



October 27, 2023

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RE: LCD Reconsideration Request – L38726 Transurethral Waterjet Ablation of the Prostate

Greetings Medical Affairs Team:

PROCEPT BioRobotics (PROCEPT) is writing to formally request reconsideration of Local Coverage Decision (LCD) Transurethral Waterjet Ablation of the Prostate (L38726).

PROCEPT is an innovative, U.S.-based medical device company that manufactures the AQUABEAM® System, which is a transurethral waterjet ablation (Aquablation) system for treating individuals with symptomatic benign prostatic hyperplasia (BPH).

Specifically, PROCEPT is requesting three (3) revisions to remove the following limitations:

1. On use of Aquablation in patients over 80 years of age. The information below summarizes new evidence regarding the clinical outcomes for individuals who were over 80 years old at the time they received Aquablation (also called transurethral waterjet ablation) for lower urinary tract symptoms (LUTS) due to BPH. The information is drawn from two studies in peer-reviewed literature and unpublished reports recently obtained from urologists in the United States.
 - a. **The requested revision will update and align your LCD with the recently finalized revision to other final or soon to be final Medicare Administrative Contractor LCDs (CGS, Palmetto, NGS, Noridian, WPS) as well as with the clinical evidence in octogenarians summarized below and the FDA-cleared indication for use (that does not include any age limitation).**
2. Of known or suspected prostate cancer or prostate specific antigen (PSA) > 10 ng/mL and the indication for prostate volume size under this LCD. **The FDA removed the limitation on known prostate cancer or PSA > 10 ng/mL, effective 8/30/2023.** The updated FDA 510k approval (K231024) is attached.
3. On prostate volume. **Newly published clinical data supports the conclusion that transurethral waterjet ablation is reasonable and necessary for prostate volume size > 150 cc.** The evidence is detailed below and is attached.

PROCEPT appreciates your review of this formal request for reconsideration of the coverage policy Transurethral Waterjet Ablation of the Prostate (L38726).

1. REMOVE the limitation on use of Aquablation in patients over 80 years of age.

Background

Age is a significant contributor to the prevalence of LUTS in BPH patients with reports showing the prevalence of LUTS increases to 80% in men at 70 years of age. Given the incidence and severity of LUTS generally increases with age, the age limitation in the current LCD warrants reevaluation to determine whether retaining this limitation on patient access is fair and necessary.

Transurethral waterjet ablation of the prostate is a robotic technology that promotes safety and provides highly reproducible, consistent results. Waterjet ablation uses real-time transrectal ultrasound imaging guidance to allow the surgeon to define the target anatomic resection contour on a computer console. Contours are selected to avoid damage to the bladder neck, ejaculatory ducts, and urinary sphincter. In addition, apical treatment can be planned to ensure that no injury occurs to the verumontanum and its underlying ejaculatory ducts. Tissue is resected using an automated, robotic-executed, high-velocity waterjet with up to 2.4 cm treatment depth.

Summary of Clinical Outcomes for Individuals Over 80 Years Old

Aquablation therapy has been well-researched, including two landmark studies that are commonly referred to as “WATER”¹ (Waterjet Ablation Therapy for Endoscopic Resection of prostate tissue) and “WATER II.”² The two prospective trials demonstrated excellent safety and effectiveness in men with smaller (30 – 80 mL) and larger (80 – 150 mL) prostates. Both studies were limited to men between the ages of 45 and 80. The age inclusion criteria for WATER and WATER II were similar to many clinical trials evaluating other BPH surgical techniques.

After the conclusion of the enrollment of the WATER and WATER II studies, investigators initiated two “real-world” registries to evaluate the outcomes of Aquablation in the community-based setting. Accordingly, many of the exclusion criteria observed in the WATER and WATER II studies were removed, including the age restrictions. The OPEN WATER³ study and the Kasraeian⁴ study were published in April and October of 2020, respectively.

The OPEN WATER study is a multi-center, prospective, all-comers study of Aquablation therapy in a real-world setting enrolling 178 patients in five community-based sites. This study evaluated Aquablation with prostates ranging in size from 20 to 150 mL with patients ranging in age from 39 to 88 years.

