

Original Article***Urethral Perfusion for Cryoablation of the Prostate***

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ABSTRACT

Cryosurgery is an emerging treatment method for prostate cancer patients that may expand the scope of practice for perfusionists. Because of the low temperatures needed to cryogenically destroy cancerous tissue, damage to the urethra and bladder may cause incontinence and impotence. As a result of this associated morbidity, an extracorporeal circuit was constructed by the perfusionists at the University of Nebraska Medical Center (Omaha, NE). This urethral perfusion circuit provides a way to maintain normothermic urethral and bladder temperatures during cryogenic procedures, thus preventing trauma to the urethra and bladder.

Five patients with a mean age of 73.3 ± 3.0 years diagnosed with localized prostate cancer (Stage A, B, C) were offered cryosurgery using urethral perfusion to treat their cancer. After induction of general anesthesia, a specially designed urethral catheter was inserted. Quarter-inch tubing was attached to barbed connections on the catheter and the free ends were then attached to the circuit. This extracorporeal circuit consisted of a heater/cooler, a twin roller pump, a cardioplegia heat exchanger, and temperature and pressure monitoring devices at the inlet and outlet sites on the catheter. Normal saline was circulated through the tubing of the urethral perfusion circuit to maintain flow rates of 200-400 ml/min, with the circuit pressure not exceeding 300 mmHg.

Average urethral perfusion time was 139.3 ± 17.7 minutes. Inlet temperature of the catheter was kept at 42°C to maintain an average bladder temperature of $38.2 \pm 2.3^\circ\text{C}$. All of the patients tolerated the procedure well and were ambulating without assistance on postoperative day one. With the exception of one patient with acute postoperative anuria, patients were discharged on the first postoperative day. Cryosurgery of prostate cancer using urethral perfusion has the potential to serve as a unique practice opportunity for perfusionists.

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INTRODUCTION

Prostate cancer is the most frequently diagnosed male carcinoma in the United States, with 200,000 new cases detected in 1996 (1). Controversy exists concerning the most appropriate method for treating prostate cancer which traditionally has included radiation therapy or radical prostatectomy. Each therapy is associated with significant morbidity including impotency, incontinence, radiation cystitis, and proctitis (2-5). Because of these serious complications, investigation of a new therapeutic method to treat prostate cancer led urologists to reconsider the technique of cryosurgical ablation.

Cryosurgical ablation is an *in situ* freezing of prostatic tissue, initially applied in 1966 by Gonder et al with the use of transurethral cryoprobes (6). Unfortunately, unacceptable complications including incontinence and impotence occurred, primarily due to an inability to monitor and control the freezing process, prohibited the widespread use of this technique (7,8). Technological advances, such as the development of a cryosurgical machine to deliver liquid nitrogen through small probes to achieve colder temperatures and more homogeneous freezing of the prostate, as well as real time ultrasound to guide accurate placement of the probes and monitoring of the freezing process, have recently made this treatment option viable (9).

In 1993, Onik et al reported on their early experience with this improved technique, achieving an 80% negative biopsy rate at three months and an initial morbidity rate of about 5% (2). Since then, other studies using this technique have shown a 70% negative biopsy rate without significant morbidity (8).

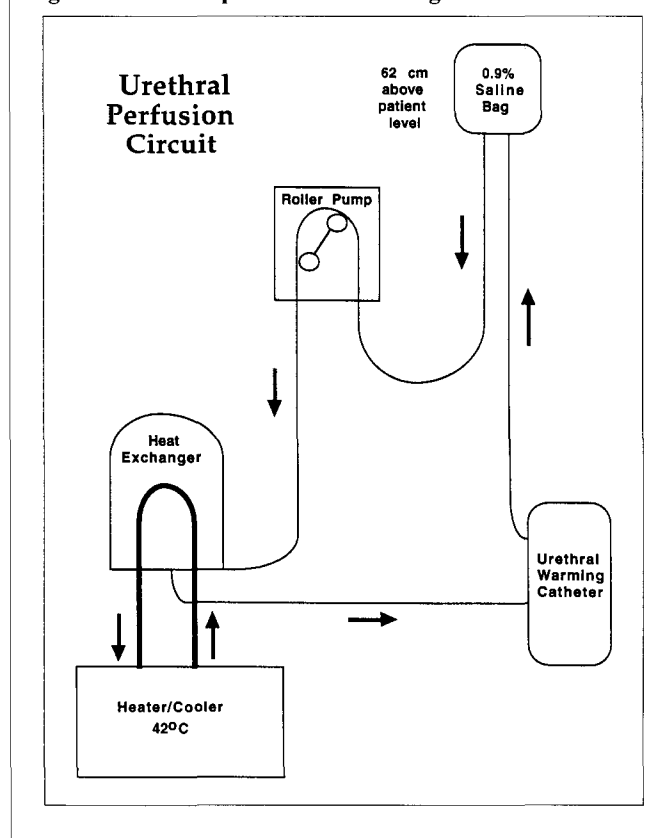
The potential advantages of cryosurgical ablation are numerous, including shorter operating time, rapid recovery, and decreased hospital stay. Cryosurgical ablation of the prostate also shows potential cure rates for localized prostate cancer are at least as good as, if not better, than radiation therapy. However, long term data is currently unavailable as the first patients had surgery only three years ago.

