



PROACT[™]
ProACT[™] Adjustable Continence Therapy for Men

Physician Instructions for Use

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MEDICA

P/N: 900136 Rev. A

ProACT Physician IFU

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**ProACT™ Adjustable Continence Therapy for Men
INSTRUCTIONS FOR USE**

Rx Only

DEVICE DESCRIPTION

The ProACT system consists of the following components:

- Device (Figure 1): two implantable balloons, pre-mounted on push-wires (push-wires not shown). Provided sterile.
- Accessories: inflation syringe, 23-gauge needle, and an extra push-wire. All accessories are provided sterile in the package with the device.



Figure 1. ProACT balloons at varying inflation levels

Table 1 - ProACT Model Numbers

Model Number	Device Length	Description
800018-12	12 cm	ProACT Patient Pack: 2 implantable devices with needle and syringe
800018-14	14 cm	ProACT Patient Pack: 2 implantable devices with needle and syringe
800022-12	12 cm	ProACT Patient Pack: 1 implantable device with needle and syringe
800022-14	14 cm	ProACT Patient Pack: 1 implantable device with needle and syringe

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INDICATIONS FOR USE

The ProACT system is indicated for the treatment of adult men who have stress incontinence arising from intrinsic sphincter deficiency of at least twelve months duration following radical prostatectomy or transurethral resection of the prostate (TURP) and who have failed to respond adequately to conservative therapy.

CONTRAINDICATIONS

The ProACT system is contraindicated for use in patients:

- with active systemic or urinary tract infections,
- with incontinence due to detrusor instability or over activity,
- with reduced bladder compliance,
- with significant residual volume greater than 100cc after voiding,
- who are presently receiving, or plan to receive within 6 months, radiotherapy and those patients who have received radiotherapy within the last six months,
- with primarily urge incontinence,
- with a suspected bladder cancer,
- with unsuccessfully treated bladder stones,
- with hemophilia or bleeding disorders.

WARNINGS

- Do not re-sterilize. The device is an implantable device and is intended for a single use only. Re-sterilization could result in mechanical failure of the device and place the patient at undue risk of procedural failure.
- Do not fill balloons with contrast solution in patients with a known allergy to contrast solution. Use isotonic saline solution in place of contrast solution in patients with a known allergy to contrast solution.
- Do not use excessive force to advance or withdraw the ProACT device. If marked resistance is encountered, damage to the device can occur.
- To ensure appropriate device delivery, do not attempt to place or introduce the device without the supplied push-wire.
- Do not inflate the balloon with more than 8.0 ml of fluid. Higher volumes can result in balloon leakage.
- Do not handle the ProACT device with any sharp instruments or lay it against an abrasive material, which may damage the device.

- If urethral perforation occurs, do not place the device on the perforated side. The opposing, non-perforated side, may be implanted. Implant may proceed on the perforated side after the wound heals.
- Carefully evaluate the implant location:
 - Improper placement of the balloons can result in suboptimal results, patient discomfort, or problems with urinary retention or erosion.
 - Device wear or puncture may result if the balloon component of the ProACT device comes in contact with its tubing, another ProACT device, or other implantable materials such as surgical staples or suture.
- Device leak may result due to long-term calcification on the surface of the balloon.
- ProACT Adjustable Continence Therapy for Men is MR-Conditional. A patient with this device can be scanned safely in an MR (Magnetic Resonance Imaging) system immediately after placement under certain conditions as detailed in the MRI Information section provided in these Instructions for Use (IFU).
- Radiation therapy with ProACT devices in vivo may cause an increased risk of device erosion.

PRECAUTIONS

- Do not use the ProACT system prior to completely reading and understanding the Instructions for Use.
- Use only 23-gauge needles for balloon volume adjustments, or damage to the device may occur.
- The long-term safety and effectiveness of ProACT have not been established.
- Safety and efficacy of the ProACT device have not been determined for men who received adjuvant/salvage radiation therapy.
- The effectiveness of the ProACT device is reduced in the reimplant setting.
- The sterile packaging should be inspected prior to use. If the sterile packaging is damaged, do not use the device.
- The ProACT system should only be used by a physicians trained in urologic surgical procedures and specifically trained to perform the ProACT implantation procedure.
- Patients undergoing a surgical implantation of the ProACT device should be pre-medicated with an antibiotic to reduce the possibility of a post-operative infection.

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- Do not implant the ProACT device without the Uromedica, Inc. Implantation Instrument Set. Do not use the Implantation Instrument Set without prior cleaning and steam sterilization.
- Do not implant a single ProACT balloon (unilateral implantation) EXCEPT in the case of urethral perforation on the opposing side. If a urethral perforation does occur on one side, do not implant the patient on the perforated side until the wound has healed.
- Maintain sterility throughout the procedure.
- Do not grasp the port or strain relief with clamps.
- If the Implantation Instrument Set is misdirected during dilation of the tissue, perforation of the bladder, urethra, or rectum may occur.
- Use of either isotonic saline or the correct solution of sterile water and contrast media is required to provide an isotonic solution for inflation of the ProACT balloons. See attached reference chart (Appendix A) for contrast media dilution instructions.
- To maintain isotonicity, use the same inflation media (diluted contrast media or saline) when performing a balloon volume adjustment as was used during the initial inflation.

ADVERSE EVENTS

The following three serious adverse events related to the device or procedure were observed in the Clinical Study:

Table 2 - Device or Procedure Related Serious Adverse Events through the 18 Months

Event Type	Device or Procedure Relatedness	Events	Patients with an Event	
		N	N	%
Retention	Device or Procedure Related	1	1	0.8
Low Heart Rate	Not device related; procedure related unknown	1	1	0.8
Ulcerative colitis	Not procedure related; device related unknown	1	1	0.8

Table 3 - Device or Procedure Related Adverse Events Reported through 24 Months

There were 574 total adverse events reported through 24 months in 114 of 123 implanted subjects. Ninety-eight patients experienced adverse events that were non-serious and that were related, or possibly related, to the device or procedure. Patients may have experienced more than one adverse event.