The Kasraeian study is a single-center, retrospective analysis of prospectively collected data to evaluate the safety and efficacy of Aquablation therapy in a community-based setting. The study

¹ Gilling P, et al. WATER: A Double-Blind, Randomized, Controlled Trial of Aquablation[®] vs Transurethral Resection of the Prostate in Benign Prostatic Hyperplasia. J Urol. 2018 May;199(5):1252-1261.

² Desai M, et al. Aquablation for benign prostatic hyperplasia in large prostates (80-150 mL): 6-month results from the WATER II trial. BJU Int. 2019 Aug;124(2):321-328.

³ Bach T, et al. First Multi-Center All-Comers Study for the Aquablation Procedure. J Clin Med. 2020 Feb 24;9(2):603.

⁴ Kasraeian A, et al. Aquablation for BPH. Can J Urol. 2020 Oct;27(5):10378-10381.

included 55 patients treated between July 2018 and December 2019 and compared outcomes in patients with prostates less than 100 mL and greater than 100 mL. This study included prostates ranging from 27 to 252 mL in volume (mean of 100 mL) with patient ages ranging from 50 to 84 years.

The OPEN WATER and Kasraeian studies included 13 patients (8 and 5 patients, respectively) with ages greater than 80 at the time of the transurethral waterjet ablation procedures. Three-month follow up on 12 of the 13 patients demonstrated a 14-point decline in the International Prostate Symptom Score (IPSS), which is consistent with the overall findings across all ages in both the OPEN WATER and Kasraeian studies (as well as consistent with the findings in the WATER and WATER II studies). In addition, the maximum urinary flow rate (Qmax) more than doubled in the patients over 80 where 12-month follow up data are available.

We also received clinical information on Aquablation patients over 80 years old at the time of treatment from urologist. This information was provided by:

- Northshore University Urology (Evanston, Illinois) – Dr. Brian Helfand (bhelfand@northshore.org)
- Potomac Urology (Alexandria, Virginia) – Dr. Inderjit Singh (isingh@potomacurology.com)
- Georgia Urology (multiple locations, Georgia) – Dr. Lewis Kriteaman (lkriteaman@gaurology.com)

The surgeons treated a total of 30 patients who were over 80 years old with Aquablation between June 2018 and December 2021. The mean age was 82.7 years, and the average prostate volume was 90.4 mL. For the patients with available baseline demographic information, the clinical variables (other than age) were similar to WATER and WATER II (see chart below).

	>80 years data set	WATER	WATER II
Prostate volume (mL)	90.4	54.1	107.4
Baseline IPSS	20	22	23
Baseline Qmax	8.8 mL/s	9.4 mL/s	8.7 mL/s

All 30 cases were completed successfully, and no cases were aborted or converted to another surgical resection technique. In reviewing and discussing the outcomes with the providers noted above, the overall outcomes of improvement in symptom scores and peak urinary flow rates were comparable to those seen in WATER and WATER II. Twenty-seven of the 30 patients were treated in the outpatient setting with three patients treated in the inpatient setting. Two adverse events were reported with one patient contracting sepsis and one patient requiring clot evacuation following the Aquablation procedure. There were no transfusions, ICU admissions, or deaths within 30 days.

These findings for patients over 80 years old treated with Aquablation (described above) are noteworthy and compelling given the consistency with the outcomes demonstrated in younger patients, and this consistency is exactly what one would expect for a surgical resection

technique. This same consistency exists with other surgical resection techniques. As one example, TURP is the gold-standard resection technique for treating younger patients for LUTS due to BPH, and TURP has also demonstrated clinically acceptable results for patients over 80 years old.⁵

In summary, we have obtained data on 43 patients over 80 years old who underwent Aquablation and the results demonstrate outstanding clinical efficacy and safety consistent with reports in the peer-reviewed literature for younger patients.

See Appendix A for more information.

2. REMOVE the limitation “Known or suspected prostate cancer (based on NCCN Prostate Cancer Early Detection guidelines) or a prostate specific antigen (PSA) > 10 ng/mL unless the patient has had a negative prostate biopsy within the last 6 months.”

