SUMMARY OF SAFETY AND EFFECTIVENESS

I. GENERAL INFORMATION

Device Generic Name:	Transurethral Microwave Thermo Therapy System
Device Trade Name:	ProstaLund® CoreTherm™
Applicant:	ProstaLund Operations AB Höstbruksvägen 10 SE-226 60 Lund, Sweden
U.S. Representative:	EXPERTech Associates, Inc. 100 Main Street Concord, MA
Premarket Approval (PMA) Number:	P010055
Date of Panel Recommendations:	None
Date of Notice of Approval to Applicant:	December 23, 2002

II. INDICATIONS FOR USE

The ProstaLund® CoreTherm™ Microwave Thermotherapy System hereinafter called CoreTherm™ is a non-surgical, minimally invasive, device intended to relieve symptoms associated with symptomatic Benign Prostatic Hyperplasia (BPH) by ProstaLund® Feedback Treatment® (PLFT®) and is indicated for men with a prostate size of 30 to 100g and length $\geq$35 mm.

III. CONTRAINDICATIONS

Contraindications for PLFT® treatment with the ProstaLund® CoreTherm™ System include:

- Severe urethral stricture preventing easy catheterization;
- Patients with penile or urinary sphincter implants;
- Previous radiation of pelvic region;
- Prostate size < 30 g; prostate length < 35 mm;
- Clinical or histological evidence of bladder cancer;
- Active prostatitis;
- Active urinary tract infection;
- Previous prostate or rectal surgery;
- Interest in the preservation of fertility;
- Implanted defibrillators, pacemakers or any other active implant;

• Metallic implant in the prostate treatment area;
• Peripheral arterial disease with intermittent claudication.

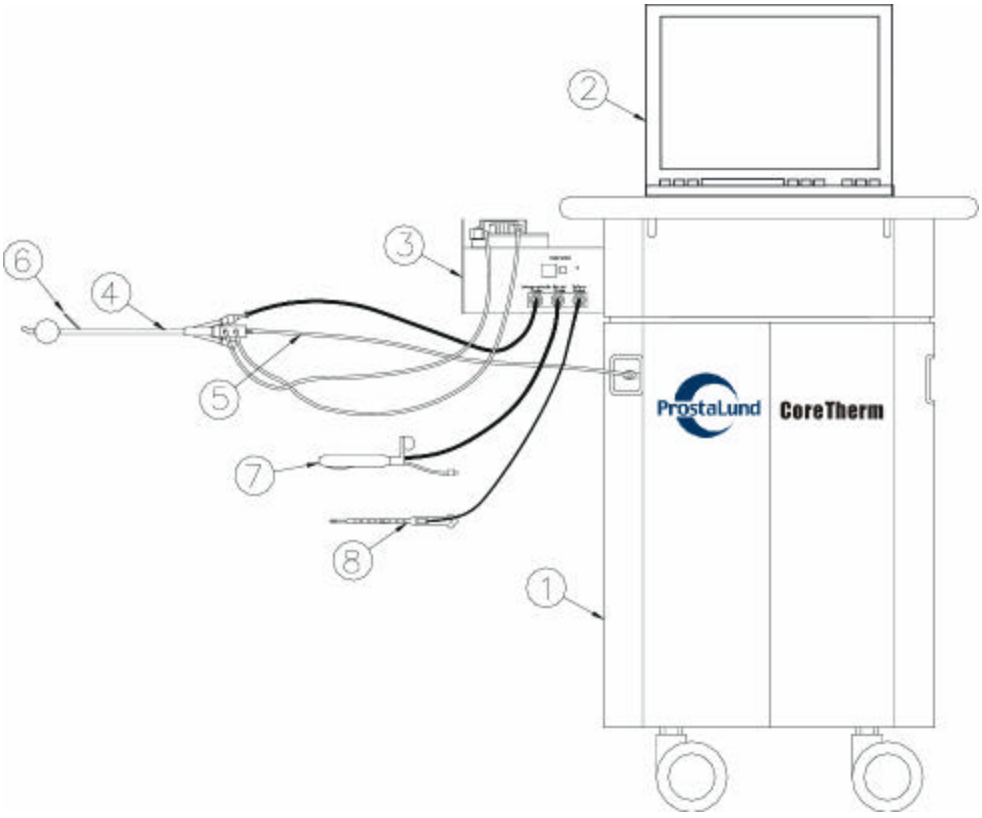
IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the labelling for the CoreTherm™

V. DEVICE DESCRIPTION

The ProstaLund® CoreTherm™ is an operator-controlled device designed to deliver microwave energy to the prostate for treatment of BPH. The treatment, PLC, is performed as a single session, and treatment duration is about 30 to 60 minutes. The device utilizes a transurethral microwave antenna to heat the prostate tissue. This heating process is regulated by the operator, through temperature feedback from an intraprostatic temperature probe. During treatment the system also continuously records rectal temperature and penile skin temperature at the penoscrotal angle, in order to ensure a safe treatment session and to avoid overheating. The power to the microwave generator is automatically shut down if any of these probes record temperatures above pre-set safety limits. The operator can follow the information, such as temperatures, calculated amount of cell kill, treatment time and power, during the treatment session on the computer screen.

Figure I



The ProstaLund® CoreTherm™ comprises:

1 CoreTherm™ Control Unit
2 Laptop PC with CoreTherm™ SW Pac
3 Pull Out Drawer
4 CoreTherm™ Catheter
5 Microwave Antenna
6 Intraprostatic Temperature Probe
7 Rectal Temperature Probe
8 Penis Safety Probe

CoreTherm™ Control Unit

The CoreTherm™ Control Unit includes a microwave generator, a temperature recording system, a water circulation system and computer-controlled delivery of microwave energy to the prostate with continuous monitoring of the intraprostatic temperature. The control unit is a portable unit approximately 890 mm high, 450 mm deep and 607 mm wide.

Laptop PC

A laptop PC with the software is connected to the control unit of the CoreTherm™. The software handles the user interface and allows the operator to register patients and set treatment parameters. It also works as a monitor displaying information, for example, the intraprostatic temperatures may be monitored continuously during treatment.

CoreTherm™ Catheter

The CoreTherm™ Catheter is primarily used to house the microwave antenna and guide the intraprostatic temperature probe. Circulating water passes through the catheter. The catheter has an inflatable balloon close to the tip, to anchor the catheter at the bladder neck during treatment. The catheter has separate channels for the microwave antenna, for the intraprostatic temperature probe, for water inlet and outlet, and for inflating the balloon.

The CoreTherm™ Catheter is for single use and should be used only once. It is provided in a sealed sterile package.

Microwave Antenna

The microwave antenna directs the microwave radiation into the prostate tissue. The antenna has to be fitted into the CoreTherm™ Catheter prior to use. The microwave antenna is delivered in a separate package, and it may be re-used a maximum of 10 times.

Temperature Probes

The *Intraprostatic Temperature Probe* records the intraprostatic temperature during treatment. It contains three temperature sensors, located 10 mm apart at the tip of the probe. A fourth sensor is placed further back in the probe and measures the temperature of the circulating water.

The operator controls the amount of microwave power applied during treatment according to the intraprostatic temperature probe. If the temperature exceeds the pre-set safety limit, the microwave generator will shut off automatically.