Adverse Event	Patients with an Event		Events N	Device-Related			Procedure-Related		
	N	%		Yes	Ukn	No	Yes	Ukn	No
Total	98	79.7%	310	155	78	77	105	64	141
Pain or discomfort	33	26.8%	44	13	18	13	16	10	18
Worsening incontinence	35	28.5%	38	19	15	4	9	9	20
Device migration	23	18.7%	35	34	0	1	3	10	22
Urinary retention	19	15.4%	24	13	5	6	8	7	9
Perforation of bladder or urethra	19	15.4%	23	0	0	23	23	0	0
Device failure	18	14.6%	21	19	1	1	5	1	15
Device leakage	15	12.2%	17	17	0	0	1	1	15
Difficulty urinating	10	8.1%	12	8	4	0	1	4	7
Device erosion	11	8.9%	12	11	1	0	2	3	7
Urinary urgency	11	8.9%	11	2	9	0	4	4	3
Urinary frequency	10	8.1%	10	1	4	5	6	3	1
Urinary tract Infection	8	6.5%	8	2	5	1	1	2	5
Erythema of perineum, penis, or scrotum	6	4.9%	7	1	3	3	6	0	1
Device occlusion	3	2.4%	3	3	0	0	0	0	3
Hematuria	3	2.4%	3	1	2	0	0	1	2
Induration in perineum or scrotum	3	2.4%	3	1	1	1	2	0	1
Abdominal pain	2	1.6%	2	0	1	1	1	1	0
Allergic reaction to antibiotic	2	1.6%	2	0	0	2	2	0	0

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Bladder spasm	2	1.6%	2	0	2	0	0	1	1
Cellulitis	2	1.6%	2	0	0	2	1	1	0
Procedural failure	2	1.6%	2	1	0	1	1	0	1
Anesthetic-related bradycardia	1	0.8%	1	0	0	1	0	1	0
Asymptomatic heart murmur	1	0.8%	1	0	0	1	0	1	0
Bruising of the scrotum	1	0.8%	1	0	0	1	1	0	0
Decreased urine stream	1	0.8%	1	0	1	0	0	0	1
Device kinking	1	0.8%	1	1	0	0	1	0	0
Doesn't feel empty after urinating	1	0.8%	1	1	0	0	0	0	1
Drainage from incision site	1	0.8%	1	0	1	0	0	0	1
Ecchymosis	1	0.8%	1	1	0	0	1	0	0
Enuresis	1	0.8%	1	0	1	0	0	0	1
Fever 100 degrees	1	0.8%	1	0	1	0	0	1	0
Foley greater than 24 hours	1	0.8%	1	1	0	0	1	0	0
Increased incontinence due to urge	1	0.8%	1	0	1	0	0	0	1
Infection: Proximal portion of surgical site for the ProACT	1	0.8%	1	0	0	1	1	0	0
Infection: Superficial infection at site of induration right scrotum	1	0.8%	1	0	0	1	1	0	0
Infection: Superficial scrotal infection	1	0.8%	1	1	0	0	0	0	1
Inguinal hernia	1	0.8%	1	0	0	1	1	0	0
Minor bleeding at incision site	1	0.8%	1	0	0	1	1	0	0
Not passing urine through catheter	1	0.8%	1	0	0	1	1	0	0
Numbness at incision site	1	0.8%	1	0	0	1	1	0	0

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Numbness at the end of penis	1	0.8%	1	1	0	0	0	1	0
Other (no improvement of incontinence symptoms)	1	0.8%	1	1	0	0	0	0	1
Pulmonary edema	1	0.8%	1	0	0	1	1	0	0
Purulent discharge from Foley catheter	1	0.8%	1	0	0	1	1	0	0
Residual volume	1	0.8%	1	0	1	0	0	0	1
Scrotal incision opened	1	0.8%	1	0	0	1	1	0	0
Small hemorrhagic cerebrovascular accident	1	0.8%	1	0	0	1	0	1	0
Swelling of right side of perineum	1	0.8%	1	1	0	0	0	1	0
Ulcerative colitis	1	0.8%	1	0	1	0	0	0	1
Urine dribbling	1	0.8%	1	1	0	0	0	0	1

In addition to the observed adverse events mentioned above, the ProACT system carries the following potential risks:

- | | |
|---|--|
| Allergic response (material, contrast media, antibiotic, other) | Induration at site of the port (perineum, scrotum) |
| Anesthesia risks (general, spinal) | Infection (urinary tract, wound) |
| Bladder spasm | Pain or discomfort from balloon or port |
| Cellulitis | Perforation (bladder wall, urethra, rectum) |
| Device calcification | Prosthetic infection |
| Device malfunction/leakage/occlusion | Prosthetic migration |
| Device wear | Sepsis |
| Erosion of tissue (bladder wall, bowel, perineum, rectum, scrotal, urethral, other) | Ulcerations (skin incision) |
| Erythema, swelling | Urethral stricture |
| False channel creation | Urinary difficulty, retention |
| Hematuria | Urinary urgency, frequency |
| Hematoma at the site of entry | Worsened incontinence |

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There were two device-related unanticipated adverse events during the clinical study. In two patients, the balloon separated from the tubing of the device during explantation. All other device-related adverse events were anticipated.

There were no device- or procedure-related deaths in the ProACT clinical study.

