DRAFT

Orthospec™

PHYSICIAN'S LABELING

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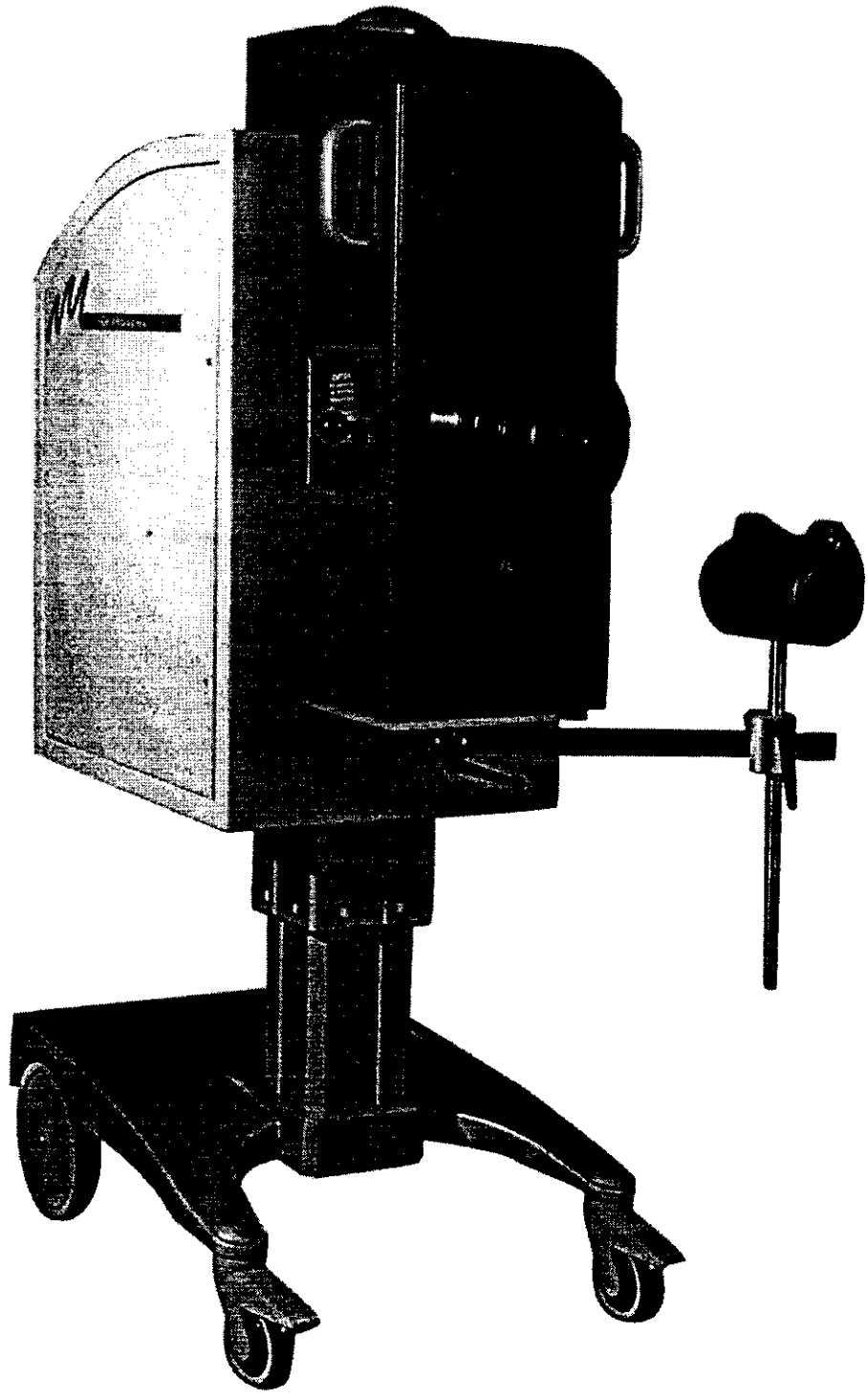
The Orthospec™



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INTRODUCTION

The **Orthospec™** is based on the shock wave therapy method and is intended to apply shock waves to the heel tissue of patients who have Proximal Plantar Fasciitis and who have failed previous conservative therapies.

CAUTION: Federal law restricts this device to sale by or on the order of a physician. The device should be used only by qualified and trained personnel under the supervision of a physician.

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.

CONTRAINDICATIONS FOR THE USE OF ORTHOSPEC™

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.

WARNINGS

1. The operator should avoid directing the device's focal point to main nerves or vessels to avoid injury to these structures.
2. 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 ecchymosis, bruising, or hematoma.
3. The safety and effectiveness of the Medispec Orthospec™ in the treatment of children have not been demonstrated. Studies indicate that there are growth plate disturbances in the epiphyses of developing long bones in rats subjected to shock waves. The significance of this finding in humans, however, is unknown.
4. This device may be sensitive to electromagnetic interference which could result in device malfunction. Do not operate in the vicinity of electrosurgery, diathermy, or nuclear magnetic resonance imaging equipment.

