

Minimally Invasive Approaches to Localized Prostate Carcinoma

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Prostate cancer is a large and increasing medical problem in most developed countries. In the United States alone it is estimated that in 2005 approximately 232,090 men will be diagnosed with the disease [1]. Widespread application of prostate specific antigen (PSA)-based screening in the early 1990s has contributed to a dramatic increase in the number of prostate cancer cases [1]. While screening may have contributed to a fall in mortality from the disease [2], effective treatment with radical surgery or high-dose radiation therapy has also contributed to the decreased death rates [3,4]. Aggressive treatment with surgery and radiation can result in significant morbidity [5,6]. Given the debate about the need for aggressive treatment for low-risk disease [7,8], it is not surprising that less invasive, less morbid treatments are being actively explored. The most established is laparoscopic and robotic prostatectomy. First performed in 1992 by Schuessler and colleagues [9,10], laparoscopic/robotic approaches have now become an established method of treatment. The debate primarily centers on whether the incremental decrease in morbidity justifies the relatively high cost. On the horizon are even less invasive procedures such as cryotherapy and high-intensity focused ultrasound (HIFU). While these technologies are not as well established as laparoscopic and robotic approaches, they offer the promise of even less morbidity while maintaining cure rates.

Of critical importance in evaluating these technologies is ensuring that they maintain the excellent oncologic outcomes documented for radical prostatectomy and radiation therapy. Long-term data on the oncologic efficacy of these relatively new treatment modalities is not currently available. In this review we will introduce the reader to some of the minimally invasive treatments being developed for the treatment of prostate carcinoma.

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CRYOTHERAPY

Cryosurgery is a tissue ablative technique that uses extreme cold temperatures to freeze and destroy a target tissue or organ. Tissue freezing has been in use since the nineteenth century, when ice was used for skin treatments. The twentieth century witnessed an expansion in cryoablative technology, including the development of novel cryogenic agents and application to different parts of the body. The modern era of cryotherapy began in 1961, when Cooper and Lee [11] developed the small caliber vacuum-insulated liquid nitrogen cryoprobe, which enabled precise organ targeting for the first time.

Cryobiology

There are a number of theories to explain the mechanism of tissue injury in cryosurgery. The most accepted theory is that freezing tissue directly causes cellular injury. According to this theory, there are four main parameters that determine the extent of injury [12–14]: (1) Cooling rate. At low cooling rates, cellular damage is initiated through an extracellular effect. Specifically, freezing causes an elevation in the extracellular solute concentration, leading to an osmotic dehydration of the cell. Conversely, when the cooling rate is sufficiently rapid to trap water within the cell, it cannot osmotically equilibrate with the extracellular space, leading to the nucleation of ice within the cell. These intracellular ice crystals cause injury to the organelles and membranes, ultimately leading to cell death. (2) Minimal temperature achieved. It is generally accepted that a temperature of -40°C should be reached to completely eradicate the viable tissue using a two-cycle method [15]. (3) Time at the minimum temperature. Maintaining the minimal temperature for at least 3 minutes is important for complete tissue destruction. (4) Thawing rate. During thawing, ice crystals fuse together, forming larger crystals that are disruptive to the cell membranes. A minimum of two freeze-thaw cycles should be performed as the coagulative necrosis area is much larger compared with one cycle [15]. Using the latest cryoprobe technology, these cycles involve argon gas freezing and active helium gas rewarming.

There are alternative theories that have possible relevance to cryotherapy. In 1877, Cohnheim hypothesized that frostbite necrosis is caused by post-thawing vascular occlusion. Specifically, freezing causes an initial period of vasoconstriction, followed by vasodilatation and increased cellular permeability. This cascade leads to endothelial cell damage, platelet aggregation and thrombotic occlusion within the blood vessels (especially the microvasculature), ultimately resulting in tissue ischemia and necrosis [13,16]. A second hypothesis is that cryotherapy causes damage via an immune-mediated mechanism, where the damaged tissue leads to a sensitization of the host immune system [14,17].

