

# LithoTron

## Abstract from the Safety and Effectiveness Data Submitted to the FDA

### 1.0 SUMMARY OF SAFETY AND EFFECTIVENESS DATA

#### 1.1 General Information

**DEVICE GENERIC NAME:** Extracorporeal shock wave lithotripter

**DEVICE TRADE NAME:** HealthTronics LithoTron Lithotripsy System

**APPLICANT:** HealthTronics  
425 Franklin Road, Suite 545  
Marietta, Georgia 30067

#### 1.2 Indications for use

The HealthTronics LithoTron is indicated for use in patients with renal and upper ureteral calculi.

#### 1.3 Device Description

The HealthTronics LithoTron Lithotripsy System utilizes spark gap technology to generate shock waves outside the patient's body to fragment urinary calculi within either the kidney or upper ureter. The device consists of (1) the shock wave unit, including the therapy head, the control cabinet and the test device ( $f_2$  phantom); (2) the C-arm fluoroscopy unit; (3) the multi-use patient table; and (4) an ECG recorder for shock wave gating. A complete description of the device is provided in the specification sheet for the LithoTron.

#### 1.4 Contraindications [Warnings and Precautions]

The Operator's Manual for the LithoTron contains contraindications, warnings, and precautions for the system which are similar to those for other lithotripsy devices. This full text also appears in the Summary of the Safety and Effectiveness Data for the LithoTron system. Users of the device should familiarize themselves with this information prior to use of the device.

#### 1.5 Summary of Clinical Studies

##### 1.5.1 Study Design

A prospective multicenter study was conducted to demonstrate the safety and effectiveness of the HealthTronics LithoTron lithotripsy system when used as indicated for performing ESW lithotripsy in subjects with upper urinary tract (renal pelvis, renal calyx, and upper ureteral) calculi.

The investigation was conducted at four investigational sites in the United States, with 215 study subjects undergoing 221 lithotripsy procedures. Data

for 166 subjects who completed all follow-up requirements by the time of PMA submission are included in the analyses of device effectiveness, with data from all 215 subjects included in the analyses of safety data. The following table presents information regarding study participation status for all subjects enrolled in this clinical study.

**Table 1: Study Participation Status**

Study Participation Status	RLS, Portland, OR		Nebraska Methodist		Arlington Memorial, TX		Cape Girardeau, MO		TOTAL	
	N	%	N	%	N	%	N	%	N	%
<b>Total Subjects Treated</b>	<b>52</b>	<b>100.0</b>	<b>50</b>	<b>96.2</b>	<b>90</b>	<b>100.0</b>	<b>23</b>	<b>95.8</b>	<b>215</b>	<b>98.6</b>
• Total subjects enrolled	52	100.0	52	100.0	90	100.0	24	100.0	218	100.0
• Enrolled; excluded, not treated	0	0.0	2	3.8	0	0.0	1	4.2	3	1.4
<b>Total Subjects Included in Both Safety and Effectiveness Analyses</b>	<b>43</b>	<b>82.7</b>	<b>48</b>	<b>92.3</b>	<b>60</b>	<b>66.6</b>	<b>15</b>	<b>62.5</b>	<b>166</b>	<b>76.1</b>
<b>Total Subjects Included in Safety Analyses Only:</b>	<b>9</b>	<b>17.3</b>	<b>2</b>	<b>3.8</b>	<b>30</b>	<b>33.3</b>	<b>8</b>	<b>33.3</b>	<b>49</b>	<b>22.5</b>
• Not yet eligible for 1 month follow up	8	15.4	0	0.0	20	22.2	6	25.0	34	15.6
• Study participation ongoing to 3 months	0	0.0	1	1.9	4	4.4	1	4.2	6	2.7
• Noncompliant / Lost to follow-up	0	0.0	1	1.9	5	5.5	1	4.2	7	3.2
• Withdrawn	1	1.9	0	0.0	1	1.1	0	0.0	2	0.9

##### 1.5.2 Study Population Demographics

Of the total 215 patients enrolled in the study, 147(68.4%) were male and 68 (31.6%) were female. This ratio of males to females is similar to that reported in prior studies of lithotripters, and is representative of previous findings that approximately 75% of stone disease patients are males. Patient age ranged from 17 to 89 years, with a mean of 48.6 years.

