Report on the Use of Extracorporeal Shockwave Therapy in Orthopaedic Conditions

Prepared for the
College of Massage Therapists of British Columbia
by
Joseph Anthony, Ph.D. P.T.
Extracorporeal Shockwave Therapy

Executive Summary

Extracorporeal Shockwave Therapy (ESWT or shockwave), is a pressure wave applied externally to the body, leading to energy transmission within and absorption by the body tissues. Shockwaves are generated in two forms – focussed and radial. These forms differ in physical characteristics, energy delivered, and method of production. When used in the management of orthopaedic conditions, shockwave is thought to have two main effects – mechanical (such as breaking up calcification) and biological (causing changes in cell behaviour). The outcome is dependent on the energy delivered. The exact details of the way by which shockwave promotes tissue healing are not yet clear, however it is generally held that shockwave energy absorption causes mechanotransduction (physical forces across a cell membrane leading to chemical changes within the cell), leading to a variety of cell signal transduction events, eventually causing alterations in cellular gene expression and behaviour. The ultimate (and anticipated) effect is tissue healing. Several contraindications (both absolute and relative) have been identified as situations or locations where shockwave should not be applied. Licensing bodies in several jurisdictions (Canada, US, UK, Europe, and others.) have granted approval for the use of shockwave in the management of certain orthopaedic conditions, usually related to chronic inflammation (e.g. fasciitis, or tendinopathy). The literature cites work being done in the treatment of other conditions, with some indication of effectiveness. The strongest evidence in support of shockwave appears to be in the management of plantar fasciitis, lateral epicondylalgia of the elbow, tendinopathy of the Achilles and Patellar tendons, and some other conditions (see text). Adverse reactions to shockwave have been reported (see text), but are usually limited in nature when the device is applied appropriately. Shockwave devices are classified as Class II by Health Canada, requiring a license to import and sell. Shockwave is considered to be safe when used appropriately, in the absence of contraindications.
Overview of Shockwave Therapy

1. What is Shockwave?

- Shockwave, or Extracorporeal Shockwave Therapy (ESWT) is a transient acoustic (sound) energy pulse or wave - a mechanical pressure disturbance that travels rapidly in three-dimensions.\(^1\) A shockwave is an “abrupt, nearly discontinuous change in pressure, having a velocity that is higher than the speed of sound in the medium through which it propagates.\(^1\)

- Being an acoustic wave, a shockwave requires a medium for travel, travels at different speeds in media of differing densities (travelling faster in denser tissue), and is transmitted, reflected and refracted at tissue interfaces where tissues of different acoustic impedances meet.\(^1\)

- Potential uses of shockwave are determined by the energy delivered.

- High-energy shockwave (> 0.5 J/mm\(^2\)) may be used in the management of calculi (lithotripsy) in the urinary, renal, biliary, and salivary systems. This application is a proposed restricted activity in BC according to the Health Professions General Regulation, Consultation Draft March 19, 2010, and may only be applied by registered physicians.\(^2\)

- Further discussion in this paper will be limited to devices delivering energy appropriate for the treatment of orthopaedic disorders (generally < ~0.6 mJ/mm\(^2\)).

- There are two forms of shockwave – focussed and radial. These forms differ in physical characteristics and method of production. Some authors argue that radial shockwave is not true shockwave, and should more accurately be called “radial pressure wave” therapy.

- Focussed shockwaves affect a small, precisely defined area; radial shockwaves affect a larger, more diffuse area. Focussed shockwaves may travel more deeply than radial shockwaves. Focussed shockwaves carry more energy than radial shockwaves. (Fig. 1 and Appendix 1).

- Focussed shockwave devices tend to be used with soft-tissue imaging for accurate “aiming” of the shockwave, and (because of this requirement) are mostly used by physicians.

- Being an acoustic wave, a shockwave requires a medium for travel, travels at different speeds in media of differing densities (travelling faster in denser tissue), and is transmitted, reflected and refracted at tissue interfaces where tissues of different acoustic impedances meet.\(^1\)

- Shockwave energy is ultimately absorbed by tissue, where (depending on energy delivered) it may induce physical changes in tissue (destruction, e.g. cracking calculi), or changes in cellular function leading to a tissue response (stimulation of healing).

\(^1\) https://physics.info/shock/ [accessed January 14th, 2018]

\(^2\) https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/professional-regulation/scope-of-practice-reform
• Both Shockwave and the older, more familiar therapeutic modality - therapeutic ultrasound - are acoustic pressure waves, but with different characteristics of the pressure wave. For example, shockwaves generally exhibit a sharp rise in pressure (~ 50 – 100 MPa), temperature and density, over a very short period of time (~ 10 ns) followed by a longer period of negative pressure, whereas ultrasound waves cause a smaller rise in pressure, (perhaps 0.05 MPa)(2) and more uniform compressions and rarefactions of the media through which they travel. Shockwaves exhibit lower, mixed frequencies and higher intensity than ultrasound waves, which are usually a single, fixed frequency for any application. These characteristics result in less shockwave energy loss (absorption) in tissues; consequently the shockwave travels deeper into tissues than therapeutic ultrasound.(3) Depth of penetration varies according to the device, but is in the order of 40 - 60 mm or more – deeper than therapeutic ultrasound. (4-6)

• The International Society for Medical Shockwave Treatment3 describes the following characteristics of both focussed and radial shockwaves:4
  Focussed shockwaves are described as:
  o a single pulse with a wide frequency range (from approx. 150 kHz up to 100 MHz),
    high pressure amplitude (up to 150 MPa), low tensile wave (up to -25 MPa), small pulse width and a short rise time of up to a few hundred nanoseconds.
  Radial shockwaves are described as:
    • “ordinary” sound waves with pressures of up to 30 MPa and much higher rise times of about 3 μs.
• Further details of the comparison between radial and focussed shockwaves are given in Appendix 1.
• Both focussed and radial shockwaves are used (with appropriate energy parameters) in the management of soft tissue disorders. See below for further information.

3 The European Society for Musculoskeletal Shockwave Therapy (ESMST) was established on 12 September 1997 in Vienna, Austria. This became the International Society for Musculoskeletal Shockwave therapy in 1999. The ISMST is a not-for-profit medical and scientific association, the purpose of which is to support the development and conduct of credible research into extracorporeal shockwave therapy, and to improve the education of shockwave therapy users. (www.shockwavetherapy.org)
Focused shockwaves (fESWT) are produced using one of three techniques: electrohydraulic; electromagnetic; piezoelectric. A description of these techniques may be found in Ogden (1) or Gerdesmeyer (7).

Radial shockwaves (rESWT) are generated in two main ways: pneumatically, or by an alternating magnetic field driving a projectile down a tube located inside the hand piece. (7,8)

In a systematic review of 106 studies in the PEDro database, Schmitz and co-authors conclude “There is no scientific evidence in favor of either rESWT or fESWT with respect to treatment outcome”. (8)

Two clinical studies directly compared differences in therapeutic outcome between focussed and radial shockwave in the treatment of orthopaedic disorders, and observed no differences in therapeutic outcome (when used appropriately). (9)

2. Uses of Shockwave

High-energy (focussed) shockwave for orthopaedic conditions has been characterised as having energy of up to 0.6 ml/mm² or more, and may be used to treat disorders of bone, and soft tissue calcifications. High-energy focussed shockwave used for orthopaedic conditions such as bony non-union usually requires anaesthesia and physician supervision (see Figure 2). (10-12)

---

5 www.pedro.org.au
• Other soft-tissue conditions may be treated using either low-energy or medium-energy focussed or radial shockwaves, without the requirement for imaging or anaesthesia.

Fig. 2. The picture shows the positioning of the patient during the shockwave treatment of a supracondylar humerus non-union under X-ray control by the C-arm. (Schaden et al, 2015) Image © Elsevier

• There appears to be no clear consensus in the literature regarding the definition of ‘high’ and ‘low’ energy shockwave in orthopaedics.

  o In 1998 Rompe and coworkers defined focussed shockwaves as low-energy (up to 0.08 ml/mm² at second focal point), medium-energy (up to 0.28 ml/mm²) and high-energy (greater than 0.6 ml/mm²)(13).
  o Porter and Shadbolt (2005)(14) suggest shockwave may be classified as high-energy or low-energy depending on whether the energy flux density (EFD) is greater or less than 0.12 ml/mm².
  o In her 2014 review Speed quotes a general guideline, from an orthopaedic conference, as low energy shockwave having an energy flux density of ≤0.12
ml/mm², and high energy having an EFD of >0.12 ml/mm². (15)
  o Lohrer cites two sources that identify low energy as < 0.08 ml/mm², medium energy
    as 0.08 – 0.28 ml/mm² and high energy as > 0.28 ml/mm². (6)
• Rompe (1998) suggests energy flux densities up to 0.28 ml/mm² as being safe for tendon,
  whereas marked damage to tendon was observed at energy flux density of 0.60 
  ml/mm². (13)
• Kaulesar Sukul et al (1993) observed major gross cortical bone changes at 0.6 ml/mm² (at 
  10,000 shocks). (16)
• Clement & Taunton (2004) suggest the following guidelines (11):
  
> High energy — energy-flux density > 0.60 ml/mm²
> Low energy — energy-flux density 0.04-0.28 ml/mm²

• Lohrer states, “With the exception of bone related conditions, modern musculoskeletal
  ESWT is performed with energy below 0.28 ml/mm² and without anaesthesia”. (6)
• In an earlier article, Cheing states, “According to our experience, patients request no local
  anaesthesia when the dosage of ESWT is below 0.37 ml/mm²”. (10)
• The International Society for Medical Shockwave Treatment Consensus Statement on 
  ESWT Indications and Contraindications (2016, attached) recommends the application of 
  focussed shockwave therapy (seemingly regardless of energy delivered) be limited to 
  trained physicians, while the Consensus Statement Terms and Definitions (2017, attached) 
  proposes that trained nurses and physical therapists may administer radial shockwave 
  after previous diagnosis by physician.

> “Only a qualified physician (certified by National or International Societies) may
  use focused shockwave therapy to treat pathologies, which have been determined 
  by diagnostic testing.”

Consensus Statement on ESWT Indications and Contraindications (2016)
International Society for Medical Shockwave Therapy

> “Trained Physicians; after previous diagnosis of physician trained, nurses or
  physiotherapist may perform Radial Pressure Waves.”

ISMST Consensus Statement Terms and Definitions (2017)
International Society for Medical Shockwave Therapy

3. What are the effects of shockwave in the tissue? (Mechanism of action)
It has been proposed that shockwave passing through tissue produces physiological effects in four 
phases, via both direct (mechanical) and indirect (chemical/biological) mechanisms: (i) direct 
(mechanical) effect, (ii) physical-chemical phase – a change in membrane permeability in response 
to cavitation, leading to movement of ions across the membrane, (iii) chemical phase – 
intracellular reaction and molecular changes, and (iv) biological phase leading to physiological 
changes. For further details of these phases, please see Chieng (2003). (10)
Shockwave at sufficient intensity (e.g. 0.6 mJ/mm$^2$) will disrupt calcifications within tendons (4), or successfully treat non-union of long bone fractures (12), however, these applications require analgesia or anaesthesia, and are performed by physicians, with imaging technology such as ultrasound imaging or fluoroscopy. (Figure 2)

Lower energy shockwave is used to promote tissue healing. Dissipation (i.e. absorption by the tissues) of the energy of the shockwave is thought to be responsible for physical and subsequent physiological (i.e. therapeutic) effects. The exact mechanism by which shockwave is able to cause biological changes in tissues is still being investigated. Current understanding is that shockwaves cause:

(i) mechanical deformation of cells, and
(ii) possible tissue destruction at the cellular level.

The pressure distribution, energy density and total acoustic energy are the most important physical parameters for the treatment of soft tissue. (1) Physical forces result in a mechanical effect on cells, leading to a biological response, namely mechanotransduction – the signalling of cellular events in response to mechanical forces on the cell. The cell wall is deformed by the shockwave, and structures within the cell (cytoskeleton) register that deformation. This results in molecular changes within the cell leading to such events as a change in gene transcription (expression), or protein production, causing a change in cell behaviour, such as increased likelihood of survival if damaged. That is, deformation of cells leads, via mechanotransduction, to activation of cell membrane ion channels, and changes in cell signalling pathways leading to alterations in gene expression and cellular behaviour. (reviewed in Dietz-Laursonn et al(17); Zelle et al(18); Romeo et al (19))

The principle mechanical effects of shockwave are:

(i) a pressure wave resulting from the rapid rise time of the initial phase of the shockwave, and
(ii) the rapid negative pressure phase (the tensile phase) causing tissue cavitation, which is the formation of tiny (10$^{-6}$ m) gas bubbles in the tissues. This effect occurs in both focussed and radial shockwave. (20)

The gas bubbles collapse at the end of the tensile phase, causing shear forces, potentially leading to controlled damage within the tissues. (1) Cellular damage results in release of free radicals, which stimulate an inflammatory response, which may lead to tissue healing. For reference, it is believed that cavitation bubbles are also caused by the application of therapeutic ultrasound, and these are understood to be one of the mechanisms by which therapeutic ultrasound has a beneficial effect in tissue. Destruction of calcifications, pain relief and mechanotransduction-initiated tissue regeneration and remodelling of tendon are considered to be the most important working mechanisms in tissue healing. (9)
Proposed therapeutic effects

Mechanical
Treatment (destruction?) of calcifications within tendons (see, e.g. (21) (22) (23))

Cell signalling
Stimulate extracellular matrix (ECM)-binding proteins and the nucleus via the cytoskeleton (e.g. (24))
Activation of bioactive molecules such as G proteins and extracellular integrin, inducing an angiogenic response (25)
Increase local blood flow (26)
Induce reversible conformational and possibly orientation changes in collagen (27)
Stimulation of inflammatory response to promote tissue healing (release of Substance P and prostaglandin E2 (28), Nitric Oxide (29), TGF β1 (29), VEGF (30), possibly other pro-inflammatory cytokines)
Transient analgesia (direct effect on nerve conduction, secondary effects)
Apoptosis (cell death, if dose is too high, e.g > 0.16 mJ/mm2) (31)
Possible protection from cell apoptosis at a low dose (e.g. up to 0.13 mJ/mm2) – e.g. chondrocytes in osteoarthritis, resulting in less cartilage destruction (32) (31) (33)

4. How is shockwave applied to a client?
Shockwave therapy is applied using a hand-held applicator, connected by an electrical cable to a control unit that operates on mains voltage (110V in Canada). Applicator shape and size varies according to manufacturer, intended use, and whether the shockwave is radial or focussed. (e.g. see Figs 3 and 4).

Fig. 3. Focussed shockwave applicator. Image © DJO Global
5. How is tissue targeted for treatment?
Shockwave therapy must be accurately delivered to the structure requiring treatment, while avoiding structures that could be potentially damaged by shockwave, such as major blood vessels or major nerves. The application of low energy shockwave requires sensitive palpation by the clinician, and patient feedback to accurately target the structure for treatment. In low-energy applications, there is no requirement for use of imaging techniques (ultrasound or fluoroscopy) to localize the structure for treatment, such as would be employed when using high-energy shockwave (See Fig. 2). Detailed knowledge of anatomy is essential to ensure only appropriate structures are targeted, and that tissue that may be damaged by shockwave is avoided.

Licensing authorities approval for the use of shockwave as a therapeutic modality.

Health Canada regulates the safety, effectiveness and quality of medical devices imported into and sold in Canada. Medical Devices in Canada are classified by Health Canada into four classes, using a set of sixteen rules in Schedule 1 (Section 6) of the Medical Devices Regulations (http://laws-lois.justice.gc.ca/eng/regulations/SOR-98-282/page-11.html#h-68) Class I is the lowest risk category, and Class IV the highest. Devices are classified according to level of risk as determined by such factors as degree of invasiveness, hazards of energy transmission, and the potential consequences to the patient in case of device malfunction or failure.

Class II, III, and IV devices sold in Canada require a product-specific Canadian Medical Device License. Devices are licensed for their specific intended use/purpose as determined by the legal manufacturer of the device. Low-energy shockwave devices are generally classified as Class II
devices, although ultimately the classification depends on the specific intended use of the product. A distributor of Class II and above medical devices cannot legally sell an unlicensed device in Canada.

“26 Subject to section 37, no person shall import or sell a Class II, III or IV medical device unless the manufacturer of the device holds a licence in respect of that device or, if the medical device has been subjected to a change described in section 34, an amended medical device licence.”  

The decision to sell a licensed Class II, or above, device to a registered professional seems to be based on the manufacturer's and retailer's perception of the potential for harm to the public, although this does seem to be a grey area.

Appendix 2 gives the results of a search of the database for shockwave devices licensed in Canada, and the licensing information also gives an indication of the proposed conditions amenable to treatment.
Indications for shockwave therapy

Proposed current indications for shockwave therapy given here were determined in three ways:

(i) Device licensing documentation in three jurisdictions was reviewed (see Appendix 2 for details)
(ii) Recommendations from the International Society for Shockwave Therapy were accessed (see below)
(iii) A (non-exhaustive) review of the peer-reviewed literature was conducted to identify the list of conditions reported as being amenable to treatment by shockwave. The literature reports a more extensive list of conditions than the list of conditions approved by licensing authorities, however the ISMST list seems to neatly represent the current state of work in this area.

Recommendations from the International Society for Medical Shockwave Treatment

The international Society for Medical Shockwave Treatment lists the following superficial soft tissue conditions as treatable (or for consideration for treatment) with shockwave therapy.6 Note four levels of evidence supporting these recommendations: approved standard indications; common empirically-tested clinical uses; exceptional indications – expert indications; and experimental indications.

Indications
1. Approved standard indications
   1.1. Chronic Tendinopathies
   1.1.1. Calcifying tendinopathy of the shoulder
   1.1.2. Lateral epicondylopathy of the elbow (tennis elbow)
   1.1.3. Greater trochanter pain syndrome
   1.1.4. Patellar tendinopathy
   1.1.5. Achilles tendinopathy
   1.1.6. Plantar fasciitis, with or without heel spur
   1.2. Bone Pathologies*
   1.2.1. Delayed bone healing
   1.2.2. Bone Non-Union (pseudarthroses)
   1.2.3. Stress fracture
   1.2.4. Avascular bone necrosis without articular derangement
   1.2.5. Osteochondritis Dissecans (OCD) without articular derangement
   1.3. Skin Pathologies
   1.3.1. Delayed or non-healing wounds
   1.3.2. Skin ulcers
   1.3.3. Non-circumferential burn wounds

---

* highlighted conditions are outside the scope of practice for RMTs
2. Common empirically-tested clinical uses
   2.1. Tendinopathies
       2.1.1. Rotator cuff tendinopathy without calcification
       2.1.2. Medial epicondylopathy of the elbow
       2.1.3. Adductor tendinopathy syndrome
       2.1.4. Pes-Anserinus tendinopathy syndrome
       2.1.5. Peroneal tendinopathy
       2.1.6. Foot and ankle tendinopathies
   2.2. Bone Pathologies
       2.2.1. Bone marrow edema
       2.2.2. Osgood Schlatter disease: Apophysitis of the anterior tibial tubercle
       2.2.3. Tibial stress syndrome (shin splint)
   2.3. Muscle Pathologies
       2.3.1. Myofascial Syndrome
       2.3.2. Muscle sprain without discontinuity
   2.4. Skin Pathologies
       2.4.1. Cellulite

3. Exceptional indications – expert indications
   3.1. Musculoskeletal pathologies
       3.1.1. Osteoarthritis
       3.1.2. Dupuytren disease
       3.1.3. Plantar fibromatosis (Ledderhose disease)
       3.1.4. De Quervain disease
       3.1.5. Trigger finger
   3.2. Neurological pathologies
       3.2.1. Spasticity
       3.2.2. Polyneuropathy
       3.2.3. Carpal Tunnel Syndrome
   3.3. Urologic pathologies
       3.3.1. Pelvic chronic pain syndrome (abacterial prostatitis)
       3.3.2. Erectile dysfunction
       3.3.3. Peyronie disease
   3.4. Others
       3.4.1. Lymphedema

4. Experimental Indications
   4.1. Heart Muscle Ischemia
   4.2. Peripheral nerve lesions
   4.3. Pathologies of the spinal cord and brain
   4.4. Skin calcinosis
   4.5. Periodontal disease
   4.6. Jawbone pathologies
   4.7. Complex Regional Pain Syndrome (CRPS)
   4.8. Osteoporosis
Contraindications for shockwave therapy

Both Health Canada and the US FDA license shockwave devices for application in specific soft tissue conditions. Part of that licensing process in the US consists of a determination of the safety of the device. Consequently, the US licensing documents list contraindications for application. The US FDA lists contraindications for the application of shockwave as:

1. Over or near bone growth centre until bone growth is complete 
2. When a malignant disease is known to be present in or near the treatment area 
3. Infection in the area to be treated 
4. Over ischemic tissue in individuals with vascular disease 
5. Patient has a coagulation disorder or if taking anti-coagulant medications 
6. Patient has a prosthetic device in the area to be treated.

The US FDA does not differentiate between focussed and radial shockwave when listing these contraindications – both device types list similar contraindications in the licensing documents (see attached).

The International Society for Musculoskeletal Shockwave Therapy gives the following list of contraindications.

Radial and focused waves with low energy
1.1. Malignant tumour in the treatment area (not as underlying disease)  
1.2. Fetus in the treatment area

2. High energy focused waves
2.1. Lung tissue in the treatment area  
2.2. Malignant tumour in the treatment area (not as underlying disease)  
2.3. Epiphyseal plate in the treatment area  
2.4. Brain or Spine in the treatment area  
2.5. Severe coagulopathy  
2.6. Fetus in the treatment area

To place these contraindications into context, the table below compares contraindications for the use of shockwave therapy with contraindications for the use of two other common therapeutic modalities - Therapeutic Ultrasound and Low Level Laser. These two modalities were chosen (i) because of both Ultrasound and Shockwave are physical pressure waves, and may be used to treat similar conditions, and (ii) both Shockwave and LASER may be used to treat similar conditions,

---

and both modalities are thought to produce beneficial effects by way of cell signal transduction. (source of ultrasound and LASER information – Physiotherapy Canada. (34)\(^8\)

In the table below, symbols are used to represent the terms “contraindication”, “precaution”, and “safe” using the following definitions.

Table 1 Legend

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>The modality should NOT be used to treat in the presence of this condition or in this body location.</td>
</tr>
<tr>
<td>P</td>
<td>Experienced clinicians may elect to treat using this modality for this condition/location with caution (e.g., at lower intensities and/or with closer monitoring).</td>
</tr>
<tr>
<td>S</td>
<td>Application of the modality for this condition/scenario or at this body location is NOT contraindicated.</td>
</tr>
</tbody>
</table>

---

\(^8\) This document synthesizes a consensus among North American and international experts, which was established by surveying experts within Canada and the United States, reviewing textbook resources, and interpreting guidelines from the Chartered Society of Physiotherapy in the United Kingdom and the Australian Physiotherapy Association.
Table 1 Summary of Contraindications for the Application of Shockwave Therapy

<table>
<thead>
<tr>
<th>Contraindication</th>
<th>Shockwave</th>
<th>Ultrasound</th>
<th>Low-level Laser</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over or near bone growth centre until bone growth is complete</td>
<td><img src="image" alt="C" /></td>
<td><img src="image" alt="P" /></td>
<td><img src="image" alt="P" /></td>
</tr>
<tr>
<td>Over or near malignancy</td>
<td><img src="image" alt="C" /></td>
<td><img src="image" alt="C" /></td>
<td><img src="image" alt="C" /></td>
</tr>
<tr>
<td>Infection in the area to be treated</td>
<td><img src="image" alt="C" /></td>
<td><img src="image" alt="P" /></td>
<td><img src="image" alt="C" /></td>
</tr>
<tr>
<td>Over ischaemic tissue in individuals with vascular disease</td>
<td><img src="image" alt="C" /></td>
<td><img src="image" alt="C" /></td>
<td><img src="image" alt="S" /></td>
</tr>
<tr>
<td>Patient has coagulopathy or is taking anti-coagulant medications</td>
<td><img src="image" alt="C" /></td>
<td><img src="image" alt="C" /></td>
<td><img src="image" alt="C" /></td>
</tr>
<tr>
<td>Over a prosthetic device</td>
<td><img src="image" alt="C" /></td>
<td><img src="image" alt="C" /></td>
<td><img src="image" alt="S" /></td>
</tr>
<tr>
<td>Fetus in the treatment area</td>
<td><img src="image" alt="C" /></td>
<td><img src="image" alt="C" /></td>
<td><img src="image" alt="C" /></td>
</tr>
</tbody>
</table>

- **Contraindicated if infection is with mycobacterium tuberculosis, or virulent bacteria. Precaution (i.e. not contraindication) in persons with non-virulent bacterial infection and immune compromise.**
Risk for Harm Caused by Shockwave Therapy

Adverse Effects Reported
Note: adverse effects have been reported in cases where shockwave was appropriately applied – that is, in the absence of contraindications, and to appropriate tissue.

US FDA reports recorded adverse effects in its “Summary of Safety and Effectiveness” documents for specific devices. The following reported and potential adverse effects have been collated from the Summary of Safety and Effectiveness documents (see attached). See below for discussion of incidence of adverse effects.

Reported Adverse Effects in US FDA “Summary of Safety and Effectiveness documents.
  - Pain or discomfort during treatment
  - Pain post-treatment
  - Skin reddening
  - Swelling and pain post-treatment
  - Numbness post-treatment
  - Mild local swelling
  - Ecchymosis (bruising)
  - Hyperesthesia, neuralgia, paresthesia
  - Nausea
  - Myalgia
  - Joint disorder
  - Pallor
  - Dizziness
  - Hypertonia
  - Tremor
  - Vasodilation
  - Application site reaction
  - Sweating

Potential Adverse effects in US FDA “Summary of Safety and Effectiveness documents
  - Bruising
  - Rupture of the plantar fascia
  - Temporary or permanent damage to blood vessels
  - Petechia (haemorrhage)
  - Haematoma
  - Tendon rupture
Misdirection of energy
Rare allergic or sensitivity reaction to the Latex membrane or to the coupling solution applied to the skin during treatment

A further review of the literature indicates that the above adverse reactions have been reported in various studies. In addition to those adverse effects listed above, Ogden states “There is no question that lung tissue is highly susceptible to disruption by shock waves, minimizing the applicability to thoracic disorders (stress fractures of the first rib). Such susceptibility also necessitates specific targeting of shock waves to avoid lung tissue when treating shoulder disorders”. (35) In vitro studies have shown serious adverse effects on embryos from the application of both focussed and radial shockwave. (e.g. (36))

Incidence of Adverse Effects
In a 2017 paper, Roerdink et al. (37) report on the results of a systematic review of complications of shockwave therapy (ESWT) in the treatment of plantar fasciitis. Thirty-nine studies published between 2005 and 2016 were included in the review, covering a total of 2493 patients and almost 6500 shockwave treatment sessions. Energy flux densities reported were between 0.01mJ/mm² (low) and 0.64 mJ/mm² (high for orthopaedic treatments). The review included studies using both focussed shockwave and radial shockwave. Average follow-up was 14.7 months. The report distinguishes between complications, and side effects.

Complications
Two complications (0.09% of study population) occurred in two different studies: one patient developed precordial chest pain and an ECG showed partial bundle branch block; a second patient developed a superficial skin infection at the site of a tibial nerve block.

Side Effects
403 patients (20.7% of the 1946 patients in studies reporting incidence of side-effects) had side effects from shockwave – pain during treatment (11.6%), transient red skin after treatment (12.8%), dysesthesia (n = 9), swelling (n = 9), ecchymosis (n = 3), throbbing sensation (n = 2) and pain after treatment for longer than one week (n = 2). The authors conclude “This study showed that both low- and high-dose ESWT are safe treatments for PF [plantar fasciitis].”

Risk of unexpected adverse outcome
There are four ways by which any electrophysical modality may cause unanticipated harm:

(i) application in the presence of a contraindication (not reported by client, or unknown by client – e.g. pregnancy, malignancy);

(ii) inappropriate dose for the condition/ client at the time of treatment;
(iii) inappropriate body area/ tissue; and
(iv) faulty equipment. With the exception of faulty equipment, the likelihood of which may be diminished by regular equipment servicing, treatment in the presence of contraindication, or at an inappropriate dose, or over inappropriate body tissue would be considered an inappropriate application.

**Inappropriate application** – contraindications present, inappropriate location (e.g. undeclared/unknown pregnancy or malignancy), inappropriate dose, faulty equipment = RISK of harm

**Appropriate application** – no contraindications, appropriate area of body, appropriate dosage, equipment functioning correctly = LOW risk of harm.

In general, shockwave is believed to be safe when appropriately applied. A systematic review on the efficacy and safety of appropriately applied shockwave therapy for orthopaedic conditions concludes:

“The safety of ESWT was also clearly supported by the cumulative data. There were no reports of serious adverse events in any of the studies included in this analysis.” (8)

**Risk Reduction**
In order to reduce risk of adverse effects, there are several recommendations:

- Operator training
- Requirement for accurate and complete medical history
- Requirement for accurate soft tissue assessment
- Requirement to clear client for any contraindications, as well as understand any site- or tissue-specific contraindications – major nerves and blood vessels, etc.

Additionally, the requirement for informed consent must not be ignored.
Appendix 1

Comparison between Radial and Focussed Shockwaves

Shockwaves are described in terms of the following parameters:

- **Pressure field** (dependent on type of shockwave, duration of shockwave and area of focus)
- **Energy flux density** (energy per square area released by the acoustic pulse at a specific time point, given in mJ/mm²)
  
  - Energy flux density (EFD) (mJ/mm²) and peak pulse energy (MPa) are determined by the temporal and spatial distribution of the pressure wave; both are generally higher in focussed shockwave.
- **Focal area** – defined as the area in which 80% of the maximum energy is reached. 55 (Rompe 1996) This is smaller, and more defined in focussed shockwave.
- Other characteristics include: speed of pressure rise, pulse width, magnitude and duration of negative pressure. These may be dependent on the method of shockwave generation.

Table 1. Comparison of focussed and radial shockwave waveform characteristics.

<table>
<thead>
<tr>
<th>Focussed Shockwave</th>
<th>Parameter</th>
<th>Radial Shockwave</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 – 100 MPa</td>
<td>Pressure</td>
<td>0.1 – 1 MPa</td>
</tr>
<tr>
<td>&lt; 1.5 mJ/mm²</td>
<td>Energy</td>
<td>&lt; 0.3 mJ/mm²</td>
</tr>
<tr>
<td>&lt; 10 microseconds</td>
<td>Pulse time</td>
<td>&gt; 1 milliseconds</td>
</tr>
<tr>
<td>focussed</td>
<td>Activity range</td>
<td>radial, distracted</td>
</tr>
<tr>
<td>deeper</td>
<td>Penetration depth</td>
<td>superficial</td>
</tr>
</tbody>
</table>
Appendix 2

This appendix lists the conditions believed suitable for treatment by shockwave from three licensing sources: Health Canada, The US Federal Drug Administration, and the UK National Institute for Care and Excellence in Health (NICE).

Health Canada - Device Licensing Documentation

Health Canada reviews medical devices to assess their safety, effectiveness and quality before being authorized for sale in Canada. Health Canada licenses shockwave devices for their specific intended use/purpose as determined by the legal manufacturer of the device. A manual search was carried out of current and archival licenses in the Health Canada Medical Devices Active Licence Listing ([https://health-products.canada.ca/mdall-limh/index-eng.jsp](https://health-products.canada.ca/mdall-limh/index-eng.jsp)) using the search term “shock”. Also, individual devices for sale in Canada were identified and then searched in the database by company name or device name.