History of Prostate Cryoablation

Gonder and Soanes were the first to describe the use of cryoablation for benign and malignant prostate disease [18–21]. A single cryoprobe was inserted initially transurethraly and often re-inserted through a perineal window to target

the prostatic apex. The freezing process was monitored by digital rectal palpation, in conjunction with a temperature sensor placed in Denonvilliers fascia. Unfortunately, this method almost invariably led to urethral sloughing and urinary dysfunction. Urethrorectal fistula and urinary incontinence were not uncommon, since there was no precise way to monitor the extent of the frozen area.

Prostate cryosurgery improved in the late 1980s with the development of transrectal ultrasonography (TRUS), enabling real-time imaging of the prostate gland. In 1988, Onik and colleagues [22] described the imaging characteristics of the frozen prostate and then described a novel type of cryotherapy, involving multiple cryoprobes guided by sonography, as well as the placement of a urethral warming catheter [23]. The surgeon could now monitor probe insertion and location, and precisely define the freeze area borders to better preserve the rectum. The introduction of a urethral warming catheter helped prevent urethral sloughing and the resultant strictures [22,23]. Because of the continued incidence of severe complications such as rectourethral fistula and urethral sloughing combined with unsatisfactory oncologic outcomes, the procedure fell out of favor.

The introduction of gas-driven probes in the late 1990s ushered in the third generation of prostate cryotherapy. These probes function by the Joule-Thompson rule, which predicts temperature changes for a high pressure gas as it expands through a narrow port and depressurizes. In these probes, argon gas cools to -186°C and is used for active freezing, while helium gas warms to around $+40^{\circ}\text{C}$ and is used for active thawing. The new cryoprobes are smaller (17 gauge = 1.47 mm) and a brachytherapy template is used to facilitate accurate transperineal placement of probes. Multiple temperature sensors are used for better control of the freeze area and a urethral warming catheter is routinely placed to protect the urethra [16,24]. In addition, patient selection has improved. The optimal prostate size is less than 50 g and Gonadotropin-releasing hormone (GNRH) analogs can be given to men with larger prostates to reduce volume.

Technique

Bowel preparation is typically done on the day before surgery. The procedure itself is performed with the patient in an exaggerated lithotomy position under general anesthesia. A TRUS probe is then placed in the rectum, which allows realtime visualization of the expanding ice-ball. The TRUS probe is attached to a holding device for the probe insertion template, and cryoneedles are placed in three to four rows with approximately 1 cm between them. Up to five thermocouples can be placed to monitor temperatures in critical areas. Denonvilliers fascia and the rectum are protected by clear ultrasound visualization of the ice-ball as it reaches the posterior prostatic capsule. At both the apex and lateral borders a minimum of 2 to 4 mm of ice-ball expansion should be used for adequate cancer treatment.

Once the probes are in place, cystoscopy is performed to rule out any urethral or bladder perforation. Based on the surgeon's preference, a suprapubic

tube may also be inserted at the beginning of the procedure. The warming catheter, which is connected to a circulating pump of 43°C warmed saline, is then inserted. It is recommended that two full freeze-thaw cycles (approximately 10 minutes freezing followed by 4 to 6 minutes of active helium thawing) be performed. At the end of the procedure, the cryoprobes are removed, while the warming catheter is left in place for another 5 to 10 minutes. The warming catheter is then removed and replaced with a standard urinary catheter, unless a suprapubic tube was placed at the beginning of the case. Patients are usually discharged the same day.

Results

Katz and Rewcastle [25] recently published a comparison of published 5-year biochemical progression-free survival rates between different forms of primary therapy for prostate cancer. Their comparisons were based on literature published between 1992 and 2002, and included data from the largest series of cryotherapy follow-up to date [26,27]. Biochemical progression was defined using the American Society for Therapeutic Radiology and Oncology (ASTRO) criteria, and patients were classified into low-, intermediate-, and high-risk groups for purposes of comparison [28,29]. According to this review, radical prostatectomy was superior in the low-risk group [25]. In the intermediate- and high-risk groups, however, there was a decline in efficacy for all treatment options with the exception of cryotherapy, which had the highest PSA progression-free survival within the 5 years of follow-up currently available in the literature.

