Summary of Safety and Effectiveness Data

I. General Information

Device Generic Name: Orthopedic Extracorporeal shock wave system

Device Trade Name: HealthTronics OssaTron®

Applicant Name: HealthTronics Surgical Services, Inc.
1841 W. Oak Parkway, Suite A
Marietta, Georgia 30062

Date of Panel Recommendation: None

Premarket Approval (PMA) Number: P990086/S3

Date of Notice of Approval to Applicant: March 14, 2003

This device was originally approved on October 12, 2000, for the limited indication for use for performing extracorporeal shock wave (ESW) treatment in patients with chronic proximal plantar fasciitis that has failed to respond to conservative treatment. Chronic proximal plantar fasciitis is defined as heel pain in the area of the insertion of the plantar fascia on the medial calcaneal tuberosity that has persisted for six months or more. The sponsor submitted this supplement to expand the clinical indications. The updated clinical data to support the expanded clinical indication for use for performing extracorporeal shock wave (ESW) treatment in patients with chronic lateral epicondylitis (tennis elbow) that has failed to respond to conservative treatment. The preclinical test data were presented in the original PMA application. For more information on the data which supported the original indication, the summary of safety and effectiveness data for the original PMA should be referenced. Written requests for copies of the summary of safety and effectiveness data can be obtained from the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD, 20852 under Docket # 01M-0271.

II. Indications for Use

The OssaTron is indicated for use for performing extracorporeal shock wave (ESW) treatment in patients with chronic lateral epicondylitis (tennis elbow) that has failed to respond to conservative treatment.

Chronic Lateral Epicondylitis is defined as lateral epicondylitis that has persisted for 6 months or more with a history of unsuccessful conservative treatment.

III. Contraindications

None known.

IV. Warnings and Precautions

Please refer to the device labeling for a list of warnings and precautions.

V. Device Description

Principles of Operation:

The HealthTronics OssaTron ESW system utilizes electrohydraulic "spark gap" technology to generate shock waves: that is, a spark plug with two opposing electrodes is positioned under water such that an electrical discharge is directed to the first focal point (F_1) of an ellipsoid reflector. The electrodes are connected to a capacitor, which is charged to the maximal voltage and then abruptly discharged. The underwater discharge causes the explosive formation of a plasma channel and evaporation of the water surrounding the electrodes. The spherical shock wave that is released expands in the surrounding water and is reflected by the walls of the ellipsoid reflector. Because of the geometric properties of an ellipsoid reflector, all shock waves generated at F_1 are reflected at its second focus (F_2). Therefore, during an ESW procedure, the device shock head and the patient are carefully aligned and positioned such that target area to be treated is located at F_2.

The OssaTron system incorporates all device components into a single transportable unit. The major components include the Therapy Head, the Control Cabinet, and the Control Console. A single-use electrode is placed in the Therapy Head for each treatment.

Therapy Head: The Therapy Head integrates the brass ellipsoid, the coupling membrane, the ELC 114 single-use electrode, the locating bow, and the dummy electrode. The brass ellipsoid houses the electrode, and reflects and focuses the shock waves. The therapy head is coupled to the patient via the water filled coupling membrane covering the ellipsoid. The ELC 114 electrode fits into the Therapy Head and extends into the brass ellipsoid. The electrode receives a high energy current from the Shock Wave Generator across the electrode tips, which produces the shock wave. A dummy electrode that is incapable of firing is provided for use only when transporting the device or when the device is stored. It is installed in the ellipsoid in the same fashion as an active electrode.

The Therapy Head includes an anti-collision device that halts shock wave generation and any mechanical movement of the device in the event of therapy head collision with the patient or table. A Locating Bow affixed to the Therapy Head allows for approximating the location of the shock wave therapy focus and aligning it with the desired target site during treatment. The Locating Bow can be rotated in 2 planes via the Control Console. The therapy head unit is connected to the Control Cabinet via an arm with 350-degree

rotation capability. The water supply and voltage cables attach to and rotate with the therapy arm.

Control Console: The Control Console includes a touch pad user interface with LED display and a hand held shock wave release button. The Control Console houses the two position key switch for turning power supply to the device on and off. Touch keys are provided for setting the desired shock wave energy (i.e., capacitor charge voltage in kV), and the frequency of shock wave delivery (Hz). The Control Console display shows these settings along with the total number of shocks delivered per procedure. Movement of the Therapy Head and the locating bow are also driven from the Control Console.

