Minimally Invasive Prostate Convective Water Vapor Energy Ablation: A Multicenter, Randomized, Controlled Study for the Treatment of Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia

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Purpose: This report reveals the results of a multicenter, randomized, controlled study using transurethral prostate convective water vapor thermal energy to treat lower urinary tract symptoms associated with benign prostatic hyperplasia.

Materials and Methods: Men 50 years old or older with an International Prostate Symptom Score of 13 or greater, maximum flow rate of 15 ml per second or less and prostate size 30 to 80 cc were randomized 2:1 between thermal therapy with the Rezūm® System and control. Thermal water vapor was injected into the transition zone and median lobe as needed. The control procedure was rigid cystoscopy with simulated active treatment sounds. The primary end point compared International Prostate Symptom Score reduction at 3 months. Treatment subjects were followed for 12 months.

Results: There were 197 men randomized (active 136, control 61). Thermal therapy and control International Prostate Symptom Score was reduced by 11.2 ± 7.6 and 4.3 ± 6.9 respectively ($p < 0.0001$). Treatment subject baseline International Prostate Symptom Score of 22 decreased at 2 weeks (18.6,

Abbreviations and Acronyms

AE = adverse event

BPH = benign prostatic hyperplasia

BPHII = BPH impact index

HRQL = health related quality of life

ICS male IS-SF = International Continence Society Male Incontinence Scale questionnaire-Short Form

I-PSS = International Prostate Symptom Score

ITT = intent to treat

LUTS = lower urinary tract symptoms

OAB-q SF = Overactive Bladder Questionnaire Short Form

PSA = prostate specific antigen

PVR = post-void residual volume

Qmax = peak urinary flow

QoL = quality of life

RF = radio frequency

TUMT = transurethral microwave thermotherapy

TUNA = transurethral needle ablation

TURP = transurethral resection of the prostate

UTI = urinary tract infection

VAS = visual analog scale

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Editor's Note: This article is the fifth of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 1628 and 1629.

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p=0.0006) and by 50% or greater at 3, 6 and 12 months, p <0.0001. The peak flow rate increased by 6.2 ml per second at 3 months and was sustained throughout 12 months (p <0.0001). No de novo erectile dysfunction was reported. Adverse events were mild to moderate and resolved quickly.

Conclusions: Convective water vapor thermal therapy provides rapid and durable improvements in benign prostatic hyperplasia symptoms and preserves erectile and ejaculatory function. Treatment can be delivered in an office or hospital setting using oral pain medication and is applicable to all prostate zones including the median lobe.

Key Words: prostate, prostatic hyperplasia, lower urinary tract symptoms, thermal conductivity

LOWER urinary tract symptoms develop in almost a third of all men, primarily from BPH. Thus, health care costs for BPH are included in the top 10 most prominent and costly diseases in men older than 50 years in the United States.[1]

The most common indications for TURP have shifted considerably in the last few decades. While previously TURP was offered for any voiding symptoms without formal objective quantification, the indication now is moderate to severe lower urinary tract symptoms attributed to BPH refractory to medical therapy. In the past this was nearly exclusively the domain of monopolar TURP. Bipolar TURP was introduced to reduce side effects from the procedure. The expanding endoscopic options, including many minimally invasive treatments, allowed the practitioner to add other treatments into the continuum between medical management and surgical options.

Less invasive treatments included active prostatic urethral expanders, eg prostatic urethral stent[2] and the prostatic urethral lift.[3] Electromagnetic energy thermal therapies to ablate tissue include microwave (TUMT) and RF (TUNA) induced transurethral needle ablation. TUMT and TUNA use heat transfer by conduction, requiring variable treatment times that may last up to an hour and high energy deposition to optimize the temperature gradient to produce tissue destruction.[4] Lack of sufficient durability, high rates of re-treatment, and patient selection regarding prostate size and the contraindication to treat median lobes are negative attributes preventing their widespread adoption.[5,6]

In this study we introduce the Rezūm System (NxThera, Inc., Maple Grove, Minnesota) that provides convective water vapor energy (WAVE™) as a minimally invasive thermal therapy involving no discernible thermal gradient as seen with conductive heat transfer (eg TUNA, TUMT). This transurethral thermal therapy uses RF to generate wet thermal energy in the form of water vapor. Convection uniformly disperses vapor thermal energy at slightly higher than interstitial pressure, intercalating the tissue interstices and rapidly disrupting tissue cell membranes effecting cell death and necrosis. The therapy can be targeted to defined areas such as the transition zone because steam will travel between cells until it encounters natural collagen barriers (forming a pseudocapsule) between the prostatic zones and it will not cross the true prostate capsule.[7,8] No thermal effects occur outside the prostate or targeted treatment zone.[9]

The principles of this WAVE technology and effective ablation of human prostatic adenomas were validated in 2 separate BPH studies. The histological evaluation of extirpated prostate tissue confirms demarcation of viable and necrotic tissue, and radiographic studies with gadolinium-enhanced magnetic resonance imaging demonstrate thermal lesion characteristics in patients with LUTS-BPH. [9,10] Single-arm BPH studies using WAVE technology show rapidly achieved improved I-PSS, flow rates and QoL sustained over 12 months.[11,12] We report the results of the first multicenter, randomized, controlled and single blinded study of this thermal therapy for LUTS associated with BPH (Rezūm II Study).

MATERIALS AND METHODS

Study Subjects, Protocol and Objectives

Institutional review board approval was obtained for the 15 participating sites in the United States (Clincaltrials.gov: NCT01912339). The Appendix provides the major inclusion and exclusion criteria for the trial.

The primary objective was to determine the efficacy and safety of the convective water vapor energy ablation of prostatic tissue. The treating physician was not blinded in order to perform the treatments but did not participate in the followup or the administration of outcomes questionnaires. Study participants and study personnel administering questionnaires were double-blinded until the 3-month followup. An independent data monitoring committee reviewed safety. All AEs reviewed were adjudicated by an independent clinical evaluation committee.

Randomization

Qualified subjects were randomized with an electronic program before treatment using permuted blocks of random sizes, stratified by investigational site, in a 2:1 ratio allocation to treatment and control arms,