Evaluation of the TULSA-PRO MRI-Guided Transurethral Ultrasound Prostate Ablation Device in Patients with Localized Prostate Cancer: a Prospective, Single-Arm, Pivotal Clinical Study

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The primary objective of this study is to further evaluate the safety and effectiveness of the MRI-guided TULSA-PRO device intended to ablate prostate tissue of patients with localized, organ-confined prostate cancer.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON42845

Source
ToetsingOnline

Brief title
MRI-TULSA-PRO

Condition

- Reproductive neoplasms male malignant and unspecified

Synonym
Prostate cancer, Prostate carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Profound Medical, Inc.
Source(s) of monetary or material Support: Profound medical;Inc.

Intervention

Keyword: Ablation, MRI-guided, Prostate cancer, Treatment

Outcome measures

Primary outcome

* Safety Endpoint: Frequency and severity of adverse events deemed related or possibly related to the TULSA-PRO device, procedure, or ablative process will be evaluated and reported in accordance with the Common Terminology Criteria for Adverse Events (CTCAE) standard published by the National Cancer Institute (NCI).

* Efficacy Endpoint: Prostate ablation efficacy will be evaluated using the proportion of patients achieving a PSA nadir * 25% of the pre-treatment baseline value.

Secondary outcome

* Adverse Event Endpoint: Frequency and severity of all adverse events, described using the NCI CTCAE.

* Erectile Dysfunction Endpoint: Rate of erectile dysfunction, determined by the change from baseline of the proportion of patients with erection firmness sufficient for penetration (IIEF item 2 * 2).

* Urinary Incontinence Endpoint: Rate of urinary incontinence, determined by the change from baseline of the proportion of patients who use one or more pads per day (EPIC item 5 * 1).

* PSA Nadir Endpoint: Proportion of patients achieving PSA nadir * 0.5 ng/ml.

* PSA Stability Endpoint: Proportion of patients with PSA * 0.5 ng/ml at the most recent follow-up visit.

* Prostate Volume Endpoint: Prostate volume reduction, evaluated on MRI between the treatment day and 12-month follow-up visits.

* Prostate Biopsy Endpoint: Proportion of patients with negative prostate biopsy at the 12-month follow-up visit, determined by TRUS-guided 10-core biopsy.

* IPSS Endpoint: Change in International Prostate Symptom Score (IPSS), between the baseline and most recent follow-up visit.

* IIEF Endpoint: Change in the Erectile Function, Orgasmic Function, Sexual Desire, Intercourse Satisfaction and Overall Satisfaction domains of the International Index of Erectile Function (IIEF-15), between the baseline and most recent follow-up visit.

* EPIC Endpoint: Change in Urinary, Bowel, Sexual and Hormonal domains of the Expanded Prostate Cancer Index Composite (EPIC), between the baseline and most recent follow-up visit.

* Targeting Accuracy Endpoint: Conformal prostate ablation, measured quantitatively between the target prostate volume and the target temperature isotherm on MRI thermometry acquired during the TULSA-PRO procedure, and described using three measures of targeting accuracy:

o Dice Similarity Coefficient (DSC * unitless from 0 to 1), is a statistical validation metric to measure the degree of spatial overlap between two regions [Dice 1945].

o Over- and under-targeted volumes (outside the target volume ± * voxel margin), representing the amount of tissue * target temperature outside the target volume and < target temperature inside the target volume, respectively. The over- and under-targeted volumes are expressed in absolute cc, and as a % of the target volume.

o Linear targeting in mm, representing the spatial accuracy (average) and precision (standard deviation) of the TULSA-PRO to heat the target boundary to the target temperature.

* CE-MRI Endpoint: Conformal prostate ablation, assessed qualitatively by visualizing the peripheral region of enhancement surrounding the non-perfused volume (NPV) on contrast-enhanced (CE)-MRI acquired immediately after treatment.

* mpMRI Endpoint: Characterize the effect of the TULSA-PRO ablation on diagnostic multi-parametric prostate MRI (mpMRI), determined using PI-RADS v2 performed at the Baseline and 12-month follow-up visits.

Study description

Background summary

Prostate cancer is the most prevalent cancer among men in economically developed countries, and is now recognized as one of the principal medical problems facing the male population [GLOBOCAN 2008]. In Canada, prostate cancer is the most frequently diagnosed cancer, with the number of cases expected to double within the next 15 years, and is the second leading cause of cancer-related death in men [Ellison and Wilkins 2009].
While conventional radical treatments for localized prostate cancer (surgery, radiation therapy) provide good local control of disease, they leave many men with significant long-term complications affecting urinary, bowel and sexual function, which can reduce the patient*s quality of life significantly [Potosky et al 2004, Thompson et al 2007]. This reduction in Quality of Life (QOL) is becoming increasingly problematic as now younger men screened for the disease,