The *Rectal Temperature Probe* records rectal temperature during treatment. It contains three temperature sensors. The sensors are located near the tip of the probe, against the inner wall of the anterior side. If the temperature exceeds the pre-set safety limit, the microwave generator will be shut off automatically.

The *Penis Safety Probe* records the surface temperature at the base of the penis during treatment. If the temperature exceeds the pre-set safety limit, the microwave generator will shut off automatically. The penis safety probe, that contains one sensor, should be fastened at the base of the penis, with the sensor at the penoscrotal angle.

The temperature probes have color-coded connectors. Each connector has a hardware key to prevent incorrect connection to the control unit. All the temperature probes contain an electronic chip that identifies the specific probe in use. The temperature probes may all be re-used after proper disinfection/sterilization according to the Instructions for Use.

VI. ALTERNATE PRACTICES OR PROCEDURES

The treatment of BPH has been based predominantly on patient symptomatology and degree of associated urinary obstruction. The following are currently available BPH treatment options, listed in order from least to most invasive:

- watchful waiting;
- medical therapy (alpha blockers, finasteride);
- thermal ablation (laser, TUNA, hot water, or microwave energy);
- transurethral incision of the prostate;
- Transurethral Resection of the Prostate (TURP);
- open prostatectomy.

VII. MARKETING HISTORY

Between 1991 and 1998, roughly 80 ProstaLund® microwave thermotherapy treatment devices (without intraprostatic temperature measurement) have been sold in about 12 countries since 1991

In 1998 the ProstaLund® Microwave Thermotherapy (ProstaLund® Standard PLS) device and the ProstaLund® Feedback Treatment® (PLFT®) with intraprostatic temperature measurement, was implemented. Subsequently, the PLS was upgraded to ProstaLund® Compact (PLC). The ProstaLund® Compact will be marketed under the name ProstaLund® CoreTherm™.

The device has been marketed in the following countries: Argentina, Austria, Chile, Denmark, France, Germany, Greece, Hong Kong, Italy, Lebanon, the Netherlands, Norway, Poland, South Africa, Sweden, and Switzerland.

The ProstaLund® devices have not been withdrawn from marketing for any reason relating to safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The vast majority of adverse events after PLFT® treatment with either PLS or CoreTherm™ device emanated from the urinary tract. In most cases, the events were of mild or moderate intensity. A complete listing of adverse events observed in the clinical study is presented in section X.

Listed below are other possible side effects of thermotherapy treatment. However, these side effects were not experienced during the clinical studies of the CoreTherm™ device.

- Rectal damage/fistula
- Burn injuries outside the treatment area
- Incontinence caused by injuries to the external sphincter
- Impotence and/or Sterility

IX. SUMMARY OF PRECLINICAL STUDIES

1. Validation of Device Changes*

A. Bench testing to compare the performance of the CoreTherm™ (PLC) to the PLS device component changes included the following:

- Microwave Generator: testing designed to compare the microwaves in the PLC to the PLS, in terms of output power, power measurement, output power variability, and security.
- Mechanical Design and Material Comparison of the PLC Feedback Treatment (PLS®) Catheter to the PLS Precision™ Treatment Catheter: testing designed to compare physical and performance in terms of specifications, materials, cooling capacity.
- Microwave Antenna: testing designed to compare electromagnetic radiation. properties in the specific absorption rate (SAR), electromagnetic field (EM-field) and the return loss.
- Stub Tuner: testing designed to compare the ability of the semi-automatic stub tuner in PLC to the PLS manual stub tuner in terms of minimizing reflected microwave power
- Temperature Probes: designed to compare 1) the temperature measuring accuracy of the PLC vs. PLS, and 2) test the identify check of the probes

* See Clinical Studies for support of device effectiveness.

B. *Electrical safety has been tested and found to be in conformity with:*
Medical Electrical Equipment
Part 1: General Requirements for Safety
IEC 60601-1, Second edition, 1998 with Amendment 1, 1991 and Amendment 2, 1995
(EN 60601-1: 1990 with A1 and A12: 1993, A2: 1995 and A13: 1996)

Medical Electrical Equipment
Part 2: Particular Requirements for the Safety of Microwave Therapy Equipment
Applicable parts of IEC 60601-2-6, First edition, 1984

C. *Electromagnetic compatibility (EMC) has been tested and found to be in conformity with:*
Medical Electrical Equipment
Part 1: General Requirements for Safety
Chapter 2: Electromagnetic Compatibility – Requirements and tests
EN 60601-1-2: 1993
Emission in according to CISPR 11, group 2, class B

D. *Protection against Water Ingress:* IP20, ordinary equipment without protection against water ingress according to IEC 60529: Edition 2.1: Degrees of protection provided by enclosures (IP Code)

E. *Microbiological Studies*
Microbiological studies of the CoreTherm™ catheter according to SS-EN 1174-2, *Sterilization of medical devices, Estimation of the population of microorganisms on product,* has been performed. Average microbiological count is less than 10/cfu per product.

F. *Sterility Assurance*

The CoreTherm™ catheter is sterilized by Ethylene Oxide by a validated sterilization process in accordance with AAMI ANSI ISO 11135-Medical Devices- Validation and Routine Control of Ethylene Oxide Sterilization.

The routine process is controlled by established process parameters and Biological Indicators. The package seal is evaluated to guarantee seal integrity. The package seal is tested according to ASTM D 4169-01 Standard Practice for Performance Testing of Shipping Containers and Systems, ASTM F 1886 – 98. Standard Test Method for Determining Integrity of Seals for Medical Packaging by Visual Inspection, ASTM E 515 -95 (Reapproved 2000) Standard Test Method for Leaks With Bubble Emission Techniques1.ASTM F 1929 – 98. Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration. and ASTM F 88 – 00. Standard Strength Test of Flexible Barrier Materials.

G. *Ethylene Oxide Residual Testing*

Tests for potential presence of Ethylene Oxide (EO) residues after sterilization were performed on samples of the CoreTherm™ catheter. Less than 0.3 mg EO was found, which is well below the recommended average daily dose of EO: 20 mg – limited exposure. According to AAMIANSI ISO 10993-7 Biological Evaluation of Medical Devices – Part 7 Ethylene Oxide Residuals.

H. *Biocompatibility Testing*

There are four patient contacting components used with the CoreTherm™ system: the CoreTherm™ catheter, the intraprostatic temperature probe, the penis safety probe and the rectal temperature probe. To investigate the possible irritancy and sensitization properties on these components, several in vivo and in vitro animal studies have been performed on all these components. The tests were selected based on the Categorization criteria in ISO/EN 10993-1. The tests selected include intracutaneous reactivity, sensitization, hemocompatibility, genotoxicity and cytotoxicity.

Data indicates that there was a high degree of biocompatibility in the material and that no significant irritation, sensitizing, hemolytic, cytotoxic or mutagenic effects could be expected from the device components.

I. *Other Performance Testing*

The CoreTherm™ and its components underwent numerous tests to ensure proper operation. Performance testing addressed the electrical, mechanical and software properties of the device and its components and included: output power of the microwave generator, microwave antenna radiation characteristics, catheter properties, tensile strength testing, leakage testing, system/ simulation testing, durability/ reliability, and functional performance. Additionally, environmental conditioning, and shelf life studies were conducted.