CLINICAL STUDIES

The ProACT pivotal IDE trial was a prospective, multi-center, single-arm study. One hundred and sixty subjects were enrolled. Of these 160 enrolled subjects, 124 subjects at 11 clinical sites qualified for implantation (68 subjects at 8 US sites and 56 subjects at 3 sites outside the US), and 123 subjects were implanted.

The primary efficacy endpoint was evaluated at 18 months after initial implantation. Patient follow-up continued annually for a median of 63.9 months (mean 58.6 months).

The patient population consisted of adult males, primarily white (90%), with an average age of 70 (50-93 years). Mean baseline 24-hour pad weight was 399 g (SD 435, range 9 – 2483 g).

Primary Efficacy Endpoint

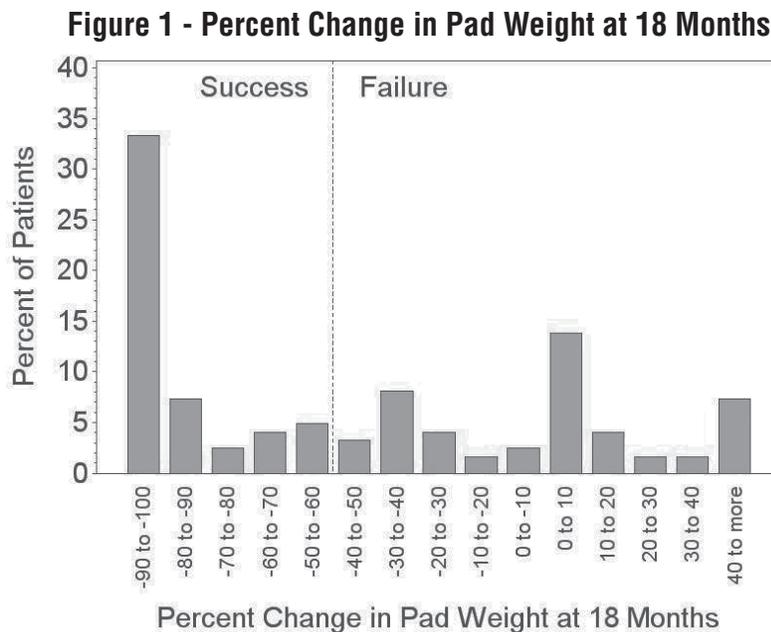
The primary efficacy endpoint was defined as the percentage of patients with \geq 50% reduction in 24-hour pad weight at 18 months from initial implantation. The table below presents intent-to-treat (ITT) analysis results. All patients for whom implantation was attempted (124) are included in this analysis. Patients were considered failures if they were explanted (regardless of whether or not they were reimplanted), withdrew from the study, were lost to follow-up, or died prior to their 18-month follow-up date. The table below summarizes these ITT results.

Table 4 - Primary Efficacy Overview at 18 Months (Intent to Treat)

	Result
24-hour Pad Weight Reduction of \geq 50% (all reimplants as failures)	
Patients with 50% or more reduction (n/N, %)	57/124, 46.0%
95% confidence interval	(37.0%, 55.1%)
Exact one-sided p-value testing $>$ 50%	0.82

In addition to the above analysis, the efficacy results in a cohort of 86 subjects with 100 grams or greater of urine loss in a 24-hour pad weight test at baseline was conducted on FDA recommendation. In this cohort of 86 patients with an average pre-implant urine loss of 552 grams in 24-hours, 24/86 (28%) improved to less than 30 grams at 18 months.

The distribution below indicates that approximately one third of patients achieved a large reduction (90-100%) in their 24-hour pad weight from baseline. Patients who were explanted, died, or withdrew prior to 18 months are counted within the 0-10% change in pad weight category.



Secondary Efficacy Endpoints

The secondary efficacy endpoints for the ProACT pivotal IDE trial were: change in number of pads per day, change in number of incontinence episodes per day, change in quality of life (as measured by the I-QoL validated questionnaire), change in urinary function (as measured by the UCLA-PCI questionnaire), and assessment of the effects of the ProACT device on sexual functioning (as measured by the International Index of Erectile Function (IIEF)).

All secondary endpoints outcomes are given in the table on the next page.

**Table 5 - Secondary Endpoints, Change at 18 Months
(Intent-to-Treat Cohort, n=124)**

	Number of Incontinence Episodes per Day	Number of Pads Used per Day¹	Incontinence Quality of Life	International Index of Erectile Function	UCLA-PCI Urinary Function
Baseline Mean	9.9	4.1	49.9	16.7	21.7
SD (range)	6.0 (0.0, 24.0)	2.3 (1.0, 13.0)	22.7 (6.0, 97.7)	15.9 (2.5, 69.0)	16.2 (0.0, 63.4)
18 Month Mean	6.0	2.4	72.9	16.2	48.9
SD (range)	7.3 (0.0, 24.0)	1.8 (1.0, 10.0)	25.9 (6.8, 100.0)	13.9 (2.5, 70.0)	30.0 (0.0, 100.0)
Mean Change	3.8	1.7	23.0	-0.4	27.2
SD (range)	7.2 (-20.3, 23.8)	2.3 (-3.0, 9.5)	28.5 (-34.3, 94.0)	11.0 (-54.0, 46.0)	28.6 (-26.6, 100.0)

