Prostate and Renal Cryoablation Clinical Review Published Literature

Research compiled by the International Society of Cryosurgery

Made possible by a grant from Endocare, Inc.

The information contained in this booklet is being provided for informational purposes only and does not contain all available published data on cryotherapy.

No specific claims (e.g., treatment of prostate cancer) are being made.

PM-3456 10/05

C O N T E N T S

Renal Cryoablation

Salvage Cryoablation

Primary Cryoablation

Focal Cryoablation

* ***Indicates an up-to-date noteworthy/important paper.***

Renal Cryoablation

1. "RADIOFREQUENCY ABLATION OF RENAL TUMORS"

Author: Mahnken AH, Gunther RW, Tacke J

Institution: Department of Diagnostic Radiology, Aachen University of Technology in Aachen, Germany

Date/Publication: August 2004, Eur Radiol. Vol. 14 (8)

Indication: Renal

Key Words: Kidney, thermal ablation, radiofrequency

Summary:
Thermal ablation is a minimally invasive and nephron sparing procedure that is ideally suited for patients with a single kidney, multiple tumors or contraindications for resective surgery. Although cryotherapy is the most extensively studied technique RF has become the most accepted. This is largely due to the technical simplicity of the procedure and equipment needed to perform it. This is counterintuitive given the clinical evidence presented in the paper. All publications in the medical literature regarding renal RF and cryoablation were surveyed. A total of 276 RF patients were found with an average follow up of 7.7 months. The disease free rate of this group was 81.8%. This is significantly lower than the 97.2% disease free rate of the 154 patients who underwent cryoablation with an average follow-up of 14.4 months. It is surprising that RF's technical simplicity has overshadowed its efficacy limitation which yields a recurrence rate over six times that of cryoablation (18.2% for RF versus 2.8% for cryoablation).

---

2. "CRYOTHERAPY AND RADIOFREQUENCY ABLATION: PATHOPHYSIOLOGIC BASIS AND LABORATORY STUDIES"

Author: Finelli A, Rewcastle JC, Jewett MAS

Institution: Department of Surgical Oncology, Princess Margaret Hospital and University of Toronto, Ontario and Department of Radiology, University of Calgary, Alberta, Canada

Date/Publication: 2003, Current Opinion in Urology Vol. 13

Indication: Renal

Key Words: Renal, radiofrequency ablation, cryotherapy

RENAL CRYOABLATION

Summary:
With an increase in the diagnosis of incidental and slow growing renal tumors, novel energy-base treatments, such as radiofrequency and cryotherapy, present important options for renal cancer patients as less invasive treatments. Cryoablation is the most studied modality and its ability to both directly and indirectly damage cells is generally understood. Recent data suggests that an active thaw can be used instead of the previously accepted passive thaw since it can effectively cryoablate renal tissue as well as significantly reduce overall operative time. Clinical experience is needed to further refine knowledge about optimal freezing temperature and freeze-thaw cycles. Radiofrequency ablation is an effective means of destroying cancerous tissue but targeting this energy has been difficult. Challenges monitoring interstitial needle placement and visualization during the procedure also limit radiofrequency's application.

---

3. "LAPAROSCOPIC RENAL CRYOABLATION IN 32 PATIENTS"

Author: Gill IS, Novick AC, Meraney AM, Chen RN, Hobart MG, Sung GT, Hale J, Schweizer DK, Remer EM

Institution: Department of Urology and Radiology, Cleveland Clinic Foundation in Cleveland, Ohio and Department of Urology, Cleveland Clinic Florida in Fort Lauderdale, Florida

Date/Publication: November 2000, Urology Vol. 56 (5)

Indication: Renal

Patient Selection: Enhancing renal mass had to be 4 cm or less, circumscribed, and peripherally located

Number of Patients: 32 total (22 retroperitoneal and 10 transperitoneal)

Length of Follow-up: 16.2 months

Efficacy: 23 of 23 show no evidence of renal cell carcinoma at 3 to 6 months postoperatively

Measurement of Efficacy: CT-directed needle biopsy of the cryolesion

Morbidity: 3.1% superficial liver laceration, 3.1% perirenal hematoma, 3.1% herpes esophagitis

Key Words: renal, cryotherapy, short-term efficacy

Summary:
Renal cryoablation has been performed by open, percutaneous, and laparoscopic techniques. Complete necrosis is thought to be achieved at -19.4oC or lower. To ensure complete cell death, the iceball must extend well beyond the visible margins of the targeted tumor. The primary criticism of renal cryoablation is the lack of histologic data about the completeness of tumor destruction and the adequacy of negative surgical margins. While laparoscopic renal cryoablation is still in development, the early results from this study are very encouraging. Of the 23 patients who underwent CT-directed needle biopsy of the cryolesion at 3 to 6 months postoperatively, none of the patients showed evidence of renal cell. Longer follow-up is needed but the initial experience is cautiously optimistic.

---

4. "PRELIMINARY EXPERIENCE WITH CRYOABLATION OF RENAL LESIONS SMALLER THAN FOUR CENTIMETERS"

Author: Khorsandi M, Foy RC, Chong W, Hoenig DM, Cohen JK, Rukstalis DB

Institution: MCP Hahnemann University in Philadelphia, PA

Date/Publication: May 2002, J Am Osteopath Assoc. Vol. 102 (5)

Indication: Renal

Patient Selection: Patients had lesions smaller than 4 cm in diameter

Number of Patients: 17

Length of Follow-up: 30 months

Efficacy: 94%

Measurement of Efficacy: reduction of lesion size

Morbidity: 12% capsular fracture, 6% diarrhea, 6% congestive heart failure, 17.6% fever, 6% intravenous infiltration, 6% ileus, 12% wound separation, 1% syncope

