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In Patients with LUTS due to BPH,

℞ **CONTIFLO ICON™**

Tamsulosin Hydrochloride 0.4mg **Prolonged Release Tablets**

Tamsulosin with Innovative CONtrolled absorption technology

Delivers consistent drug levels over 24hrs[1]

- Better control of bothersome night-time symptoms of LUTS/ BPH, including nocturia
- Better QoS and QoL

Offers 24-hr symptom control[1,2]

- OD dose sufficient

Lower C-max & Drug intake independent of food consumption[1,2]

- Better cardiovascular safety profile
- Patient compliance

Abbreviated Prescribing Information. CONTIFLOTM ICON.

GENERIC NAME: Tamsuosin Hydrochloride Prolonged Release Tablets. COMPOSITION:Each film-coated tablet contains: Tamsulosin HCl IP…0.4 mg (prolonged release.DOSAGE Form: Tablets for oral use. Description: CONTIFLO ICON contains tamsulosin hydrochloride, which is an antagonist of alphaIA adrenoceptors in the prostate. Indications: For the treatment of sign and symptoms of benign prostatic hyperplasia (BPH). DOSE AND METHOD OF ADMINISTRATION: The recommended dose of CONTIFLO ICON (Tamsulosin HCl Prolonged Release Tablet) is 0.4mg once daily. It should be administered approximately one-half hour following the same meal each day. For those patients who fail to respond to the 0.4mg dose after 2 to 4 weeks of dosing, the dose of tamsulosin HCl prolonged release tablet can be increased to 0.8mg once daily. If discontinued or interrupted for several days at either the 0.4mg or 0.8mg dose, therapy should be started again with the 0.4mg once daily doseThe tablet should be swallowed whole and should not be crunched or chewed as this will interfere with the prolonged release of the active ingredient. Pregnancy: Pregnancy category B: Tamsulosin is not indicated for use in women. CONTRAINDICATIONS: Patients with known hypersensitivity to tamsulosin or any other component of this product. Reactions have included skin rash, urticaria, pruritus, angioedema and respiratory symptoms. WARNINGS AND PRECAUTIONS: Possibility of postural hypotension. Patients should be cautioned to avoid situations where injury could result should syncope occur. Tamsulosin should not be used in combination with other alpha adrenergic blocking agents. Caution is advised when alpha adrenergic blocking agents including tamsulosin are co-administered with PDE5 inhibitors. Alpha adrenergic blockers and PDE5 inhibitors are both vasodilators that can lower blood pressure. Concomitant use of these two drug classes can potentially cause symptomatic hypotension. Caution should be exercised with concomitant administration of warfarin and tamsulosin. Patients must be advised about the possibility & seriousness of Priapism. Intraoperative floppy iris syndromehas been observed during cataract surgery in some patients treated with alpha1 blockers, including tamsulosin. Advice patients considering cataract surgery to tell their ophthalmologist about use of contiflo Icon. DRUG INTERACTIONS: Tamsulosin 0.4mg should not be used in combination with strong inhibitors of CYP3A4 (e.g., ketoconazole). Tamsulosin should be used with caution in combination with moderate inhibitors of CYP3A4 (e.g., erythromycin), in combination with strong (e.g., paroxetine) or moderate (e.g., terbinafine) inhibitors of CYP2D6, in patients known to be CYP2D6 poor metabolizers particularly at a dose higher than 0.4mg (e.g., 0.8mg).. SHELF-LIFE: Please see Mfg. Date. Expiry date printed on pack. Do not use product after expiry date which is stated on packaging. Expiry date refers to last day of that month. STORAGE AND HANDLING INSTRUCTIONS: Store below 25 ̊C, protected from light and moisture. Keep all medicines out of reach of children. For more information kindle write to : SUN HOUSE, 201 B/1,WESTERN EXPRESS HIGHWAY, GOREGAON EAST, MUMBAI-400063

1.Phillip V. Kerrebroeck, Journal compilation BJU International, 2006; 98(2): 1-2
2. M.C. Michel et al. The Pharmacokinetic Profile of Tamsulosin Oral Controlled Absorption System. European Urology Supplements , 2005; (4): 15–24 QOL= Quality of life
QOS= Quality of sleep

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Robotic Simple Prostatectomy

Carlos Eduardo Schio Fay, Sameer Chopra, Monish Aron

Abbreviations

BPH	Benign prostatic hyperplasia
CBI	Continuous bladder irrigation
DRE	Digital rectal exam
IPSS	International prostate symptom score
JP	Jackson–Pratt
LUTS	Lower urinary tract symptoms
OSP	Open simple prostatectomy
PSA	Prostate-specific antigen
RSP	Robotic simple prostatectomy
SHIM	Sexual health inventory for men
TRUS	Transrectal ultrasound
TURP	Transurethral resection of the prostate
UTI	Urinary tract infection

Introduction

Surgical treatment for BPH is indicated in patients with moderate-to-severe lower urinary tract symptoms (LUTS), who have failed medical therapy or desire a more effective treatment option, and for patients who develop BPH-related complications such as acute urinary retention, recurrent urinary tract infection (UTI), renal insufficiency, gross hematuria, and bladder stone(s) secondary to BPH. Bladder diverticulum associated with recurrent UTI and bladder dysfunction is also an indication for surgical intervention [1].

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The type of surgery recommended to the patient will depend on patient and prostate anatomy, patient comorbidities, surgeon's experience and training. Transurethral resection of the prostate (TURP) remains the gold standard for the treatment of prostates less than 80 g, and open simple prostatectomy (OSP) has been the gold standard for the treatment of prostates larger than 80 g [2]. However, OSP is associated with a significant risk for complications [3, 4].

In 2002, laparoscopic simple prostatectomy was first described as a minimally invasive alternative to OSP to reduce perioperative complications, especially blood loss, blood transfusions, reoperation, and to decrease the length of hospital stay [5–7]. Robotic simple prostatectomy (RSP) was first described in 2008 and since then its role for surgical treatment of BPH is increasing [8, 9].

Using robotics has demonstrated benefit in providing stereoscopic magnified 3-D vision, tremor filtration, seven degrees of freedom wristed instruments, and enhanced ergonomics. The benefits of these have resulted in a shorter learning curve for RSP than for laparoscopic simple prostatectomy [4]. We have previously reported on our experience of using the transperitoneal approach [4, 10]. The transperitoneal approach is usually preferred, which is reflective of the surgeon's background experience with robotic radical prostatectomy.

Preoperative Preparation

Preoperative Evaluation

Preoperative evaluation includes history, physical examination, digital rectal exam (DRE), and laboratory testing including kidney function tests, urinalysis, reflex culture, and prostate-specific antigen (PSA). We also administer the International Prostate Symptom Score (IPSS) and Sexual Health Inventory for Men (SHIM) questionnaires, and obtain uroflowmetry with peak flow rate (Qmax) measurement, transrectal ultrasound to estimate prostate size, and perform a bladder scan to assess post-void residual volume. A transrectal prostate biopsy is performed, to rule out prostate cancer, if the patient has an elevated PSA or abnormal DRE, if clinically indicated.

Patients are counseled as to all treatment alternatives and surgical options. Risks and benefits, potential complications, and the possibility of conversion to open surgery are discussed. Informed consent is obtained.

Antiplatelet and anticoagulant medications are discontinued or bridged before surgery, as clinically indicated. Medical and anesthesia clearance are obtained if necessary. No bowel preparation is usually required unless the patient is habitually constipated, and the patient is made NPO after midnight on the day of surgery. Prophylactic intravenous antibiotics are administered at induction of anesthesia prior to skin incision and are usually discontinued 24 h after surgery.

Operative Room Setup

For RSP, we use a four-arm robotic technique. The additional arm allows for the need of only one assistant who is positioned on the patient's left side. The scrub technician is positioned on the patient's left side as well with video monitors on both sides of the patient for easy viewing by the

surgical team. A Mayo stand is placed next to the assistant where frequently used instruments are placed. The da Vinci® Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA) will be docked in between the patient's legs for the Si robot (Fig. 1) or on the right side of the patient for the Xi robot.

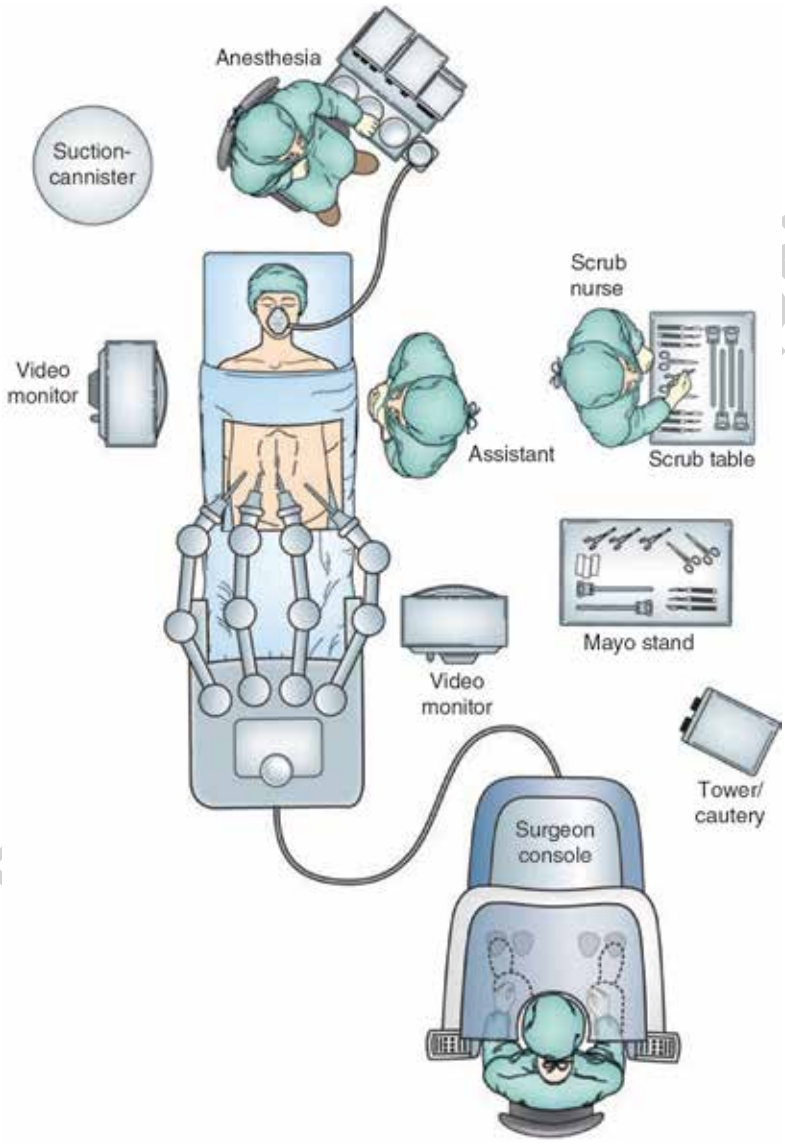

Fig. 1: Operating room setup for robotic simple prostatectomy. Schematic demonstrating the typical operating room setup for robotic simple prostatectomy utilized at our institution.

Patient Positioning

Under general endotracheal anesthesia, the patient is placed in a modified lithotomy position (Fig. 2) over a nonskid foam pad. The patient is secured using the Yellofin® stirrups and an upperbody warming blanket is applied. Care is taken to adequately pad all pressure points to avoid positioning injuries. The abdominal skin is shaved with clippers, and the patient is prepped and draped in standard sterile fashion for a transperitoneal pelvic robot-assisted surgery. An 18-French urethral catheter is inserted and an orogastric tube is placed. A standard time-out is called prior to incision.

Instrumentation and Equipment List

Equipment

- Si or Xi da Vinci®
- 0° robotic scope (Intuitive Surgical, Inc., Sunnyvale, CA)
- Monopolar Scissors (Intuitive Surgical, Inc., Sunnyvale, CA) × 1
- ProGrasp™ Forceps (Intuitive Surgical, Inc., Sunnyvale, CA) × 2
- Needle Drivers (Intuitive Surgical, Inc., Sunnyvale, CA) × 2
- Clip Appliers (Intuitive Surgical, Inc., Sunnyvale, CA) × 2
- Tenaculum Forceps (Intuitive Surgical, Inc., Sunnyvale, CA) × 1

Fig. 2: Patient positioning. For robotic simple prostatectomy, the patients are positioned in lithotomy and modified Trendelenburg.

Trocars

- 12 mm trocars × 2 (1 for the Xi)
- 8 mm trocars × 3 (4 for Xi)

Assistant Instruments

- Suction irrigator device (Bariatric length)
- Laparoscopic spoon forceps
- Hem-o-lok applier (Teleflex Medical, Research Triangle Park, NC)
- Medium (purple) Hem-o-lok clips (Teleflex Medical, Research Triangle Park, NC)
- Laparoscopic needle driver
- Laparoscopic scissor
- 10 mm specimen entrapment bag

Step-by-Step Technique (Videos 21.1, 21.2, 21.3, 21.4, 21.5, 21.6, 21.7, 21.8, and 21.9)

Step 1: Pneumoperitoneum and Trocar Placement

The first incision is made approximately 1–2 fingerbreadths above the umbilicus. Through this incision we establish pneumoperitoneum to 15 mmHg with a Veress needle. A 12-mm port (8 mm for the Xi) is inserted through this incision into the peritoneal cavity. The peritoneal cavity is then inspected using the 0° scope to ensure absence of any intra-abdominal injury from the Veress needle or the trocar. Four additional trocars are then inserted under direct vision. The 8-mm da Vinci® working trocars are all placed at the horizontal level of the umbilicus with a separation of 8–10 cm between trocars. We prefer to keep the fourth robotic arm on the right side of the patient. A 12-mm assistant trocar is placed in the left upper quadrant in the midclavicular line taking care to avoid being too close to the camera trocar or the left robotic arm. Thus, a 4-arm, 5-trocar transperitoneal approach is employed (Fig. 3).