##### 1.5.3 Compliance with Protocol Requirements

Fifteen study subjects (6.9%) of the 215 treated did not meet all of the inclusion/exclusion criteria described in the study protocol. Seven subjects (3.2%) with renal or ureteral abnormalities were enrolled in the study; four subjects (1.9%) who had taken aspirin within 2 weeks of treatment were enrolled; three subjects (1.4%) were enrolled with stones to be treated greater than 20 mm; and one subject was enrolled (0.4%) who at 17 years old was younger than the minimum age for study participation. All subjects enrolled with deviations from the study enrollment criteria remained in the PMA study cohort and data from these subjects are included in safety and effectiveness analyses.

### 1.5.4 Stone Characteristics

**Total Stone Burden Measured:** Each study subject was required to undergo either a radiographic assessment of the kidneys, ureter, and bladder (KUB) with ultrasound examination; or an intravenous pyelogram (IVP) prior to the study procedure to determine the total number and size of the calculi on the side to be treated. Mean total stone burden appreciated pretreatment was 11.8 mm, maximum 60.0 mm, minimum 4.0 mm.

**Table 2: Total Stone Burden Measured at Pretreatment**

	RLS, Portland, OR		Nebraska Methodist		Arlington Memorial, TX		Cape Girardeau, MO		TOTAL	
	N	%	N	%	N	%	N	%	N	%
<b>Total Stone Burden Measured</b>										
4 mm to 9 mm	22	42.3	23	46.0	35	38.9	10	43.5	90	41.9
10 mm to 14 mm	22	42.3	14	28.0	33	36.7	9	39.1	78	36.3
15 mm to 20 mm	8	15.4	10	20.0	11	12.2	1	4.3	30	14.0
Greater than 20 mm	0	0.0	3	6.0	11	12.2	3	13.0	17	7.9
<b>TOTAL</b>	52	100.0	50	100.0	90	100.0	23	100.0	215	100.0

**Total Stone Burden Treated:** The total stone burden treated exceeded the maximum 20 mm size described by the study protocol in 3 subjects; in all other cases, the stone burden treated fell within the 4 mm to 20 mm range described by the study protocol. The total stone burden treated was 10 mm or greater in 53.5% of the 215 study subjects.

**Table 3: Total Stone Burden Treated**

	RLS, Portland, OR		Nebraska Methodist		Arlington Memorial, TX		Cape Girardeau, MO		TOTAL	
	N	%	N	%	N	%	N	%	N	%
<b>Total Stone Burden Treated</b>										
4 mm to 9 mm	22	42.3	24	48.0	40	44.4	14	60.9	100	46.5
10 mm to 14 mm	22	42.3	16	32.0	35	38.9	8	34.8	81	37.7
15 mm to 20 mm	8	15.4	9	18.0	13	14.4	1	4.3	31	14.4
Greater than 20 mm	0	0.0	1	2.0	2	2.2	0	0.0	3	1.4
<b>TOTAL</b>	52	100.0	50	100.0	90	100.0	23	100.0	215	100.0

**Stone Location:** The majority of stones to be treated (44.6%) were located in the renal calyx, with relatively similar distribution of the remaining stones located in the renal pelvis (22.3%), the ureteropelvic junction (16.7%), and the upper ureter (20.9%). Note that the total number of stones identified for treatment (n=231) exceeds the total number of subjects treated (n=215).