Key Words: open renal cryoablation, low morbidity, efficacy

RENAL CRYOABLATION

Summary:
The widespread use of imaging instruments (MRI, CT scan, and ultrasound) has caused an increase in the number of small renal lesions being detected. Therefore, nephron-sparing procedures are being used more frequently on small lesions when the localized cancer is present bilaterally or in a patient with an anatomic or functional solitary kidney. Renal cryoablation is advantageous because it is as effective as surgery but with fewer morbidities. In this study, the open renal approach was used since it allows complete mobilization, access to any part of the kidney, and continual ultrasound monitoring. Lesions greater than 4 cm were not treated due to fear of undertreating the lesion. The only attributable complication in the study was capsular fracture found in two patients. However, both of these fractures resulted from the use of more than one cryoprobe, and when the switch to only one cryoprobe was made there were no more incidences of capsular fracture. Follow-up studies demonstrate infarction and a reduction of lesion size in 15 to 16 cases.

---

5. "RETROPERITONEAL LAPAROSCOPIC CRYOABLATION OF SMALL RENAL TUMORS: INTERMEDIATE RESULTS"

Author: Lee DI, McGinnis DE, Feld R, Strup SE

Institution: Department of Urology, University of California, Irvine Medical Center in Orange, CA; Bryn Mawr Hospital in Bryn Mawr, PA; Department of Radiology and Urology, Thomas Jefferson University School of Medicine in Philadelphia, PA

Date/Publication: January 2003, Urology Vol. 61 (1)

Indication: Renal

Patient Selection: Preoperative CT or MRI showing a solid or complex renal mass less than 4 cm in size

Number of Patients: 20

Length of Follow-up: up to 3 years

Efficacy: 95%

Measurement of Efficacy: reduction of lesion size

Morbidity: 5% (1/20) pancreatic injury

Key Words: laparoscopic renal cryoablation, low morbidity, efficacy

Summary:
The data from this study demonstrates that small renal lesions can be successfully ablated by cryosurgery. The morbidity using laparoscopic renal cryosurgery was extremely low. Other than transient laboratory changes, no specifically cryosurgery-related morbidities occurred. No urinary fistulas developed and only one injury to an adjacent structure (pancreas) occurred. With limited experience published, the most widely regarded criterion for success is a lack of postoperative enhancement of the treated lesion. By using a retroperitoneal approach, there is slightly lower morbidity than using a transperitoneal approach.

---

6. "RENAL CRYOTHERAPY: 2003 CLINICAL STATUS"

Author: Lowry PS, Nakada SY

Institution: University of Wisconsin Medical School in Madison, Wisconsin

Date/Publication: 2003, Current Opinion in Urology Vol. 13

Indication: Renal

Patient Selection: Patients had lesions smaller than 4 cm in diameter

Number of Patients: 18

Length of Follow-up: 3 months

Efficacy: 100%

Measurement of Efficacy: decrease in lesion size

Key Words: renal cryosurgery, nephron-sparing surgery, laparoscopy

Summary:
Clinical studies have shown that long-term cancer control and renal function after partial nephrectomy has equivalent results to radical nephrectomy. Cryoablation of small renal masses represents an alternative method for performing nephron-sparing surgery. Cryoablation may be performed under open conditions, but laparoscopy provides equivalent efficacy with less morbidity.

Cryotherapy can also be performed percutaneously with MRI monitoring. After cryotherapy, patients require diligent radiographic monitoring, more frequently than after surgery. Durability of renal cryotherapy appears promising but more data is required to provide reliable treatment. Currently, cryoablation of small renal lesions is minimally invasive, safe, and efficacious for select peripheral lesions in carefully selected patients.

---

7. "LAPAROSCOPIC RENAL CRYOSURGERY: THE NORTHWESTERN EXPERIENCE"

Author: Nadler RB, Kim SC, Rubenstein JN, Yap RL, Campbell SC, User HM

Institution: Northwestern Memorial Hospital

Date/Publication: October 2003, Journal of Urology Vol. 170 (4 Pt 1)

Indication: Renal

Patient Selection: Lesions must be less than 4 cm, solid, solitary, peripheral, exophytic, and fit radiographic criteria for suspected renal malignancies

Number of Patients: 15

Length of Follow-up: 15.1 months

Efficacy: 86% (6/7)

Measurement of Efficacy: lack of lesion enhancement

Morbidity: 7% postoperative intubation (1/15), 7% postoperative ileus (1/15)

Key Words: clinical experience, laparoscopic renal cryosurgery

Summary:
In this study laparoscopic renal cryosurgery was applied in the clinical arena and produced comparable results to academia renal cryosurgery studies. Both a transabdominal approach was used as well as a retroperitoneal approach for small, exophytic renal lesions. The data demonstrates that this procedure can be performed in the clinical setting safely and efficiently. Patients recovered rapidly with little need of narcotics and returned to

work approximately two weeks after the procedure. The efficacious results demonstrate that laparoscopic renal cryosurgery is a viable and safe treatment, especially for small incidental lesions and patients with many comorbidities. The maximum lesion size should be around 3 to 4 cm. Cryosurgery has many advantages over partial nephrectomy including less blood loss, no renal hilar clamping, no technically difficult suturing, no urine leaks, decreased need for ureteral stenting, and is effective in patients on anticoagulation. It is also easier to treat less exophytic tumors because of ultrasonic monitoring of the iceball. One probe can be used to treat tumors up to 2 cm while larger tumors can be treated with triangulation. Larger tumors should be treated with laparoscopic partial nephrectomy or laparoscopic radical nephrectomy.