At this point, the patient is placed in Trendelenburg position, and the da Vinci® is docked (Fig. 4) between the legs for the Si or from the right side of the patient for the Xi. The instruments are inserted into the peritoneal cavity under direct vision. We initially start with a ProGrasp™ in the left and fourth arm and a monopolar scissor in the right arm.

Step 2: Cystotomy (Table 1)

The sigmoid colon is initially mobilized out of the pelvic cavity for better exposure of the target anatomy (Fig. 5a–d). The bladder is filled with approximately 200 mL of saline through the urethral catheter and a vertical midline cystotomy is created with monopolar scissors gaining access to the bladder lumen (Fig. 6a, b).

Table 1: Instrumentation required for step 2: cystotomy.

Surgeon instrumentation			Assistant instrumentation
Left arm	**Right arm**	**Fourth arm**	• Laparoscopic suction irrigator
• ProGrasp™ forceps	• Monopolar scissors	• ProGrasp™ forceps	
• **Endoscope lens**: 0°			

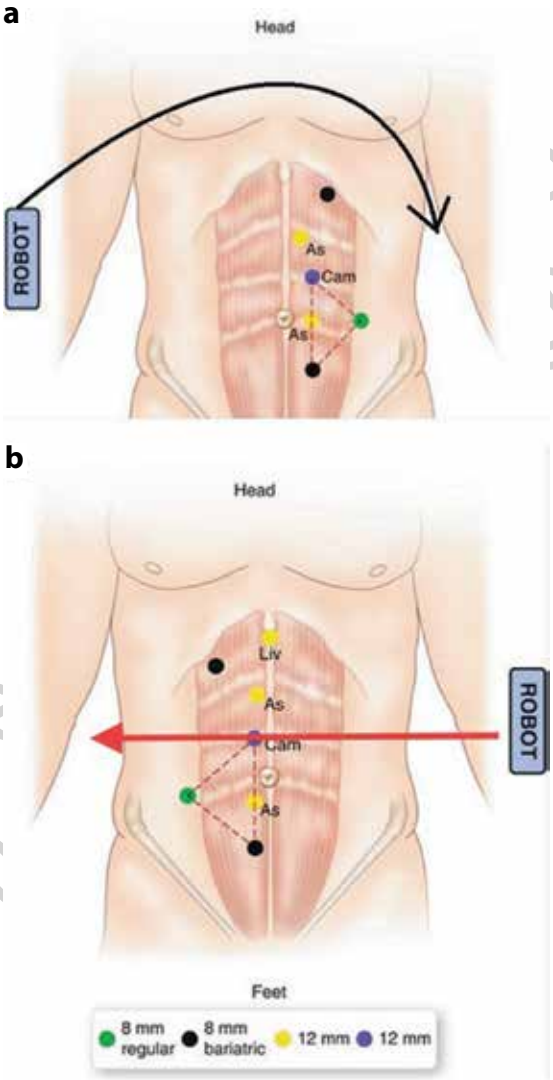

Fig. 3: Trocar placement. For transperitoneal robotic simple prostatectomy, a five-trocar placement is utilized. This placement is identical to that for robotic radical prostatectomy.

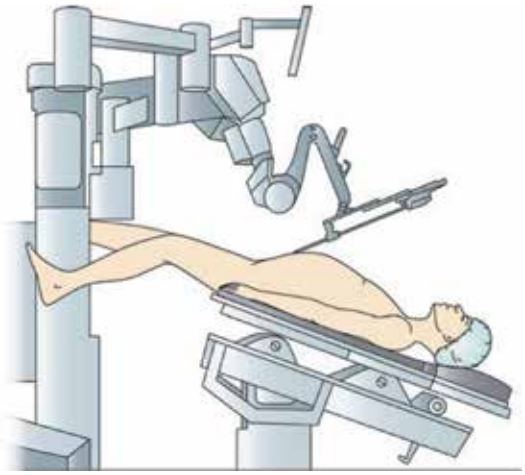

Fig. 4: Robot docking. With the patient placed in lithotomy position and modified Trendelenburg, the da Vinci® Si is docked in between the patient's legs.

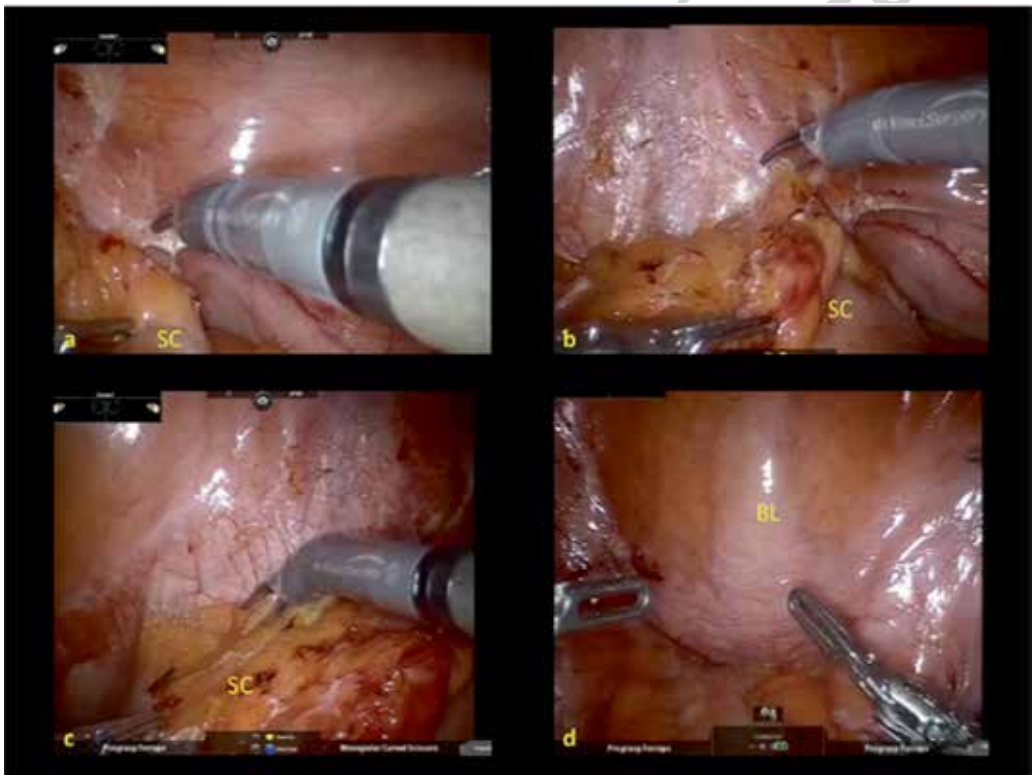

Fig. 5: (**a–d**) Mobilization of the sigmoid colon. The sigmoid colon (SC) is mobilized to allow for better exposure of the bladder (BL).

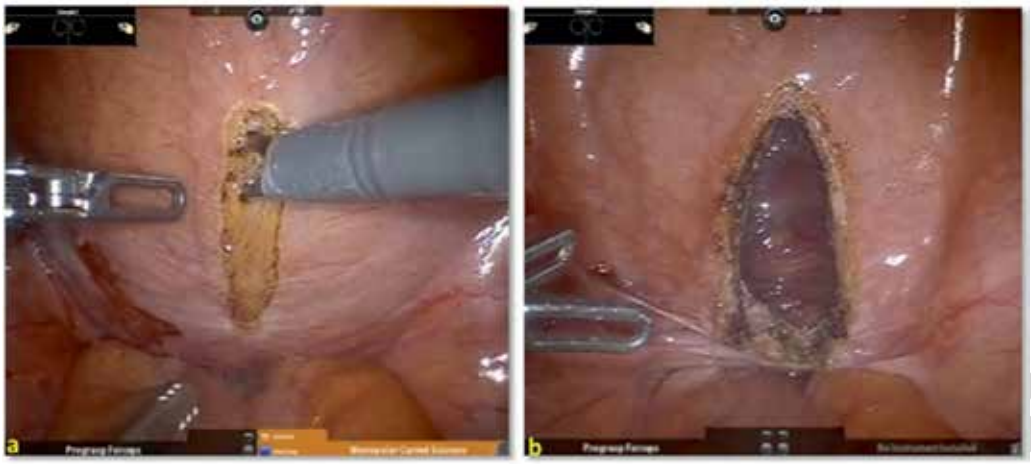

Fig. 6: (**a, b**) Midline vertical cystostomy. A midline vertical cystostomy is created to gain access to the anterior portion of the bladder.

Step 3: Deploying Stay Sutures (Table 2)

All the fluid is suctioned out and 2–4 stay sutures are deployed to keep the edges of the cystotomy widely retracted. These stay sutures are 2-0 Polyglactin sutures, 6-in. long, on a CT-1 needle with a medium Hem-o-lok clip tied into the end of the suture. The stay suture is passed outside-in through the bladder wall at the edge of the cystotomy, anchored laterally to the abdominal wall, then pulled taut and secured with an additional Hem-o-lok clip (Fig. 7a, b).

Typically, a large prostatic adenoma that bulges into the bladder is immediately apparent. A 2-0 Polyglactin suture on a CT-1 needle stay suture is placed in the median lobe to provide traction and countertraction during the procedure using the ProGrasp forceps in the fourth robotic arm (Fig. 8). Bilateral ureteral orifices are then carefully identified and care is taken to keep them safe throughout the procedure.

If simultaneous bladder diverticulectomy is to be performed, or if the intravesical adenoma is extremely large and very close to the ureteral orifices, ureteral double J stents can be placed using a 2 mm mini-port deployed in the suprapubic area. A 0.035-in. guide wire is inserted through the miniport, floppy end first, and then a 4.8–6 French ureteral stent is advanced over the wire (Fig. 9a–d).

Table 2: Instrumentation required for deploying stay sutures.

Surgeon instrumentation			Assistant instrumentation
Left arm	**Right arm**	**Fourth arm**	• Hem-o-lok applier
• Needle driver	• Needle driver	• ProGrasp™ forceps	• Laparoscopic scissors
• **Endoscope lens**: 0°			

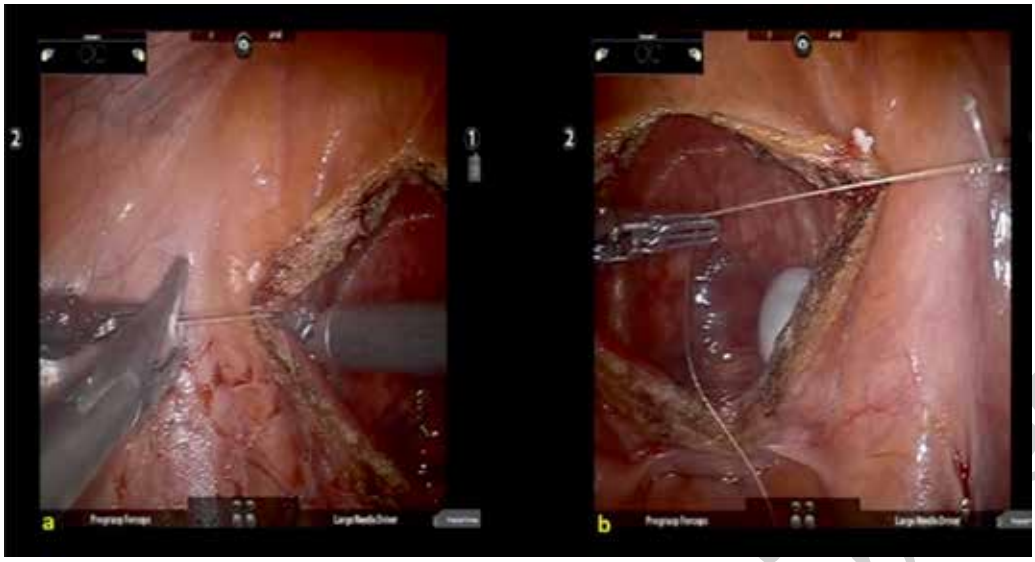

Fig. 7: (**a, b**) Exposing the operative space of the bladder. A 2-0 Polyglactin suture on a CT-1 needle stitch with a Hem-o-lok at the end is passed through the bladder, anchored laterally to the abdominal wall, then pulled and secured with a Hem-o-lok to expose the bladder and keep open the operative space.

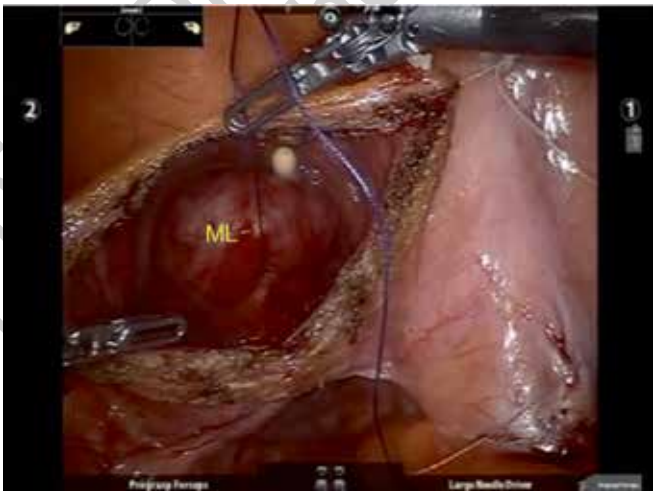

Fig. 8: Prostatic median lobe control. A large prostatic adenoma is identified from within the bladder and a 2-0 Vicryl on a CT-1 needle stay suture is placed within the median lobe (ML) to provide traction and countertraction during the procedure.