**Table 4: Stone Location at Pretreatment**

	RLS, Portland, OR		Nebraska Methodist		Arlington Memorial, TX		Cape Girardeau, MO		TOTAL	
	N	%	N	%	N	%	N	%	N	%
<b>Stone Location at Pretreatment</b>										
<b>Renal calyx:</b>	20	38.5	27	54.0	36	40.0	19	56.5	102	44.6
Upper	3	5.8	3	6.0	5	5.6	2	8.7	13	6.0
Middle	3	5.8	4	8.0	11	12.2	3	13.0	21	9.8
Lower	14	26.9	20	40.0	20	22.2	8	34.8	62	28.8
<b>Renal pelvis</b>	17	32.7	13	26.0	17	18.9	1	4.3	48	22.3
<b>Ureteropelvic junction</b>	9	17.3	9	18.0	13	14.4	5	21.7	36	16.7
<b>Upper ureter</b>	9	17.3	7	14.0	26	28.9	3	13.0	45	20.9

**Number of Stones:** For 163 of the 215 subjects treated (75.8%), a single stone comprised the total stone burden treated. The following table presents pretreatment findings regarding the number of stones identified at pretreatment at each study site.

**Table 5: Number of Stones at Pretreatment**

	RLS, Portland, OR		Nebraska Methodist		Arlington Memorial, TX		Cape Girardeau, MO		TOTAL	
	N	%	N	%	N	%	N	%	N	%
<b>Number of Stones at Pretreatment</b>										
Single stone	46	88.5	33	66.0	69	76.7	15	65.2	163	75.8
Two stones	5	9.6	11	22.0	10	11.1	1	4.3	27	12.6
Three stones	1	1.9	4	8.0	7	7.8	4	17.4	16	7.4
Four stones	0	0.0	1	2.0	4	4.4	1	4.3	6	2.8
Five stones	0	0.0	1	2.0	0	0.0	1	4.3	2	0.9
Six stones	0	0.0	0	0.0	0	0.0	1	4.3	1	0.5
<b>TOTAL</b>	52	100.0	50	100.0	90	100.0	23	100.0	215	100.0

### 1.5.5 Number of LithoTron Procedures

A total of 224 lithotripsy procedures have been performed on the 215 subjects enrolled in the study. Two hundred and seven (207) study subjects (96.2%) were treated with a single lithotripsy procedure; seven subjects (3.3%) each were treated with two procedures and one subject (0.5%) was treated with the maximum three procedures allowed by the study protocol. The retreatment rate for the PMA study cohort is therefore 4.1%.

**Table 6: Total Number of LithoTron Procedures Performed**

	RLS, Portland, OR	Nebraska Methodist	Arlington Memorial, TX	Cape Girardeau, MO	TOTAL
<b>Total Stone Burden Treated</b>	N	N	N	N	N
Total patients treated	52	46	84	22	204
Patients re-enrolled for bilateral / ipsilateral disease	0	4	6	1	11
Total subjects treated	52	50	90	23	215
Subjects treated with a single procedure	51	48	86	22	207
Subjects treated with two procedures	1	2	3	1	7
Subjects treated with three procedures	0	0	1	0	1
<b>TOTAL PROCEDURES PERFORMED</b>	53	52	95	23	224

Of the 224 lithotripsy procedures performed, information regarding the lithotripsy procedure is available for 221 procedures. Three of the repeat procedures were scheduled or performed too close to the date of database closure for these data to be available.

### 1.5.6 Treatment Parameters

**Number of Shock Waves:** An average of 2482.7 shocks were delivered per treatment session, with 186 of 221 procedures (84.1%) performed with 2000-3000 shocks. No procedure exceeded the 3000 shock maximum mandated by the study protocol. All procedures were performed with ECG gated shock wave delivery, with the exception of one case that deviated from the protocol requirements for gated delivery. The study subject sustained no adverse effects as a result of non-gated shock wave delivery.

**Power Level Used:** The maximum kV setting per treatment ranged from 16 kV to 26 kV, with an average maximum power setting of 23.6 kV used per procedure. The majority of cases (n=110, 51.1%) were performed with a maximum power setting of 24 kV; two procedures (0.9%) were performed with a maximum power setting of 16 kV; five (2.3%) were performed at a maximum 18 kV; 27 (15.5%) at a maximum 20 kV; 54 (25.1%) were performed at a maximum of 22 kV; and 17 (12.0%) at a maximum 26 kV.