In terms of complications, impotence remains a significant problem after prostate cryotherapy (80% to 100%). Some authors have suggested performing a one-sided nerve-sparing procedure, in which only the side with a positive biopsy is treated with cryotherapy. The untreated side is followed with repeat biopsies. In the small initial series, seven of nine patients maintained potency; however, this technique remains controversial [30,31].

With the advent of third generation cryotherapy technology, there has been a substantial decline in the morbidity. In fact, rectal and bladder complications (<0.5%) are now rare in patients undergoing primary treatment [26,27,32]. In the recent literature, prostate cryotherapy is associated with an incontinence rate of up to 5.4%, and approximately 1.3% to 5.5% of patients have required transurethral resection of the prostate (TURP) for bladder outlet obstruction following cryotherapy [26,32]. Scrotal swelling and pelvic pain are additional complications and are reported in up to 5.9% of patients [33].

Cryoablation has also been used to treat local recurrences following external beam radiation therapy and brachytherapy. In this setting, cryotherapy may be associated with a lower risk of incontinence than salvage radical prostatectomy (6.7% to 7.9%) [34,35]. Salvage prostate cryotherapy is associated with an 18-month PSA progression-free survival of 34% to 74% [16,34,35], which compares favorably to progression-free survival for salvage radical prostatectomy [36].

Future Directions

In light of the tremendous advances in the field of radiation oncology over the past few decades, it is likely that cryotherapy will continue to evolve. New and improved imaging devices, combined with computerized treatment planning, and more accurate cryoprobes and thermocouples will enhance current capabilities for tissue destruction with less damage to the surrounding tissues. Long-term outcomes of patients treated with third generation cryotherapy technology will define the oncological efficacy of cryosurgery for prostate cancer compared with other therapies.

HIGH-INTENSITY FOCUSED ULTRASOUND

Background

High-Intensity Focused Ultrasound (HIFU) is an innovative minimally invasive approach. In contrast to cryosurgery, the probes do not need to be inserted directly into the prostatic tissue. Instead, a probe is inserted transrectally and a high-energy ultrasound beam is focused into the prostate. Acoustic energy absorbed by the prostate tissue is converted into thermal energy with intraprostatic temperatures reaching upwards of 98.6°C. The result is a focal area of coagulative necrosis. Tissue outside of the focal zone, including rectal mucosa and serosa, has no significant temperature rise and therefore no tissue damage [37,38]. HIFU is widely available in Europe, but outside of clinical trials, it is not widely available in the rest of the world.

Technique

Prostatic HIFU is performed in the operating room under spinal or general anesthesia. The patient is placed in a lateral position. The imaging and treatment probes are positioned transrectally. The prostate is imaged using a diagnostic probe and a treatment plan is created. A series of adjacent, oval shaped target zones, approximately 24 mm in height and 1.6 mm in diameter, are mapped to each cross-sectional level of the prostate (Fig. 1). The machine is activated and automatically cycles through the treatment plan delivering upwards of 600 adjacent lesions to treat the entire prostate. Since it is critical that the patient does not move during the procedure, a monitoring device automatically deactivates the machine if the patient moves. In addition, cooling fluid is circulated around the treatment probe to protect the rectal wall.

It is important to recognize that prostatic HIFU is still evolving and that other techniques, such as perineal probes, are being actively explored. While preclinical models have demonstrated tissue ablation and safety, further work is needed to demonstrate efficacy and superiority to the more mature transrectal approach [39].

Results

Studies evaluating HIFU in prostate cancer have predominantly focused on patients who were not candidates for radical prostatectomy because of significant

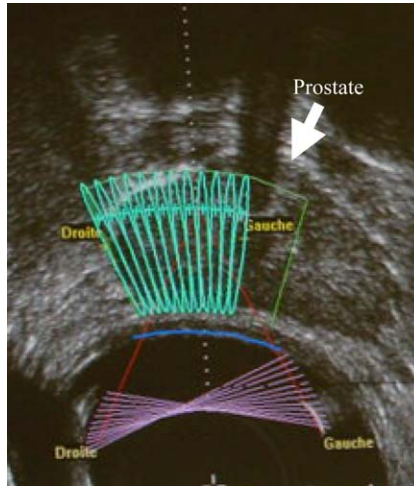


Fig. 1. Prostatic High-Intensity Focused Ultrasound.

comorbidity or prior external beam radiation therapy. In addition, many studies included patients who did not wish to risk the morbidity associated with surgery.

