

# LABELING

## **Section X. Device Labeling**

### **Part 3: Patient Labeling**

# Prolieve™

## A Transurethral Microwave Therapy Device Patient Information

Version 2.0



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The **Prolieve™** Patient information is *directed to you, the patient.*

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## Glossary

<b>BPH</b>	Benign prostatic hyperplasia
<b>Benign prostatic hyperplasia</b>	Enlargement of the prostate with no cancer
<b>Bladder spasm</b>	Involuntary contraction of muscles affecting the bladder wall
<b>Catheter</b>	A flexible tube for withdrawing fluids from (or introducing fluids into) a cavity of the body, especially one for inserting into the bladder, through the urethra, to remove urine
<b>Cystourethroscopy</b>	A procedure used to look at the inside of the bladder and urethra. A flexible tube with a small camera attached is inserted through the urethra and into the bladder
<b>Erectile dysfunction</b>	Unable to have or maintain an erection of the penis
<b>Intermittent Claudication</b>	Limping or lameness in your legs
<b>Invasive</b>	A puncture or incision of the skin or insertion of an instrument or foreign material into the body
<b>Leriches Syndrome</b>	A syndrome caused by blocking of the abdominal aorta. It usually occurs in men and is characterized by fatigue in the hips, thighs, or calves during exercise; no pulse in the femoral arteries; impotence; and pale, cold legs
<b>Parameter</b>	A variable whose measure is indicative of a quantity or function that cannot itself be precisely determined by direct methods, for example, blood pressure and pulse rate are parameters of heart function
<b>Prolieve™</b>	A Transurethral Microwave Therapy Device
<b>Prostatitis</b>	Inflammation of the tissue of the prostate
<b>Rectal Temperature Monitor</b>	A device inserted into the rectum to measure the temperature of the rectal tissue near the prostate gland
<b>Retrograde ejaculation</b>	Ejaculation backwards into the bladder instead of forward through the urethra
<b>The device</b>	Prolieve™
<b>Transurethral</b>	To the urethral tube through the penis
<b>Ultrasound</b>	A technique in which high-frequency sound waves are bounced off internal organs and the echo pattern is converted into a 2 dimensional picture of the structures beneath the transducer
<b>Urethra</b>	The tube through which urine is passed from the bladder. The length of the urethra is about 25 centimeters in men
<b>Urinary incontinence</b>	The involuntary discharge of urine
<b>Urinary retention</b>	Unable to empty the bladder
<b>Urinary sphincter</b>	A muscle that is normally tight, but when relaxed, allows urine to flow from the bladder
<b>Uroflowmetry</b>	A procedure used to measure the rate of urine flow

## What is the Prostate?

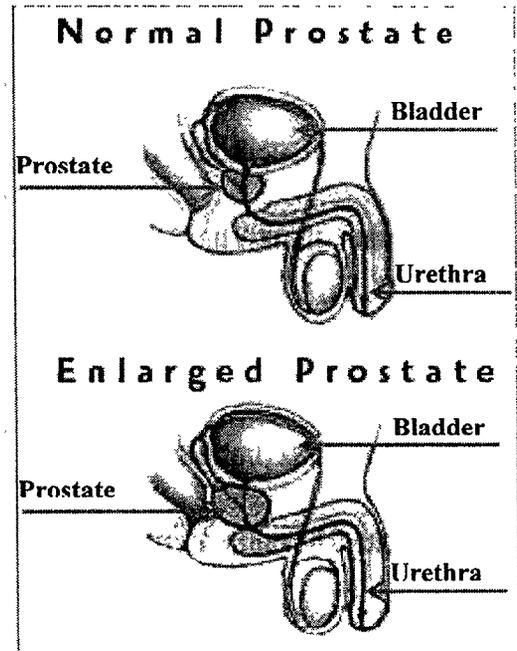
It is a walnut-sized gland in men that surrounds the neck of the bladder where it joins the **urethra**. The prostate gland produces a fluid that is part of semen.

## Why am I being treated with the Prolieve™ System?

Your physician has determined that you are suffering from symptomatic **benign prostatic hyperplasia (BPH)**. This means that your prostate has become enlarged (see images below). **BPH** is not life threatening and it is not a type of cancer, but you may have found it to be embarrassing and inconvenient. You are not alone. **BPH** is common in men 50 years of age and older. The symptoms are:

- ⇒ Feeling a repeated and instant need to urinate.
- ⇒ Interrupting your sleep to urinate.
- ⇒ Waiting for urine to start flowing.
- ⇒ Having a weak, variable or dribbling stream of urine.
- ⇒ Feeling pain or burning when urinating.
- ⇒ Feeling that your bladder does not empty.

The **Prolieve™** System has been successful in treating patients with **BPH** symptoms. The following information has been written *especially for you*. Please read it and ask your physician if you have any additional questions.



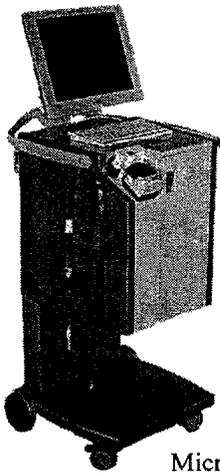
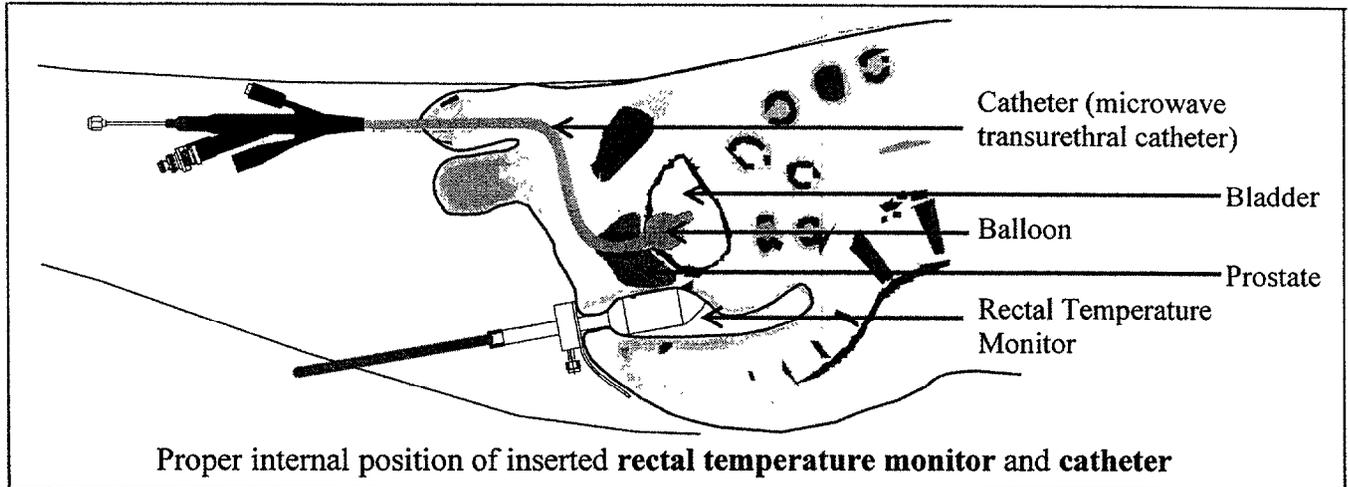
### Purpose of the device (indications for use)

**Prolieve™** is a medical **device** that is used to destroy part of the prostate to treat symptomatic **BPH** in men with an enlarged prostate who would benefit from drug or surgical therapy.