**Fluoroscopy Time:** The average fluoroscopy time for the 221 LithoTron procedures for which data is available is 6.5 minutes. The relative radiation exposure associated with fluoroscopy time for the LithoTron can be estimated by using the rem value (roentgen equivalent, man; 1 rem = 1 rad x relative biological effectiveness) calculated for a 5'10" 180 pound male, which is 1.53 rem / min. Therefore, a total fluoroscopy time of 6.5 minutes during a LithoTron procedure would result in a total radiation exposure of 9.94 rem. For comparative purposes, the fluoroscopy exposure with the original ESW lithotripsy system, the Dornier HM-3, was associated with a rem of 4.50/minute for a 5'10" 180 pound male, and fluoroscopy exposure of 6.5 minutes would translate to a total of 29.5 rem.

**Table 7: Number of Shock Waves, Power Setting, and Fluoroscopy Time**

Treatment Parameters	RLS, Portland, OR		Nebraska Methodist		Arlington Memorial, TX		Cape Girardeau, MO		TOTAL	
	Av.	Max.	Av.	Max.	Av.	Max.	Av.	Max.	Av.	Max.
Number of Shocks	2643.4	3000	2672.6	3000	2348.5	3000	2559.3	3000	2482.7	3000
Power setting (kV)	24.0	26	22.9	26	23.2	26	19.9	22	23.6	25
Fluoroscopy Time	3.2	8.4	7.0	22.3	5.9	19.4	6.1	33	5.5	33

**Anesthesia Use:** The majority of the 221 lithotripsy procedures for which data are available were performed without anesthesia and with the use of conscious IV sedation only (n=168, 76.0%). One subject received neither anesthesia nor analgesia. One investigational site performed the majority of procedures conducted under general anesthesia; 66% of the procedures performed at this site were conducted under general anesthesia.

**Table 8: Anesthesia / Analgesia Use during Lithotripsy**

Total Stone Burden Treated	RLS, Portland, OR		Nebraska Methodist		Arlington Memorial, TX		Cape Girardeau, MO		TOTAL	
	N	%	N	%	N	%	N	%	N	%
<b>General Anesthesia</b>	35	66.0	2	3.8	13	14.0	1	4.3	51	23.1
<b>IV Sedation</b>	17	32.1	49	94.2	80	86.0	22	95.7	168	76.0
<b>Spinal</b>	1	1.9	0	0.0	0	0.0	0	0.0	1	0.5
<b>None</b>	0	0.0	1	2.0	0	0.0	0	0.0	1	0.5
<b>TOTAL</b>	53	100.0	52	100.0	93	100.0	23	100.0	221	100.0

### 1.5.7 Summary of Effectiveness Results

The effectiveness of treatment with the HealthTronics LithoTron was based upon two criteria: 1) the presence and size of stone fragments retained at final assessment and 2) the need for any additional procedures required to achieve stone-free status. "Success" was defined as radiographic evidence of stone-free status or the presence of stone fragments small enough to pass spontaneously (less than or equal to 4 mm), and no additional surgical procedure(s) or treatment(s) with another approved ESW lithotripter or intracorporeal lithotripter performed following the lithotripsy treatment to achieve stone-free status. The study protocol called for patients to be fol-

lowed for up to three months following treatment; however, a final status could be assigned for any patient demonstrating a stone-free status or treatment failure at the one month follow up.

As previously discussed, 215 study subjects are included in the PMA study cohort, including 166 subjects who completed all protocol requirements and who were assigned a final status, and 40 subjects who continued to participate in the study and who were not yet eligible for assessment of final status. Seven subjects were lost to follow-up, and 2 subjects were withdrawn from the study.

