Impact of a cryotherapy training workshop on the adoption and utilization of cryotherapy in the community setting

Janice M. Mayes, BSc, Vladimir Mouraviev, MD, Thomas J. Polascik MD
Duke Prostate Center and Division of Urologic Surgery, Duke University Medical Center, Durham, North Carolina, USA

MAYES JM, MOURAVIEV V, POLASCIK TJ. Impact of a cryotherapy training workshop on the adoption and utilization of cryotherapy in the community setting. The Canadian Journal of Urology. 2008;15(4):4147-4152.

Introduction: *Given the improved therapeutic efficacy and acceptable side effect profile with current cryotechnology, we wish to better understand the attitudes of community urologists expressing interest in this treatment modality toward the adoption of cryotherapy in their practice.*

Methods: *A retrospective survey was conducted with information gathered on 50 responding physicians who attended a cryosurgery workshop between February 2004 and September 2006. Specifics such as demographics and professional background, reasons for interest in cryosurgery, and the current status of cryosurgery in the physicians' practice were collected and analyzed using SPSS, version 14 (Chicago, IL).*

Results: *Of the responding 50 physicians who attended a cryotherapy training workshop, 33 (66%) had been in practice for ≥ 15 years. The most frequently cited reasons for interest in cryosurgery were the intention to introduce cryosurgery into routine practice for treatment of primary (70%) and salvage (62%) prostate cancer and treatment of renal neoplasms (62%). Most physicians reported the learning curve to be short. Of the 22 (44%) physicians currently practicing cryotherapy, most are using the technique for treatment of primary prostate cancer and as a salvage procedure for radiorecurrent prostate cancer. Twenty-eight (56%) physicians reported that they were not practicing cryosurgery yet, mainly citing lack of patient interest/appropriate patients and/or a lack of institutional support.*

Conclusions: *This study provides insight into the attitudes of community urologists to adopt cryotherapy into their practice following a training course. Although some surgeons successfully integrate cryotherapy into their practice, further efforts must be made to remove barriers to allow adoption of this technology in the community setting.*

Key Words: cryosurgery, cryotherapy, prostatic neoplasms, kidney neoplasms, education

Introduction

In 1961, Cooper and Lee[1] introduced the first cryotherapy apparatus. Since then, cryotherapy has gone through phases of clinical adoption as well as disinterest. Early cryotechnology relied on liquid nitrogen as the cryogen, a difficult substance to precisely control and manipulate iceball growth. A number of complications demonstrated with early liquid nitrogen systems tempered enthusiasm, and cryotherapy was all but abandoned by the mid 1990's. However, at the end of the last century the introduction of third generation, gas-driven cryosystems based on the Joule-Thompson effect revolutionized cryotherapy.[2-4] With the current use of argon gas instead of liquid nitrogen, iceball growth can be precisely controlled. This, paired with ultrasound guidance and temperature monitoring, reduces the probability of freezing normal structures such as the anterior rectal wall and urinary sphincter. Additionally, the urethral warming catheter dissuades freezing of the urethra and helps prevent urethral slough and stricture. With such improvements, side effects have drastically decreased resulting in a resurgence in the use of cryotherapy.[5] Additionally, the use of ultra thin 17-gauge needles with sharp tips evolved cryotherapy

Disclosure: Dr. Polascik is a research consultant to Galil Medical

Accepted for publication June 2008

Address correspondence to Dr. Thomas J. Polascik, Associate Professor of Urology, Duke University Medical Center, Box 2804, Yellow Zone, Durham, NC 27710 USA

into a truly minimally invasive procedure with direct transperineal skin penetration and precise insertion of the cryoprobes into the prostate through a conventional brachytherapy-type grid template.[4,5] Recent technical improvements allow for a simpler, quicker freezing-thawing process that has significantly shortened the operative time.[6,7] In 1997, Medicare provided a limited, noncoverage policy for cryosurgery that by 1999 evolved to cover primary treatment of patients with clinically localized prostate cancer. By 2001, Medicare expanded its coverage to include salvage treatment for patients who had failed radiation therapy and met one of the following conditions: stage ≤ T2b, Gleason score < 9 or prostate-specific antigen (PSA) of < 8ng/ml.[8] In addition, with current, intermediate-term results supporting the increasing acceptance of cryoablation as an efficient treatment choice for patients with small renal lesions, the American Medical Association established a CPT code for laparoscopically guided renal cryotherapy in 2003 prompting many Medicare and commercial carriers to provide coverage for the procedure since that time.[9,10]

Given the improved therapeutic efficacy and acceptable side effect profile with current cryotechnology, we wish to better understand the attitudes of community urologists expressing interest in this treatment modality toward the adoption of cryotherapy in their practice.