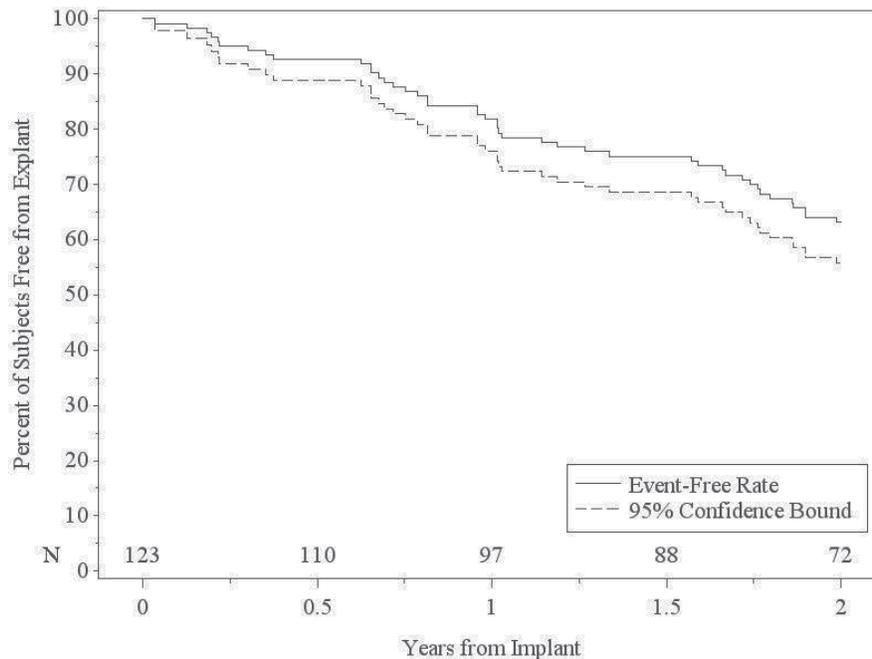
¹Patients had to wear at least one pad for pad weight test, so zero pads would not occur.

Explantation, Reimplantation, and Long-term Device Survival

Twenty-two subjects were explanted and reimplanted with the ProACT device prior to the 18-month study endpoint. At the 18 month endpoint, reimplanted subjects had a much lower success rate than the success rate in subjects with index devices only.

In the ProACT pivotal IDE trial, 8 of 123 implanted subjects were permanently explanted prior to the 18 month study endpoint.

The graph below depicts the survival in vivo of index devices over time. For example, at one year post implant, 82% of the implanted subjects had their index devices still implanted (not explanted), with a lower one-sided 95% confidence interval of 76%.

Figure 2 - Kaplan-Meier Probability of Remaining Free of Device Explant

Balloon Volume Adjustments in the Clinical Study

Balloon volume adjustments are necessary for gradual balloon inflation to a therapeutic level. Adjustments involved inserting a needle through the skin into the ports of each ProACT balloon and adding or removing fluid. Adjustments were initially expected to be completed within six months of implant. However, many adjustments were performed beyond 6 months after implantation.

Subgroup Analyses

The effects of a number of variables on the primary efficacy endpoint (50% reduction in pad weight at 18 months) and the primary safety endpoint (complications between implant and 18 month) were analyzed. The variables included the following:

- age
- body mass index
- type of prior prostate surgery

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- time since prior prostate surgery
- previous incontinence severity
- baseline incontinence severity
- urodynamic parameters
- receiving balloon volume adjustments between 6-18 months
- having devices explanted and reimplanted within 18 months.

Receiving balloon volume adjustments between 6-18 months was a factor associated with a higher probability of efficacy. This association was since late-occurring adjustments would be anticipated in patients who had poorer outcomes and who were seeking to achieve a therapeutic benefit. Factors associated with higher complication rates included (1) body mass index > 25kg/m², (2) less than one year since prior prostate surgery, (3) more severe incontinence at baseline, (4) receiving balloon volume adjustments between 6-18 months, and (5) having devices explanted and reimplanted within 18 months. In general, patients with severe or moderate incontinence at baseline had more complications than patients with mild incontinence. Furthermore, ProACT reimplants and re-adjustments were associated with lower success relative to the index ProACT devices.

MRI Information



MR Conditional

Non-clinical testing demonstrated that the ProACT system is MR Conditional. A patient with this device can be scanned safely in an MR system immediately after placement under the following conditions:

- Static magnetic field of 3-Tesla or less
- Maximum spatial gradient magnetic field of 10,000-Gauss/cm (extrapolated) or less
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 4-W/kg for 15 minutes of scanning (i.e., per pulse sequence) in the First Level Controlled Operating Mode of operation for the MR system
- Under the scan conditions defined about the ProACT device is expected to produce a maximum temperature rise of 1.6°C after 15-minutes of continuous scanning (i.e., per pulse sequence).

Artifact Information

In non-clinical testing, the image artifact caused by the ProACT device extends approximately 10-mm from the ProACT device when imaged using a gradient echo pulse sequence and a 3-Tesla MR system.

Instructions for Implantation

Equipment Requirements

- Image Intensifier and sterile cover
- Sterile drill sleeve (Optional for Post Radical Prostatectomy, essential for post Transurethral Resection or enucleation)
- Camera and light source

Device Requirements

- 2 kits each size (12 cm and 14 cm) ProACT device (dual patient pack kits) recommended

Instrument Requirements

- Basic rigid cystoscopy set up
- Regular surgical instrument set
- No. 10 blade and handle
- Debakey Forceps
- Rubber shod plain forceps
- Adson Forceps
- Cairns Tissue Forceps
- McIndoe / Metzenbaum Scissors
- Dressing Scissors
- 7" Needleholder
- Uromedica Implantation Instruments:
 - Implantation Instrument Set
 - U-Channel Sheath
 - Sharp Trocar
 - Blunt Trocar
 - Tissue Expanding Device

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Accessories

- Jug
- Gallipots x2
- Kidney dish x2
- Bladder syringe
- 10 ml syringe
- 3-0 Vicryl rb needle
- 4-0 skin suture

Solutions

A) One (1) liter H₂O or saline bag for cystoscopic irrigation.

B) Solution of contrast and sterile water for injection mix (see Appendix A for example solutions). **In the case of a patient with a contrast allergy, use isotonic saline only.**

C) Five hundred (500) ml of 0.9% saline for injection with 80g Gentamycin (or equivalent) for soaking ProACT device. This can be prepared in a jug and then poured into a kidney dish. Devices should not be exposed to the air for long periods of time.