The current LCD L38726, originally effective in 2020, reflects now outdated FDA language that excluded patients with “diagnosed or suspected cancer of the prostate.” A recent FDA clearance (K231024) removed this contraindication. We are requesting that FCSO update and align the LCD with the recent updated FDA label, which allows Aquablation therapy in patients that have known or suspected prostate cancer.

For many men diagnosed with prostate cancer, the disease does not threaten life expectancy or quality of life impairment, to the extent that there is an ongoing debate on whether low risk disease (Gleason Grade Group 1) should even be termed “cancer” due to its essentially non-existent metastatic potential.⁶ Within the NCCN guidelines⁷ for prostate cancer, conservative management is a preferred or recommend course of treatment for all prostate cancer risk groups (and PSA levels) depending on life expectancy and symptomatology. See Table 1.

⁵ Brierly RD, et al. Is transurethral resection of the prostate safe and effective in the over 80-year-old? *Ann R Coll Surg Engl.* 2001 Jan;83(1):50-3.

⁶ Eggener SE, et al. Low-Grade prostate Cancer: Time to stop calling It Cancer. *J Clin Oncol.* 2022 Sep 20;40(27):3110-3114.

⁷ NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]): Prostate Cancer Version 1.2023. National Comprehensive Cancer Network.

Table 1: Life expectancy for which active surveillance, observation and no imaging or treatment are indicated by risk group with the NCCN prostate cancer treatment guidelines.

NCCN Risk Group	Active Surveillance	Observation	No Imaging or Treatment
Very Low and Low	≥ 10 years*	5-10 years*	< 5 years*
Favorable Intermediate	≥ 10 years	5-10 years*	< 5 years*
Unfavorable Intermediate	NR	5-10 years*	< 5 years*
High or very high	NR	< 5 years	NR

Active surveillance includes regular follow-up with PSA measurement and biopsy.
Observation involves monitoring with a history and physical exam no more often than every 12 months without surveillance biopsies.

*Preferred treatment; NR=Not Recommend

Conservative management for localized prostate cancer has become more common in the United States. In the early 2000s, just 7% and 5% of men with low and intermediate risk disease, respectively, chose conservative management as their initial treatment. The utilization has grown substantially in recent years and the most recent data shows 60% and 20% of men with low risk and intermediate risk disease chose conservative management, respectively. These men tend to be older and, as such, are at increased risk from LUTS due to BPH but are currently, through NGS, unable to access to the symptom relief offered by Aquablation.

A body of evidence presented to FDA establishes a positive benefit to risk profile of Aquablation for men with diagnosed or suspected prostate cancer. The data addresses theoretical concerns, and provides compelling evidence leading the FDA to remove the contraindication:

- The American Urological Association (AUA) guidelines⁸ do not recommend against resective BPH therapies such as Aquablation in patients with diagnosed or suspected prostate cancer, as BPH treatment is not proven in literature to increase oncological risk.

⁸ Lerner LB, et al.; Management of lower urinary tract symptoms attributed to benign prostatic hyperplasia: AUA Guideline part II, surgical evaluation and treatment. J Urol 2021; 206: 818.

- Many men with undiagnosed prostate cancer are treated with resective BPH therapies including Aquablation. but there is no evidence that this creates oncologic risk.⁹
 - The WATER study included men with undiagnosed prostate cancer and no adverse oncological outcomes were observed in the Aquablation arm.
- The theoretical routes for potential exposure to metastatic hazards during Aquablation therapy are demonstrated to pose negligible risk.
 - Physiological evidence through direct measurement of circulating tumor cells (CTCs) does not reveal increased potential for metastasis during Aquablation therapy.¹⁰
 - Tumor spill and CTC seeding of metastases from Aquablation is a theoretical concern that is not borne out by the scientific, clinical evidence or within the peer reviewed literature.¹¹
- Restricting access to men with suspicion of prostate cancer disproportionately impacts groups with certain demographic characteristics, such as older men and black men who have higher suspicion of prostate cancer.¹²

FDA, by removing the contraindication for patients diagnosed or suspected of prostate cancer, has acknowledged that Aquablation therapy is beneficial in effectively alleviating LUTS due to BPH without negligible oncologic risk.