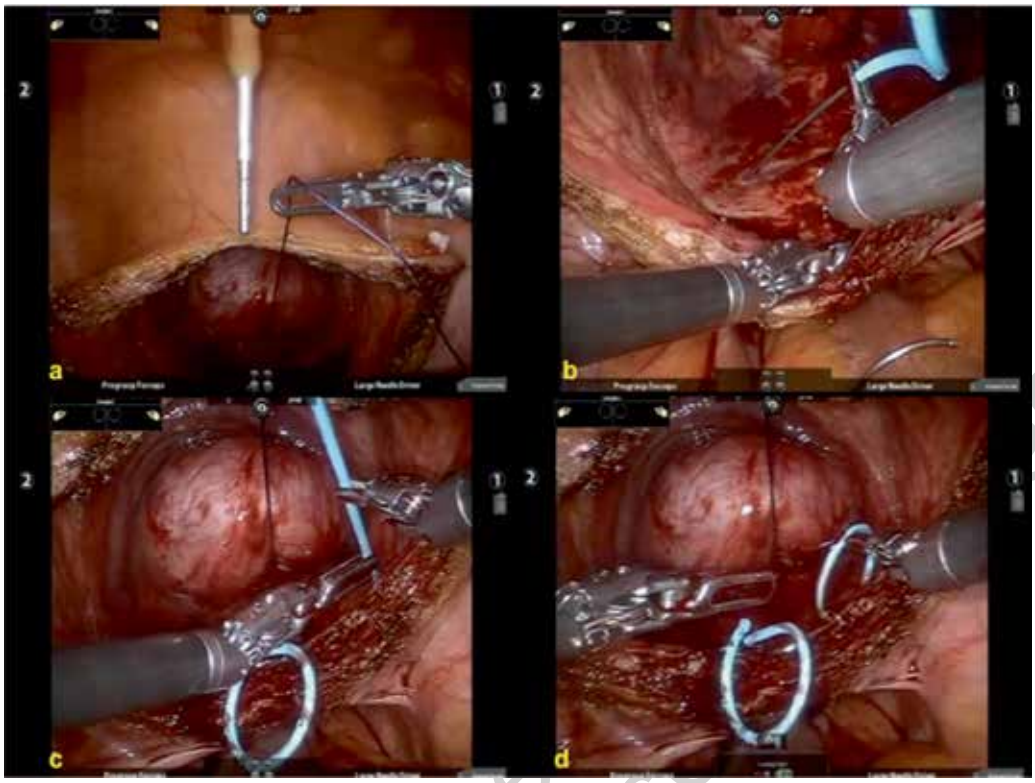

Fig. 9: Insertion of bilateral ureteral stents. (**a**) A 2-mm mini-port is inserted into the suprapubic area. (**b**) Guide wire insertion and left ureteral stent placement. (**c**) Right ureteral stent placement. (**d**) Final aspect showing bilateral ureteral stents.

Step 3: Adenoma Dissection (Table 3)

The urethral catheter is pulled back into the urethra after deflating the balloon, and a stay suture is used to elevate the median lobe using the fourth robotic arm. With the median lobe retracted anteriorly, a mucosal incision is made at the junction between the median lobe and the trigone using hot monopolar scissors. This incision is deepened to reach the plane of the adenoma at the junction between the adenoma and the compressed peripheral zone and capsule of the prostate (Fig. 10).

Table 3: Instrumentation required for step 3: adenoma dissection.

Surgeon instrumentation			Assistant instrumentation
Left arm	**Right arm**	**Fourth arm**	• Laparoscopic suction irrigator
• ProGrasp™ forceps	• Monopolar scissors	• ProGrasp™ forceps	
		• Tenaculum forceps	
• **Endoscope lens**: 0°			

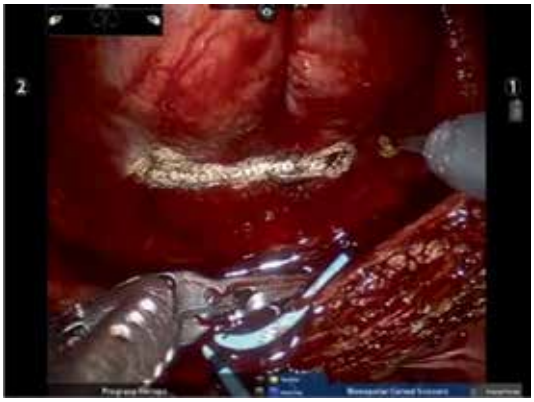

Fig. 10: Bladder mucosa incision. With traction stitch retracted with fourth arm, bladder mucosa is incised between median lobe and bladder trigone.

After a plane of dissection has been established posteriorly, the surgeon progresses both laterally and distally using a combination of blunt and sharp dissection (Fig. 11a). Bleeding vessels are coagulated concurrently using monopolar electrocautery. Once the posterior aspect of the adenoma has been separated from the compressed peripheral zone and prostate capsule, the dissection proceeds along the lateral surface of the prostate adenoma, mobilizing the lateral aspect of the adenoma (Fig. 11b). The plane of dissection should hug the pearly white surface of the adenoma. Care should be taken to avoid transgressing the compressed peripheral zone and the prostate capsule. Once enough of the adenoma has been freed up, the previously placed stay suture in the median lobe is removed and the adenoma is grasped with a robotic tenaculum forceps brought in under vision through the fourth robotic arm. The tenaculum provides an excellent grip on the adenoma, and allows excellent traction and countertraction to aid in the dissection of the adenoma. During dissection of the adenoma, we maintain a ProGrasp™ in the left arm and the monopolar scissors in the right arm. As the dissection of the lateral aspect of the adenoma progresses distally, the previously made posterior mucosal incision is carried laterally in a circumferential fashion. The lateral aspect of the adenoma is mobilized down towards the apical tissue where the lateral shoulders of the adenoma start tapering medially towards the membranous urethra. The anterior aspect of the adenoma mobilization is done last and the anterior bladder neck mucosa is incised with hot scissors at the 12 o'clock position and the dissection progresses distally along the anterior surface of the adenoma (Fig. 11c, d).

The dissection continues distally to the point the urethra is visualized (Fig. 12). The urethra is then sharply transected using cold scissors. The adenoma is completely released from the prostate and then placed in a 10-mm specimen entrapment bag. The prostate fossa is examined for any residual adenoma, which can be excised separately and removed with a laparoscopic spoon forceps.

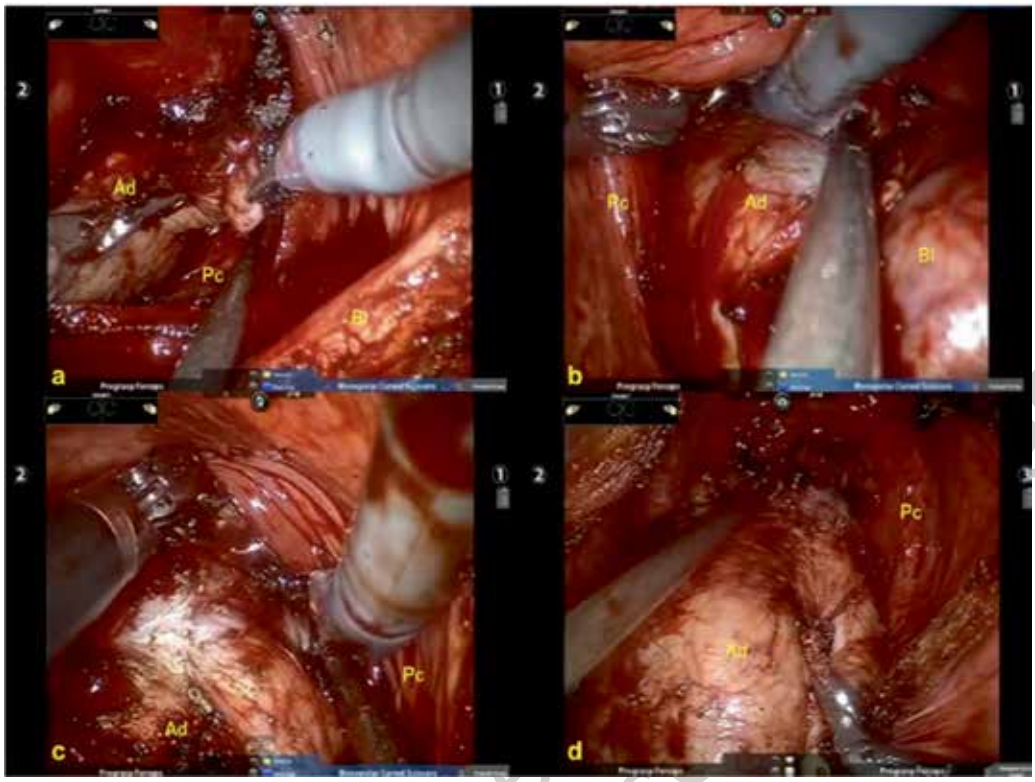

Fig. 11: Adenoma dissection. (**a**) Posterior dissection (**b**) Dissection of the lateral aspect of the adenoma (**c, d**). Anterior dissection. *Pc* prostate capsule, *Bl* bladder, *Ad* adenoma

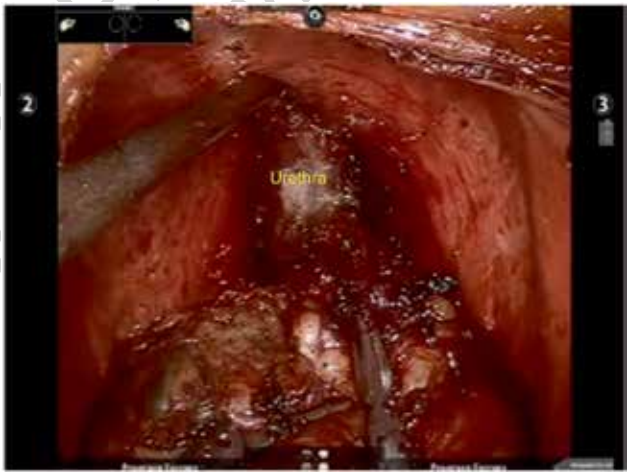

Fig. 12: Urethral exposure. The urethra is exposed.

Table 4: Instrumentation required for step 4: hemostasis.

Surgeon instrumentation			Assistant instrumentation
Left arm	**Right arm**	**Fourth arm**	• Laparoscopic suction irrigator
• Needle driver	• Needle driver	• ProGrasp™ forceps	• Laparoscopic needle driver
	• Monopolar scissors (for pinpoint coagulation)		
• **Endoscope lens:** 0°			

Step 4: Hemostasis (Table 4)

The key to excellent hemostasis is being in the correct plane during enucleation of the adenoma and obtaining concurrent hemostasis while the adenoma is being enucleated. This will significantly decrease the amount of time spent in obtaining hemostasis after the adenoma has been anchored laterally to the abdominal wall, then pulled and secured with a Hem-o-lok to expose the bladder and keep open the operative space enucleated. Post-enucleation hemostasis is obtained using a combination of electrocautery and sutures. Discrete arterial bleeders can be point coagulated with the monopolar scissors while venous bleeding is best secured with sutures. We use either 2-0 V-loc™ sutures or figure-of-eight, 2-0 Polyglactin sutures for hemostatic suturing in the prostatic fossa (Fig. 13a–d). Small bleeders near the sphincter are suture ligated with 4-0 Polyglactin sutures. The suturing is done with robotic needle drivers in the left and right robotic arm. The fossa is thoroughly irrigated to ensure excellent hemostasis.

Step 5: Retrigonization

We do not routinely retrigonize the prostatic fossa. If retrigonization is considered appropriate, we do this after carefully obtaining perfect hemostasis and a clean prostatic fossa. This is accomplished using a 2-0 V-loc™ suture on a GS-21 needle placed at the 6 o'clock position in the bladder neck mucosa and advancing it into the prostatic fossa at a convenient location, usually in the midfossa. The stitch is then advanced along the left side of the bladder neck to advance the lateral mucosa down into the prostatic fossa. An additional 2-0 V-loc™ suture on a GS-21 needle is used for the advancement of the right-sided bladder neck mucosa. The goal of retrigonization is to cover the raw surface of the prostatic fossa and theoretically decrease the risk of postoperative hemorrhage and irritative symptoms. Retrigonization is done with robotic needle drivers in the left and right robotic arm.