D) Two hundred and fifty (250) ml normal saline for irrigation with 50 – 100 ml of contrast. Two hundred (200) ml is used for visualizing the bladder, and a further 50 ml will be used for the urethrogram. **In the case of a patient with a contrast allergy, use isotonic saline only.**

Cleaning and Sterilization of Surgical Tools

Recommended sterilization for reusable surgical tools: The Uromedica surgical tools are supplied non-sterile. Clean and sterilize the tools before first use and after each use. Follow the cleaning and sterilization instructions provided within the labeling for each of the surgical tools. General guidelines are listed below and other recommended guidelines may be available within your facility. For first time use, begin with Step 5 below. For all subsequent uses, begin with Step 1 below.

1. Immediately after removal of the surgical tools from the patient, separate the sharp-tipped trocar from the U-channel sheath.
2. Immerse and soak the instrument components in warm tap water (20 - 40°C) and pH neutral enzymatic detergent for 10 minutes. Follow detergent manufacturer's recommendations for concentration levels.

3. With instruments completely immersed, scrub all individual components for 5 minutes with a soft bristle brush to visually remove any contaminant. Use tight-fitting brushes to get inside the grooves, crevices, and hinge locations. Note: Pay special attention to crevices and slots.
4. Visually inspect each component to verify that the cleaning steps have properly removed blood or other visible contaminant. Do not proceed if instruments are not visibly clean.
5. For 30 seconds, rinse the components thoroughly with warm tap water (20 - 40°C).
6. For 10 minutes, ultrasonically clean the component in room temperature purified water (Ultrafilter, RO, DU, and/or distilled) and pH neutral enzymatic detergent. Follow the detergent manufacturer's recommendations for the correct concentration levels.
7. For 1 minute, rinse the components thoroughly with room temperature purified water (Ultrafilter, RO, DU, and/or distilled).
8. Visually inspect each component for any residual contaminants. If any residual contaminants remain on the components, repeat steps 2 -7.
9. Dry the components using a low linting, non-abrasive soft cloth to minimize contamination that could occur from wet instruments.
10. As needed, dip components into lubricant/rust inhibitor.
11. Pack and steam sterilize the Implantation Instrument(s). Make sure that the parts are separated, including the actuating jaw for the Tissue Expanding Device. The individual parts may be sterilized in the same package.
12. Steam sterilize pre-vacuum cycle at 132° - 135° C for a minimum of three [3] minutes.

Preparing the Patient

1. Start oral antibiotic therapy prior to anesthesia.
2. Place patient in lithotomy position with acute abduction to enable access to perineum. Shave performed at discretion of surgeon.
3. Prep perineal and groin region using Betadine. Position and drape C arm.

Administering Anesthetic/Cystourethroscopy

1. Administer either general or spinal anesthetic which should be the preference of the urologic surgeon.
2. Perform cystourethroscopy (Solution A). Drain bladder and inflate a Foley catheter to 100 - 200cc using a bladder syringe and Solution D. Cystoscope sheath/obturator retained in place during procedure to visualize and palpate the urethra.

Preparing the Contrast Media (Solution B)

Note: In the case of a patient with a contrast allergy, use isotonic saline only.

Prepare an isotonic filling solution by diluting a contrast media chosen from Appendix A with the prescribed amount of sterile water. The full volumes indicated need not be mixed but the ratios should remain the same so that water does not pass into or out of the device over time due to osmosis. Larger volumes facilitate more accurate mixing.

Implantation in Post Radical Prostatectomy Patients

1. Two transverse perineal incisions are made about 1 cm long and 1 cm posterior to base of the scrotum, immediately posterior to urethra on either side of the midline.
2. Metzenbaum / McIndoe scissors to dissect adipose and muscle layers on each side of the midline.
3. Using finger palpation (or Metzenbaum Scissors) through the incision, identify the tip of the fascial triangle created between the urethra and inferior pubic rami. Using a pair of artery forceps, open the incision large enough to allow the introduction of the U-Channel Sheath. The U-Channel Sheath should be directed toward the inferior pubic rami and should push through the pelvic floor.
4. Advance the U-Channel Sheath (with sharp trocar) and, using controlled force and a twisting motion (rather than pushing), move proximally towards the bladder neck. By retaining the cystoscope in a horizontal position, you can use this as a guide by directing the Implantation Instrument parallel in a superolateral plane to the membranous urethra. Use fluoroscopy frequently to observe position and avoid bladder or

urethral perforation or being more lateral than 5 mm or too medially into the urethra. Given the expected presence of scar tissue around the bladder neck, the manipulation of the Implantation Instrument should be done slowly using only a twisting motion to prevent bladder perforation. As fluoroscopy creates only a 2 dimensional view, it is not possible to distinguish whether the trocar tip is anterior or posterior to the bladder neck. Once the tip of the sharp trocar appears to be at the bladder neck, stop and remove the sharp trocar. Extra care should be taken in reaching the last 0.5 cm to 1 cm distal to the bladder neck, as this is where bladder perforation is most likely to occur. The blunt trocar can be used to advance the last 0.5 to 1.0 cm up to the bladder neck to reduce the likelihood of perforation of the bladder or urethra. Urethral or bladder perforation can be identified when the internal trocar is removed and urine is lost out of the U-channel sheath. In the event that a urethral perforation occurs, the U-channel sheath should be withdrawn gently, and a balloon should not be implanted on the perforated side. Once recognized, the perforation can be treated by the placement of a urethral Foley catheter for three (3) days.