The search yielded the following partial list of licensed devices, with manufacturer-specified uses, to give the indications for which these devices have been licensed for use in Canada.

<table>
<thead>
<tr>
<th>Manufacturer and Product (Health Canada License Number)</th>
<th>Manufacturer-stated indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>R. Wolf GmbH Piezoson 300 (31533) Also Piezowave (78054)</td>
<td>Rotator cuff in the shoulder, tennis or golfer’s elbow, patellar tip syndrome in the knee, plantar fasciitis, conditions of insertion tendinitis (enthesiopathies)</td>
</tr>
<tr>
<td>Medispec OrthoSpec (67798)</td>
<td>Shoulder Tendinosis (with or without calcification), Shoulder Bursitis, Lateral &amp; Medial Epicondylitis, Patellar Tendonitis, Trochanteric Bursitis Achilles Tendonitis, Plantar Fasciitis (with or without Heel Spur), Non-union fractures, Trigger points (“muscle knots”), Avascular Necrosis, Stress Fracture</td>
</tr>
<tr>
<td>Storz Medical AG Medipuls MP200 (74491)</td>
<td>Treatment Of Tendinopathies, Hamstrings, Myofascial Trigger Points,</td>
</tr>
</tbody>
</table>
Achilles Tendinopathy, Bursitis
Hallux Rigidus, Non-Healing Ulcers
Tendonitis, Scar Tissue
Jumpers Knee, Calcific Rotator Cuff
Tendinitis, Trigger Point Therapy
Non Unions, Shoulder Pain, Tennis
Elbow, Patellar Tendonitis, Plantar
Fasciitis/Heel Spur, Shin Splints, Stress
Fractures, Enhancement Of Bone
Healing, Muscle And Connective Tissue
Activation With V-Actor®

Guangzhou Longest Science &
Technology LGT-2500S (94714)
Musculoskeletal disease and chronic
pain in shoulder, back, heel, knee or
elbow.

The Health Canada – Summary Basis of Decision database may be searched at this URL
https://hpr-rps.hres.ca/reg-content/summary-basis-decision.php

**US FDA**
The United States Food and Drug Administration has approved devices for the application
of shockwave therapy for three soft tissue conditions in adults 18 years of age or more:
chronic plantar fasciitis (2000, 2005), chronic lateral epicondylitis (2002, 2003), and for
the treatment of diabetic foot ulcers (2017). See attached “Summary of Data and
Effectiveness Documents”, and the Medical Devices Database:
https://www.fda.gov/medicaldevices/deviceregulationandguidance/databases/default.htm
**UK National Institute for Care and Health Excellence (NICE)**\(^9\) – Recommendations for Treatable Conditions

The United Kingdom NICE lists the following four conditions as potentially treatable with shockwave.\(^10\) Any explanatory statements by NICE are shown below the condition.

1. **Achilles tendinopathy**
   a. The evidence on extracorporeal shockwave therapy (ESWT) for Achilles tendinopathy raises no major safety concerns. Current evidence on efficacy of the procedure is inconsistent and limited in quality and quantity. Therefore, ESWT for Achilles tendinopathy should only be used with special arrangements for clinical governance, consent and audit or research.

2. **Refractory greater trochanteric pain syndrome**
   a. Evidence on the efficacy and safety of extracorporeal shockwave therapy (ESWT) for refractory greater trochanteric pain syndrome is limited in quality and quantity. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

3. **Refractory lateral epicondylitis**
   a. The evidence on extracorporeal shockwave therapy (ESWT) for refractory tennis elbow raises no major safety concerns; however, current evidence on its efficacy is inconsistent. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

4. **Refractory plantar fasciitis**
   a. The evidence on extracorporeal shockwave therapy (ESWT) for refractory plantar fasciitis raises no major safety concerns; however, current evidence on its efficacy is inconsistent. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

---

\(^9\) NICE is a Non-Departmental Public Body in the United Kingdom. NICE is accountable to the Department of Health and Social Care, but operates independently of the government. NICE is an independent organisation responsible for providing evidence-based guidance on health and social care.

References


Naples, Italy, October 12th, 2016

Consensus Statement on
ESWT Indications and Contraindications

The members of the managing board, the Advisory board and the Senators of the International Society for Medical Shockwave Treatment (ISMST), have decided at the managing board meeting in Naples, Italy held on October 13th, 2016, to publish a set of clinical recommendations for using therapeutic shockwaves in clinical practice.

The recommendations were assembled based on an assessment of the current published scientific and clinical information and accepted approaches to treatment.

The recommendations are meant to aid the clinician in the use of shockwave medicine. In particular, the Guidelines are intended to clarify the indications and contraindications to treatment.

The recommendations are not intended to be a fixed protocol, as some patients may require more or less treatment depending on the clinical scenario. Patient care and treatment should always be based on a clinician’s independent medical judgment, given the individual patient’s clinical circumstances.

On behalf of the ISMST Managing Board,

Dr. José Eid
General Secretary of the ISMST
A. Introduction and prerequisites and minimal standards of performing ESWT

In order to prevent improper treatment, the following list contains the minimum prerequisites and standard examinations performing ESWT:

1. Clinical examination
2. Radiological imaging
3. Neurological and/or laboratory-diagnostic tests and/or other investigations may be necessary to corroborate the diagnosis.

Only a qualified physician (certified by National or International Societies) may use focused shockwave therapy to treat pathologies, which have been determined by diagnostic testing.

For the treatment on bones, a high-energy, focused shockwave with positioning technology has to be used.

In accordance with most scientific evidence ISMST recommends to use focused generators and high energy levels to treat calcifications.

To treat superficial soft tissue conditions, devices with or without focusing technology may be utilized; close attention must be paid to the depth of penetration of the shockwave source when treating deep tissue structures.

B. INDICATIONS

1. Approved standard indications
   1.1. Chronic Tendinopathies
      1.1.1. Calcifying tendinopathy of the shoulder
      1.1.2. Lateral epicondylopathy of the elbow (tennis elbow)
      1.1.3. Greater trochanter pain syndrome
      1.1.4. Patellar tendinopathy
      1.1.5. Achilles tendinopathy
      1.1.6. Plantar fasciitis, with or without heel spur
   1.2. Bone Pathologies
      1.2.1. Delayed bone healing
      1.2.2. Bone Non-Union (pseudarthroses)
      1.2.3. Stress fracture
      1.2.4. Avascular bone necrosis without articular derangement
      1.2.5. Osteochondritis Dissecans (OCD) without articular derangement
   1.3. Skin Pathologies
      1.3.1. Delayed or non-healing wounds
      1.3.2. Skin ulcers
      1.3.3. Non-circumferential burn wounds
2. Common empirically-tested clinical uses
   2.1. Tendinopathies
      2.1.1. Rotator cuff tendinopathy without calcification
      2.1.2. Medial epicondylopathy of the elbow
      2.1.3. Adductor tendinopathy syndrome
      2.1.4. Pes-Anserinus tendinopathy syndrome
      2.1.5. Peroneal tendinopathy
      2.1.6. Foot and ankle tendinopathies
   2.2. Bone Pathologies
      2.2.1. Bone marrow edema
      2.2.2. Osgood Schlatter disease: Apophysitis of the anterior tibial tubercle
      2.2.3. Tibial stress syndrome (shin splint)
   2.3. Muscle Pathologies
      2.3.1. Myofascial Syndrome
      2.3.2. Muscle sprain without discontinuity
   2.4. Skin Pathologies
      2.4.1. Cellulite

3. Exceptional indications – expert indications
   3.1. Musculoskeletal pathologies
      3.1.1. Osteoarthritis
      3.1.2. Dupuytren disease
      3.1.3. Plantar fibromatosis (Ledderhose disease)
      3.1.4. De Quervain disease
      3.1.5. Trigger finger
   3.2. Neurological pathologies
      3.2.1. Spasticity
      3.2.2. Polyneuropathy
      3.2.3. Carpal Tunnel Syndrome
   3.3. Urologic pathologies
      3.3.1. Pelvic chronic pain syndrome (abacterial prostatitis)
      3.3.2. Erectile dysfunction
      3.3.3. Peyronie disease
   3.4. Others
      3.4.1. Lymphedema

4. Experimental Indications
   4.1. Heart Muscle Ischemia
   4.2. Peripheral nerve lesions
4.3. Pathologies of the spinal cord and brain
4.4. Skin calcinosis
4.5. Periodontal disease
4.6. Jawbone pathologies
4.7. Complex Regional Pain Syndrome (CRPS)
4.8. Osteoporosis

C. CONTRAINDICATIONS

1. Radial and focused waves with low energy
   1.1. Malignant tumor in the treatment area (not as underlying disease)
   1.2. Fetus in the treatment area

2. High energy focused waves
   2.1. Lung tissue in the treatment area
   2.2. Malignant tumor in the treatment area (not as underlying disease)
   2.3. Epiphyseal plate in the treatment area
   2.4. Brain or Spine in the treatment area
   2.5. Severe coagulopathy
   2.6. Fetus in the treatment area
Naples, Italy, October 12th, 2016

Consensus Statement on ESWT Indications and Contraindications

The members of the managing board, the Advisory board and the Senators of the International Society for Medical Shockwave Treatment (ISMST), have decided at the managing board meeting in Naples, Italy held on October 13th, 2016, to publish a set of clinical recommendations for using therapeutic shockwaves in clinical practice.

The recommendations were assembled based on an assessment of the current published scientific and clinical information and accepted approaches to treatment.

The recommendations are meant to aid the clinician in the use of shockwave medicine. In particular, the Guidelines are intended to clarify the indications and contraindications to treatment.

The recommendations are not intended to be a fixed protocol, as some patients may require more or less treatment depending on the clinical scenario. Patient care and treatment should always be based on a clinician’s independent medical judgment, given the individual patient’s clinical circumstances.

On behalf of the ISMST Managing Board,

Dr. José Eid
General Secretary of the ISMST
A. Introduction and prerequisites and minimal standards of performing ESWT

In order to prevent improper treatment, the following list contains the minimum prerequisites and standard examinations performing ESWT:

1. Clinical examination
2. Radiological imaging
3. Neurological and/or laboratory-diagnostic tests and/or other investigations may be necessary to corroborate the diagnosis.

Only a qualified physician (certified by National or International Societies) may use focused shockwave therapy to treat pathologies, which have been determined by diagnostic testing.

For the treatment on bones, a high-energy, focused shockwave with positioning technology has to be used.

In accordance with most scientific evidence ISMST recommends to use focused generators and high energy levels to treat calcifications.

To treat superficial soft tissue conditions, devices with or without focusing technology may be utilized; close attention must be paid to the depth of penetration of the shockwave source when treating deep tissue structures.

B. INDICATIONS

1. Approved standard indications
   1.1. Chronic Tendinopathies
      1.1.1. Calcifying tendinopathy of the shoulder
      1.1.2. Lateral epicondylopathy of the elbow (tennis elbow)
      1.1.3. Greater trochanter pain syndrome
      1.1.4. Patellar tendinopathy
      1.1.5. Achilles tendinopathy
      1.1.6. Plantar fasciitis, with or without heel spur
   1.2. Bone Pathologies
      1.2.1. Delayed bone healing
      1.2.2. Bone Non-Union (pseudarthroses)
      1.2.3. Stress fracture
      1.2.4. Avascular bone necrosis without articular derangement
      1.2.5. Osteochondritis Dissecans (OCD) without articular derangement
   1.3. Skin Pathologies
      1.3.1. Delayed or non-healing wounds
      1.3.2. Skin ulcers
      1.3.3. Non-circumferential burn wounds
2. Common empirically-tested clinical uses
   2.1. Tendinopathies
      2.1.1. Rotator cuff tendinopathy without calcification
      2.1.2. Medial epicondylopathy of the elbow
      2.1.3. Adductor tendinopathy syndrome
      2.1.4. Pes-Anserinus tendinopathy syndrome
      2.1.5. Peroneal tendinopathy
      2.1.6. Foot and ankle tendinopathies
   2.2. Bone Pathologies
      2.2.1. Bone marrow edema
      2.2.2. Osgood Schlatter disease: Apophysitis of the anterior tibial tubercle
      2.2.3. Tibial stress syndrome (shin splint)
   2.3. Muscle Pathologies
      2.3.1. Myofascial Syndrome
      2.3.2. Muscle sprain without discontinuity
   2.4. Skin Pathologies
      2.4.1. Cellulite

3. Exceptional indications – expert indications
   3.1. Musculoskeletal pathologies
      3.1.1. Osteoarthritis
      3.1.2. Dupuytren disease
      3.1.3. Plantar fibromatosis (Ledderhose disease)
      3.1.4. De Quervain disease
      3.1.5. Trigger finger
   3.2. Neurological pathologies
      3.2.1. Spasticity
      3.2.2. Polyneuropathy
      3.2.3. Carpal Tunnel Syndrome
   3.3. Urologic pathologies
      3.3.1. Pelvic chronic pain syndrome (abacterial prostatitis)
      3.3.2. Erectile dysfunction
      3.3.3. Peyronie disease
   3.4. Others
      3.4.1. Lymphedema

4. Experimental Indications
   4.1. Heart Muscle Ischemia
   4.2. Peripheral nerve lesions
4.3. Pathologies of the spinal cord and brain
4.4. Skin calcinosis
4.5. Periodontal disease
4.6. Jawbone pathologies
4.7. Complex Regional Pain Syndrome (CRPS)
4.8. Osteoporosis

C. CONTRAINDICATIONS

1. Radial and focused waves with low energy
   1.1. Malignant tumor in the treatment area (not as underlying disease)
   1.2. Fetus in the treatment area

2. High energy focused waves
   2.1. Lung tissue in the treatment area
   2.2. Malignant tumor in the treatment area (not as underlying disease)
   2.3. Epiphyseal plate in the treatment area
   2.4. Brain or Spine in the treatment area
   2.5. Severe coagulopathy
   2.6. Fetus in the treatment area
Summary of Safety and Effectiveness Data

I. General Information

**Device Generic Name:** Extracorporeal Shock Wave Therapy Device

**Device Trade Name:** Dornier Epos™ Ultra

**Applicant's Name and Address:** Dornier Medical Systems, Inc.
1155 Roberts Boulevard
Kennesaw, Georgia 30144

**PMA Number:** P000048

**Date of Panel Recommendation:** none

**Date of Notice of Approval to Applicant:** January 15, 2002
II. Indications for Use

The Dornier Epos™ Ultra is a non-surgical alternative for the treatment of chronic plantar fasciitis for patients with symptoms of plantar fasciitis for 6 months or more and a history of unsuccessful conservative therapy. Plantar fasciitis is defined as the traction degeneration of the plantar fascial band at its origin on the medial tubercle of the calcaneus.

III. Contraindications

None known.

IV. Warnings and Precautions

The warnings and precautions can be found in the device labeling.

V. Device Description

The Dornier Epos™ Ultra is an extracorporeal shock wave therapy (ESWT) system. The Epos™ Ultra consists of a transportable cart housing the electromagnetic shock wave circuit, the hand held control unit, the CPU, a water circuit and the ultrasound subsystem. A therapy head mounted to the articulated arm, the hand control unit and the power cable are attached to the exterior of the cart. An ultrasound imaging system with a 7.5 MHz transducer is located on top of the cart. An isocentric locating arm fixed to the therapy head is used for positioning the therapy focus into the treatment area. In addition, the ultrasound is used to observe and monitor the shock wave treatment.

The shock wave source of the Epos™ Ultra uses electromagnetic technology to generate shock waves. Shock waves are acoustic waves that are characterized by a quick rise time of a few nanoseconds to a high maximum positive pressure (amplitude) of more than 80 Mpa (1 Mpa = 10 bar). A pulse of electrical energy flowing through a disc coil at the base of the therapy head induces strong magnetic fields, which produce forces that propel the membrane producing a plane pressure wave. The shock waves travel through the water filled coupling cushion mounted to the therapy head, where they are precisely focused by an acoustic lens to the target tissue.

Figure 1 gives a pictorial view of the Dornier Epos™ Ultra System.
VI. Alternative Practices and Procedures

Chronic plantar fasciitis is a common cause of heel pain. It is the most common diagnosis for pain in the inferior aspect of the heel.

Current conservative treatments for plantar fasciitis include:

- Rest
- Physical therapy
- Heel cushions
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Corticosteroid injections
- Taping
- Orthotics
- Shoe modifications
- Night splinting
- Casting

Current non-conservative treatments for plantar fasciitis include:

- Shockwave therapy by another commercially available shockwave generator
- Surgery

VII. Marketing History

Epos™ Ultra devices have been marketed in Europe, Russia, Africa, Middle East, Asia, Japan, Australia, Canada and South America. The Epos™ Ultra devices received a CE mark and were first distributed in November 1996. The Epos™ Ultra has not been withdrawn from marketing for any reason relating to its safety or effectiveness.

VIII. Adverse events of the Device on Health

The adverse events that occurred during the clinical study are listed under Tables 6 & 7.

The adverse events observed during treatment with the Dornier Epos™ Ultra include:

- Pain and/or discomfort during treatment
- Pain or swelling for a brief period following treatment
- Localized numbness, tingling or decreased sensation in the foot or at the site of shock wave delivery; and
- Local subcutaneous hematoma, minor bruising, or petechial bleeding in the foot or at the treatment site
Other potential adverse events may include:

- Rupture of the plantar fascia
- Possible bleeding and/or infection at the injection site related to injection of local anesthetic
- Temporary or permanent nerve damage associated with the injection or shock wave treatment
- Misdirection of extracorporeal shock wave energy to a major nerve or blood vessel, resulting in injury; and/or
- Anesthesia complication, including allergic reactions to local anesthetic agents

**IX. Summary of Non-clinical Studies**

**Shock Wave Characterization Produced by the Epos™ Ultra**

The Dornier Epos™ Ultra's therapy head with the 140mm diameter EMSE O-80 is designed as a standard lithotripsy therapy head for orthopedic shock wave applications. The 140mm diameter EMSE, which produces the shock waves, was previously approved for use in the Dornier Compact S Lithotripter in P840008, Supplement 62. Shock wave measurements produced by the EMSE O-80 shock wave emitter were characterized and documented in accordance with the parameters defined in the FDA Draft of Suggested Information for Reporting Extracorporeal Shock Wave Lithotripsy Device Shock Wave Measurements and IEC 1846. Measurements were recorded using a fiber optic hydrophone.

Measurements of the shock wave field of the EMSE O-80 were recorded at the minimal, typical and maximum energy settings as defined in the study protocol. Calculations of focal energy per pulse are based upon equation (4) in section 2.3, Beam Energy, of the draft guidance. The values were calculated including positive and rarefaction portions of the waves. Completion of calculations determined minimal shock-to-shock variation over the minimum, typical and maximum intensity settings for 5mm, 10mm and 12mm diameters of the pulse frequency ranges, demonstrating the accuracy of the EMSE pressure pulse generator.

The testing also included measurements of pulse intensity integral and effective energy as defined in the guidance. Both parameter values for positive signal and for the complete signal including rarefaction were measured and documented.

**EMI / EMC Testing**

Testing was conducted on the Epos™ Ultra without ultrasound to demonstrate compliance with EN 60601-1-2. This standard regulates the EMI/EMC of medical equipment that includes compliance with EN 55011 for radio frequency emissions. IEC 801-2, IEC 801-3, IEC 801-4, and IEC 801-5 represent immunity to electrostatic discharge (ESD), immunity to radio frequency electromagnetic fields, immunity to fast transients (bursts), and immunity to surges.

Testing was conducted on the ultrasound unit used in this study to demonstrate compliance with IEC 60601-1-2 (for EMC) and IEC 950 (for external TV monitors and other peripherals).
Other Testing

Testing was conducted with the Epos™ Ultra in accordance with 21 CFR 1010, Performance Standards for Electronic Products: General.

In Vitro and Animal Studies

In vitro or animal experiments were not conducted with the Dornier Epos™ Ultra. Previous studies with similar Dornier lithotripters were used to support safety of the Epos Ultra because shock waves are produced similarly.

X. Clinical Studies

Study Design and Objectives

The study was designed as a multicenter, randomized, placebo-controlled, prospective, double masked clinical study of patients with plantar fasciitis with at least moderate pain for at least six months and a history of prior conservative therapy with two groups: a group receiving ESWT with the Epos™ Ultra and a control group receiving a sham treatment. A total of 150 patients were enrolled at six clinical centers. The original randomization provided allocation for 75 Active and 75 Sham patients, i.e., one Active patient to one Sham patient; however, one patient in the Sham group erroneously received an Active treatment making the allocation 76 in the Active group and 74 in the Sham group. The study was conducted to determine whether a single, outpatient extracorporeal shock wave treatment can safely and effectively relieve the pain associated with plantar fasciitis. The follow-up visits occurred at 3-5 days, 6 weeks, 3 months, 6 months, and 12 months after treatment. After 3 months, patients who were treated with Sham treatment were offered an Active unmasked treatment in the open label extension study if they still met inclusion criteria. This was done after the masked 3 month safety and effectiveness outcome assessments were collected.

The primary efficacy endpoint was the difference between the active Epos™ Ultra treatment and the sham Epos™ Ultra treatment at 3 months post-treatment in the improvement from baseline in the VAS score for pain while walking for the first few minutes in the morning using a repeated measures analysis with covariates. In addition to evaluating the actual changes in pain score, the proportion of patients achieving at least 60% improvement in pain while walking for the first few minutes in the morning was compared between treatment groups at 3 months.

The secondary efficacy endpoints were the difference between groups in the improvement from baseline at 3 months post-treatment of the pain evaluation from the AOFAS Ankle-Hindfoot Scale Score, the Roles and Maudsley Score, the SF-12 health status questionnaire, pain measurement on palpation with a pressure threshold meter, and the ROM Assessment from the AOFAS Ankle-Hindfoot Scale Score. Safety was assessed as the number of adverse events and severity of complications that were related to extracorporeal shock wave therapy.

Subject Inclusion and Exclusion

The principal inclusion criteria were:

- Greater than 18 years old
- Symptoms present for greater than 6 months as assessed by patient history
- Visual Analog Scale (VAS) score of >5 for pain during the first few minutes of walking in the morning
- History of 6 months of unsuccessful conservative therapy to include any NSAIDS and two other conservative therapies
- Roles and Maudsley Score of 3 or 4
- Signed informed consent
- Single site of tenderness with local pressure over the medial calcaneal tuberosity on passive dorsiflexion of the foot

The principal exclusion criteria were:

- Previous treatment with any other conservative therapies within two weeks of treatment; corticosteroid injection within one month of treatment
- Previous surgery for plantar fasciitis
- History or documented evidence of autoimmune disease
- History or documented evidence of peripheral vascular disease
- History or documented evidence of Type I or Type II diabetes mellitus
- History or documented evidence of peripheral neuropathy such as nerve entrapment, tarsal tunnel syndrome, etc.
- History or documented evidence of systemic inflammatory disease such as rheumatoid arthritis, ankylosing spondylitis, Reiter's syndrome, etc.
- History or documented evidence of a bleeding disorder or hemophilia
- Pregnancy

Study Methodology

At screening and follow up, data collection included: history and physical exam, pain measurement on palpation with pressure threshold meter, VAS pain score questionnaires, SF-12 health status questionnaire, AOFAS Ankle-Hindfoot Scoring System questionnaire, and Roles and Maudsley questionnaire. Patients were asked which treatment they believed they received as an assessment of masking.

Study Enrollment

A total of three patients from the Active group and one patient from the Sham group discontinued prior to the 3 month follow up visit. Enrolled patients underwent a single, outpatient ESWT session after being randomized to an active (76 patients) or sham (74 patients) treatment. Follow up compliance at 3 months was 96.1% in the Active group and 98.6% in the Sham group. Two females and one male in the Active group and 1 female in the Sham group discontinued prior to the 3 month follow-up visit. Table 1 provides a summary of patients enrolled and treated.
Table 1: Patient Accounting up to 3 month follow-up visit

<table>
<thead>
<tr>
<th>Reason</th>
<th>Active Treatment Pts (N = 76)</th>
<th>Sham Treatment Pts (N = 74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient lost to follow-up</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Adverse event(^1)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Lack of effectiveness of treatment</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Follow-up frequency</td>
<td>73 (96.1%)</td>
<td>73 (98.6%)</td>
</tr>
</tbody>
</table>

1. This event was reported as severe pain during treatment despite local anesthesia use

Baseline Characteristics

There were differences between treatment groups in gender (p=0.02), height (p=0.01), and the use of taping as a pre-treatment conservative therapy (p=0.02) of baseline characteristics. No significant differences were found between treatment groups in any of the other characteristics which included age, weight, affected foot, participation in a weekly exercise program, duration of plantar fasciitis symptoms, and the requirement of standing while at work. Table 2 below provides patient demographics for both active and sham treatment groups. Table 3 provides baseline values for the primary and secondary endpoints.

Table 2: Patient Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Active Treatment Patients (n = 76)</th>
<th>Sham Treatment Patients (n = 74)</th>
<th>p-value(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean 50, Range 26-69</td>
<td>Mean 53, Range 31-72</td>
<td>NS</td>
</tr>
<tr>
<td>Gender</td>
<td>Male 14 (18.0%), Female 62 (81.6)%</td>
<td>Male 27 (36.5%), Female 47 (63.5%)</td>
<td>NS, 0.0156</td>
</tr>
<tr>
<td>Height (inches)</td>
<td>Mean 66, Range 60.4-77.0</td>
<td>Mean 68, Range 56.0-79.5</td>
<td>0.0131</td>
</tr>
<tr>
<td>Weight (lbs)</td>
<td>Mean 180, Range 120.0-294.0</td>
<td>Mean 186, Range 115.0-390.0</td>
<td>NS</td>
</tr>
<tr>
<td>Affected Foot</td>
<td>Right 46%, Left 54%</td>
<td>Right 55%, Left 45%</td>
<td>NS, NS</td>
</tr>
<tr>
<td>Required to Stand</td>
<td>55%</td>
<td>66%</td>
<td>NS</td>
</tr>
<tr>
<td>Participation in weekly exercise</td>
<td>55%</td>
<td>60%</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of symptoms (months)</td>
<td>Mean 22, Range 6-120</td>
<td>Mean 24.1, Range 3.0-99.0</td>
<td>NS</td>
</tr>
</tbody>
</table>

1. p-value associated with 2-way ANOVA for continuous parameters, & Cochran-Mantel Haenszel for categorical variables.

P0000048
Summary of Safety and Effectiveness Data
### Table 3: Baseline Values for Primary and Secondary Endpoints

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Active Treatment Patients (n = 76)</th>
<th>Sham Treatment Patients (n = 74)</th>
<th>p-value (n = 150)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VAS Pain</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1° Endpoint (0-10)</td>
<td>Mean 7.7 5.0-10.0</td>
<td>Mean 7.7 4.7-10.0</td>
<td>.9644</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean AOFAS Pain</td>
<td>13.4</td>
<td>12.2</td>
<td>.4746</td>
</tr>
<tr>
<td>Severe = 0</td>
<td>Moderate = 20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild = 30</td>
<td>None = 40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Roles &amp; Maudsley Score</td>
<td>3.8</td>
<td>3.8</td>
<td>.3217</td>
</tr>
<tr>
<td>Excellent = 1</td>
<td>Good = 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fair = 3</td>
<td>Poor = 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean SF-12 (Mental)</td>
<td>53</td>
<td>52</td>
<td>.2410</td>
</tr>
<tr>
<td>Mean SF-12 (Physical)</td>
<td>39</td>
<td>38</td>
<td>.4733</td>
</tr>
<tr>
<td>Mean AOFAS ROM-Sagittal</td>
<td>7.4</td>
<td>7.0</td>
<td>.0710</td>
</tr>
<tr>
<td>Normal/Mild = 8</td>
<td>Moderate = 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe = 0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean AOFAS ROM-Hindfoot</td>
<td>5.5</td>
<td>5.5</td>
<td>.6954</td>
</tr>
<tr>
<td>Normal/Mild = 6</td>
<td>Moderate = 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marked = 0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain on Palpation (kg)</td>
<td>Mean 5.8 1.1-15.9</td>
<td>Mean 5.6 1.3-13.3</td>
<td>.4533</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Treatment Characteristics

The procedure for active and sham treatments was performed identically except that for patients randomized to sham, a thin air cushion was placed on the therapy head prior to the patients arrival to the treatment room. The treatment was administered by a physician who did not perform follow-up evaluations. All patients received an injection of 5ml of 1% Xylocaine into the medial calcaneal branch of the tibial nerve. Eleven percent (10.5%, 8/76) of patients in the Active group and 4.1% (3/74) of patients in the Sham group received additional anesthesia during treatment.

The average treatment time was 21 minutes in the Active group and 19.8 minutes in the Sham group. The therapy was delivered by administering a total of 3800 shock waves to reach an approximated total energy delivery of 1300 mJ/mm². The mean number of shocks delivered was 3742 in the Active group and 3744 in the Sham group. Patients were not informed of their randomization until after 3 months.
In the Active group, 45/76 patients (59.2%) correctly guessed that they received an Active treatment and 31/76 (40.8%) believed they received a Sham treatment or were not sure. Eighty-four percent (84.4%, 38/45) of patients who believed they received an Active treatment also experienced pain during treatment. Of the 31 patients who guessed that they received a Sham treatment or were not sure, 17/31 (54.8%) experienced pain during treatment. Although Active patients who reported pain during treatment were more likely to have reported active therapy in the blinding verification, there was no difference at any follow-up visit in the change from baseline in the VAS score as assessed by the patient for pain with the first few steps in the morning between active patients who believed they received an active treatment and those who believed they received a sham treatment (p>0.51).

In the Sham group, 11/74 (14.9%) patients correctly guessed that they received the Sham treatment and 63/74 (85.1%) believed they received an Active treatment or were not sure. No patient who correctly guessed they received a Sham treatment experienced pain during treatment. Five patients who believed they received an Active treatment experienced pain during treatment. Sixty-nine patients (93.2%) in the Sham group did not experience pain during treatment.

The incidences of device malfunctions were also recorded during the clinical trial. Table 4 summarizes the device malfunctions that occurred for both Active and Sham patients. A total of eight device malfunctions occurred during the clinical study, four in the Active group and four in the Sham group. Two malfunctions, one in the Active group and one in the Sham group, were related to the printer, which is used in conjunction with the ultrasound to print images from the ultrasound screen. The malfunction in the Sham group occurred prior to treatment when the printer would not print. After adjusting the printer cable, the video printer functioned as intended and treatment began. The malfunction in the Active group occurred during treatment. The printer cable had to be adjusted in order to obtain an image of the patient's foot. Treatment continued and was completed according to protocol.

One device malfunction occurring in the Active group during treatment was related to a drop in the frequency of the shock wave delivery. It was determined that this occurred due to overheating of the device. The treatment continued with the patient receiving the appropriate amount of shocks at a reduced intensity level.

One device malfunction occurring in the Sham group was related to an intermittent display problem with the hand control unit which did not affect the delivery of shock waves. Treatment was completed according to protocol.

Four malfunctions, two in the Active group and two in the Sham group, occurred during treatment when the machine would not deliver shocks. These malfunctions were determined to be related to a connection problem with the hand switch, which allows the delivery of shock waves.