Step 6: Bladder Closure (Table 5)

A 22-French 3-way hematuria catheter is inserted into the bladder via the urethra and 30 mL of sterile water is used to inflate the balloon. The previously placed stay sutures are now cut and removed. The Hem-o-lok clips on the stay sutures, on the bladder wall and the abdominal wall,

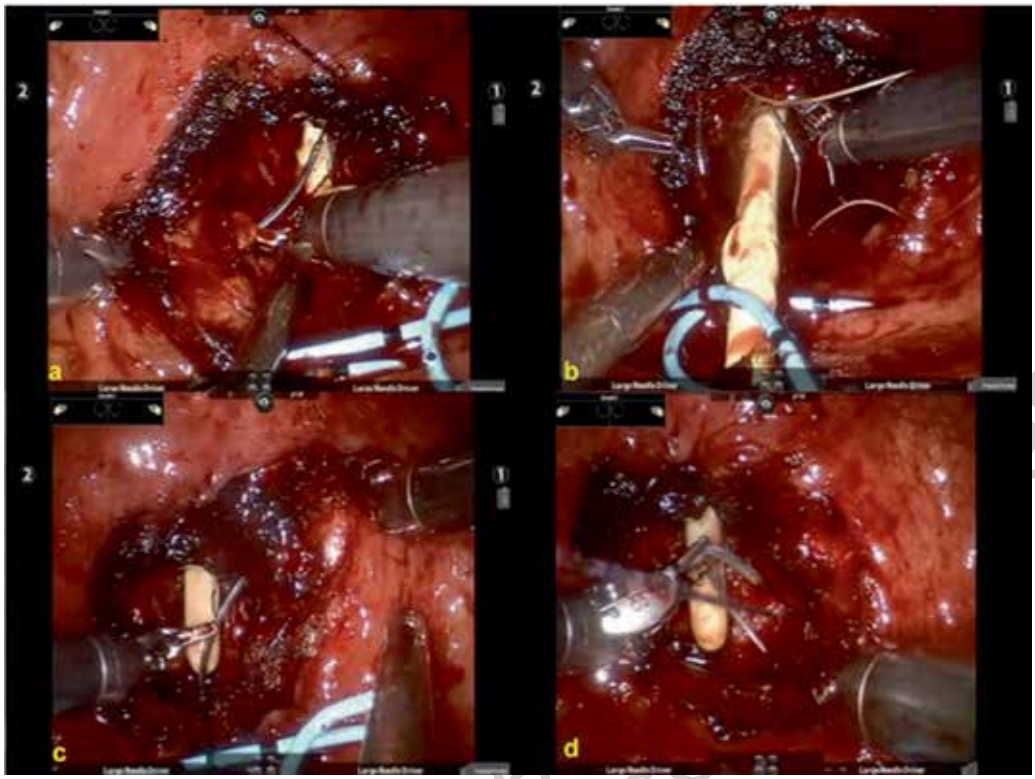

Fig. 13: Hemostasis. (**a–d**) Hemostatic sutures are placed at bleeding sites within the fossa to provide hemostasis. 4-0 Vicryl sutures and spot coagulation are performed to complete this step.

are removed by the assistant using a laparoscopic spoon forceps. The midline cystotomy is now closed in two layers; the first is an inner full thickness layer using 2-0 V-loc™ sutures on a GS-21 needle (Fig. 14) and the second layer is also a full thickness layer using the same sutures (Fig. 15). After the first layer is complete, the bladder is filled with 200 mL of saline to ensure the closure is watertight and also to avoid hitting the urethral catheter balloon with the second layer closure.

Table 5 : Instrumentation required for step 5: bladder closure.

Surgeon instrumentation			Assistant instrumentation
Left arm	**Right arm**	**Fourth arm**	• Laparoscopic suction irrigator
• Needle driver	• Needle driver	• ProGrasp™ forceps	• Laparoscopic spoon—to remove Hem-o-lok clips from stay sutures
			• Laparoscopic needle driver
• **Endoscope lens**: 0°			

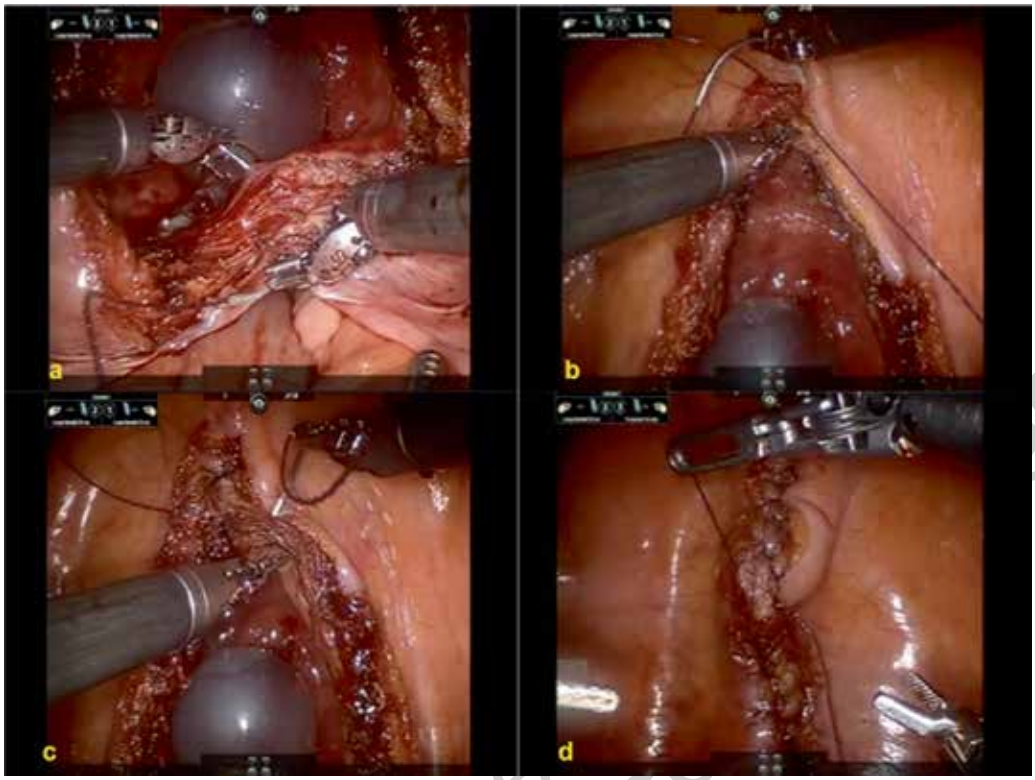

Fig. 14: First layer of bladder closure. (**a–c**) First layer of bladder closure. A 2-0 V-loc suture on a GS-21 needle is used to perform the first layer of bladder closure. (**d**) Final aspect of the first layer of bladder closure.

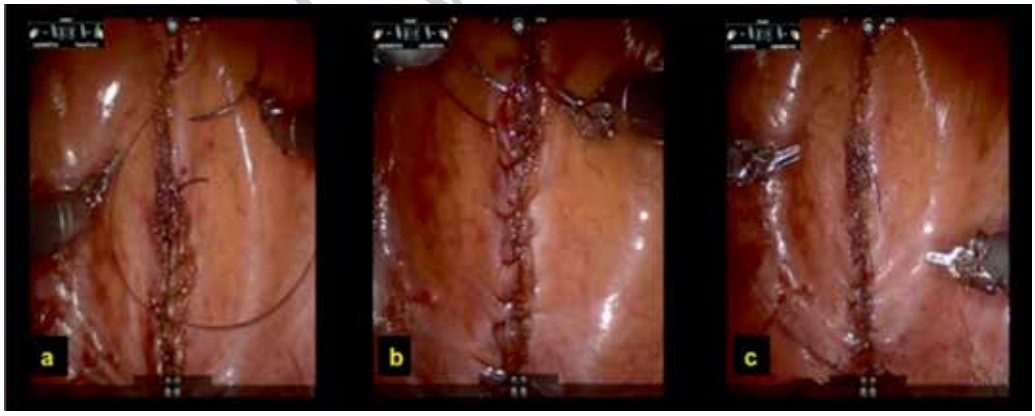

Fig. 15: Second layer of bladder closure. (**a, b**) Second layer of bladder closure. A 2-0 V-loc suture on a GS-21 needle is used to perform the second layer of bladder closure. (**c**) Final aspect of the second layer of bladder closure.

To confirm a watertight closure, the bladder is now distended with 300 mL of saline and continuous bladder irrigation (CBI) is now commenced after irrigating out any clots. CBI is titrated to ensure a clear return of irrigant.

Hemostasis is now confirmed in the peritoneal cavity and a 19-French Jackson–Pratt (JP) drain is placed in the retrovesical space and brought out through the right lateral 8-mm trocar site and affixed to the skin using 2-0 Nylon. Robotic instruments are now removed under vision and the robot is undocked.

The midline camera trocar incision is now enlarged as needed to allow extraction of the adenoma specimen within the specimen entrapment bag. The fascia of the extraction site is closed using 0 PDS figure-of-eight stitches. The 12-mm assistant trocar site is closed using the Carter-Thomason Port Closure System® and 0 Polyglactin sutures. Subcutaneous tissue is reapproximated using 3-0 Polyglactin suture and the skin is closed using 4-0 Monocryl® in subcuticular fashion. Dermabond® is applied over the incisions. The patient is then extubated and transferred to recovery room.

Special Considerations

Potential Bladder Tumor

To rule out a potential bladder tumor in smokers or patients with a history of hematuria, a flexible cystoscopy is performed either at the time of preoperative office visit or at the start of the case. The presence of a bladder tumor is a contraindication to opening the bladder.

Previous Open Abdominal Surgery

In a patient with a prior midline abdominal incision from an open procedure, pneumoperitoneum is obtained either with a Veress needle away from the incision, or with the open (Hasson) technique. The cavity is carefully inspected, and adhesions, if present, are taken down laparoscopically prior to docking the robot.

Bladder Diverticulum

A bladder diverticulectomy can be performed at the same time as a RSP. We prefer to place a JJ stent on the side of the diverticulum to protect the ipsilateral ureter during dissection of the diverticulum. Also the vertical cystotomy is moved slightly off center away from the side of the diverticulum to avoid having the two suture lines very close together.

Bladder Calculi

Bladder calculi can be easily and expeditiously removed at the time of RSP since the bladder is wide open.

Potential Complications

The most common complication from this procedure is ongoing hematuria. This can lead to prolonged CBI, prolonged length of stay, and even potential clot retention and possible bladder rupture. The best way to avoid this is to spend the necessary amount of time in the operating room to get perfect hemostasis prior to bladder closure.

If there is persistent ongoing hematuria which looks arterial, it may become necessary to take the patient back to the operating room. Often it is a simple matter to address this cystoscopically and fulgurate the arterial bleeder with a resectoscope loop.

Rarely, if the urethral catheter gets blocked and is not recognized in a timely fashion, the bladder closure may give way and there can be an intraperitoneal leak. In this situation, the best approach is to go back robotically, open the bladder, wash it out, get hemostasis, and close the bladder again.

Transient incontinence and erectile dysfunction can occur rarely, in less than 5 % of patients. Some patients have symptoms of overactive bladder and dysuria for a few weeks to months after surgery. Most of these are self-limiting and resolve spontaneously.

Rarely, if residual adenoma is left behind at the apex, patients may not be able to void well postoperatively. This can be diagnosed at the 3-month visit and confirmed with an office cystoscopy. Residual adenoma at the apex associated with poor flow and high IPSS score can be treated with a TURP directed at this residual tissue.

Follow-up

Intermittent compression stockings and subcutaneous heparin are used during the hospital stay to prevent thromboembolic events. Continuous bladder irrigation is stopped on the first postoperative day if the urine is clear or light pink. The JP drain is removed prior to discharge after confirming absence of urine leak. The median length of hospital stay in our experience is 3 days. The urethral catheter is removed on postoperative day 7 with a voiding trial. A follow-up visit is scheduled at 3 months for symptom check, uroflowmetry, postvoid residual urine measurement, and administration of IPSS and SHIM questionnaires.

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Interventional Ultrasound: Transperineal and Transrectal Prostatic Biopsy

Andrea Fandella, Pietro Pepe

Indications for Baseline Biopsy

PSA and/or rectal examination suspects remain the main indications for biopsy [1–4]. A prostate biopsy may be indicated for PSA values that exceed the thresholds of common use and almost always for values above 10 ng/ml; in this regard it is suggested to always repeat the PSA before making a decision. PSA level should be verified after a few weeks using the same assay under standardized conditions (i.e., no ejaculation, manipulations, urinary tract infections, prostate inflammation, and trauma) in the same laboratory [2, 3]. Empiric use of antibiotics in an asymptomatic patient in order to lower the PSA should not be undertaken [4].

Age, comorbidity of the patient, and therapeutic consequences are variables to consider when prescribing this procedure. Risk stratification is a potential tool for reducing unnecessary biopsies [1].

The transrectal ultrasound is considered the standard method to guide prostate biopsy and the removal of frustules done with transperineal or transrectal technique.

In rare cases, such as rectal amputation, it may require a transperineal guide.

It suggests a careful informed consent that explains to the patient the consequences of a possible clinical diagnosis of cancer before the biopsy [5].

Preparation for Prostate Biopsy

Sampling of the frustules of the prostate can result in bleeding inside the lodge and bladder. This occurrence is more frequent and severe in patients taking medications that interfere with clotting. For this reason it is wise to suspend, whenever possible, these drugs before the biopsy (aspirin, ticlopidine). In particular, the Coumadin and the Sintrom must be replaced by low molecular weight heparins [5].

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To minimize the risk of infections, it is appropriate to take an antibiotic before the examination; oral or intravenous antibiotics are state of the art. Quinolones are the drugs of choice, with ciprofloxacin being superior to ofloxacin [6]; prophylaxis should be made taking into account the proportion of bacterial resistance in the region where biopsy is performed, and then the patient choose the antibiotic accordingly. In addition, the patient should be questioned about previous urinary infections and if he/she has taken antibiotics for 3 months prior to biopsy. If this occurs, he/she should choose an antibiotic different from the previous.

Increased quinolone resistance [7] is associated with a rise in severe post-biopsy infection [8].

In cases of doubt, and if there has already been a prostatitis, the resistance of the intestinal germs by culture obtained by rectal swab should be tested [9–12]. Furthermore, to reduce the risk of infections, the preparation involves running the morning of an enema to clear the rectum [5].

How to Do the Biopsy?