5. On removal of the internal trocar, it is important to advance gently the U-Channel sheath proximally to occupy the space created by the tip of the internal trocar. At this point, if the patient has fibrotic tissue, the Tissue Expanding Device (TED) may be used to dilate the tissue, creating a space for the ProACT balloon. The TED can be locked within the U-Channel sheath. The TED handles are then squeezed together to open the jaw, facilitating tissue dilation. Failure to dilate the tissue may cause undue pressure on the balloon surface, causing a distal migration of the balloon on inflation.
6. ProACT sizing is determined using the 1cm incremental markings on the internal trocar, measuring the length of the periurethral space. An additional 4 cm should be added to total length to accommodate the positioning of the ProACT port from the incision. (Usually size 14 cm is required.)

REMINDER: Both devices implanted must be the same length.

7. Prime the devices. Remove device from packet, and, draw using prepared isotonic filling solution (Solution B) into the syringe provided. Attach 23-gauge non-coring needle (included) to syringe and inflate up to 1.5 ml into the balloon via the port. Hold the syringe with plunger towards the

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ceiling, and withdraw solution and any air bubbles. Micro bubbles will not affect device. Aim to remove all the air leaving a fluid lining within the ProACT device. Once primed, remove the needle and syringe, and submerge in antibiotic solution (Solution C).

8. Remove one device from the antibiotic solution and ensure that the push-wire is pushed to the tip of the balloon. Lubricate and slide device along U-channel sheath trough, with one of the three “wings” of the primed balloon at the 6 o’clock position relative to the U-Channel sheath. Push on the push-wire rather than the tubing between the balloon and the port. This will keep the push-wire in correct position and ease delivery of the device. Check that the balloon is at the bladder neck using fluoroscopy. Once the balloon is in the correct position, the U-Channel sheath should be pulled back approximately 2 cm to allow for the balloon to be unencumbered during inflation. Prior to inflating the balloon, check to see that the balloon has not moved back with the 2 cm withdrawal of the U-Channel sheath. Inflate the balloon using a needle to inject up to 1.5 ml of Solution B into the port. Check the position and inflation using fluoroscopy again. Leaving the push-wire in place, move to the contralateral side.

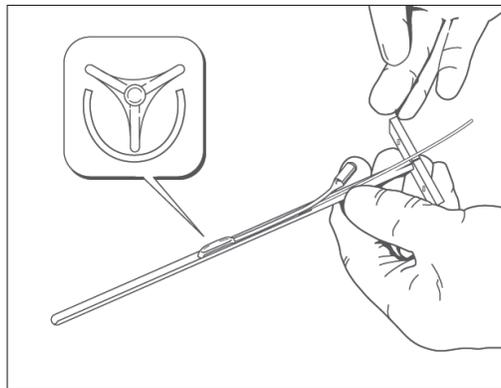


Figure 3 - ProACT device in U-channel with one “wing” in 6 o’clock Position

9. Repeat the procedure on the contralateral side. Once the second balloon is in place, use fluoroscopy to check that both balloons are positioned correctly. If one or both balloons are judged to be too distal to the bladder neck, deflate the balloon, remove the device (soak in antibiotic), and re-dilate the same tract using the Implantation Instrument to enable placement

at a more proximal position at the bladder neck. If the balloons are in the correct position, remove the push-wires.

10. Confirm the absence of urethral perforation by cystoscopic examination. If a urethral perforation has occurred, the balloon on the side of the perforation must not be implanted or must be removed if already implanted (see precautions and warnings).

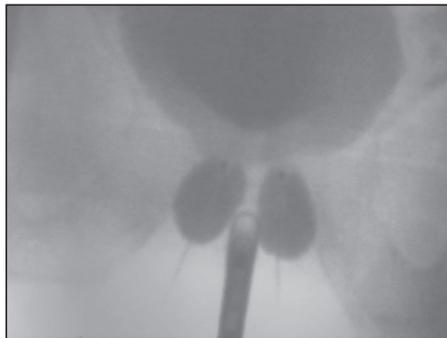


Figure 4 - Properly Positioned ProACT Balloons with Rigid Cystoscopy Sheath

11. Remove the cystoscope and perform a urethrogram using Solution D through a bladder syringe to identify urethral closure effect created by the balloons. It is believed that a pseudo-capsule will form around the balloons after approximately four to six weeks. This allows for further adjustments even though total continence may not occur initially. Edema may result from the surgical trauma, which if combined with pressure resulting from over inflation of the devices may cause tissue necrosis. Some patients may be initially dry because of post procedural edematous effect but become incontinent after the edema has subsided.
12. A cystourethroscopy may be performed. Gentle manipulation of the ports will identify location of the balloons relative to the urethra.
13. Using artery forceps, create a pocket passing from the initial incision into the postero-lateral wall of the scrotum to place the ports. Ports should be placed under the skin in the scrotum so that they will not cause discomfort to the patient when seated, and should be superficial enough to permit easy access should further adjustment be necessary. Care should be taken when handling the port so as not to tear the silicone. Rubber shod clamps or forceps should be used when grasping the ports during implantation.

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14. Close the incision in two layers using 3-0 resorbable suture for the subcutaneous tissue and 4-0 resorbable suture for the skin. Dressing applied.
15. Post-operatively, the patient should receive the initially given oral antibiotic.
16. Confirm the patient can void spontaneously. If the patient cannot void spontaneously, place a Foley catheter until anaesthesia effects have subsided, then have patient void. If the patient is still unable to void, decrease the balloon volume in 0.5 ml increments from both balloons until spontaneous voiding is achieved.

