure of the mean distance the stone is from the focus. In general the mean distance between the stone and the focal point of the lithotripter was about one third of the measured inspiration to expiration distance. However there was substantial scatter in the data and therefore measuring inspiration-to-expiration distance should not be used as a proxy for the distance between the stone and focus, rather the distance should be determined by direct measurement.

We had hypothesised that during the treatment patient pain would increase and that this would result in more stone motion and a change in respiration rate. We did find that the pain score increased during treatment over the first 1500 SWs. However, the data did not show a change in either stone movement or respiratory rate during treatment. This suggests that the pain patients felt did not affect their respiration activity during lithotripsy.

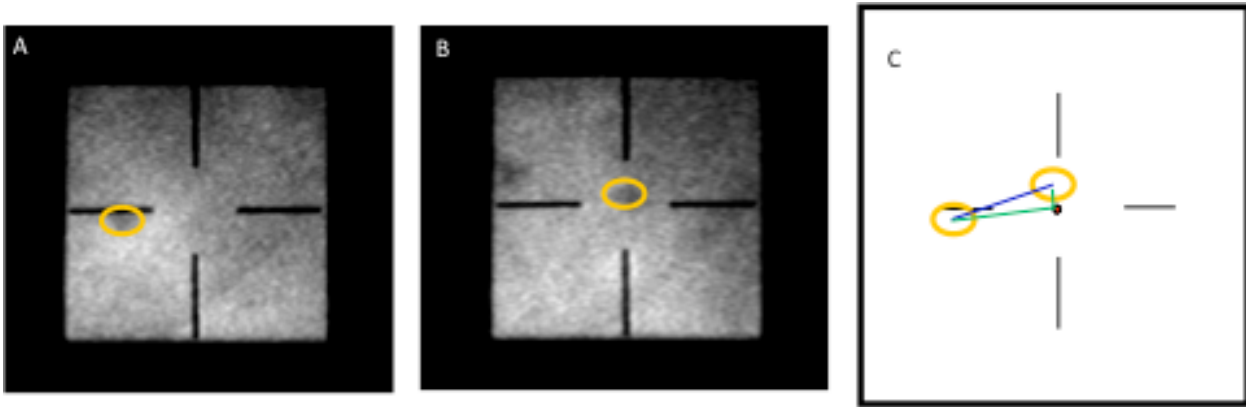
Data on stone movement is important because previous *in vitro* work has suggested that increased movement results in a significant reduction in fragmentation efficiency [3]. Lithotripsy systems with a small focus may produce more powerful fragmentation at the expense of some shocks missing the stone if there is significant movement. Even with the relatively small range of movement observed in our study, modelling suggests that on average stones in the kidney were subject to 55% of the energy that they would have had if they were not moving. For stones in the ureter, where the motion was less, on average received 73% of the energy they would be subject to if they did not move. These values are not sensitive to respiration rate, as long as breathing and shock wave delivery are not synchronised. The lithotripter employed in these studies has the capability to be employed with either a narrow focus or a broad focus. The data is supportive of the manufacturers statement for this particular that the narrower focus be used for ureteric stones, due to the lower amount of motion, and the broader focal zone for kidney stones, which had greater motion.

In summary, kidney stone motion was measured to be less than reported in anaesthetised patients which suggest that more shock wave energy may be incident on the stone for conscious patients. For the patients studies here the respiratory motion was not correlated with stone fragmentation outcomes suggesting that the range of motion did not affect stone fragmentation for this lithotripter. However, we estimated that about half the available energy was incident on stones in the kidney which suggests if a system that tracks and triggers shock wave delivery in real-time based on stone location could almost double the energy delivered to the stone which presumably would result in better fragmentation and less collateral damage.