Of the 166 subjects who completed final follow-up requirements, 143 (86.1%) were stone-free, or retained stone fragments 4 mm or less in size. These subjects were assigned a final status of "Success". Twenty-three (13.9%) had either undergone an additional procedure for the treatment of the calculi, or had retained fragments larger than 4 mm. These subjects were assigned a final status, "Failure".

**Table 9: Final Status: Effectiveness Results, by Study Site**

	RLS, Portland, OR	Nebraska Methodist	Arlington Memorial, TX	Cape Girardeau, MO	TOTAL
Final Status	N (%)	N (%)	N (%)	N (%)	N (%)
<b>SUCCESS</b>	<b>34 (79.1)</b>	<b>37 (77.1)</b>	<b>57 (95.0)</b>	<b>15 (100.0)</b>	<b>143 (86.1)</b>
Stone-free	30	23	44	12	109
Fragments 4 mm or less	4	14	13	3	34
<b>FAILURE</b>	<b>9 (20.9)</b>	<b>11 (22.9)</b>	<b>3 (5.0)</b>	<b>0 (0.0)</b>	<b>23 (13.9)</b>
Fragments > 4 mm	5	4	2	0	11
Additional procedure	4	7	1	0	12
<b>TOTAL</b>	<b>43</b>	<b>48</b>	<b>60</b>	<b>15</b>	<b>166 (100.0)</b>

Among the 166 subjects included in the study cohort analyzed for effectiveness parameters, the success rate varied across study sites, ranging from a success rate of 77.1% to 100.0%. This difference was found to be statistically significant, although explained by the differences among study sites.

**Table 10: Summary of Overall Success Rate by Site**

Site	Total Subjects	Total Successes	Success Rate (%)	Confidence Bounds for Success		Comparison to 0.65	
				Lower Limit	Upper Limit	Z-score	P-value
All sites combined	166	143	86.1	80.9	91.4	7.9	<0.001
RLS, Portland, OR	43	34	79.1	66.9	91.2	2.3	0.023
Nebraska Methodist	48	37	77.1	65.2	89.0	2.0	0.046
Arlington Memorial	60	57	95.0	89.5	100.5	10.7	<0.001
Cape Girardeau	15	15	100.0				

P-value for Fishers Exact Test for homogeneity of success by site equal to 0.007.

Two hundred and seven (207) study subjects (96.2%) were treated with a single lithotripsy procedure; seven subjects (3.3%) each were treated with two procedures and one subject (0.5%) was treated with the maximum three procedures allowed by the study protocol. This number is too small to allow any meaningful statistical analysis of the impact of retreatment on the overall success rate.

Analyses of stone-free status and success rates in the cohort of 166 subjects followed to final assessment showed the device to be equally effective for patients with large stone sizes, large stone burdens, and more than 3 stones at pretreatment.

Other pretreatment characteristics including gender, race, age, weight, pretreatment stone location, and history of prior lithotripsy treatment did not appear to affect the outcome of treatment.

### 1.5.8 Summary of Safety Results: Adverse Reactions and Complications

There were no unanticipated adverse events reported during the course of the study for any of the 215 subjects in the PMA study cohort. No subject required prolonged follow up due to a complication, and all complications resolved without permanent effects or serious clinical sequelae. Twenty-three of the 215 subjects experienced a total of 36 complications (16.7%), and an additional 3 complications were reported unrelated to the study procedure (1.4%). All complications and adverse events reported during the course of the study included those known and expected to be associated with ESW lithotripsy.

The following table summarizes the complications reported for all study subjects during the course of the study.