Implantation in patients who have undergone Transurethral Resection or enucleation for Benign Prostatic Hyperplasia

1. Two transverse perineal incisions are made, each about 1cm long and 1cm posterior to base of the scrotum, immediately posterior to urethra.
2. Metzenbaum / McIndoe scissors are used to dissect adipose and muscle layers on each side of the midline.
3. Using finger palpation through the incision, identify the tip of the fascial triangle created between the urethra and inferior pubic rami. Using a pair of artery forceps, open the incision large enough to allow the introduction of the U-Channel Sheath (with sharp trocar). The U-Channel Sheath should be directed toward the inferior pubic rami and should push through the pelvic floor.
4. Advance the U-Channel Sheath (with sharp trocar) and, using controlled force and a twisting motion (rather than pushing), move proximally towards the prostatic remnant. By retaining the cystoscope in a horizontal position, you can use this as a guide by directing the Implantation Instrument parallel in a superolateral plane to the membranous urethra. Care should be taken to avoid puncturing the prostate. Use fluoroscopy frequently to observe position and avoid bladder or urethral perforation or being more lateral than 5mm or too medially into the urethra. The absence of scar tissue should allow for the creation of a space at the level of the membranous urethra, lateral to the external sphincter and dorsolateral to the apex of the prostatic remnant. The use of fluoroscopy can assist in determining the length of the prostatic urethra in order to estimate anatomic position of the apex more easily. The measurements should be taken when the trocar

is stationary, as the prostate and bladder base will move when prodded by the trocar. Once the tip of the sharp trocar appears to be at the level of the apex, stop and remove the sharp trocar. A space can be created by a simple maneuver of the U-Channel sheath. Extra care should be taken in reaching the last 0.5 cm to 1 cm distal to the apex of the prostate, as this is where perforation is most likely to occur. The blunt trocar can be used to advance the last 0.5 to 1.0 cm up to the apex of the prostate to reduce the likelihood of perforation. Perforation can be easily identified when the internal trocar is removed and urine is lost out of the U-channel sheath. In the event that this occurs, the U-channel sheath should be withdrawn gently, and the ProACT device should not be implanted until perforation is healed. Once recognized, the perforation can be treated by the placement of a urethral Foley catheter for three (3) days.

5. On removal of the internal trocar, it is important to advance gently the U-Channel sheath proximally to occupy the space created by the tip of the internal trocar. At this point, if the patient has fibrotic tissue, the Tissue Expanding Device (TED) can be used to dilate the tissue, creating a space for the ProACT balloon. The TED can be locked within the U-Channel sheath. The TED handles are then squeezed together to open the jaw, facilitating tissue dilation. Failure to dilate the tissue may cause undue pressure on the balloon from the fibrotic tissue, causing a distal migration of the balloon on inflation.
6. ProACT sizing is determined using the 1cm incremental markings on the internal trocar. An additional 4 cm should be added to the total length to accommodate the positioning of the ProACT port from the incision. (Usually size 14 cm is required.)
REMINDER: Both devices implanted must be the same length.
7. Prime the devices. Remove device from packet, and using prepared isotonic filling solution (Solution B), draw solution into the syringe. Attach non-coring needle (included) to syringe and inflate up to 1.5 ml into the balloon via the port. Hold the syringe with plunger towards the ceiling, and withdraw solution and any air bubbles. Micro bubbles will not affect device. Aim to remove all the air leaving a fluid lining within the ProACT device. Once primed, remove needle and syringe, and submerge in antibiotic solution (Solution C).

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8. Remove one device from the antibiotic solution and ensure that the push wire is pushed to the tip of the balloon. Lubricate and slide device along U-channel sheath trough, with one of the three 'wings' of the primed balloon at the 6 O'clock position relative to the U-Channel sheath. Push on the push wire rather than the tubing between the balloon and the port. This will keep the push wire in the correct position and ease delivery of the device. Check that the balloon is exterior to the prostatic fossa at the level of the apex using fluoroscopy. Once the balloon is in the correct position, the U-Channel sheath should be pulled back approximately 2 cm to allow for the balloon to be unencumbered during inflation. Prior to inflating the balloon, check to see that the balloon has not moved back with the 2 cm withdrawal of the U-Channel sheath. Inflate the balloon by using a needle to inject up to 1.5 ml isotonic solution (Solution B) into the port. Check position and inflation using fluoroscopy again. Leaving the push wire in place, move to the contralateral side.

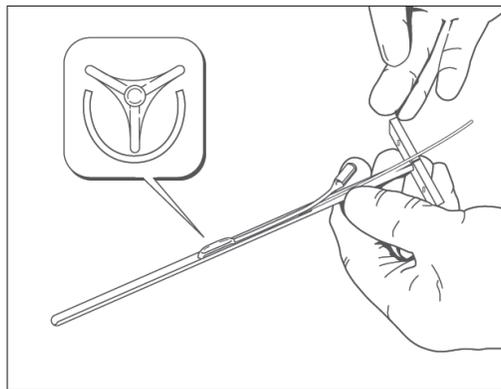


Figure 5 - ProACT device in U-channel with one "wing" in 6 o'clock Position

9. Repeat the procedure on contralateral side. Once the second balloon is in place check using fluoroscopy to make sure both are positioned correctly. If one or both balloons are judged to be too distal to the apex of the prostatic remnant, deflate the balloon, remove the device (soak in antibiotic) and re-dilate the same tract using the Implantation Instrument to enable placement at a more proximal position at the bladder neck. If the balloons are in the correct position, remove the push wires.