Materials and methods

The company sponsored cryosurgery workshop is held at an academic medical center. The cryosurgery workshop consists of a day of lectures on the basic science of cryobiology, patient selection, oncologic outcomes and complications. Instruction of how to perform cryotherapy for kidney neoplasms and prostate cancer is provided. A live demonstration of prostate cryotherapy is performed in the operative suite, with video and two-way sound transmission to the lecture hall. In this fashion, urologists are able to ask questions during the procedure. Following the live surgery, participants are able to try the technique using the cryotherapy equipment and a phantom tissue model. Although there is not a coinciding dry lab for renal cryotherapy, the techniques involved (laparoscopic approach, thermocouple placement, real-time ultrasound monitoring of iceball growth, etc) are covered in lecture.

A retrospective survey was conducted with information gathered from 50 of the 136 physicians who attended a cryosurgery training workshop between February 2004 through September 2006 for both kidney and prostate cancer. Physician information such as demographics and professional background, reasons for interest in cryosurgery, and the current status of cryosurgery in their practice was collected. Specifically for this study, participants were surveyed to evaluate the impact of the course on the adoption of the technique into clinical practice. Non-parametric statistical analysis—Kruskal-Wallis and Mann-Whitney—was performed using SPSS, version 14 (Chicago, IL).

Results

Demographics

Of the responding 50 physicians (response rate: 37%, maximum of two contact attempts) who attended a cryotherapy workshop, the majority were urologists practicing in a community setting, Table 1. Table 2 details the level of experience for performing similar type procedures, such as brachytherapy. Only six (12%) physicians had previously attended a cryotherapy course while the remaining 44 (88%) had not.

Reasons for interest

Of the reasons reported for attending the cryosurgery course, physicians more frequently cited the intention to introduce cryosurgery into their routine practice for the management of primary prostate cancer (70%), small renal tumors (62%), and as a salvage procedure for radiorecurrent prostate cancer (62%). A total of 28 (56%) physicians responded that cryosurgery would be useful for treating men with clinically localized cancer instead of surgery while 27 (54%) wanted to offer cryosurgery as an option for radiation failures. In addition, 23 (46%) physicians wished to utilize cryosurgery to treat patients who would otherwise elect radiation as their primary treatment.

TABLE 1. **Characterization of physicians' practices**

Demographics	**No. (%)**
Type of practice	
Community based group practice	35 (70%)
Community based solo practice	13 (26%)
Full time academic setting	1 (2%)
Military/veterans affairs setting	1 (2%)
Length of time in practice	
> 20 years	19 (38%)
15 < 20 years	14 (28%)
10 < 15 years	4 (8%)
5 < 10 years	9 (18%)
< 5 years	4 (8%)

TABLE 2. **Levels of responding physicians' experience**

Techniques	No. (%)
Ultrasonography of prostate (TRUS) and/or prostate biopsy	
No experience	1 (2%)
50-100 cases	3 (6 %)
> 100 cases	46 (92%)
Brachytherapy	
No experience	15 (30%)
< 25 cases	7 (14%)
25-50 cases	5 (10%)
> 50 cases	23 (46%)
Prostate cryoablation	
No experience	40 (80%)
< 10 cases	5 (10%)
10-25 cases	3 (6%)
> 25 cases	2 (4%)
Open renal cryoablation	
No experience	46 (92%)
< 10 cases	2 (4%)
> 25 cases	1 (2%)
No response	1 (2%)
Laparoscopic technique	
No experience	27 (54%)
< 10 cases	12 (24%)
10-25 cases	3 (6%)
> 25 cases	8 (16%)
Robotic technique	
No experience	30 (60%)
< 10 cases	11 (22%)
10-25 cases	2 (4%)
> 25 cases	5 (10%)
No response	2 (4%)
Hand-assisted laparoscopic technique	
No experience	20 (40%)
< 10 cases	13 (26%)
10-25 cases	8 (16%)
> 25 cases	9 (18%)