No patient in either group experienced any adverse events as a result of the device malfunction, and all patients remained blinded to their treatment randomization.
Table 4: Device Malfunctions

<table>
<thead>
<tr>
<th></th>
<th>Active Treatment Patients (n = 76)</th>
<th>Sham Treatment Patients (n = 74)</th>
<th>Total (n = 150)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Malfunctions</td>
<td>4 (5.3%)</td>
<td>4 (5.4%)</td>
<td>8 (5.3%)</td>
</tr>
<tr>
<td>Before Treatment</td>
<td>0 (0.0%)</td>
<td>1 (25.0%)</td>
<td>1 (12.5%)</td>
</tr>
<tr>
<td>During Treatment</td>
<td>4 (100%)</td>
<td>3 (75.0%)</td>
<td>7 (87.5%)</td>
</tr>
</tbody>
</table>

Primary Effectiveness Endpoint

In the Active group, the mean pain score decreased from 7.7 ±1.4 at baseline to 3.4 ± 2.8 at 3 months post-treatment, a mean percent improvement of 56.5%. In the Sham group, the mean score decreased from 7.7 ± 1.5 at baseline to 4.1 ± 3.1 at 3 months post-treatment, a mean percent improvement of 46.6%. The change from baseline to 3 months in VAS pain due to treatment was statistically significant using a repeated measures analysis (p=0.0149), with covariate analysis and without imputing missing data (3 active patients and 1 sham patient) as summarized in Table 5.

The proportion of patients achieving at least 60% improvement in pain during the first few minutes of walking in the morning was compared between treatment groups at 3 months. Fifty-six percent (56.2%) of the Active group demonstrated 60% improvement from baseline in their VAS scores or greater reduction in their pain, compared to 45.2% of the patients in the Sham group. This was not statistically significant.

Table 5: VAS Scores for Active and Sham Patients Baseline Through 3 months Post Treatment

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3-5 days</th>
<th>6 weeks</th>
<th>3 months</th>
<th>Change from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Treatment</td>
<td>N</td>
<td>76</td>
<td>74</td>
<td>72</td>
<td>73</td>
</tr>
<tr>
<td>Treatment Patients</td>
<td>Mean</td>
<td>7.7</td>
<td>5.0</td>
<td>4.6</td>
<td>3.4</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>1.4</td>
<td>2.8</td>
<td>3.1</td>
<td>2.8</td>
</tr>
<tr>
<td>Sham Treatment</td>
<td>N</td>
<td>74</td>
<td>74</td>
<td>71</td>
<td>73</td>
</tr>
<tr>
<td>Treatment Patients</td>
<td>Mean</td>
<td>7.7</td>
<td>5.7</td>
<td>5.0</td>
<td>4.1</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>1.5</td>
<td>2.8</td>
<td>3.0</td>
<td>3.1</td>
</tr>
</tbody>
</table>

The clinical data showed that on average, patients with a lower baseline VAS score, a shorter duration of symptoms, or a lower body mass index (BMI) had a higher improvement in VAS pain score.

Secondary Effectiveness Endpoint

The Roles and Maudsley pain score was used as a secondary endpoint. At 3 months post-treatment, the distribution of patients in the four categories, excellent, good, fair, and poor, was
found to be statistically significant between the treatment groups (p=0.03) with 61.6% of Active patients having good to excellent results, compared to only 39.7% of Sham patients.

The AOFAS Ankle-Hindfoot Scale and the SF12 Health Status Questionnaire, which did not show statistically significant change between active and sham patients, over time were also used as secondary endpoints.

Safety Results

Adverse events were evaluated by type, nature, severity and intensity during treatment and at each follow up visit. No study subject experienced an unanticipated serious device-related adverse event during the course of the study.

All but one complication resolved with little or no intervention. The most common complications were pain during treatment and pain 3-5 days post-treatment. Pain during treatment occurred in 72.4% Active patient group and 6.8% Sham patient group. Pain during treatment was recorded on a scale of 1-10 (mild-severe) with a mean score during treatment of 3.5 in the Active group and 0.2 in the Sham group. Pain post-treatment at 3-5 days was reported in 40.8% of Active patients (31/76) and 35.1% of Sham patients (26/74).

Table 6 summarizes the adverse events related to ESWT at treatment through 3 month follow up. Other than pain during treatment, there were no differences in the nature or type of adverse events reported between the Active and Sham groups. There were no serious unanticipated adverse device effects to report related to ESWT.

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Active Treatment Patients (n = 76)</th>
<th>Sham Treatment Patients (n = 74)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Patients</td>
<td>Number of Occurrences</td>
<td>% of Patients</td>
</tr>
<tr>
<td>Pain During Treatment</td>
<td>55</td>
<td>55</td>
<td>73%</td>
</tr>
<tr>
<td>Pain Post Treatment</td>
<td>28</td>
<td>31</td>
<td>37%</td>
</tr>
<tr>
<td>Edema</td>
<td>5</td>
<td>5</td>
<td>7%</td>
</tr>
<tr>
<td>Ecchymosis</td>
<td>5</td>
<td>5</td>
<td>7%</td>
</tr>
<tr>
<td>Petechiae</td>
<td>0</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Rash</td>
<td>1</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Hypesthesia</td>
<td>2</td>
<td>3</td>
<td>3%</td>
</tr>
<tr>
<td>Neuralgia</td>
<td>1</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>3</td>
<td>3</td>
<td>4%</td>
</tr>
<tr>
<td>Total Events</td>
<td>104</td>
<td>53</td>
<td>---</td>
</tr>
</tbody>
</table>

1. Number of patients experiencing at least one occurrence
2. Pain during shock wave application: statistical significance with p-value <0.0001 by Fischer's Exact Test
3. Pain experienced immediately after treatment through 3 month follow-up
All but one adverse event was reported by the investigator as not serious: one patient reported strong pain at the 3 month follow-up visit. The event resolved without intervention before the patient was exited from the study.

All but one adverse event had resolved: one patient in the Active group reported paresthesia of the lateral distal part of the plantar surface at the 3-5 day follow-up visit. The ankle-foot sensation testing was abnormal for all four locations at the 3-5 day follow-up visit. The patient was prescribed ibuprofen, ice, and rest and was referred to a neurologist for further evaluation, with abnormal ankle/foot sensation testing at locations 1, 2, 3, but normal at location 4. The neurologist report noted irritation of the N. plantaris lateralis with no loss of muscle strength. This adverse event was reported as unresolved at the 3 month visit. The patient was seen at the 6 month follow-up visit and the adverse event was again reported as unresolved. The patient discontinued from the study before the 12 month follow-up.

Adverse events were evaluated through 12 months for Active and Sham patients. No adverse events were reported in the Active group after the 3 month follow-up visit. Adverse events for patients who originally received Sham treatment who elected Active unmasked treatment were also evaluated. The events, which are summarized in Table 7 below, were evaluated through 12 months after initiating Active unmasked treatment. Of the 73 Sham patients remaining at the 3 month follow-up visit, 51 elected to receive the unmasked Active treatment. Adverse events reported through 12 months for these patients are presented in Table 7 below.

Table 7: Adverse Events for Open Label Active Treatment of Patients Originally Randomized to Sham Treatment Through 12 Months Follow Up

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>X-over Treatment (n = 51)</th>
<th>3-5 day</th>
<th>6 weeks</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pts¹ occur</td>
<td>pts¹ occur</td>
<td>pts¹ occur</td>
<td>pts¹ occur</td>
<td>pts¹ occur</td>
<td>pts¹ occur</td>
</tr>
<tr>
<td>Pain during Treatment</td>
<td></td>
<td>28</td>
<td>26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain post Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Edema</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ecchymosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Petechiae</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paresthesia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection Site</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemorrhage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Patients experiencing at least one occurrence within each interval

Conclusions drawn from the Studies

The preclinical and clinical data provide reasonable assurance that the Dornier Epos™ Ultra device is safe and effective when used in accordance with the device labeling.
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 was not referred to the Orthopedics and Rehabilitation Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CDRH Decision:
FDA inspection of the manufacturing facility determined that the applicant was in compliance with the Quality System Regulation (21 CFR 820). Approval for this PMA application was issued on January 15, 2002.

XII. Approval Specifications:
Directions for use: See the Labeling.

Hazard to health from the use of the device: See the Warnings, Precautions, and Adverse effects section in the Labeling.

Postapproval Requirements and Restrictions: See Approval order.
1. Summary of Safety and Effectiveness

A. General Information

Device Generic Name: Extracorporeal Shock Wave Therapy (ESWT) system

Device Trade Name: SONOCUR® Basic

Applicant Name and Address: Siemens Medical Solutions USA, Inc.
Sales and Service Group
186 Wood Avenue South
Iselin, NJ 08830

Application Number: P010039

Date of Panel Recommendation: None

Date of Notice of Approval to Applicant: July 19, 2002

B. Indications for Use

The Siemens SONOCUR Basic is a non-surgical alternative for the treatment of chronic lateral epicondyliitis (commonly referred to as tennis elbow) for patients with symptoms of chronic lateral epicondyliitis for 6 months or more and a history of unsuccessful conservative treatments.

C. Contraindications

There are no known contraindications to ESWT with the SONOCUR Basic for treatment of chronic lateral epicondyliitis.

D. Warnings

The following warnings pertain to the use of the SONOCUR Basic for treatment of chronic lateral epicondyliitis (tennis elbow).

- Operators of the SONOCUR Basic should be aware of the proper use of the device in delivering the correct number of shocks and in localizing the proper area to be treated.
• ESWT with the SONOCUR Basic should be prescribed by and performed under the supervision of a physician trained and experienced in the care of patients with lateral epicondylitis.

• If the patient moves after correct positioning, re-perform localization if necessary. Failure to maintain correct positioning could result in misdirection of the shockwave and injury to adjacent nerves or blood vessels.

• If patients experience severe pain/discomfort at the application site during treatment, the system operator should decrease the penetration depth of the therapeutic shock wave focus by increasing the water level in the coupling bellows.

• If patients experience a vaso-vagal reaction during treatment, the patient should be reclined to a supine position until symptoms disappear.

• Patients currently undergoing systemic anticoagulation therapy (example—coumadin, heparin) should consult their physicians regarding temporary discontinuation of such medications before ESWT to prevent potential ecchymosis/bruising.

• Patients on daily aspirin therapy should temporarily discontinue aspirin intake 1 week before ESWT therapy.

E. Precautions
The following are precautions for the SONOCUR Basic system for treatment of chronic lateral epicondylitis (tennis elbow):

• Electromagnetic compatibility (EMC):
  If electromagnetic interference between the extracorporeal shock wave system and nearby electronic equipment is suspected (as evidenced by erratic behavior with either device), it is recommended that their distance be increased until proper operation resumes. If it is necessary to operate an electronic device in close proximity to the ESWT system during treatment, the device and the ESWT system should be tested for proper simultaneous operation prior to clinical use.

• Never remove any of the cabinet covers to the system’s electronics. The high voltage power supply circuits utilized by extracorporeal shock wave systems use voltages that are capable of causing serious injury or death from electric shock.

• If the device malfunctions during treatment or the treatment is discontinued, the therapeutic effects may not be as noticeable.

The safety and effectiveness of the SONOCUR Basic has not been established for:
• Pregnant women
• Patients younger than 18 years of age.
• Patients with a coagulation abnormality, thrombopathy, infection, tumor, cervical compression syndrome, cervical or upper extremity arthritis, local arthrosis, neurologic abnormality, or radial nerve entrapment
• Patients who have had previous surgery for lateral epicondylitis
• Patients who suffer from severe systemic diseases that may lead to sensory changes or neuropathic pain. For example, this may include diseases such as gout, diabetes mellitus, rheumatoid arthritis.
• Patients with cardiac pacemaker
• Patients who received physical or occupational therapy less than four (4) weeks prior to ESWT
• Patients who received a local steroid injection less than six (6) weeks prior to ESWT
• Patients with tennis elbow affecting both arms or who have had previous surgery for this condition

F. Device Description

Overview
The design of the SONOCUR Basic is based on Siemens extracorporeal shock wave lithotripsy (ESWL) devices. A shock wave is generated at the base of the shock head by an electromagnetic acoustic source (EMAS) within the shock head. When a high voltage pulse from a capacitor discharge is transmitted via the slab coil, a current is induced in the aluminum-foil membrane. The membrane is then rapidly repelled, which causes a shock wave. This shock wave travels through the water filled shock head to the focusing lens. This acoustic lens focuses the energy of the propagated pressure wave to a small concentrated point some known distance from the lens. The shock wave passes through the lens and into a water-filled coupling head (bellows).

By palpation, the treatment area (lateral epicondyle) is located. The shock head is positioned using the articulating device arm, aligned with the treatment area, and coupled to the patient’s skin using ultrasonic gel. The release of shock waves is controlled by the user via the system control console, which is menu-driven. The repetition frequency of shock wave release ranges from 1Hz to 4Hz, and is adjusted by the user at the control console. Shock wave pulses are released either by manually pressing the release button on the handswitch or by holding down the release button for a preset number of pulses.
**Component List**
The SONOCUR Basic device consists of the following components in a transportable unit:

A. Electromagnetic acoustic source (EMAS) with coupling bellows and keys for the shock wave release, the brakes and controlling the pump
B. Trolley with high tension capacitor charging unit and water conditioning system
C. Control console with controls for system parameter setting such as energy and pulse frequency
D. Articulating arm to position the EMAS (or shock head)

![Figure 1: SONOCUR Basic Components](image)

**Electromagnetic acoustic source (EMAS)**
The electromagnetic acoustic source (EMAS) is mounted at the base of the shock head. The shock head housing connects the polystyrene acoustic lens with the EMAS. The lens end of the head is fitted with a water-filled silicon coupling bellows.

The spaces between the EMAS and the lens and between the lens and the coupling bellows (or between the EMAS and the coupling head for the elliptical-spherical lens shock head) are filled with water.

The coupling head provides an acoustically favorable path for the focused pressure wave as it moves from the shock head to the patient. A water reservoir, pump, and valve system are used to adjust penetration depth to individual patients' anatomy.

When the pressure pulse capacitor charging unit discharges, it sends a short current pulse through the slab coil of the EMAS. By the law of induction, the...
increasing current in the slab coil induces a magnetic field around the coil. Similarly, as this magnetic field builds, it induces eddy currents in the metal diaphragm (made of an aluminum-alloy disk), which, in turn, induces a magnetic field near the metal diaphragm.

The magnetic field that is induced in the diaphragm has the opposite polarity of the field set up near the slab coil. Since these magnetic fields have opposite polarities, they repel each other and the diaphragm is forced away from the rigidly fixed slab coil. The resulting motion of the diaphragm creates a compression wave, which travels through the water within the shock head.

A polystyrene acoustic lens is mounted in the shock head above the diaphragm. This lens focuses the compression wave to a small focal region.

**Pressure Pulse Capacitor Charging Unit**
The large current impulse used to create the compression wave in the pressure pulse generator is a result of a capacitive discharge through the EMAS. Initiating the capacitive discharge is accomplished with a spark gap, which consists of two electrodes in a cavity. This potential difference across the capacitor can be varied for the EMAS and ultimately determines the pressure of the wave created by the EMAS and the pressure pulse which forms in the focal region.

**Water systems**
The water conditioning system, which has a compact design, fits with all its components in the housing of the transportable trolley. The water conditioning system is composed of two independent water circuits:
- cooling system and
- coupling system (the area between the lens and coupling bellows).

**Control Console**
The system parameters can be controlled and displayed on the control console. In the main menu, the following parameters can be selected and/or displayed
- number of pulses per treatment
- number of pulses currently applied during session
- energy level indication
- warning and error messages

**Articulating arm to position the shock head**
The shock head is mounted on a unique articulating arm. This arm can be flexibly moved in three planes after releasing the electromagnetic brakes. The pain is identified by palpation by the physician or by subjective assessment of the patient. The shock head is coupled to the patient’s skin, using ultrasonic gel. After applying a sufficient amount of ultrasound gel to the patient’s skin and to the coupling bellows, the shock head and pressure pulse focus are positioned to the location of the pain and the brakes are locked.
The penetration depth of the therapeutic pressure pulse focus in the patient body can be set by varying the water level in the bellows. To decrease or increase the penetration depth, water is pumped into or out of the bellows.

G. Adverse Effects of the Device on Health
Adverse events observed during a clinical study of 114 patients that were associated with extracorporeal shock wave therapy (ESWT) include those listed below, categorized by frequency:

Adverse events reported in >20% of patients:
- pain at, or surrounding the treatment site

Adverse events reported in <20% of patients
- nausea
- myalgia
- joint disorder
- pallor
- dizziness
- hypertonia
- hypesthesia
- paresthesia
- tremor
- vasodilation
- application site reaction
- sweating

The number and frequency of each reported event is summarized in Table 1 below:

<table>
<thead>
<tr>
<th>Event</th>
<th>Active</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Patients [1]</td>
<td>Number of Occurrences</td>
</tr>
<tr>
<td>Pain</td>
<td>28</td>
<td>60</td>
</tr>
<tr>
<td>Nausea</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Application Site Reaction</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Sweating</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Dizziness</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Hypertonia</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Hypesthesia</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Joint Stiffness</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Myalgia</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Tremor</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Vasodilation</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Pallor</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Accidental Injury</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Peripheral Edema</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
During the study, three patients exhibited benign, non-life threatening EKG changes that were determined by the investigators and cardiologists not to be treatment related.

Other potential adverse events not seen during the clinical study include:
- Neuropathy
- Tendon rupture
- Local hematoma
- MisdIRECTION of energy

H. Alternate Practices and Procedures

Alternative therapies can be divided into nonsurgical and surgical treatment. Among the most common initial treatments are rest and application of cold to the symptomatic region. The use of aspirin very often is a first choice. Nonsteroidal anti-inflammatory medications including indomethacin seem to be helpful in some patients. The physical therapy modality of high-voltage electric stimulation has been helpful in relieving pain and inflammation. If the process does not respond to the above treatment choices, a cortisone injection may be appropriate. Various surgical treatments can also be considered as an alternative to ESWT.

I. Marketing History

In October 1996, SONOCUR Basic was made commercially available in the European Market. Since then, it has been available in countries other than the United States, Japan and Taiwan. SONOCUR Basic has never been withdrawn from marketing for any reason related to safety or effectiveness of the device.

J. Summary of Preclinical Testing

**Shock wave characterization**

Shock wave output from the SONOCUR Basic was characterized according to the draft FDA guidance, “Draft of Suggested Information for Reporting Extracorporeal Shock Wave Lithotripsy Device Shock Wave Measurements”. The following figure (figure 2) shows the peak positive pressure at the focus as a function of Energy Level (system output range):
Figure 2. Peak Positive Pressure versus Energy Level

Energy Flux Density Output versus SONOCUR Basic Energy setting

<table>
<thead>
<tr>
<th>Energy setting</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy Flux Density in mJ/mm²</td>
<td>0.03</td>
<td>0.06</td>
<td>0.12</td>
<td>0.17</td>
<td>0.25</td>
<td>0.32</td>
<td>0.41</td>
<td>0.50</td>
</tr>
</tbody>
</table>

All values based on measurements with PVDF membrane hydrophone.
Manufacturer: GEC-Marconi Research Center
Type: Y-33-7603

**Biocompatibility**
The material of the coupling bellows which contacts the patient conforms to the international standard ISO-10993 “Biological Evaluation of Medical Devices Part 1: Evaluation and Testing”. Sensitivity and irritation testing, USP biological testing (classification VI), intracutaneous toxicity, and implantation testing were performed. The ISO-10993 testing showed that there were no reactions identified as sensitization and no irritant/corrosive effects.
**Noise level testing**
The amplitude of the noise generated by the shock head of the SONOCUR Basic system was measured with a Larson Davis sound meter. The equipment conforms to Class I requirements according to IEC 804. The sound measurements were performed at a distance of 1m from the SONOCUR Basic unit with the following parameters: energy levels 1 – 8, minimal (1 Hz) and maximum (4 Hz) repetition frequency, and with and without patient simulation. The surface sound pressure levels measured are below the Occupational Safety and Health Administration (OSHA) standard for all exposure times (from 0.5 hours/day to 8 hours/day).

**Animal testing**
Animal studies were conducted using an early prototype of the Sonocur Basic system, which used the same mechanism of electromagnetic shock-wave generation, by Rompe et. al [Dose related effects of shock waves on rabbit tendon Achilles: A Sonographic and Histological Study. Journal of Bone and Joint Surgery (Br) 1998.80-B:546-52]. For this study, forty-two (42) New Zealand rabbits (84 total tendons) were randomized into four treatment groups:

1) Group A: 1000 shock-wave impulses of an energy flux of 0.08mJ/mm²
2) Group B: 1000 shock-wave impulses of an energy flux of 0.28mJ/mm²
3) Group C: 1000 shock-wave impulses of an energy flux of 0.60mJ/mm²
4) Group D: no shock-wave therapy (control group)

During the study, sonographic and histological tests were performed and the results showed no changes in Group A, transient swelling of the tendon in Group B. With Group C (energy flux of 0.60mJ/mm²), there was the formation of paratendinous fluid with a significant increase in the anteroposterior diameter of the tendon. In addition, there was marked histological changes with increased eosin staining, fibrinoid necrosis, fibrosis in the paratenon and infiltration of inflammatory cells. It was concluded that energy flux densities greater than 0.28mJ/mm² should not be used clinically to treat tendon disorders. The Sonocur Basic system uses 0.08mJ/mm² for the treatment of lateral epicondylitis.

**K. Summary of Clinical Studies**
As a first step in its clinical development for the U.S. market, Siemens sponsored a small randomized, double-blinded, placebo-controlled pilot study to assess the feasibility of using the Sonocur Basic system in the treatment of lateral epicondylitis. An analysis of the three-month study data showed that the ESWT system is safe, with the most frequently reported adverse event being pain during treatment. The results also showed an efficacy advantage for the active treatment group in reducing pain at 12 weeks post-treatment compared with baseline, even though there was a higher than expected “placebo effect” that was consistently observed over the entire three month follow-up period. To reduce this placebo effect and increase the active treatment effect, certain adjustments to the study design were made (including the inclusion/exclusion criteria and treatment
application) and Siemens continued further clinical testing of the Sonocur Basic ESWT system. This additional testing was conducted as a multi-center clinical trial, which is described below in further detail.

**Study Design and Objectives**
The Siemens Sonocur Basic multi-center pivotal trial was a randomized, double-blind (patients and evaluators), placebo-controlled, parallel treatment study. A total of 114 patients were enrolled in the study at 3 investigational sites.

Patients with chronic tennis elbow were examined and randomized to one of two treatment groups (active, placebo). Each patient was scheduled to receive three treatments: once a week for a three-week period. For all completed treatments, a maximum of 2100 impulses per treatment session was delivered for a total energy delivery of 9.27J for all three sessions. The procedure for the active and placebo treatments was performed identically except that for patients receiving the placebo treatment, a sound-reflecting pad was placed between the treatment site and the shock wave head. No local anesthetic injection or analgesic was allowed during treatment.

During the study, assessments of pain level and functional activity were performed. At each visit, the pain intensity was evaluated using the Thomsen provocation test (resisted wrist extension). The patient was asked to record the level of pain that he/she was experiencing on a visual analog scale (VAS), which was a 100mm scale with 0 for no pain and 100 for intolerable pain. In addition, functional improvement was also examined using an Upper Extremity Functional Scale, or UEFS, test. For this test, patients in the study were asked to score their ability to perform specific daily chores (such as opening jars/doors, washing dishes) on a scale from 1 to 10, with a score of 1 meaning that the patient had no problem at all and a score of 10 meaning that the patient could not perform the activity. Additional measures of efficacy were examined including the patient’s overall impression, grip strength, activity evaluation (ability to perform activities that were limited by his/her tennis elbow condition), and pain medication consumption. Safety assessments included an assessment of adverse events, physical examination, X-rays, vital signs, 12-lead EKG, clinical labs, and proportion of patients who couldn’t tolerate treatment.

Patients were scheduled for follow-up evaluations, occurring at 1-, 4-, 8-, 12-weeks, 6-months, and 12-months post-treatment. The primary analysis of the safety and efficacy data was performed after all patients were enrolled, treated, and completed their 12-week follow-up requirements.

**Primary and Secondary Efficacy Endpoints:**
The primary efficacy endpoint was at least a 50% reduction from baseline to Week 12 post-treatment in the pain visual analog scale (VAS) during resisted wrist extension.

The secondary efficacy endpoint was an improvement from baseline to Week 12 post-treatment in the patient's mean upper extremity function score. Function was assessed using the Upper Extremity Function Scale (UEFS) (Pransky et al.).

Subject Inclusion and Exclusion

The inclusion criteria included:

- history of lateral epicondylitis for at least 6-months;
- pain that is unresponsive to two of three conventional therapy programs (local steroid injections, physical/occupational therapy, non-steroidal anti-inflammatories);
- pain by palpation of the lateral epicondyle;
- baseline pain that was = 40 during resisted wrist extension (“Thomsen provocation test”) on a 100mm visual analog scale (VAS); and

The exclusion criteria included:

- < 18 years of age;
- received local steroid injections within 6 weeks, physical/occupational therapies within 4 weeks, or non-steroidal anti-inflammatory within 1 week prior to randomization;
- received systemic therapeutic anticoagulants;
- active bilateral epicondylitis;
- history and/or physical findings of cervical compression syndrome, cervical or upper extremity arthritis, local arthrosis or neurologic abnormality, rheumatoid disease, or radial nerve entrapment;
- previous surgery for lateral epicondylitis;
- participated in a Workman’s Compensation Program or planned to apply for the Program;
- thrombopathy, infection, tumor, or other severe systemic diseases;
- arthrosis of the elbow, as confirmed by X-ray diagnosis (AP, lateral views);
- pregnancy;
- participated in a study with any experimental therapy within the last 30 days.
Study Population
Of the 114 patients enrolled in the study and included in the intent-to-treat (ITT) cohort, 56 patients were assigned to the active treatment group and 58 patients were assigned to the placebo group. Two (3.6%) active treatment group patients could not tolerate treatment and discontinued from the study prior to completing all three scheduled treatments. A third active treatment group patient was discontinued due to a low platelet count, which was found to be a pre-existing condition prior to study participation. Of the 58 placebo patients, 3 (5.2%) patients discontinued prior to the 12-week follow-up period to seek alternative therapy.

Patient demographics and treatment history are summarized in Table 2, below. The mean age for the active treatment group was 47 years (ranging from 35-71 years), and the mean age for the placebo group was 47 years (ranging from 35-60 years). There were 27 male (48.2%) and 29 female (51.8%) patients in the active treatment group and 27 male (46.6%) and 31 female (53.4%) patients in the placebo group. The mean height was 171 cm and the mean weight was 76 kg. Physical exam and medical histories at baseline were also similar between the treatment groups.

Table 2: Patient Demographics and Treatment History

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Active Treatment Patients (N=56)</th>
<th>Placebo Treatment Patients (N=58)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>47</td>
<td>47.3</td>
</tr>
<tr>
<td>Range</td>
<td>35-71</td>
<td>35-60</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>27 (48.2%)</td>
<td>27 (46.6%)</td>
</tr>
<tr>
<td>Female</td>
<td>29 (51.8%)</td>
<td>31 (53.4%)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>170.9</td>
<td>171.8</td>
</tr>
<tr>
<td>Range</td>
<td>152.4-188.0</td>
<td>149.9-190.5</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>75.9</td>
<td>78.9</td>
</tr>
<tr>
<td>Range</td>
<td>50.9-120.0</td>
<td>53.0-120.2</td>
</tr>
<tr>
<td>Affected Arm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>35 (62.5%)</td>
<td>41 (70.7%)</td>
</tr>
<tr>
<td>Left</td>
<td>21 (37.5%)</td>
<td>17 (29.3%)</td>
</tr>
<tr>
<td>Prior Therapies*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All three</td>
<td>41 (73.2%)</td>
<td>43 (74.1%)</td>
</tr>
<tr>
<td>Steroid Injections &amp; PT/OT</td>
<td>4 (7.1%)</td>
<td>6 (10.3%)</td>
</tr>
<tr>
<td>Steroid Injections &amp; NSAIDs</td>
<td>6 (10.7%)</td>
<td>5 (8.6%)</td>
</tr>
<tr>
<td>PT/OT &amp; NSAIDs</td>
<td>5 (8.9%)</td>
<td>4 (6.9%)</td>
</tr>
<tr>
<td>Symptom Duration (months)**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>21.3</td>
<td>20.8</td>
</tr>
<tr>
<td>Range</td>
<td>6.0-178.0</td>
<td>6.0-176.0</td>
</tr>
</tbody>
</table>

* PT/OT= physical and occupational therapy, NSAIDs= non-steroidal anti-inflammatory
** from date of initial diagnosis by a physician to enrollment into the study
Each treatment group (active, placebo) had lateral epicondylitis for an average of
21 months (12-month median) prior to randomization. In total, seventy-six (66.7%)
patients had their right arm affected and 38 (33.3%) patients had their left arm
affected. More than 70% of the patients in each treatment group had all three
types of therapies (injections, PT/OT, NSAIDs) prior to enrollment, and 54 (93.1%)
placebo patients and 51 (91.1%) active treatment patients had steroid injections.

**Treatment Characteristics:**
All patients were scheduled to receive three treatments: once a week for a three
week period. For all completed treatments, a maximum of 2100 impulses per
treatment session was delivered for a total energy delivery of 9.27J for all three
sessions. The procedure for the active and placebo treatments was performed
identically except that for patients receiving the placebo treatment, a sound
reflecting pad was placed between the treatment site and the shock wave head.
No local anesthetics were used for treatment application.

During the study, the majority of patients (96.5%) completed all three treatments
without any treatment interruptions or abortions. As summarized in Table 3,
below, two active treatment patients had treatments aborted due to adverse patient
reactions (elbow pain, nausea, diaphoresis, light headedness) and two patients (1
active, 1 placebo) had treatments interrupted due to temporary device
malfunctions.

<table>
<thead>
<tr>
<th>Table 3: Number of patients with treatments interrupted or aborted</th>
<th>Active (n=56)</th>
<th>Placebo (n=58)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with Treatments Interrupted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse Event</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Machine Malfunction</td>
<td>1 (1.8%)</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>Patients with Treatments Discontinued</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse Event</td>
<td>2 (3.6%)</td>
<td>0</td>
</tr>
<tr>
<td>Machine Malfunction</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Overall, the systems performed reliably over the course of the study with few
reported problems. For two of the three systems used in the clinical trials, device
malfunctions were reported. One device malfunction was due to a broken system
cable that prevented shock wave delivery, and one reported malfunction was due
to a defective shock wave module that needed to be replaced (with the water
cooling system cleaned and serviced). Given their low frequency of occurrence, its
unlikely that these system malfunctions significantly affected the overall study
results.
**Efficacy and Safety Results**

**Efficacy Results:**
For the ITT population (refer to Table 4, below), the placebo and active treatment groups had comparable pain scores at the baseline evaluation. The average pain score for patients who received the active treatment was 74 at baseline and 37.6 at 12 weeks. The average score for the placebo patients was 75.6 at baseline and 51.3 at 12 weeks.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Baseline</th>
<th>Week 1</th>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Active</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>56</td>
<td>56</td>
<td>56</td>
<td>56</td>
<td>56</td>
</tr>
<tr>
<td>Mean</td>
<td>73.98</td>
<td>55.55</td>
<td>49.09</td>
<td>40.77</td>
<td>37.59</td>
</tr>
<tr>
<td>SD</td>
<td>15.79</td>
<td>25.18</td>
<td>26.79</td>
<td>28.67</td>
<td>28.68</td>
</tr>
<tr>
<td><strong>Placebo</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>58</td>
<td>58</td>
<td>58</td>
<td>58</td>
<td>58</td>
</tr>
<tr>
<td>Mean</td>
<td>75.57</td>
<td>63.97</td>
<td>60.57</td>
<td>54.81</td>
<td>51.33</td>
</tr>
<tr>
<td>SD</td>
<td>16.00</td>
<td>23.19</td>
<td>25.48</td>
<td>25.12</td>
<td>29.65</td>
</tr>
</tbody>
</table>

N=number of patients  
SD= standard deviation  

The primary efficacy endpoint was at least a 50% reduction from baseline to 12-weeks post-treatment in the pain visual analog scale (VAS) during resisted wrist extension. For the intent-to-treat cohort, the results show that the active treatment group had 34/56 (60.7%) of the patients and the placebo group had 17/58 (29.3%) of the patients achieving at least a 50% reduction in pain during provocation at Week 12 compared with baseline. There was a statistically significant (p=0.001) between group difference.