Biopsy without complications does not require hospitalization. The overall duration of the procedure is less than 30 min.

Based on the operator's preferences, the patient is encouraged to take the following positions: the side (Fig. 1), gynecological, and knee-chest positions. The first two positions are the most frequently used.

In Fig. 2, the instruments needed are biopsy gun, syringe with anesthetic, 18 cm needle, and sterile container for the samples.

The next stage involves the introduction of an ultrasound probe in the rectum. This tool will allow the operator to view the loggia, the prostate, and the bladder. In particular, the operator will proceed to the measurement of the volume of the prostate. The most important function of the ultrasound probe is to provide an image of the area and to drive accurately the operator in the selection of the different areas in which to execute withdrawal prostate.

A biopsy gun with a hook cutting edge (crypt) is able to take small frustules of suspicious tissue. The quick-snap mechanism with which the needle is pushed and withdrawn from the prostate minimizes the feeling of discomfort.

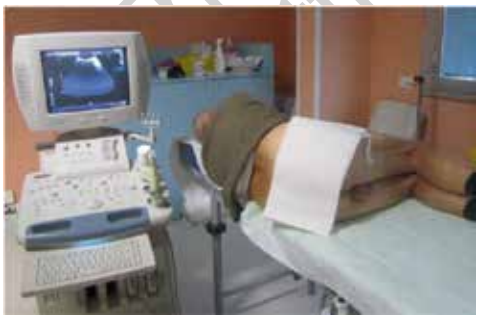

Fig. 1: Patient in positions on the side ready for transrectal biopsy.

Fig. 2: Instruments: biopsy gun 25 cm 18 gauge needle, syringe with anesthetic with a 25 cm 22 gauge echogenic needle tip, and the sterile cassettes for the samples.

The biopsy needle may reach the prostate through the rectum (transrectal approach) or the skin of the area located between the testicles and anus (transperineal approach). Both of these methods have proved particularly effective and safe. The choice essentially depends on the operator's preference.

Transrectal Approach

The procedure can be performed both in the lateral decubitus position (lying on your side and with your legs bent) (Fig. 1) and in gynecological position.

Before any operation is practiced, rectal examination to rule out the presence of concomitant abnormalities of the rectal wall should be performed.

Transrectal biopsy is performed under local anesthesia. The ultrasound probe introduced into the rectum is provided with a channel for the passage of fine needles. So with an 18 gauge 25 cm needle, it is possible to reach every part of the prostate (Figs. 3, 4, and 5).

Only patients with high comorbidity may require the procedure in the operating room under sedation or anesthesia.

Local Anesthesia Prior to Biopsy

Ultrasound-guided periprostatic block is state of the art [13] (Video 26.1). It is not important whether the depot is apical or basal. Intrarectal instillation of local anesthesia is inferior to periprostatic infiltration [14].

Transperineal Approach

The procedure is performed in gynecological position. The doctor performs a rectal examination to rule out the presence of concomitant abnormalities of the rectal wall. The patient is asked to raise a hand with the testicles, or claims are with gauze fixed with patches to "hammock" groin.

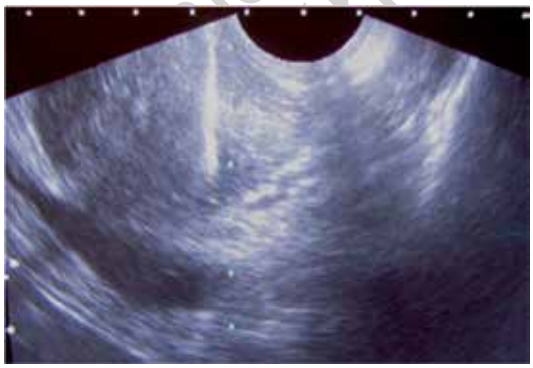

Fig. 3: Transrectal biopsy in the peripheral rear area.

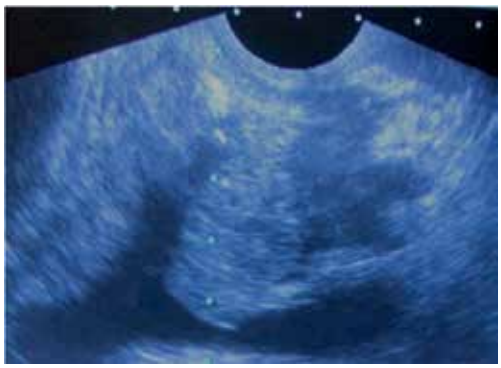

Fig. 4: Transrectal biopsy in the apex.

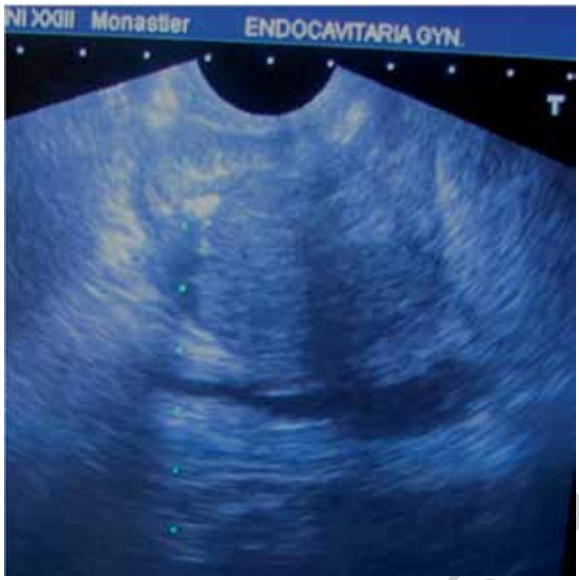

Fig. 5: Transrectal biopsy in the peripheral right area.

The skin located between the testicles and the anus is shaved and disinfected. The entry point of the needle is located 1.5 cm above the anus. At this level, it injects a few ml of local anesthetic with a needle thin and short. In point prior anesthesia, a thin needle of greater length that allows the injection of the local anesthetic around the prostate is then introduced.

A thin metal channel cable is introduced along the path anesthetized until reaching the suspected area. This system will make it easy and not annoying for the patient because of the repeated passage of the needle biopsy. The ultrasound probe allows the patient to see at any time the areas that are reached by the needle biopsy. When the procedure is performed, a mild compression dressing is performed with the entry of the needle.

Transperineal prostate biopsy has come to the foreground as a result of lower incidence of sepsis, better detection rate for anterior prostate cancer (PCa), and the opportunity to perform the template-guided prostate biopsy [15, 16]. Transrectal and transperineal prostate biopsy procedures require different techniques and are recommended with the same level of evidence [17]. Candidates for transperineal biopsy should be studied with coagulation blood tests and receive antibiotic prophylaxis; if sedation is required (saturation or template-guided biopsy), both blood tests and cardiologic evaluation are recommended. Transperineal biopsy needs multifrequency linear or biplanar probes to show perineal passage of the needle; this approach is recommended for patients that have been previously subjected to abdominoperineal amputation or that are affected by severe disease of the rectum (Figs. 6 and 7).

Transperineal and transrectal prostate biopsy provides similar detection rates for prostate cancer (PCa) both for first procedure (34–40 %) and for repeat procedure (22–43 %) performing at least 12 (extended biopsy) vs. >20 (saturation biopsy) cores, respectively [18–31]. Transperineal

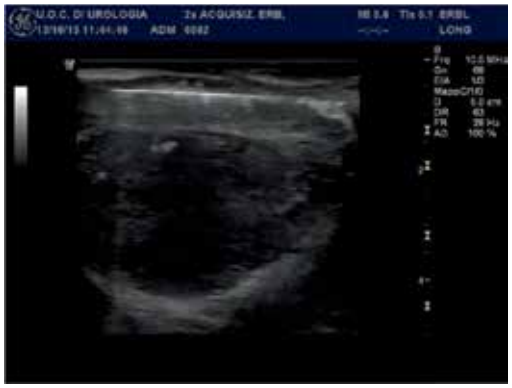

Fig. 6: Transperineal prostate biopsy (longitudinal scan): the needle (18 gauge tru-cut) is used to perform the biopsy in the periphery of the gland.

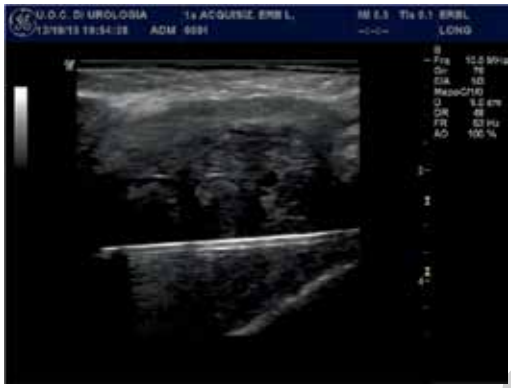

Fig. 7: Transperineal prostate biopsy (longitudinal scan): the needle (18 gauge tru-cut) is used to perform the biopsy in the anterior zone of the gland.

route allows for easier access to the anterior zone of the gland, where incidence of PCa is from 10 to 20 % at repeat biopsy [32–36]. Transperineal template-guided biopsy, utilizing 30–60 cores, is suggested for men with previously negative biopsies and persistent suspicious of cancer, in local PCa staging and in the re-evaluation of patients enrolled in active surveillance (AS) protocols [37–40].

Despite ultrasound sensitivity improvement through combined use of color power Doppler (CDU) and a contrast medium agent [41–43] or elasto-sonography [44], the accuracy of transperineal and transrectal approach in the diagnosis of PCa performing targeted biopsies has not improved. On the contrary, combined use of multiparametric MRI (magnetic resonance imaging) and MRI/TRUS transperineal fusion targeted biopsy has high accuracy in detecting significant PCa [44–51]. In fact, multiparametric MRI/TRUS targeted biopsy produces a higher detection rate of PCa for each single core compared to extended biopsy schemes (15–20 % vs. 5–10 %) [50, 51] (Video 26.7) (Figs. 8, 9, 10, and 11); multiparametric MRI/TRUS transperineal targeted biopsy improves diagnosis of significant PCa most notably in AS protocols [44, 48–52].

Prostate biopsy is the gold standard in re-evaluation of men enrolled in AS protocols, and the highest percentage of patients being reclassified at confirmatory prostate biopsy repeat biopsy (25–30 % of the cases) [48] following unfavourable histology results (i.e., Gleason score >6, number of positive cores >2, greatest percentage of cancer "GPC" >50 %). Despite the fact that both the appropriate number of biopsy cores (extended vs. saturation vs. template-guided schemes) and the approach (transrectal vs. transperineal) [43–55] have not been established, transperineal biopsy seems more accurate in the identification of patients at risk of PCa in AS protocols [48], resulting in a lower incidence of adverse definitive histology specimens compared to transrectal approach [53– 56]. Multiparametric MRI/TRUS fusion targeted biopsy has improved staging in AS giving 10 % reassignment [57] in patients undergoing standard biopsy [58, 59]; moreover, MRI/TRUS fusion transperineal targeted biopsy has good accuracy in the diagnosis of anterior PCa [59–63] and in the re-evaluation of micro-focal cancer (a single positive core of Gleason score equal to 6

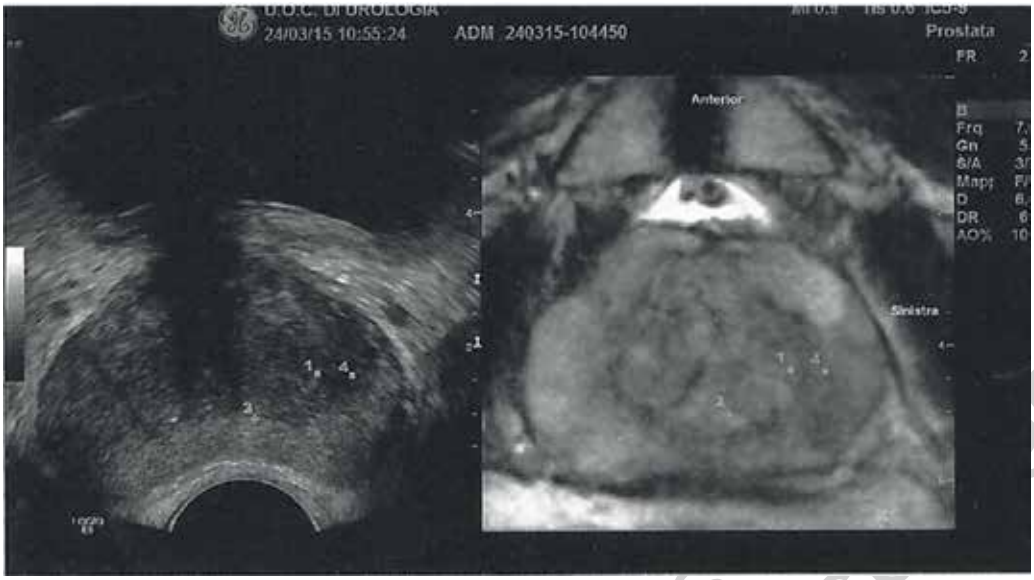

Fig. 8: 3.0 Tesla pelvic multiparametric MRI/TRUS fusion imaging (axial scan) (ACHIEVA 3.0 Tesla; Philips Healthcare Best, the Netherlands – Logiq E9 General Electric; Milwaukee, WI): multiparametric MRI/TRUS fusion procedure and the application of markers.