Control Cabinet: The Control Cabinet is the main body of the device. It connects to standard hospital main 120 VAC single phase electrical power supply. The Control Cabinet is mounted on a locking wheelbase and incorporates 6 subcomponents: the charging unit, the shock wave generator, the electric module, the water supply unit, the water valve unit, and the motor drive units.

The charging unit delivers the high voltage to the shock wave generator, which in turn triggers transformers that discharge high-voltage energy across the electrode tips. The electric module is where power connections are made; it supports and controls most of the high and low power supplies to the system components. The water supply unit contains a water tank, a safety thermostat for temperature control, a desalination unit to set conductivity, and a small circulation pump and provides conditioning, de-gassing and de-ionizing capabilities. The water valve unit allows pressure control for setting the coupling pressure during treatment, and for emptying and filling the therapy head following electrode change. The Motor drive units enable rotation of the Therapy Arm and Locating Bow, and movement of the Control Cabinet on the wheelbase.

VI. Adverse Effects of the Device on Health

A total 98 complications or adverse events were reported for the 225 treated subjects participating in this study. These 225 subjects received 273 active ESW treatments and 90 placebo treatments. No unanticipated adverse events or serious adverse events have occurred to date in any subject participating in this investigation.

The most commonly reported procedure or device related complications occurred during or shortly after the study procedure and included localized swelling, bruising or petechiae at the treatment site (n=19) and reactions to anesthetic agents (n=9). It is noted that all of the reactions to anesthetic agents occurred at a single site, and may have been related to the method of administering a regional block.

Table 1: All Complications or Adverse Events, All Study Procedures

	Active Treatment Group (n= 93)	Nonrandomized Group (n= 42)	Placebo Treatment Group (n= 90)	
Event	Total ESW Procedures (n= 131)[1]	Total ESW Procedures (n= 56)[2]	ESW Procedures (n= 86)[3]	Placebo Procedures (n= 90)
Procedure related				
Anesthesia	3 (2%)	1 (2%)	2 (2%)	3 (3%)
Local	8 (6%)	7 (13%)	1 (1%)	3 (3%)
Neuro	2 (2%)	0 (0%)	1 (1%)	0 (0%)
Pain	5 (4%)	0 (0%)	1 (1%)	0 (0%)
Subtotal	**18 (14%)**	**8 (14%)**	**5 (6%)**	**6 (7%)**
Not Procedure related				
Other	28 (21%)	4 (7%)	15 (17%)	14 (16%)
Tear	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Subtotal	**28 (21%)**	**4 (7%)**	**15 (17%)**	**14 (16%)**
TOTAL	**46 (35%)**	**12 (21%)**	**20 (23%)**	**20 (22%)**
Total events: Active treatment Placebo treatment	**78/273 (29%)**			**20/90 (22%)**

[1]Total ESW procedures include 93 primary procedures and 38 repeat treatments in 38 subjects who failed to meet success criteria at 8 weeks
[2]Total ESW procedures include 42 primary procedures and 14 repeat treatments in 13 subjects who failed to meet success criteria at 8 weeks
[3]A total of 86 placebo treatment patients underwent primary ESW treatment after failing to meet success criteria at 8 weeks post placebo treatment

Potential Adverse Effects

The potential adverse effects of ESW treatment with the OssaTron include:

- Pain during the ESW treatment;
- Localized numbness, tingling or decreased sensation in the foot or at the site of shock wave delivery;
- Local subcutaneous hematoma, bruising, or petechial bleeding in the foot/elbow or at the treatment site;
- Misdirection of ESW energy to a major nerve or blood vessel, resulting in injury;
- Anesthesia complications, including allergic reactions to local or regional anesthetic agents; and
- Rupture of plantar fascia.

VII. Alternate Practices or Procedures

Alternative therapies include:

- Rest
- Application of cold to the symptomatic region
- Non-steroidal anti-inflammatory medications
- Physical therapy

- Surgical treatments

VIII. Marketing History

The OssaTron has been marketed in the European Union, Switzerland, Iran, Saudi Arabia, Thailand, People's Republic of China, Australia and Taiwan. HealthTronics Surgical Services Inc. has placed approximately 56 OssaTron systems throughout the United States since PMA approval on October 12, 2000. The OssaTron system has never been withdrawn from marketing for any reason related to safety or effectiveness of the device.

IX. Summary of Preclinical Testing

A summary of the preclinical testing of the OssaTron may be found in SSED for the original PMA application.