The secondary efficacy endpoint was an improvement from baseline to Week 12 post-treatment in the patient’s mean upper extremity function scale (UEFS) score. For the ITT population (refer to Table 5, below), the placebo and active treatment groups had comparable mean upper extremity function scores (UEFS) at the baseline evaluation. The mean UEFS score for the active treatment group was 4.68 at baseline (SD=1.78) and the mean UEFS score for the placebo group was 4.63 (SD=1.8) at baseline. At Week 12, there was a statistically significant (p=0.01) difference between groups in the mean UEFS scores, compared with baseline.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Baseline</th>
<th>Week 1</th>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Active</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>56</td>
<td>53</td>
<td>51</td>
<td>52</td>
<td>53</td>
</tr>
<tr>
<td>Mean</td>
<td>4.68</td>
<td>3.23</td>
<td>2.80</td>
<td>2.54</td>
<td>2.25</td>
</tr>
<tr>
<td>SD</td>
<td>1.78</td>
<td>1.89</td>
<td>1.70</td>
<td>1.52</td>
<td>1.57</td>
</tr>
<tr>
<td><strong>Placebo</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>58</td>
<td>57</td>
<td>57</td>
<td>55</td>
<td>54</td>
</tr>
<tr>
<td>Mean</td>
<td>4.63</td>
<td>3.71</td>
<td>3.79</td>
<td>3.54</td>
<td>3.23</td>
</tr>
<tr>
<td>SD</td>
<td>1.80</td>
<td>1.77</td>
<td>1.98</td>
<td>2.12</td>
<td>2.09</td>
</tr>
</tbody>
</table>

N=number of patients, SD=standard deviation
The percent improvement in the average efficacy scores (pain, UEFS, patient’s overall impression, activity level, and grip strength testing) at 12-weeks compared with baseline is summarized in Table 6, below.

Table 6: Percent Improvement in Average Efficacy Scores at 12 Weeks, Compared with Baseline

<table>
<thead>
<tr>
<th></th>
<th>SONOCUR Basic ESWT</th>
<th>Placebo (Mock)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>average score at beginning of study</td>
<td>average score at 12 weeks</td>
</tr>
<tr>
<td>Pain *</td>
<td>74</td>
<td>37.6</td>
</tr>
<tr>
<td>UEFS *</td>
<td>4.7</td>
<td>2.3</td>
</tr>
<tr>
<td>Activity Evaluation *</td>
<td>7.7</td>
<td>3.5</td>
</tr>
<tr>
<td>Overall Impression *</td>
<td>70.3</td>
<td>32.8</td>
</tr>
<tr>
<td>Grip Strength Testing</td>
<td>71</td>
<td>87.1</td>
</tr>
</tbody>
</table>

* statistically significant (p<0.05) between group difference. p-value is calculated using one way ANOVA

Safety Results:
In general, the nature, severity, frequency, duration and resolution of adverse events were similar in the active and placebo group, with the exception of certain vasovagal responses (i.e. nausea, sweating, dizziness, hypesthesia) and reports of pain during treatment for the active group.

Table 1 (page 6: Adverse Device Effects of the Device on Health) summarizes the type and frequency of adverse events that were categorized as being possibly or probably related to the study treatment.

The following table (Table 7) shows the occurrence of adverse events for the active treatment group that were judged to be possibly or probably treatment related over the course of the 12-month study period.
## Table 7. Active Treatment Group: Adverse Events Through 12 Months of Follow-up

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Treatment Period</th>
<th>Follow-up Period [1]</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>24</td>
<td>46</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Application Site Reaction</td>
<td>4</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>*</td>
</tr>
<tr>
<td>Sweating</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dizziness</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hypertonia</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Hypesthesia</td>
<td>3</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Joint Stiffness</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>*</td>
</tr>
<tr>
<td>Myalgia</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tremor</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vasodilation</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pallor</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

[1] relative to the last treatment, using protocol defined windows. No new adverse events judged as being possibly or probably related to treatment were reported after the 6-month follow-up period.

[2] number of patients experiencing at least one occurrence within each time interval

* patient discontinued from study during the 6-month follow-up visit and subsequently had surgery for tennis elbow. No additional study data is available for this patient after the 6-month follow-up period.
At the time of the 12-week follow-up visit, all device related adverse events had resolved, except for one patient who had moderate elbow stiffness and mild swelling that was still ongoing at the time of the 6-month follow-up visit. This patient, who had an x-ray with normal findings at baseline and 12 weeks, was unresponsive to treatment and terminated study participation soon after the 6-month follow-up visit for surgery. There were no new device related adverse effects reported during the long-term (3-12month) follow-up period.

In addition to adverse events, lab values, physical exam results, X-rays, vital signs, and EKGs were assessed. No significant between group differences were observed.

L. 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 was not referred to the General and Plastic Surgery Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicated information previously reviewed by this panel.

FDA Decision:

This clinical study has demonstrated that use of the Siemens Sonocur Basic system for the treatment of patients with chronic lateral epicondylitis is a safe and effective alternative for patients who have a history of unsuccessful conservative treatments. The results show a good safety profile for the system and show that the system can be used to relieve pain and improve functional activity.

The preclinical and clinical data provide reasonable assurance that the Siemens SONOCUR Basic is safe and effective when used in accordance with the device labeling. In addition, the applicant’s manufacturing facility was inspected and found to be in compliance with the Quality Systems Regulation (21CFR 820).

CDRH issued an approval order on July 19, 2002.

M. Approval specifications:

Directions for Use: see labeling

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

Conditions of Approval: see approval order
SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

DEVICE GENERIC NAME: Orthopedic Extracorporeal Shock Wave Therapy Device

DEVICE TRADE NAME: Orthospec™ Orthopedic ESWT

APPLICANT'S NAME AND ADDRESS: Medispec Ltd.
12850 Middlebrook Road, Suite 1
Germantown, MD 20874
Phone: 301-944-1575
Fax: 301-972-6098

PREMARKET APPROVAL
APPLICATION (PMA) NUMBER: P040026

DATE OF PANEL RECOMMENDATION: None

DATE OF NOTICE OF APPROVAL TO THE APPLICANT: April 1, 2005

II. INDICATIONS FOR USE

Orthospec™ Extracorporeal Shock Wave Therapy (ESWT) is indicated for the treatment of Proximal Plantar Fasciitis with or without heel spur in patients 18 years of age or older. Orthospec™ ESWT is a non-invasive alternative method for patients with symptoms of Proximal Plantar Fasciitis for 6 months or more and a history of unsuccessful conservative therapies to relieve heel pain.

Proximal Plantar Fasciitis is defined as heel pain in the area of the insertion of the plantar fascia on the plantar calcaneal tuberosity.

III. CONTRAINDICATIONS

Use of the Orthospec™ is contraindicated in the following situations:

1. Over or near bone growth centers until bone growth is complete.
2. When a malignancy is known to be present in or near the treatment area.
3. Over ischemic tissues in individuals with vascular disease where the blood supply would be unable to follow the increase in metabolic demand and tissue necrosis may result.
4. Patient has coagulation disorder or is taking anticoagulant medications, either for acute or chronic anticoagulant therapy.
5. Patient has infection at the area to be treated with Orthospec™. This is due to the risk of spreading infection.
6. This product contains natural rubber latex which may cause allergic reactions.
IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the physicians labeling.

V. DEVICE DESCRIPTION

The Orthospec™ Extracorporeal Shock Wave Therapy device provides a non-invasive method of therapy for the treatment of Proximal Plantar Fasciitis with or without heel spur. The Orthospec™ employs an electro-hydraulic, or "spark gap" method of creating the shock wave. With this technique, an electrode (spark plug) ignites an electrical charge within a water-containing stainless steel semi-ellipsoid chamber and contact membrane, evaporating a small portion of the water and creating a shock wave reflecting outward off the ellipsoid. The shock wave is generated within the reflector chamber and transmitted through the skin surface of the patient to the treatment site. The reflector chamber is an apparatus used to apply the shock wave to the treatment zone. Water enters the chamber through an intake valve that is controlled from the control panel. The water cushion can be inflated or deflated from the control panel to assure contact with the skin. This chamber must remain filled during the treatment procedure.

The energy of the shock wave can be adjusted between levels 1 and 7. The frequencies of shock waves are 96, 120 and 160 shocks per minute. Coupling solution is used on both the contact membrane and the patient's skin to enhance conductivity. The device has a linear motor for height adjustment and casters for lateral positioning of the reflector towards the treatment area. Imaging or sedation is not required with use of the Orthospec™.

The Orthospec™ is a portable, self-contained unit and does not require special installation. The operational platform consists of a cast iron base with a high voltage generator, contained in a locked cabinet, operating from a standard 115 or 230 voltage electrical wall socket. The major components consist of the Main Frame, Shock Wave Head and Control Panel.

Main Frame

The main frame is a single, mobile unit that cases the high voltage generator. It includes the shock wave unit and control panel.

Shock Wave Head

The Shock Wave Head is integrated within the main frame. It consists of a stainless steel semi-ellipsoid reflector, a dry natural rubber membrane filled with water, an underwater electrode, and a high voltage power supply. These components together form a water chamber in which the shock wave is generated. The shock wave is generated from the electrode by an electric spark and transmitted to the treatment site via the contact membrane.

Control Panel

The control panel allows for the operation of the device. It is a touch panel built with an array of switches with transparent regions through which the system indication lights and displays can be seen. The main power key switch, energy and frequency levels, water inflate and deflate operation, height control and shock wave counter are all functions of the control panel.
VI. ALTERNATIVE PRACTICES AND PROCEDURES

Conservative therapies to treat Plantar Fasciitis consist of physical therapy, anti-inflammatory pharmaceuticals, steroid injections, deep heat treatments, and orthotics. Surgical options include endoscopic plantar fasciotomy or open plantar fascia release.

VII. MARKETING HISTORY

The Orthospec™ device has been commercially marketed and sold in over 25 countries outside the United States since 1998. Currently there are 65 devices placed in 25 countries around the world including, Europe, Asia, and South America. The Orthospec™ system been recalled for safety and/or effectiveness reasons.

VIII. ADVERSE EVENTS OF THE DEVICE ON HEALTH

ADVERSE EVENTS

During the Orthospec™ clinical study, there were 3 reported cases of adverse events out of 172 treated patients. They included two cases of bruising and one case of mild local swelling observed by the patient but not by the physician. None of the adverse events was severe, and none required medical intervention or subsequent medical care.

<table>
<thead>
<tr>
<th>Summary of All Adverse Events</th>
<th>Orthospec™ (N = 115)</th>
<th>Placebo (N = 57)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Adverse Event</td>
<td>3 (2.6%)</td>
<td>0 (0%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Bruising</td>
<td>2 (1.7%)</td>
<td>0 (0%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Mild local swelling</td>
<td>1 (0.9%)</td>
<td>0 (0%)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

POTENTIAL ADVERSE EVENTS

Potential adverse events when using the Orthospec™ device include:

- Pain during ESW treatment
- Petechia
- Superficial hematoma
- Neurosensory conditions (Hypesthesia or Paresthesia)
- Rare allergic or sensitivity reaction to the Latex membrane or to the coupling solution applied to the skin during treatment
- Tendon rupture

IX. SUMMARY OF PRECLINICAL STUDIES

Shock Wave Characterization (Pressure Measurements)
Shock Wave Characterization Produced by the Orthospec™ Shock wave pressure measurements were performed in accordance with IEC 61846, "Ultrasonics - Pressure pulse lithotripters - Characteristics of fields" (1998). The Orthospec™ was typically configured with a fluid-filled membrane and a 25 um spot-poled membrane-type Polyvinylidene Difluoride PVDF hydrophone with a 0.5 mm geometrical diameter.
Measurements of the shock wave field were based on an average of over thirty measurements at the focal location. The mean peak positive pressure and mean peak negative pressure were 340±127 bar and 49±15 bar, respectively, at 24kV. From the integration of the pressure-time waveform, and the scans through the focal region, the integrated energy per pulse was 0.11 J at 24kV.

Calculations of the focal energy per pulse were based upon equation 3 in Clause 7.3.3 of IEC 61846. The measurement was conducted by integrating over the focal plane in an approach similar to that used to measure diagnostic ultrasound equipment. The measured pressure-time waveforms were squared to get pressure-squared vs. time, and then integrated.

In order to measure the rise time and pulse duration of the shock waveform, the measurement was repeated with the oscilloscope sampling rate increased to 100 Msmp/s. From a series of measurements, the average rise time was 400±100 ns; the average pulse width was 1200±45 ns.

These results indicate that the device was designed to produce output characteristics that fall within the range of those used in extracorporeal shock wave lithotripsy. Preclinical data was extracted from the animal study using the Medispec Econolith™ Shockwave Lithotripsy System (P950043). The intended use for the Econolith™ Shockwave Lithotripsy System is for internal tissues, to fragment upper urinary tract calculi, which provides much more energy and pressure than the Orthospec™, intended for orthopedic applications. The Orthospec™ ESWT device is a low energy shock wave modification of the Econolith™ Shockwave Lithotripsy System by Medispec, Ltd. Medispec, Ltd. includes this study as part of the Orthospec™ PMA based on its FDA approval as a validated demonstration of safety and effectiveness. The animal study was conducted under more severe energy and intensity parameters than the Orthospec™. Both devices work on the same range of voltage, however for orthopedic applications, the shock wave pressure is greatly reduced from that utilized in kidney stone treatments (ESWL). Soft tissue effects of the lower energy shockwaves were quantified in animal studies. Based on these soft tissue animal study results, Medispec, Ltd. developed their performance parameters for the Orthospec™ device.

Standards Testing
Testing was conducted on the Orthospec™ ESWT to demonstrate compliance with IEC 60601-1, IEC 60601-2-36, IEC 60601-1-2, ISO 14971 and IEC 61846.

In Vitro and Animal Studies
Animal study data and acoustic characteristic data were extracted from the FDA approved PMA P950043 of the Econolith Lithotripter Shock Wave Lithotripsy System to show both safety and effectiveness. Both devices are technically equivalent in terms of the primary component, the Shock Wave Generator, and functionality. The Econolith’s applied use is for internal tissues to fragment upper urinary tract calculi, thus the Orthospec™ uses less energy and less pressure on less sensitive body tissue during treatment than the Econolith™ Lithotripter, which uses more energy and operates on more sensitive tissue of the body.

1 IEC 60601-1: Safety Requirements for Electrical Equipment for Measurement, Control, and Laboratory Use, Part I: General Requirements
2 IEC 601-2-36: Medical Electrical Equipment Part 2: Particular Requirements for the Safety of Equipment for Extracorporally Induced Lithotripsy
4 ISO 14971: Medical Devices – Application of Risk Management to Medical Devices
X. SUMMARY OF CLINICAL STUDIES

Clinical Investigation

Study Design

A multicenter, double-blind, randomized, placebo-controlled clinical investigation of 172 patients was conducted to determine the safety and effectiveness of the Orthospec™ ESW treatment in patients with chronic Proximal Plantar Fasciitis with or without heel spur who had not responded to conservative therapy.

Proximal Plantar Fasciitis is defined as heel pain in the area of the insertion of the plantar fascia on the plantar calcaneal tuberosity.

Patients were randomized 2:1 to either the active Orthospec™ treatment or placebo. Patients were followed out 1, 2, 3 months post-treatment for efficacy and safety evaluations, and then 6 and 12 months post-treatment for further safety assessment. Three clinical sites participated including up to two blinded investigators and one unblinded investigator at each site. The blinded investigators conducted pre- and post-evaluations and the unblinded investigator performed all treatments.

Treatment Procedure

Up to two blinded investigators and one unblinded investigator participated at each of the three clinical sites. Blinded investigators conducted all pre- and post-treatment evaluations and the unblinded investigators performed the ESW treatments. Patients were randomized to either the active treatment group or placebo control group. Both treatments were performed in parallel with each patient receiving 3,800 shocks. For patients who received the placebo treatment the contact membrane of the device was lined with an internal foam insert to absorb the shock waves. No anesthetic was given during or after treatment.

Inclusion/Exclusion Criteria

Patients with the following criteria were eligible for enrollment:

- Male or female eighteen years of age or older. If female is of childbearing potential, she must not be pregnant at the time of enrollment and she must be using an accepted form of birth control during the study.
- Diagnosed with proximal plantar fasciitis on the basis of history and physical examination with symptoms present for more than 6 months and has been treated by a licensed healthcare professional for at least 4 months
- Pain intensity score of ≥ 5 cm on the VAS scale in the investigator’s heel pain assessment and the subject’s self-assessment of pain upon the first few minutes of walking in the morning
- Failed two pharmacological and two nonpharmacological treatment modalities for relief of pain and will not undergo such treatments within the following time windows prior to treatment:
  - Local steroid injections – 6 weeks
  - NSAIDS – 1 week
  - Physical therapy – 2 weeks
- Single site of tenderness with local pressure over the plantar calcaneal tuberosity on passive dorsiflexion of the foot
- Chronic conditions such as osteoarthritis, diabetes, peripheral vascular diseases that do not affect foot pain
Patients with the following criteria were excluded:

- Recent history of significant cardiac, neurological, hepatic, renal, metabolic, or hematological disease or impairment. Significance determined by pre-admission testing, medical history (recent and previous), and specialist evaluations
- Previous surgery for plantar fasciitis
- Chooses to continue physical therapy or other conservative treatments during the time he/she is enrolled in the study
- Corticosteroid injection within 6 weeks of treatment
- Neuropathic, malignant, or infectious causes of pain
- Coagulation disorders or is taking anticoagulant medications, either for acute or chronic anti-coagulant therapy
- Tears of the fascia
- Bilateral plantar fasciitis
- Condition in which the exposure to radiation is not advisable (i.e. pregnancy)
- Infection or malignancy at the area to be treated with Orthospec™
- Simultaneously participating in another device or drug study, or who has participated in any clinical trial involving an experimental device or drug within 30 days of entry into this study. Patients may be enrolled only one time in this study.
- Significant medical illness that may cause the patient to be non-compliant with the protocol or confound the data interpretation
- Require narcotics for plantar pain relief or other medical conditions prior to treatment

Evaluation Methods

Only blinded investigators performed pre- and post-treatment evaluations. Evaluations consisted of:

- Investigator's heel pain assessment
- Subject's self-assessment of heel pain
- Subject's self-assessment of activity and function
- The use of heel pain medications

During the investigator's evaluation of heel pain, a pressure sensor (PressureSpec®) was used to apply and record the amount of pressure that elicited a pain response at baseline, and then used the pressure sensor to apply the same amount of pressure at each subsequent follow-up visit for consistency in the evaluation.

Primary Objective

- The primary objective was to demonstrate a statistically significant difference between the Orthospec™ treatment and placebo treatment with respect to the change in pain intensity from baseline to 3 months post-treatment as measured on the Visual Analog Pain Score (VAS scale 0-10 cm) in the investigator's heel pain assessment. The investigator's heel pain assessment for a successful response required a minimum improvement from baseline of at least 50% with a VAS score of ≤ 4.0 cm.

Secondary Objectives

The secondary objectives of the study were to demonstrate statistically significant differences between the Orthospec™ treatment and placebo treatment with respect to:

- The change in pain intensity from baseline to 3 months post-treatment as measured on the Visual Analog Pain Score (VAS scale 0-10 cm) in the subjects self-assessment of pain (upon
the first few minutes of walking in the morning). The subject's heel pain assessment for a successful response required a minimum improvement from baseline of at least 50% with a VAS score of $\leq 4.0$ cm.

- Subject's self-assessment of activity and function measured by the distance the subject is able to walk without heel pain
- The use of pain medications

**Study Enrollment**

As shown in Table 1, a total of 196 subjects were screened. 172 patients were enrolled and randomized (2:1) to either the active Orthospec™ treatment group or the placebo treatment group. One patient randomized to the Orthospec™ treatment group received placebo treatment by mistake. This patient was kept in the Orthospec™ treatment group for all analyses except where indicated otherwise. The subjects had a mean age of 51 years, and the mean duration of foot pain was 30 months. Thirty-three percent (33%) were male, 87% were white, and the mean weight was 184 pounds. Of the 172 enrolled patients, a total of 152 patients (88.4%) completed the study out to 3 months post-treatment and 20 patients terminated prematurely. The protocol specified that all patients who return for at least one post-treatment visit would be included in the primary efficacy analysis; a total of 168 patients were thus included.

<table>
<thead>
<tr>
<th>Screened</th>
<th>Orthospec™</th>
<th>Placebo</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized</td>
<td>115</td>
<td>57</td>
<td>172</td>
</tr>
<tr>
<td>Completed 3 Months</td>
<td>101 (87.8%)</td>
<td>51 (89.5%)</td>
<td>152 (88.4%)</td>
</tr>
<tr>
<td>Terminated Prematurely</td>
<td>14 (12.2%)</td>
<td>6 (10.5%)</td>
<td>20 (11.6%)</td>
</tr>
<tr>
<td>Condition Worsened</td>
<td>5 (4.3%)</td>
<td>0 (0%)</td>
<td>5 (2.9%)</td>
</tr>
<tr>
<td>Healed</td>
<td>1 (0.9%)</td>
<td>0 (0%)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0%)</td>
<td>1 (1.8%)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Lost to Follow-up</td>
<td>8 (7.0%)</td>
<td>5 (8.8%)</td>
<td>13 (7.6%)</td>
</tr>
<tr>
<td>Included in primary analysis of effectiveness</td>
<td>112 (97.4%)</td>
<td>56 (98.2%)</td>
<td>168 (97.7%)</td>
</tr>
</tbody>
</table>

- Completed Month 1 Visit: 111 (96.5%), 54 (94.7%), 165 (95.9%)
- Completed Month 2 Visit: 97 (84.3%), 48 (84.2%), 145 (84.3%)
- Completed Month 3 Visit: 101 (87.8%), 51 (89.5%), 152 (88.4%)

1 Had at least one investigator assessment of heel pain post treatment.

**Effectiveness Analysis**

**Primary Effectiveness Results**

The primary endpoint, mean change from baseline in the investigator’s Assessment of heel pain at three months achieved statistical significance ($p=0.045$). Table 2 summarizes the mean changes from baseline in investigator's assessment of heel pain at each monthly follow-up visit.
Table 2 – Mean Change from Baseline in Investigator’s Assessment of Heel Pain Last Observation Carried Forward

<table>
<thead>
<tr>
<th>Month 1</th>
<th>Orthospec™</th>
<th>Placebo</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>111</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Mean¹</td>
<td>-1.61</td>
<td>-1.27</td>
<td>0.34</td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>-0.34 (-1.06, 0.37)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>111</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Mean¹</td>
<td>-2.30</td>
<td>-1.31</td>
<td>0.026</td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>-0.99 (-1.86, -0.12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>112</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Mean¹</td>
<td>-2.51</td>
<td>-1.57</td>
<td>0.045</td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>-0.94 (-1.87, -0.02)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ Estimated from an analysis of variance and adjusted for baseline assessment and clinical site.

Table 3 summarizes the mean change from baseline in investigator’s assessment of heel pain as a function of the maximum tolerated energy applied. The patient mistakenly treated with placebo is included in the placebo group for this analysis. These results show that patients who received a maximum energy level of 4.5 or less is not therapeutic.

Table 3 – Mean Change from Baseline to Month 3 in Investigator’s Assessment of Heel Pain by Maximum Shock Wave Energy Applied Last Observation Carried Forward

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>57</td>
<td>-1.53</td>
</tr>
<tr>
<td>Level 2 – 4.5</td>
<td>14</td>
<td>-1.09</td>
</tr>
<tr>
<td>Level 4.6 – 5.9</td>
<td>12</td>
<td>-1.71</td>
</tr>
<tr>
<td>Level 6 – 6.9</td>
<td>53</td>
<td>-2.87</td>
</tr>
<tr>
<td>Level 7</td>
<td>32</td>
<td>-2.93</td>
</tr>
</tbody>
</table>

¹ Adjusted for clinical site and baseline assessment

Secondary Effectiveness Results

Table 4 summarizes the results for each of the secondary effectiveness endpoints at three months. As seen in this table, the patient self-assessment of heel pain and the change in use of pain medication achieved statistical significance, supporting the findings of the primary effectiveness endpoint. Patients in the Orthospec™ treatment group had a higher point estimate of the response rate with regard to activity and function than patients in the placebo group, although this endpoint was not statistically significant.
Table 4 – Summary of Secondary Effectiveness Results at Three Months

<table>
<thead>
<tr>
<th>Measure</th>
<th>Orthospec™</th>
<th>Placebo</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=115</td>
<td>N=57</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean change from baseline</td>
<td>-3.39</td>
<td>-1.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Response rate</td>
<td>52.7%</td>
<td>28.6%</td>
<td>0.003</td>
</tr>
<tr>
<td>Patient’s Assessment of Activity and Function Response Rate</td>
<td>64.3%</td>
<td>57.1%</td>
<td>0.33</td>
</tr>
<tr>
<td>Change in the use of Pain Medication</td>
<td>Increased</td>
<td>1.0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>No change</td>
<td>65.0%</td>
<td>74.5%</td>
</tr>
<tr>
<td></td>
<td>Decreased</td>
<td>34.0%</td>
<td>13.7%</td>
</tr>
</tbody>
</table>

1 The last value was carried forward for all patients missing an assessment at month 3 and all analyses (except change in pain medication, which was adjusted for clinical site) were adjusted for clinical site and the corresponding baseline assessment.

As noted in Table 3 above, patients treated with an energy level of ≤ 4.5 did not, as a group, obtain a therapeutic benefit. To demonstrate the effectiveness among patients treated with an energy level > 4.5, the primary analysis and each of the secondary analyses are repeated in Table 5 excluding Orthospec™ patients who received an energy level of ≤ 4.5.

As these tables demonstrate, there is a higher rate of pain relief and improvement in activity and function when patients were treated at energy level higher than 4.5.

Table 5 – Summary of Effectiveness Results at Three Months

<table>
<thead>
<tr>
<th>Orthospec Patients With Energy Level &gt; 4.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure</td>
</tr>
<tr>
<td>N=97</td>
</tr>
<tr>
<td>Investigator’s Assessment of Heel Pain</td>
</tr>
<tr>
<td>Mean change from baseline</td>
</tr>
<tr>
<td>Response rate</td>
</tr>
<tr>
<td>Patient’s Assessment of Heel Pain</td>
</tr>
<tr>
<td>Mean change from baseline</td>
</tr>
<tr>
<td>Response rate</td>
</tr>
<tr>
<td>Change in the use of Pain Medication</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

1 The last value was carried forward for all patients missing an assessment at month 3 and all analyses (except change in pain medication, which was adjusted for clinical site) were adjusted for clinical site and the corresponding baseline assessment.

Gender Analysis/Bias

The statistical analysis showed no significant correlation between age, gender, weight, and treatment effectiveness.
Complications and Adverse Events

The adverse events are presented in Section VIII above.

Device Failures and Replacements

There were six treatment interruptions and one aborted treatment. Five interrupted treatments were due to minor device malfunctions, i.e., shock wave counter and spark plug adjustment (user error). One interrupted treatment was due to pain. All treatments that were interrupted satisfied the required number of shocks or the required duration of treatment, and therefore the patients were able to complete the full treatment session. During the aborted treatment, a minor malfunction caused the treatment session to abort after the patient received 3,011 shocks. The Orthospec™ device was replaced at two sites due to service logistics.

Additional Clinical Experience

Medispec Ltd. previously conducted clinical studies of the Orthospec™ Extracorporeal Shock Wave Therapy (ESWT) for various orthopedic therapeutic indications including the treatment of pain of Plantar Fasciitis. A total of 1,117 Orthospec™ ESWT treatments were performed at 17 medical centers and clinics in 12 countries.

No significant adverse events were reported by any of the investigation sites. Minor adverse events included mild bruising, weakness, diaphoresis, and vomiting which all resolved without medical intervention.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

All assessments of the reduction of heel pain were found to be statistically significant when compared to placebo. During the clinical investigation, there were three reported cases of adverse events, all reported from the active treatment group. They included two mild cases of bruising and one case of mild local swelling noted only by the patient. These reported cases required no medical intervention or subsequent medical care.

The investigation demonstrates that the Orthospec™ device provides a reasonable assurance of safety and effectiveness for patients with symptoms of Proximal Plantar Fasciitis for 6 months or more and a history of unsuccessful conservative therapies to relieve heel pain.

XII. PANEL RECOMMENDATIONS

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 application was not referred to the General Surgical Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH DECISION

FDA issued an approval order on April 1, 2005.

The applicant’s manufacturing facility was inspected and found to be in compliance with the Quality System Regulation (21CFR 820).
XIV. APPROVAL SPECIFICATIONS

Directions for Use: See the Device Labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in the label.

Post Approval Requirements and Restrictions: See Approval Order.
SUMMARY OF SAFETY AND EFFECTIVENESS

I General Information
Device Generic Name: Orthopedic Extracorporeal Shock Wave Therapy Device
Device Trade Name: EMS Swiss DolorClast®
Applicant Name and Address: Electro Medical Systems (EMS) S.A.
Chemin de la Vuarpillière 31
CH – 1260
Nyon, Switzerland
PMA Number: P050004
Date of Panel Recommendation: None
Date of Notice of Approval to Applicant: May 8, 2007

II Indications for Use
The EMS Swiss DolorClast® is a non-surgical alternative for the treatment of chronic proximal plantar fasciitis for patients 18 years of age or older with symptoms for 6 months or more and a history of unsuccessful conservative therapy. Chronic proximal plantar fasciitis is defined as heel pain in the area of the insertion of the plantar fascia on the medial calcaneal tuberosity.

III Contraindications
Use of the EMS Swiss DolorClast® is contraindicated in the following situations:

1. Over or near bone growth center until bone growth is complete
2. When a malignant disease is known to be present in or near the treatment area
3. Infection in the area to be treated
4. Over ischemic tissue in individuals with vascular disease
5. Patient has a coagulation disorder or if taking anti-coagulant medications
6. Patient has a prosthetic device in the area to be treated.
IV  Warnings and Precautions

The warnings and precautions for use of the EMS Swiss DolorClast® for the treatment of chronic proximal plantar fasciitis can be found in the device labeling.

V  Device Description

The EMS Swiss DolorClast® consists of a control unit and a handpiece. An applicator is mounted onto the distal end of handpiece, fixed by a screw cap. A pressure pulse from the compressed air supply causes a projectile within the handpiece to be driven forward and to strike the inner surface of the applicator probe. The impact generates a shock wave in the applicator that travels to the distal surface of the probe and is transferred to the treatment target by direct contact. The shock wave propagates radially into the tissue from the point of contact. Thus, the device has no “focusing” characteristics, per se, because the maximum energy is directly at the coupling point on the skin surface, targeting the treatment areas of interest that are close to the skin. The maximum possible energy flux density ($E_{D,max}$) is $0.18 \text{ mJ/mm}^2$.

The EMS Swiss DolorClast® system consists of the following components:

- Control unit (100 – 240 VAC / 50 Hz – 60 Hz)
- Handpiece set with a 15 mm applicator
- Foot pedal
- Coupling gel bottle
- Power supply cord (hospital grade)
- Compressed air tube
- Component case

An air compressor and a mobile cart are provided as optional accessories.