---

8. "MINIMALLY INVASIVE MANAGEMENT OF THE SMALL RENAL TUMOR: REVIEW OF LAPAROSCOPIC PARTIAL NEPHRECTOMY AND ABLATIVE TECHNIQUES"

Author: Ogan K, Cadeddu JA

Institution: The Clinical Center for Minimally Invasive Urologic Cancer Treatment, Department of Urology, The University of Texas Southwestern Medical Center in Dallas, Texas

Date/Publication: November 2002, Journal of Endourology Vol. 16 (9)

Indication: Renal

Key Words: laparoscopic partial nephrectomy techniques, ablative techniques

Summary:
The establishment of nephron-sparing surgery and the emergence of laparoscopic partial nephrectomy are the two most profound changes in renal cancer. This article outlines the various LPN and ablative techniques currently in development. LPN techniques include duplication of the open technique, hand-assisted laparoscopic partial nephrectomy, double-loop renal tourniquet, cable-tie tourniquet, ultrasound shears, RF-assisted LPN, microwave tissue coagulator, laser surgery, and endosnare.

RENAL CRYOABLATION

The major disadvantages of LPN techniques are high morbidities, limitations in which tumors can be treated, and the need for highly skilled and experienced surgeons for some techniques. Ablative technologies minimize the risk and morbidity traditionally associated with open or laparoscopic partial nephrectomy. Ablative technologies include cryoablation, RF ablation, and high-intensity focused ultrasound (HIFU). HIFU is ideal for treatment of small renal tumors but problems of imprecise targeting and thermal burns prevent its use. RF show promising short term results with low morbidities, but its use is recommended for small tumors (<3 cm) only. Cryoablation has shown very promising short term results with high efficacy and minimal morbidity, but a longer follow-up is necessary. However, if cryoablation is able to withstand the test of time, it may be the least morbid technique for its delivery to small renal tumors. Exploration into these techniques is important since treatment of renal cancer will ultimately shift from open to minimally invasive methods.

---

9. "CLINICAL EXPERIENCE WITH OPEN RENAL CRYOABALTION"

Author: Rukstalis DB, Khorsandi M, Garcia FU, Hoenig DM, Cohen JK

Institution: Division of Urology, MCP Hahnemann University School of Medicine, Philadelphia and Allegheny General Hospital in Pittsburgh, PA

Date/Publication: January 2001, Urology Vol. 57 (1)

Indication: Renal

Patient Selection: Radiologic (CT or MRI) identification of at least one solid or indeterminate renal mass less than 4 cm in size

Number of Patients: 29

Length of Follow-up: 16 months

Efficacy: 91.3%

Measurement of Efficacy: Either complete resolution of the treated mass or only a residual nonenhancing cyst

Key Words: open renal cryoablation, efficacy, safety

Summary:
Data from this study demonstrates that open renal cryoablation is a safe and efficacious surgical technique for the destruction of renal cancer. The open transperitoneal approach facilitates renal exploration, ultrasound imaging, and cryoablation with multiple probes without significant morbidity. Data shows little blood loss in the procedure and a median hospital stay of 3 days indicating that this technique is well tolerated and likely to be competitive with other methods in terms of cost. Additional advantages include the ability to inspect the renal unit and convert the procedure to radical nephrectomy if necessary. Since one tumor was not completely eradicated, the study has emphasized the need for precise temperature monitoring during the procedure for lesions larger than 3 cm. It is recommended that reliable tissue destruction is achieved at temperatures less than -40oC

---

10. "LAPAROSCOPIC CRYOTHERAPY FOR RENAL TUMORS"

Author: Spaliviero M, Moinzadeh A, Gill IS

Institution: Glickman Urological Institute in Cleveland, Ohio

Date/Publication: April 2004, Technology in Cancer Research and Treatment Vol. 3 (2) Indication: Renal

Key Words: laparoscopic cryotherapy, low morbidity, short-term results

Summary:
This study looks at key laboratory and clinical discoveries and the future direction of renal cryotherapy. Laboratory experience demonstrates that the temperature of the cooling probe, freeze time, and vascularity of the tissue all play a significant role in size and growth of the ice ball. Clinical experience demonstrates that renal cryosurgery has a major role in treatment of small (< 3cm) solid tumors in patients with medical comorbidity. Advantages compared to partial nephrectomy are reduced blood loss, no renal hilar clamping and warm ischemia requirement, and no need for suture-repairing of renal parenchyma and collecting system. The primary limitation of cryo is the lack of pathologic confirmation of negative surgical margins and complete kill throughout the tumor. Long-term follow-ups are needed to confirm its efficacy and durability.

RENAL CRYOABLATION

11. "EFFECT OF INTENTIONAL CRYO-INJURY TO THE RENAL COLLECTING SYSTEM"

Author: Sung GT, Gill IS, Hsu TH, Meraney AM, Skacel M, Brainard JA, Remer EM

Institution: Urological Institute and Departments of Pathology and Radiology, Cleveland Clinic Foundation in Cleveland, Ohio

Date/Publication: February 2003, Journal of Urology Vol. 170

Indication: Renal

Patient Selection: all female swine weighing 35 to 47 kg

Number of Patients: 12

Length of Follow-up: 1 month

Key Words: warming of pelvicaliceal system, bilateral renal cryoablation

Summary:
This study evaluates whether continuous irrigation of the renal pelvicaliceal system with warm saline protects it against cryo-injury. The protective effect of local warming of vital hollow structures, such as the urethra during prostate cryoablation, is well described in recent literature. This same effect was tested in the pelvicaliceal system by warming all 12 right kidneys and leaving all 12 left kidneys without warming. However, the results demonstrate that continuous irrigation of the ureter and renal pelvis with warm saline during cryoablation do not provide any cryoprotective advantage to the calix at risk. The data suggests that mere extension of the ice ball into the intact pelvicaliceal system does not seem to result in urinary extravasation or caliceal fistula formation. This type of injury appears to be associated with favorable, watertight healing characteristics. This study has clinical relevance for facilitating cryoablation of a small, localized central or polar renal tumor located in proximity to the pelvicaliceal system.