Learning curve

When asked "If you have had no previous experience in cryosurgery/brachytherapy or transrectal ultrasound (TRUS) guided prostate biopsy, how would you characterize the ease or difficulty in learning this technique?" Twenty urologists responded with half reporting the challenge to learn this technique as "easy" while the remainder responded it was of "moderate" difficulty. Of the physicians with previous experience in TRUS-guided techniques, 47.2% characterized the ability to learn this technique as "easy", 50% as "moderately difficult", and 2.8% as "difficult". When asked to estimate the learning curve for prostate cryosurgery, 32% responded that < 5 cases would suffice while 42% cited 5-10 cases, and 16% cited over 10 cases. The learning curve for cryosurgery of renal tumors was estimated by 40% of the physicians as < 5 cases, 24% as 5-10 cases, and 6% as > 10 cases, while 8% did not respond citing that they were unsure or did not treat renal tumors. A total of 29 (58%) physicians reported that the cryosurgery course was effective in reducing the number of cases that constituted their normal learning curve for the procedure while 6% reported it to be ineffective and 32% were unsure. Overall, 98% would recommend the course to a colleague.

A total of 98% of the attending urologists had prior experience in TRUS and/or prostate biopsies that significantly ($p < 0.005$) decreased the number of mentored cases for urologists performing prostate cryosurgery. Those with ultrasound experience also required fewer cases to become comfortable when performing cryotherapy on patients with in situ brachytherapy seeds ($p < 0.005$). As ultrasound guidance is such an integral part of cryosurgery, those with previous experience were able to perform comfortably after fewer cases. Significant differences in the adoption of cryosurgery were also found between physicians with experience in laparoscopic and robotic techniques versus those with none. Specifically, physicians with minimal experience (< 10 cases) in either laparoscopic or robotic techniques were more likely to introduce cryosurgery into their practice compared to those with no previous cases ($p = 0.030$ and $p = 0.026$, respectively). However, there was no significant difference between the physicians with more experience (≥ 10 cases) in minimally invasive laparoscopic or robotic surgery compared to those with no previous cases; however, this is likely due to the small sample size.

Current status

Of the physicians attending the course, as of December 2006, 28 (56%) had not yet started practicing cryosurgery. Of the physicians who are now practicing, 13 (59.1%) are using the technique for treatment of primary prostate cancer, 7 (31.8%) use it as a salvage procedure for radiorecurrent prostate cancer, and 5 (22.7%) use the technique to treat renal tumors, with some using the technique for more than one treatment type. Details about proctorship and learning curves as well as current cryosurgery case specifics are outlined in Table 3 and Table 4. The techniques involved in cryotherapy are transferable between operative sites as seen in the urologists with previous experience in renal cryotherapy

TABLE 3. **Mentorship during the learning process***

	No. (%)
Who mentored you?	
Company-sponsored cryosurgeon	19 (86.4%)
Colleague	2 (9.1%)
None	1 (4.5%)
Number of cases mentored: prostate cancer	
1-2	8 (36.4%)
3-5	10 (45.5%)
6-10	1 (4.5%)
Not reported	3 (13.6%)
Number of cases mentored: renal	
0	12 (54.5%)
1-2	6 (27.3%)
3-5	1 (4.5%)
Not reported	3 (13.6%)
Learning curve (no. cases) involving patients with brachytherapy implants present	
< 5	10 (45.5%)
5-10	4 (18.2%)
10-20	4 (18.2%)
> 20	1 (4.5%)
Not reported	3 (13.6%)