Early data demonstrating coagulative necrosis in treated prostate tissue [37] and potential efficacy in phase I trials [40], led to a large open-label multicenter study in Europe. Four hundred and two patients were treated from 1995 to 1999. Twenty-eight percent of the patients were treated with multiple sessions, highlighting a potential strength of HIFU: the ability to retreat if necessary. Eighty-seven percent of the 288 patients who were rebiopsied after treatment had negative biopsies. The average PSA nadir was 1.8 ng/mL. Complications reported included rectourethral fistulas in 1.3% and incontinence in 13.1%. Follow-up was relatively short at 407 days. The treatment protocol evolved during the trial making interpretation of results and complications difficult [41].

Later studies have standardized the technique. An early study by Beerlage and colleagues [42] treated 111 patients with T1-3NxM0 prostate cancer. The first 49 patients were treated selectively; focusing the ultrasound on the region of the prostate believed to harbor the tumor. In this selectively treated cohort only 19% achieved a PSA less than 0.5 ng/mL, while 30% had PSA nadirs of greater than 4 ng/mL; 72% of patients in this study had residual cancer on repeat biopsy. The lack of efficacy in this patient population probably reflects the multifocal nature of prostate cancer and the limitation of prostate-sparing HIFU.

The remaining 62 patients received treatment to the entire prostate. Fifty-five percent achieved a nadir less than 0.5 ng/mL and only 9% had a nadir greater than 4 ng/mL. The repeat positive biopsy rate of 32% was relatively high in this study. No long-term progression-free survival data were presented. There were

significant side effects to the treatment with three patients developing rectourethral fistulas, nine patients developing stress incontinence, and one patient developing urethral stenosis [42].

Blana and colleagues [43] treated 146 patients with cT1-2N0M0, Gleason Sum less than or equal to 7 and PSA levels less than 15 ng/mL. PSA nadir was achieved after 3 months. Fifty-six percent of patients had a nadir less than 0.1 ng/mL, 83% had a nadir less than 0.5 ng/mL, and 92% had a nadir less than 1 ng/mL. Control biopsies following treatment were negative in 93% of cases. At 22-month follow-up, the median PSA was 0.15 ng/mL and 87% of patients had a PSA less than 1 ng/mL. Complications remained a significant problem. Suprapubic tubes were used routinely to prevent retention and 12% required TURP. Stress incontinence was present in 10% of the patients immediately following HIFU but this improved to 6% at last follow-up. Fifty-three percent of patients who were potent preoperatively developed impotence. Only one patient developed a rectourethral fistula.

In an effort to decrease complications, groups have continued to modify their techniques. Gelet and colleagues [44] spared tissue at the apex in an effort to improve continence rates. They treated 102 patients and found that 22.5% continued to have some degree of incontinence. At 19-month follow-up, 66% of the patients had no evidence of disease. The authors also advocated sparing tissue along the neurovascular bundle to preserve potency in selected patients. In an effort to decrease postoperative retention, Vallancien and colleagues [45] performed transurethral resections of the prostate before HIFU. Treating 30 patients staged cT1-2N0M0, PSA less than 10 and Gleason Sum less than or equal to 7, they found that 73% had negative biopsies at 1 year and 3 patients had a PSA greater than 4 ng/mL. Two patients developed urinary retention, one patient developed urinary incontinence, and no patients developed a rectourethral fistula. These results demonstrate that the technique has evolved, resulting in improved cure rates. However, urinary and sexual functional outcomes remain a significant issue for HIFU treatment.