■ ■ ■

Salvage Cryoablation

1. "SALVAGE CRYOSURGERY FOR RECURRENT PROSTATE CANCER AFTER RADIATION THERAPY: A SEVEN- YEAR FOLLOW-UP"

Author: Bahn DK, Lee F, Silverman P, Bahn E, Badalament R, Kumar A, Greski J, Rewcastle JC

Institution: Prostate Institute of America, Community Memorial Hospital in Ventura, California

Date/Publication: September 2003, Clinical Prostate Cancer Vol. 2 (2)

Indication: Salvage

Patient Selection: Patients must have previous radiation therapy treatment at least 24 months before treatment and biopsy-proven recurrent prostate cancer without evidence of distant metastasis

Number of Patients: 59

Length of Follow-up: 7 years

Efficacy: 59%

Measurement of Efficacy: PSA level less than or equal to 0.5 ng/mL

Morbidity: 4.3% incontinence and 3.4% rectal fistula formation

Key Words: Biochemical relapse, radiation failure, salvage therapy

Summary:
Radiation therapy remains a prominent treatment of prostate cancer, yet it has multiple drawbacks. For example, the procedure cannot be repeated and some tumors are resistant to radiation. Salvage radical prostatectomy has been an option for salvage treatment but it is a complex and risky procedure associated with high comorbidity and extended hospitalization. Hormonal treatment may reduce tumor size and cause slower growth, but it is not curative. Since the mid-1990s cryosurgery has had success in treating radiation-resistant prostate cancer. Through a 7-year retrospective analysis, the results of this study demonstrate that salvage cryosurgery is a promising form of treatment. It shows a success rate comparable with salvage radical prostatectomy and hormonal therapy. Results are especially favorable when the PSA is less than 10 and tumor stage is T1-T2. The data shows minimal morbidity rates and no known latent complications. In addition, the procedure is minimally invasive, requiring a short hospital stay.

SALVAGE CRYOABLATION

2. "SELECTION OF SALVAGE CRYOTHERAPY PATIENTS"

Author: Katz AE, Ghafar MA

Institution: Department of Urology, College of Physicians and Surgeons of Columbia University in New York, New York

Date/Publication: 2002, Reviews in Urology Vol. 4 (Supp 2)

Indication: Salvage

Key Words: Failed Radiation, Patient Selection

Summary:
Approximately 1/3 of prostate cancer patients choose radiation therapy for treatment, and between 20% and 66% of these patients fail in radiation treatment. Salvage cryosurgery is the preferential option for those patients requiring a secondary treatment after their first failure. Before performing salvage cryosurgery, patients might need hormonal therapy in order to reduce the size of the prostate gland and allow more working space for the cryosurgeon. Certain refinements can make salvage cryosurgeon especially effective such as using an argon-based system with thermocoupling, using an external sphincter temperature probe, or continuing urethral warming in the recovery room for 2 additional hours.

3. "SALVAGE CRYOSURGERY – HOW I DO IT"

Author: Donnelly BJ, Saliken JC

Institution: Tom Baker Cancer Center and Calgary Prostate Institute in Calgary, Alberta, Canada

Date/Publication: 2002, Reviews in Urology Vol. 4 (Supp 2)

Indication: Salvage

Key Words: Salvage Cryo technique, patient selection

Summary:
Appropriate patient selection is imperative for successful salvage cryosurgery. For it to be successful, the cancer must be confined to the prostate and its immediate area. Of those patients whose cancer recurs after radiation therapy, only 24.3% have isolated local recurrence without distant disease. Identifying this population can

be difficult. The minimal requirements of identification include a positive prostatic biopsy and negative bone scan. Other selection criteria include PSA level, Gleason score, and absence of T3 and T4 disease. The technique used by Donnelly is a modification of that originally described by Onik. Cases are treated by the combined efforts of an urologist and radiologist. Patient positioning is important to allow good access to the perineum. A flexible cystoscope is used to visualize the prostate and bladder and to guide the pigtail catheter. A urethral warming catheter is placed in the bladder over the guidewire. A biplane TRUS probe is inserted into the rectum to visualize and measure the prostate. Usually six cryoprobes are used but more or fewer can be used if the prostate is exceedingly large or small, or unusually shaped. Lateral placement of the probes is important because the temperature between probes is much lower than the temperature at the edge of the iceball. Another critical factor is the thermocouples that are placed where specific temperatures need to be achieved. The temperature of the posterolateral probes (3 & 4) impact how rapidly the iceballs form on the other probes. The operator should continue the freeze longer than he or she thinks is necessary in order to achieve a truly adequate ablation. The second freeze is initiated after a complete thaw and should progress faster than the first.

---

4. "SALVAGE CRYOTHERAPY FOR RECURRENT PROSTATE CANCER AFTER RADIOTHERAPY: VARIABLES AFFECTING PATIENT OUTCOME"

Author: Izwawa JI, Madesen LT, Scott SM, Tran JP, McGuire EJ, Von Eschenbach AC, Pisters LL

Institution: Department of Urology, University of Texas M.D. Anderson Cancer Center in Houston, Texas

Date/Publication: June 2002, Journal of Clinical Oncology Vol. 20 (11)

Indication: Salvage

Patient Selection: no exclusion criteria related to local extent of disease, PSA level, or Gleason score, provided there was a

reasonable expectation that the local tumor burden could be encompassed in the freezing process

Number of Patients: 131

Length of Follow-up: 5 years

Efficacy: 90% T1-T2, 69% T3-T4

Measurement of Efficacy: 5 year disease-free rates

Key Words: Patient selection, salvage cryo

Summary:
This report is the first long-term study on patients undergoing a salvage therapy for recurrent prostate cancer after radiation therapy. The purpose of the study is to identify the pretreatment factors that have an impact on the success of salvage cryosurgery. The results indicate that patient selection is very important for cryosurgery since not all locally recurrent prostate cancers have the same natural history. The results indicate that cryosurgery is an optimal treatment for patients who have locally recurrent androgen-dependent disease, a PSA level of less than 10 ng/mL, Gleason scores of less than 9, and pre-XRT clinical stages of T1 to T2. On the other hand, salvage cryotherapy is more likely to fail in patients who have locally recurrent androgen-independent PCa, a PSA level of greater than 10 ng/mL, a Gleason score of 9 and 10, or a pre-XRT clinical stage greater than T2. What is not known is whether the unfavorable patients would receive a significantly greater benefit from another therapy.