*22 of 50 surveyed are now practicing

TABLE 4. **Current physicians' cryosurgery case load***

	No. (%)
Who do you perform cryosurgery with?	
Alone	15 (68.2%)
With partner	2 (9.1%)
With partner and proctor	1 (4.6%)
With interventional radiologist	3 (13.6%)
Not reported	1 (4.6%)
Prostate cancer case frequency (per month)	
≥ 5	2 (9.1%)
1-2	16 (72.7%)
< 1	1 (4.6%)
None	1 (4.6%)
Not reported	2 (9.1%)
Renal case frequency (per month)	
≥ 5 cases	1 (4.5%)
1-2	2 (9.1%)
< 1 case	1 (4.5%)
None	9 (40.9%)
Not reported	9 (40.9%)

*22 of 50 surveyed are now practicing

who were mentored for significantly fewer prostate cryotherapy cases than those without previous renal cryotherapy experience ($p < 0.005$). Interestingly, the urologists with prior experience in prostate cryotherapy reported a significantly shorter estimated learning curve for prostate procedures ($p < 0.005$) suggesting that once starting to practice cryotherapy, one might find the adaptive period much shorter than originally expected. When asked if the physicians changed their previous treatment modality towards cryosurgery 18 (82%) had. The main reasons cited were the treatment of a select group of patients (primary or salvage prostate cryosurgery, or renal cryosurgery) (38.9%), and offering cryotherapy in lieu of brachytherapy (33.3%), external beam radiotherapy (27.8%), or radical prostatectomy (22.2%). Several physicians changed their treatment approach due to multiple reasons.

Of the physicians who had not introduced cryosurgery into their practice, perceived impediments were a lack of patient interest or appropriate patients, reported by 12 (28%) physicians, a lack of institutional support by 5 (10%), and the need for additional training by 5 (10%). When physicians were asked if they had any concerns regarding cryotherapy, the main responses were concern of treatment efficacy/cancer control by 25 (50%), impotence rates by 16 (32%), and concern for causing a rectourethral fistula by 15 (30%) urologists. The ideal patients were reported by 31 (62%) and 28 (56%) physicians to be those who have failed radiation therapy and those who are not suitable surgical candidates, respectively. In addition, 25 (50%) and 21 (42%) physicians agreed that patients with a small renal tumor or primary organ-confined prostate cancer, respectively, would be good candidates for cryosurgery.

A total of 31 (62%) physicians believe that the future of cryosurgery will depend on its efficacy in clinical trials and future advancements. Overall, 29 (58%) felt that cryosurgery is an additional tool to the growing number of therapeutic options available for renal cell carcinoma and prostate cancer.

Discussion

The first cryotherapy systems in clinical practice used liquid nitrogen as a cryogen and were performed without the guidance of imaging systems. In addition, there was no means to monitor iceball formation either with temperature thermocouples or TRUS. Protection of the urethra from cold injury was not standard. Liquid nitrogen, although an effective cryogen, was not very precise or controllable. Thus, reports of complications were common during the early evolution of this technology and were not surprising

given the limitations at that time.[11,12] However, as with any evolving technology, improvements have occurred both in the delivery of cryosurgery as well as the imaging systems. Argon/helium gas systems based on the Joule-Thompson principle provide greater control over the iceball formation.[2,5] TRUS guidance has allowed the treating physician to precisely place each cryoprobe and image the freezing process in real-time. Temperature thermocouples allow for multiple temperature measurements, thereby ensuring lethal temperatures to be achieved in the target tumor/organ while preventing lethal temperatures from injuring critical normal structures such as the rectum and urinary sphincter. Since the routine adoption of an FDA-approved urethral warming catheter, urethral slough, once a common occurrence without a protective catheter, is now rare.[5,13] In addition, rectourethral fistula is now rarely seen given the precise control of argon gas systems and sonographic monitoring.[14,15] With the exception of erectile dysfunction, prostate cryosurgery has become a very safe procedure with a low complication profile.[2,5,15,16]

Due to previous reports of complications with early techniques and technology, the adoption of cryosurgery as a treatment option has been relatively slow. In the present study, we were surprised to find that the level of concern reported by some urologists (30%) for causing a rectourethral fistula was disproportionately high and not reflective of the current cryotherapy complication profile in the literature, with results between 0% and 1% in some series due to the high accuracy of targeted ablation under TRUS guidance and thermocouple mapping.[2,16,17]

The reported interests in cryotherapy as a treatment modality for primary prostate cancer and salvage cases as well as for renal tumors are well founded and complimented by today's literature. Complication rates are low making cryotherapy competitive for implementation as a minimally invasive surgery. However, as seen in 25 (50%) of the physicians, paucity of long-term data using newer cryotechnology creates an interest to see results regarding long-term cancer control using third generation cryotechnology.