Testing indicated that the CoreTherm™ and its components performed properly, according to product specifications, in all testing conditions, demonstrating the performance of the device for its intended use.

Package integrity of the CoreTherm™ catheter was established for one year following testing in accordance with ASTM F 1980-02: Standard Guide for Accelerated Aging of Sterile Medical Device Packages. Testing included visual inspection, dye penetration, bubble

emission, and tensile strength to ensure sterility is maintained for one year. Shelf life testing was performed on 26-month aged catheters and consisted of balloon inflation, balloon leakage, burst strength, and tensile strength testing to ensure the catheter performs in accordance with specifications after real time aging.

X. SUMMARY OF CLINICAL STUDIES

Study Design

Study A

Study A was prospectively planned and was conducted under an IDE at ten centers in Scandinavia and the USA. The results of the PLS device used for PLFT® treatment was compared to TURP (Trans Urethral Resection of the Prostate). The treatment allocation was double-blind and sealed randomization envelopes were used. Approximately 150 patients with BPH were planned for enrollment to either PLFT® treatment with PLS device or TURP with a randomization ratio of 2:1 (with twice as many patients in the PLS/PLFT® treatment group).

The patients were seen at screening (0-6 weeks pre-treatment), at treatment (day 1) and at follow-up visits at 3, 6 and 12 months post-treatment. After study completion the patients will be followed-up on a long-term basis up to 5 years post-treatment. The latter results will be documented and reported separately and submitted to FDA in the beginning of 2005.

The primary objective was the subjective improvement of patients treated with the PLS device compared to TURP after 12 months, in patients with BPH. The primary efficacy variable was the International Prostate Symptom Score (IPSS), which is commonly used when evaluating patients with BPH.

The statistical hypothesis was to test for non-inferiority of treatment with the PLS device as compared to TURP with IPSS as the primary variable. One-sided confidence intervals (95%) for the difference in IPSS between PLFT® treatment with the PLS device as compared to TURP according to the t-distribution are presented, including the change from baseline. Noninferiority of PLFT® treatment with PLS device as compared to TURP could be claimed if the one-sided 95% confidence interval of the treatment difference in IPSS of PLFT® treatment with the PLS device as compared to TURP is 125% or less.

The same principle of statistical analysis was stated also for the secondary variable Qmax. A higher value for Qmax indicated a better response; hence a lower one-sided 95% confidence interval within 80% of PLFT® treatment with PLS device as compared to TURP represented the statistical target.

The responder rate was regarded as a secondary variable. Noninferiority in responder rate for PLFT® treatment with the PLS device as compared to TURP could be claimed if the 95% one-sided confidence interval for the difference in the proportion of responders is not lower than 20% of the proportion responders in the TURP group. Calculations according to the t-distribution were used.

A responder was defined as:

- IPSS of 7 or less, and/or
- 50% or greater improvement in IPSS from baseline, and/or

- Q_{max} of 15 ml/s or more, and/or
- 50% or greater improvement in Q_{max} from baseline.

If there was data missing at the one-year visit in the responder analysis results from the previous visit replaced the missing value ("last observation carried forward", LOCF).

Secondary objectives were to study the clinical efficacy in terms of objective improvement, as well as to study the safety of PLFT® treatment with PLS device compared to TURP after 12 months regarding:

- max urinary free flow rate (Q_{max});
- detrusor pressure [at maximum flow rate (P_{det} at Q_{max})] (as measured by urodynamics);
- residual urine volume;
- prostate volume (as determined by TRUS);
- post-treatment indwelling catheter time;
- adverse events;
- sexual function (i.e. query regarding penetrating coitus and ejaculation ability);
- distribution of patients into responder and non-responder groups.

Study B and C were conducted at single centers in Switzerland and in the Netherlands, respectively. In both cases the subject device ProstaLund® CoreTherm™ was used. These studies were conducted to support the clinical data of Study A performed with the PLS device to ensure outcomes of both devices were comparable.

Study B

Study B was prospectively planned and was conducted at one center in Switzerland. PLFT® treatment with the CoreTherm™ device was compared to TURP. The treatment allocation was double blind and sealed randomization envelopes were used. It was intended to enroll 51 patients with BPH to treatment with either PLFT® treatment with the CoreTherm™ device or TURP, with a randomization ratio of 2:1.

The patients were seen at screening (0-6 weeks pre-treatment), at treatment (day 1) and at follow-up visits at 3, 6 and 12 months post-treatment.

The primary objective was to study the clinical efficacy of PLFT® treatment with the CoreTherm™ device as compared to TURP in patients with BPH in terms of the proportion of responders (see study A for definition) after 12 months of treatment.

The responder rate was regarded as the primary variable. The Objective of the study was to demonstrate that the proportion responders in the PLFT® treatment group with the CoreTherm™ device had a 95% one-sided confidence interval that was not lower than 70%, furthermore, noninferiority of PLFT® treatment with CorTherm™ device as compared to TURP was tested by the same principle as in study A. For the secondary variables IPSS and Q_{max} 95% one-sided confidence intervals for the treatment difference were calculated, and noninferiority of PLFT® treatment with CorTherm™ device as compared to TURP tested as in study A.

Secondary objectives were to study the clinical efficacy in terms of subjective and objective improvement, as well as to study the safety of PLFT® treatment with CorTherm™ device with TURP as a reference after 12 months regarding:

- IPSS;
- Q_{max};

- detrusor pressure [at maximum flow rate (P_{det} at Q_{max})] (as measured by urodynamics);
- residual urine volume;
- prostate volume (as determined by TRUS);
- adverse events;
- post-treatment indwelling catheter time;
- sexual function (i.e. query regarding penetrating coitus and ejaculation ability).

Study C

Study C was also prospectively planned and was conducted at one center in the Netherlands. It was intended to evaluate PLFT® treatment with CoreTherm™ device in 35 patients with BPH. There was no reference group.

The patients were seen at screening (0-4 weeks pre-treatment), at treatment (day 1) and at follow-up visits at 3, 6 and 12 months post-treatment.

The primary objective was to study the clinical efficacy of PLFT® treatment with CoreTherm™ device in patients with BPH in terms of the proportion of responders (see study A for definition) after 12 months of treatment.

The responder rate was regarded as a primary variable. This study had no comparative group, and the statistical hypothesis was to test, if the proportion responders in the PLFT® treatment group with CoreTherm™ device had a 95% one-sided confidence interval that was not lower than 70%. Secondary objectives were identical to those established under Study B.

Patient Classification

Patients were classified into a Per-Protocol (PP) sample and an Intention-to-Treat (ITT) sample. The ITT sample represented all patients treated, and the PP sample represents patients who had no major violations* to visit schedules or protocol procedures.