The control unit houses the power supply, impulse circuitry, and pneumatic switches used to generate the pressure impulses to the handpiece. The pressure regulator controls the external compressed air supply, which is preset at 5 to 6 bar, providing a user-adjustable driving pressure of 0 to 4 bar for the handpiece. An increase in driving pressure results in an increase in projectile speed in the handpiece and a corresponding increase in applied energy to the tissue. The impulse frequency can be set from 1 to 15 Hz. Other user-selectable treatment parameters include the operating mode (single versus multiple impulses) and
number of impulses (1 to 9999). Treatment parameters (impulse pressure, impulse frequency and number of impulses) are displayed on the front panel of the pressure regulator/control unit. The device incorporates a microprocessor for control of the operating parameters.

VI Alternative Practices and Procedures

Chronic proximal plantar fasciitis is generally treated conservatively with a variety of pharmacological and nonpharmacological therapies. Pharmacological therapies may include OTC or prescription analgesics or non-steroidal anti-inflammatory agents (NSAIDs), local anesthetic injections or local corticosteroid injections. Nonpharmacological therapies may include physical therapy such as ice, heat or ultrasound; physiotherapy such as massage and stretching; orthotics, heel pads, shoe modifications, taping, night splints, immobilization, or casting. Current nonconservative treatments for chronic proximal plantar fasciitis include shockwave therapy with another commercially available shock wave therapy device or surgery.

VII Marketing History

The EMS Swiss DolorClast® received the CE Mark in July 1999. Since that time, approval to market the EMS Swiss DolorClast® has been granted in Brazil, Canada, Switzerland, the Czech Republic, Hungary, Russia, China, Korea, and Australia. The EMS Swiss DolorClast® is also commercially available in Hong Kong, where government marketing approval is not required. The EMS Swiss DolorClast® has not been withdrawn from marketing for any reason related to safety and effectiveness of the device in any country.

VIII Adverse Effects of the Device on Health

During the EMS Swiss DolorClas® clinical study, a total of 73 non-serious adverse events were reported during the 12 week follow-up period in 41 of the 129 patients (31.8%) receiving active treatment. Of these reports, 23 adverse events in 16 patients were considered to be not device related and 50 adverse events in 33 patients were considered to be device related. Eight patients reported both device related and non-device related adverse events.

In the placebo group, a total of 36 adverse events were reported in 27 of the 122 patients (22.1%) during the 12 week follow-up period. Of these reports, 25 adverse events in 19 patients were considered to be not device related, and 11 adverse events in 10 patients were considered to be device related. Two of these patients reported both device related and non-device related adverse events.
Table 1 summarizes the adverse events that were considered to be related to the device. The most common adverse event associated with use of the EMS Swiss DolorClast is pain or discomfort during treatment. This side effect was noted by 23% of the patients treated with the EMS Swiss DolorClast in the clinical study, but all patients except for one were able to complete their treatments without any anesthesia. In the majority of cases the duration of treatment pain was reported to be a maximum of less than 10 minutes.

Table 1: Summary of Device Related Adverse Events, Safety Population (n=251) at Visit 7 (12-Week Follow-up)

<table>
<thead>
<tr>
<th>Event</th>
<th>ESWT Group (N=129)</th>
<th>Placebo Group (N=122)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># Events</td>
<td># Subjects</td>
</tr>
<tr>
<td>Pain or discomfort during treatment</td>
<td>43</td>
<td>30¹</td>
</tr>
<tr>
<td>Pain post-treatment</td>
<td>5</td>
<td>5²</td>
</tr>
<tr>
<td>Skin reddening</td>
<td>1</td>
<td>1³</td>
</tr>
<tr>
<td>Swelling and pain post-treatment</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Numbness post-treatment</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

¹Twenty subjects with pain during one treatment session, seven during two sessions, and three during three sessions
²Three subjects also reported pain during treatment.
³This subject also reported pain during treatment.

In the active ESWT treated group, a total of 23 non-device related adverse events were reported in 16 of the 129 patients (12.4%). These were as follows: wasp sting (1), common cold disease (3), cough (1), sinusitis (2), headache (6), body aches (1), pain of the hip (1), toe (1) or neck (1), intermittent back pain of unknown etiology (1), aggravated neuroma (1), tinnitus (1), occasional knee weakness due to knee injury (1), developing tendonitis (1), and heart murmur (1).

In the placebo group, there were a total of 25 non-device related adverse events reported in 19 of the 122 patients (15.6%). These reports were as follows: gastric ulcer (1), upset stomach (2), irregular heart "movement" (1), pain long after treatment end in heel (1)/right shoulder (1)/body aches (1), infection of nose, ear and throat (1), fracture of the toe (right foot) (1), pain and swelling of left knee.
(1), acute nausea (1), adductor-strain (1), headache (10), common cold disease (2) and congestion (1).

Only six additional adverse events in five patients (1 in the active ESWT treated group and four in the placebo group) were reported during the 6-month and 12-month follow-up period. All of these reports were considered to be not related to the device. There was one report of ischiatic pain plus lumbar back pain in one patient in the active ESWT treated group. There were five non-device related adverse event reports in four patients in the placebo treated group. These were as follows: lateral right foot pain along metatarsus (1), acute nausea (1), teeth inflammation (1), zoster neuralgia (1), and umbilical hernia (1).

Other potential adverse events that have not been observed in clinical studies of the EMS Swiss DolorClast® may include:

- Bruising
- Rupture of the plantar fascia (tissue along the bottom of the foot)
- Temporary or permanent damage to the blood vessels
- Petechia
- Temporary or permanent nerve damage causing hypesthesia or paresphesia
- Hematoma
- Tendon Rupture

IX Summary of Non-Clinical Testing

Shock Wave Characterization

Acoustic output measurements were performed to measure the maximum shock wave output of the EMS Swiss DolorClast®. In addition, other shock wave performance characteristics as specified in FDA’s Guidance for the Content of Premarket Notifications (510(k)s) for Extracorporeal Shock Wave Lithotripters Indicated for the Fragmentation of Kidney and Ureteral Calculi, were measured where applicable. The experimental setup complied with the requirements of IEC 61846 (1998): Ultrasonecs - Pressure pulse lithotripters - Characteristics of fields. Measurements were made using a fiberoptic hydrophone, at maximum pressure setting, in a container of degassed water with the hydrophone positioned within an accuracy of 100 μm. Pressure signals from the hydrophone amplifier were
recorded using an oscilloscope through an average value calculation of 20 single impulses. Results are given in Table 2.

Table 2: Shockwave Characteristics

<table>
<thead>
<tr>
<th>Physical quantities</th>
<th>Symbol</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak positive acoustic pressure</td>
<td>( p_{+\text{max}} )</td>
<td>11.92 MPa</td>
</tr>
<tr>
<td>Peak negative acoustic pressure</td>
<td>( p_{-\text{max}} )</td>
<td>-5.86 MPa</td>
</tr>
<tr>
<td>Rise time</td>
<td>( t_r )</td>
<td>3 ( \mu \text{s} )</td>
</tr>
<tr>
<td>Compressional impulse duration</td>
<td>( t_p )</td>
<td>2.5 ( \mu \text{s} )</td>
</tr>
<tr>
<td>Compressional impulse duration</td>
<td>( t_p )</td>
<td>2.5 ( \mu \text{s} )</td>
</tr>
<tr>
<td>Pressure decrease time</td>
<td>-</td>
<td>0.91 ( \mu \text{s} )</td>
</tr>
<tr>
<td>Max. pos. Energy flux density</td>
<td>( \text{ED}_{+\text{max}} )</td>
<td>0.18 mJ/mm²</td>
</tr>
<tr>
<td>Maximum focal width (-6dB focal size ( x, y ))</td>
<td>( f_{x,\text{6db}} )</td>
<td>8.0 ( \times 10^3 ) m</td>
</tr>
<tr>
<td>Orthogonal focal width (-6dB focal size ( z ))</td>
<td>( f_{y,\text{6db}} )</td>
<td>8.0 ( \times 10^3 ) m</td>
</tr>
<tr>
<td>Focal extent</td>
<td>( f_{z,\text{6db}} )</td>
<td>8.0 ( \times 10^3 ) m</td>
</tr>
<tr>
<td>Focal volume</td>
<td>( f_{V,\text{6db}} )</td>
<td>268 ( \times 10^9 ) m³</td>
</tr>
<tr>
<td>Distance between the focus and target location</td>
<td>-</td>
<td>N.A. (not a focused device)</td>
</tr>
<tr>
<td>Derived focal acoustic impulse energy</td>
<td>( E_{-\text{6db}} )</td>
<td>5.4 mJ</td>
</tr>
<tr>
<td>Derived acoustic impulse energy</td>
<td>( E )</td>
<td>8.6 mJ</td>
</tr>
</tbody>
</table>

**Handpiece Longevity**

The longevity of the handpiece was validated to have a lifetime in excess of 500,000 impulses (equivalent to about 250 uses). Four handpieces were tested until failure or 1,000,000 impulses, whichever came first. One blocked after 500,000 impulses, another after 800,000 impulses and the remaining two were still functioning at 1,000,000 impulses.

**Electrical Safety and Electromagnetic Interference Testing**

The EMS Swiss DolorClast® was tested by Montena, a test laboratory certified by the Swiss Federal Office of Metrology, and found to be in conformance with the electrical safety requirements of IEC 60601-1: Medical Electrical Equipment - Part 1: General Requirements for Safety, and the electromagnetic compatibility requirements of IEC 60601-1-2: Medical Electrical Equipment - Part 1: General Requirements for Safety; Electromagnetic Compatibility -- Requirements and Tests.
Software Verification and Validation

Software verification and validation testing was conducted in accordance with the EMS Swiss DolorClast® Software Verification and Validation Plan and the device was found to meet all tests requirements, with no known unresolved anomalies remaining.

Biocompatibility Testing

Biocompatibility testing was conducted on the applicator, the only portion of the EMS Swiss DolorClast® intended to come in contact with the patient. Testing for in vitro cytotoxicity, sensitization, and intracutaneous reactivity was conducted in accordance with the applicable requirements of ISO 10993: Biological evaluation of medical devices - Part 1: Evaluation and Testing, and as specified in FDA’s guidance Required Biocompatibility Training and Toxicology Profiles for Evaluation of Medical Devices (May 1, 1995) and in accordance with the principles of Good Laboratory Practice. All test criteria were successfully met.

In addition, the manufacturer of the contact gel conducted a human patch test for primary skin irritation and allergic hypersensitivity to the gel. Thirty (30) volunteer subjects with no visible skin diseases and no known allergic hypersensitivities were tested for 24 hours and examined at patch removal and at 48 and 72 hours after removal. There was no evidence of primary irritation or allergic hypersensitivity in any of the subjects.

X. Summary of Clinical Investigations

Study Design

A multicenter, randomized, placebo-controlled, prospective, double blind clinical study was conducted to assess the safety and effectiveness of the EMS Swiss DolorClast® when used to treat unsuccessful conservatively treated subjects with symptoms of chronic proximal plantar fasciitis. A total of 251 subjects were randomized with a 1:1 allocation ratio to one of two groups: a group receiving ESWT with the EMS Swiss DolorClast® and a control group receiving a sham treatment. The study was conducted at eight clinical sites: three in the United States and five in Germany. For the purpose of this study, chronic proximal plantar fasciitis was defined as painful tenderness localized at the inferomedial aspect of the calcaneal tuberosity close to the insertion area of the plantar fascia that had persisted for at least 6 months prior to study enrollment.
**Subject Eligibility**

Subjects were required to meet the following eligibility criteria in order to be enrolled into the study:

**Inclusion Criteria**

1. Age greater than 18 years
2. Ability of subject or legal respondent to give written informed consent after being told of the potential benefits and risks of participating in the study
3. Signed informed consent
4. Diagnosis of painful heel syndrome (i.e., chronic proximal plantar fasciitis) proven by clinical examination
5. Six months of unsuccessful conservative treatment i.e., have undergone at least 2 unsuccessful non-pharmacological treatments and at least 2 unsuccessful pharmacological treatments. The following conservative treatments may have been completed as single, combined or consecutive treatments:
   - **Non-pharmacological treatments**
     - Physical therapy e.g., ice, heat or ultrasound
     - Physiotherapy e.g., massage and stretching
     - OTC-devices like orthosis, taping and heel pads
     - Prescribed orthosis
     - Shoe modification like higher heels
     - Cast/immobilization
     - Night splints
   - **Pharmacological treatments**
     - External (topical) application of analgesics and/or anti-inflammatory gels
     - Therapy with prescription analgesic and/or NSAIDs
     - Local anesthetic injections
     - Local corticosteroid injections
6. Time gap of at least:
   - 6 weeks since the last cortisone injection;
• 4 weeks since the last iontophoresis, ultrasound and electromyostimulation;
• 1 week since the last NSAIDs and
• 2 days since the last analgesics, heat, ice, massage, stretching, night splinting and orthosis
7. VAS Scores of ≥ 5 on two VAS pain scales (heel pain when taking first steps of the day and heel pain while doing daily activities)
8. Willingness to refrain from the following painful heel related, concomitant therapies: iontophoresis; electromyostimulation; ultrasound; NSAIDs; steroid injections or surgery – Until Visit 7 of this study (shoe modifications and rescue pain medication are allowed during the entire study)
9. Willingness to keep a Subject Heel Pain Medication and Other Heel Pain Therapy Diary until 12 months after the last ESWT treatment
10. Females of childbearing potential may be entered if they provide a negative urine pregnancy test immediately before the first ESWT treatment
11. Willingness of females of childbearing potential to use contraceptive measures for 2 months after enrollment into the study

Exclusion Criteria
1. Subjects suffering from tendon rupture, neurological or vascular insufficiencies of the painful heel
2. Inflammation of the lower and upper ankle
3. History of rheumatic diseases, and/or collagenosis and/or metabolic disorders
4. Subjects with a history of hyperthyroidism
5. Malignant disease with or without metastases
6. Subjects suffering from Paget disease or calcaneal fat pad atrophy
7. Subjects suffering from Osteomyelitis (acute, subacute, chronic)
8. Subjects suffering from fracture of the Calcaneus
9. Subjects with an immunosuppressive therapy
10. Subjects with a long-term-treatment with corticosteroid
11. Subjects suffering from diabetes mellitus, severe cardiac or respiratory disease
12. Subjects suffering from coagulation disturbance and/or therapy with Phenprocoumon, Acetylsalicylicacid or Warfarin
13. Bilateral painful heel, if both feet need medical treatment

14. Subjects who, at entry, are known to have treatment planned within the next 8 weeks, which may abruptly alter the degree or nature of pain experiences such that the shock wave therapy will no longer be necessary (e.g., surgery)

15. Time gap of less than:
   - 6 weeks since the last cortisone injection;
   - 4 weeks since the last iontophoresis, ultrasound and electromyostimulation;
   - 1 week since the last NSAIDs and
   - 2 days since the last analgesics, heat, ice, massage, stretching, night splinting and orthosis

16. Previous surgery of the painful heel syndrome

17. Previous unsuccessful treatment of the painful heel with a similar shock wave device

18. History of allergy or hypersensitivity to bupivacaine or local anesthetic sprays

19. Subjects with significant abnormalities in hepatic function

20. Subjects in a poor physical condition

21. Pregnant female

22. Infection in the treatment area recently or in medical history

23. History or documented evidence of peripheral neuropathy such as nerve entrapment, tarsal tunnel syndrome, etc.

24. History or documented evidence of systemic inflammatory disease such as rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, aseptic bone necrosis, Reiter's syndrome, etc.

25. History or documented evidence of worker's compensation or litigation

26. Participation in an investigational device study within 30 days prior to selection, or current inclusion in any other clinical study or research project

27. Subjects who, in the opinion of the investigator, will be inappropriate for inclusion into this clinical study or will not comply with the requirements of the study

Clinical Study Procedures

Subjects who signed the study informed consent form and met the study eligibility criteria were randomized to receive either the active or placebo device treatment in a 1:1 allocation, but were not told of their randomization assignments. The
placebo handpiece and applicator were constructed so that the pressure impulses were blocked from being transferred to the treatment site, but otherwise were the same as the active handpiece and applicator in terms of sound, vibration and appearance.

After a screening visit to determine eligibility (Visit 1), the study started at Visit 2 with the first treatment (after randomization). The treatment protocol was the same for active and placebo subjects. The protocol specified up to 2500 impulses at each of three visits (Visits 2, 3 and 4), spaced 2 weeks apart. The first 500 impulses were applied at gradually increasing pressure (from 2 to 4 bar at 8 Hz) in order to desensitize the subjects to the pain of the impulses. After the 500 introductory impulses, 2000 treatment impulses were performed at a pressure of 4 bar. If the patient could not tolerate the pain during the first 250 introductory impulses, the investigator was allowed to administer a local anesthesia in these subjects using 5-10 ml of 0.5% bupivacaine in a medial injection or a local anesthetic spray.

The follow-up period began 1 week after the last treatment (Visit 5, 5 weeks after randomization). Follow-up evaluations were performed by study investigators who were not involved in the subject’s treatment and were blinded as to the subject’s randomization. Follow-up visits continued at 6 weeks (Visit 6), and 12 weeks (Visit 7) following the last treatment (or 10 weeks and 16 weeks following randomization, respectively).

Subjects considered to be “responders” to the EMS Swiss DolorClast® treatment were to continue to return for follow-up visits at 6 months (Visit 8), and 12 months (Visit 9) following the last treatment (7 months and 13 months following randomization, respectively). A “responder” was defined in the study protocol as a subject with at least 60 percent reduction in pain when taking first steps of the day and while doing daily activities or, if less than 60 percent reduction on the above, then the subject was satisfied with the outcome of the treatment, was able to work (if applicable) and did not require concomitant therapy to control heel pain. Data through Visit 7 is presented to support the PMA approval of the EMS Swiss DolorClast®.

**Efficacy Endpoints**

As a result of a blinded review of the study data, it was determined that a high correlation existed between the three heel pain measurements recorded using a visual analog scale (VAS): 1) heel pain upon taking first steps of the day; 2) heel pain while doing daily activities; and 3) heel pain after application of the
Dolormeter (a standardized pressure device) \((r=0.85, r=0.79, \text{ and } r=0.80, \text{ respectively})\). Therefore, a composite of these three measures was used as the primary efficacy endpoint, calculated two ways, first on a continuous scale as the sum score of the three measurements and second on a binary scale (success/failure) with “success” being defined as greater than 60 percent reduction in VAS score from baseline to Visit 7 (12 weeks after the last ESWT treatment) on at least two of the three heel pain measurements.

The secondary efficacy endpoints were the differences between groups at Visit 7 on the Roles and Maudsley Score, the SF-36 Quality of Life questionnaire, the investigator’s global judgment of effectiveness of the treatment, and the subject’s satisfaction with the outcome of the treatment.

**Safety Endpoints**

The safety of the EMS Swiss DolorClast\textsuperscript{®} treatment was evaluated by comparing the type, device relationship, intensity and seriousness of adverse events reported by the subjects in both groups during treatment and during the study follow-up period.

**Patient Accountability**

All subjects who were enrolled in the study and received at least one treatment were evaluated for safety as the Safety Population \((N = 251: 129 \text{ ESWT and } 122 \text{ placebo})\). Subjects who received at least one treatment and had at least one follow-up evaluation were evaluated for efficacy as the Intent to Treat (ITT) population \((N=243; 125 \text{ ESWT and } 118 \text{ placebo})\). Efficacy was determined in the ITT patients who dropped out before completing all treatments or evaluations using the “Last Value Carried Forward” technique. Subjects who completed all three treatment sessions and all follow-up evaluations through Visit 7 (12 weeks after the last treatment) were considered the Per Protocol (PP) population \((N=219: 111 \text{ ESWT and } 108 \text{ placebo}; \text{ for a total follow-up rate through Visit 7 of } 87.3\% (219/251))\). Both ITT and PP populations were used in primary efficacy analysis. All missing values in both data analyses were handled using the “Last Value Carried Forward” (LVCF) technique.

The Safety Population included 152 subjects enrolled in five German centers (78 ESWT and 74 placebo) and 99 subjects enrolled in three United States centers (51 ESWT and 48 placebo).
Baseline Characteristics

The baseline characteristics and demographic data presented in Table 3 below for the ITT patient population demonstrate that the ESWT and placebo groups were comparable at baseline as all effect sizes using the Wilcoxon-Mann-Whitney test indicate equality and all p-values are not statistically significant (p > 0.1).

The ESWT and placebo groups were also very similar with respect to the prior failed therapies. All subjects met the study entry criteria of having tried and failed at least two pharmacological and two nonpharmacological therapies for their chronic proximal plantar fasciitis with the exception of one subject in the ESWT group and two subjects in the placebo group (ITT population).

Table 3: Baseline Characteristics, ITT Population (Intention-to-Treat)

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>ESWT ITT (N = 125)</th>
<th>Placebo ITT (N = 118)</th>
<th>Effect Size¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>52.4 (11.98)</td>
<td>52.0 (10.54)</td>
<td>0.5174</td>
</tr>
<tr>
<td>Range</td>
<td>23-77</td>
<td>18-78</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>69.60% (87/125)</td>
<td>66.95% (79/118)</td>
<td>0.4867</td>
</tr>
<tr>
<td>Male</td>
<td>30.40% (38/125)</td>
<td>33.05% (39/118)</td>
<td></td>
</tr>
<tr>
<td>Ethnic Origin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White, Non-Hispanic</td>
<td>92.0% (115/125)</td>
<td>95.8% (113/118)</td>
<td>See footnote 2</td>
</tr>
<tr>
<td>Hispanic</td>
<td>4.0% (5/125)</td>
<td>0.8% (1/118)</td>
<td></td>
</tr>
<tr>
<td>Afro-American</td>
<td>0.8% (1/125)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>2.4% (3/125)</td>
<td>2.5% (3/118)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0.8% (1/125)</td>
<td>0.8% (1/118)</td>
<td></td>
</tr>
<tr>
<td>Body Weight (kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>79.0 (14.67)</td>
<td>81.1 (16.25)</td>
<td>0.4678</td>
</tr>
<tr>
<td>Range</td>
<td>48-118</td>
<td>50-131</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>170.5 (10.06)</td>
<td>170.4 (8.36)</td>
<td>0.4945</td>
</tr>
<tr>
<td>Range</td>
<td>138-202</td>
<td>154-197</td>
<td></td>
</tr>
</tbody>
</table>
Table 3: Baseline Characteristics, ITT Population (Intention-to-Treat) (Continued)

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>ESWT ITT (N = 125)</th>
<th>Placebo ITT (N = 118)</th>
<th>Effect Size$^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heel Pain Duration (months)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>25.6 (26.09)</td>
<td>24.9 (25.27)</td>
<td>0.5023</td>
</tr>
<tr>
<td>Range</td>
<td>6-99</td>
<td>6-99</td>
<td></td>
</tr>
<tr>
<td>Heel pain (VAS) when taking first steps in the morning</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>7.5 (1.49)</td>
<td>7.5 (1.57)</td>
<td>0.4941</td>
</tr>
<tr>
<td>Range</td>
<td>3-10</td>
<td>5-10</td>
<td></td>
</tr>
<tr>
<td>Heel pain (VAS) while doing daily activities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>7.3 (1.48)</td>
<td>7.1 (1.53)</td>
<td>0.4525</td>
</tr>
<tr>
<td>Range</td>
<td>3-10</td>
<td>4-10</td>
<td></td>
</tr>
<tr>
<td>Heel pain (VAS) after application of the Dolormeter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>7.2 (1.73)</td>
<td>7.1 (1.75)</td>
<td>0.4701</td>
</tr>
<tr>
<td>Range</td>
<td>0-10</td>
<td>2-10</td>
<td></td>
</tr>
<tr>
<td>Roles and Maudsley score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>3.5 (0.52)</td>
<td>3.5 (0.57)</td>
<td>0.4917</td>
</tr>
<tr>
<td>Range</td>
<td>2-4</td>
<td>2-4</td>
<td></td>
</tr>
<tr>
<td>SF-36 Physical Health Score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>45.0 (20.05)</td>
<td>46.7 (20.58)</td>
<td>0.5248</td>
</tr>
<tr>
<td>Range</td>
<td>5-88</td>
<td>9-86</td>
<td></td>
</tr>
<tr>
<td>SF-36 Mental Health Score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>29.9 (20.07)</td>
<td>29.9 (19.38)</td>
<td>0.5055</td>
</tr>
<tr>
<td>Range</td>
<td>0-78</td>
<td>0-90</td>
<td></td>
</tr>
</tbody>
</table>

$^1$The Mann-Whitney estimator is the corresponding standardized effect size measure of the Wilcoxon-Mann-Whitney test. Benchmarks for group differences: 0.5 equality, 0.44/0.56 small, 0.36/0.64 medium, 0.29/0.71 large.

$^2$Differences between groups not significant, p=0.4995 using the Fisher Exact Test (Mann-Whitney not appropriate for categorical variables).
Treatment Characteristics

The majority of subjects in the Safety Population completed all three treatment sessions 90.7\% (117/129) ESWT and 95.9\% (117/122) placebo. The average number of impulses delivered per treatment session ranged between 2413 and 2451 and was very similar between the two treatment groups (p-value>0.5 for all three treatments). Although 30 ESWT and five placebo subjects complained of pain during treatment, only one subject requested local anesthesia for the pain. Only one device malfunction was reported during the study (placebo applicator did not function and treatment was conducted with a second applicator). No subject in either group experienced an adverse event as a result of a device malfunction.

Primary Efficacy Results

The time point for evaluating the primary efficacy of the treatments was at Visit 7 (12 weeks following the third treatment session). Results are presented for both the ITT population (subjects who completed at least one treatment session and one evaluation session) and the Per Protocol population (subjects who completed all three treatment sessions and all follow-up evaluations). Missing data was handled using the Last Value Carried Forward (LVCF) approach. Pain scores were adjusted for subjects who took interfering analgesics or had other therapies for their chronic proximal plantar fasciitis within predefined timeframes prior to evaluation visits by adding 2 points to their VAS scores for the affected visit. EMS conducted supportive sensitivity analyses to confirm the results obtained using these methods.

Table 4 presents the primary efficacy results for the ITT population. In the ESWT group, the mean composite pain score (sum of VAS scores for the three pain measures) decreased from 22.0 ± 3.24 at baseline to 9.7 ± 8.56 at Visit 7, for a mean percent decrease (i.e., improvement) of 56 percent. In the placebo group, the mean composite pain score decreased from 21.6 ± 3.22 at baseline to 12.3 ± 9.39 at Visit 7, for a mean percent decrease of 44 percent. These results show a significant improvement in the mean composite VAS score for the ESWT group as compared to the placebo group (p=0.022).
The result for overall success rate, defined as greater than 60 percent reduction in VAS pain scores on at least two of the three pain measures, was also superior for the ESWT group as compared to the placebo group. Sixty-one percent (75/123) of the ESWT subjects met this success criterion as compared to 42 percent (49/116) of the placebo subjects group (p=0.002).

Table 4: Primary Efficacy Results for ITT Population at Visit 7 - Composite Scores for Three VAS Measures

<table>
<thead>
<tr>
<th></th>
<th>ESWT (N=125)</th>
<th>Placebo (N=118)</th>
<th>Effect Size</th>
<th>P-Value One Sided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite VAS Score:</td>
<td></td>
<td></td>
<td>0.5753</td>
<td>0.0220</td>
</tr>
<tr>
<td>Percent Change from</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline at Visit 7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>-56.0 (39.31)</td>
<td>-44.1 (41.81)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>-72.1</td>
<td>-44.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall Success Rate</td>
<td></td>
<td></td>
<td>0.5937</td>
<td>0.0020</td>
</tr>
<tr>
<td>(&gt;60% reduction in</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS on at least two</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pain measures)</td>
<td>60.98%</td>
<td>42.24%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(75/123)</td>
<td>(49/116)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1Mann-Whitney (MW) effect size
2Wilcoxon-Mann-Whitney test
3Unconditional Exact Röhmel-Mansman test

Table 5 presents the results for the Per Protocol population. In this population, where all subjects received the full prescribed three treatments, the results for the ESWT group improved (as compared to the ITT population) while the results for the placebo group stayed essentially the same (as compared to the ITT population). The superiority of the Per Protocol ESWT group as compared to the Per Protocol placebo group is confirmed by this analysis (p<0.01 on both composite VAS score and overall success).
Table 5: Primary Efficacy Results for Per Protocol Population at Visit 7 - Composite Scores for Three VAS Measures

<table>
<thead>
<tr>
<th></th>
<th>ESWT (Npp=111)</th>
<th>Placebo (Npp=108)</th>
<th>Effect Size¹</th>
<th>P-Value One sided</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Composite VAS Score:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent Change from Baseline at Visit 7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>-60.6 (35.97)</td>
<td>-44.2 (42.11)</td>
<td>0.6037</td>
<td>0.0041²</td>
</tr>
<tr>
<td>Median</td>
<td>-75.0</td>
<td>-44.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Overall Success Rate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(&gt;60% reduction in VAS on at least two pain measures)</td>
<td>64.55% (71/110)</td>
<td>43.40% (46/106)</td>
<td>0.5788</td>
<td>0.0011³</td>
</tr>
</tbody>
</table>

¹Mann-Whitney (MW) effect size
²Wilcoxon-Mann-Whitney test
³Unconditional Exact Röhmel-Mansman test

Secondary Efficacy Results

Table 6 presents the results of the secondary efficacy criteria, including the Roles and Maudsley Score, SF-36 Quality of Life evaluation, investigator’s global judgment of effectiveness, and subject’s satisfaction with their therapy outcome. The ESWT group demonstrated greater improvements from baseline to Visit 7 on all secondary measures as compared to the placebo group (P < 0.025 one-sided).
Table 6: Secondary Efficacy Results for ITT Population

<table>
<thead>
<tr>
<th></th>
<th>ESWT (N=125)</th>
<th>Placebo (n=118)</th>
<th>Effect Size&lt;sup&gt;1&lt;/sup&gt;</th>
<th>P-Value One Sided</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Roles and Maudsley Score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent or Good</td>
<td>58.40%</td>
<td>41.52%</td>
<td>0.5973</td>
<td>0.031&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(73/125)</td>
<td>(49/118)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fair or Poor</td>
<td>41.60%</td>
<td>58.48%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(52/125)</td>
<td>(69/118)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SF-36 Physical&lt;sup&gt;1&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent Change from Baseline at Visit 7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean / SD</td>
<td>-37.2 (48.42)</td>
<td>-19.5 (52.13)</td>
<td>0.6191</td>
<td>0.013&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Median</td>
<td>-44.1</td>
<td>-23.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SF-36 Mental&lt;sup&gt;1&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent Change from Baseline at Visit 7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean / SD</td>
<td>-14.6 (62.89)</td>
<td>+8.4 (99.06)</td>
<td>0.5850</td>
<td>0.016&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Median</td>
<td>-22.8</td>
<td>-14.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Investigator Judgment of Effectiveness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very good or Good</td>
<td>70.80%</td>
<td>40.91%</td>
<td>0.6335</td>
<td>0.0002&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(80/113)</td>
<td>(45/110)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>10.62%</td>
<td>20.91%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(12/113)</td>
<td>(23/110)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unsatisfactory or Poor</td>
<td>18.58%</td>
<td>38.18%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(21/113)</td>
<td>(42/110)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Patient Judgment of Therapy Satisfaction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very or Moderately Satisfied</td>
<td>63.16%</td>
<td>46.36%</td>
<td>0.5984</td>
<td>0.0045&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(72/114)</td>
<td>(51/110)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slightly Satisfied or Neutral</td>
<td>18.42%</td>
<td>10.00%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(21/114)</td>
<td>(11/110)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dissatisfied</td>
<td>18.42%</td>
<td>43.64%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(21/114)</td>
<td>(48/110)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup>SF-36 scores standardized using a scale from 0 (best score) to 100 (worst score); negative percent change from baseline indicates improvement.