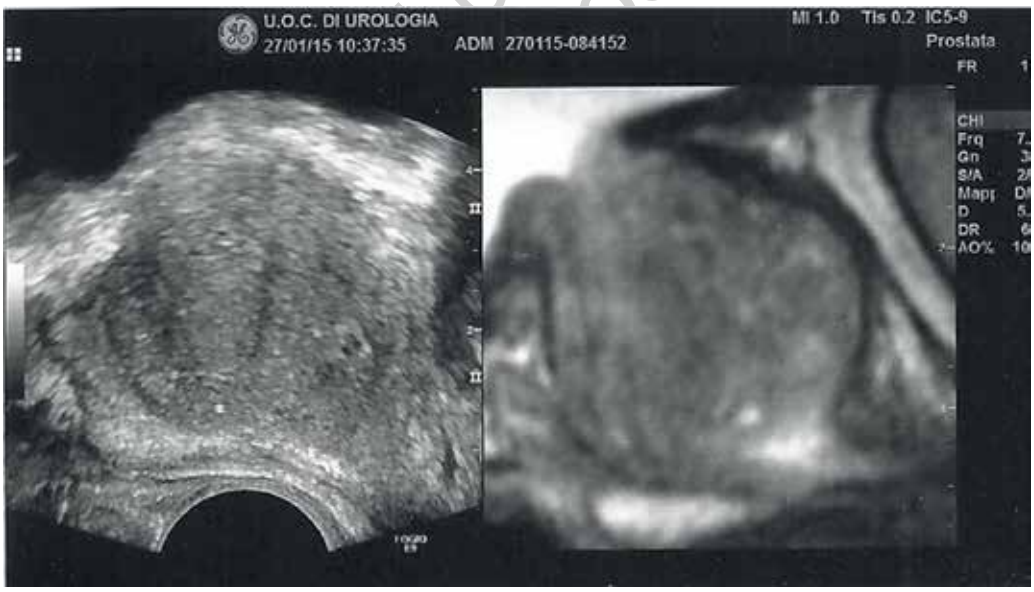

Fig. 9: 3.0 Tesla pelvic multiparametric MRI/TRUS fusion imaging (longitudinal scan) (ACHIEVA 3.0 Tesla; Philips Healthcare Best, the Netherlands – Logiq E9 General Electric; Milwaukee, WI).

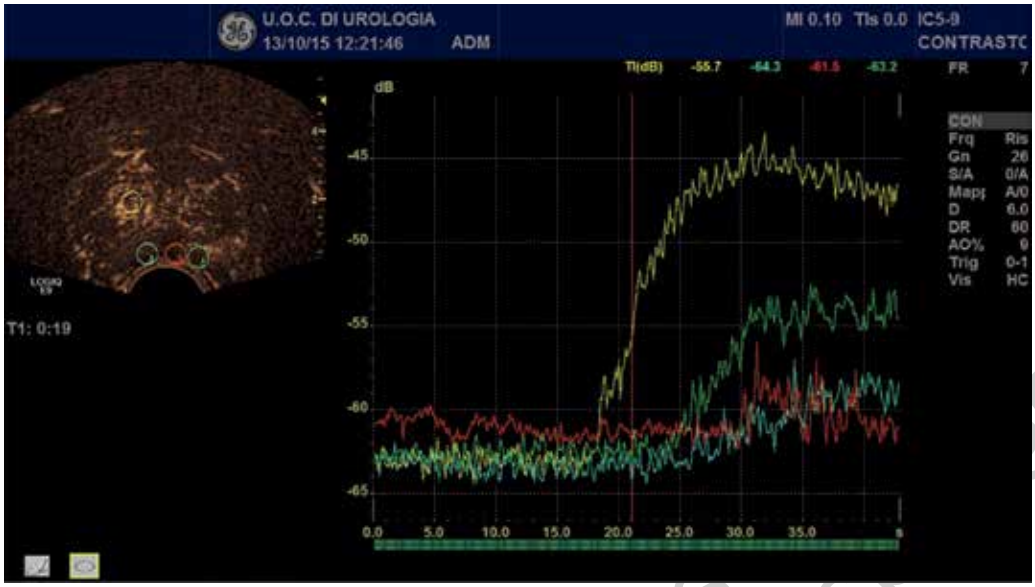

Fig. 10: Visual and quantitative analysis of SonoVue® concentration in the prostate after intravenous administration of ultrasound contrast medium: the markers evaluate the concentration of SonoVue® in different areas of the gland.

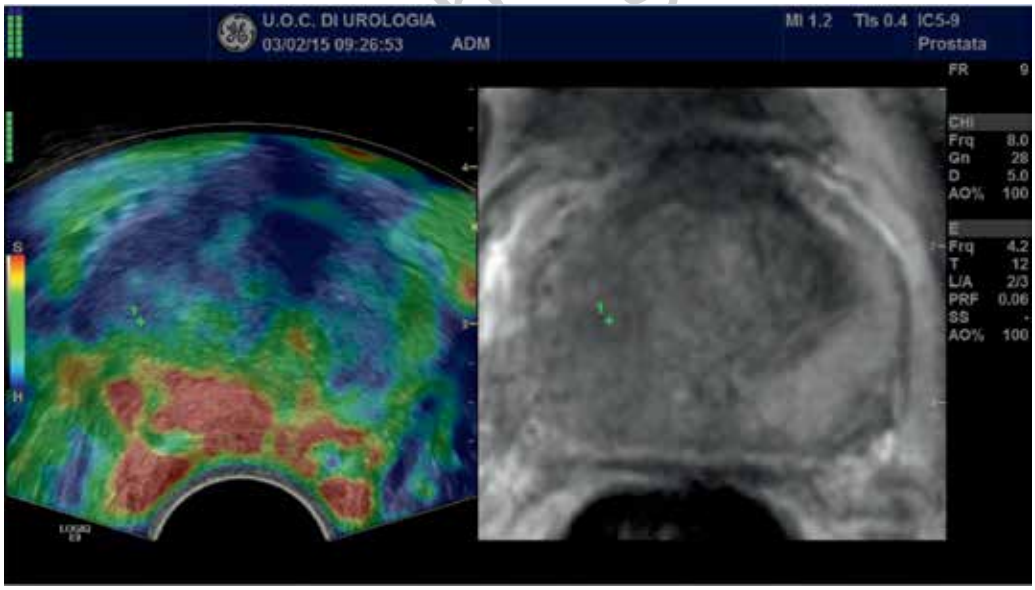

Fig. 11: 3.0 Tesla pelvic multiparametric MRI/TRUS/elasto-sonography fusion imaging (ACHIEVA 3.0 Tesla; Philips Healthcare Best, the Netherlands – Logiq E9 General Electric; Milwaukee, WI): ultrasound evaluation of multiparametric MRI suspicious lesion (marker) is also conducted using elasto-sonography.

and GPC <5 %) [64] at risk for clinically insignificant PCa. Highest diagnostic accuracy of clinically significant PCa in the re-evaluation of men in AS [65] is still, at present, obtained through extended or saturation prostate biopsy schemes combined with MRI/TRUS targeted biopsy.

Finally, the transperineal approach reduces the incidence of sepsis (at most 0.07 %) compared with 1–2 % for the transrectal approach [11, 61, 66–74].

In conclusion, the transperineal approach could be recommended in persistent suspicion of PCa following one or more negative transrectal biopsies as this approach increases the detection of anterior PCa; furthermore, the transperineal route significantly reduces the incidence of sepsis in patients with previous prostatitis and/or recurrent urinary tract infection [75–77].

Sampling Sites and Number of Cores

On baseline biopsies, the sample sites should be bilateral from apex to base as far as posteriorly and laterally as possible in the peripheral gland (Videos 26.2, 26.3, 26.4, 26.5, and 26.6). Additional cores should be obtained from suspect areas by DRE/TRUS and MRI (Video). Sextant biopsy is no longer considered adequate. Ten to 12 core biopsies are recommended [78], with >12 cores not being significantly more conclusive [79, 80].

Transition Zone Biopsy

Transition zone sampling during baseline biopsies has a low detection rate and should be confined to repeat biopsies [81].

Indications for Re-biopsy

After a Previous Negative Biopsy

Indications include (a) persistent increase in PSA, (b) suspicious DRE, (c) ASAP (atypical small acinar proliferation), and (d) extended PIN (prostatic intraepithelial neoplasia). The number of frustules taken must be higher than the first biopsy; you should also perform the transitional zone biopsy.

Alternatively, the re-biopsy can be done by technical saturation (20–24 samples). Approximately, 20 % re-biopsies are positive.

Repeat Biopsy After Previously Negative Biopsy

Isolated high-grade PIN in one or two biopsy sites is no longer an indication for repeat biopsy [82–85].

After a Previous Positive Biopsy

The re-biopsy is provided in most of the protocol for the patient in the active surveillance.

Possible Complications of Biopsy

The prostate biopsy is a safe procedure and generally associated with few complications.

During the execution of the biopsy, with both transperineal and transrectal approaches, the patient may experience pain even after executing anesthesia. Rarely, the patient may experience a general malaise characterized by increased sweating and feeling of loss of consciousness. Exceptional is the appearance of allergic reactions to the local anesthetic.

After the procedure, a rare complication (less than 2 % of cases) can be represented by the inability to empty the bladder spontaneously. In such a case, the placement of a urinary catheter which may be held in place for a few days or removed immediately is necessary.

For a few weeks after the biopsy with transrectal approach, you can assist in the loss of blood from the rectum (rectal). Such event is observed in 10–40 % of cases. The presence of blood in urine (hematuria) and/or urethrorrhagia is common in both the transrectal and the transperineal biopsies. Both are observed in approximately 30–60 % of cases; they persist for some days and generally disappear spontaneously.

Table 1: Complications following transperineal prostate biopsy in 3,000 patients submitted to 12 vs. 18 vs. >24 needle cores.

Complications	12 cores* 915 pts	vs.	18 cores*° 1330 pts	vs.	>24 cores° 630 pts
Hematuria	92 (8.1 %)		130 (9.7 %)		66 (10.4 %)
Urethrorrhagia	20 (2 %)		30 (1.5 %)		19 (3 %)
Hematospermia	98 (10.7 %)		280 (21 %)		192 (30.4 %)
Acute urinary retention	38 (4.1 %)		95 (7.1 %)		70 (11.1 %)
Prostatitis	6 (0.6 %)		10 (0.7 %)		6 (0.9 %)
Sepsis	–		–		–
Orchiepididymitis	4 (0.4 %)		7 (0.5 %)		4 (0.6 %)
Urinary tract infection	27 (3 %)		30 (2.2 %)		16 (2 %)
Perineal hematoma	3 (0.3 %)		4 (0.3 %)		5 (0.8 %)
Vagal syndrome	9 (0.9 %)		–		–
Fever	4 (0.4 %)		8 (0.6 %)		5 (0.8 %)
Systemic adverse events[a,b]	1 (0.1 %)		–		–
Hospital admission (within 20 days)	9 (1 %)		18 (1.3 %)		10 (1.6 %)
Emergency department visit (within 20 days)	55 (6 %)		128 (9.6 %)		91 (14.4 %)

[a] Prostate biopsy performed under local anesthesia (*) or sedation (°) [72]
[b] Acute cardiac ischemia

Prostate biopsy is considered a safe technique, with incidence of severe complications <1 %; among these are the most dangerous infections of antibiotic-resistant germs. Severe postprocedural infections were initially reported in 1 % of cases, but have increased as a consequence of antibiotic resistance [8–11].

Low-dose aspirin is no longer an absolute contraindication [86]. Percentage of complications per biopsy session, irrespective of the number of cores, are as follows: hematospermia 37.4 %, hematuria >1 day 14.5 %, rectal bleeding <2 days 2.2 %, prostatitis 1 %, fever >38.5 °C 0.8 %, epididymitis 0.7, rectal bleeding >2 days +/− surgical intervention 0.7 %, urinary retention %, and other complications requiring hospitalization 0.3 % [11].

After transperineal biopsy, seldom is the formation of a hematoma at the site of entry of the needle (less than 0.5 % of cases). The clinical complications following transperineal prostate biopsy in men submitted to extended vs. saturation biopsy are listed in Table 1 [68].

In less than 1 % of cases, it is possible to observe the onset of high fever with shivering that may require hospitalization.

After the "execution of the procedure is an appropriate observation period of about a" time to highlight the appearance of any immediate complications. After transperineal biopsy, a mild compression level with the entry of the needle could be instituted.

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Ultrasound MRI Fusion Biopsy in Prostate Gland

Francesco Porpiglia, Matteo Manfredi

Introduction

Until recently, the diagnosis of prostate cancer (PCa) has been based on blinded, systematic, template-based sampling strategy under transrectal ultrasound (TRUS) guidance. This test has undergone considerable modification in order to improve the sampling efficiency: from the original six cores [1] to the standardized 12 cores [2, 3]. Nevertheless, 12-core TRUS biopsy conferred an incremental benefit in terms of detection; there is a wide consensus that it remains prone to errors. These principally comprise undersampling of significant and oversampling of insignificant PCa [4–6].

The introduction of multiparametric magnetic resonance imaging (mp-MRI) has made it possible to change the way in which prostate biopsy is done, allowing to direct biopsies to suspicious lesions rather than randomly. The subject of this chapter relates to the use of a software to assist in targeting an MRI-derived suspicious lesion.

Interpretation of Multiparametric MRI

The MRI acquisition and reporting by the radiologist is the initial step of all MRI targeted biopsy strategies. mp-MRI includes three components: high-resolution T2-weighted MR images (T2WI) and at least two functional MRI techniques including diffusion-weighted imaging (DWI) and dynamic contrast-enhanced MRI (DCE-MRI) [7–9] (Fig. 1). MR spectroscopic imaging (MRSI) remains an optional technique in most centers. The use of an endorectal coil (ERC) to increase the spatial resolution of the technique is still under debate, especially with the recent improvement in signal-to-noise ratios achieved by the use of the 3-T scanner [10].