**Major violation was defined as:*

- *patients who at inclusion had, or during the study developed withdrawal criteria but were not withdrawn*
- *patients who had too short wash-out period of 5-alpha reductase inhibitors or alpha blockers prior to treatment*

In addition, patients were excluded from the PP analysis if three or more of the following deviations occurred;

- *one or more missing visits 3-5,*
- *patients who had too long screening period*
- *patients with a too old IPSS result at baseline*
- *patients who had missing IPSS at visit 1 or 3-5*
- *patients who have been seen significantly early or late for one or more of their post treatment visits*

Patient Selection and Exclusion Criteria

The same patient inclusion and exclusion criteria were used in all three clinical study protocols (except for three minor differences in the definitions in exclusion criteria 5, 8 and 14).

Inclusion Criteria:

1. Patients 45 years or older.
2. Symptomatic BPH.
3. I-PSS ≥13.
4. Prostate size: 30-100 g.
5. Q_{max} <13 ml/s on a voided volume >125 ml.
6. Informed consent.

Exclusion Criteria:

1. Medically and/or psychologically unable to tolerate procedures.
2. Previous microwave thermotherapy, TURP, laser prostatectomy or other surgical treatment of the prostate.
3. Previous pelvic irradiation or radical pelvic surgery.
4. History of urethral strictures, bladder neck contracture, or potentially confounding bladder pathology.
5. Evidence of prostatitis.
6. Prostatic Specific Antigen (PSA) >10 µg/l.
7. Evidence of prostate cancer or bladder cancer.
8. Evidence (as determined by cystoscopy) of median lobe.
9. Neurogenic bladder and/or sphincter abnormalities.
10. Symptomatic UTI at time of treatment.
11. Indwelling catheter or on self-catherization.
12. Concomitant medication with 5-alpha reductase inhibitors, alpha blockers, anticholinergics, androgens, and gonadotropin-releasing hormonal analogs within 6 weeks of treatment.
13. Residual urinary volume >300 ml.
14. Acontractile or hypocontractile detrusors.
15. Moderate to severe renal failure (defined as level twice the upper limit of the reference range for the serum creatinine (S-Cr) concentration).
16. Patients interested in future fertility.

Demographic Data and Baseline Characteristics

In terms of demographics, medical history, concurrent diseases and other baseline characteristics, both treatment groups (PLFT® treatment with either the PLS or the CoreTherm™ device and TURP) in Study A and Study B were considered to be comparable.

At baseline, mean patient age ranged from 65 to 69 years, mean IPSS from 19.2 to 21.9 and mean Q_{max} from 7.0 to 8.4 ml/s in the different study groups. Mean prostate volume in both Study A and Study B was somewhat smaller (48.9 and 51.9 ml, respectively) than that for the treatment group in Study C (58.3 ml). Mean detrusor pressure [P_{det} at Q_{max}] for PLFT® treatment group with the CoreTherm™ device was slightly higher for Study B (80.9 cmH_2O) as compared to Study A and, in particular, Study C (73.7 and 67.5 cmH_2O, respectively).

Table I Demographic data and baseline characteristics in Study A, B and C.

Variable (unit)	Mean				
	Study A		Study B		Study C
	PLFT® with PLS (n = 100)	TURP (n = 46)	PLFT® with CoreTherm™ (n = 42)	TURP (n = 19)	PLFT® with CoreTherm™ (n = 41)
Age (years)	67	69	67.5	67.7	65
Weight (kg)	83	81	80	82	80
Height (cm)	178	177	175	175	178
Prostate volume [by TRUS] (ml)	48.9	52.7	51.9	56.0	58.3
PSA (µg/l)	3.3	3.6	4.3	4.6	3.4
IPSS	21.0	20.4	20.0	19.2	21.9
Q_{max} (ml/s)	7.6	7.9	7.0	7.0	8.4
Detrusor pressure [P_{det} at Q_{max}] (cmH_2O)	73.7	79.4	80.9	79.8	67.5

Number of centers and study population

Ten centers, six in Sweden, two in Denmark and two in the USA participated in Study A. A total of 154 patients were randomized and 146 were treated. At 12 months, 133 patients had completed the study and 13 patients had been withdrawn (nine in the PLFT® treatment group with the PLS device and four in the TURP group).

One center in Switzerland participated in Study B. A total of 62 patients were randomized and 61 were treated. At 12 months, 55 patients had completed the study and six patients had been withdrawn (three in the PLFT® group with the CoreTherm™ device and three in the TURP group).

One center in the Netherlands participated in Study C. A total of 42 patients were enrolled and 41 were treated. At 12 months, 33 patients had completed the study and eight patients had been withdrawn.

Table II Centers and number of patients in study A, B and C

Country	Center no. & city	Patients enrolled/included:			
		Total	PLFT® with PLS	TURP	SF*
- Study A					
Sweden	01. Uppsala	33	21	11	1
	02. Hudiksvall	19	11	6	2
	03. Lund	18	11	6	1
	04. Ljungby	15	9	3	3
	05. Kristianstad	21	15	6	-
	06. Kalmar	25	17	8	-

Denmark	07. Frederiksberg	7	5	2	-
	08. Herlev	5	3	2	-
The USA	09. Scottsdale, AZ	3	3	-	-
	10. Toledo, OH	8	5	2	1
Total number of patients in Study A:		**154**	**100**	**46**	**8**
- Study B		**Total**	**PLFT® with CoreTherm™**	**TURP**	**SF***
Switzerland	13. Aarau	**62**	**42**	**19**	**1**
- Study C		**Total**	**PLFT® with CoreTherm™**	**na****	**SF***
The Netherlands	14. Nijmegen	**42**	**41**		**1**
Total number of patients:		**258**	**183**	**65**	**10**

**) Screening Failure not treated (i.e. withdrawn before treatment but after allocation of a randomization/patient number)*

***) There was no control group in Study C*

Study Period

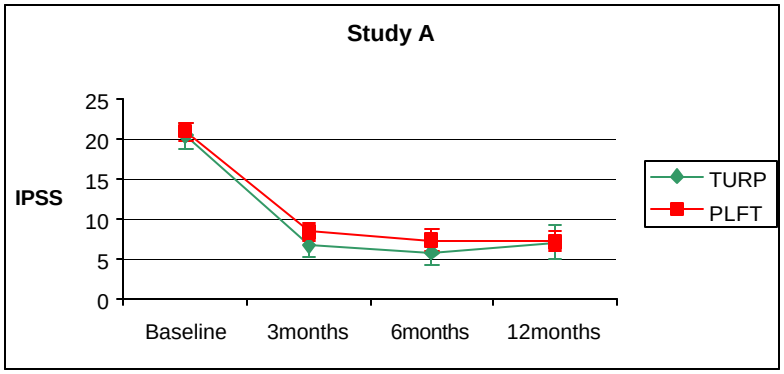
The three studies were conducted during the period October 1998 to October 2001. Study A will continue in a long-term follow-up study up to 5 years post treatment.

Data Analysis and Results

Study A

There was a marked post-treatment decrease in IPSS at the 3-month follow-up visit both in the PLFT® treatment group with the PLS device and TURP group (see graph below). The decrease in IPSS was maintained up to 12 months post-treatment for both groups.

Figure II



Mean IPSS values and 95% confidence intervals for PLFT® and TURP data in study A. The ITT analysis demonstrated the ratio of the PLFT® treatment with the PLS device to TURP for mean IPSS was 113.2% with a one-sided 95% confidence interval of 137.0%. The statistical target set

was = 125%. Results were similar when the baseline-adjusted IPSS were considered as well as the results for the PP analysis. Analysis of the percent responders are presented below for the ITT and PP data.