HIFU has been frequently used for primary treatment of localized prostate cancer, but it has also been widely used for PSA failures following external beam radiation therapy. Because of the significant morbidity associated with salvage prostatectomy, investigators have explored this treatment option [36]. Gelet and colleagues [46] treated 71 patients with recurrent disease following external beam radiation therapy. Many of these patients had high-risk disease before External Beam Radiation Therapy; 15 patients had cT3 disease, the mean PSA was 20.4 ng/mL (range 3.5 to 60.0) and 7 patients had Gleason sum 8 to 10. Before HIFU all patients had a biopsy to prove local recurrence and a negative metastatic work-up. The mean PSA at the time of HIFU was 7.7 ng/mL with a range of 0.5 to 54 ng/mL. Forty (56%) of the patients received additional systemic therapy in addition to the HIFU. At 14.8-month follow-up, 57 had negative biopsies, 9 patients developed metastatic disease, and 4 patients died of prostate cancer. Side effects were substantial with 4 rectourethral fistulas, 25 cases of incontinence, and 12 bladder neck strictures. This significant

side effect profile must be balanced against the side effects that occur in patients who fail radiation therapy and are treated with other modalities [36].

In summary, HIFU is still evolving as a treatment modality. Rebiopsy results generally demonstrate low residual cancer rates in the prostate. Unfortunately, long-term biochemical, disease-specific, and overall survival data are not available at the current time. The procedure continues to undergo modifications to spare tissue near the neurovascular bundle and at the apex, in an effort to decrease impotence and incontinence, respectively [44,47]. The effect these modifications will have on cure rates is unclear. Introduction of rectal cooling has decreased the risk of fistulas substantially [41] and TURP at the time of treatment appears to decrease risk of retention [45].

LAPAROSCOPIC AND ROBOTIC RADICAL PROSTATECTOMY

Background

Laparoscopic prostatectomy was first described in 1992 [9] and the first series was reported in 1997, but consisted of only 9 cases [10]. The authors concluded that the procedure was technically difficult and did not offer a clear advantage over open radical prostatectomy. The technique was limited by instrumentation and the difficulty of performing the vesicourethral anastomosis. Interest in laparoscopic prostatectomy was renewed in 1999, when two separate groups of urologists reported successful adoption of laparoscopic radical prostatectomy with greatly reduced operative times [48,49]. The description of a standardized technique with initial oncologic outcomes similar to open procedures and the promise of decreased morbidity led to a newfound interest in the technique [50]. The procedure was still limited by the intracorporeal suturing skill level required to perform a laparoscopic vesicourethral anastomosis.

The introduction of surgical robotics has helped to speed the application of endoscopic techniques to radical prostatectomy [51–54]. The use of robotic-assisted systems facilitates endoscopic suturing, one of the most technically demanding steps of the procedure. Robotic prostatectomy may have a shorter learning curve than standard laparoscopy [52]. While providing some advantages to the surgeon, the cost of the robotic system is prohibitive to many centers and is a limiting factor in the spread of this technology.

Technique

Laparoscopic techniques have been developed to emulate established procedures for open nerve-sparing radical prostatectomy [55,56]. Surgeons at the Montsouris Institute described one of the first standardized techniques to be used in a large series of patients [50]. Many other groups have reported variations of the operation. The major difference in surgical approaches is whether the operation is performed intraperitoneally or extraperitoneally (as an open nerve-sparing radical prostatectomy). Extraperitoneal approaches keep the peritoneal contents out of the operative field, lessening the chance for injury and can help to confine postoperative urine leaks or hematomas [57]. While

this offers some advantages, the extraperitoneal approach can be more difficult because the working space is limited [58].