3. REMOVE the Covered Indication “Prostate volume of 30-150 cc by transrectal ultrasound (TRUS)”

This section summarizes new evidence regarding the clinical outcomes for individuals with prostates greater than 150 cc at the time they received Aquablation for lower urinary tract symptoms (LUTS) due to BPH. The information is drawn from two studies in the peer-reviewed literature and unpublished reports from procedure information collected by the company. **Also, like our request for removal of the limitation for patients with prostate cancer, the FDA documentation does not contain any language limiting the use of the device based on prostate volume.**

Summary of Clinical Outcomes for Individuals with Prostates Greater Than 150 cc

Aquablation in patients with prostates greater than 150 cc has been well-researched, including two recent studies.

In a retrospective study by Helfand et. al (2021),¹³ Aquablation was demonstrated as both safe

⁹ Hilscher M, et al. Risk of prostate cancer and death after benign transurethral resection of the prostate-A 20-year population-based analysis. *Cancer*. 2022 Oct;128(20):3674-3680.

¹⁰ PROCEPT BioRobotics Corporation. Data on file.

¹¹ Eschwège P, et al. Prognostic value of prostate circulating cells detection in prostate cancer patients: a prospective study. *Br J Cancer*. 2009 Feb 24;100(4):608-10

¹² Jahn JL, et al. The high prevalence of undiagnosed prostate cancer at autopsy: implications for epidemiology and treatment of prostate cancer in the Prostate-specific Antigen-era. *Int J Cancer*. 2015 Dec 15;137(12):2795-802. doi: 10.1002/ijc.29408. Epub 2015 Jan 8.

and effective in men with very large (> 150 cc) prostates. In this study, the mean prostate size was 209 cc (range: 151 – 362) and the average age was 69 years (range: 54-83). At baseline, subjects reported severe LUTS as demonstrated by the mean pre-procedure IPSS of 19±6. At 6 months post Aquablation, the mean IPSS decreased to 7±5 (p<0.001). The maximum flow rate (QMax) increased from 7±4 cc/sec to 19.5 ± 5 at 6 months (p<0.001). This IPSS reduction and QMax increase are consistent with that observed in the WATER and WATER II studies of Aquablation which included men with prostates ranging from 30-80 cc and 80-150 cc, respectively. There were no reports of adverse events (incontinence, erectile dysfunction, or ejaculatory dysfunction) in the very large prostate group. Importantly, the authors reported that a statistically significantly lower rate of clinically significant bleeding within the very large cohort. Quality-of-life measures from the very large patient group were similarly in line with the outcomes reported in WATER and WATER II.

From efficacy, safety and quality-of-life standpoints, the compelling outcomes observed in WATER and WATER II, which only included prostates less than 150 cc, have been reproduced in a population with prostate volumes greater than 150 cc.

Operative time for the very large prostate patients was higher. However, the increase was not statistically significant, and the authors note that it was not proportional to the increase in prostate size. The study concluded that Aquablation provides reproducible results in relatively uniform time regardless of prostate size or shape.

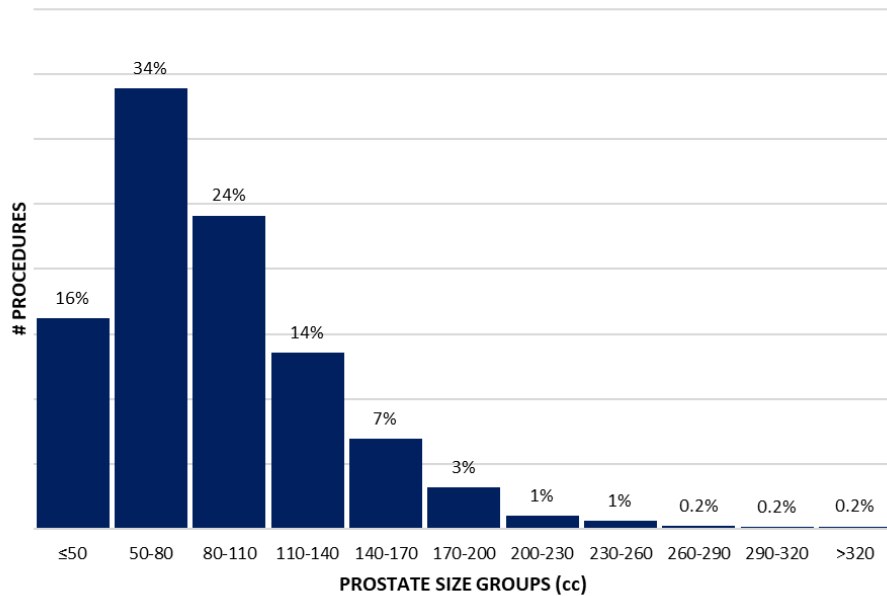
A published paper on surgical technique provides instruction on best practices for using Aquablation in patients with prostate volumes with prostates greater than 150 cc.¹⁴ Patient selection along with additional considerations and technique for these patients are discussed. These additional considerations and maneuvers are reported to be simple and follow the same planning and execution steps used during Aquablation for smaller prostates.