---

5. "SALVAGE CRYOTHERAPY USING AN ARGON BASED SYSTEM FOR LOCALLY RECURRENT PROSTATE CANCER AFTER RADIATION THERAPY: THE COLUMBIA EXPERIENCE"

Author: Ghafar MA, Johnson CW, De La Taille A, Benson MC, Bagiella E, Fatal M, Olsson CA, Katz AE

Institution: Department of Urology, College of Physicians and Surgeons of Columbia University in New York, New York

Date/Publication: October 2001, Journal of Urology Vol. 166 (4)

Indication: Salvage

Patient Selection: Must have biochemically and biopsy proven disease recurrence and negative bone scan

Number of Patients: 38

Length of Follow-up: 20.7 months

Efficacy: 86% at 1-year, 74% at 2 years

Measurement of Efficacy: biochemical recurrence-free survival calculated from Kaplan-Meier curves

Morbidity: 39.5% rectal pain, 2.6% urinary tract infection, 7.9% incontinence, 7.9% hematuria, 10.5% scrotal edema, 0% rectourethral fistula, urethral sloughing and urinary retention

Key Words: argon based system, efficacy, safety, salvage

Summary:
There are limited options for recurrent cancer patients. Additional radiation is not acceptable since tumors are clearly radio resistant. Cytotoxic chemotherapy and hormonal therapy are not curative. Salvage radical prostatectomy is a technically challenging procedure that is associated with high comorbidity and long hospitalization. The modernization of cryotherapy, including the new argon based CRYOCare machine, make cryotherapy a suitable option for salvage therapy since it has little complication and successful disease-free survival rates. With the introduction of ultrasound monitoring, thermocouples, and the urethral warming system, morbidities associated with salvage cryotherapy have remained low. The results of this study indicate that cryosurgery is an effective clinical therapy for recurrent localized prostate cancer. It is less invasive, causes little trauma, and has fewer side effects than salvage radical prostatectomy.

---

6. "RESULTS OF SALVAGE CRYOABLATION OF THE PROSTATE AFTER RADIATION: IDENTIFYING PREDICTORS OF TREATMENT FAILURE AND COMPLICATIONS"

Author: Chin JL, Pautler SE, Mouraviev V, Touma N, Moore K, Downey DB

Institution: Division of Urology and Department of Diagnostic Radiology, London Health Sciences Center, University of Western Ontario in London, Ontario, Canada

Date/Publication: June 2001, Journal of Urology Vol. 165 (6 Pt1)

SALVAGE CRYOABLATION

Indication: Salvage

Patient Selection: Patients must have increasing PSA levels on 3 consecutive determinations at least 2 years after administration of radical radiation therapy

Number of Patients: 118

Length of Follow-up: 18.6 months

Efficacy: 87%

Measure of Efficacy: Patients free of histological failure

Morbidity: 3.3% rectourethral fistulas, 6.7% severe incontinence

Key Words: salvage, radiation failure, patient selection, complication predictions

Summary:
Salvage cryotherapy has been reported as technically more challenging than primary cryotherapy and the complications more significant. However, through this study predictors of treatment failure and complications can be identified in order to find a patient selection criteria that will produce positive salvage cryotherapy results. Data from this study identifies bulky stage T3B and T4A disease as a predictive factor for urinary fistula formation and prior transurethral surgery as a predictive factor for incontinence. Results from cases without these factors demonstrate postoperative complications that are acceptable. The quality of life assessment indicates favorable patient satisfaction and acceptance of cryoablation. Factors that would predict an unfavorable outcome include PSA level greater than 10 ng/mL, a high Gleason score, stage T3/T4 disease, and increasing PSA levels despite hormone therapy. However, this patient group probably has systemic disease, which is not curative with any form of local therapy.

---

7. "LOCAL TUMOR CONTROL WITH SALVAGE CRYOTHERAPY FOR LOCALLY RECURRENT PROSTATE CANCER AFTER EXTERNAL BEAM RADIOTHERAPY"

Author: Izawa JI, Perrotte P, Greene GF, Scott S, Levy L, McGuire E, Madsen L, Von Eschenbach AC, Pisters LL

Institution: Department of Urology and Biomathematics, University of Texas M.D. Anderson Center in Houston, Texas

Date/Publication: March 2001, Journal of Urology Vol. 165 (3)

Indication: Salvage

Patient Selection: no study exclusion criteria for local disease extent, PSA, or Gleason score if there was a reasonable expectation that the local tumor burden would be encompassed in the freezing process

Number of Patients: 145

Length of Follow-up: 6 months

Efficacy: 77%

Measurement of Efficacy: negative biopsy after salvage cryosurgery

Key Words: Radiation failure, salvage cryosurgery efficacy, patient selection, technique

Summary:
This study focuses on determining which patients are the most appropriate candidates and the optimal cryotherapy procedure. The results demonstrate that a higher initial clinical stage and PSA level greater than 10.3 ng/mL correlate with a positive biopsy after salvage cryosurgery. Therefore, patients with clinical stage T1-TN0M0 disease and PSA level less than 10.3 ng/mL are likely to benefit from salvage cryosurgery. In addition to this, patients with a life expectancy of 10 years or more are more likely to benefit from the procedure and justify the potential morbidity. The cryosurgery technique that optimizes local control while minimizing morbidity includes a minimum of 5 probes, 2 freeze-thaw cycles and a urethral warming catheter. Multivariate analysis shows that PSA level and the number of cryotherapy probes are the strongest predictors of a positive biopsy.