For reference and illustration, we will briefly describe the Montsouris technique as first reported [50]. Technical updates and minor variations in technique among different centers are beyond the scope of this review. With the patient under general anesthesia, the peritoneal cavity is insufflated with CO₂ gas. A 10-mm trocar or laparoscopic port is placed at the umbilicus and a video camera is inserted through this for visualization. A voice-controlled robotic arm (AESOP, Computer Motion, Goleta, CA) is frequently used to control the camera movements. An additional 10-mm port and three 5-mm ports are placed in a fan-like configuration across the midportion of the abdomen to allow access to the pelvis. An incision is made in the Pouch of Douglas and the seminal vesicles and vasa deferentia are dissected. Denonvillier's fascia (the fascial layer between the prostate and rectum) is divided and the posterior prostatic dissection is completed. The space of Retzius (the potential space between the bladder and the anterior abdominal wall) is developed. The endopelvic fascia covering the prostate is then divided and the dorsal venous complex is ligated. The plane between the prostate and bladder is then developed. When the bladder has been separated from the prostate, dissection is continued until the surgeon identifies the seminal vesicles and vas in the previously dissected area posterior to the bladder and prostate. At this point the vascular pedicles of the prostate are divided in an antegrade (prostatic base to apex) fashion (different from open radical prostatectomy, where the procedure proceeds retrograde [prostatic apex to base]). Nerve-sparing is also performed during this step. When the apex of the prostate is reached, the previously ligated dorsal venous complex is divided as is the urethra. Although blood loss is usually minimized at this step in laparoscopy, significant hemorrhage can still occur, as in open surgery. The specimen is placed in a laparoscopic extraction bag and placed out of the surgical field for removal at the end of the procedure. The urethrovesical anastomosis is sewn in an interrupted fashion, using eight or more sutures (compared with four to six typically used in open surgery). The more watertight anastomosis may allow earlier catheter removal than in open surgery [59]. Many surgeons, especially those using robotic techniques have used a running vesicourethral anastomotic suture to limit the number of intracorporeal knots that need to be tied.

The largest series of robotic-assisted prostatectomies reported so far has used a modification of the Montsouris technique (antegrade, intraperitoneal) [60]. Robotic-assisted prostatectomy makes use of the da Vinci robot (Intuitive Surgical, Sunnyvale, CA) (Fig. 2). The configuration of ports is similar to a standard laparoscopic approach; the robotic camera lens is placed through the umbilical port and two other ports are for two robotic arms. Additional ports are used for the surgical assistant to provide retraction, suction or to pass sutures. The surgeon sits at a console remote from the operating table. The da Vinci robotic system offers several potential advantages over standard laparoscopy including improved depth perception for the surgeon and additional



Fig. 2. The da Vinci Surgical System. The surgeon sits at a remote console and controls the robotic arms, while an assistant is at the patient's side to provide retraction and suction when needed. (Courtesy of Intuitive Surgical Inc., Sunnyvale, CA. ©2006 Intuitive Surgical Inc.)

degrees of freedom of motion. The console provides improved ergonomics for the surgeon. Whether these advantages will translate into improved surgical outcomes remains to be shown. Of note, a disadvantage of the robotic system is the lack of tactile feedback.

Results

For the advantages of the decreased morbidity of laparoscopic and robotic prostatectomy to be worthwhile, functional and oncologic outcomes for the procedures had to be equivalent to open radical prostatectomy. Initial reports of laparoscopic and robotic prostatectomy focused on feasibility, complications, and perioperative outcomes. As the procedure became more well established, researchers began to report functional outcomes, most importantly urinary control and sexual function. Because prostate cancer tends to be a slow-growing cancer, early reports of the technique focused on pathologic parameters such as margin status as a surrogate for long-term progression-free survival. However, now that many of the surgical series are more mature, intermediate-term oncologic outcomes are becoming available.

The initial reports of the French groups showed that laparoscopic prostatectomy could be accomplished safely [48,49]. These initial series showed that complications decreased with increasing surgeon experience. As other centers adopted the procedure, it became apparent that there was a steep learning curve to the procedure [61]. In the first large (>100 patients) series of patients, reported operative times decreased with increasing surgeon experience [48]. The patients were divided into three groups: first 40 cases, middle 40 cases, and last 40 cases. Other outcomes such as blood loss, transfusion rate, and the rate of conversion to open surgery all improved in the latter group of cases compared with the first group of cases. The overall positive margin rate was 15%, which compares favorably to a series of open prostatectomies with

reported positive margin rates reported by Hull and colleagues (12.8%) [62] and Lepor and colleagues (19.9%) [63]. Another French group reported on their first 134 patients [64]. In this series the mean operative time was 4.7 hours, transfusion rate was 3%, and no cases were converted to open surgery.