X. Summary of Clinical Studies

A. Study Design

The clinical study of the OssaTron was a multicenter, randomized, sham controlled clinical trial to determine the safety and effectiveness of ESW treatment for chronic lateral epicondylitis. The study protocol was approved for a total enrollment of 250 subjects, including 100 subjects randomized to either active ESW treatment or sham treatment with the OssaTron and 50 nonrandomized subjects to allow each investigator to complete training requirements for performing the OssaTron procedure. The patients were followed up at 4 weeks and 8 weeks after the treatment, at the 8 weeks post treatment follow up a success / fail assignment was made based on three criteria: Investigator assessment of pain, subject self-assessment of pain and the use of pain medications.

A minimum of two investigators participated in the study at each site so that one investigator could serve as the blinded evaluator for baseline and post treatment follow up visits. The non-blinded investigator performed the study procedures as follows: Each study subject received a local anesthetic or a bier block prior to the study procedure. The affected arm was then draped from the view of the study subject. Each subject assigned to active treatment then underwent an ESW procedure with a total of 1500 shocks delivered at a power setting of 18kV. The average active treatment time was 20.5 minutes. For subjects assigned to sham treatment, a Styrofoam block was placed against the coupling membrane of the shock head to absorb the shock waves. A fluid-filled IV bag was then placed between the Styrofoam block and the subject's elbow to mimic the feel of the coupling membrane, and 1500 shocks were then delivered at 18kV.

B. Inclusion and Exclusion Criteria

Enrollment was limited to patients with the following criteria:

- History of chronic lateral epicondylitis persisting for at least 6 months;
- Failure to respond to at least 3 attempts at conservative treatment: one prior courses of non-invasive treatment, including physical therapy (e.g., stretching exercises) and the use of an orthotic device; and two prior course of pharmacological treatment such as NSAID's or cortisone injections;

- Investigator assessment of pain at the point of tenderness over the affected lateral epicondyle $\geq$5.0 on a 10 cm. Visual Analog Scale (VAS) and subject self-assessment of pain during activity $\geq$5.0 cm on a 10 cm VAS;
- Female subjects must not be pregnant;
- Other causes for elbow pain have been ruled out, such as vascular insufficiency or neuropathy of the upper extremities;
- Concomitant pathology has been ruled out, including severe osteoarthritis; rheumatoid arthritis, osteoporosis; metabolic disorders, malignancies; Paget's disease; an acute, subacute or chronic osteomyelitis or systemic infection; or fracture of the affected arm; and
- 21 years of age or older to assure all subjects would be skeletally mature.

Table 2
Demographics of Patients Enrolled in Lateral Epicondylitis Study

Characteristics	Active Treatment Patients (N=93)	Placebo Treatment Patients (N=90)
Age (years)		
Mean:	44	46
Range:	22-66	32-71
Gender		
Male:	46	41
Female:	47	49
Affected Arm		
Right:	64	69
Left:	29	21
Prior Therapies		
Cortisone	26	25
Injections:	15	12
NSAID's:	52	53
Both:	93	90
Physical Therapy:		
Symptom Duration (Days)		
Mean:	684.37	783.79
Range:	161-4920	126-8089

C. Evaluation Methods

1. Investigator Assessment:

The investigator blinded to randomization assignment assessed the subject's elbow pain by applying pressure on the affected lateral epicondyle. The investigators used a pressure sensor to record the amount of pressure applied to elicit the baseline response, and thereafter to apply the same amount of pressure at each follow up assessment to assure consistency in this evaluation. To be eligible for study participation, a subject must have reported a pain score of 5.0 or greater on a 10 cm VAS during the investigator's initial assessment.

2. Subject Self-Assessment of Pain:

Each subject was asked to provide a self-assessment of the amount of pain experienced in the affected elbow during activity, reported according to a 10 cm VAS. To meet study inclusion criteria, the subject's initial VAS must have been moderate to severe, i.e., 5.0 cm or greater on a 10 cm VAS.

D. Primary Effectiveness Measurements

The investigator who was blinded to randomization assignment determined the initial "success/fail" status for each study subject, who must meet all 3 of the following criteria in order for an overall status of "success" to be assigned at the 8 week follow-up visit.

- Investigator's assessment of elbow pain: A minimum 50% improvement over baseline, and a score no greater than 4.0 on VAS.
- Subject's self-assessment of pain with activity: A minimum 50% improvement over baseline with a score no greater than 4.0 on VAS.
- Use of pain medications: None or rare pain medication use at the 8 week visit. Rare medication use was defined as no more than three does of medication during the week immediately prior to being evaluated.

