1 GENERAL STUDY INFORMATION

1.1 Study Confidentiality

This document contains confidential and privileged information. As such, it should not be disclosed unless written permission is obtained from PROCEPT BioRobotics Corp, also referred to as the "sponsor," and the principal investigator, or if disclosure is mandated by law. Individuals who receive this information must be made aware that it is confidential. These restrictions on disclosure also extend to any future privileged or confidential information provided.

1.2 Study Summary

Title:	WATER IV Prostate Cancer: Aquablation versus Active Surveillance for the Treatment of Localized Prostate Cancer
Primary Objective:	To evaluate the safety and efficacy of Aquablation Therapy with the AQUABEAM Robotic System and the HYDROS Robotic System to reduce unfavorable prognosis for men with GG1 or 2 localized prostate cancer in comparison to active surveillance.
Study Design:	This is a multicenter prospective, randomized clinical trial where subjects will be randomized to active surveillance or Aquablation. Aquablation therapy can consist of one or more Aquablation procedures. Patients can undergo any additional prostate cancer treatments and that data will be collected. The primary endpoint is superiority in the Aquablation arm with respect to freedom from Grade Group ≥ 2 prostate cancer at 12 months compared to the active surveillance arm. The key secondary endpoint is superiority in the Aquablation arm with respect to freedom from persistent or increased MRI suspicion (PRECISE 3, 4 or 5) AND additional prostate cancer treatment at 3 years compared to the active surveillance arm. Active surveillance is a standard of care prostate cancer treatment and subjects in this arm will be followed for a total of 10 years after randomization. Subjects in the Aquablation arm will be followed for a total of 10 years after initial study treatment. Subjects will not be withdrawn if they undergo additional prostate cancer treatments.
Device Names:	AQUABEAM Robotic System HYDROS Robotic System

Clinical Site(s):	Up to 50 sites in the United States, Canada, Japan, Europe, United Kingdom, Hong Kong, South Korea, Taiwan, and mainland China.
Target Population:	Biological men with GG2 or MRI visible GG1 localized prostate cancer.
Proposed Indication:	The AQUABEAM Robotic System and the HYDROS Robotic System are intended for the management of prostate cancer.
Planned Enrollment:	Up to 333 subjects will be randomized in a 2:1 ratio (Aquablation: Active Surveillance). The assumed lost to follow-up rate at the primary endpoint is 10%. At least 50% of the subjects randomized will have GG2 disease at baseline. No center will enroll more than 20% of the population and at least 50% of subjects will be enrolled in the United States.
Treatment:	Aquablation: A near total gland resection with the waterjet will be performed. Aquablation can be repeated and not be considered an additional prostate cancer treatment. Active surveillance: Active surveillance treatment will be performed according to institutional standards of care. In addition, subjects will undergo study-specific assessments after consent. Patients can undergo additional prostate cancer treatments at their study physician's discretion. This will not exit them from the study.
Study Follow-up Schedule:	Catheter removal visit (Aquablation arm only), 6 months, 12 months, 24 months, 36 months, 48 months, 60 months, 6 years, 7 years, 8 years, 9 years and 10 years.
Inclusion Criteria:	1. Biological male with age ≥ 45 years at the time of consent 2. Biopsy positive Grade Group 2 prostate cancer or biopsy positive Grade Group 1 MRI visible lesion (PI-RADS/Likert ≥ 3) 3. First prostate cancer diagnoses within 18 months (545 days) of consent 4. Are candidates for active surveillance 5. Clinical Stage ≤ T2c 6. PSA < 15 ng/ml 7. Prostate volume ≥ 25 ml
Exclusion Criteria:	1. Any prior or current local or systemic treatment for prostate cancer, including but not limited to surgery, radiation therapy (external or brachytherapy), tissue ablation, hormone therapy or chemotherapy. 2. Patients with previous surgical or minimally invasive treatment of benign prostatic hyperplasia within the prior 3 months of study treatment. 3. Evidence of lymph node, bone metastasis, extracapsular extension or seminal vesicle invasion. 4. Patient is unwilling to accept a blood transfusion if required.

	5. Any condition or history of illness or surgery that may pose an additional risk to patients undergoing the Aquablation procedure such as: 5a. Medical conditions that preclude the use of anesthesia; 5b. Any condition or history of active rectal inflammatory bowel disease or other factors which might increase the risk of rectal injury (i.e. fistula formation); 5c. Patient is unable to stop anticoagulants or antiplatelet agents prior to study treatment per standard of care; 5d. Any other condition or history of infection, illness or surgery that in the opinion of the investigator might affect the outcome of the study procedure, study conduct, and study results; or pose additional risks to the patient (e.g., other cancer, active urethral stricture disease). 6. Patients who are unable to provide informed consent due to cognitive impairment, legal status (such as incarceration), or other factors limiting autonomy or unwilling or unable to follow study instructions including randomization and complete all required study visits through 10 years. This includes individuals with severe cognitive disabilities, those under legal guardianship, or those currently incarcerated. 7. Patient currently participating in other studies unless approved by Sponsor in writing. 8. More than one complete biopsy beyond the diagnostic biopsy comprising both a systematic biopsy and biopsy of any MRI visible lesion (PI-RADS/Likert ≥ 3). 9. GG2 disease with PSA ≥ 10 OR stage ≥ T2b OR ≥ 50% of biopsy cores positive (multiple cores taken from any MRI visible lesion are counted as one continuous core).
Primary Endpoints	Freedom from GG ≥ 2 prostate cancer at 1 year
Key Powered Secondary Endpoints	Freedom from persistent or increased MRI suspicion (PRECISE 3, 4 or 5) AND additional prostate cancer treatment at 3 years
Secondary Endpoints	All secondary endpoints will be assessed based on the follow-up timepoints where data is collected unless otherwise specified. • Modeled area under the curve months of urinary incontinence with urinary incontinence rates following failure of the primary endpoint being that of radical prostatectomy as observed in the radical prostatectomy arm of the WATERIV RP study • Modeled area under the curve months of erectile dysfunction with erectile dysfunction rates following failure of the primary endpoint being that of radical prostatectomy as observed in the radical prostatectomy arm of the WATERIV RP study