SALVAGE CRYOABLATION

8. "CRYOSURGERY: IS IT AN EFFECTIVE OPTION FOR PATIENTS FAILING RADIATION?"

Author: de la Taille A, Katz AE

Institution: Department of Urology, Columbia University College of Physicians and Surgeons in New York, New York

Date/Publication: September 2000, Current Opinion in Urology Vol. 10 (5)

Indication: Salvage

Key Words: salvage, new technology, low morbidity, cost

Summary:
De la Taille and Katz give an overview of salvage cryosurgery. Primary treatment of prostate cancer using radical prostatectomy and radiation therapy have a recurrent and residual disease rate ranging from 25% to 93%. Therefore, many patients turn toward the four options of salvage surgery: salvage prostatectomy, salvage brachytherapy, hormonal therapy, and salvage cryotherapy. Continuing advances and refinements in cryotechnology have made it a safe and efficacious treatment for prostate cancer. For example, the addition of temperature probes and ultrasound monitoring have helped lower morbidities associated with cryotherapy compared to what was previously reported. Cryotherapy produces cancer cell death though three key factors: direct mechanical shock, osmotic shock, and cellular hypoxia. Since cost becomes a critical factor in healthcare, it is important to note that cryotherapy is half of the usual cost for either radical prostatectomy or radiation therapy.

---

9. "SALVAGE CRYOTHERAPY FOR RECURRENT PROSTATE CANCER AFTER RADIATION THERAPY: THE COLUMBIA EXPERIENCE"

Author: de la Taille A, Hayek O, Benson MC, Bagiella E, Olsson CA, Fatal M, Katz AE

Institution: Departments of Urology and Biostatistics, Columbia University College of Physicians and Surgeons in New York, New York

Date/Publication: January 2000, Urology Vol. 55 (1)

Indication: Salvage

Patient Selection: Patients must have completed external beam radiation therapy at least 18 months before evaluation, a rising serum PSA value, biopsy-proven recurrent prostate cancer without seminal vesicle invasion, negative bone scans, and no evidence of disease in the lymph nodes

Number of Patients: 43

Length of Follow-up: 21.9 months

Efficacy: 79% at 6 months and 66% at 12 months

Measurement of Efficacy: biochemical recurrence-free survival (bRFS) defined as a PSA value less than 0.1 ng/mL

Morbidity: 9% incontinence, 5% obstruction, 5% urethral stricture, 26% rectal pain, 9% urinary infection, 12% scrotal edema, and 5% hematuria

Key Words: salvage, low morbidity, efficacy

Summary:
Cryosurgical technology has been applied in the past to a wide variety of neoplasms. The cold environment created has proven to destroy both cancerous and normal cells. Advances have been made in cryoablation to make it a safe and efficacious treatment. For example, the procedure is now performed percutaneously and uses real-time transrectal ultrasound guidance and FDA approved urethral-warming devices. When consulting a patient for salvage therapy the first step should consist of a prostate and seminal vesicle ultrasound-guided biopsy. If the biopsy reveals seminal vesicle involvement, cryosurgery is not recommended. Androgen deprivation is usually used before salvage cryosurgery to decrease the prostate and facilitate a faster freeze with less gas required. The results from this study support the current safety and efficacy profile that cryotherapy is a viable option in the treatment of patients who have biopsy-proven local failure after radiation therapy.

■ ■ ■

Primary Cryoablation

1. "IN TREATING LOCALIZED PROSTATE CANCER THE EFFICACY OF CRYOABLATION IS INDEPENDENT OF DNA PLOIDY TYPE"

Author: Bahn DK, Silverman P, Lee F Sr, Badalament R, Bahn ED, Rewcastle JC

Institution: University Laboratories, Detroit Medical Center

Date/Publication: June 2004, Technology in Cancer Research and Treatment Vol.3 (3)

Indication: Primary

Patient Selection: Patients with prostate cancer and whose DNA ploidy was known prior to treatment

Number of Patients: 447

Length of Follow-up: 5 years

Efficacy: 78% (diploid), 75% (tetraploid), 79% (aneuploid)

Measurement of Efficacy: Used Kaplan-Meier analysis with a PSA cutoff of 1.0 ng/mL

Key Words: DNA Ploidy and Cryotherapy, broad range of use

Summary:
There is substantial evidence indicating that differences in DNA ploidy are highly predictive of differential treatment responses of patients to radical surgery and radiation therapy. It has been found that patients with aneuploid tumors suffer substantially worse than patients with diploid tumors in terms of progression and spread of disease and biochemical disease free status (bDFS). However, the results of this experiment demonstrate that the efficacy of cryoablation is independent of DNA ploidy type. Since cryoablation damages cells regardless of their individual characteristics, all ploidy types of tumors are killed. Therefore, cryoablation is a preferential treatment to radiation and radical surgery since it treats non-diploid tumors as well as it treats diploid tumors.