Table III Responders at 12 months follow-up - ITT analysis

Study	**Percentage of responders, LOCF (95% confidence interval)**		**Difference (PLFT® with PLS - TURP)**	**One-sided 95% confidence interval (CI) for difference**
	PLFT® with PLS (n=100)	**TURP (n=46)**		
Study A	82.0% (74.4% - 89.6%)	87.0% (77.0% - 97.0%)	-5.0%	CI: -15.4%

Table IV Responders at 12 months follow-up - PP analysis

Study	**Percentage of responders, LOCF (95% confidence interval)**		**Difference (PLFT® with PLS - TURP)**	**One-sided 95% confidence interval (CI) for difference**
	PLFT® with PLS (n=93)*	**TURP (n=42)***		
Study A	82.8% (75.0% - 90.6%)	88.1% (78.0% - 98.2%)	-5.3%	CI: -15.8%

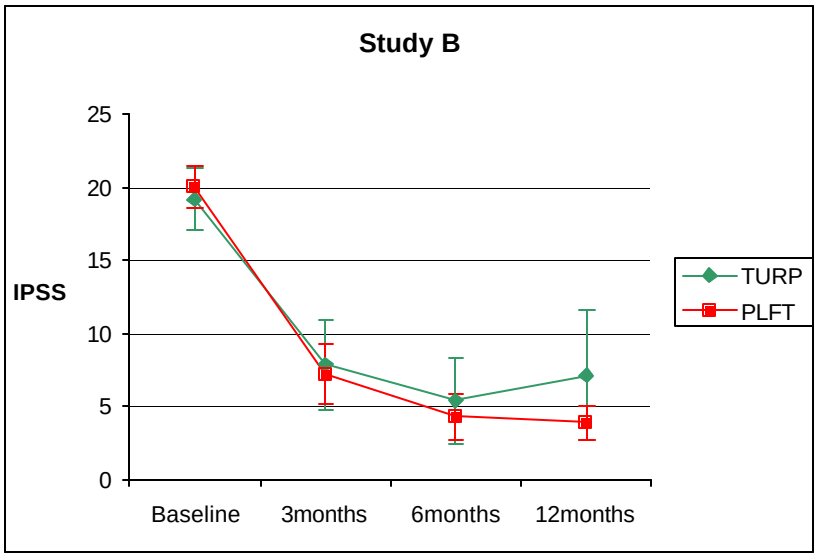
*One patient in each group with missing data (patients withdrawn due to adverse events) excluded from PP sample (PLFT®: patient withdrawn due to prostate cancer; TURP: patient expired)

Mean Q_{max} improved from a baseline value of 7.6 ml/s to 13.3 ml/s at 12 months for the PLFT® group. In comparison, mean value for the TURP group improved from 7.9 ml/s to 15.2 ml/s. The ITT analysis demonstrated the ratio PLFT to TURP for mean Q_{max} was 93.3% with a one-sided 95% confidence interval of 80.9%, which was within the statistical target of = 80%. For the baseline adjusted Q_{max} the ratio for PLFT® using the PLS device to TURP was similar (92.4%), but the one-sided confidence interval slightly lower than 80% (78.3%). Results of the PP analysis were in accordance with these data.

Study B

In accordance with results seen in study A, IPSS improved for both treatment groups post-treatment (see graph below). The decrease in IPSS was maintained up to 12 months post-treatment for both groups.

Figure III



Mean IPSS values and 95% confidence intervals for PLFT® and TURP data in study B. The ITT analysis demonstrated the ratio PLFT® to TURP for mean IPSS was 80.3% with a one-sided 95% confidence interval of 111.4%. The statistical target set was = 125%. Results were similar when the baseline-adjusted IPSS were considered as well as the results for the PP analysis. Analysis of the percent responders are presented below for the ITT and PP data.

Table V Responders at 12 months follow-up - ITT analysis

Study	**Percentage of responders, LOCF (95% confidence interval)**		**Difference (PLFT® with CoreTherm™ - TURP)**	**One-sided 95% confidence interval (CI) for difference**
	PLFT® with CoreTherm™ (n=42)	**TURP (n=19)**		
Study B	88.1% (78.0% - 98.2%)	79.0% (59.3% - 98.6%)	9.2%	CI: -8.6%

Table VI Responders at 12 months follow-up - PP analysis

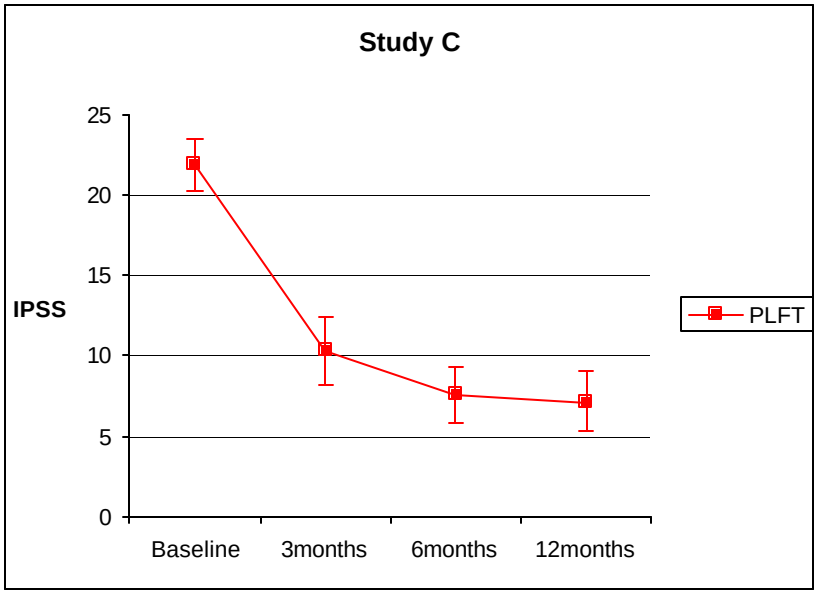
Study	**Percentage of responders, LOCF (95% confidence interval)**		**Difference (PLFT® withCoreTherm™ - TURP)**	**One-sided 95% confidence interval (CI) for difference**
	PLFT® with CoreTherm™ (n=40)	**TURP (n=17)**		
Study B	92.5% (84.1% - 100.9%)	82.4% (62.7% -102.0%)	10.2%	CI: -6.8%

Mean Q_{max} improved from a baseline value of 7.0 ml/s to 19.9 ml/s at 12 months for the PLFT® with CoreTherm™ device group. In comparison, mean value for the TURP group improved from 7.9 ml/s to 25.2 ml/s. The ITT analysis demonstrated the ratio PLFT® with CoreTherm™ device to TURP for mean Q_{max} was 69.9% with a one-sided 95% confidence interval of 54.6%, which was not within the statistical target of = 80%. Results for the baseline adjusted Q_{max} the ratio for PLFT® with CoreTherm™ device to TURP and the PP analysis were in accordance with these data.

Study C

In accordance with results seen in study A, IPSS improved post-treatment (see graph below). The decrease in IPSS was maintained up to 12 months post-treatment.