To describe suspected lesions diagnosed by MRI in a standardized manner, radiologists use standardized suspicion scores and graphical templates to show locations. The most used scores

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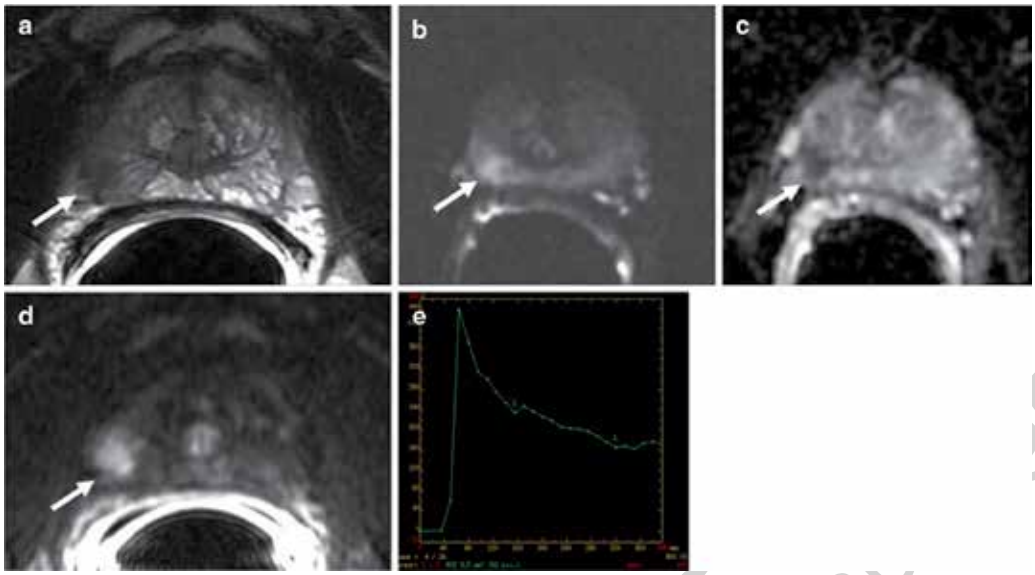


Fig. 1: Images from a 59-year-old male with serum PSA 7.92 ng/mL, and one previous biopsy underwent an mp-MRI. The MRI demonstrated a PI-RADS 5 right posterior apex to mid-peripheral zone lesion (*white arrow*) on axial T2W (**a**), DWI (**b**), ADC (**c**), and DCE (**d, e**). MRI/US fusion software-based targeted biopsy demonstrated Gleason score 7 (3 + 4) prostate cancer (67 % in three cores).

are the 1–5-point Likert scale (based on radiologist's subjective score) or the prostate imaging reporting and data system (PI-RADS) score (based on determined criteria) [11–13]. In particular, concerning PI-RADS score, the interreader agreement performs well, and the inter-reader reproducibility improves with increasing experience.

MRI-Guided Targeted Biopsy

An MRI targeted biopsy can be performed in three ways: in-bore MRI targeted biopsy, MRI/US fusion visual targeted biopsy, and MRI/US fusion software-based targeted biopsy. These three approaches are all informed by tumor location diagnosed by the MRI. It is just the manner in which the target volume is "represented" to the operator that differentiates them.

Concerning in-bore MRI targeted biopsies, needles are introduced only into the areas of interest by performing a transrectal or transperineal biopsy. Serial MRI scans are performed to confirm biopsy needle placement (Fig. 2). Multiple studies demonstrated that in-bore MRI targeted biopsies are feasible with a median detection rate significantly higher than random biopsies. Moreover, this approach reduces the number of sampled cores with a real-time feedback of its placement, allowing a high likelihood of hit target [14, 15]. Nevertheless, in-bore MRI targeted biopsy is time-consuming and costly, not commonly available, and performed in prone position under general anesthesia.

The simplest targeted strategy concerns the use of MRI/US fusion visual targeted biopsies directed to the suspicious areas highlighted on the MRI. The first step, as in the other strategies, is

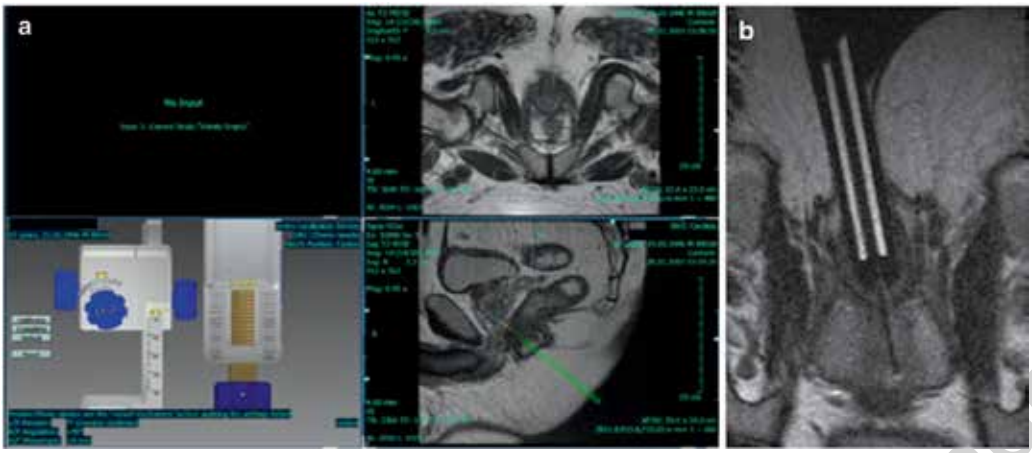


Fig. 2: In-bore biopsy. (**a**) Needle-in control scans are performed in two different planes (axial and coronal); (**b**) targeted cores are taken from each lesion using an MRI-compatible, 18G, fully automatic biopsy gun.

represented by the detection of suspicious lesions on MRI. Then the urologist performs a standard US-guided biopsy, either by a transrectal or a transperineal approach, trying to direct the needles toward the areas suspicious on mp-MRI. Many authors suggest better efficiency and accuracy compared to standard biopsy [16, 17]. The most important disadvantage relates to the learning curve and reproducibility of this strategy. This approach requires an experienced urologist to translate the information of the mp-MRI onto real-time US, which can be challenging according to the deformation and the anatomical characteristics of the prostate.

Finally, MRI/US fusion software-based targeted biopsies represent a novel approach developed to improve the accuracy of prostate biopsy, allow dissemination of the technique, and permit the storage of images for future resampling. MRI/US fusion software-based targeted biopsy devices allow to align the pre-biopsy MR images with intraoperative TRUS in order to enable the urologist to perform targeted biopsy directed toward MR-visible lesions. This approach combines the high diagnostic accuracy of MRI for detecting PCa with TRUS, which represents a procedure well mastered by urologists. The process of coregistration of MRI and US images is automatized by the use of a fusion device, and therefore the results are likely to be more consistent across different centers.

Coregistration of MRI and US Images

MRI to US cognitive fusion is complicated by the significant deformation of the prostate shape that occurs between TRUS and MRI (with or without an endorectal coil). The software-based registration method corrects this effect to achieve better diagnostic accuracy [18].

There are two different methods to register MR images to live TRUS: rigid and elastic registration. Both of them aim to align the MR and US images through the identification of landmarks present on both corresponding images. The outer shape of the prostate is used to match the MRI contour to the live US image.

Elastic registration allows deformation, warping, and dimensional changes between images, based on mathematical algorithms. As every prostate is different in density and elasticity, these calculations are estimations. Rigid registration permits only rotational and translational variations between images, without changing the images themselves. The urologist needs to make some adjustments in case of error due to the rigid registration, using manual correction of the alignment and targeting or using different degrees of pressure/insertion depth of the US probe (Fig. 3) [19].

While overlapped images obtained from rigid registration usually have discontinuous borders looking less pleasant to the eye than elastic registration, it is difficult to define which method is able to achieve better accuracy. Elastic registration should guarantee better matching, but some experts think the cognitive adjustment might overcome the issues encountered with rigid registration and allow better spatial precision, especially in patients having unusual gland dimensions.

Fusion Platforms

MRI/US fusion software-based targeted biopsy first of all requires a diagnostic mp-MRI with a report scheduling all the suspicious lesions edited by an expert uro-radiologist (Fig. 4). mp-MRI images are loaded in the specific software and regions of interest are then outlined. The patient is positioned, and a TRUS is performed, with MR images superimposed on real-time US images (Fig. 5). Targeted biopsies directed to mp-MRI-suspicious lesions are then performed (Figs. 6 and 7).

A standardized report of the biopsy session should be provided, including a detailed notification of MRI/US fusion software-based targeted biopsies, and eventually standard biopsies, that were performed. It can be done in the same manner as for mp-MRI, using a standardized diagram of the prostate, including drawings of the sampled lesions. The report must underline how good the MRI/US fusion software-based targeted biopsy matched the mp-MRI one (e.g., visibility of the lesion). All this information will be useful for analyzing the final histopathology results (Fig. 8).

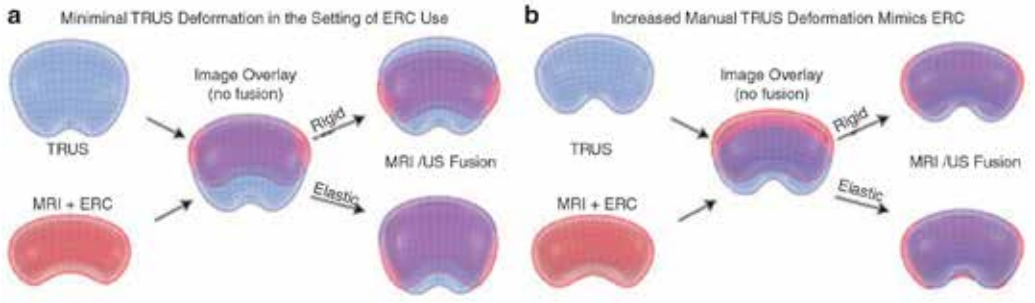
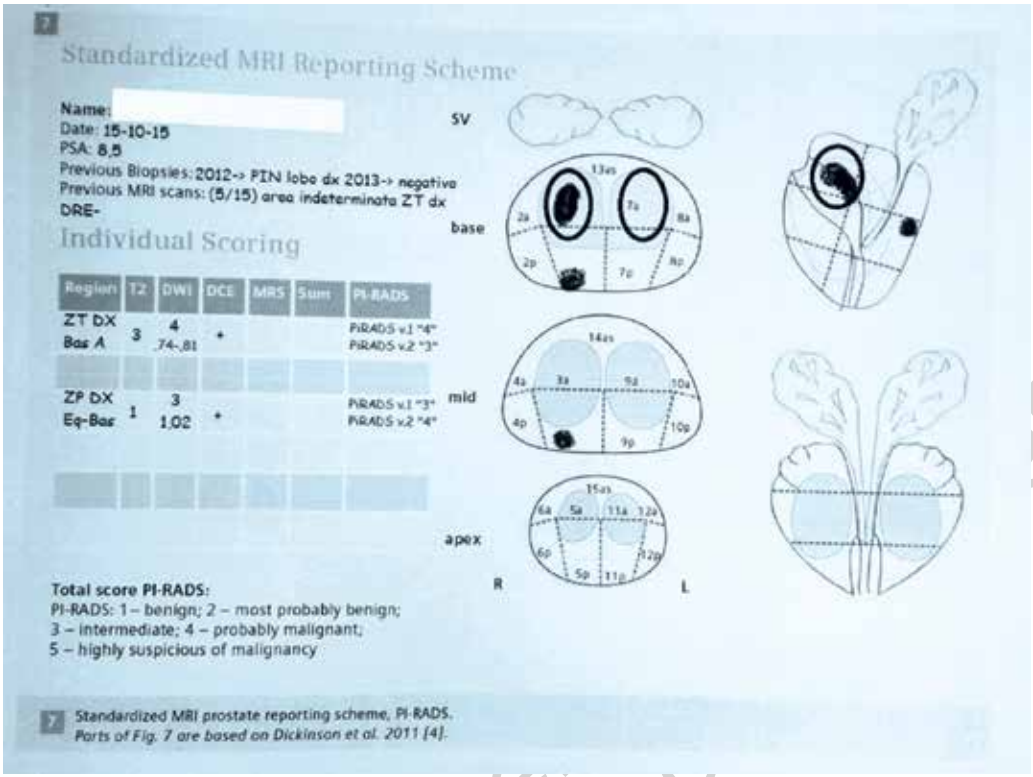


Fig. 3: Elastic and rigid methods to register MR images to live TRUS. (**a**) MRI/US registration with minimal US-probe deformation and use of an endorectal coil (ERC) for MRI; (**b**) MRI/US registration with increased manual US-probe deformation that can mimic ERC deformation. In middle images in (**a**) and (**b**) is shown the simple overlap of US and MR images, resulting in reduced correlation between imaging modalities. Rigid registration permits only rotational and translational variations between images. Elastic registration allows local deformation, e.g., caused by an endorectal coil or TRUS probe. ERC endorectal coil (Reproduced from Logan *et al*. [19]).



Standardized MRI prostate reporting scheme, PI-RADS. Parts of Fig. 7 are based on Dickinson et al. 2011 [4].

Fig. 4: mp-MRI report scheduling all the suspicious lesions classified by PI-RADS score.