The role perfusionists have in this surgical procedure is in designing and implementing a circuit to safely circulate warm saline through a urethral catheter using readily available materials and equipment, thus maintaining the integrity of the urethral epithelium, limiting the destruction of healthy prostatic parenchyma, and preventing the sloughing of urethral tissue during cryosurgery (10).

MATERIALS AND METHODS

After obtaining Institutional Review Board approval and informed consent, a total of five patients with a mean age of 73.3 ± 3.0 years diagnosed with prostate cancer (Stage A, B, C) were offered cryosurgical ablation of the prostate. Patients included in this study had to be able to tolerate the procedure under general anesthesia, adhere to required follow-up, and be candidates for the alternative standard therapies should the cryosurgical therapy fail. At our institution, these subjects included patients

Figure 1: Urethral perfusion circuit diagram



who were not candidates for a radical prostatectomy, patients where radiation treatment had failed, elderly males (average age 70 years) or young males who were otherwise healthy. Patients were excluded from this study if their medical history was such that standard treatment options would not be offered.

After induction of general anesthesia, the patient was placed in the dorsal lithotomy position. Using sterile technique, a suprapubic bladder catheter was placed under cystoscopic guidance. The cystoscope was removed and a 22 Fr balloon sleeve was passed through the urethra and into the bladder. The scrotum and urethral catheter were elevated and attached to a Buchwalter surgical retractor to reveal the surgical field.

The urethral perfusion circuit consisted of a twin roller pump^a calibrated to quarter inch tubing, two lengths of sterile ten foot quarter inch tubing, a heater/cooler^b, a cardioplegia heat exchanger^a, pressure and temperature monitoring devices, and a three liter bag of normal saline with a rapid prime line. The two lengths of tubing were brought to the sterile field and connected to the urethral warming catheter. The inlet to the catheter connection was distal to the heat exchanger and the outlet from the catheter was into the three liter normal saline bag (Figure 1). This bag, which receives returning fluid from the catheter, should be elevated above the patient to maintain a hydro-

a Sorin Biomedical, Irvine, CA

b Sarns/3M Health Care, Ann Arbor, MI

der of both urine and necrotic tissue. Since the initial attempts of cryoablation of the prostate by Gonder et al (6) in 1966, several important technological advances have been developed to provide a greater margin of

Table 1: Demographic data

Patient	Age	Cancer Type	Previous Treatment	Urethral Perfusion Time	LOS (hours)
A	74	Adenocarcinoma	External Beam Radiation	128	31
B	70	Adenocarcinoma	Laparoscopic Lymph Node Dissection	125	24
C	74	Adenocarcinoma	External Beam Radiation	140	24
D	68	Adenocarcinoma	External Beam Radiation	145	26
E	76	Adenocarcinoma	Watchful Waiting	164	69*

LOS: length of stay in hospital from operative time to discharge. *Over postoperative 24 hours, patient was anuric and was not discharged because of low urine output.

static pressure column on the catheter. Normal saline warmed to 42° C circulated through the catheter to achieve a normothermic urethral temperature. Flow ranges through the catheter were maintained between 200-400 mL/min with line pressures not exceeding 300 mmHg.

Following transrectal ultrasound-guided cryoablation of the prostate, the urethral perfusion catheter was removed and a Foley bladder catheter was placed as a stent. The patient was then transferred to PACU and later admitted to the hospital with an anticipated hospital stay of 24 to 48 hours. The Foley catheter was removed prior to discharge while the suprapubic tube remained in place. Study patients returned to the urology clinic for their post-surgical visit one week after the operation.

RESULTS

Average outlet temperatures at the catheter, which reflected the temperature of the bladder, were $38.2 \pm 2.3^\circ$ C. Flows in the circuit were maintained at 200-400 mL/min and the transurethral pressure readings did not exceed 300 mmHg. This pressure was much lower than that required to rupture the system, yet adequate enough to keep the balloon sleeve of the catheter fully dilated. Average perfusion time for the cryoablation was 139.3 ± 17.2 minutes.

All of the study patients tolerated the procedure well and were ambulating without assistance on the initial postoperative day. With the exception of one patient who developed acute postoperative anuria and was later discharged on postoperative day three, the remaining study patients were discharged on the first postoperative day (Table 1).