One trend seen in the responses of the physicians interested in beginning a cryotherapy program is the struggle over the ideal patient for cryotherapy. For prostate cancer, 62% and 28% of physicians identified patients not responding to radiation or those not considered candidates for surgery, respectively, as the ideal patient. However, the literature also supports the use of cryotherapy as a first-line therapy for primary prostate cancer[2,7,16,18] and those patients with high risk features.[12,15]

Based on the reported conversions from previous treatment modalities, many physicians are switching from treating patients with other offered forms of radiation (27.8% previously using brachytherapy and 22.2% using external beam therapy) to cryosurgery. This allows the urologists to utilize cryosurgery, an effective treatment modality with an acceptable side effect profile, to treat patients without potentially affecting their surgical volume. The data suggests that almost one in five urologists participating in the training workshop accepted cryotherapy in their practice in place of other established treatment options.

While the technique itself is not complicated, often integrating a new therapy into clinical practice can be challenging. Start up costs, such as purchasing or leasing new equipment, can be problematic for some institutions and is reflected by 10% of physicians as one of the main deterrents to adapting the technique. In addition, when counseling a patient about his treatment options, patients tend to gravitate toward familiar treatments with well established data and outcomes. Thus following cryosurgery's resurgence, it may be that fewer patients are interested or exposed to the option of cryotherapy as reported by 28% of the physicians. Moreover, some physicians who lack experience or, quite the opposite, are settled into their usual prostate cancer treatment options feel as though they need more training before utilizing a new treatment modality as expressed by 10% of physicians. It is important to note that 74% of the responding physicians have been in practice for ≥ 10 years, with only 8% practicing for < 5 years. Often "younger" physicians more readily adopt newer techniques and treatment modalities due to previous exposure during residency or fellowship training.[19] Training concerns can easily be alleviated by utilizing a mentorship program by working with an experienced cryosurgeon. In addition there are also seminars for training nursing staff.

In spite of the 56% of responding physicians who had not yet begun using cryosurgery, it is clear that those who start tend to integrate the procedure as seen in the 86% of the practicing physicians who are now using cryosurgery as a primary treatment modality. The large percentage of treatment adaptation may be due to the minimally invasive nature of the procedure that allows for quicker recovery that can be especially important for older patients.[20,21] A study by Anastasiadis et al[22] shows that the quality of life after primary or salvage cryotherapy for localized prostate cancer is comparable to traditional treatment modalities. Likewise, the transferability of laparoscopic skills to renal cryosurgery may also help a select group of physicians to adapt the treatment modality.[19]

A limitation of the present study is that the responding physicians reflect those with an interest in cryotherapy and not necessarily all practicing urologists who may not have an interest. Also, based on the study's design there are no generalizations to practice. Second, this is a retrospective study based on physician's responses that may have been affected by the passing of time or later adoption of cryotherapy into clinical practice. In addition, with the responding physicians working in the community setting, adoption of a new technology may not be the physician's decision alone. Factors such as patient interest, equipment costs, and hospital privileges can have varying effects on the implementation rate.

Cryotherapy is a treatment option for primary and salvage prostate and renal cancer with a majority of the responding physicians, 62%, agreeing that the future of cryosurgery will depend on its efficacy in clinical trials and future advancements in technology. Although some surgeons successfully integrate cryotherapy into their practice, further efforts must be made to remove barriers to allow adoption of this technology in the community setting. □