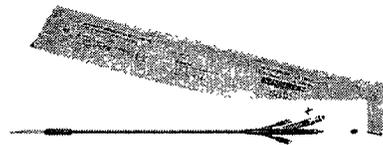
### Description of the device

The **device** is made up of a microwave, computer and a single-use Prolieve™ Procedure Kit. The **device** delivers microwave energy (heat) to the prostate for the treatment of symptomatic **BPH**. The **device** uses a microwave antenna that is inside a **catheter**, which is placed inside the **urethra** to heat the prostate. At the same time, a balloon on the **catheter** inflates and pushes against the wall of the **urethra** to help in the heating process. A heat-exchanger cartridge is responsible for warming the fluid that circulates through the balloon **catheter**. A **rectal temperature monitor** is placed in the rectum near the prostate to monitor temperature. The heating process is controlled by a computer in the machine that reads the temperature measured by the **rectal temperature monitor**.

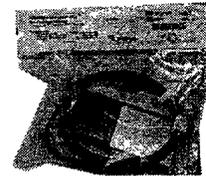
The heat from the microwave may get high enough to cause tissue damage inside the **prostate**. The tissue that gets damaged will, over time, get reabsorbed by the **prostate** and will relieve the pressure to your prostate which maybe the cause of your symptoms. The water is used to inflate the balloon, which may open the blockage and reduce symptoms.



Microwave, computer, and rectal temperature monitor

Sterile microwave  
transurethral catheter

500 mL sterile water

Heat exchanger  
cartridge system

## How does the device work?

Patient information is entered by a physician into the computer system of the **device**. A sterile microwave **transurethral catheter**, a heat exchanger cartridge system, and a 500 mL bag are hooked to the instrument console. The physician will insert the flexible **catheter** into the **urethra** of the patient. When the microwave energy is turned on, it will be transmitted from a special antenna inside the **catheter** to provide continuous heat to the patient's **prostate**. The heat will reduce the enlarged tissue of the **prostate**. A small balloon that is also part of the **catheter** will inflate within the section of **urethra** close to where the **prostate** is located. The inflated balloon will cause the tissue to expand, which may cause some discomfort to the patient. During the entire 45-minute procedure, warm water will be circulating inside the **catheter** to protect the **urethra** from the heat generated by the microwave energy. For the safety of the patient, the instrument console monitors the temperature surrounding the treatment area by means of a **rectal temperature monitor**. If the patient's rectal temperature reaches 42°C, the system will shut off automatically.

The **Prolieve™** System has been through testing and has been found to comply with all the required conformance standards regarding manufacturing. Moreover, the system design and operating protocol have been investigated in clinical studies of other men suffering from **BPH**. The results show that the **device** is safe and effective and it has obtained approval from the FDA.

## What are the alternative treatments for **BPH**?

You should discuss these with your doctor.

- Watchful waiting
- Drug therapy
- Surgery
- Other microwave therapies

The microwave therapy takes 45 minutes, but your physician will need additional time to get you prepared for the procedure. Please allow at least 2 hours for the entire treatment visit.

## When should the **device** not be used (contraindications)?

Please inform your physician if:

- You are *not able to feel pain*. Microwave treatment is not indicated in patients whose response to pain has been reduced. This reduced pain response may result from surgery, regional or local anesthetic, or other relevant condition that is determined by the physician upon evaluation).
- A **catheter** cannot be passed through your **urethra**.
- You have a urinary infection.
- You have a prostate infection.
- You have undergone a penile or **urinary sphincter** implants.
- You have clogging of the arteries with **intermittent claudication** or **Leriches Syndrome**.
- You had your prostate removed.
- You have been cancer of the prostate or the bladder.
- You have metallic hip or leg implants.
- You have an implanted cardiac pacemaker, or defibrillator.
- You are interested in having children.
- You have had any history of pelvic radiation.
- You have an abnormality of your blood that prevents it from clotting.
- You have any kidney disease.
- You cannot urinate without help of some kind.
- You have stones in your bladder.

## General warnings and precautions

It is very important that you are awake during this procedure. Your doctor will rely on your sensations of pain or heat as a guide during treatment.

## What to expect during treatment?

First, the physician will evaluate you to see if you are a candidate for this therapy. The following is a list of tests your physician may order: urine analysis, urine culture, blood tests, **uroflowmetry, ultrasound, and cystourethroscopy**. Your physician will choose which tests you may have.

Then, on the day that the two of you choose, you will come to the treatment center. You should bring a partner to drive you home since this is an outpatient procedure.

You may be given an antibiotic by your physician, but it will be up to your physician to make that decision.

On the day of treatment, you will remain in a comfortable position on the treatment bed. You may be able to listen to music or read a book while the treatment is being done.

When the small balloon is inflated, you may feel a slight pain or discomfort. This is normal. It is possible also that during treatment you may experience some discomfort such as **bladder spasms**, bleeding, feeling the need to empty your bladder or have a bowel movement. You will also feel a warming sensation as the temperature increases during treatment. This is also normal. Keep in mind that there is water circulating through the **catheter** to keep your **urethral** channel warm, but not hot.

If you experience severe pain, please inform your physician right away.

Each physician's office and hospital outpatient department is different. Therefore, treatment procedures may vary a bit. In general, here is what you can expect:

1. At least one hour before treatment, your physician may give you medication to help you keep calm during the procedure. Other medications that your physician may give you are to help avoid infections.
2. You will be asked to empty your bladder.
3. You will be asked to lie on your back on the treatment table. The physician will then apply anesthesia to the tip of your penis. This will help you to not feel pain while he/she inserts the **catheter** through the **urethra** of the penis.
4. To keep you warm and comfortable, you will remain covered throughout the procedure.
4. Your physician will enter your personal information into the system and will scan the bar codes from the procedure kit.
5. As your physician proceeds with each step, he/she may continue to prepare the system for your treatment.
6. Before your physician inserts the **catheter**, he/she will use a large syringe, without a needle, to apply KY Jelly lubrication directly into the **urethra**.
7. Your physician will then insert the **catheter** through the **urethra** into the bladder. This is the same as inserting a regular **catheter**.

8. Your physician will double check that the **catheter** is in place. The physician may do this by using **ultrasound**. When the **catheter** is in place, your physician will secure it so that it does not move.
9. Next your physician will prepare the **rectal temperature monitor** for insertion.
  - a. Your physician will place a sterile cover on the **rectal temperature monitor**.
  - b. Your physician will lubricate the surface of the cover on the **rectal temperature monitor** with KY Jelly.
10. Your physician will then insert the rectal monitor and secure it so that it does not shift position. During the treatment, the rectal monitor will be checked frequently to ensure proper positioning.

Treatment will then be initiated. It will last approximately 45 minutes. Your physician will continue to monitor you at all times.

### What to expect following treatment?

You will be able to go home right after treatment. You should have someone drive you home after the procedure.