<sup>2</sup>Mann-Whitney (MW) effect size

<sup>3</sup>p-values of one-sided test for superiority using the Wilcoxon-Mann-Whitney test
Safety Results

Adverse events are presented in section VIII above.

Follow-up Results at 6-Months and 12-Months

Treatment Responders at Visit 7 continued in the study and returned for two additional follow-up visits, Visit 8 at 6 months following the last treatment and Visit 9 at 12 months following the last treatment.

Results at both the 6-month and 12-month follow-up visits were similar to the results presented in Table 4 for visit 7. Results at the 12-month follow-up (Visit 9) are shown in Table 7 for the ITT population. Results include the composite scores and overall success rate in accordance with the same criteria used for the primary efficacy results at Visit 7 (Table 4). Missing data was handled using the Last Value Carried Forward (LVCF) approach. Pain scores were adjusted for subjects who took interfering analgesics or had other therapies for chronic proximal plantar fasciitis within predefined timeframes prior to evaluation visits by adding 2 points to their VAS scores for the affected visit.

In both the ESWT group and the placebo group, the mean composite scores increased slightly from the scores at Visit 7. The results continue to show an improvement in the mean composite VAS score for the ESWT group as compared to the placebo group. Likewise, the overall success rate (defined as greater than 60 percent reduction in VAS pain scores on at least two of the three pain measures) for the ESWT group continued to be superior to that of the placebo group. These results confirm that the results obtained at the 3-month primary efficacy endpoint are maintained over a period of up to 12 months.
Table 7: Efficacy Results for ITT Population at Visit 9 (12-months) - Composite Scores for Three VAS Measures

<table>
<thead>
<tr>
<th></th>
<th>ESWT (N=125)</th>
<th>Placebo (N=118)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Composite VAS Score:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent Change from Baseline at Visit 9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>-61.9(43.62)</td>
<td>-46.5 (45.52)</td>
</tr>
<tr>
<td>Median</td>
<td>-84.8</td>
<td>-43.2</td>
</tr>
<tr>
<td><strong>Overall Success Rate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(&gt;60% reduction in VAS on at least two pain measures)</td>
<td>63.41% (78/123)</td>
<td>43.97% (51/116)</td>
</tr>
</tbody>
</table>
XIII  CDRH Decision

FDA issued an approval order on May 8, 2007.

The applicant’s manufacturing facility was inspected and was found to be in compliance with the Quality Systems Regulation (21 CFR 820).

XIV  Approval Specifications

Directions for Use: See the Device Labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in the labeling.

Post Approval Requirements and Restrictions: See Approval Order.
EMS
Swiss DolorClast®

PHYSICIAN’S LABELING

CAUTION! Federal law restricts this device to sale by or on the order of a physician.

Manufacturer
EMS Electro Medical System S.A
Chemin de la Vuarpillière 31
CH-1260 Nyon, Switzerland

US Distributor
EMS Corporation
11886 Greenville Avenue #120
Dallas, Texas 75243 - USA

Release date: April 5, 2007
1. INTRODUCTION

The EMS Swiss DolorClast® is an extracorporeal shock wave device intended for use in applying shock waves to the heel of patients who have chronic proximal plantar fasciitis and who have failed prior conservative therapies. Shock waves generated by the EMS Swiss DolorClast® propagate radially into the tissue from the point of contact. Thus, the device has no “focusing” characteristics, per se, because the maximum energy is directly at the coupling point on the skin surface, targeting the treatment areas of interest that are close to the skin.

The EMS Swiss DolorClast® is intended to be used by medical professionals who have been trained in its operation.

2. INDICATIONS FOR USE

The EMS Swiss DolorClast® is a non-surgical alternative for the treatment of chronic proximal plantar fasciitis for patients 18 years of age or older with symptoms for 6 months or more and a history of unsuccessful conservative therapy. Chronic proximal plantar fasciitis is defined as heel pain in the area of the insertion of the plantar fascia on the medial calcaneal tuberosity.

3. CONTRAINDICATIONS

Use of the EMS Swiss DolorClast® is contraindicated in the following situations:
- Over or near bone growth center until bone growth is complete
- When a malignant disease is known to be present in or near the treatment area
- Infection in the area to be treated
- Over ischemic tissue in individuals with vascular disease
- Patient has a coagulation disorder or is taking anti-coagulant medications
- Patient has a prosthetic device in the area to be treated.

4. WARNINGS

- This EMS Swiss DolorClast® device must be operated by personnel trained in Radial Extracorporeal Shock Wave Therapy
- The EMS Swiss DolorClast® may only be used by qualified and trained persons in medical facilities for its intended purpose.
- Operators of the EMS Swiss DolorClast® should carefully read the Operator Instruction Manual before use.
Operators of the EMS Swiss DolorClast® should be aware of the proper use of the device in delivering the correct number of impulses and in localizing the proper area to be treated.

The EMS Swiss DolorClast® handpiece must be carefully positioned and treatment should be performed by a physician trained and experienced in the care of patients with foot and ankle disorders who has been instructed in the operation of the EMS Swiss DolorClast®.

Avoid treatment over main nerves or vessels to avoid injury to these structures.

Patients currently undergoing systemic anticoagulation therapy, or other medications that might prolong bleeding time (such as aspirin) should consult with their physicians regarding temporary discontinuation of such medications before beginning treatments to prevent potential, bruising, or hematoma.

The safety and effectiveness of the EMS Swiss DolorClast® in the treatment of pregnant women, children under the age of 18 years, or patients who have had prior surgery for plantar fasciitis have not been demonstrated. The EMS Swiss DolorClast® is indicated only for patients 18 years of age or older.

Studies indicate that there are growth plate disturbances in the epiphyses of developing long bones in rats subjected to shockwaves. The significance of these findings in humans is unknown.

For safety reasons, never connect the handpiece to the housing when the handpiece is not fully assembled. Before assembling/disassembling the handpiece, the quick connector of the connecting tube must be disconnected from the housing; otherwise, there is a potential risk of injury by the projectile in the handpiece if the foot pedal is pressed accidentally.

This device should not be operated in an explosion hazardous environment.

To avoid danger of spreading germs and cross contamination of patients it is essential to clean the EMS Swiss DolorClast® before each treatment and sterilize the patient contacting parts if they come in contact with compromised skin.

5. PRECAUTIONS

Patient pain tolerance is enhanced by starting at a low pressure (i.e., 2 bar) and gradually increasing the pressure to 4 bar over approximately 500 impulses. However, if the patient is not able to tolerate the treatment, then local anesthesia should be administered. Patients who are unable to tolerate local or regional anesthetic or cannot tolerate the treatment pain even with a local or regional anesthetic should not be treated with this device and should consider alternative therapies. All but
one patient treated in the EMS Swiss DolorClast® clinical study were able to tolerate the treatment without anesthesia.

- Although no patients in the clinical study experienced a vaso-vagal reaction during treatment, this reaction has been reported with other types of extracorporeal shock wave therapy. If this reaction occurs, the treatment should be interrupted and the patient reclined to a supine position until symptoms disappear.

- The housing of the EMS Swiss DolorClast® is not watertight. The handpiece is neither watertight nor autoclavable and should not be immersed into liquids nor chemically disinfected.

- The safety and effectiveness of the EMS Swiss DolorClast® to treat painful heel has not been established for patients with the following conditions:

  - Under 18 years of age
  - Diseases or disorders of the nerves in the foot to be treated
  - Diseases or disorders of the bones in the foot to be treated
  - Infection in the area to be treated
  - Current or recent therapy that would compromise tissue healing
  - Problems with circulation or bleeding
  - History or documented evidence of immune system deficiencies (autoimmune disease)
  - Significant disease of the blood vessels in the foot to be treated
  - Rheumatoid arthritis (pain, stiffness or swelling of the joints)
  - Malignant disease with or without metastases in heel
  - Previous treatment of the painful heel with corticosteroid injections within 6 weeks of the EMS Swiss DolorClast® treatment or previous treatment with non-steroidal anti-inflammatory drugs within 1 week of the EMS Swiss DolorClast® treatment
  - Previous surgery for painful heel
  - Pregnant female

6. ADVERSE EVENTS

During the EMS Swiss DolorClast® clinical study, a total of 73 non-serious adverse events were reported during the 12 week follow-up period in 41 of the 129 patients (31.8%) receiving active treatment. Of these reports, 23 adverse events in 16 patients were considered to be not device related and 50 adverse events in 33 patients were considered to be device related. Eight patients reported both device related and non-device related adverse events.
In the placebo group, a total of 36 adverse events were reported in 27 of the 122 patients (22.1%) during the 12-week follow-up period. Of these reports, 25 adverse events in 19 patients were considered to be not device related, and 11 adverse events in 10 patients were considered to be device related. Two of these patients reported both device related and non-device related adverse events.

Table 1 summarizes the adverse events that were considered to be related to the device. The most common adverse event associated with use of the EMS Swiss DolorClast® is pain or discomfort during treatment. This side effect was noted by 23% of the patients treated with the EMS Swiss DolorClast® in the clinical study, but all patients except for one were able to complete their treatments without any anesthesia. In the majority of cases the duration of treatment pain was reported to be a maximum of less than 10 minutes.

<table>
<thead>
<tr>
<th>Event</th>
<th>ESWT Group (N=129)</th>
<th>Placebo Group (N=122)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># Events</td>
<td># Subjects</td>
</tr>
<tr>
<td>Pain or discomfort during treatment</td>
<td>43</td>
<td>30¹</td>
</tr>
<tr>
<td>Pain post-treatment</td>
<td>5</td>
<td>5²</td>
</tr>
<tr>
<td>Skin reddening</td>
<td>1</td>
<td>1³</td>
</tr>
<tr>
<td>Swelling and pain post-treatment</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Numbness post-treatment</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

¹ Twenty subjects with pain during one treatment session, seven during two sessions, and three during three sessions.
² Three subjects also reported pain during treatment.
³ This subject also reported pain during treatment.

In the active ESWT treated group, a total of 23 non-device related adverse events were reported in 16 of the 129 patients (12.4%). These were as follows: wasp sting (1), common cold disease (3), cough (1), sinusitis (2), headache (6), body aches (1), pain of the hip (1), toe (1) or...
neck (1), intermittent back pain of unknown etiology (1), aggravated neuroma (1), tinnitus (1), occasional knee weakness due to knee injury (1), developing tendonitis (1), and heart murmur (1).

In the placebo group, there were a total of 25 non-device related adverse events reported in 19 of the 122 patients (15.6%). These reports were as follows: gastric ulcer (1), upset stomach (2), irregular heart "movement" (1), pain long after treatment end in heel (1)/right shoulder (1)/body aches (1), infection of nose, ear and throat (1), fracture of the toe (right foot) (1), pain and swelling of left knee (1), acute nausea (1), adductor-strain (1), headache (10), common cold disease (2) and congestion (1). Only six additional adverse events in five patients (1 in the active ESWT treated group and four in the placebo group) were reported during the 6-month and 12-month follow-up period. All of these reports were considered to be not related to the device. There was one report of sciatic pain plus lumbar back pain in one patient in the active ESWT treated group. There were five non-device related adverse event reports in four patients in the placebo treated group. These were as follows: lateral right foot pain along metatarsus (1), acute nausea (1), teeth inflammation (1), zoster neuralgia (1), and umbilical hernia (1).

Other potential adverse events that have not been observed in clinical studies of the EMS Swiss DolorClast® may include:

- Bruising
- Rupture of the plantar fascia (tissue along the bottom of the foot)
- Temporary or permanent damage to the blood vessels
- Petechia
- Temporary or permanent nerve damage causing hypesthesia or parasthesia
- Hematoma
- Tendon rupture
7. CLINICAL STUDY

A multi-center, randomized, placebo-controlled, prospective, double-blind clinical study was conducted with two groups: a group receiving radial ESWT with the EMS Swiss DolorClast® and a control group receiving a sham treatment. A total of 251 patients, randomized in a 1:1 allocation ratio, were treated at eight clinical sites. For the purpose of this study, chronic proximal plantar fasciitis was defined as painful tenderness localized at the inferomedial aspect of the calcaneal tuberosity close to the insertion area of the plantar fascia that had persisted for at least six months prior to study enrollment.

7.1 Subject Eligibility

The eligibility criteria described in the study protocol were as follows:

**Inclusion Criteria**

All of the following criteria have to be met for inclusion of a subject into the study:

1. Age greater than 18 years,
2. Ability of subject or legal respondent to give written informed consent after being told of the potential benefits and risks of participating in the study,
3. Signed informed consent,
4. Diagnosis of painful heel syndrome (i.e., chronic proximal plantar fasciitis) proven by clinical examination,
5. 6 months of unsuccessful conservative treatment i.e., must have undergone at least 2 unsuccessful non-pharmacological treatments and at least 2 unsuccessful pharmacological treatments. The following conservative treatments may have been completed as single, combined or consecutive treatments:

**Non-pharmacological treatments**

- Physical therapy e.g., ice, heat or ultrasound
- Physiotherapy e.g., massage and stretching
- OTC-devices like orthosis, taping and heel pads
- Prescribed orthosis
- Shoe modification like higher heels
- Cast/immobilization
- Night splints

**Pharmacological treatments**

- External (topical) application of analgesics and/or anti-inflammatory gels
- Therapy with prescription analgesic or NSAIDs
- Local anesthetic injections
- Local corticosteroid injections
6. Time gap of at least:
   - 6 weeks since the last cortisone injection;
   - 4 weeks since the last iontophoresis, ultrasound and electromyostimulation;
   - 1 week since the last NSAIDs and
   - 2 days since the last analgesics, heat, ice, massage, stretching, night splinting and orthosis

7.Scores of ≥ 5 on both VAS pain scales (heel pain when taking first steps of the day and heel pain while doing daily activities)

8. Willingness to refrain from the following painful heel related, concomitant therapies: iontophoresis; electromyostimulation; ultrasound; NSAIDs; steroid injections or surgery – Until Visit 7 of this study (shoe modifications and rescue pain medication are allowed during the entire study)

9. Willingness to keep a Subject Heel Pain Medication and Other Heel Pain Therapy Diary until 12 months after the last treatment,

10. Females of childbearing potential may be entered if they provide a negative urine pregnancy test immediately before the first ESWT treatment

11. Willingness of females of childbearing potential to use contraceptive measures for 2 months after enrollment into the study

**Exclusion Criteria**

Any of the following excludes a subject from the study:

1. Subjects suffering from tendon rupture, neurological or vascular insufficiencies of the painful heel;
2. Inflammation of the lower and upper ankle;
3. History of rheumatic diseases, and/or collagenosis and/or metabolic disorders;
4. Subjects with a history of hyperthyroidism;
5. Malignant disease with or without metastases;
6. Subjects suffering from Paget disease or calcaneal fat pad atrophy;
7. Subjects suffering from Osteomyelitis (acute, sub acute, chronic);
8. Subjects suffering from fracture of the Calcaneus;
9. Subjects with an immunosuppressive therapy;
10. Subjects with a long-term-treatment with corticosteroid;
11. Subjects suffering from diabetes mellitus, severe cardiac or respiratory disease;
12. Subjects suffering from coagulation disturbance and/or therapy with Phenprocoumon, Acetylsalicylic acid or Warfarin;
13. Bilateral painful heel, if both feet need medical treatment;
14. Subjects who, at entry, are known to have treatment planned within the next 8 weeks, which may abruptly alter the degree or nature of pain experienced such that the radial extracorporeal shock wave therapy will no longer be necessary (e.g., surgery);
15. Time gap of less than:
   - 6 weeks since the last cortisone injection;
4 weeks since the last iontophoresis, ultrasound and electromyostimulation;
1 week since the last NSAIDs and
2 days since the last analgesics, heat, ice, massage, stretching, night splinting and orthosis;
16. Previous surgery of the painful heel syndrome;
17. Previous unsuccessful treatment of the painful heel with a similar shock wave device;
18. History of allergy or hypersensitivity to bupivacaine or local anesthetic sprays;
19. Subjects with significant abnormalities in hepatic function;
20. Subjects in a poor physical condition;
21. Pregnant female;
22. Infection in the treatment area recently or in medical history;
23. History or documented evidence of peripheral neuropathy such as nerve entrapment, tarsal tunnel syndrome, etc.;
24. History or documented evidence of systemic inflammatory disease such as rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, aseptic bone necrosis, Reiter's syndrome, etc.;
25. History or documented evidence of worker's compensation or litigation;
26. Participation in an investigational device study within 30 days prior to selection, or current inclusion in any other clinical study or research project;
27. Subjects who, in the opinion of the investigator, will be inappropriate for inclusion into this clinical study or will not comply with the requirements of the study.

7.2 Study Design

Subjects who signed the study informed consent form and met the study eligibility criteria were randomized to receive either the active or placebo device treatment in a 1:1 allocation, but were not told of their randomization assignment. The placebo handpiece and applicator were constructed so that the pressure impulse was blocked from being transferred to the treatment site, but otherwise was the same as the active handpiece and applicator in terms of sound, vibration and appearance.

After a screening visit to determine eligibility (Visit 1), the study started at Visit 2 with the first treatment (after randomization). The treatment protocol was the same for active and placebo subjects. The protocol specified up to 2500 impulses at each of three visits (V2, V3 and V4), spaced 2 weeks apart. The first 500 shocks were applied at gradually increasing pressure (from 2 to 4 bar) in order to desensitize the patient to the pain of the impulses. After the 500 introductory impulses, 2000 treatment impulses were performed at a pressure of 4 bar. If the patient could not tolerate the pain during the first 250 introductory impulses, the investigator was allowed to perform a local anesthesia in these subjects using 5-10 ml of 0.5% bupivacaine in a medial application or a local anesthetic spray.
The follow-up period began 1 week after the last treatment (Visit 5, 5 weeks after randomization). Follow-up evaluations were performed by study investigators who were not involved in the subject’s treatment and were blinded as to the subject’s randomization. Follow-up visits continued at 6 weeks (Visit 6), and 12 weeks (Visit 7) following the last treatment (or 10 weeks and 16 weeks following randomization, respectively). Patients who had sufficient pain relief to meet the study definition of “responders” continued in the study at this point and were followed again at 6 months (Visit 8) and 12 months (Visit 9) following the last treatment. A “responder” was defined in the study protocol as a subject with at least 60 percent reduction in pain when taking first steps of the day and while doing daily activities or, if less than 60 percent reduction on the above, then the subject was satisfied with the outcome of the treatment, was able to work (if applicable) and did not require concomitant therapy to control heel pain.

7.3 Study Population.

A total of 251 subjects formed the Safety Population for the study: 152 in five German centers and 99 in three US centers. Of these, 129 were randomized to the active group and 122 to the placebo group. Ninety-seven percent of this patient population (243/251) received at least one treatment and had at least one follow-up evaluation, and formed the core patient population for efficacy analysis (Intent to Treat population, ITT). Of these 243 patients, 125 were in the ESWT group and 118 were in the placebo group. Eighty-seven percent of the Safety Population had all three treatments and completed all follow-up visits through Visit 7 (Per Protocol population, PP). Of the 219 Per Protocol patients, 111 were in the ESWT group and 108 were in the placebo group.

Analysis of the subject baseline characteristics and demographic data for the ITT patient population demonstrate that the ESWT and placebo groups were well comparable at baseline on all variables and all p-values were statistically not significant (p > 0.1).

7.4 Treatment Information

The majority of subjects in the Safety Population completed all three treatment sessions 90.7% (117/129) ESWT and 95.9% (117/122) placebo. The average number of impulses delivered per treatment session ranged between 2413 and 2451 and was very similar between the two treatment groups (p-value >0.5 for all treatment sessions. Placebo impulses were blocked from reaching the treatment area. Although 30 ESWT and 5 placebo subjects complained of pain during treatment, only one subject requested local anesthesia for the pain. Only one device malfunction was reported during the study (placebo applicator did not function and treatment was conducted with a second applicator). No subject in either group experienced an adverse event as a result of a device malfunction.
### 7.5 Primary Efficacy Results

The primary efficacy endpoint was a composite of three measures of chronic proximal plantar fasciitis, evaluated using a 10 cm Visual Analog Scale (VAS): heel pain upon taking first steps of the day, heel pain while doing daily activities, and heel pain after application of the Dolormeter (a standardized pressure device). The composite result was calculated two ways, first on a continuous scale as the sum score of the three measurements and second on a binary scale (success/failure) with success being defined as greater than 60 percent reduction in VAS score from baseline to Visit 7 (12 weeks after the last ESWT treatment) on at least two of the three heel pain measurements.

The primary timepoint for evaluating the efficacy of the treatments was at Visit 7, or 12 weeks following the third treatment session. Results are presented in Tables 2 and 3 for both the Intent-to-treat (ITT) population (subjects who completed at least one treatment session and one evaluation session) and the Per Protocol population (subjects who completed all three treatment sessions and all follow-up evaluations). Missing data was handled using the Last Value Carried Forward (LVCF) approach. Pain scores were adjusted for subjects who took interfering analgesics or had other therapies for their painful heel within predefined timeframes prior to evaluation visits by adding 2 points to their VAS scores for the affected visit. EMS conducted supportive sensitivity analyses to confirm the results obtained using these methods.

#### Table 2: Primary Efficacy Results for ITT Population at Visit 7 - Composite Scores for Three VAS Measures

<table>
<thead>
<tr>
<th></th>
<th>Swiss DolorClast (N=125)</th>
<th>Placebo (N=118)</th>
<th>Effect Size</th>
<th>P-Value One Sided</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Composite VAS Score:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent Change from Baseline at Visit 7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>-56.0 (39.31)</td>
<td>-44.1 (41.81)</td>
<td>0.5753</td>
<td>0.0220</td>
</tr>
<tr>
<td>Median</td>
<td>-72.1</td>
<td>-44.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Overall Success Rate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(&gt;60% reduction in VAS on at least two pain measures)</td>
<td>60.98% (75/123)</td>
<td>42.24% (49/116)</td>
<td>0.5937</td>
<td>0.0020</td>
</tr>
</tbody>
</table>

1. *Mann-Whitney (MW) effect size*
2. *Wilcoxon-Mann-Whitney test*
3. *Unconditional Exact Rühmel-Mansman test*
Table 3: Primary Efficacy Results for Per Protocol Population at Visit 7 - Composite Scores for Three VAS Measures

<table>
<thead>
<tr>
<th>Composite VAS Score: Percent Change from Baseline at Visit 7</th>
<th>Swiss DolorClast (Np=111)</th>
<th>Placebo (Np=108)</th>
<th>Effect Size</th>
<th>P-Value One Sided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>-60.6 (35.97)</td>
<td>-44.2 (42.11)</td>
<td>0.6037</td>
<td>0.0041</td>
</tr>
<tr>
<td>Median</td>
<td>-75.0</td>
<td>-44.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall Success Rate (&gt;60% reduction in VAS on at least two pain measures)</td>
<td>64.55% (71/110)</td>
<td>43.40% (46/106)</td>
<td>0.5788</td>
<td>0.0011</td>
</tr>
</tbody>
</table>

1Mann-Whitney (MW) effect size
2Wilcoxon-Mann-Whitney test
3Unconditional Exact Röhmel-Mansman test

The primary efficacy results for the ITT population demonstrate that the mean composite pain score for the ESWT group (sum of VAS scores for the three pain measures) decreased from 22.0 ± 3.24 at baseline to 9.7 ± 8.56 at Visit 7, for a mean percent decrease (i.e., improvement) of 56 percent. In the placebo group, the mean composite pain score decreased from 21.6 ± 3.22 at baseline to 12.3 ± 9.39 at Visit 7, for a mean percent decrease of 44 percent. These results show a significant improvement in the mean composite VAS score for the ESWT group as compared to the placebo group (p=0.022).

The result for overall success rate, defined as greater than a 60 percent reduction in VAS pain scores on at least two of the three pain measures, was also superior for the ESWT group as compared to the placebo group. Sixty-one percent (75/123) of the ESWT subjects met this success criterion as compared to 42 percent (49/116) of the placebo subjects group (p=0.002).

The results for the Per Protocol population further support the efficacy of ESWT with the EMS Swiss DolorClast®. In this population, where all subjects received the full prescribed three treatments, the results for the ESWT group improved (as compared to the ITT population) while the results for the placebo group stayed essentially the same (as compared to the ITT population). The superiority of the Per Protocol ESWT group as compared to the Per Protocol placebo group is confirmed by this analysis (p<0.01 on both composite VAS score and overall success).

7.6 Secondary Efficacy Results

The secondary efficacy criteria included the Roles and Maudsley Score, SF-36 Quality of Life evaluation, investigator’s global judgment of effectiveness, subject’s satisfaction with their therapy outcome, and whether the subjects
would recommend the EMS Swiss DolorClast® therapy to a friend. Results are summarized in Table 4. The ESWT group demonstrated greater improvements from baseline to Visit 7 on all secondary measures as compared to the placebo group (P < 0.025 one-sided).

Table 4: Secondary Efficacy Results for ITT Population

<table>
<thead>
<tr>
<th>Roles and Maudsley Score</th>
<th>Swiss DolorClast (N=125)</th>
<th>Placebo (N=118)</th>
<th>Effect Size²</th>
<th>P-Value One Sided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent or Good</td>
<td>58.40% (73/125)</td>
<td>41.52% (49/118)</td>
<td>0.5973</td>
<td>0.0031³</td>
</tr>
<tr>
<td>Fair or Poor</td>
<td>41.60% (52/125)</td>
<td>58.48% (69/118)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SF-36 Physical

<table>
<thead>
<tr>
<th>Percent Change from Baseline at Visit 7</th>
<th>Mean / SD</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean / SD</td>
<td>-37.2 (48.42)</td>
<td>-44.1</td>
</tr>
<tr>
<td>Median</td>
<td>-19.5 (52.13)</td>
<td>-14.3</td>
</tr>
</tbody>
</table>

SF-36 Mental

<table>
<thead>
<tr>
<th>Percent Change from Baseline at Visit 7</th>
<th>Mean / SD</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean / SD</td>
<td>-14.6 (62.89)</td>
<td>-22.8</td>
</tr>
<tr>
<td>Median</td>
<td>+8.4 (99.06)</td>
<td>-14.3</td>
</tr>
</tbody>
</table>

Investigator Judgment of Effectiveness

| Very good or Good | 70.80% (80/113) | 40.91% (45/110) | 0.6335 | 0.0002³ |
| Moderate         | 10.62% (12/113) | 20.91% (23/110) |       |        |
| Unsatisfactory or Poor | 18.58% (12/113) | 38.18% (42/110) |       |        |

Patient Judgment of Therapy Satisfaction

| Very or Moderately Satisfied | 63.16% (72/114) | 45.36% (51/110) | 0.5984 | 0.0045⁵ |
| Slightly Satisfied or Neutral | 18.42% (21/114) | 10.00% (11/110) |       |        |
| Dissatisfied               | 18.42% (21/114) | 43.64% (46/110) |       |        |

SF-36 scores standardized using a scale from 0 (best score) to 100 (worst score); negative percent change from baseline indicates improvement.

²Mann-Whitney (MW) effect size.

³P-values of one-sided test for superiority using the Wilcoxon-Mann-Whitney test

7.7 Follow-up Results at 6-Months and 12-Months

Treatment Responders at Visit 7 continued in the study and returned for two additional follow-up visits, Visit 8 at 6 months following the last treatment and Visit 9 at 12 months following the last treatment. The evaluations/procedures conducted at Visit 8 were the same as conducted at Visits 5 and 6, while the evaluations/procedures conducted at Visit 9 were the same as conducted at Visit 7. Subject Diaries for Responders were collected at Visit 9.
Results at both the 6-month and 12-month follow-up visits were similar to the results presented above for visit 7. Results at the 12-month follow-up (Visit 9) are shown in Table 5 below for the ITT population. Results include the composite scores and overall success rate in accordance with the same criteria used for the primary efficacy results at Visit 7. Missing data was handled using the Last Value Carried Forward (LVCF) approach. Pain scores were adjusted for subjects who took interfering analgesics or had other therapies for chronic proximal plantar fasciitis within predefined timeframes prior to evaluation visits by adding 2 points to their VAS scores for the affected visit.

In both the EMS Swiss DolorClast® ESWT group and the placebo group, the mean composite scores increased slightly from the scores at Visit 7. The results continue to show an improvement in the mean composite VAS score for the ESWT group as compared to the placebo group. Likewise, the overall success rate (defined as greater than 60 percent reduction in VAS pain scores on at least two of the three pain measures) for the ESWT group continued to be superior to that of the placebo group. These results confirm that the results obtained at the 3-month primary efficacy endpoint are maintained over a period of up to 12 months.

Only six additional adverse events in five patients were reported during the 6-month and 12-month follow-up period (one patient in the ESWT group and four patients in the placebo group). None of these reported adverse events were considered to be related to the device.

Table 5: Efficacy Results for ITT Population at Visit 9 (12-months) - Composite Scores for Three VAS Measures

<table>
<thead>
<tr>
<th></th>
<th>Swiss DolorClast (N=125)</th>
<th>Placebo (N=118)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Composite VAS Score:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent Change from</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline at Visit 9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>-61.9 (43.62)</td>
<td>-46.5 (45.52)</td>
</tr>
<tr>
<td>Median</td>
<td>-84.8</td>
<td>-43.2</td>
</tr>
<tr>
<td><strong>Overall Success Rate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(&gt;60% reduction in VAS</td>
<td>63.41% (78/122)</td>
<td>43.97% (51/116)</td>
</tr>
<tr>
<td>on at least two pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>measures)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
7.8 Safety Results

See Section 6.0 above for adverse events reported during the study.

7.9 Conclusions

The results of the clinical study summarized above provide reasonable assurance that the EMS Swiss DolorClast® is safe and effective when used in accordance with the device labeling. The results of the multi-center, randomized, placebo-controlled, double-blinded clinical study demonstrate that treatment with the EMS Swiss DolorClast® provides relief to patients with symptoms of proximal plantar fasciitis of at least 6 months duration who had failed previous conservative therapy.
1. The treatment site is located using palpation and patient feedback regarding the area of pain.

2. After locating the treatment site, the skin of the treatment area is marked.

3. Local anesthesia, if necessary, should be by subcutaneous injection or anesthesia spray. Do not inject directly into the treatment site.

4. Use EMS Swiss DolorClast® coupling gel for improved coupling.

5. Gently rub the applicator tip over the site of treatment in multiple impulse mode. Exert as much pressure as the patient can reasonably tolerate (use the ø15 mm applicator).
EMS
Swiss DolorClast®

For Treatment of Chronic Proximal Plantar Fasciitis (Painful Heel Syndrome)

Patient Information
Manufacturer
EMS Electro Medical System S.A
Chemin de la Vuarpillière 31
CH-1260 Nyon, Switzerland

U.S. Subsidiary / US Distributor
EMS Corporation
11886 Greenville Avenue #120
Dallas, Texas 75243 - USA
Phone +001 972 690 8382
Fax +001 972 690 8981

Release date: March 06, 2007

Regulatory Statement for the United States

CAUTION! Federal law restricts this device to sale on or by the order of a physician.
CONTENTS

1. What is the EMS Swiss DolorClast®? ............................................................ 1
2. What is chronic proximal plantar fasciitis? ............................................... 2
3. Who should have treatment with the EMS Swiss DolorClast®? .............. 3
4. Who should not have treatment with the EMS Swiss DolorClast®? ........ 3
5. What are the precautions about this treatment? ....................................... 4
6. What are the risks of the treatment? ........................................................... 5
7. What are the potential benefits of the treatment? ..................................... 6
8. What are the alternative treatments? .......................................................... 6
9. How is treatment with the EMS Swiss Dolorclast® performed? ............. 7
10. What are the results of the clinical study? ............................................... 7
11. Who should I contact if I have questions about treatment with the EMS Swiss Dolorclast®? ................................................................. 10
1. WHAT IS THE EMS SWISS DOLORCLAST®?