DISCUSSION

Cryosurgical ablation of the prostate is potentially a more successful method of treating prostate cancer than radiation treatment (11). Prostatic cryoablation was initially abandoned because of the significant associated morbidity, most notably, urethral sloughing from the transmural freezing of the urethra and extrusion of the necrotic tissue (17). This led to urinary retention with repeat catheterization necessary to drain the blad-

safety for patients undergoing this procedure. The use of 5 cryogenic probes, which allow for continuous cooling of liquid nitrogen and improved distribution of the freezing process, as well as modern ultrasound technology which permits more accurate probe placement in the prostate gland, have led to decreased complications during this procedure (2,18). Thus, cryosurgical ablation of the prostate is gaining popularity as an alternative treatment protocol for prostate cancer.

Due to these technological advances, Onik et al successfully reintroduced cryosurgery of the prostate in the late 1980s (1, 12). Their prospective study compared two treatment groups, each receiving cryosurgical ablation of the prostate (2). Group 1 consisted of 8 patients who were treated when the cryogenic systems had only one probe per instrument. Freezing of the entire prostate was done with two instruments and each probe placed into the gland multiple times. Early biopsy and PSA results indicated that this procedure was not adequate for effective ablation. With this in mind, a new system was developed in which 5 probes could be used simultaneously (Cryomedical Sciences, Inc., Rockville, MD), applying a standard treatment protocol and placement of a urethral warming device. Forty-seven patients treated using the new cryoablation method made up Group 2.

Because of the difference in treatment methods between the two groups, analysis of Group 1 and 2 patients were done separately and then together. Three of the 8 patients in Group 1 had residual disease after 1 procedure with 2 of the 3 opting for treatment with the new system. In Group 2, only 15 patients had enough follow-up data and postoperative biopsy results for analysis. At three months, only one patient (6.7%) had residual disease and the other 14 patients all demonstrated negative biopsy reports. Combining the two groups of patients with data available at three months or longer, 4 of 23 patients had residual disease (17.4%) while the rest of the patients had no evidence of residual cancer. Furthermore, none of these patients suffered from incontinence, demonstrating the efficacy of the urethral warming catheter. Results from this surgical procedure showed an overall rate of negative findings on biopsy of 82.6% with residual rate of positive findings on biopsy at three months of 17.4% (1).

These preliminary studies indicate that cryoablation of the prostate can destroy prostate cancer with minimal or no com-

plications. With 5 probe placement, freezing of the entire prostate gland at one time was made possible, resulting in better outcomes and decreased morbidity for Stage A and B prostate cancer. In the Onik et al study, positive biopsy rates for patients with large tumors (Stages B2 and C) were higher (31%) than that of the total population.

A study by Cohen and Miller of 8 patients undergoing cryosurgical ablation of the prostate using 5 cryoprobes placed simultaneously, further confirms the efficacy of this therapy when combined with the use of a warming device (17). None of the patients in this study sloughed the urethral tissue or required post-operative drainage longer than 12 hours.

In centers performing cardiac surgical procedures, a circuit set-up for the urethral warming device can be constructed from readily available equipment and materials. Advantages of this arrangement are, most notably, the use of perfusionists already trained in this type of circuitry as well as a fairly inexpensive circuit design. Hospitals wishing to perform cryoablation of the prostate who do not have a cardiac surgical program can also perform this procedure. If a commercial urethral warming device is unavailable, an 11 Fr nephrostomy tube can be threaded through a piece of cystoscopic tubing (18) or a urethral warming device can be constructed according to Cohen et al (10). (Recently, Cryomedical Sciences (CMS) has received FDA approval for a CMS urethral warming system.)

To provide a successful urethral perfusion system, the perfusionist must anticipate and avoid potential areas of failure in the mechanical design of the system. Suggested options for warming may include a commercially available blood warming device or a cell-culture warming device if these temperatures cannot be obtained with the heater/cooler. Pressure monitors on both the inlet and outlet of the catheter are imperative as they may indicate catheter dislodgement, kinking or urethral rupture. The urethral catheter should be water-tested prior to insertion to ensure the balloon expands and that there is no water leak. The 3L-normal saline bag, which receives returning fluid from the catheter, should be elevated above the patient to maintain a hydrostatic pressure column on the catheter, facilitate patency, and therefore result in a homogeneous temperature gradient throughout the catheter and urethra. We experienced no problems associated with the design and implementation of the perfusion equipment and urethral warming device.

In conclusion, urethral warming is an important component in decreasing the morbidity associated with cryoablation of the prostate. Urethral bladder perfusion offers a unique opportunity for perfusionists to assist patients with this debilitating disease while at the same time expanding the scope-of-practice for perfusionists.

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