There is a chance that your physician will send you home with a **catheter**. Sixteen percent (16%) of patients that were involved in previous clinical studies were catheterized after treatment. Do not worry; the **catheter** will let the urine drain from your bladder while the swelling, if any, goes down. In most cases the **catheter** will need to remain for three days or less. Please remember it may be different in your situation and that your physician knows best. Please follow his/her instructions carefully.

Some patients have experienced side effects following treatment. The most common side effects are:

- Bladders spasm
- Pain
- Soreness
- Blood in the urine

These side effects cleared within a few days. Other side effects reported were frequency, urgency and **urinary retention**. These were most likely symptoms of **BPH** and not caused by the treatment.

Remember *you are unique* and you may experience other symptoms. Please notify your physician if you experience **bladder spasms**, pain, soreness, or blood in your urine or if you have any other concerns about how you are feeling.

As with any **transurethral** microwave therapy procedure, there are rare cases of serious side effects. Please consult with your physician.

## Risks of the Prolieve™ System

There have been serious, but rare, side effects with **transurethral** microwave therapy **device** treatments. However, none of these have been experienced by any of the patients treated with the **Prolieve™** System. Please consult with your physician.

During the clinical study of the **Prolieve™** System, the following events were directly attributed to the procedure: **bladder spasms**, **urethral irritations**, and complete **urinary retention** (requiring catheterization). Other side effects reported were those associated with **BPH**. The majority of the side effects resolved within 2 weeks to 1 month and required little or no medication.

## Benefits of the Prolieve™ System

- The side effects reported have been few.
- It is a single 45-minute treatment that is performed at your physician's office or at a local hospital in the outpatient department.
- It eliminates the need for multiple-office visits for **BPH** medications and the related costs and inconvenience.
- Quality of life has been shown to improve.
- It is not a surgical procedure.

## Disadvantages of the Prolieve™ System

- Unlike medication, treatments with the **Prolieve™** System are performed at a physician's office or at a local hospital in the outpatient unit.
- The patient must be a good candidate for the treatment.
- The procedure requires some exposure and may be a bit embarrassing and or uncomfortable.
- There are side effects including: anal irritation, **bladder spasms**, bleeding (mild to excessive), bowel irritation, chronic pain at the site, complete **urinary retention**, incomplete **urinary retention**, **erectile dysfunction**, pressure sensation (minimal), **prostatitis**, **retrograde ejaculation**, **urethral injury** (irritation), urinary clot retention, **urinary incontinence**, urinary tract infection, urinary urgency.

## Importance of keeping up with your regimen of care

For your safety and prompt recuperation, it is important that you follow your physician's instructions. Go to all of your follow-up visits. Do not be embarrassed to ask questions. Communicate with your physician and discuss your concerns.

**Date of print:** February 2004.

## **Section X. Device Labeling**

### **Part 1: Essential Prescribing Information (EPI)**

February 12, 2004

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# Prolieve™ System

## A Transurethral Microwave Therapy Device

### Essential Prescribing Information

Version 1.0

**CELSION™**

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**CAUTION: Federal Law restricts this device to sale and use by or on the order of a physician (or properly licensed practitioner).**

The Prolieve™ Thermodilatation System (Prolieve™) Essential Prescribing Information (EPI) is directed to the prescribing physician. For details concerning the operation of the device, please see the User Manual for Prolieve™.

### DEVICE DESCRIPTION

Prolieve™ is a transurethral microwave therapy device equipped with automated controls designed to deliver microwave energy to the prostate and balloon-administered compression (thermodilatation) for the treatment of symptomatic benign prostatic hyperplasia (BPH). This device utilizes a transurethral microwave antenna to heat the prostate to a temperature between 41°C and 46°C, with simultaneous 46 Fr. prostatic urethral catheter balloon-administered compression over a treatment length of 1.2 to 5.5cm. Warm water is circulated through the transurethral catheter system and compression balloon to protect the wall of the urethra. The microwave heating process is regulated through temperature feedback from three sensors mounted on the surface of a rectal temperature monitor (temperature monitor). The temperature monitor is placed against the rectal mucosa adjacent to the prostatic capsule. A treatment consists of applying microwave energy at 915 MHz  $\pm$  5 MHz (50 Watts maximum) to the prostate for 45 minutes reaching an intraprostatic temperature of 41°C to 46°C, at a rectal control temperature up to 41°C and a maximum rectal temperature of 42°C.

The device consists of a permanent instrument and a single-use Prolieve™ Procedure Kit (Procedure Kit). The permanent instrument generates the microwave power, provides temperature-controlled water circulation, monitors treatment parameters with built in safety alerts, and records treatment data. A monitor screen with graphic user interface (GUI) provides a visual display. The permanent instrument is configured as a single integrated cart unit, which provides computer control, microwave power and temperature measuring capabilities, constant temperature thermoelectric plates, circulatory fluid pump, and rectal temperature monitor. The thermoelectric plates are coupled to the heat exchanger

cartridge, which is part of the Procedure Kit. In this way, the device can maintain the circulating water at a temperature of  $34.5^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$  at the point of entry into the transurethral catheter system.

The single-use Procedure Kit contains a single sterile 18 Fr diameter 36 cm long microwave transurethral catheter, a heat exchanger cartridge system, and a 500 mL bag of sterile water. The transurethral catheter includes a 5cc retention balloon as well as a 3.7 cm long compression balloon for dilatation that reaches 46 Fr diameter when inflated. The microwave antenna consists of a coaxial cable; the active portion is positioned towards the distal end of the compression balloon.

## INDICATIONS FOR USE

Prolieve™ is a transurethral microwave therapy device that provides a non-surgical, minimally invasive procedure for the treatment of symptomatic Benign Prostatic Hyperplasia (BPH) in men with a prostate size of 20 to 80 grams, a prostatic urethra length between 1.2 cm and 5.5 cm and in whom drug therapy (e.g., Finasteride (Proscar®)) is typically indicated.

## CONTRAINDICATIONS

The contraindications for Prolieve™ are:

- Patients whose pain response has been significantly decreased by any means (previous surgery, regional or local anesthetic, or other relevant condition which is determined by the physician upon evaluation) because the patients' ability to detect pain is a treatment safety mechanism.
- Severe urethral stricture preventing catheterization.
- Current urinary or prostatic infection.
- Presence of a penile or urinary sphincter implant.
- Prostate size <20g or >80g.
- Peripheral arterial disease with intermittent claudication or Leriche's Syndrome (i.e., claudication of the buttocks or perineum).
- Protruding median lobe resulting in a "ball-valve" type of obstruction at the bladder neck.
- Evidence of prostatic cancer or bladder cancer.
- Presence of metallic implants, e.g. pelvic, femur, penile prosthesis, etc.
- Presence of implanted cardiac pacemakers, or defibrillators.
- Previous transurethral prostatectomy.
- Patients interested in the preservation of future fertility.
- Patients with a previous history of pelvic radiation.
- Patients with coagulation disorders.
- Patients with renal impairment.
- Patients with neurological disorders that might affect bladder function.
- Patients with bladder stones and large post voiding residual (greater than 250 mL).

## WARNINGS

The following is a list of warnings for the safe and effective use of Prolieve™

### Warning – Patient Safety

**Warning:** The physician must monitor patient condition during the treatment. Patient comments regarding pain or excess heat in regions not associated with the expected treatment location should be fully investigated. Failure to monitor adequately and deliver the procedure per recommendations of the labeling may lead to serious patient injury.