PRECAUTIONS

1. 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.
2. It is recommended that there be no less than a one month interval between treatments and not over 4 treatments in a session. The number of shock waves per session should not exceed 3,800. As the clinical study has shown, patients' relief of pain should continue for up to 3 weeks after a treatment session. Therefore, a one month time window between treatments is recommended.
3. Clinical study results indicate utilizing the Orthospec™ at energy level settings of less than or equal to 4.5 will not lead to a successful outcome. If the patient can not tolerate the Orthospec™ procedure at energy levels higher than 4.5 after 10 minutes into the procedure, it is recommended, per the physician's discretion, that the treatment be terminated.
4. Safety and effectiveness in patients who are pregnant, who are under 18 years of age, or who have had prior surgery for plantar fasciitis have not been established.
5. If the patient has significant tears of the plantar fascia, shock wave treatment may be ineffective.
6. The operator should direct the maximum energy mark (yellow dot which represents the focal point) at the point of maximum pain intensity (pain origin and not referred pain zone); however, mild misdirection should not significantly change the effectiveness of the treatment.
7. If the patient experiences a vaso-vagal reaction during treatment, the patient should be reclined to a supine position until symptoms disappear.

ADVERSE EVENTS

During the Orthospec™ clinical study, there were 3 reported cases of adverse reactions 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.

Summary of All Adverse Events			
	Orthospec™ (N = 115) n (%)	**Placebo** (N = 57) n (%)	**P-Value**
Any Adverse Event	3 (2.6%)	0 (0%)	0.55
Bruising	2 (1.7%)	0 (0%)	1.0
Mild local swelling	1 (0.9%)	0 (0%)	1.0

POTENTIAL ADVERSE EVENTS

Potential adverse effects that could occur when using the Orthospec™ treatments include:

- Pain
- Petechia
- Superficial hematoma
- Neurosensory conditions: Hypesthesia or Parasthesia
- Rare allergic or sensitive reaction to the coupling solution applied to skin during treatment, or to the Latex membrane.
- Tendon rupture

CLINICAL STUDY

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.

Inclusion criteria were:

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.

Exclusion criteria were:

- 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™.

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- 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.
- Requires narcotics for plantar pain relief or other medical conditions prior to treatment.

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.

Primary Objective

- The primary objective of the study 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 $\leq$ 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. The subjects had a mean age of 51 years, and the mean duration of foot pain was 30 months. Thirty-three (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 1 - Patient Accountability

	Orthospec™ n (%)	**Placebo** n (%)	**Total** n (%)
Screened	196		
Randomized	115	57	172
Completed 3 Months	101 (87.8%)	51 (89.5%)	152 (88.4%)
Terminated Prematurely	14 (12.2%)	6 (10.5%)	20 (11.6%)
Condition Worsened	5 (4.3%)	0 (0%)	5 (2.9%)
Healed	1 (0.9%)	0 (0%)	1 (0.6%)
Other	0 (0%)	1 (1.8%)	1 (0.6%)
Lost to Follow-up	8 (7.0%)	5 (8.8%)	13 (7.6%)
Included in primary analysis of effectiveness[1]	112 (97.4%)	56 (98.2%)	168 (97.7%)
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 heal 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). The following table 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

	Orthospec™	Placebo	P-Value
Month 1			
N	111	54	
Mean[1]	-1.61	-1.27	0.34
Difference (95% CI)	-0.34 (-1.06, 0.37)		
Month 2			
N	111	54	
Mean[1]	-2.30	-1.31	0.026
Difference (95% CI)	-0.99 (-1.86, -0.12)		
Month 3			
N	112	56	
Mean[1]	-2.51	-1.57	0.045
Difference (95% CI)	-0.94(-1.87, -0.02)		

[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. These results show that 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

	N	Mean[1]
Placebo	57	-1.53
Level 2 – 4.5	14	-1.09
Level 4.6 – 5.9	12	-1.71
Level 6 – 6.9	53	-2.87
Level 7	32	-2.93

[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 pain and the 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[1]			
Measure	**Orthospec™ N=115**	**Placebo N=57**	**P-Value**
Patient's Assessment of Heel Pain			
Mean change from baseline	-3.39	-1.78	<0.001
Response rate	52.7%	28.6%	0.003
Patient's Assessment of Activity and Function Response Rate	64.3%	57.1%	0.33
Change in the use of Pain Medication			
Increased	1.0%	11.8%	<0.001
No change	65.0%	74.5%	
Decreased	34.0%	13.7%	

[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, patients treated with an energy level of ≤ 4.5 did not, as a group, receive a therapeutic benefit. To demonstrate the effectiveness among patients receiving 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 level of improvement in pain relief and activity and function when patients were treated at energy level higher than 4.5.

Table 5 – Summary of Effectiveness Results at Three Months[1] Orthospec Patients With Energy Level > 4.5			
Measure	**Orthospec™ N=97**	**Placebo N=57**	**P-Value**
Investigator's Assessment of Heel Pain			
Mean change from baseline	-2.75	-1.52	0.011
Response rate	46.4%	19.3%	<0.001
Patient's Assessment of Heel Pain			
Mean change from baseline	-3.69	-1.72	<0.001
Response rate	57.7%	28.1%	<0.001
Patient's Assessment of Activity and Function Response Rate	67.0%	56.1%	0.16

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Change in the use of Pain Medication			
Increased	1.1%	11.5%	<0.001
No change	61.4%	75.0%	
Decreased	37.5%	13.5%	

[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.

Conclusion

This investigation demonstrates the Orthospec™ ESWT modality is a safe and effective tool in treating chronic pain caused by Proximal Plantar Fasciitis that is not responsive to conservative therapy.

NOTE: *To achieve the most effective treatment results, the treatment energy should reach levels 4.5 and higher.*