for whom continence and potency are of major concern, are faced with earlier detection of less severe disease. The quandary faced is then how to proceed due to a lack of intervention options that can treat the disease but not cause substantial life-long side-effect issues.
As a result, men are seeking new ways to treat prostate cancer that allow them to avoid surgery or radiation and their potential complications. In order to address this shortcoming in the management of the disease, it is desirable to offer treatments that can achieve good control of local disease, with low morbidity.
Magnetic Resonance Imaging (MRI)-guided Transurethral Ultrasound Ablation (MRI-TULSA) is a novel minimally-invasive technology to precisely ablate the prostate gland using real-time MRI monitoring and active temperature feedback control. High-energy ultrasound is delivered by a device inserted in the urethra and is used to heat prostate tissue, both benign and malignant, to the point of thermal coagulation (thermal ablation). MRI is used during the procedure to measure in real-time the temperature distribution in the prostate, enabling closed-loop feedback control of the heating pattern and precise ablation of the prostate gland. MRI thermometry is based on a physical property of water protons [Ishihara et al 1995], and has been demonstrated to control ultrasound ablation by many groups [Vanne and Hynynen 2003, Mougenot et al 2009, Chopra et al 2012, Fuentes et al 2009]. In addition, MRI is used pre-treatment to guide device positioning and perform treatment planning. Post-treatment, Contrast Enhanced (CE)-MRI can be used to visualize the Non-Perfused Volume (NPV) and assess the extent of thermal ablation.
Profound Medical Inc. (PMI) has developed an MRI-TULSA system, the TULSA-PRO, which has the advantages of a non-invasive procedure with short treatment times. The TULSA-PRO has the potential to offer accurate and precise prostate ablation with low rates of complications and low morbidity.
Phase I clinical study of the TULSA-PRO in thirty prostate cancer patients has demonstrated precise thermal ablation of the prostate gland with low rates of serious or long-term adverse events, though with conservative safety margins around the prostate capsule. The purpose of this Pivotal clinical study is to establish the safety and effectiveness of the TULSA-PRO for accurate and precise ablation of the prostate gland, with reduced safety margins and in a larger prostate cancer population. In this Pivotal study, men with localized (organ-confined) prostate cancer will undergo MRI-TULSA with the aim of whole-gland prostate ablation. Patients will then be followed for twelve months to check on the progress of the ablative therapy and associated adverse events, monitor indicators of quality of life, and indicators of residual prostate cancer. Additional patient monitoring for long-term effects will continue annually for a period of up to five years after the MRI-TULSA procedure. This study will provide confirmatory data that will become the basis for seeking regulatory approval of the PMI TULSA-PRO in the USA.

Study objective

The primary objective of this study is to further evaluate the safety and

effectiveness of the MRI-guided TULSA-PRO device intended to ablate prostate tissue of patients with localized, organ-confined prostate cancer.

Study design

Phase 1, single arm, international multicenter trial

Intervention

MRI-guided transurethral ultrasoundablation of the prostate.

Study burden and risks

Risks associated with the TULSA procedure:
The TULSA-PRO device has had limited testing in humans. The likelihood of the risks below is estimated based on results of a 30-patient Phase I clinical trial.

Likely (21% or more)
* Pain and inflammation in the pelvic area post-procedure
* Hematuria (blood in the urine)
* Urinary complications including increased urinary frequency and urgency
* Penile discharge or bleeding
* Retrograde (back into the bladder) or absence of or diminished ejaculation
* Urinary tract infection
* Reduced erectile function

Less Likely (5 * 20%)
* Post-ablation urinary retention after the supra-pubic catheter removal which will require catheterization
* Bladder spasms
* Hematospermia (blood in the semen or ejaculation fluid)
* Bloating
* Erectile dysfunction (erection insufficient for penetration)

Rarely (less than 4%)
* Short term fever
* Stress incontinence (spontaneous urine passing with coughing or sneezing)
* Rectal discomfort or hemorrhoid pain
* Diarrhea
* Epididymitis (inflammation of the cord at the back of the testicle)
* Urethral stricture (narrowing of the tube you pass urine through)
* Urinary incontinence (uncontrolled leakage of urine)
* Osteitis pubis* (non-infectious inflammation of the pubic bone)
* Rectal wall injury and/or rectal fistula*

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Men diagnosed with biopsy-proven, organ-confined, low- to intermediate-risk prostate cancer will be eligible for participation in this study, provided they have not received prior treatment of their prostate cancer.

Exclusion criteria

Extraprostatic extension, lesion within 3mm of the urethra or sphincter plane, previous TURP, calcifications or cysts in the prostate, use of hormones

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-12-2017
Enrollment:	12
Type:	Actual

Medical products/devices used

Generic name:	TULSA-PRO
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	12-12-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL57803.091.16