Figure IV



Mean IPSS values and 95% confidence intervals for PLFT® in study C.

Table VII Responders at 12 months follow-up - ITT analysis

Study	**Percentage of responders, LOCF (95% confidence interval)**	**One-sided lower 95% confidence interval**
	PLFT® with CoreTherm™ (n=41)	**PLFT® with CoreTherm™ (n=41)**
Study C	80.5% (68.0% - 93.0%)	70.1%

Table VIII Responders at 12 months follow-up - PP analysis

Study	**Percentage of responders, LOCF (95% confidence interval)**	**One-sided lower 95% confidence interval**
	PLFT® with CoreTherm™ (n=37)	**PLFT® with CoreTherm™ (n=37)**
Study C	86.5% (75.1% - 97.9%)	77.0%

Mean Q_{max} improved from a baseline value of 8.4 ml/s to 17.8 ml/s at 12 months for the patients in this study.

Summary Study A, B and C

IPSS

In all three studies and in each of the treatment groups, there was a decrease in IPSS at the 3-month follow-up. At 12 months post-treatment, mean scores of IPSS for the PLFT® group with either PLS or CoreTherm™ device in Study A, Study B and Study C had decreased significantly as compared to baseline (see graphs). This was also seen for the TURP group in Study A and Study B.

Responders to treatment

As can be seen in the tables, patients in the PLFT® group with either PLS or CoreTherm™ device had responder rates that were comparable to those in the TURP group. Data for PLFT patients in Study C were in agreement with results in Study A and Study B. There were no major differences seen between the PP and ITT sample of patients.

Responder rate and percentage of patients with 50% or greater improvement in IPSS, or IPSS and Q_{max}, at 12 months follow-up in the ITT sample are shown below.

Study	**Percentage and number (n) of responders, LOCF**	
Study A	**PLFT® with PLS N=100**	**TURP N=46**
Responders (overall definition)	82.0% (82/100)	87.0% (40/46)
50% or greater improvement from baseline in IPSS	71.0% (71/100)	71.7% (33/46)
50% or greater improvement from baseline in both IPSS and Q_{max}	34.0% (34/100)	39.1% (18/46)
Non responders*	18.0% (18/100)	13.0% (6/46)
Study B	**PLFT® with CoreTherm™ N=42**	**TURP N=19**
Responders (overall definition)	88.1% (37/42)	79.0% (15/19)
50% or greater improvement from baseline in IPSS	85.7% (36/42)	73.7% (14/19)
50% or greater improvement from baseline in both IPSS and Q_{max}	81.0% (34/42)	63.2% (12/19)
Non responders	11.9% (5/42)	21.1% (4/19)
Study C	**PLFT® with CoreTherm™ N=41**	**
Responders (overall definition)	80.5% (33/41)	-
50% or greater improvement from baseline in IPSS	65.9% (27/41)	-

50% or greater improvement from baseline in both IPSS and Q_{max}	51.2% (21/41)	-
Non responders*	19.5% (8/41)	-

* Non-responders included also a few patients with missing data for both IPSS and Q_{max}
** Study C had no control group

Other Secondary variables

Bother score
In accordance, the results of bother score indicated a pronounced improvement in all study treatment groups. From baseline to 12 months after treatment, mean bother score for the PLFT® group with either PLS or CoreTherm™ device in Study A, Study B and Study C decreased with 67, 78 and 68%, respectively (i.e. went from 4.3, 3.7 and 4.2 to 1.4, 0.8 and 1.4, respectively). For the TURP group in both Study A and Study B, the decrease in mean bother score was 64 and 65%, respectively (i.e. change from 4.2 and 3.7 to 1.5 and 1.3, respectively).

Detrusor pressure
Mean detrusor (voiding) pressure [at max urinary flow rate (P_{det} at Q_{max})] decreased from baseline to 12 months with 34 and 47% for the PLFT® group with the PLS device and TURP groups in Study A, respectively (i.e. decreased from 73.8 to 48.4 cmH_2O in the PLFT group and from 79.4 to 41.8 cmH_2O in the TURP group). In Study B the mean detrusor pressure decreased from baseline to 12 months from 80.9 to 46.7 cmH_2O in the PLFT group with CoreTherm™ device the and from 79.8 to 42.3 cmH_2O in the TUR-P group. In Study C the detrusor pressure decreased from 67.5 to 62.6 cmH_2O in the PLFT® group with CoreTherm™ device.

Prostate volume
Mean prostate volume as determined by TRUS for the PLFT® group treatment with either PLS or CoreTherm™ device in Study A, Study B and Study C was 48.9, 51.8 and 58.3 ml at baseline and 34.2 ml, 32.2 and 36.4 ml at 12 months, respectively. The corresponding relative changes were 30, 38 and 38%, respectively. For the TURP group in Study A and Study B, mean prostate volume as measured by TRUS decreased with 51 and 64%, respectively (i.e. went from 52.7 and 56.0 ml to 25.6 and 20.2 ml at 12 months, respectively).

Post-treatment indwelling catheter time
The mean post-treatment indwelling catheter time was 14, 20 and 18 days for the PLFT® group treatment with either PLS or CoreTherm™ device in Study A, Study B and Study C, respectively. For the TURP groups it was shorter i.e. 3.1 days in both Study A and Study B, as expected due to the two different types of intervention (coagulation vs. resection of prostate tissue).

Safety
A total of 183 patients in three studies were treated with PLFT® treatment with either PLS or CoreTherm™ device and evaluated in the clinical investigation. In all three studies the patients were treated once with PLFT® with either PLS or CoreTherm™ device: in Study A, 100 patients were treated; in Study B, 42 patients were treated; in Study C, 41 patients were treated. The vast majority of adverse events after PLFT® treatment with either PLS or CoreTherm™ device emanated from the urinary tract. In most cases, the events were of mild or moderate intensity. A single patient may report several different adverse events.

The treatments were performed with twelve (12) different ProstaLund® control units. No deaths were reported assessed by the investigator as probably or possibly related to PLFT® treatment with either PLS or CoreTherm™ device. No patient was discontinued from the study due to a device- related adverse event. Patients with symptoms of urinary tract infection recovered with antibiotics following treatment.

The following table identifies the adverse events reported in the three studies. The PLFT® treatment columns with either PLS or CoreTherm™ device represent pooled adverse event data from study A, B and C. The column for the TURP group presents pooled data from study A and B.