**Warning:** There are unlikely but serious thermal (heat-related) injuries that may occur which include fistula formation and tissue damage to the penis or urethra requiring urostomies, partial amputation of the penis, and/or other therapeutic interventions, and narrowing of the penile urinary tube at any time after the treatment.

**Warning:** The physician must ensure the careful and correct placement of the catheter and temperature monitor as shown in the User Manual before heating commences. The recommended procedures for catheter and temperature monitor placement will minimize the probability of excessive temperature in normal tissue and non-therapeutic temperature in the treated area.

**Warning:** The physician must adhere to the recommended applicator placement and sterile field preparation to reduce the likelihood of surface burns and blistering from the subsequent delivery of therapeutic heat.

**Warning:** The emission of microwave energy must be off during placement and removal of the catheter to avoid stray microwave radiation directed towards the eyes (or testes) of the patient or the operator.

**Warning:** A single high dose of microwave radiation to the testes, or testicular heating for a prolonged period, may result in temporary or permanent sterility. Elevated temperatures may be expected to affect the pharmacological activity of some drugs, with unpredictable results. Altered vascular perfusion may dramatically affect the local tissue effects of systemic or infused drugs

## PRECAUTIONS

### Treatment Related

**Caution** - The safety and effectiveness of Prolieve™ for men <50 and >80 years old has not been established in clinical studies.

**Caution** - The use of Prolieve™ must be prescribed and administered under the direct supervision of a qualified and trained physician following appropriate urological evaluation of the patient.

**Caution** - No anesthetic other than aqueous-based topical intraurethral anesthetic used for catheter placement is recommended.

**Caution** – The user must comply with strict adherence to aseptic techniques during the placement of applicators to avoid localized infections. If the Procedure Kit seal or internal sterile packaging seals are damaged or broken, the contents may not be sterile and could cause infection. Damaged or broken seal devices should be discarded or returned.

**Caution** - Treatment with Prolieve™ applies compression and deposits microwave energy, which converts to heat within the patient's prostate and in the immediately adjacent tissue. Some animal studies in the literature suggest there may be unknown health effects from exposure to microwave radiation, including an increased incidence of tumors. Although it is not possible to extrapolate these studies to humans, they suggest that unnecessary microwave radiation exposure should be avoided.

### Device Related

**Caution** – Failure to use all the components of Prolieve™ with temperature sensors in accordance with the User Manual may result in insufficient therapy and/or increased risk of injury or infection to the patient.

**Caution** - Any nearby equipment operating on a similar frequency to that of Prolieve™ should be operated at a distance of at least 2 meters (6.5 ft.) (including locations behind adjacent walls) to avoid device-to-device interference. Such devices include but are not limited to cell phones and/or other sensitive treatment and monitoring equipment, e.g., drug infusion devices, physiological monitoring devices.

**Caution** – Prolieve™ is designed to operate in a room with adequate space for the patient, treatment bed, permanent instrument, with adequate lighting, and clinical personnel. The treatment room should also be clean and support the needs of the physician to treat in a sterile field. Failure to provide these may have a deleterious effect on the patient and or treatment result.

**Caution** - Any modifications made to equipment or software without explicit approval from the manufacturer poses a potential safety threat to the operators and patients. Only qualified, trained personnel should be allowed to operate the equipment. Please consult the User Manual for specific technical warnings and precautions on device operation.

### Operator Related

**Caution** - Equipment covers must never be removed with primary power connected to the equipment due to a risk of electrical shock.

### POTENTIAL ADVERSE EVENTS

Microwave heating devices and dilatation have the potential for producing adverse events as a result of the delivery of therapeutic heat, or of the exposure to electromagnetic radiation. Those adverse events

not seen in the clinical trials include: urethral stricture, pelvic abscess, allergic reaction including anaphylaxis, bladder neck contracture, urethral tear, rectal wall injury, infertility, and fistula.

### ADVERSE EVENTS

The adverse events that were directly attributed to the procedure were urethral irritation, bladder spasms and complete urinary retention resolving by the 2-week visit.

A summary of the adverse events at treatment and during the follow-up evaluation of 1-year is presented in Table 1. The patients included in the Reported at Treatment column are the 125 randomized to Prolieve™ plus the 20 patients who crossed over from the Proscar® treatment arm. There were five patients in whom the treatment was cancelled and they are not included in the 140 patients followed in the post-treatment period for safety.

Adverse events experienced by the Proscar® patients were not recorded other than those events associated and similar to the Prolieve™ patients and are therefore not reported.

**Table 1: Number and Rate of Adverse Events Reported During the Pivotal Investigation**

Symptom	Reported at Treatment (N=145)	Reported During Post-Treatment (N=140)*				
		2-Week (N=131)	1-M (N=131)	3-M (N=129)	6-M (N=121)	12+M (N=103)
Anal irritation	1 (0.7%)					
Bladder spasm	17 (12%)	3 (2.3)		1 (0.8 %)	1 (0.8 %)	
Bleeding (mild to excessive)	5 (3.4%)					
Bowel irritation	1 (0.7%)					
Chronic pain at site		2 (1.5 %)	1 (0.8 %)	1 (0.8 %)	1 (0.8 %)	
Complete urinary retention	22 (15.2 %)	6 (4.6 %)				
Incomplete urinary retention		7 (5.3 %)	9 (6.9 %)	5 (3.9 %)	3 (2.5 %)	4 (3.9 %)
Erectile Dysfunction		1 (0.8 %)	2 (1.5 %)	1 (0.8 %)	1 (0.8 %)	1 (0.8 %)
Pressure sensation (minimal)	1 (0.7%)					
Prostatitis		1 (0.8 %)		1 (0.8 %)	1 (0.8 %)	1 (1.0 %)
Retrograde ejaculation					1 (0.8 %)	
Urethral injury (irritation)	2 (1.4%)	2 (1.5 %)				
Urinary clot retention			1 (0.8 %)			
Urinary incontinence		2 (1.5 %)	1 (0.8 %)	1 (0.8 %)	1 (0.8 %)	1 (1.0 %)
Urinary tract infection		1 (0.8 %)			1 (0.8 %)	1 (1.0 %)
Urinary urgency	3 (2.1%)					
Total	52 (35.9 %)	25 (19.1 %)	14 (10.7 %)	10 (7.8 %)	10 (8.3 %)	8 (7.8 %)

\*Does not include the 5 patients in whom treatment was cancelled.

Catheterizations associated with treatment: Sixteen percent (22/140) of the patients was catheterized post treatment. Sixty-four percent (14/22) of these catheterizations were for three days or less. All but one patient were catheterized for less than one week. There were 3 patients

who were catheterized for reasons other than urinary retention. One patient experienced bladder spasms requiring catheterization and a second patient had the catheter replaced during treatment due to a leak. The third patient had a false passage, Prolieve™ treatment was not initiated and the patient was catheterized for 3 days.