E. Data Analysis and Results

1. Study Enrollment

A total of 225 subjects were enrolled and treated, of these 42 subjects were nonrandomized subjects enrolled to accomplish investigator training requirements, leaving 183 randomized subjects.

Twenty-one of the 225 subjects (9.0%) withdrew from the study or were lost to follow up prior to the 8 week follow up visit. Three of the 21 subjects lost to follow-up were nonrandomized subjects, and the remaining 18 were randomized subjects. A total of 165 randomized and 39 nonrandomized subjects were assigned a "success/fail" status based on 8 week follow up findings.

The Table 3 summarizes the 8 week follow up status for all study subjects.

Table 3: Study Participation Status-Follow Up at 8 Weeks

	ACTIVE TREATMENT SUBJECTS	PLACEBO TREATMENT SUBJECTS	NONRANDOMIZED SUBJECTS	TOTAL
Total Subjects Treated	93	90	42	225
Subjects less than 8 Weeks since Treatm	0	0	0	0
Total Subjects Eligible for 8 Week Follow Up	93	90	42	225
Total Lost to Follow Up or Withdrawn	11	7	3	21
Total Subjects with 8 Week Status	82	83	39	204

2. Gender Analysis:

The study population was evenly divided between male and female. Subjects' ages at the time of study enrollment ranged from 22 years to 72 years, mean 45.7 years. Subjects were predominantly Caucasian.

3. Duration of Symptoms at Baseline:

The study protocol required that each subject must have had symptoms of chronic lateral epicondylitis for at least six months prior to study enrollment. The table above shows the mean duration of symptoms for subjects randomized to active treatment was 684 days (1.9 years), range 5 months to 13 years. For subjects randomized to placebo treatment, the mean duration of symptoms was 783.79 days (2.1 years), range 4 months to 22 years.

4. Effectiveness Analysis

a. Investigator Assessment:

The subjects randomized to active ESW treatment improved from a mean baseline VAS score of 7.73 to 3.64 at 8 weeks as shown in the table below. The median 8 week VAS score was 3.35. Forty-three of the 82 subjects (52.4%) met the success criteria for this parameter. The subjects randomized to placebo treatment improved from a mean baseline VAS score of 7.81 to 5.17 at 8 weeks. The median 8 week VAS score was 5.5. Twenty-six of the 83 subjects (31.3%) met the success criteria (minimum 50% improvement and VAS score of 4.0 or less) for this parameter. The difference between the active treatment and placebo group was statistically significant.

Table 4: Investigator Assessment – Baseline through 8 Weeks

		Baseline	4 Weeks	8 Weeks
Active ESW Treatment	*N*	93	84	82
	Mean (StD)	7.73(1.38)	5.02(2.73)	3.64(2.52)
	Median	7.6	5.3	3.35
	Range	4.7-10	0-10	0-9.7
Placebo Treatment	*N*	90	80	83
	Mean (StD)	7.81(1.50)	5.48(3.31)	5.17(3.13)
	Median	7.7	6.05	5.5
	Range	4.9-10	0-10	0-10

b. Subject Self-Assessment of Pain:

At each study visit subjects were asked to report the amount of pain experienced over the past week during activity. The subject recorded the response on the 10 cm VAS scale. The subjects randomized to active ESW treatment improved from a mean VAS baseline score of 7.37 to 3.53 at 8 weeks. The median 8 week VAS score was 2.9. Forty-eight of the 82 subjects (58.6%) met the success criteria (minimum 50% improvement and VAS score of 4.0 or less) for this parameter.

The subjects randomized to placebo treatment improved from a mean baseline VAS score of 7.76 to 4.37 at 8 weeks. The median 8 week VAS score was 4.2. Thirty-six of the 83 subjects (43.4%) met the success criteria (minimum 50% improvement and VAS score of 4.0 or less) for this parameter. The difference between the active treatment and placebo group was not statistically significant.