Because most commercial insurers that cover Aquablation do not limit access based on prostate volume, many surgeons already treat these large glands. Over the last few years, PROCEPT has tracked the number of procedures performed along with the size of the prostate treated. See Figure 1.

¹³ Helfand BT, et al.; Men with lower urinary tract symptoms secondary to BPH undergoing Aquablation with very large prostates (> 150 mL). Can J Urol. 2021 Dec;28(6):10884-10888.

¹⁴ Helfand BT, et al.; How I do it: Aquablation in very large prostates (> 150 mL). Can J Urol. 2022 Apr;29(2):11111-11115.

Figure 1: Prostate Size Histogram – U.S. Data
 1/1/2021 – 6/30/2023
 Avg: 92cc, Median: 80cc



Roughly 12% of Aquablation procedures were performed on very large prostates. In reviewing and discussing the outcomes of these procedures with the providers, the overall outcomes of improvement in symptom scores and peak urinary flow rates were reportedly comparable to those seen in Helfand et. al (2021), WATER and WATER II.

These findings for patients with prostates over 150 cc treated with Aquablation support the consistency with the outcomes obtained in smaller prostates. This consistency is exactly what one would expect for a surgical resection technique.

Proposed Language for the revision of the current LCD L38726:

1. Indications including all of the following:

~~Age ≤ 80~~

~~Prostate volume 30–150 cc by transrectal ultrasound (TRUS)~~

- a. Persistent moderate to severe symptoms despite maximal medical management including all of the following:
 - i. International Prostate Symptom Score (IPSS) ≥ 12
 - ii. Maximum urinary flow rate (Qmax) of ≤ 15 mL/s (voided volume greater than 125 cc)



- iii. Failure, contraindication or intolerance to at least 3 months of conventional medical therapy for LUTS/BPH

Limitations

The following are considered not reasonable and necessary:

1. Body mass index $\geq 42\text{kg/m}^2$
2. ~~Known or suspected prostate cancer (based on NCCN Prostate Cancer Early Detection guidelines) or a prostate specific antigen (PSA) $>10\text{ ng/mL}$ unless the patient has had a negative prostate biopsy within the last 6 months~~
2. Bladder cancer, neurogenic bladder, bladder calculus or clinically significant bladder diverticulum
3. Active urinary tract or systemic infection
4. Treatment for chronic prostatitis
5. Diagnosis of urethral stricture, meatal stenosis, or bladder neck contracture
6. Damaged external urinary sphincter
7. Known allergy to device materials
8. Inability to safely stop anticoagulants or antiplatelet agents preoperatively

Attached are relevant publications along with the updated FDA documentation. PROCEPT can facilitate a call with urologists to speak to their outcomes of Aquablation in this patient set. Please do not hesitate to contact me with any questions regarding the content of this request. Thank you for your consideration of this formal request for the revision of LCD L38726.

Sincerely,

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Appendix A: Age Limitation-Additional Considerations

As you consider the new information regarding the use of Aquablation in patients over 80, we also urge you to consider the potential that the lack of age limitations for other BPH interventions could skew treatment decisions, even if Aquablation provides a superior safety profile for patients over 80 years old. By removing the age limitation for transurethral waterjet ablation (Aquablation), NGS can better ensure that each patient and treating physician can select the best possible treatment option without counterproductive discrepancies between Medicare beneficiaries who happen to be, for example, 78 years old versus 81 years old.