## SUMMARY OF CLINICAL STUDY

### Study Design

This multi-center, randomized, open-label trial compared a single outpatient treatment of symptomatic BPH with Prolieve™ lasting 45 minutes to that of a daily regimen of 5mg Proscar® (Finasteride). 166 patients were randomized at 14 centers in a 3:1 ratio of Prolieve™ to Proscar®. At the completion of the 6-month evaluation, patients randomized to Proscar® who had failed treatment and met the inclusion criteria, were permitted to crossover to receive treatment with Prolieve™.

The treatment consisted of applying microwave energy at 915 MHz  $\pm$  5 MHz (50Watts maximum) to the prostate for 45 minutes at a rectal control temperature up to 41°C and a maximum rectal temperature of 42°C; the automatic treatment abort temperature of the device. Effectiveness and safety were assessed during treatment and at post-treatment follow-up visits at 2 weeks, 1, 2, 3, 6, and 12 months.

### Patient Assessment

*Effectiveness:* The primary objective of the study was to assess whether treatment with Prolieve™ would demonstrate clinical equivalency to treatment with Proscar®. Clinical equivalency was defined as having no less than 80% of the effectiveness of Proscar®. The primary endpoint of the study was the change in AUA Symptom Index score from baseline to 6 months. The response to treatment in the Prolieve™ treatment was evaluated out to 12 months post-treatment or longer for durability. The secondary effectiveness outcome measures included peak flow rate (PFR), post void residual (PVR) as well as evaluation of the following:

- The International Index of Erectile Function (IIEF-5): This section consists of questions asking the patient about their erectile function.
- Quality of Life (QOL): Six questions focused on the patient's feelings about his urinary condition, perception of urinary difficulties, sexual functions, activities of daily living, general well-being and social activities.
- Impact of Lower Urinary Tract Symptoms (LUTS) on Quality of Life: Six questions related to the patient's urinary problems and if these problems interfered with the patient's life.
- BPH Impact Index (BII): Four questions related to the patient's concern over his urinary problems and the amount of physical discomfort experienced.
- BPH Specific Interference with Activities (BSI): Seven questions related to the degree to which the patient's urinary problems interfered with some common activities.
- Sexual Function: Six questions pertaining to the patient's sexual function.
- Pain or discomfort: Four questions related to the presence, location, frequency and severity of pain or discomfort in the urethra.

*Safety:* The objective was to substantiate the safety profile of Prolieve™. Safety was assessed by the frequency of local and systemic side effects during treatment, and the occurrence of anticipated and unanticipated adverse effects during follow-up.

### **Accountability**

A total of 190 patients were randomized in the study, 142 to Prolieve™ and 48 to Proscar®. Before the initiation of treatment, 24 patients chose to withdraw from the study prior to any attempt at treatment (17 Prolieve™ / 7 Proscar®). Therefore, while still maintaining the 3:1 ratio, a total of 125 patients in the Prolieve™ arm and 41 patients in the Proscar® arm were included in the statistical analysis and comprise the intent-to-treat population (Table 2). At the time the database was closed for analysis 92/125 (74%) of the patients in the treatment arm completed their 12-month follow-up. There were 20 patients treated with Prolieve™ following their participation in the pivotal trial in the Proscar® arm. The information for these 20 patients is included in the safety summary with the 125 patients originally randomized to Prolieve™. Five of the patients in the Prolieve™ intent-to-treat population went for treatment but treatment was canceled during the preparatory steps and these five patients are not included in the safety presentation for the post-treatment period.

### **Demographic Data**

Eighty-three percent of the patients in both treatment arms were Caucasian (104/125, 34/41). The mean age of the patients in the Prolieve™ arm was 63.7 (43-87) years compared to 64.3 (50-83) years for patients in the Proscar® arm. The difference in the mean age between the treatment arms was not statistically significant.

### **Data Analysis and Results on Intent-to-Treat Population**

*Effectiveness:* The primary effectiveness analysis was a repeated measure analysis using the least squares model for each follow-up evaluation comparing the two treatment arms. All patients with missing data at any follow-up evaluation or who did not attend a visit were included in the analysis as failures.

### **Repeated Measures Mean Improvement Comparison on Intent to Treat Population**

#### *Primary Effectiveness Variable: AUA Total Score*

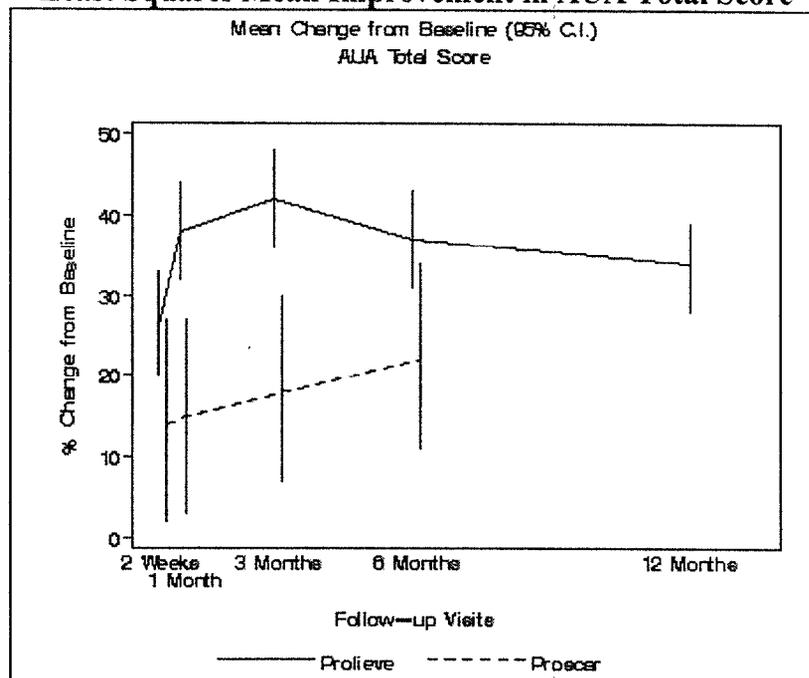
The mean improvement in AUA total score for the patients treated with Prolieve™ was greater than the mean improvement observed for patients treated with Proscar® at each follow-up evaluation (2 week, 1 month, 3 months, and 6 months) except the 12-month visit at which Proscar® patient data was not collected and are presented below in Table 2. Graph A below presents this information in graphic format. The vertical lines represent the confidence intervals.

**Table 2: Repeated Measures Analysis  
Least Squares Mean Improvement in AUA Total Score**

Visit	Treatment Arm	Absolute Mean Improvement (95% CI)	Percent Improvement (95% CI)
2-week	Prolieve™	5.7 (4.3, 7.1)	26% (20, 33)
	Proscar®	2.8 (0.4, 5.3)	14% (2, 27)
1-month	Prolieve™	8.4 (7.1, 9.7)	38% (32, 44)
	Proscar®	3.0 (0.7, 5.2)	15% (3, 27)
3-month	Prolieve™	9.2 (8.0, 10.5)	42% (36, 48)
	Proscar®	3.6 (1.4, 5.8)	18% (7, 30)
6-month	Prolieve™	8.1 (6.9, 9.4)	37% (31, 43)
	Proscar®	4.4 (2.2, 6.7)	22% (11, 34)
12+ month	Prolieve™	7.4 (6.2, 8.6)	34% (28, 39)

\*note: the data above is based on the Prolieve™ treated patients, N=125, and Proscar® treated patients, N=41.