2. "THE CURRENT AND POTENTIAL ROLE OF CRYOABLATION AS PRIMARY THERAPY FOR LOCALIZED PROSTATE CANCER"

Author: Katz AE, Rewcastle JC

Institution: Department of Urology, College of Physicians and Surgeons of Columbia University, Columbia-Presbyterian Medical Center

Date/Publication: May 2003, Current Oncology Reports Vol. 5 (3)

Indication: Primary (and smaller discussion on Focal)

Length of follow-up: 5 year follow-up on various prostate treatments conducted over the past 10 years (1992-2002)

Key Words: High efficacy, low morbidity, comparison with other treatments, focal cryo

Summary:
Katz and Rewcastle compiled 5 year follow-up reports on various treatments of prostate cancer including cryoablation, radical prostatectomy, brachytherapy, 3-D conformal radiation, and external-beam radiation performed over the past ten years. Through this comparison they were able to provide sufficient data to show that cryotherapy is comparable if not superior in treating prostate cancer. The recent advances in cryo technology have made targeted cryoablation much more effective than its use during its reintroduction in the early 1990's. A comparison of recent publications demonstrates that cryotherapy's efficacy is equivalent to other treatments in treating low-risk disease and possibly superior for moderate- to high-risk prostate cancer. In addition, morbidity in cryotherapy is mild in comparison with other procedures with the exception of impotence. However, studies demonstrate that sexual function returns to a large number of impotent patients (cf. Robinson studies below). While morbidity declines for cryotherapy over time, results of other treatments reveal the emergence of late-onset morbidity. Therefore, cryoablation proves to be an effective treatment preserving the quality of life for patients. The article also discusses the potential role of focal cryoablation as an ideal treatment for targeting less aggressive forms of prostate cancer.

PRIMARY CRYOABLATION

3. "TARGETED CRYOABLATION OF THE PROSTATE: 7-YEAR OUTCOMES IN THE PRIMARY TREATMENT OF PROSTATE CANCER"

Author: Bahn DK, Lee F, Badalament R, Kumar A, Greski J, Chernick M

Institution: Crittenton Hospital in Rochester, Michigan

Date/Publication: August 2002, Urology Vol. 60 (Supp 2A)

Indication: Primary

Patient Selection: patients eligible if they exhibited localized or locally advanced prostate cancer (TNM stage T1 or T3)

Number of Patients: 590

Length of Follow-up: 7 years

Efficacy: 92% (low), 89% (medium), 89% (high)

Measurement of Efficacy: ASTRO definition of biochemical failure based on 3 successive increases of PSA level

Morbidity: 4.3% incontinence, 94.9% impotence (5.1% recovered potency), 5.5% transurethral resection of the prostate (TURP), <0.1% Fistula

Measurement of Morbidity: Measurements based on rates immediately after surgery and adjusted to include 7-year follow-up on patients

Key Words/Concepts: high efficacy, broad range of use, superiority to RF

Summary:
The procedure and results of this experiment show the evolution of cryoablation as the modern transrectal ultrasound-guided percutaneous method differentiates itself from the early 1960's use of cryotherapy. With the results of this 7-year data, cryotherapy can be compared with 7 year follow-up data on radiation therapy. Through this comparison it can be seen that cryotherapy's high efficacy rate make it comparable if not superior to radiation and other traditional treatments. While cryotherapy has been accepted as advantageous for treatment of older patients or patients having too much comorbidity, the data from this report indicates a broader role for cryoablation. The high efficacy seen

in local and locally advanced cases shows that cryoablation can be applied as a primary treatment for various cases. A comparison with radiation also demonstrates that cryoablation is a quick procedure (one night stay), less expensive than competing procedures, and comparable, if not lower, in morbidity rates. Therefore the results from this experiment should induce a greater acceptance of cryoablation as a viable primary treatment option for local to locally advanced cancer.

---

4. "CRYOSURGERY AS PRIMARY TREATMENT FOR LOCALIZED PROSTATE CANCER: A COMMUNITY HOSPITAL EXPERIENCE"

Author: Ellis DS

Institution: Arlington Memorial Hospital in Arlington, Texas and Baylor Medical Center in Coppell, Texas

Date/Publication: August 2002, Urology Vol. 60 (Supp 2A)

Indication: Primary (small % of salvage patients)

Patient Selection: Biopsy-proven adenocarcinoma of the prostate, PSA testing, full routine clinical staging, and Gleason score evaluations

Number of Patients: 93 (75 primary, 18 salvage)

Length of Follow-up: 1 year

Efficacy: 84%

Measurement of Efficacy: PSA levels of less than or equal to 0.4 ng/mL

Morbidity: 1.4% severe incontinence, 4% mild incontinence, 1.3% transurethral resection, 6.7% urethral sloughing, 82.4% impotence

Measurement of Morbidity: Measured up to a year after surgery. Severe incontinence = requiring > 2 pads per day, mild incontinence = requiring < 2 pads per day

Key Words: community hospital setting, safety and efficacy, salvage, training of physician

PRIMARY CRYOABLATION

Summary:
Ellis demonstrates that cryosurgery as a primary treatment for prostate cancer is an effective and safe procedure that can be performed in a community hospital setting with outcomes comparable to outcomes achieved in academic hospital settings. The efficacy and morbidity results of those treated in the community hospital compare favorably with the published results of procedures performed in academic hospital settings. The procedures were done by a single urologist suggesting that cryosurgery is possible for any urologist to perform provided he or she has: 1) imaging, interventional, and surgical skills; 2) competence with a cystoscope; 3) an understanding of ice ball thermodynamics and cryobiology; and 4) cryosurgery-specific experience.