At Treatment	***Number PLFT® Treatment* with PLS or CoreTherm™**	***Rate PLFT® Treatment* with PLS or CoreTherm™**	***Number TURP***	***Rate TURP***
Urgency	19	10.4%	1	1.5%
Suprapubic and General Pain including Penile Pain	12	6.6%	0	0.0%
Bladder Spasm	7	3.8%	0	0.0%
Hypertension	4	2.2%	0	0.0%
Hypotension	4	2.2%	1	1.5%
Bleeding	2	1.1%	0	0.0%
Impotence*	1	0.5%	0	0.0%
Hematuria	1	0.5%	1	1.5%
Dysuria	1	0.5%	0	0.0%
Hemorrhage non-specific	0	0.0%	5	7.7%
Urinary Incontinence	0	0.0%	2	3.1%
Urinary Tract Infection	0	0.0%	1	1.5%
Post-operative hemorrhage	0	0.0%	1	1.5%
Neoplasm non-specific	0	0.0%	1	1.5%
Chest pain	0	0.0%	1	1.5%

Day 2-5	***Number PLFT® Treatment* with PLS or CoreTherm™**	***Rate PLFT® Treatment* with PLS or CoreTherm™**	***Number TURP***	***Rate TURP***
Bladder Spasm	10	5.5%	0	0.0%
Urgency	6	3.3%	2	3.1%
Urinary Retention	3	1.6%	4	6.2%
Dysuria	2	1.1%	0	0.0%
Hematuria	2	1.1%	1	1.5%
Suprapubic and General Pain including Penile Pain	2	1.1%	0	0.0%

Micturition Frequency	1	0.5%	0	0.0%
Bleeding	1	0.5%	0	0.0%
Epididymitis	1	0.5%	0	0.0%
Urinary Tract Infection	0	0.0%	4	6.2%
Urinary Incontinence	0	0.0%	3	4.6%
Post-operative hemorrhage	0	0.0%	1	1.5%
Neoplasm non-specific	0	0.0%	1	1.5%
Chest pain	0	0.0%	1	1.5%

Day 6 to 1 Month	***Number PLFT®* *Treatment* with PLS or CoreTherm™**	***Rate PLFT®* *Treatment* with PLS or CoreTherm™**	***Number TURP***	***Rate TURP***
Urgency	25	13.7%	3	4.8%
Urinary Retention	22	12.0%	4	6.3%
Bladder Spasm	17	9.3%	0	0.0%
Urinary Tract Infection	13	7.1%	5	7.9%
Dysuria	10	5.5%	0	0.0%
Hematuria	6	3.3%	5	7.9%
Micturition Frequency	3	1.6%	0	0.0%
Suprapubic and General Pain including Penile Pain	3	1.6%	0	0.0%
Epididymitis	2	1.1%	1	1.6%
Urinary incontinence	2	1.1%	3	4.8%
Post-operative hemorrhage	1	0.5%	4	6.3%
Neoplasm non-specific	1	0.5%	2	3.2%
Impotence*	2	1.1%	2	3.2%
Ejaculation disorder	0	0.0%	1	1.6%
Urethral stricture	1	0.5%	1	1.6%

Adverse Events at Treatment until 1 Month

All patients in the PLFT® treatment group with either the PLS or CoreTherm™ device were discharged with an indwelling catheter. The mean post-treatment indwelling catheter time was 14, 20, and 18 days for the PLFT® treatment group with either PLS or CoreTherm™ device in the A, B, and C studies, respectively. As seen in the table above, urgency and bladder spasm was the major adverse event seen during the time period. Suprapubic/general pain and penile pain were reported during treatment, but thereafter in a considerably lower frequency. A few cases of hypertension or hypotension occurred during treatment. Dysuria, hematuria, bleeding and micturition frequency were reported occasionally. During Day 6 to 1 month post treatment urinary retention and urinary tract infection were relatively common. There were two cases of epididymitis and urinary incontinence (1.1% of patients).

In the TURP group, i.e. the patients treated with TURP in the A and B studies, urinary incontinence and urinary tract infection were relatively common during the time period. At the day of treatment also hemorrhage non-specific was reported (7.7%). During Day 6 to 1 month hematuria (7.9%) and postoperative hemorrhage (6.3%) were the most common adverse events.

Urgency and urinary tract infection was reported for 24 patients (13.1%) in the PLFT® treatment group with either PLS or CoreTherm™. Bladder spasm and urinary retention were decreasing in

frequency compared to the previous time period and was reported for 9 patients (4.9%). Dysuria, 4.4%, hematuria, 2.2%, micturition1.6%, frequency, 1.1%, prostatitis, ejaculation disorder 1.1% (i.e., retrograde ejaculation) and impotence were reported occasionally and of patients, respectively). The same was true for epididymitis and urinary incontinence (2.2% and 1.6% of patients, respectively).

In the TURP group urinary incontinence (9.5%) and urinary tract infection (6.3%) were still rather common. Urgency was experienced by 7.9% of the patients, while impotence was reported by 4.3%.

Adverse Events After 3 Months Post-Treatment
There were 181 patients available for follow-up in the PLFT® treatment groups with either PLS or CoreTherm™ device during this time period. The tendency for urgency and urinary tract infection was lower as compared to the previous time period (7.7% and 6.6%, respectively). Bladder spasm and urinary retention were uncommon (2.2% of patients), as well as hematuria, micturition frequency, and prostatisis (1.7% of patients). There were a low number of patients with urinary incontinence (3.3%), urethral stricture (2.2%), and epididymitis (1.7%). Three cases of bladder calculus (1.7%) have been reported. Both impotence and ejaculation disorder were reported for 9 patients (4.9%). Ejaculation disorder (i.e., retrograde ejaculation) is anticipated to occur to a certain extent.

Urgency and urinary incontinence were still rather common and reported by 10.3% and 8.6% of the patients in the TURP group, respectively. The cases of impotence increased to 8.6% and ejaculation disorder were reported by 6.9%.

Duration of Adverse Events
Urgency, bladder spasm, and urinary tract infection had all a median duration of 11 days. Urinary retention was treated successfully, generally with placement of a catheter, and median duration of the event was one day. Suprapubic and general pain including penile pain had also a median duration of one day. Hematuria and bleeding had median duration of 1 and 3 days, respectively, and dysuria 19 days. Micturition frequency, prostatitis, urinary incontinence, urinary stricture, and epididymitis had intermediate duration, and were typically resolved within 22, 29, 99, 51, and 33 days, respectively (median values).

In comparison, urgency in the TURP group had a median duration of 73 days, urinary incontinence lasted typically 165 days and urinary tract infection 20 days. Hematuria, urinary retention, hemorrhage non-specific and post-operative hemorrhage were resolved within a few days: 3 days, 1.5, 1 and 1 day respectively.

At 12 months ongoing adverse events were as follows for the PLFT® treatment group with either PLS or CoreTherm™ device**.** There was one patient (0.5%) each with bladder spasm, hematuria, prostatitis, pain, or urinary tract infection, two patients (1.1%) with micturition frequency, urgency, or urethral stricture, and 3 patients (1.6%) with urinary incontinence. In addition there were 9 patients each with impotence and ejaculation disorder (4.9%) ongoing at 12 months.

Ongoing adverse events after 12 months are as follows in the TURP group. Impotence (8.6%), ejaculation disorder (6.9%), neoplasm non-specific and urgency (5.2%) were the most common

adverse events ongoing after 12 months. There was one patient (1.7%) each with PSA increase, urethral disorder, urethral stricture and urethral incontinence.

Serious Adverse Events

A serious adverse event was defined as any untoward medical occurrence that:
- resulted in death;
- was life-threatening;
- required in-patient hospitalization or prolongation of existing hospitalization;
- resulted in persistent or significant disability or incapacity;
- was cancer; or
- required intervention to prevent permanent damage to body function or structure,

PLFT® treatment with either PLS or CoreTherm™ device.-
The following table identifies all the Serious Adverse Events (SAE) reported for patients treated with PLFT® with either the PLS or device CoreTherm™ in Study A, Study B and Study C during the 12-month follow-up period (possibly/probably related or non-related to PLFT® treatment with the PLS or CoreTherm™ device).