References

1. Cooper IS, Lee AS. Cryostatic congelation: a system for producing a limited, controlled region of cooling or freezing of biologic tissues. *J Nerv Ment Dis* 1961;133:259-263.
2. Han KR, Belldegrun AS. Third-generation cryosurgery for primary and recurrent prostate cancer. *BJU Int* 2004;93:14-18.
3. Johnson DB, Nakada SY. Cryoablation of renal and prostate tumors. *J Endourol* 2003;17:627-632.
4. Zisman A, Leibovici D, Siegel YI, Lindner A. Prostate cryoablation without an insertion kit using direct transperineal placement of ultrathin freezing probes. *Tech Urol* 2000;6:34-36.
5. Mouraviev V, Polascik TJ. Update on cryotherapy for prostate cancer in 2006. *Curr Opin Urol* 2006;16:152-156.
6. Mouraviev V, Joniau S, Van Poppel H, Polascik TJ. Current status of minimally invasive ablative techniques in the treatment of small renal tumours. *Eur Urol* 2007;51:328-336.
7. Zisman A, Pantuck AJ, Cohen JK, Belldegrun AS. Prostate cryoablation using direct transperineal placement of ultrathin probes through a 17-gauge brachytherapy template-technique and preliminary results. *Urology* 2001;58:988-993.
8. <http://www.cms.hhs.gov/mcd/viewncd.asp?ncd_id=230.9&ncd_version =1&basket=ncd%3A230%2E9%3A1%3ACryosurgery+of+Prostate> 3/26/07.
9. Davol PE, Fulmer BR, Rukstalis DB. Long-term results of cryoablation for renal cancer and complex renal masses. *Urology* 2006;68:2-6.
10. Schwartz BF, Rewcastle JC, Powell T, Whelan C, Manny T Jr, Vestal JC. Cryoablation of small peripheral renal masses: a retrospective analysis. *Urology* 2006;68:14-18.
11. Pisters LL, von Eschenbach AC, Scott SM, Swanson DA, Dinney CP, Pettaway CA, Babaian RJ. The efficacy and complications of salvage cryotherapy of the prostate. *J Urol* 1997;157:921-925.
12. Miller RJ Jr, Cohen JK, Merlotti LA. Percutaneous transperineal cryosurgical ablation of the prostate for the primary treatment of clinical stage C adenocarcinoma of the prostate. *Urology* 1994;44:170-174.
13. Cohen JK, Miller RJ, Shuman BA. Urethral warming catheter for use during cryoablation of the prostate. *Urology* 1995;45:861-864.
14. Cohen J. Cryosurgery of the prostate: techniques and indications. *Reviews in Urology* 2004;6:S21-S26.
15. Prepelica KL, Okeke Z, Murphy A, Katz AE. Cryosurgical ablation of the prostate: high risk patient outcomes. *Cancer* 2005;103:1625-1630.
16. Polascik T, Nosnik I, Mayes J, Mouraviev V. Short-term cancer control after primary cryosurgical ablation for clinically localized prostate cancer using third generation cryotechnology. *Urology* 2007;70:117-121.
17. Ghafar MA, Johnson CW, De La Taille A, Benson MC, Bagiella E, Fatal M, Olsson CA, Katz AE. Salvage cryotherapy using an argon based system for locally recurrent prostate cancer after radiation therapy: the Columbia experience. *J Urol* 2001;166:1333-1337;discussion 7-8.
18. Ellis DS. Cryosurgery as primary treatment for localized prostate cancer: a community hospital experience. *Urology* 2002;60:34-39.
19. Marguet CG, Young MD, L'Esperance JO, Tan YH, Ekeruo WO, Preminger GM, Albala DM. Hand assisted laparoscopic training for postgraduate urologists: the role of mentoring. *J Urol* 2004;172:286-289.
20. Mouraviev V, Nosnik I, Sun L, Robertson CN, Walther P, Albala D, Moul JW, Polascik TJ. Financial comparative analysis of minimally invasive surgery to open surgery for localized prostate cancer: a single-institution experience. *Urology* 2007;69:311-314.
21. Mouraviev V, Nosnik I, Robertson C, Albala D, Walther P, Polascik TJ. Comparative financial analysis of minimally invasive surgery to open surgery for small renal tumours < or =3.5 cm: a single institutional experience. *Eur Urol* 2007;51:715-720;discussion 20-21.
22. Anastasiadis AG, Sachdev R, Salomon L, Ghafar MA, Stisser BC, Shabsigh R, Katz AE. Comparison of health-related quality of life and prostate-associated symptoms after primary and salvage cryotherapy for prostate cancer. *J Cancer Res Clin Oncol* 2003;129:676-682.