The EMS Swiss DolorClast®, illustrated in Figure 1, is an extracorporeal shock wave therapy device intended for use in treating chronic proximal plantar fasciitis (painful heel). Proximal means near to the heel. The therapeutic shock waves (high intensity sound waves) are delivered from outside of the body (i.e., "extracorporeally"), so the treatment is completely non-invasive.

The device consists of a control unit and a handpiece, with the treatment applicator mounted on the end of the handpiece. The treatment applicator is held in contact with the heel at the point of maximum tenderness as illustrated in Figure 2. Compressed air is used to drive a projectile (metal cylinder) within the handpiece toward the applicator. When the projectile hits the applicator inside the handpiece, a shock wave is generated (high intensity sound wave) that is then transferred to the treatment site. The highest energy density will be at the point of contact of the applicator (the treatment site), but the shock wave will travel outward (i.e., radially) into the soft tissue surrounding the point of contact.

Figure 1. EMS Swiss DolorClast®
2. WHAT IS CHRONIC PROXIMAL PLANTAR FASCIITIS?

Chronic proximal plantar fasciitis, also called painful heel syndrome, is a condition in which there is painful tenderness in the area around the medial (middle part) plantar calcaneal tuberosity (heel bone). See Figure 3 below:

Figure 3: Location of Heel Pain
3. WHO SHOULD HAVE TREATMENT WITH THE EMS SWISS DOLORCLAST®?

The EMS Swiss DolorClast® is intended to apply shock waves to the heel for the treatment of chronic proximal plantar fasciitis (painful heel syndrome). It is intended to be used for patients who are 18 years of age or older who have symptoms of painful heel syndrome that have lasted for 6 months or more and who have tried other conservative therapies but without success.

4. WHO SHOULD NOT HAVE TREATMENT WITH THE EMS SWISS DOLORCLAST®?

Treatment with the EMS Swiss DolorClast® should not be performed if any of the following conditions exist:

- You have incomplete bone growth over or near the area to be treated
- There is malignant disease (cancer) in or near the treatment area
- You have an infection in the area to be treated.
- You have ischemic tissues (tissues that have poor blood circulation) at the treatment site
- If you have a coagulation (bleeding) disorder or if you are taking anti-coagulation medications
- You have a prosthetic device in the area to be treated.

In addition, if you have any of the conditions listed in Section 5 below you should consult with your doctor to determine if this therapy is appropriate for you.
5. WHAT ARE THE PRECAUTIONS ABOUT THIS TREATMENT?

The safety and effectiveness of the EMS Swiss DolorClast® for treatment of painful heel has not been established for patients with the following conditions:

- Under 18 years of age
- Diseases or disorders of the nerves in the foot to be treated
- Diseases or disorders of the bones in the foot to be treated
- Infection in the area to be treated
- Current or recent therapy that would compromise tissue healing
- Problems with circulation or bleeding disorders
- History or documented evidence of immune system deficiencies (autoimmune disease)
- Disease of the blood vessels in the foot to be treated
- Rheumatoid arthritis (pain, stiffness or swelling of the joints)
- Malignant disease (cancer) in any part of the body, including the heel
- Previous treatment of the painful heel with corticosteroid (steroid) injections within 6 weeks of the EMS Swiss DolorClast® treatment or previous treatment with non-steroidal anti-inflammatory drugs (such as ibuprofen) within 1 week of the EMS Swiss DolorClast® treatment
- Previous surgery for painful heel
- Pregnant female

If you have any of the above conditions you should consult with your doctor to determine if this treatment is appropriate for you.
6. WHAT ARE THE RISKS OF THE TREATMENT

The most likely risk associated with use of the EMS Swiss DolorClast® is pain or discomfort during treatment. This side effect was noted by 23% of the patients treated with the EMS Swiss DolorClast® in a clinical study, but all patients except for one were able to complete their treatments without any anesthesia. Other adverse events associated with use of the EMS Swiss DolorClast® that were reported during the study were continued pain after treatment (in 3.9% of patients), skin reddening after treatment (in less than 1 percent of patients), and swelling with pain after treatment (in less than 1 percent of patients).

Other potential adverse events that have not been observed in clinical studies of the EMS Swiss DolorClast® may include:

- Bruising
- Rupture of tissue along the bottom of the foot (plantar fascia)
- Temporary or permanent damage to the blood vessels
- Petechia (small reddish or purple spots on the skin)
- Temporary or permanent nerve damage causing loss of feeling
- Hematoma
- Tendon rupture

During the clinical study, a total of 23 other adverse events that were not believed to be related to the EMS Swiss DolorClast® were reported in 16 of the 129 patients who were treated with the EMS Swiss DolorClast® (12.4%). These were as follows: wasp sting (1), common cold disease (3), cough (1), sinusitis (2), headache (6), body aches (1), pain of the hip (1), toe (1) or neck (1), intermittent back pain of unknown etiology (1), aggravated neuroma (1), tinnitus (1), occasional knee weakness due to knee injury (1), developing tendonitis (1), and heart murmur (1).

Your doctor will be able to discuss all of the potential risks of the treatment with you. Make sure that you tell your doctor if you experience any side effects during or following treatment of your painful heel with the EMS Swiss DolorClast®.
7. **WHAT ARE THE POTENTIAL BENEFITS OF THE TREATMENT?**

This therapy may relieve the pain in your heel and it might eliminate the need for surgery. However, it is possible that the therapy may not completely eliminate your pain or it may not work at all. A clinical study of the EMS Swiss DolorClast® demonstrated that the treatment is both safe and effective in relieving heel pain in some patients who had suffered from painful heel for at least 6 months and had failed numerous conservative therapies prior to radial extracorporeal shock wave therapy. The treatment was considered to be successful in 61 percent of the patients who were treated with the EMS Swiss DolorClast®, while only 42 percent of patients who received a “sham” (simulated) treatment were considered to be successes. A treatment was considered to be “successful” if the patient reported that his/her pain was improved by 60 percent or more on two out of three different tests (see details of the clinical study below).

8. **WHAT ARE THE ALTERNATIVE TREATMENTS?**

Heel pain is generally treated conservatively with a variety of drug and non-drug therapies, including the following:

- Over-the-counter or prescription pain medication or non-steroidal anti-inflammatory agents (NSAIDs, e.g., Ibuprofen)
- Injections of anesthetics around the painful heel
- Corticosteroid (steroid) injections around the painful site
- Physical therapy (i.e., ice, heat, ultrasound)
- Physiotherapy (i.e., massage, stretching)
- Orthotics, heel pads, and shoe modifications
- Taping, night splints, immobilization, or casting

Prior to treatment with the EMS Swiss DolorClast®, you should have tried and failed a variety of these other conservative therapies over a period of at least 6 months. Talk with your doctor about the most appropriate alternative therapies for your painful heel.
9. HOW IS TREATMENT WITH THE EMS SWISS DOLORCLAST® PERFORMED?

If your doctor determines that treatment with the EMS Swiss DolorClast® is appropriate for your painful heel, you will be placed in prone position and your doctor will palpate your heel to locate the tenderest position. Your feedback to your doctor will be important to locate the center of your pain. Coupling gel will be applied to your heel and the treatment applicator will be held in contact with your heel at this location.

When the treatment begins, the impulses will be delivered at a low pressure and slowly increased to the target treatment pressure (4 bar). This should allow you to get used to the moderate treatment pain so that you should not need any anesthesia to complete the treatment. However, if you do experience pain that you cannot tolerate, you should tell your doctor who can then administer a local anesthesia (using a shot or an anesthesia spray). Once the treatment pressure of 4 bar is reached, treatment will continue until a total of 2000 impulses at 4 bar have been delivered.

You will be expected to undergo a total of three treatment sessions within 2 weeks in order to realize the maximum benefits of the treatment. Your doctor may also want you to return for short follow-up visits to assess your response to the treatments. You should notice a gradual improvement in your heel pain over time, and it may take up to 3 months before you notice significant improvement. Be sure to tell your doctor about any changes in your heel pain and any side effects you experience from the treatment.

10. WHAT ARE THE RESULTS OF THE CLINICAL STUDY?

A clinical study using the EMS Swiss DolorClast® to treat painful heel was conducted at eight hospitals or medical centers: three in the United States and five in Germany. A total of 251 subjects were treated in the study. Half of the subjects received treatment with an active device and half with a sham device. The sham device looks and sounds like the active one, but did not emit any impulses to the heel. All subjects were blinded, that is, they did not know whether they had received the active or sham treatment. All subjects in the study had symptoms of painful heel for at least 6 months that had not responded to prior conservative therapies.
Before starting the treatment, all subjects underwent testing to establish the level of their pain using a Visual Analog Scale (VAS, a line to indicate pain level, with 0 equal to no pain and 10 equal to unbearable pain). To qualify for the study, subjects had to have levels of at least 5 out of 10 for heel pain when taking the first steps in the morning and heel pain during daily activities. Subjects were also asked to evaluate their heel pain on a four point scale (the Roles and Maudsley scale) and to evaluate their general quality of life using a questionnaire called the SF-36 score.

Subjects returned for follow-up at three time periods: 1 week, 6 weeks and 12 weeks following their third treatment. In addition, patients were asked to return for follow-up evaluation 6 months and 12 months after treatment. At each follow-up visit, the subjects were evaluated by a doctor that did not know what treatment (active or sham) they had received. The results at the 12 week evaluation were used to assess the effectiveness of the treatment.

Subjects were considered to be a success in the study if they had greater than 60% improvement in their heel pain (as measured using the VAS three months after treatment) on at least two of the following three tests: heel pain when taking the first steps of the day, heel pain during daily activities, and heel pain upon application of external pressure.

A summary of the effectiveness results at 3 month following treatment with the Swiss DolorClast® is given in Table 1.

The results of the study (Intent to Treat Group) demonstrated that the active treatment group had a significantly better outcome than the sham treatment group as 61% of the active treated subjects met the definition of success as compared to 42% of the sham subjects. When considering only subjects who completed all three treatments and all follow-up visits (Per Protocol Group), as shown in Table 1, the results in the active group improved as 65% met the definition of success in the study. Results at the 6 month and 12 month follow-up were similar to, or better than, the results at the 12 week evaluation.

The other measures of effectiveness also demonstrated that the active treated subjects had better outcomes in the study as compared to the sham treated subjects. The results on the Roles and Maudsley Score, SF-36 Quality of Life evaluation, and investigator’s judgment of effectiveness were all significantly better for the active treated subjects as compared to the group who received a sham treatment. In addition, the subjects in the active treated group had a
significantly higher level of satisfaction with their therapy outcome and were significantly more likely to recommend the EMS Swiss DolorClast® therapy to a friend.

Table 1: Summary of Effectiveness Results 3 Months after Treatment with the Swiss DolorClast®

<table>
<thead>
<tr>
<th>MEASUREMENT</th>
<th>Active (Dolorclast) Treated at 3 month</th>
<th>Sham Treated at 3 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall success rate, Patients with more than 60% heel pain improvement on 2 of 3 VAS tests (mean value)</td>
<td>64.5%</td>
<td>43.4%</td>
</tr>
<tr>
<td>Roles and Maudsley Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent or Good</td>
<td>58.40%</td>
<td>41.52%</td>
</tr>
<tr>
<td>Fair or Poor</td>
<td>41.60%</td>
<td>58.48%</td>
</tr>
<tr>
<td>SF-36 Physical (quality of life assessment)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent Change from Baseline (average value); negative value indicates improvement</td>
<td>-37.2 %</td>
<td>-19.5%</td>
</tr>
<tr>
<td>SF-36 Mental (quality of life assessment)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent Change from Baseline (average value); negative value indicates improvement</td>
<td>-14.6 %</td>
<td>+8.4%</td>
</tr>
<tr>
<td>Investigator Judgment of Effectiveness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very good or Good</td>
<td>70.80%</td>
<td>40.91%</td>
</tr>
<tr>
<td>Moderate</td>
<td>10.62%</td>
<td>20.91%</td>
</tr>
<tr>
<td>Unsatisfactory or Poor</td>
<td>18.58%</td>
<td>38.18%</td>
</tr>
<tr>
<td>Patient Judgment of Therapy Satisfaction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very or Moderately Satisfied</td>
<td>63.16%</td>
<td>46.36%</td>
</tr>
<tr>
<td>Slightly Satisfied or Neutral</td>
<td>18.42%</td>
<td>10.00%</td>
</tr>
<tr>
<td>Dissatisfied</td>
<td>18.42%</td>
<td>43.64%</td>
</tr>
<tr>
<td>(21/114)</td>
<td>(48/110)</td>
<td></td>
</tr>
<tr>
<td>Patient Recommendation of Therapy to a Friend</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive (yes)</td>
<td>91.23%</td>
<td>69.09%</td>
</tr>
<tr>
<td>Negative (no)</td>
<td>8.77%</td>
<td>30.91%</td>
</tr>
</tbody>
</table>
No study subjects experienced any unexpected or serious device-related adverse events during the course of the study. The most common event was pain or discomfort during treatment, reported by 30 out of 129 subjects (23.26%) in the active treatment group. Twenty out of 129 reported pain during only one of the treatments, seven of 129 subjects during two of the treatments and only three out of 129 subjects during all three treatments. Three out of 129 subjects reported pain during and after treatment. Eighteen of the reports rated pain during treatment as severe, 22 reports pain rating as moderate, and three reports rated pain as mild. Only one subject requested local anesthesia because of pain during treatment. All other subjects who complained of pain during treatment complete the treatments without local anesthesia. One active treated subject reported mild swelling and pain following treatment and one reported skin reddening that faded following treatment.

11. WHO SHOULD I CONTACT IF I HAVE QUESTIONS ABOUT TREATMENT WITH THE EMS SWISS DOLORCLAST®?

You should contact your doctor to ask any questions about your painful heel syndrome and how treatment with the EMS Swiss Dolorclast® may be helpful.
SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Orthopedic Shock Wave Unit

Device Trade Name: Storz Medical Duolith SDI Shock Wave Therapy Device

Device Procode: NBN

Applicant's Name and Address: Storz Medical AG
Lohstamfestrasse 8
CH-8274 Tagerwilen
Switzerland

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P080028

Date of FDA Notice of Approval: January 8, 2016

II. INDICATIONS FOR USE

The Duolith SDI is indicated for extracorporeal shock wave treatment of heel pain due to chronic proximal plantar fasciitis for patients of age greater than 18 years with a history of failed alternative conservative therapies for at least 6 months. Chronic proximal plantar fasciitis is defined as traction degeneration of the plantar fascial band at the origin on the medial calcaneal tuberosity that has persisted for six months or more.

III. CONTRAINDICATIONS

- Over or near bone growth center until bone growth is complete
- When a malignant disease is known to be present in or near the treatment area
- Infection in the area to be treated
- Patient has a coagulation disorder or taking anti-coagulant medications
- Patient has a prosthetic device in the area to be treated

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Duolith SD1 device labeling.

V. DEVICE DESCRIPTION

The Duolith SDI is an extracorporeal shock wave (ESWT) treatment device. Key components of the Duolith SDI are the control unit, hand piece (with two (2) stand-offs), and optional foot pedal. The depth of penetration is determined by the standoff that is attached to
the distal end of the hand piece.

The principle of operation of the Duolith SD1 is functionally similar to that of Storz Medical Lithotripters. It uses an electromagnetically generated shock wave produced within a hand-held applicator (F-SW Hand piece). The shock wave is generated by discharging a high voltage capacitor located in the Control Unit into a cylindrically shaped coil system in the Hand piece which is surrounded by a cylindrical metallic membrane. The transient magnetic field produced by the coil induces eddy currents in the metal membrane, causing it to repel from the coil, producing a pressure wave. The membrane is immersed in water and the pressure wave produced by the membrane propagates through the water to a concentric parabolic reflector, where it is reflected to a focal point outside of the Hand piece in front of the reflector.

The Duolith SD1 incorporates micro-processor control of the operating parameters. The software was determined to be a minor level of concern (as described in FDA Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices (May 11, 2005) and based on a software hazard analysis conducted by Storz Medical AG).

The Duolith SD1 F-SW Hand piece and Stand-Offs are provided non-sterile to the user. Instructions for cleaning and low level disinfection are provided in the Operating Instructions. The hand piece and applicator can be cleaned using a soft cloth and a general purpose surface disinfectant. Because the device is for use in intact skin only, neither high level disinfection nor sterilization are necessary.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of heel pain due to chronic proximal plantar fasciitis, including non-surgical alternatives. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle. Most patients with chronic proximal plantar fasciitis do not require surgery to relieve the symptoms. The use of shoe inserts (cups and pads), orthotics, oral non-steroidal anti-inflammatory agents, and local steroid injections provide pain relief in most patients. However, symptoms may persist in some patients over an extended period of time despite all forms of conservative management. These patients can be offered a variety of surgical procedures. However, even surgical intervention does not always result in success and could be associated with surgical complications.

VII. MARKETING HISTORY

The Duolith SD1 is marketed worldwide except for in the United States and is authorized to bear the CE Mark. The Duolith SD1 has not been withdrawn from marketing for any reason related to its safety and effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH
Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device: petechiae, hematoma, tendon rupture, bruising, rupture of plantar fascia (a very rare side effect), temporary or permanent damage of nerve and blood vessels.

For the specific adverse events that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF PRECLINICAL STUDIES

A. Shock Wave Characterization

Measurements to characterize the Duolith SD1 shock waves are listed in Table 1 below and are in accordance with the performance criteria, stated in the guidance document outline in FDA's "Guidance for the Content of Premarket Notifications [510(k)s] for Extracorporeal Shock Wave Lithotripters Indicated for the Fragmentation of Kidney and Ureteral Calculi," issued n August 2000, with the exception that the parameter "Distance between the focus and target location" is not applicable to the Duolith SD1 since there is no localization system or target marker. The testing showed that typical value for the different parameters met the acceptance/performance criteria.

Testing was conducted for energy flux density settings of 0.10, 0.35, and 0.55mJ/mm², which is the operational range of the Duolith SD1. In addition, peak positive and negative acoustic pressures were also determined for the minimum flux density setting of 0.01mJ/mm². Test results are summarized in Table 1 below.

Table 1: Summary of Shock Wave Characterization Tests

<table>
<thead>
<tr>
<th>Energy Flux Density Setting: mJ/mm²</th>
<th>0.01</th>
<th>0.10</th>
<th>0.35</th>
<th>0.55</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak-positive acoustic pressure (MPa)</td>
<td>3</td>
<td>14</td>
<td>36</td>
<td>62</td>
</tr>
<tr>
<td>Peak-negative acoustic pressure (MPa)</td>
<td>3</td>
<td>9</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>Rise Time (ns, 1 0% to 90%)</td>
<td>--</td>
<td>330</td>
<td>190</td>
<td>100</td>
</tr>
<tr>
<td>Compressional pulse duration (ns, FWHM)</td>
<td>--</td>
<td>620</td>
<td>350</td>
<td>200</td>
</tr>
<tr>
<td>Fx-Maximum focal width (mm, -6 dB)</td>
<td>--</td>
<td>5.4</td>
<td>3.8</td>
<td>2.8</td>
</tr>
<tr>
<td>Fy-Orthogonal focal width (mm, -6 dB)</td>
<td>--</td>
<td>5.4</td>
<td>3.8</td>
<td>2.8</td>
</tr>
<tr>
<td>Fz-Focal extent (mm, -6 dB)</td>
<td>--</td>
<td>57</td>
<td>49</td>
<td>34</td>
</tr>
<tr>
<td>Focal volume (cm³)</td>
<td>--</td>
<td>0.87</td>
<td>0.37</td>
<td>0.14</td>
</tr>
<tr>
<td>Distance between focus and target location</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Derived focal acoustic pulse energy (mJ)</td>
<td>--</td>
<td>2.0</td>
<td>3.8</td>
<td>3.5</td>
</tr>
<tr>
<td>Derived acoustic pulse energy for 5 mm diameter focal area (mJ)</td>
<td>--</td>
<td>1.7</td>
<td>5.5</td>
<td>8.5</td>
</tr>
<tr>
<td>Derived acoustic pulse energy for 8 mm diameter focal area (mJ)</td>
<td>--</td>
<td>3.3</td>
<td>12</td>
<td>18</td>
</tr>
</tbody>
</table>

B. Hand piece Longevity

Duolith F-SW hand piece longevity was demonstrated to exceed 1,000,000 shocks and ranged from 1,154,201 to 3,184,414 shocks (mean: 2,105,739.143; SD: 735,653.976).
The guaranteed service life of the F-SW hand piece is 1,000,000 SW. When it reaches the limit of 1,000,000 SW the F-SW hand piece should be replaced as soon as possible.

C. **Electrical Testing**

The Duolith SD1 was tested for electrical safety and found in conformance with all applicable requirements of IEC60601-1 (1988), Amendment 1 (1991), and Amendment 2 (1995). EMC testing has been repeated for both the investigational T-Top and the PMA Tower versions.

The Duolith SD1 was tested for EMC safety and for safety of the extracorporeally induced lithotripsy and was found to be in conformance with all applicable requirements of EN 60601-1-2:2001 (Medical electrical equipment, General requirements for safety, EMC) and EN 60601-1-2-36:1997 (Particular requirements for safety of equipment for extracorporeally induced lithotripsy). The Duolith SD1 complied with the emissions requirements for Class B equipment and the minimum immunity requirements of these standards. Test results are summarized in Table 2 below.

The Duolith SD1 complies with UL60601.1 and CAN/CSA C22.2 No.601- M90 by CSA International.

<table>
<thead>
<tr>
<th>Description</th>
<th>Criteria*</th>
<th>Results</th>
<th>T-Top Report Numbers:</th>
<th>Tower Report Number:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>2005-1294-2347</td>
<td>2005-1294-2138</td>
</tr>
<tr>
<td><strong>Emissions Tests</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiated Emissions (30 to 1000 MHz)</td>
<td>Class B</td>
<td>Pass</td>
<td>Pass</td>
<td></td>
</tr>
<tr>
<td>Conducted Emissions at AC mains terminals</td>
<td>Class B</td>
<td>Pass</td>
<td>Pass</td>
<td></td>
</tr>
<tr>
<td>(0.15 to 30 MHz)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Harmonic current emissions</td>
<td>Class A</td>
<td>Pass</td>
<td>Pass</td>
<td></td>
</tr>
<tr>
<td>Voltage fluctuations and flicker</td>
<td>IEC 61000-3-3</td>
<td>Pass</td>
<td>Pass</td>
<td></td>
</tr>
<tr>
<td><strong>Immunity Tests</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electrostatic Discharge Immunity</td>
<td>8 kV air</td>
<td>Pass</td>
<td>Pass</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 kV contact</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiated RF Electromagnetic Field Immunity</td>
<td>3 V/m, 80%</td>
<td>Pass</td>
<td>Pass</td>
<td>Pass</td>
</tr>
<tr>
<td></td>
<td>1kHzAM</td>
<td>(80-2500 MHz)</td>
<td></td>
<td>(80-1000 MHz)</td>
</tr>
<tr>
<td>Electric Fast Transient (Burst)</td>
<td>2 kV-AC mains</td>
<td>Pass</td>
<td>Pass</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1kV-Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surge Immunity (AC mains)</td>
<td>1kV/2kV</td>
<td>Pass</td>
<td>Pass</td>
<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>---------</td>
<td>------</td>
<td>------</td>
<td></td>
</tr>
<tr>
<td>Radio Frequency, conducted</td>
<td>0.15-80 MHz</td>
<td>Pass</td>
<td>Pass</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 V, 80% 1 kHz AM</td>
<td>Pass</td>
<td>Pass</td>
<td></td>
</tr>
<tr>
<td>Magnetic fields</td>
<td>50-160 Hz, 3 Nm</td>
<td>Pass</td>
<td>Pass</td>
<td></td>
</tr>
<tr>
<td>Voltage Dip and Interrupt Immunity</td>
<td>30%-100% main voltage, 0.01-5 sec. duration</td>
<td>Pass</td>
<td>Pass</td>
<td></td>
</tr>
</tbody>
</table>

* Class A equipment is equipment suitable for use in all establishments other than domestic and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.

* Class B equipment is equipment suitable for use in all establishments, including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.

**D. Software Verification and Validation Testing**

System level software verification and validation testing was conducted and the Duolith SDI was found to meet all test requirements according to the FDA Guidance “Guidance for the Content of Pre-Market Submissions for Software Contained in Medical Devices,” issued on May 11, 2005, with no known unresolved anomalies remaining.

**E. Biocompatibility Testing**

The only portions of the Duolith SDI intended to come in contact with the patient are the polyurethane coupling membrane and the stand-offs (made of the same polyurethane membrane). These components are classified as having short duration contact on intact skin according to FDA's guidance "Required Biocompatibility Training and Toxicology Profiles for Evaluation of Medical Devices,” issue on May 1, 1995, which was subsequently superseded by "AAMI/ANSI/ISO 10993-1:2003." Biocompatibility testing included cytotoxicity testing, irritation, and sensitization testing performed in compliance with FDA’s biocompatibility guidance and demonstrated that the materials in direct contact with the patient are non-toxic and biocompatible. The ultrasound coupling gel recommended for use with the Duolith SDI is legally marketed in the United States.

**X. SUMMARY OF PRIMARY CLINICAL STUDY**

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of ESWT procedure with Duolith SDI device for the treatment of heel pain due to plantar fasciitis in the US under IDE G050236. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.
A. Study Design

Patients were treated between June 12, 2006 and June 9, 2007. The database for this PMA reflected data collected through September 5, 2007 and included 233 patients. The study was conducted at six (6) clinical sites, all in the United States, with two (2) of the six (6) geographic sites for a single investigator. Therefore, results are based on a five (5) clinical sites.

The study was a multicenter, randomized, placebo-controlled, prospective, double-blind clinical study enrolling 250 subjects (in 1:1 allocation to active treatment with the Duolith SD1 or the placebo-control which received a sham treatment with a device identical to the active device but in which the transmission of the shockwaves to the patient was blocked). The study was conducted to assess the safety and effectiveness of the Duolith SD1 when used to treat unsuccessful conservatively treated subjects suffering from painful heel syndrome. For the purpose of this study, painful heel syndrome was defined as chronic proximal plantar fasciitis that had persisted for at least 6 months before study enrollment. The patient and the clinician performing the efficacy assessments were blinded; the clinician administering the treatment (active and placebo) was not blinded. All study procedures for both groups were identical except that of the stand-off used. Active or sham procedures were administered at three (3) treatment visits approximately 1 week apart, with subsequent follow-up visits at 6 weeks, 3 months, 6 months, and 12 months after the last treatment session. The primary endpoint of comparison between the Duolith Group and Placebo Group is 3 months after the last treatment session (approximately 14 weeks after randomization). Subjects considered to be "responders" at the three (3) month follow up, continued to be followed at 6 and 12 months after the last treatment session. A responder is a subject whose heel pain percentage decrease is > 60% from baseline at Visit 6 (3 months) for at least two (2) of the three (3) heel pain Visual Analog Scale (VAS) measurements: Heel pain when taking the first steps of the day, Heel pain while doing daily activities, and Heel pain after application of a standardized pressure device (F-meter). The VAS has an 11 point scale of 0 to 10 with 0 being no pain and 10 being the highest pain.

1. Clinical Inclusion and Exclusion Criteria

   After a screening visit to determine eligibility (Visit 1), the study started at Visit 2 with the first treatment (after randomization). However, Visit 1 and 2 procedures could be performed at a single visit.

   a. Enrollment in the clinical study (G050236) was limited to patients who met the following inclusion criteria:

      i. Age greater than 18 years

      ii. Ability of subject or legal respondent to give written informed consent after being told of the potential benefits and risks of participating in the study
iii. Singed informed consent

iv. Diagnosis of painful heel syndrome (i.e., chronic proximal plantar fasciitis) proven by clinical examination. Chronic proximal plantar fasciitis is defined as heel pain in the area of the insertion of the plantar fascia on the medial calcaneal tuberosity

v. Six (6) months of unsuccessful conservative treatment (i.e., must have undergone at least 2 unsuccessful non-pharmacological treatments and at least 2 unsuccessful pharmacological treatments within the past year). The following conservative treatments could have been completed as single, combined, or consecutive treatments:

- Non-pharmacological treatments
  - Physical therapy (e.g., ice, heat or ultrasound)
  - Physiotherapy (e.g., massage and stretching)
  - Over The Counter (OTC) devices like orthosis, taping, and heel pads
  - Prescribed orthosis
  - Shoe modification like higher heels
  - Cast/immobilization
  - Night splints

- Pharmacological treatments
  - External (topical) application of analgesic and/or anti-inflammatory gels
  - Therapy with prescription analgesics and/or Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)
  - Local anesthetic injections
  - Local corticosteroid injections

vi. Time gap of at least:
  - Six (6) weeks since the last corticosteroid injection
  - Four (4) weeks since the last anesthetic injection; iontophoresis, ultrasound, and electro-myostimulation
  - One (1) week since the last NSAIDs
  - Two (2) days since the last prescription or non-prescription analgesics, heat, ice, massage, stretching, night splinting, and orthosis

vii. Scores of $\geq 5$ on the three (3) VAS pain scales

viii. Score of 3 (fair) or 4 (poor) on the Roles and Maudsley Scale

ix. Willingness to refrain from the following painful heel related, concomitant therapy: iontophoresis; electro-myostimulation; ultrasound; NSAIDs; steroid injections or surgery - Until Visit 6 (3 months) of this study (shoe modifications and rescue pain medication are allowed during the entire
study)

x. Willingness to keep a Subject Heel Pain Medication and Other Heel Pain Therapy Diary until 12 months after the last treatment

xi. Females of childbearing potential may be entered if they provide a negative urine pregnancy test immediately before the first ESWT treatment

xii. Willingness of females of childbearing potential to use contraceptive measures for 2 months after enrollment into the study

b. Patients were not permitted to enroll in the clinical study if they met any of the following exclusion criteria:

i. Inflammation of the lower and upper ankle

ii. History of rheumatic diseases, and/or collagenosis and/or metabolic disorders

iii. Patients with a history of hyperthyroidism

iv. Active malignant disease with or without metastases

v. Patients suffering from Paget disease or calcaneal fat pad atrophy

vi. Patients suffering from Osteomyelitis (acute, sub-acute, chronic)

vii. Patients suffering from fracture of the Calcaneus

viii. Patients with an immunosuppressive therapy

ix. Patients with a long-term (≥6 months duration) treatment with any corticosteroid

x. Patients suffering from insulin-dependent diabetes mellitus, severe cardiac, or respiratory disease

xi. Patients suffering from coagulation disturbance and/or therapy with Phenprocoumon, Acetylsalicylic acid, or Warfarin

xii. Bilateral painful heel, if both feet need medical treatment

xiii. Patients who, at entry, are known to have treatment planned within the next 8 weeks, which may abruptly alter the degree or nature of pain experienced such that the extracorporeal shock wave therapy will no
longer be necessary (e.g., surgery)

xiv. Time gap of less than:
- 6 weeks since the last corticosteroid injection
- 4 weeks since the last anesthetic injection; iontophoresis, ultrasound, and electro-myostimulation
- 1 week since the last NSAIDs
- 2 days since the last prescription or non-prescription analgesics, heat, ice, massage, stretching, night splinting, and orthosis

xv. Previous surgery of the painful heel syndrome

xvi. Previous unsuccessful treatment of the painful heel with a similar shock wave device

xvii. History of allergy or hypersensitivity to bupivacaine or local anesthetic sprays

xviii. Patients with significant abnormalities in hepatic function

xix. Patients in a poor physical condition

xx. Pregnant female

xxi. Active infection or history of chronic infection in the treatment area

xxii. History or documented evidence of peripheral neuropathy such as nerve entrapment, tarsal tunnel syndrome, etc.

xxiii. History or documented evidence of systemic inflammatory disease such as rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, aseptic bone necrosis, Reiter's syndrome, etc.

xxiv. History or documented evidence of worker's compensation or litigation

xxv. Participation in an investigational device study within 30 days prior to selection, or current inclusion in any other clinical study or research project

xxvi. Patients who, in the opinion of the investigator, will be inappropriate for inclusion into this clinical study or will not comply with the requirements of the study

xxvii. Patients with implanted pacemakers, insulin pumps, defibrillators, and/or neuro-stimulators
xxviii. Patients with prosthetic devices implanted in the area of treatment

xxix. Patients with open wounds or skin rashes

xxx. Patients suffering from tendon rupture, neurological, or vascular insufficiencies of the painful heel, as assessed using the Semmes-Weinstein Monofilament test and the Ankle Brachial Index

2. **Follow-up Schedule**

All patients were scheduled to return to follow up examination at Visits 5 (6 week) and 6 (3 month) after the last treatment session (Visit 4; 2 week after the last ESWT treatment session).

a. **Patient Eligibility for Long Term Follow Up (FII):**

Patients defined as "responders" according to the definitions provided below were also being followed at Visits 7 (6 month) and 8 (12 month).