**Graph A: Repeated Measures Analysis  
Least Squares Mean Improvement in AUA Total Score**



**Effectiveness Results on Evaluable Patients-Prolieve™ Patients Only**

*AUA Responder Rates for Treated Patients:* All patients having a 30% or greater improvement in AUA total score from baseline during the follow-up evaluation were considered responders. Only patients treated with Prolieve™ who were present at the

visit were included in the analysis, i.e., evaluable patients. The improvement percentages are shown in Table 3.

**Table 3: Response for Total AUA Symptom Score in Percent Improvement**

Visit	Group	Percent Response			
		Worsened	No Change 0 to 29%	Improved 30 to 100%	Missing
2 week	Prolieve™	27 (23%)	29 (24%)	59 (49%)	5 (4%)
	Proscar®	10 (24%)	20 (49%)	10 (24%)	1 (2%)
1 month	Prolieve™	14 (12%)	26 (22%)	74 (62%)	6 (5%)
	Proscar®	13 (32%)	11 (27%)	13 (32%)	4 (10%)
3 month	Prolieve™	8 (7%)	27 (23%)	79 (66%)	6 (5%)
	Proscar®	11 (27%)	8 (20%)	16 (39%)	6 (15%)
6 month	Prolieve™	6 (5%)	30 (25%)	69 (58%)	15 (13%)
	Proscar®	8 (20%)	14 (34%)	13 (32%)	6 (15%)
12 month	Prolieve™	8 (7%)	16 (13%)	68 (57%)	28 (23%)

\*note: the data above is based on the Prolieve™ treated patients, N=120, and Proscar® treated patients, N=41.

*Mean Improvement and Responder Analysis for Treated Patients:* Only patients treated with Prolieve™ who were present at the visit were included in the analysis. The mean improvement of 10.1 (47%) (95% CI, 8.5, 11.6) for 92/120 patients observed at the 12+month visit indicates the improvement was sustained.

*Secondary Effectiveness Parameters:* The results for these secondary endpoints and analysis are described below. The secondary effectiveness analysis is performed on the intent-to-treat population, N=125 for the Prolieve™ patients and N=41 on the Proscar® patients.

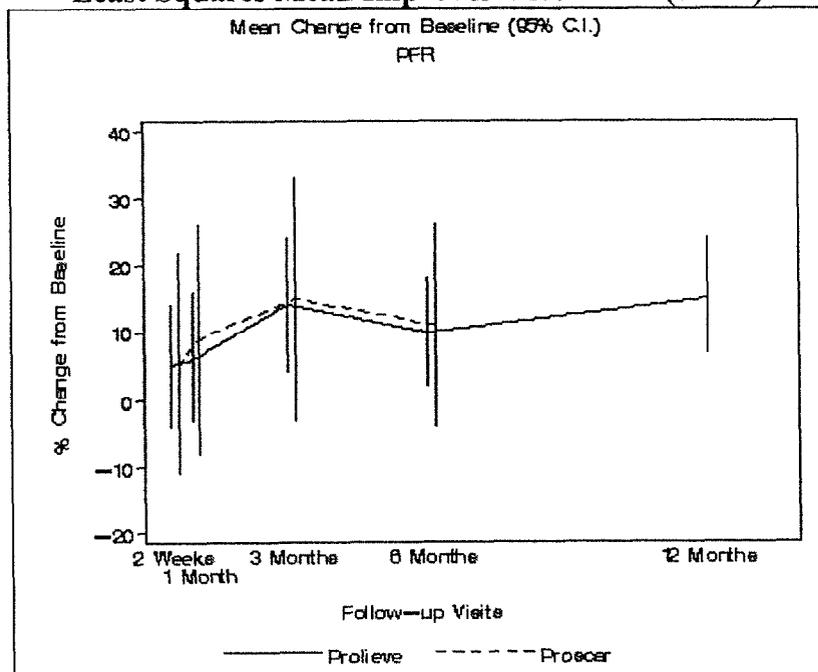
- *PFR:* The least squares mean improvement in peak flow rate data for the patients treated with Prolieve™ are shown in Table 4 below. A plot of these data is provided in Graph B.

**Table 4: Repeated Measures Analysis  
Least Squares Mean Improvement in PFR (cc/sec)**

Visit	Treatment Arm	Absolute Mean Improvement (95% CI)	Percent Improvement (95% CI)
2 week	Prolieve™	0.5 (-0.4, 1.3)	5% (-4, 14)
	Proscar®	0.5 (-1.0, 2.0)	5% (-11, 22)
1 month	Prolieve™	0.6 (-0.3, 1.5)	6% (-3, 16)
	Proscar®	0.8 (-0.7, 2.4)	9% (-8, 26)
3 month	Prolieve™	1.4 (0.4, 2.3)	14% (4, 24)
	Proscar®	1.4 (-0.3, 3.0)	15% (-3, 33)
6 month	Prolieve™	1.0 (0.2, 1.7)	10% (2, 18)
	Proscar®	1.0 (-0.3, 2.4)	11% (-4, 26)
12+ month	Prolieve™	1.5 (0.7, 2.3)	15% (7, 24)

\*note: the data above is based on the Prolieve™ treated patients, N=125, and Proscar® treated patients, N=41.

**Graph B: Repeated Measures Analysis  
Least Squares Mean Improvement in PFR (cc/sec)**



- **QOL:** The mean improvement for the patients treated with Prolieve™ was 4.5 (19%) compared to 1.1 (5%) for the patients treated with Proscar® at the 6-month

visit (95% CI, 5, 25). This improvement was sustained to the 12+-month visit where the mean improvement was 4.2 or 18% (95% CI, 14, 22).

- *LUTS*: The mean improvement for the patients treated with Prolieve™ was 2.3 (17%) compared to 0.8 (6%) for the patients treated with Proscar® at the 6-month visit (95% CI, 3, 18). The improvement observed in the patients treated with Prolieve™ was sustained to the 12+-month visit where the mean improvement was 2.0 or 14% (95% CI, 11, 18).
- *BSI*: The mean improvement for the patients treated with Prolieve™ was 3.4 (19%) compared to 0.8 (5%) for the patients treated with Proscar® at the 6-month visit (95% CI, 2, 27). The improvement observed in the patients treated with Prolieve™ was sustained to the 12+-month visit where the mean improvement was 3.8 or 20% (95% CI, 15, 26).
- *BII*: The mean improvement for the patients treated with Prolieve™ was 2.2 (23%) compared to 1.0 (12%) for the patients treated with Proscar® at the 6-month visit (95% CI, 0, 24). The improvement observed in the patients treated with Prolieve™ was sustained to the 12+-month visit where the mean improvement was 2.1 or 23% (95% CI, 17, 28).
- *IIEF-5*: The comparison between the two treatment arms with respect to erectile function appear to be similar at each of the follow-up visits.
- *PVR*: The PVR mean change from baseline for the two treatment arms appear to be similar at each of the follow-up visits.
- *Sexual Function*: A comparison of responses by patients in the two treatment arms was made for the questions asking if the patient experienced pain with erections, intercourse and/or ejaculations. Less than 1% of patients treated with Prolieve™ experienced some form of erectile dysfunction following treatment.
- *Pain and Discomfort*: No differences were observed between the two treatment arms at any of the follow-up evaluations with respect to pain and discomfort.
- *Prostate weight and response rates*: A covariate analysis based on prostate weight was performed to assess the impact of treatment success with respect to prostate size. A comparison in response rates based on AUA total score and prostate weight was made for the patients treated with Prolieve™. Those patients with prostate weights of ≤40grams were included in one group while patients with prostate weights >40 grams were placed in the other group. At the 6-month visit the patients in the ≤40gram group had a 71% (51/72) AUA responder rate (percent improvement of 30% or greater compared to baseline) compared to 34% (18/53) for the patients in the >40gram group (95% CI, 20.4, 53.4). These results demonstrated that patients with prostates >40grams did not demonstrate as significant a response as patients with prostate weights of ≤40grams.