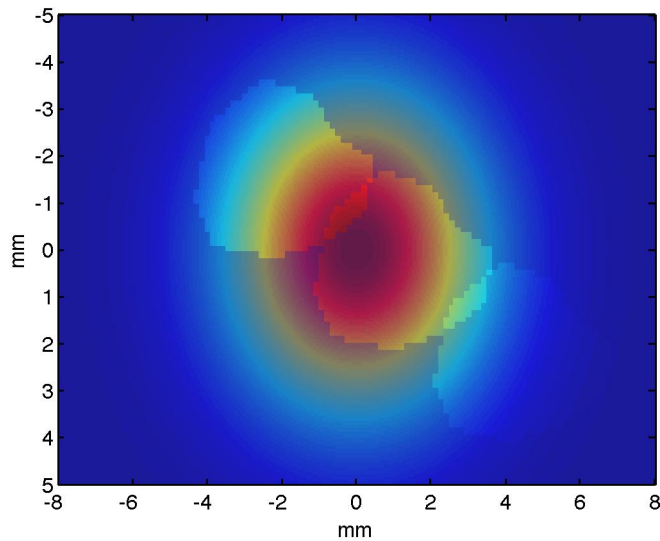
## **Acknowledgements**

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## Figures

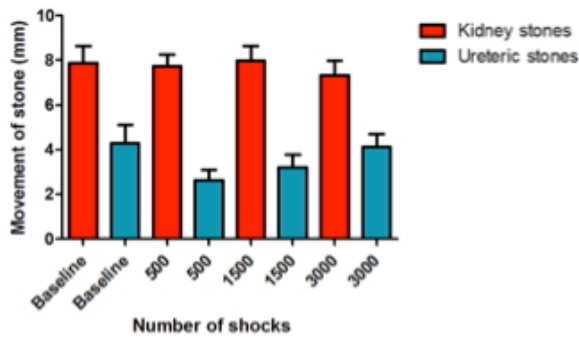


**Figure 1:** Example fluoroscopy images taken at inspiration (A) and expiration (B) during lithotripsy. Images were overlaid and the distance between the centroids of the two outlines and the distance from the nominal focal point calculated (C).

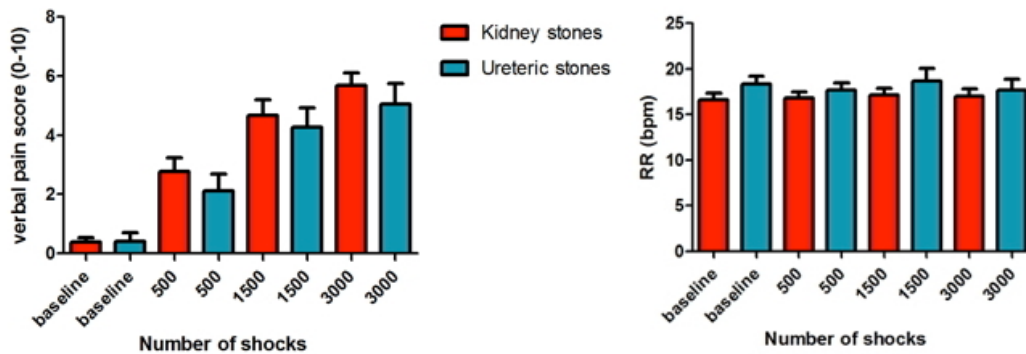


**Figure 2:** Example images from the Matlab simulation showing the spatial distribution of the energy density as a colour map and the overlay of the stone at three locations: expiration, mid-point and inspiration.

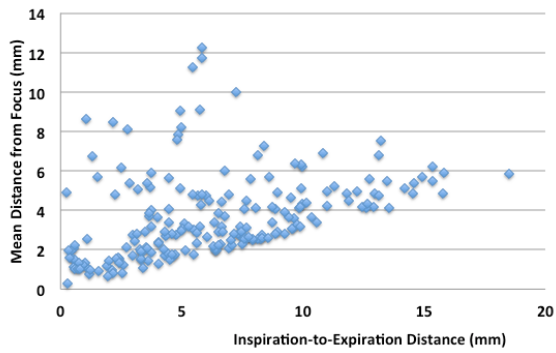




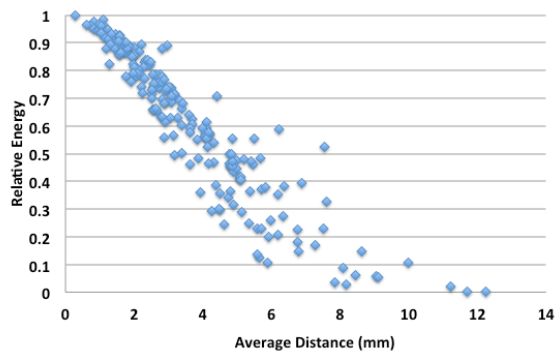
**Figure 3.** Stone movement due to respiration as a function of the number of shock waves delivered. Ureteric stones demonstrated less movement than stones in the kidney ( $p < 0.05$ ) at all timepoints throughout treatment. Overall, the range of stone movement did not change as treatment progressed for either kidney or ureteric stones.



**Figure 4.** Reported pain and respiratory rate during lithotripsy treatment. Although reported pain score increased as SWL treatment progressed it was not significant enough to impact on respiratory rate or stone movement.



**Figure 5** Scatter plot of mean distance to focus against inspiration-to-expiration distance. In general the mean distance is about one third of the inspiration-to-expiration distance however the correlation is not strong.



**Figure 6** Relative energy delivered to the stone for each condition and the average distance the stone was from the focus.

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