A responder was defined as follows:

- A patient whose percentage decrease of heel pain was greater than 60 percent from baseline to Visit 6 (3 months) for at least two (2) of the three heel pain (VAS) measurements, or

- A patient that fulfilled three (3) conditions at the 3 month follow up visit (Visit 6): (1) Able to return to work, (2) satisfied with the treatment outcome, and (3) required no concomitant therapy to control heel pain

In addition, all patients with at least one FII visit were included in the long term follow up analysis. There were no exclusion criteria.

b. **Study Procedures**

The primary follow-up visit for comparison of the Duolith SD1 and the placebo-controlled sham groups is 3 months after the last treatment (Visit 6, 3 months after randomization). At this visit, the decision was made whether a patient had a sufficient response to the extracorporeal shock wave treatment to continue in the study. Sufficient response was considered as a reduction in pain larger than 60% on at least two (2) of the three (3) VAS measurements or, if the reduction in pain was < 60%, then the patient must be able to work and complete activities of daily living, must be satisfied with the outcome of the treatment, and must not require any other treatment to control heel pain. Patients who showed sufficient response to the treatment during the follow-up I period (visit 6) continued in the follow-up II period (visit 8). Otherwise, the patient was discontinued from the study and may receive further treatment for painful heel as necessary.
Patients who consented to enrollment were randomized but were blinded to treatment assignment. The treatment was repeated three (3) times approximately one week (± 4 days) apart (at Visits 1 or 2, 3, and 4). The study procedures, except for the treatment devices, were the same for all patients. The protocol specified up to 2000 impulses at each of the three (3) treatment visits. Follow up for all patients consisted of Visits 5 and 6. Subjects defined as responders are also being followed at Visits 7 (6 month) and 8 (12 Month). A responder is a patient who fulfills the conditions as stated above. Safety and effectiveness data were analyzed through the Visit 6 (3 months) follow up performed for all subjects and the 12 month follow up of responders.

In general, therapy was performed without local anesthesia. Due to a possible pain sensation caused by the shock wave treatment, the applied energy was increased smoothly from lowest energy level of 0.01 mJ/mm² up to a level of 0.25 mJ/mm² within the first 500 impulses. After these 500 introductory impulses, 2000 treatment impulses were performed with the regular working application level of 0.25mJ/mm². Only one subject in the Duolith Group required local anesthesia at Visit 2 (baseline visit with first ESWT application).

Post-operative parameters measured during the study included the following:

At Visit 5: Follow-Up I (6 weeks ± 1 week after the last ESWT treatment)

- Investigation of the primary criteria (VAS, Roles and Maudsley-Score)
- Investigation of the secondary criteria (analgesic medication consumption)
- Safety Criteria: Adverse reactions related to previous ESWT and local anesthesia
- Assessment of local tissue effects
- Documentation of concomitant therapy and medication
- Review entries in the Subject Heel Pain Medication and Other Painful Heel Therapy Diary and reissuing

Visit 6: Primary Endpoint: Follow-Up I (3 month ± 7 days after the last ESWT treatment)

- Physical examination
- Vital signs
- Investigation of the primary criteria (VAS, Roles and Maudsley-Score)
• Investigation of the secondary criteria (analgesic medication consumption, Physician's Judgment; Subject's Satisfaction, and Subject's Treatment Recommendation)

• Safety Criteria: Investigator's global assessment of tolerability

• Response to ESWT treatment

• Assessment of local tissue effects

• Subject's satisfaction and treatment recommendation, Physician's judgment

• Record Adverse Events (AE)/Serious Adverse Events (SAE)

• Documentation of concomitant therapy and medication

• Review entries in the Subject Heel Pain Medication and Other Painful Heel Therapy Diary

Visit 7: Follow-Up II (6 month ± 1 month after the last ESWT treatment)

• Investigation of the primary criteria (VAS, Roles and Maudsley-Score)

• Investigation of the secondary criteria (analgesic medication consumption)

• Assessment of local tissue effects

• Record AE/SAE

• Documentation of concomitant therapy and medication

• Review entries in the Subject Heel Pain Medication and Other Painful Heel Therapy Diary

Visit 8: Secondary Endpoint: Follow-Up II (12 months± 1 month after the last ESWT treatment)

• Investigation of the primary criteria (VAS, Roles and Maudsley-Score)

• Investigation of the secondary criteria (analgesic medication consumption,
- Physician's Judgment; Subject’s Satisfaction and Subject's Treatment Recommendation
- Safety Criteria: Investigator's global assessment of tolerability
- Response to ESWT treatment
- Assessment of local tissue effects
- Record AE/SAE
- Documentation of concomitant therapy and medication

Adverse events and complications were recorded at all visits. The key time points are shown below in the tables for safety and effectiveness (Tables 7-12).

3. Clinical Endpoints

a. Safety:

Safety endpoints were adverse events (type, intensity, severity, relationship to treatment, etc.) and the investigator's rating of treatment tolerability. The safety population consisted of all subjects receiving at least one (1) treatment.

b. Effectiveness:

The determination of effectiveness was based on two (2) criteria: a composite score for pain (using a 10 cm or 100 mm visual analog scale) and Roles and Maudsley scores when measured at the 3-month follow up visit (Visit 6). The composite score is the sum of three (3) pain measurements for the following:

i. Heel pain when taking the first steps of the day
ii. Heel pain while doing daily activities
iii. Heel pain after application of a standardized pressure device (F-meter)

Heel pain after application of a standardized pressure device (F-Meter) was based on the subject-specific force level at Visit 2 (baseline visit with first ESWT application). Using this same pressure at subsequent visits, the pain level was assessed using the same anchored VAS.

The second primary criterion for effectiveness was the four (4) point Roles and Maudsley score (JBJS(A) 1972; Aug 54 3; 499-508) as follows:

i. Excellent (No pain, full movement, full activity)
ii. Good (Occasional discomfort, full movement, and full activity)
iii. Fair (Some discomfort after prolonged activity)
iv. Poor (Pain limiting activities)

There were eight (8) secondary criteria for effectiveness criteria as follows:

i. Physician's Global Judgment of Effectiveness at Visits 6 (3 month) and 8 (12 month) rated as very good (0), good (1), moderate (2), unsatisfactory (3), or poor (4)

ii. Satisfaction with the Outcome of the Treatment as rated by subjects on a 7-Point Numeric Rating Scale (at Visit 6 and 8 only) rated as very dissatisfied (-3), moderately dissatisfied (-2), slightly dissatisfied (-1), neutral (0), slightly satisfied (1), moderately satisfied (2), or very satisfied (3)

iii. Willingness to recommend treatment as judged by patient (at visit 6 and 8 only): Yes/No

iv. Patient's analgesic medication consumption for painful heel (Acetaminophen (Tylenol®), Non-prescription analgesics, Prescription analgesics, or others as specified in concomitant therapy form in the Case Report Form (CRF) and patient's diary)

v. Heel pain overall success defined as percentage decrease of heel pain (VAS) larger than 60% from baseline at the 3 month follow up visit (Visit 6) for at least two (2) of the three (3) heel pain measurements.

vi. Heel pain single success when taking the first steps of the day defined as percentage decrease of heel pain (VAS) larger than 60% from baseline at the 3 month follow up visit (Visit 6)

vii. Heel pain single success while doing daily activities defined as percentage decrease of heel pain (VAS) larger than 60% from baseline at 3 month follow up visit (Visit 6)

viii. Heel pain single success after application of a standardized pressure device (F-meter) defined as percentage decrease of heel pain (VAS) larger than 60% from baseline at 3 month follow up visit (Visit 6)

The intent-to-treat (ITT) population consisted of all subjects who received at least one treatment and who had at least one evaluation visit. Missing values were handled using the Last Observation Carried Forward (LOCF) technique.

B. Accountability of PMA Cohort

Patients were randomized immediately before treatment at Visit 1 (before first application of ESWT) or Visit 2 (baseline visit with first ESWT application) using a block randomization scheme with sealed randomization envelopes. At the time of database lock, there were 126 subjects assigned to the Duolith Group and 124 subjects assigned to the Placebo Group. Treatment allocation and the numbers of subjects in each of the data sets (safety population, intent-to-treat population (ITT), and per-protocol population (PP)) are summarized in Table 3 below. A total of 17 subjects discontinued the study prematurely before Visit 6 (3 month) (Duolith Group: 7 subjects, Placebo Group: 10 subjects). Reasons for premature discontinuation are summarized by
treatment group in Table 4 below.

Table 3: Distribution of Subjects by Treatment Group and Data Set

<table>
<thead>
<tr>
<th>Data Set</th>
<th>Number of Subjects (Percent of Subjects)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Duolith Group</td>
<td>Placebo Group</td>
<td>Total Subjects</td>
<td></td>
</tr>
<tr>
<td>Safety Population</td>
<td>126</td>
<td>124</td>
<td>250 (100%)</td>
<td></td>
</tr>
<tr>
<td>ITT Population</td>
<td>125 (99.2%)</td>
<td>121 (97.6%)</td>
<td>246 (98.4%)</td>
<td></td>
</tr>
<tr>
<td>PP Population</td>
<td>122 (96.8%)</td>
<td>117 (94.4%)</td>
<td>239 (95.6%)</td>
<td></td>
</tr>
</tbody>
</table>

Missing values were handled using Last Observation Carried Forward (LOCF) technique.

Table 4: Reasons for Premature Discontinuation of Patients in the Safety Population (by Treatment Group)

<table>
<thead>
<tr>
<th>Reason for Premature Discontinuation</th>
<th>Duolith Group (N=126)</th>
<th>Placebo Group (N=124)</th>
<th>Total (N=250)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worsening of condition</td>
<td>2 (1.6%)</td>
<td>4 (3.2%)</td>
<td>6 (2.4%)</td>
</tr>
<tr>
<td>Adverse Event</td>
<td>2 (1.6%)</td>
<td>1 (0.8%)</td>
<td>3 (1.2%)</td>
</tr>
<tr>
<td>Worsening of condition and Adverse Event</td>
<td>1 (0.8%)</td>
<td>2 (1.6%)</td>
<td>3 (1.2%)</td>
</tr>
<tr>
<td>Administrative Reason</td>
<td>0</td>
<td>2 (1.6%)</td>
<td>2 (0.8%)</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>2 (1.6%)</td>
<td>1 (0.8%)</td>
<td>3 (1.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>7 (5.6%)</td>
<td>10 (8.1%)</td>
<td>17 (6.8%)</td>
</tr>
</tbody>
</table>

C. Study Population Demographics & Baseline Parameters

The demographics of the study population are typical for a primary study performed in the U.S. A tabular summary of subject demographics and baseline characteristics for the ITT population is provided by treatment group in Table 5 and a summary of the baseline characteristics for the efficacy criteria is provided in by treatment group Table 6. Differences between groups in demographic and baseline characteristics are minimal and the largest effect size (0.56 observed for age) is categorized as "small."

Table 5: Summary of Demographic and other Baseline Characteristics by Treatment Group- ITT Population

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Duolith Group (N= 125)</th>
<th>Placebo Group (N= 121)</th>
<th>Effect Size Mann-Whitney*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>Mean(SD, Range)</td>
<td>50.0 (11.18, 27 - 79)</td>
<td>47.4 (10.63, 23 - 77)</td>
</tr>
<tr>
<td>Gender:</td>
<td>Male</td>
<td>40 (32.0 %)</td>
<td>33 (27.3 %)</td>
</tr>
<tr>
<td>Number of subjects</td>
<td>Female</td>
<td>85 (68.0 %)</td>
<td>88 (72.7 %)</td>
</tr>
<tr>
<td>Ethnic Origin:</td>
<td>White</td>
<td>111 (88.8 %)</td>
<td>104 (86.0 %)</td>
</tr>
</tbody>
</table>
### Table 6: Summary of Baseline Efficacy Characteristics by Treatment Group - ITT Population

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Duolith Group (N = 125)</th>
<th>Placebo Group (N = 121)</th>
<th>Effect Size Mann-Whitney</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heel Pain (VAS) First Steps</td>
<td>Mean (SD; Range) 7.9 (1.55; 4.0-10.0)</td>
<td>8.0 (1.61; 3.0-10.0)</td>
<td>0.5066</td>
</tr>
<tr>
<td>Heel Pain (VAS) Daily Activities</td>
<td>Mean (SD; Range) 7.9 (1.55; 5.0-10.0)</td>
<td>7.9 (1.51; 5.0-10.0)</td>
<td>0.5087</td>
</tr>
<tr>
<td>Heel Pain (VAS) After F-Meter</td>
<td>Mean (SD; Range) 9.3 (1.25; 5.0-10.0)</td>
<td>9.3 (1.28; 5.0-10.0)</td>
<td>0.4907</td>
</tr>
</tbody>
</table>

The Mann-Whitney estimator is the corresponding standardized effect size measure of the Wilcoxon-Mann-Whitney test, benchmarks: 0.5 equality, 0.44/0.56 small, 0.36/0.64 medium-sized, 0.29/0.71 large group difference.
Heel Pain (VAS)
Composite Score
Mean (SD; Range) 8.38 (0.996; 5.30-10.00) 8.38 (1.016; 5.30-10.00) 0.5084

Roles and Maudsley
Mean (SD; Range) 3.6 (0.49; 3.0-4.0) 3.7 (0.48; 3.0-4.0) 0.5184

The Mann-Whitney estimator is the corresponding standardized effect size measure of the Wilcoxon-Mann-Whitney test, benchmarks: 0.5 equality, 0.44/0.56 small, 0.36/0.64 medium-sized, 0.29/0.71 large group difference.

Treatment Characteristics: A majority of subjects in both groups completed the treatments without deviations (Duolith Group: 98.4%; Placebo Group: 98.4%). Five (5) subjects (Duolith Group: 2; Placebo Group: 3) were reported with treatment-related deviations at six (6) treatment sessions. Only one (1) subject in the Duolith Group required anesthesia for the second treatment visit.

D. Safety and Effectiveness Results

1. Safety Results
The analysis of safety was based on the evaluable cohort of 250 patients available for 3 month evaluation. The key safety outcomes for this study are presented below in Tables 7 to 9.

Treatment Tolerability: The clinician’s judgment of treatment tolerability (a safety endpoint) was rated as "very good" or "good" in 89.1% (106/119) of the patients in the Duolith Group and in 91.2% (104/114) patients in the Placebo Group at Visit 6 (3 months). This was based on the investigator's global rating of treatment tolerability. The difference between the two (2) treatment groups for tolerability was only 2.1 percentage points in favor of the Placebo Group (P = 0.1434, two-sided Wilcoxon-Mann-Whitney test, MW = 0.4522, LB-CI = 0.3888). However, 74.4% (n=93 patients) of the Duolith Group and 71.1% (n=86 patients) in the Placebo Group required one or more concomitant analgesic medications during the study.

A total of 101 adverse events (77 events in the Duolith group and 24 in the placebo group) in 250 patients (126 in Duolith and 124 Placebo groups) were reported during the main study (enrollment through Visit 6 or 3 months). Adverse events reported for the Duolith SD 1 consist primarily of pain or discomfort during and after treatment. Events are summarized by treatment group and event category in the Table 7 below.

Table7: Summary of Number and Percent of Adverse Events by Category and Treatment Group- Safety Population

<table>
<thead>
<tr>
<th>Category</th>
<th>Duolith Group (n=126)</th>
<th>Placebo Group (n=124)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of events</td>
<td>Percent of events</td>
<td>Number of events</td>
</tr>
<tr>
<td>Heel Pain (VAS) Composite Score</td>
<td>8.38 (0.996; 5.30-10.00)</td>
<td>8.38 (1.016; 5.30-10.00)</td>
<td>0.5084</td>
</tr>
<tr>
<td>Roles and Maudsley</td>
<td>3.6 (0.49; 3.0-4.0)</td>
<td>3.7 (0.48; 3.0-4.0)</td>
<td>0.5184</td>
</tr>
</tbody>
</table>
In the Duolith Group, a total of 77 events were reported for 43/126 subjects (76.2% of 101 adverse events; 34.1% of 126 subjects). In the Placebo Group, a total of 24 events were reported for 17/124 subjects (23.8% of 101 adverse events; 13.7% of 124 subjects). Pain and/or discomfort occurring during or after treatment represent 60 events in the Duolith Group (60 of 77 events; 77.9%) and 11 events in the Placebo Group (11 of 24 events; 45.8%). Swelling was observed only in the Duolith Group (5 of 77 events; 6.5%). These differences are logical since subjects in the Duolith Group received active shock wave therapy.

Table 7 shows a total of 25 events among 250 patients were categorized as "other" (Duolith Group: 12 events, Placebo Group: 13 events). These events, their rated intensity, relationship, and seriousness are listed by treatment group in Table 8 below. Of these 25 events, none in the Duolith Group were rated as related to treatment. In the Placebo Group, however, two (2) events were rated as possibly related and for two (2) events the relationship was rated as doubtful.

Table 8: Listing of "Other" Adverse Events by Treatment Group

<table>
<thead>
<tr>
<th>Event Description</th>
<th>Intensity</th>
<th>Relation</th>
<th>Serious</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duolith Group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bone fracture spontaneous</td>
<td>Severe</td>
<td>not related</td>
<td>No</td>
</tr>
<tr>
<td>false sensation</td>
<td>Moderate</td>
<td>not related</td>
<td>No</td>
</tr>
<tr>
<td>inflicted injury</td>
<td>Mild</td>
<td>not related</td>
<td>No</td>
</tr>
<tr>
<td>inflicted injury</td>
<td>Moderate</td>
<td>not related</td>
<td>No</td>
</tr>
<tr>
<td>inflicted injury</td>
<td>Moderate</td>
<td>not related</td>
<td>No</td>
</tr>
<tr>
<td>inflicted injury</td>
<td>Severe</td>
<td>not related</td>
<td>No</td>
</tr>
<tr>
<td>influenza-like symptoms</td>
<td>Mild</td>
<td>not related</td>
<td>No</td>
</tr>
<tr>
<td>Neuropathy peripheral</td>
<td>Mild</td>
<td>not related</td>
<td>No</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Severe</td>
<td>not related</td>
<td>Yes</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>Severe</td>
<td>not related</td>
<td>Yes</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>Mild</td>
<td>not related</td>
<td>No</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>Mild</td>
<td>not related</td>
<td>No</td>
</tr>
<tr>
<td><strong>Placebo Group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bone fracture spontaneous</td>
<td>Moderate</td>
<td>not related</td>
<td>No</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>Mild</td>
<td>not related</td>
<td>No</td>
</tr>
<tr>
<td>inflicted injury</td>
<td>Moderate</td>
<td>not related</td>
<td>No</td>
</tr>
</tbody>
</table>
inflicted injury    Severe    not related    No
joint pain         Severe    not related    No
painful heel       Moderate  possible     No
painful heel       Severe    not related    No
tendon disorder    Moderate  possible     No
tendon disorder    Moderate  doubtful     No
tendon disorder    Moderate  not related    No
tendon disorder    Moderate  not related    No
tendon disorder    Moderate  not related    No
tendon disorder    Moderate  not related    No
painful heel       Severe    not related    No
joint pain         Severe    not related    No
painful heel       Moderate  possible     No
painful heel       Severe    not related    No
tendon disorder    Moderate  possible     No
tendon disorder    Moderate  possible     No
tendon disorder    Moderate  possible     No
painful heel       Severe    not related    No
tendon disorder    Moderate  not related    No
painful heel       Moderate  possible     No
tendon disorder    Moderate  possible     No
painful heel       Severe    not related    No

For adverse events categorized as "other," there were 12 events in the Duolith Group (12 of 77; 15.6%) and 13 events in the Placebo Group (13 of 24 events; 54.2%). Six (6) adverse events were reported for four (4) subjects during the long term follow up period of 12 months. No event was serious but one (1) subject discontinued during study participation during long term follow up due to ankle pain*. These events are summarized in Table 9 below:

<table>
<thead>
<tr>
<th>Group</th>
<th>Reported Term</th>
<th>Intensity</th>
<th>Relation</th>
<th>Serious</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duolith</td>
<td>Sinus infection, took antibiotics</td>
<td>Moderate</td>
<td>Not Related</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Reaction to antibiotics - allergy</td>
<td>Moderate</td>
<td>Not Related</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Respiratory system involved with Asthma attack</td>
<td>Moderate</td>
<td>Not Related</td>
<td>No</td>
</tr>
<tr>
<td>Placebo</td>
<td>Fracture of 5 metatarsals while vacationing</td>
<td>Moderate</td>
<td>Not Related</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Patient believes he developed ankle pain*</td>
<td>Mild</td>
<td>Doubtful</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Feels ankle hurts from repositioning**</td>
<td>Moderate</td>
<td>Probable</td>
<td>No</td>
</tr>
</tbody>
</table>

*Either non-related or due to repositioning of ankle during sham treatment  
**Repositioning of ankle during sham treatment

2. Effectiveness Results
The analysis of effectiveness was based on the 246 evaluable patients (ITT population) at the 3 month time point. Key effectiveness outcomes are presented in Tables 10 to 12. Results for the primary effectiveness criteria are statistically significant (P < 0.025 one-sided). All sensitivity analyses agreed with confirmatory results and showed statistically significant results. The same trend was demonstrated across study centers. A summary of changes in the median VAS composite score of heel pain and changes in the Roles and Maudsley Score is provided in Table 10 and 11 below.
Table 10: Summary Comparison of Baseline and Visit 6 (3 months) Composite VAS Score for Pain with Score Correction* by Treatment Group- ITT Population (LOCF)

<table>
<thead>
<tr>
<th>Composite VAS</th>
<th>Duolith Group (N=125)</th>
<th>Placebo Group (N=121)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Visit 6</td>
</tr>
<tr>
<td>Mean</td>
<td>8.38</td>
<td>3.80</td>
</tr>
<tr>
<td>Median</td>
<td>8.30</td>
<td>2.70</td>
</tr>
<tr>
<td>SD</td>
<td>0.996</td>
<td>2.47</td>
</tr>
<tr>
<td>Min</td>
<td>5.30</td>
<td>0.00</td>
</tr>
<tr>
<td>Max</td>
<td>10.00</td>
<td>10.00</td>
</tr>
</tbody>
</table>

*Score Correction for interfering analgesic therapy as defined in the statistical analysis plan

Using the Wilcoxon-Mann-Whitney, one-sided test for superiority, the results of the Duolith Group were determined to be superior to the Placebo Group (P = 0.0027 one-sided, MW = 0.6026, LB-CI = 0.5306). The mean Roles and Maudsley score was reduced from 3.6 to 2.5 in the Duolith Group and from 3.7 to 2.9 in the Placebo Group, with a final group difference for Roles and Maudsley scores of 0.4 in favor of the Duolith Group.

Table 11: Comparison of Baseline and Visit 6 (3 months) Roles and Maudsley Scores with Score Correction* by Treatment Group- ITT Population (LOCF)

<table>
<thead>
<tr>
<th>Composite VAS</th>
<th>Duolith Group (N=125)</th>
<th>Placebo Group (N=121)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Visit 6</td>
</tr>
<tr>
<td>Mean</td>
<td>3.6</td>
<td>2.5</td>
</tr>
<tr>
<td>Median</td>
<td>4.0</td>
<td>2.0</td>
</tr>
<tr>
<td>SD</td>
<td>0.49</td>
<td>0.94</td>
</tr>
<tr>
<td>Min</td>
<td>3.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Max</td>
<td>4.0</td>
<td>4.0</td>
</tr>
</tbody>
</table>

*Score Correction for interfering analgesic therapy as defined in the statistical analysis plan

Using the Wilcoxon-Mann-Whitney, one-sided test for superiority, the results for the Duolith Group were determined to be superior to the Placebo Group (P = 0.0006 one-sided, MW = 0.6135, LB-CI = 0.5466).

Secondary Effectiveness. Results for secondary effectiveness criteria are summarized for the ITT population in Table 12 below.

Table 12: Summary of Secondary Effectiveness Results by Treatment Group
<table>
<thead>
<tr>
<th>Secondary Effectiveness Criterion</th>
<th>Rating/Result</th>
<th>Duolith Group Number of subjects (n=119) (Percent of subjects)</th>
<th>Placebo Group Number of subjects (n=114) (Percent of subjects)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigator's Global Judgment of Effectiveness at Visit 6 (3 months)</td>
<td>Very good</td>
<td>46 (38.66%)</td>
<td>41 (35.96%)</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td>42 (35.29%)</td>
<td>21 (18.42%)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>11 (9.24%)</td>
<td>11 (9.65%)</td>
</tr>
<tr>
<td></td>
<td>Unsatisfactory</td>
<td>11 (9.24%)</td>
<td>16 (14.04%)</td>
</tr>
<tr>
<td></td>
<td>Poor</td>
<td>9 (7.56%)</td>
<td>25 (21.93%)</td>
</tr>
<tr>
<td>Subject's global judgment of therapy Satisfaction</td>
<td>Very unsatisfied</td>
<td>9 (7.56%)</td>
<td>18 (15.79%)</td>
</tr>
<tr>
<td></td>
<td>Moderately unsatisfied</td>
<td>13 (10.92%)</td>
<td>20 (17.54%)</td>
</tr>
<tr>
<td></td>
<td>Less satisfied</td>
<td>6 (5.04%)</td>
<td>9 (7.89%)</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>15 (12.61%)</td>
<td>18 (15.79%)</td>
</tr>
<tr>
<td></td>
<td>In general satisfied</td>
<td>19 (15.97%)</td>
<td>11 (9.65%)</td>
</tr>
<tr>
<td></td>
<td>Satisfied</td>
<td>29 (24.37%)</td>
<td>17 (14.91%)</td>
</tr>
<tr>
<td></td>
<td>Very satisfied</td>
<td>28 (23.53%)</td>
<td>21 (18.42%)</td>
</tr>
<tr>
<td>Subject's recommendation of therapy to a friend</td>
<td>Yes</td>
<td>95 (79.83%)</td>
<td>68 (59.65%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>24 (20.17%)</td>
<td>46 (40.35%)</td>
</tr>
<tr>
<td>Heel Pain Overall Success (larger than 60% from baseline at visit 6 (3 month) for at least two (2) of the three (3) heel pain (VAS) measurements</td>
<td>Success</td>
<td>68 (54.40%)</td>
<td>45 (37.19%)</td>
</tr>
<tr>
<td></td>
<td>Failure</td>
<td>57 (45.60%)</td>
<td>76 (62.81%)</td>
</tr>
<tr>
<td>Heel pain single success when taking first steps of the day (percentage decrease of heel pain (VAS) measurements larger than 60% from baseline at visit 6 (3 month follow up))</td>
<td>Success</td>
<td>63 (50.40%)</td>
<td>44 (36.36%)</td>
</tr>
<tr>
<td></td>
<td>Failure</td>
<td>62 (49.60%)</td>
<td>77 (63.64%)</td>
</tr>
<tr>
<td>Heel pain single success</td>
<td>Success</td>
<td>62 (49.60%)</td>
<td>47 (38.84%)</td>
</tr>
<tr>
<td>Secondary Effectiveness Criterion</td>
<td>Rating/Result</td>
<td>Duolith Group Number of subjects (n=119) (Percent of subjects)</td>
<td>Placebo Group Number of subjects (n=114) (Percent of subjects)</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>---------------</td>
<td>-------------------------------------------------------------</td>
<td>-------------------------------------------------------------</td>
</tr>
<tr>
<td>while doing daily activities (percentage decrease of heel pain (VAS) measurements larger than 60% from baseline at visit 6 (3 month follow up))</td>
<td>Failure</td>
<td>63 (50.40%)</td>
<td>74 (61.16%)</td>
</tr>
<tr>
<td>Heel pain single success after application of a standardized pressure device (F-meter) (percentage decrease of heel pain (VAS) measurements larger than 60% from baseline at visit 6 (3 month follow up))</td>
<td>Success</td>
<td>67 (53.60%)</td>
<td>51 (42.15%)</td>
</tr>
<tr>
<td></td>
<td>Failure</td>
<td>58 (46.40%)</td>
<td>70 (57.85%)</td>
</tr>
<tr>
<td>Frequency count of subjects with at least one concomitant analgesic therapy during the study</td>
<td>No</td>
<td>32 (25.60%)</td>
<td>35 (28.93%)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>93 (74.40%)</td>
<td>86 (71.07%)</td>
</tr>
</tbody>
</table>

XI. PANEL MEETING RECOMMENDATION AND FDA’S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the General and Plastic Surgery Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The results of primary effectiveness criteria in composite VAS showed statistically significant pain reduction when the VAS pain scores were compared between treatment and placebo groups. The results of the Duolith group were found to be slightly superior to the placebo group (p<0.025, one-sided) in terms of pain relief.

B. Safety Conclusions

A total of 77 adverse events in the Treatment Group and 24 adverse events in the
Placebo-Controlled Sham Group were reported through Visit 6 at 3 month. The adverse events primarily consist of pain or discomfort during and after treatment. Of the twenty five (25) events reported as "other" and listed in the Table 7 none were related to the treatment in the Duolith group, but two (2) events in the Placebo Group were rated as possibly related and two (2) events were rated as doubtful. It can be concluded therefore, the Duolith SD1 Shock Wave Therapy Device and the treatment for pain due to plantar fasciitis is safe.

C. **Overall Conclusions**

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The preclinical and clinical data presented in this PMA provide reasonable assurance that the Duolith SD1 is safe when used according to the device labeling.

The results of the multi-center, randomized, placebo controlled, double-blind clinical study demonstrate that treatment of heel pain due to chronic proximal plantar fasciitis with the Duolith SD1 may provide relief for up to 12 weeks duration in a significant proportion of the patient population who have previously failed conservative treatment for 6 months or more. The most likely side effect is pain during/after treatment which was reported by 50.7% of patients in the Duolith Group and 41.6% of patients on the Placebo-Controlled Sham Group. For this study 74.4% of the Duolith Group and 71.07% of the Placebo-Controlled Sham Group required one or more concomitant analgesic therapy during the study. The clinical data from the study demonstrate that the efficacy of the device outweighs the risk and the device is safe and effective for patients having symptoms of chronic proximal plantar fasciitis, for 6 months or more, and a history of unsuccessful conservative therapy.

XIII. **CDRH DECISION**

CDRH issued an approval order on January 8, 2016.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. **APPROVAL SPECIFICATIONS**

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See Approval Order