There are several recent studies that have focused on the complications of radical prostatectomy in large series of surgeries performed by surgeons experienced in radical retropubic prostatectomy and in laparoscopic radical prostatectomy (Table 1) [59,63,65,66]. Lepor and colleagues [63] reported on the complication rate for a large single-surgeon series of radical retropubic prostatectomies. Open surgery had a higher estimated blood loss than laparoscopic prostatectomy (818.6 ml versus 380 ml), which resulted in a higher transfusion rate (9.7% versus 4.9%) [59,63]. Serious intraoperative complications such as rectal/bowel and ureteral injuries were rare in both techniques but were more common in the laparoscopic series (Table 1) [59,63]. The need for reoperation was also higher in the laparoscopic series reported by Guillonneau and colleagues (3.7%) [65] and Rassweiler and colleagues (1.8%) [59] than in the open series reported by Lepor and colleagues (0.5%) [63]. Anastomotic stricture rates were similar between a series of retropubic prostatectomies and a series of laparoscopic prostatectomies (4% versus 4.1% to 6.4%) [59,66]. Postoperative complications such as pulmonary embolism, deep vein thrombosis, myocardial infarction, and death were rare in all series, both open and laparoscopic.

As experience with laparoscopic radical prostatectomy has increased and the procedure has been promulgated, several large and mature patient series have been reported in the literature. These series have adequate numbers of patients and length of follow-up to make comparisons to contemporary series of open

Table 1

Comparison of complications of radical prostatectomy and laparoscopic and robotic prostatectomy

Institution	NYU [63]	Washington University [66]	Montsouris [65]	Heidelberg [59]
Technique	Open retropubic	Open retropubic	Laparoscopic	Laparoscopic
No. of Patients	1000	3477	567	438
Complications				
Rectal injury, %	0.05	0.05	1.4 ^a	0.7
Ureteral injury, %	0.2	0.05	0.5	—
Est. blood loss, ml	818	—	380	800–1100
Transfusion rate, %	9.7	—	380	4.9
Pulmonary embolism/ Deep vein thrombosis, %	0.4	1.3	—	<1
Myocardial infarction, %	0.5	0	0.1	<1
Reoperation, %	0.5	—	3.7	1.8
Anastomotic stricture, %	1	2.7	—	4.1–6.4
Conversion to open surgery, %	—	—	1.2	0.5

^a192% including other bowel injury.

radical prostatectomies (Table 2). In the largest published series of laparoscopic prostatectomies to date, oncologic outcomes were reported with a median follow-up of 12 months [73]. Three-year progression-free survival was improved for patients with negative surgical margins (90%) compared with positive margins (67%) ($P < .001$). The overall positive margin rate was 19.2% (6.9% pT2a, 18.6% pT2b, 30% pT3a, 34% pT3b) [73]. These results are comparable to several contemporary series of open prostatectomies. Catalona and Smith [76] reported 3-year progression-free survival rates of 93% for patients with organ-confined disease, 88% with microscopic extracapsular extension, and 75% with extracapsular extension and positive margins. Results of long-term oncologic efficacy are awaited for laparoscopic and robotic prostatectomy, but early and intermediate pathologic and oncologic results are similar to open radical prostatectomy, which suggests that similar long-term results may be expected.

While oncologic results are of paramount concern, evaluation of prostate cancer treatments must include evaluation of the effect on urinary control and sexual function. Modern radical retropubic prostatectomy, adhering to and improving on the anatomic principles and techniques described by Walsh and colleagues [55,56] has allowed contemporary surgeons to achieve outstanding functional results for radical retropubic prostatectomy (Table 2). Most authors have defined patients who did not need to wear a pad at 12 to 18 months of follow-up as continent. Large single-surgeon series of radical retropubic prostatectomy have published continence rates of 92% to 97% [67,72,77]. These results are similar to a large population-based study of patients who underwent radical retropubic prostatectomy [78]. Published continence results for laparoscopic and robotic prostatectomy range from 82.3% to 96.0%