## MAINTAINING DEVICE EFFECTIVENESS

Please refer to the User Manual for complete instruction on device maintenance required by Celsion. Celsion recommends the following actions be performed by the user:

### Weekly

- Cleaning of all cooling air inlets

### Each 12-month period

- Microwave power output calibration
  - Temperature system validation
  - System electrical safety verification
- 
- To help maintain the device's proper operation it is important to follow the specified shutdown procedure. The specified instructions are in the User Manual. In general, be certain to close all windows on the Prolieve™ computer screen by single, left mouse clicks on the upper right hand corner of each window. Select the Shut Down option and wait until the message "it is now safe to turn off your computer" appears.
  - Always place the power button in the off position when treatment is completed.
  - Backup power should be available to permit proper shutdown in the event of a power outage.
  - Prolieve™ requires no lubrication
  - For any needed service, call 888-272-1001.

## ALTERNATIVE TREATMENTS

For symptomatic bladder obstruction secondary to BPH, the alternative procedures include those shown below.

- "Watchful waiting," some patients may improve or stabilize the symptoms.
- Drug therapy with a single drug or combined therapy with an alpha blocker and Finasteride (Proscar®). The combination relaxes the bladder neck and prostatic urethra and Finasteride can shrink the volume of BPH growth.
- Microwave thermotherapy (TUMT) using intraprostatic temperatures >46°C is effective in partially relieving symptoms of BPH. There are several devices approved for this purpose.
- TUNA that uses radiofrequency energy to destroy intraprostatic tissue resulting in opening of the obstruction.
- Urethral stents placed in the prostatic urethra to expand the opening of the channel.
- Laser treatment for resection, electrovaporization or coagulation of the BPH tissue.

- TURP, transurethral removal, piece by piece of BPH growth with an electrical loop.
- Transurethral incision of the prostate (TUIP), this is limited to prostates <30gm, and
- Open surgery via different approaches (suprapubic, retropubic or perineal) removes only the inner part of the gland.

The treating physician should discuss the alternatives prior to treatment.

## **PATIENT COUNSELING INFORMATION**

Patient counseling is the responsibility of the treating physician. However, Celsion Corporation provides the following suggestions:

- **Purpose, alternatives and the desired outcomes. Discuss the following with the patient:**
  1. Reconfirm the diagnosis.
  2. The purpose of the Prolieve™ treatment.
  3. The alternative treatments and their side effects.
  4. The desired outcome of the Prolieve™ treatment including the fact that it is not a curative procedure.
- **Pretreatment instructions. Advise the patient of the following:**
  1. He may have a prophylactic antibiotic therapy recommended prior to treatment.
  2. He will be asked to empty his bladder.
  3. His vital signs will be monitored.
  4. He will feel bladder urgency during the treatment.
  5. He will have an aqueous based topical anesthetic applied.
  6. He will feel suprapubic heat during treatment; actual pain should be reported immediately to the medical team.
- **Procedure description. Advise the patient of the following to facilitate his understanding of the procedure:**
  1. The physician and technician will prepare the machine for use.
  2. A topical anesthetic will be applied to the opening of the urethra.
  3. A catheter will be inserted into the bladder, and different methods, such as x-ray or ultrasound, may be used to verify the exact location of the equipment.
  4. A temperature monitor with a prophylactic cover will be inserted to monitor the treatment.
  5. Heat generated by microwave power will be applied to the prostate gland and compression will be applied to the wall of the urethra.
  6. The catheter and temperature monitor will be removed at the conclusion of the treatment.
  7. The preparation and procedure should take about 60 to 90 minutes.

- **Adverse events. Advise the patient of all potential adverse events associated with the procedure: (See Table 1).**
- **Follow up expectations. Advise the patient of the following:**
  1. Follow up visits or tests are required.
  2. Adverse events such as blood in the urine are common for 3 to 5 days after the procedure.
  3. Pain and discomfort may last for up to 7 days after the procedure.
  4. Patient should take pain medication as recommended by the physician.
  5. When he is to contact the physician.

## **HOW SUPPLIED**

The main components of Prolieve™ are the permanent instrument and the single-use Procedure Kit.

The permanent instrument consists of:

- Instrument cabinet
- Cables
- Rectal Temperature Monitor

The single-use Procedure Kit consists of:

- Sterile, Microwave Transurethral Catheter
- Heat Exchanger Cartridge
- Sterile Water, 500 mL bag

Disposable user supplies consist of:

- 5cc Syringe (for inflation of location balloon)
- KY Jelly
- Aqueous-based, 2% Lidocaine Jelly (packaged in a sterile syringe)
- General Prophylactic for use with the RTP
- Absorption pad 2 foot by 2 foot (or equivalent coverage)
- 4" x 4"sponges (sterile gauze)
- Gauze Tape
- Ultrasonic Gel (if ultrasound imaging is anticipated)

## **USER MANUAL**

The User Manual is a separate document.

## **PATIENT INFORMATION**

Patient labeling is available to assist the physician in counseling the patient about this device and the procedure. The patient labeling should be provided to the patient in a timely manner.