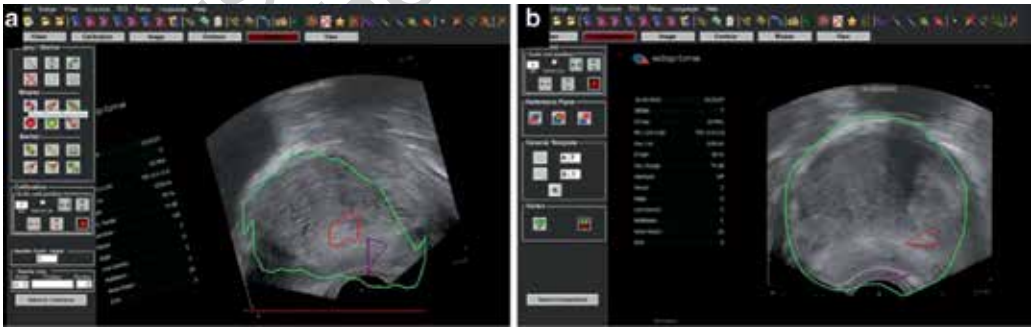


Fig. 5: Superimposition of MR and US images: the outer shape of the prostate is used to match the MRI contour to the real-time US image. (**a**) Longitudinal view; (**b**) transversal view.

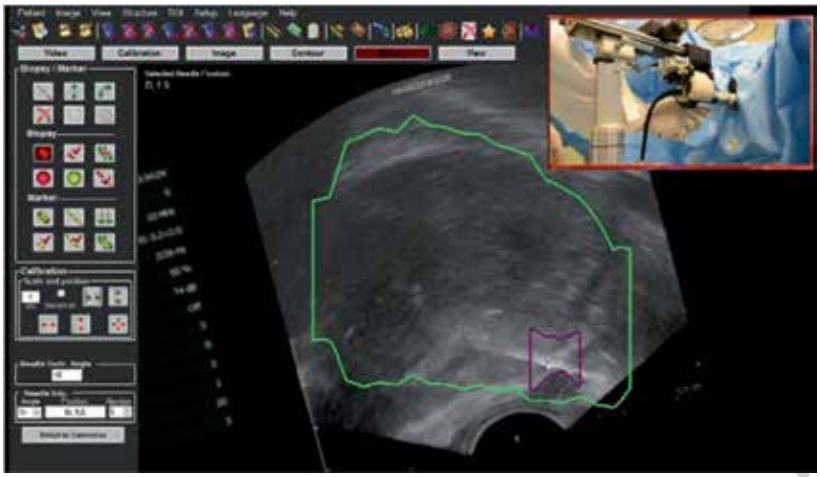


Fig. 6: Targeted biopsies directed to mp-MRI-suspicious lesions: transrectal approach.

Fig. 7: Targeted biopsies directed to mp-MRI-suspicious lesions: transperineal approach.

The different devices currently in use to allow MRI/US fusion software-based targeted biopsy are reported in Table 1. To date, there are no available studies directly comparing the different platforms in terms of accuracy, nor detection rate.

Fig. 8: Example of a report of the biopsy session.

Indications of MRI/US Fusion Software-Based Targeted Biopsy

Main Indications

- Re-biopsy in men with persistent suspicion of PCa after first negative prostate biopsy: persistently increased PSA and/or positive digital rectal examination (DRE) [20–25] and/or diagnosis of extensive high-grade prostatic intraepithelial neoplasia (HG-PIN) or atypical small acinar proliferation (ASAP) of the prostate [26]. As expected, a number of studies have shown that in this subgroup of men, MRI/US fusion software-based targeted biopsy allowed the detection of more clinically significant PCa than standard biopsy [27].
- Follow-up of patients under active surveillance (AS). Many authors evaluated fusion systems to perform confirmatory targeted biopsy in patients under AS. Hu *et al.* recently proved in a series of 113 patients that confirmatory MRI/US fusion software-based targeted biopsy resulted in reclassification in 36 % of men, ranging from 24 to 100 % according to the MRI score, from low to high grade, respectively [28]. Sonn *et al.* demonstrated that in a series of 171 patients, MRI/US fusion software-based targeted biopsy was three times more likely to identify cancer than standard biopsy (21 % versus 7 %, respectively), and of the men with clinically significant PCa initially enrolled for AS, 38 % had disease detected only on targeted biopsies [29]. Moreover, MRI/US fusion software-based targeted biopsy permits to track the location of all biopsy cores, allowing the urologist to perform a re-biopsy in the same suspicious areas, which is mandatory in the correct follow-up of patients under AS.

Other Indications

Other indications, as recommended by many authors but to be confirmed by further studies, could be:

- The follow-up of men suspicious for local recurrence after local treatment [30]
- The guidance of focal therapy [31]
- The characterization of suspicious lesions even at the first biopsy [32, 33]

Results of MRI/US Fusion Software-Based Targeted Biopsy

Standard Biopsy Versus MRI/US Fusion Software-Based Targeted Biopsy

The two approaches did not differ significantly in overall detection of PCa. When considering a core-by-core analysis, Rastinehad *et al.* reported an increased detection rate of MRI/US fusion software-based targeted biopsy with respect to standard biopsy (37.9 % vs 12.5 %, respectively, $p < 0.001$) [34]. The detection rate of clinically significant PCa seems higher performing a MRI/US fusion software-based targeted biopsy than performing a standard biopsy. In the study of Siddiqui *et al.*, MRI/US fusion software-based targeted biopsy diagnosed 30 % more high-risk cancers versus standard biopsy ($p<0.001$) and 17 % fewer low-risk cancers ($p = 0.002$) [35]. On

Table 1: Summary of MR/TRUS fusion software-based targeted biopsy platform specifications.

MRI/US fusion software (manufacturer)	US image acquisition	Method of registration	Tracking system	Manipulation	Sampling route	Year of FDA approval
Artemis (Eigen)	Manual	Elastic	Mechanical arm with encoders	Via mechanical arm	Transrectal or transperineal	2008
BioJet (D&K Technologies)	Manual	Rigid (elastic for minor deformations)	Stepper with digital encoders	Via stepper	Transrectal or transperineal	2012
BiopSee (MedCom)	Manual	Rigid (elastic for minor deformations)	Stepper with digital encoders	Via stepper	Transrectal or transperineal	NR
Real-time virtual sonography (Hitachi)	Manual	Rigid	Electromagnetic	Freehand	Transrectal or transperineal	2010
UroNav (Invivo/ Philips)	Manual	Rigid	Electromagnetic	Freehand	Transrectal or transperineal	2005
Urostation (Koelis)	Automatic	Elastic	3D ultrasound	Freehand	Transrectal	2010
Virtual Navigator (Esaote)	Manual	Rigid	Electromagnetic	Freehand	Transrectal	2014

MRI/TRUS magnetic resonance imaging/transrectal ultrasound, *FDA* Food and Drug Administration, *NR* not reported

the other hand, two recently published randomized controlled trial (RCT) concluded that detection rates for any cancer and clinically significant PCa did not significantly differ between the two approaches, [36, 37].

Concerning the length of biopsy positive cores, Puech *et al.* reported a statistically significant longest core cancer length in MRI/US fusion software-based targeted biopsy compared to standard biopsy (mean: 7.3 mm ± 3.8 vs 4.6 mm ± 3.1, respectively; $p = 0.0001$) [38].

In all studies reporting the data, MRI/US fusion software-based targeted biopsy necessitates fewer cores to diagnose PCa compared to standard biopsies. In the systematic revision of Valerio *et al.*, MRI/US fusion software-based targeted biopsies detected more clinically significant cancers using fewer cores compared with standard biopsy (median, 9.2 vs 37.1, respectively) [27].

Finally, in terms of more accurate grading of PCa, Lanz *et al.* published a study including 125 men undergoing radical prostatectomy for PCa diagnosed both by MRI/US fusion software-based targeted and standard biopsy. Targeted biopsy detected 126 lesions in 115 patients. The primary Gleason grade, secondary Gleason grade, and Gleason score of the 126 individual tumors were determined accurately in 114 (90 %), 75 (59 %), and 85 (67 %) cases, respectively [39].

Template Systematic Biopsy vs MRI/US Fusion Software-Based Targeted Biopsy

Radtke *et al.* reported a comparative analysis of 294 consecutive patients undergoing systematic transperineal biopsy and MRI/US fusion software-based targeted biopsy. The authors reported that sampling efficiency was in favor of the second method, with 46.0 % of MRI/US fusion

software-based targeted biopsy versus 7.5 % of systematic biopsy cores detecting PCa with a Gleason score ≥7. However, as 12.8 % Gleason score ≥7 was missed by the targeted approach, the authors concluded that the gold standard for cancer detection is a combination of systematic and targeted cores [40].

MRI/US Fusion Visual Targeted Biopsy vs MRI/US Fusion Software-Based Targeted Biopsy

Only two studies directly compared MRI/US fusion software-based targeted biopsy with MRI/US fusion visual targeted biopsy [37, 40], thus indicating the need for further studies. In details, Puech *et al.* reported that in 79 MR imaging targets among 95 patients, positivity for cancer was 47 % with cognitive and 53 % with MRI/US fusion software-based targeted biopsy ($p = 0.16$) [38]. The same results were reported in a prospective study in 125 consecutive men by Wysock *et al.* concluding that MRI/US fusion softwarebased targeted biopsy was more often histologically informative than visual targeting but did not increase cancer detection [41]. Moreover, Cool *et al.* reported the results of 225 simulated targeted biopsies on suspected lesions on MRI, with MRI/US fusion visual targeted biopsy sampling the 45–48 % of clinically significant lesions compared with 100 % obtained with MRI/US fusion software-based targeted biopsy [42]. Delongchamps *et al.* indirectly compared various targeted biopsy approaches in a consecutive series of patients. They reported that rigid and elastic MRI/US fusion software-based targeted biopsies performed significantly better than standard biopsies ($p = 0.0065$ and 0.0016, respectively), while MRI/US fusion visual targeted biopsy did not perform better ($p = 0.66$) [32]. Finally, in a preliminary study including 32 consecutive patients, Mouraviev *et al.* divided 32 consecutive patients into three groups based on the method used to target the suspected lesion. They concluded that MRI/US fusion software-based targeted biopsy (using two different platforms) increases diagnostic accuracy compared with MRI/US fusion visual targeted biopsy [43].

In-Bore MRI Biopsy vs MRI/US Fusion Software-Based Targeted Biopsy

Recently, Arsov *et al.* compared in a prospective randomized trial the PCa detection between inbore MRI biopsy and MRI/US fusion software-based targeted biopsy + 12-core standard biopsy in 210 patients with at least one negative standard biopsy. They reported that PCa detection ($p = 0.7$), detection rates for significant PCa ($p = 0.7$), and the highest percentage tumor involvement per biopsy core ($p = 0.4$) were similar between the arms [44].

Future Perspectives

The most important issue that will have to be addressed with the current use of MRI/US fusion software-based targeted biopsy concerns its role in the diagnostic pathway. The actual scenario is represented by an existing test, the standard 12-core biopsy. The new test, the MRI/US fusion software-based targeted biopsy, could add on or replace the existing test. In most studies, patients

underwent standard prostate biopsy in combination with MRI/US fusion software-based targeted biopsies in the same session. The first high-quality study with a very large sample size that examined the utility of MRI/US fusion software-based targeted biopsy against standard biopsy combined was published by Siddiqui *et al.* In this paper, there was little utility to include standard biopsy in the protocol as 200 men would be needed to be additionally sampled in order to diagnose one additional high-risk PCa, missed by MRI/US fusion software-based targeted biopsy. Further, the two combined approaches lead to a change in Gleason score risk stratification in 15 % of cases, of which 2 % increased to high-risk PCa [35]. Two RCT were recently published comparing MRI/US fusion software-based targeted biopsy and standard biopsy. In the study by Baco *et al.* [36], including 175 patients, the 2-core MRI/US fusion software-based targeted biopsy was comparable to 12-core standard biopsy in terms of clinically significant PCa detection (38 % vs 49 %, respectively, $p = 0.2$) and was more effective for MRI-detected PCa with a PI-RADS score of 4–5 [36]. They concluded that the traditional biopsy may be replaced by two-core MRI/TRUS targeted biopsy. Tonttila *et al.* reported similar results for one-/two-core MRI/US fusion software-based targeted biopsy and 12-core standard biopsy in terms of any cancer (64 % vs 57 %, respectively, $p = 0.5$) and clinically significant (55 % vs 45 %, respectively, $p = 0.8$) PCa [37]. Further evidence about the role of MR/US fusion software-based targeted biopsy in the pathway of PCa diagnosis will be acquired in the near future when the results of ongoing trials will be available [45–47].

The next aspect to evaluate before adopting the new procedure as a new standard of care will be cost-effectiveness. Certainly, the time spent to coregister MRI and US images and to perform the biopsy is longer for MRI/US fusion software-based targeted prostate biopsies compared to the standard approach. Recently, Shoji *et al.* reported that the number of cases to perform an MRI/US fusion software-based targeted prostate biopsy within 20 min was five [48]. With regard to cost, while the fusion biopsy itself has some intrinsic expenses, the greatest increase in cost is due to the necessity to perform MRI on each patient. Nevertheless, some initial studies have shown that the overall cost-effectiveness might be still in favor of a software-based approach [49].

Conclusions

In men at risk with mp-MRI-suspicious lesion, the MRI/US fusion software-based targeted approach seems to have valuable features to be added in the standard diagnostic pathway of PCa for achieving accurate risk stratification. Although it seems to detect more clinically significant PCa as compared to standard biopsy, whether this approach should replace or support the TRUS-guided random biopsy will be determined by ongoing trials.

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Notes:

Notes:

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