**Table 11: Complications Summary for All 215 Subjects in PMA Cohort**

Event	Number of Occurrences
Complications / Adverse Events related to lithotripsy procedure:	36 (16.7%)*
Severe pain, renal colic	11 (5.1%)
Steinstrasse or post-treatment obstruction	8 (3.7%)
Nausea, vomiting	6 (2.7%)
Mild / slight ecchymosis post treatment	5 (2.3%)
Infection or sepsis	3 (1.3%)
Urinary retention not associated with obstruction; resolved with bladder catheterization	3 (1.3%)
<b>Complications / Adverse Events not related to Lithotripsy procedure</b>	<b>3 (1.4%)*</b>
Transient ischemic attack, 2-3 weeks post treatment	1 (0.4%)
Acute myocardial infarction, CHF, 2.5 months post treatment	1 (0.4%)
Progressive coronary artery disease requiring CABG	1 (0.4%)

\*percentages for individual complications may not total to this number due to rounding to the nearest one-tenth of one percent

### 1.6 Conclusions Drawn from the Studies

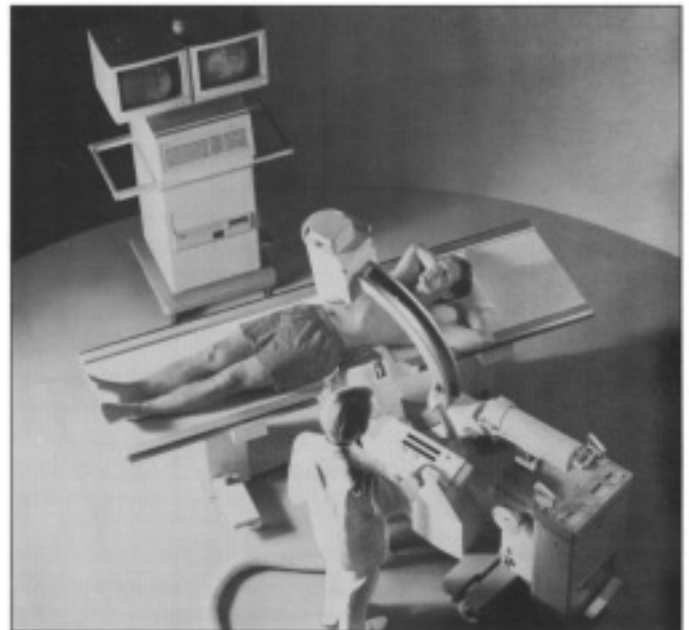
A multicenter clinical investigation was conducted at four sites within the United States to determine the safety and effectiveness of the HealthTronics LithoTron lithotripsy system to fragment renal and upper ureteral calculi. Clinical data were collected on a total of 215 subjects undergoing a total of 224 procedures. Study treatments were limited to a maximum of 3000

shocks at a maximum power setting of 26 kV, and the study protocol limited treatment to stones between 4 mm and 20 mm in maximum diameter. Distribution of stones treated according to location included 102 (44.6%) in the renal calyx, 13 (6.0%) in the upper calyx, 21 (9.8%) in the mid-calyx, and 62 (28.8%) in the lower calyx; 48 (22.3%) in the renal pelvis, 36 (16.7%) in the ureteropelvic junction, and 45 (20.9%) in the upper ureter.

One hundred and sixty-six (166) subjects were included in the analysis of effectiveness data. Successful outcome, defined as subjects being either stone-free or having fragments < 4 mm by three months post-treatment, was recorded for 86.1% of the 166 subjects. The success rate varied from 77.1% to 100.0% over the four study sites, but analyses of covariates revealed no other variables affecting outcome. Complications following treatment for all 215 study subjects included severe pain or renal colic (5.1%); steinstrasse or obstruction (3.7%); nausea and vomiting (2.7%); mild ecchymosis at the treatment site (2.3%); infection (1.3%); and urinary retention not associated with obstruction (1.3%). There were no cases of intrarenal or perirenal hematoma.

Twenty-seven subjects were included in a study cohort undergoing renal scans; complete pre- and post-treatment data are available for 24 of these subjects. Only one of these subjects had decreased renal function in the treated kidney following the procedure which was not associated with changes in BUN and creatinine.

The results of the laboratory, animal, and clinical studies of the HealthTronics LithoTron lithotripsy system provide reasonable assurance of safety and effectiveness of the device for the noninvasive fragmentation of urinary calculi of the kidneys and upper ureter.



For additional information on the LithoTron, please contact:



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