The published data on Aquablation demonstrates the procedure is safe, reproducible and an effective treatment of LUTS due to BPH. More important, Aquablation is effective for the large prostates for which treatment options are limited. For most practicing urologists (greater than 98%) who do not perform HoLEP, Aquablation can be a reasonable choice to avoid the need for open simple prostatectomy on larger prostates. Other documented advantages include a short learning curve, procedure reproducibility through image guidance and robotic execution, shorter operative time (less than one hour) and shorter length of stay, all of which are potentially associated with decreased procedure-related morbidity — factors that are highly relevant to patients over 80 years old.

Considering the new data involving the treatment of individuals over 80 (described above), policymakers should take steps to remove any age-based limitations on Aquablation treatments for BPH. Individuals over 80 years old need access to the full spectrum of treatment options, especially given the direct association that exists between age and the disease burden of BPH. Elderly individuals with LUTS due to BPH often have a very limited set of clinical options, and transurethral waterjet ablation can provide a safer, less-invasive clinical option for patients suffering from LUTS due to BPH. Individuals who are over 80 years old should have access to this important therapy under the same clinical criteria that would apply to a similarly situated 79-year-old.

In addition to the clinical data, please consider the following:

- Palmetto (L38549), WPS (L38682), and CGS (L38378) have removed the age restriction.
- Noridian (DL38705/DL38707) and NGS (DL38367) have written draft policies removing the age restriction.
- The Defense Health Agency recently updated TRICARE's systemwide coverage policy to cover transurethral waterjet ablation of the prostate for the treatment of BPH without any limitation based on age.¹⁵
- Aquablation provides a superior safety profile for patients who are both over and under 80 years old. Currently, the LCD limits access to Aquablation for patients under 80, but other clinical options are not subject to age limitations, even if Aquablation provides a safer clinical option. By removing the age limitation for transurethral waterjet ablation,

¹⁵ Defense Health Agency, Military Health System. TRICARE Policy Manual 6010, 60-M. Chapter 4 Surgery, Section 14.1, Urinary System, Revision C-107, January 6, 2023. Available at: https://manuals.health.mil/pages/DisplayManualHtmlFile/2023-01-06/AsOf/TP15/C4S14_1.html

NGS can better ensure that each patient and treating physician can select the best possible treatment option without counterproductive discrepancies between Medicare beneficiaries who happen to be, for example, 78 years old versus 81 years old.

- There are two commercial health plans — Humana and Anthem Blue Cross Blue Shield — with positive coverage policies for Aquablation that have been effective for over 24 months with no age restrictions, as well as additional commercial health plans that have added coverage of transurethral waterjet ablation without age restrictions since FCSO finalized its current LCD, including, but not limited to, United, Cigna, Health Care Service Corporation, Highmark, CareFirst, and Florida Blue.
- There is nothing in the FDA-cleared labeling to support or require an age-based restriction. The FDA cleared the AQUABEAM[®] Robotic System for the resection and removal of prostate tissue in males suffering from LUTS due to BPH under a *de novo* request in December 2017 following completion of a randomized, double-blind clinical trial (WATER), which is detailed in this letter and included in the accompanying clinical package.¹⁶ The labeling reviewed and cleared by the FDA has no restrictions or limitations based on age, prostate size, or prostate shape.
- Recent publication of the five-year follow up data for the WATER¹⁷ and WATER II¹⁸ studies further highlight the benefits of Aquablation, including the potential benefits that one would expect to apply to patients over 80 years of age. For example, the five-year follow up revealed that 12.3 percent of patients treated with TURP required a subsequent intervention (procedure or medication) while only 6.0 percent of Aquablation patients required subsequent interventions over five years.

¹⁶ DEN170024, Online Medical Device Database, U.S. Food and Drug Administration, Available at:

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm?ID=DEN170024>

¹⁷ Gillling PJ, et al. Five-year outcomes for Aquablation therapy compared to TURP: results from a double-blind, randomized trial in men with LUTS due to BPH. *Can J Urol*. 2022 Feb;29(1):10960-10968.

¹⁸ Bhojani N, et al. Aquablation Therapy in Large Prostates (80-150 mL) for Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia: Final WATER II 5-Year Clinical Trial Results. *J Urol*. 2023 Apr 28, Epub ahead of print.