Table 2

Oncologic and functional outcomes for selected large radical prostatectomy and laparoscopic/robotic prostatectomy series

Institution	Positive margin rate (%)	Freedom from biochemical progression 5/10/15 years (%)	Continence ^a (%)	Potency ^b (%)
Wash. Univ. [67,68]	19	80/68/—	93	76
NYU [63,69]	19	—	97	—
Johns Hopkins [70,71]	11	84/74/66	95	68 (25–91)
Baylor [62,72]	12	82/77/75	95	70
Laparoscopic and robotic prostatectomy series				
Montsouris [73,74]	7–34 ^c	90.5 (3 y)	82.3	85
Heidelberg [59]	24	87 (2.5 y)	90.3	—
Créteil [64]	25	89.6 (11 mo)	86.2	58.8
Henry Ford [75]	6	—	96	38–64

^aContinence most commonly defined as not using pads (follow-up usually >12 months).

^bPotency most commonly reported as ability to have intercourse with oral phosphodiesterase inhibitors.

Potency outcomes usually only reported for bilateral nerve-sparing (follow-up usually >12 months).

^cStage dependent.

(Table 2). Comparison of continence rates among multiple series of surgeries is difficult because of the varying definitions of continence, length of follow-up, and ages of the patients, all factors that have been determined to affect urinary continence outcomes [67].

Sexual function is another important functional outcome after prostate cancer surgery. Again, comparison of results between different series and techniques is somewhat difficult given the bias of patient selection. In addition, many published studies rely on physician or patient reported outcomes, not on validated measurement tools. Postoperative potency is most commonly defined as the ability to have an erection sufficient for intercourse with or without the aid of an oral phosphodiesterase inhibitor. Most series have reported on men who were potent preoperatively and had bilateral nerve-sparing procedures at a minimum of 12 to 18 months of follow-up. With these caveats in mind, reported potency rates for radical retropubic prostatectomy range from 68% to 76% in several large single-surgeon series [67,72,77]. These results are much higher than those reported in a population-based study of prostate cancer outcomes, where only 40% of men retained sexual function after surgery [78]. Laparoscopic and robotic prostatectomy series have achieved results similar to those reported for open surgery with rates of 38% to 85% reported (Table 2) [59,64,74,75].

In summary, oncologic and functional outcomes of radical retropubic prostatectomy have been excellent. Attempts to improve on these outcomes with laparoscopic and robotic prostatectomy will be difficult. Advantages of laparoscopic and robotic approaches include improved visualization of pelvic anatomy including the urethral sphincter and neurovascular bundles, less blood loss, and modest benefits in postoperative catheterization and recovery times. Early and intermediate oncologic outcomes for laparoscopic and robotic prostatectomy seem favorable and functional results in large series are comparable to similar series of radical retropubic prostatectomies. Long-term oncologic results are awaited for laparoscopic and robotic procedures. Laparoscopic and robotic prostatectomy has become the preferred surgical procedure for clinically localized prostate cancer at some centers. The benefit over open approaches is not unequivocal, however. There is a steep learning curve for these procedures and the functional and oncologic outcomes are not significantly different from those of radical retropubic prostatectomy.

SUMMARY

Prostate cancer is an increasing medical problem. Radical prostatectomy and radiation therapy are effective treatments, but have the risk of significant morbidity. Clinicians have strived to develop new modalities of treatment that can maintain the excellent treatment outcomes of radical prostatectomy, but diminish the morbidity. Improved instrumentation, optics, and robotic technology have allowed the application of laparoscopic techniques to radical prostatectomy. Patients can have less blood loss and expect more rapid recovery. Intermediate oncologic outcomes appear similar to radical prostatectomy with good functional

results. Cryotherapy and HIFU are tissue ablative approaches rather than extirpative approaches to prostate cancer treatment. They attempt to use nonsurgical methods to treat prostate cancer with the hope of providing oncologic control comparable to surgery and radiation while minimizing morbidity.

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