## REFERENCES

1. Anscher, Mitchell S.; Samulski, Thaddeus V.; Dodge, Richard; Prosnitz, Leonard R.; Dewhurst, Mark W. "Combined External Beam Irradiation and External Regional Hyperthermia for Locally Advanced Adenocarcinoma of the Prostate." *Int. J. Radiation Oncology Biol. Phys.*, Vol. 37, No. 5, pp. 1059-1065, 1997.
2. Astrahan, M.A.; Ameye, F.; Oyen, R.; Willemen, P.; Baert, L.; and Petrovich, Z. "Interstitial Temperature Measurement During Transurethral Microwave Hyperthermia." *The Journal of Urology*. Vol. 145, 304-308, February 1991.
3. Baert, L.; Ameye, F.; Willemen, P.; Vanderhove, J.; Lauweryns, J.; Astrahan, M.; and Petrovich, Z. "Transurethral Microwave Hyperthermia for Benign Prostatic Hyperplasia: Preliminary Clinical and Pathological Results." *The Journal of Urology*. Vol. 144, 1383-1387, December 1990.
4. Blute, Michael L.; Tomera, Kevin M.; Hellerstein, Daniel K.; Atkinsons, Elizabeth J.; Patterson, David E.; and Segura, Joseph W. "Transurethral Microwave Thermotherapy for Prostatism: Early Mayo Foundation Experience." *Mayo Clinic Proceedings*. Vol. 67, 417-421, May 1992.
5. Daehlin, Lars; Frugard, Jannicke. "Three-year Follow-up after Transurethral Microwave Thermotherapy (TUMT) for Benign Prostatic Hyperplasia using the Primus U + R Device." *Scand J Urology Nephrol* 33: 217-221, 1999.
6. Devonec, Marian; Ogden, Chris; and Carter St. Clair, Simon. "Microwave Thermotherapy in Benign Prostatic Hypertrophy." *Current Opinion in Urology*. Vol. 3, 202-208, 1993.
7. Devonec, Marian; Tomera, K.; and Perrin, P. "Review: Transurethral Microwave Thermotherapy in Benign Prostatic Hyperplasia." *Journal of Endourology*. Vol. 7, Number 3, 1993.
8. De La Rosette, J.J.M.C.H.; Francisca, E.A.E; Kortmann, B.B.M.; Floratos, D.L.; Debruyne, F.M.J.; Kiemeny, L.A.L.M. "Clinical Efficacy of a New 30-Min. Algorithm for Transurethral Microwave Thermotherapy: Initial Results." *BJU International* (2000), 86, 47-51.
9. De La Rosette, J.J.M.C.H.; De Wildt, M.J.A.M.; Alivizatos, F.; Frowling, F.M.J.A.; Debruyne, F.M.J. "Transurethral Microwave Thermotherapy (TUMT) in Benign Prostatic Hyperplasia: Placebo Versus TUMT." *Urology*, July 1994, Vol. 44, No. 1.
10. De Wildt, M.J.A.M.; Debruyne, F.M.J.; De La Rosette, J.J.M.C.H. "High-Energy Transurethral Microwave Thermotherapy: A Thermoablative Treatment for Benign Prostatic Obstruction." *Urology* 48 (3), 1996.
11. Djavan, Bob; Roehrborn, Claus G.; Shariat, Shahrokh; Ghawidel, Keywan; Marberger, Michael. "Prospective Randomized Comparison of High Energy Transurethral Microwave Thermotherapy Versus Blocker Treatment of Patients with Benign Prostatic Hyperplasia." *The Journal of Urology*, Vol. 161, 139-143, January 1999.
12. Djavan, Bob; Seitz, Christian; Ghawidel, Keywan; Basharkhah, Ali; Bursa, Bernd; Hruby, Stephan; Marberger, Michael. "High-Energy Transurethral Microwave Thermotherapy in Patients with Acute Urinary Retention Due to Benign Prostatic Hyperplasia." *Urology* 54 (1), 1999.

13. Floratos, Diamandis L.; Kiemeny, Lambertus A.L.M.; Rossi, Cristina; Kortmann, Barbara B.M.; Debruyne, Frans M.J.; De La Rosette, Jean J.M.C.H. "Long-Term Follow-up of Randomized Transurethral Microwave Thermotherapy Versus Transurethral Prostatic Resection Study." *The Journal of Urology*, Vol. 165, 1533-1538, May 2001.
14. Kaplan, Steven A.; Shabsigh, Ridwan; Soldo, Katherine A.; and Olsson, Carl A. "Prostatic and Periprostatic Interstitial Temperature Measurements in Patients Treated with Transrectal Thermal Therapy (Local Intracavitary microwave Hyperthermia)." *The Journal of Urology*. Vol. 147, 1562-1565, June 1992.
15. Larson, Thayne R.; Collins, Joseph M. "An Accurate Technique for Detailed Prostatic Interstitial Temperature-Mapping in Patients Receiving Microwave Thermal Treatment." *Journal of Endourology*. Vol. 9, No. 4, August 1995.
16. Larson, Thayne R.; Collins, Joseph M. "Increased Prostatic Blood Flow in Response to Microwave Thermal Treatment: Preliminary Findings in two Patients with Benign Prostatic Hyperplasia." *Urology*, 46 (4), 1995.
17. Larson, Thayne R.; Collins, Joseph M.; Corica, Alberto. "Detailed Interstitial Temperature Mapping During Treatment with a Novel Transurethral Microwave Thermoablation System in Patients with Benign Prostatic Hyperplasia." *The Journal of Urology*, Vol. 159, 258-264, January 1998.
18. Lau, K.O.; Li, M.K.; Foo, K.T. "Long-Term Follow-up of Transurethral Microwave Thermotherapy." *Urology* 52 (5), 1998.
19. Lindner, A.; Siegel, Y.I.; Saranga, D.; Korzcak, D.; Matzrin H.; and Braf, Z. "Complications in Hyperthermia Treatment of Benign Prostatic Hyperplasia." *The Journal of Urology*. Vol. 144, 1390-1392, December 1990.
20. Roehrborn, Claus G.; Preminger, Glenn; Newhall, Phil; Denstedt, John; Razvi, Hassan; Chin, L. Joseph; Perlmutter, Aaron; Barzell, Winston; Whitmore, Willet; Fritzsich, Ralph; Sanders, Jeffrey; Sech, Scott; Womack, Sean. "Microwave Thermotherapy for Benign Prostatic Hyperplasia with the Dornier Urowave: Results of a Randomized, Double-Blind, Multicenter, Sham-Controller Trial." *Urology*, 51 (1), 1998.
21. Sapozink, Michael D.; Boyd, Stuart D.; Astrahan, Melvin A.; Jozsef, Gabor; and Petrovich, Zbigniew. "Transurethral Hyperthermia for Benign Prostatic Hyperplasia: Preliminary Clinical results." *Urology*, Vol. 143, pp. 944-950, May 1990.
22. Servadio, C.; Leib, Z.; Lev, A. "Diseases of Prostate Treated by Local Microwave Hyperthermia." *Urology*. Vol. XXX, 2, 97-99, August 1987.
23. Servadio, C.; Lindner, Lev, A.; Leib, Z.; Siegel, Y.; Braf, Z. "Further Observations on the Effect of Local Hyperthermia on Benign Enlargement of the Prostate." *World J. Urology*, 6:204-208, 1989.
24. Stawarz, B.; Szmigielski, S.; Ogrodnik, J.; Astrahan, M.; Petrovich, Z. "A Comparison of Transurethral and Transrectal Microwave Hyperthermia in Poor Surgical Risk Benign Prostatic Hyperplasia Patients." *The Journal of Urology*. Vol. 146, 353-357, August 1991.
25. Sterzer, Fred; Meddecki, Jozef; Mawhinney, Daniel D.; Friedenthal, Esther; Melman, Arnold. "Microwave Treatments for Prostate Disease." *Transactions on Microwave Theory and Techniques*. Vol. 48, 11, November 2000.

26. Yerushalmi, A. "Localized, Non-Invasive Deep Microwave Hyperthermia for the Treatment of Prostatic Tumors: The First 5 Years." *Cancer Research*, Vol. 107, 141-146, 1988.
27. Muschter, Rolf; Schorsch, Isabel; Danielli, Lavy; Russel, Christoph; Timoney, Anthony; Yachia, Daniel; Jolkowsky, Eduard; Matalon, Gabriel; Roder, Thomas; Nordling, Jorgen. "Transurethral Water-Induced Thermotherapy for the Treatment of Benign Prostatic Hyperplasia: A Perspective Multicenter Clinical Trial." *The Journal of Urology*. Vol. 164, 1565-1569, November 2000.