Event	***Number***	***Rate***	***Causality***
Appendicitis	1	0.5%	Non-related
Back pain	1	0.5%	Non-related
Fever	1	0.5%	Related
Heart disorder	1	0.5%	Non-related
Dizziness	1	0.5%	Non-related
Vertigo	2	1.1%	1 Related
Faeces discoloured	1	0.5%	Non-related
Hemorrhoids thrombosed	1	0.5%	Related
Fibrillation atrial	1	0.5%	Non-related
Tachycardia ventricular	1	0.5%	Non-related
Spondylitis ankylosing	1	0.5%	Non-related
Angina pectoris	1	0.5%	Non-related
Angina pectoris aggravated	1	0.5%	Non-related
Myocardial infarction	3	1.6%	Non-related
Neoplasm malignant	1	0.5%	Non-related
Neoplasm non-specific	2	1.1%	Non-related
Epididymitis	1	0.5%	Related
Sepsis	1	0.5%	Related
Pneumonia	1	0.5%	Non-related
Post-operative hemorrhage	1	0.5%	Related

Event	*Number*	***Rate***	***Causality***
Spinal cord compression	1	0.5%	Non-related
Hematuria	2	1.1%	1 Related
Urethral disorder (perforation)	1	0.5%	Related
Urethral stricture	1	0.5%	Related
Urinary incontinence	1	0.5%	Related
Urinary retention	3	1.6%	2 Related
Cerebrovascular disorder	1	0.5%	Non-related

Hemorrhage intracranial	1	0.5%	Non-related

In total 41 SAEs were reported for the three studies. 6 of the events occurred during the screening period (i.e. pre-treatment).

In the Study A total of 21 SAEs were reported. Out of these 21 SAEs the investigator judged three to be probably or possibly related to the study treatment; hematuria, post-operative hemorrhage and urethral disorder (perforation).
The perforation occurred prior to treatment during the catheterization and no microwave treatment was performed.

In Study B a total of 13 SAEs were reported. Six out of these 13 SAEs were judged to be probably or possibly related to the study treatment; fever, urinary incontinence, hemorrhoids thrombosed, urethral stricture and two cases with urinary retention.

In Study C, a total of 7 SAEs were reported. Four out of these 7 SAEs were judged to be probably or possibly related to the study treatment; vertigo, sepsis, epididymitis and flare up of epididymitis.

In Study A, one patient had a myocardial infarction that resulted in death 12 month post treatment. The event was assessed as unlikely related to treatment.

No deaths were reported in the other studies.

TURP-group
The following table identifies all the Serious Adverse Events (SAE) reported for patients treated with TURP in Study A and B during the 12 month follow-up period (possibly/probably related or non-related to TURP).

Event	***Number***	***Rate***	***Causality***
Cardiac failure	1	1.5%	Non-related
Diverticulitis, colonic	1	1.5%	Non-related
Arrhythmia	1	1.5%	Non-related
Fibrillation atrial	1	1.5%	Non-related
Gout	1	1.5%	Related
Hypokalemia	1	1.5%	Non-related
Hyponatremia	1	1.5%	Non-related

Event	*Number*	***Rate***	***Causality***
Colon carcinoma	1	1.5%	Non-related
Neoplasm non-specific	2	3.1%	Non-related
Delirium	1	1.5%	Related
Anemia	1	1.5%	Non-related
Orchitis	1	1.5%	Related
Sepsis	1	1.5%	Related
Post-operative hemorrhage	2	3.1%	Related

Hematuria	3	4.6%	Related
Urethral stricture	1	1.5%	Related
Urinary tract infection	1	1.5%	Related
Cerebral hemorrhage	1	1.5%	Non-related
Transient ischemic attack	1	1.5%	Non-related

In total 24 SAEs were reported for the both studies. Three of the events occurred during the screening period (i.e., pre-treatment).

In Study A total of 19 SAEs were reported. Nine out of these 19 SAEs were judged to be probably or possibly related to the study treatment: gout, delirium, sepsis, post-operative hemorrhage (2), hematuria (3) and urinary tract infection.

In Study A, two deaths were reported in the TURP group. One patient had a myocardial infarction that resulted in death. The event was assessed as unlikely related to treatment. The other patient died due to a combination of acute myocardial infarction, congestive heart failure and arrhythmia. The event was assessed by the Investigator as possibly related to the treatment.

In the Study B a total of five SAEs were reported. Out of these five SAEs the investigator judged two to be probably or possibly related to the study treatment; orchitis and urethral stricture.

No deaths were reported in Study B.

Clinical Laboratory Data
There were no clinically significant changes in the laboratory variables. In all three studies, the laboratory variables; hemoglobin (Hb), serum creatinine (S-Cr) or Prostate Specific Antigen (PSA) did not show any clinically significant changes from baseline to follow-up. There were no laboratory adverse events, as related to the reference ranges of each of the local laboratories. The PSA level increased at the 6 month period for one patient in the PLFT group in Study B. While the 12 month control the level had decreased it was still above reference range.

Device Failures and Replacements

Study A
No device or accessory failure, or device replacement, was reported during the study.

Study B and Study C
No device failure or device replacement was experienced during the studies. Five accessory failures were reported in Study B and three in Study C. In all cases necessary actions were taken by the investigator. The failures were all regarded as harmless to the patients and of no or minor influence to the treatment outcome. The components were replaced by ProstaLund®.

XI. CONCLUSIONS DRAWN FROM STUDIES

The laboratory, animal and clinical data provide reasonable assurance of the safety and effectiveness of the ProstaLund® CoreTherm™ device for the treatment of symptomatic BPH, when used as indicated.

The clinical data from patients treated with either the PLS or CoreTherm™ demonstrate that the treatment provides patient benefit with low morbidity. The effectiveness results, one year after treatment, demonstrates the durability of treatment response.

Adverse events were generally transitory, resolving within one month after treatment. Adverse events that persisted beyond 12 months after treatment include bladder spasm, hematuria, Prostatitis, pain, urinary tract infection, urethral strictures, urinary incontinence, frequency, and urgency.

XII. PANEL RECOMMENDATIONS

Pursuant to section 515(c)(2) of the Food, Drug, and Cosmetic Act (the act) as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Gastroenterology and Urology Devices Panel, an FDA advisory panel, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH DECISION

Based on the data contained in the PMA, CDRH has determined that the CoreTherm™ is reasonably safe and effective for the indication to relieve symptoms associated with symptomatic BPH in men with a urethra length of = 35 mm and a total prostate size between 30 and 100 g. Furthermore, the applicant agreed to the post-approval requirement that they collect data on the long-term (5-year) effects of the device.

The applicant's manufacturing facility was inspected and determined to be in compliance with the Quality Systems Regulation. CDRH issued an approval order on December 23, 2002.

XIV. APPROVAL SPECIFICATIONS

Directions for Use: See the labeling.

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

Postapproval Requirements and Restrictions: See approval order.