Table 5: Subject Self-Assessment – Baseline through 8 Weeks

		Baseline	4 Weeks	8 Weeks
Active ESW Treatment	*N*	93	84	82
	Mean (StD)	7.37(1.21)	4.53(2.26)	3.53(2.53)
	Median	7.4	4.75	2.9
	Range	4.6-10	0-9	0-8.4
Placebo Treatment	*N*	90	80	83
	Mean (StD)	7.76(1.31)	4.92(2.49)	4.37(2.58)
	Median	7.95	4.6	4.2
	Range	4.9-10	0-9.9	.02-9.7

c. Use of Pain Medications :

Each subject was asked to report the medications he or she was taking for pain at the initial study evaluation visit, and thereafter to keep track of all medications taken for pain throughout the course of study participation. The use of pain medications was then classified according to the frequency of use: chronic, frequent, occasional, rare or none. Exact definitions for these classifications were provided in the study protocol. In order to be assigned a status "success" for this parameter, the study protocol required that the

subject could be taking none or rare pain medications at the time of the 8 week follow up visit. The results are shown in the following table.

At baseline, 56/93 (60.2%) active treatment subjects were routinely taking medication for elbow pain. This had been reduced to 24/82 (29.1%) by the 8 week visit. Seventy-one of 82 subjects followed to 8 weeks (86.6%) met the success criteria for this parameter. At baseline, 56/90 (62.2%) placebo treatment subjects were routinely taking medication for elbow pain. This had been reduced to 26/83 (31.3%) by the 8 week visit. Sixty-one of 83 subjects followed to 8 weeks (73.5%) met the success criteria for this parameter. The difference between the active treatment and placebo group was not statistically significant.

Table 6: Medication Requirements – Baseline through 8 Weeks

	Baseline	Medication Requirements	4 Weeks	8 Weeks
Active ESW Treatment	None: 37 NSAID's: 46 Other: 10	None Rare Occasional Frequent Chronic	49 14 8 5 8	58 13 2 2 7
Placebo Treatment	None: 34 NSAID's: 52 Other: 4	None Rare Occasional Frequent Chronic	48 8 9 10 5	57 4 9 8 5

d. Overall Success/Fail Status:

As shown in Table 7, the results show a statistically significant difference between the OssaTron and placebo groups for the composite endpoint at 8 weeks. Of the 82 subjects followed to 8 weeks after an active OssaTron ESW treatment, 33 (40%) met all 3 success criteria, compared to 20 of 83 placebo treated subjects (24 %) who met all 3 criteria, a difference that is significant at a *p* level of 0.043.

The majority of the treatment effect was observed in the blinded evaluator's assessment of elbow pain. The subjects' self-assessments of pain with activity did not indicate large treatment differences through 8 weeks, and were not statistically different. The active treatment subjects showed greater improvement use of pain medications and in SF-36 scores than did placebo subjects. However, none of the primary or secondary outcome measurements demonstrated statistically significant treatment differences.

Table 7:
8 Week Response to Treatment-All Components of Success, All Subjects Randomized

MEASURE	ACTIVE ESW TREATMENT (N=93)	PLACEBO TREATMENT (N=90)	P VALUE
Investigator Assessment	45 (48%)	26 (29%)	0.007
Self Assessment, Pain during activity	51 (55%)	37 (41%)	0.063
Medication Use	75 (81%)	63 (70%)	0.095
Composite: All 3 Components	33 (35%)	20 (22%)	0.043

5. Primary Safety Measurements

As shown in Table 1, a total of 98 complications or adverse events were reported for the 225 treated subjects participating in this study. These 225 subjects received 273 active ESW treatments and 90 placebo treatments. No unanticipated adverse events or serious adverse events have occurred to date in any subject participating in this investigation.

The most commonly reported procedure or device related complications occurred during or shortly after the study procedure and included localized swelling, bruising or petechiae at the treatment site (n=19) and reactions to anesthetic agents (n=9). It is noted that all of the reactions to anesthetic agents occurred at a single site, and may have been related to the method of administering a regional block.

XI. Panel Recommendation

In accordance with the provisions of Section 515(c)(2) of the Act as amended by the Safe Medical Devices Act of 1990, this PMA supplement was not referred to the Orthopedics Devices Panel or the General Surgery Devices Panel, FDA advisory committees, because the information in the PMA substantially duplicated information previously reviewed by this panel.

XII. FDA Decision

The clinical study results provide reasonable assurance that use of the HealthTronics OssaTron for the treatment of patients with chronic lateral epicondylitis is a safe and effective alternative for patients who have a history of unsuccessful conservative treatment.

In addition, the applicant's manufacturing facility was inspected and found to be in compliance with the Quality Systems Regulation (21 CFR 820).

CDRH issued an approval order on March 14, 2003.

XIII. Approval Specifications

Directions for use: See labeling

Hazard to Health from Use of the Device: see Warnings, Precautions, and Adverse Events sections in the labeling.

Conditions of Approval: See approval order