10. Confirm the absence of urethral perforation by cystoscopic examination. If a urethral perforation has occurred, the balloon on the side of the perforation must not be implanted or must be removed if already implanted (see precautions and warnings).
11. Remove cystoscope and perform a urethrogram by injecting (Solution D) through bladder syringe to identify urethral closure effect created by balloons. It is believed that a pseudo-capsule will form around the balloons after approximately four to six weeks. This allows for further adjustments even though total continence may not occur initially. Edema may result from the surgical trauma, which if combined with pressure resulting from over inflation of the devices may cause tissue necrosis. Some patients may be initially dry because of this post procedural edematous effect but become incontinent after the edema has subsided.
12. A cystourethroscopy may be performed. Gentle manipulation of the ports will identify location of the balloons relative to the urethra.
13. Using artery forceps, create a pocket passing from the initial incision into each postero-lateral wall of the scrotum in order to place the ports. Ports should be placed under the skin in the scrotum so that they will not cause discomfort to the patient when seated, and should be superficial enough to permit easy access should further adjustment be necessary. Care should be taken when handling the port so as not to tear the silicone. Rubber shod clamps or forceps should be used when grasping the ports during implantation.
14. Close the incision in two layers using 3-0 resorbable suture for the subcutaneous tissue and 4-0 resorbable suture for the skin. Dressing applied.
15. Post-operatively, the patient should receive the initially given oral antibiotic.
16. Confirm the patient can void spontaneously. If the patient cannot void spontaneously, place a foley catheter until anesthesia effects have subsided, then have patient void. If patient is still unable to void, decrease balloon volume in 0.5 ml increments from both balloons until spontaneous voiding is achieved.

Balloon Volume Adjustment Visits

The table below contains a suggested adjustment schedule.

NOTE: Increases in balloon volumes should be stopped once the patient is satisfied with their continence OR both of the balloons have been filled to their maximum volume of 8.0 ml each, whichever occurs first. For instance, if a patient is satisfied with 2.0 ml in each balloon, do not perform additional balloon volume adjustments.

NOTE: Progressive increases in balloon volumes should result in a gradual decrease in urine leakage. If no or very minimal clinical improvement is observed with increases in balloon volumes, the ProACT balloons may be incorrectly positioned. When each balloon volume has reached 4.5 ml and if no improvement has yet been observed, the device should be imaged via X-ray to confirm proper placement of the balloons. If the balloons appear misplaced, revision may be indicated.

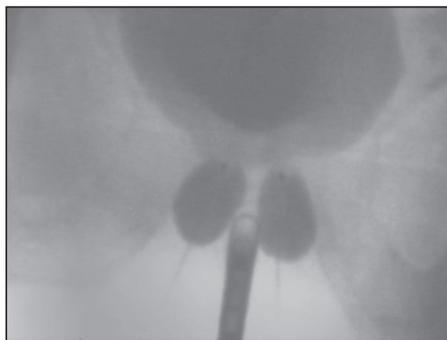


Figure 6 - Image of Proper Device Positioning (X-ray)¹

WARNING: Use only a 23-gauge needle for post-operative balloon volume adjustments. Use of other needles may result in damage to the ProACT device.

WARNING: Do not exceed 8.0 ml in either balloon at any time. Exceeding this maximum increases the risk of device failure.

CAUTION: Rapid increases in balloon volumes may increase the risk of device migration down the surgical tool dilation path.

1 Giammo et al. J. Urology. Vol. 183, 1921-1926, May 2010.

Table 6 - Suggested Adjustment Schedule

Visit	Timing after Implant	Recommended Incremental Volume Increase per Balloon (ml)	Maximum Incremental Volume Increase per Balloon (ml)
Initial Implant		1.0	1.5
6 week Visit	6 weeks	0.5	1.0
Adjustment Visit	Every 4 Weeks, <i>as required</i>	0.5	1.0

Adjustments to the volume of the ProACT balloons to achieve therapeutic results should not occur until 6 weeks after implant. Thereafter, it is recommended that adjustments be considered at 4 week intervals until the desired result is achieved. Adjustments may be up to 1.0 ml per balloon, per visit after the initial implant adjustment.

Several adjustments during the first 6 months post implantation should be expected to attain an optimal clinical result for each subject. Lower incremental adjustment volumes may result in a longer adjustment period. You may require additional adjustments (to a maximum volume of 8.0 ml per balloon) beyond 6 months post implantation to achieve an optimal clinical result.

Symptoms identified at or between follow-up visits (e.g., urinary retention or symptoms of incontinence (leaking)) should initiate the process for determining whether adjustment should be made. For subjects presenting with urinary retention, the volume of each balloon should be reduced in 0.5 ml increments until retention is alleviated.

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Appendix A

Contrast Media	Amount	+	Sterile H₂O
Cysto-Conray®	8ml	+	17ml
Cysto-Conray® II	19ml	+	6ml
Iomeron® 200	19ml	+	6ml
Iomeron® 250	18ml	+	7ml
Iomeron® 300	16ml	+	9ml
Iomeron® 350	14ml	+	11ml
Iomeron® 400	13ml	+	12ml
Isovue® 200	19ml	+	6ml
Isovue® 250	15ml	+	10ml
Isovue® 300	14ml	+	11ml
Isovue® 370	12ml	+	13ml
Omnipaque™ 140	23ml	+	2ml
Omnipaque™ 180	19ml	+	6ml
Omnipaque™ 240	16ml	+	9ml
Omnipaque™ 300	13ml	+	12ml
Omnipaque™ 350	11ml	+	14ml
Ultravist® 150	23ml	+	2ml
Ultravist® 240	17ml	+	8ml
Ultravist® 300	14ml	+	11ml
Ultravist® 370	12ml	+	13ml

WARNING: In patients with known allergy to contrast solution, fill balloons with isotonic saline in place of contrast solution.

Made in USA. US Patents apply.

Covered by U.S. Patent Nos. 5,964,806; 6,045,498; 6,645,138; 7,828,716 and patents pending. When used in conjunction with implantation apparatus, covered by U.S. Patent Nos. 6,419,624; 6,579,224; 7,364,540; 7,481,762; 7,014,606; 7,771,346; 8,926,494 and patents pending.

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