---

5. "QUALITY OF LIFE AND SEXUALITY OF MEN WITH PROSTATE CANCER 3 YEARS AFTER CRYOSURGERY"

Author: Robinson JW, Donnelly BJ, Saliken JC, Weber BA, Ernst S, Rewcastle JC

Institution: University of Calgary in Calgary, Alberta, Canada

Date/Publication: August 2002, Urology Vol. 60 (Supp 2A)

Indication: Primary

Patient Selection: Biopsy-proven adenocarcinoma of the prostate, PSA level less than or equal to 30 ng/mL, a stage of T1 to T3 NO MO by clinical evaluation, bone scan, chest x-ray and TRUS guided biopsies

Number of Patients: 76 men

Length of Follow-up: Quality of life checkups: 6 months, 1 year, and 3 years; medical and biochemical assessment ongoing

Efficacy: 5 year follow-up: 69% PSA < 0.3

Measurement of Efficacy: PSA level

Key Words: quality of life, sexual function

Summary:
This study focuses on the degree to which men who have undergone cryosurgery are able to recapture the quality of life (QOL) they enjoyed before treatment. Two questionnaires were adminis-

tered, the Functional Assessment of Cancer Treatment- Prostate (FACT-P) and the Sexuality Follow-Up Questionnaire (SFQ), to quantify the changes in QOL. While there were decreases in FACT-P scores 6 weeks after surgery, by 12 months there were no significant differences with feelings prior to surgery with the exception of sexuality. However, sexuality scores continually rose after two years due to a return of sexual function and the usefulness of sexual aids. Comparing scores at 1 year to 3 years demonstrates 47% improvement in sexual functioning. There are no other significant changes between 1 year to 3 years suggesting that life remained stable after the first year of treatment and that there are no delayed complications of prostate cryotherapy. These results can be tentatively compared to publications of other treatments to demonstrate that QOL scores 3 years after treatment are at least as high from cryosurgery as from radical prostatectomy, external-beam radiotherapy, or brachytherapy.

---

6. "IN VIVO INTERSTITIAL TEMPERATURE MAPPING OF THE HUMAN PROSTATE DURING CRYOSURGERY WITH CORRELATION TO HISTOPATHOLOGIC OUTCOMES"

Author: Larson TR, Robertson DW, Corica A, Bostwick DG

Institution: Department of Urology, Mayo Clinic, Scottsdale, Arizona

Date/Publication: April 2000, Urology Vol. 55 (4)

Indication: Primary

Patient Selection: Men with prostate cancer who had been previously scheduled to undergo radical retropubic prostatectomy as their primary treatment

Number of Patients: 6

Key Words: critical temperatures, double freeze vs. single freeze, temperature mapping

Summary:
The purpose of this study is to determine the critical temperatures below which human prostatic tissue can be cryoablated, and to compare the efficacy of single-freeze vs. double-freeze.

Thermocouple junctions placed at various radial distances from the probe allow cell ablation and temperature to be recorded. The results indicate that double-freeze can achieve cryoablation of a larger volume of target tissue than a single-freeze procedure. Definitive cryoablation is -60oC for single-freeze and -40oC for double-freeze. These results provide a basis for more optimal use of temperature monitoring during cryosurgery. This will allow for eradication of prostate cells with minimum potential for complications.

---

7. "A PROSPECTIVE TRIAL OF CRYOSURGICAL ABLATION OF THE PROSTATE: FIVE-YEAR RESULTS"

Author: Donnelly BJ, Saliken JC, Ernst DS, Ali-Ridha N, Brasher PMA, Robinson JW, Rewcastle JC

Institution: Tom Baker Center and University of Calgary

Date/Publication: October 2002, Urology Vol. 60 (4)

Indication: Primary (small % of salvage cases)

Patient Selection: histologically proven adenocarcinoma, PSA levels less than 30 ng/mL, and negative bone scans

Number of Patients: 76

Length of Follow-Up: 5 years

Efficacy: 98.6 % cancer-specific survival rate

Measurement of Efficacy: Negative biopsy

Morbidity: 3.9% sloughing, 1.3% incontinence, 1.3% testicular abscess, all experience impotency immediately after surgery but 47% regained sexual function 3 years after surgery

Measurement of Morbidity: Follow-up biopsy, quality of life questionnaire, and sexual questionnaire (FACT-P)

Key Words: efficacy, safety

Summary:
In the past, complications such as urethroperineal and urethrorectal fistulas have caused cryotherapy to be questioned. However after the development of TRUS probes, real-time imaging, well-insulated cryoprobes, and a urethral warming device,

cryosurgery has improved in efficacy and safety. Through the results of this study, Donnelly, et al have demonstrated that properly delivered cryosurgical ablation has a high efficacy providing that the cancer is confined to the prostate and immediate vicinity. The procedural complications are similar to those reported elsewhere and compare favorably to other treatments. Impotence has the highest morbidity but the nerves are frozen and not cut and therefore have the potential to recover. Other treatments show a potency rate of 25% after 18 months. Since 47% of the cryosurgery patients resumed sexual function, cryosurgery potency rates compare favorably with other treatments. As do other treatments, cryosurgery requires long training and experience.

---

8. "FIVE YEAR RETROSPECTIVE, MULTI-INSTITUTIONAL POOLED ANALYSIS OF CANCER-RELATED OUTCOMES AFTER CRYOSURGICAL ABLATION OF THE PROSTATE"

Author: Long JP, Bahn D, Lee F, Shinohara K, Chinn DO, Macaluso JN Jr

Institution: New England Medical Center, University of California at San Francisco, Urologic Institute of New Orleans, Crittenton Hospital, and Alhambra Hospital

Date/Publication: March 2001, Urology Vol. 57 (3)

Indication: Primary

Patient Selection: Clinical stages T1-T4, any PSA level, and any Gleason grade

Number of Patients: 975

Length of Follow-Up: 5 years

Efficacy: 82%

Measurement of Efficacy: biopsy after procedure

Key Words: comparison between radiotherapy and cryosurgery, efficacy, safety

Summary:
Study includes a retrospective analysis of a large database of patients from five institutions and comparison with contemporary reports of patient outcomes after radiotherapy. Because of the large sample, the cryosurgery technique was performed with some variation with only a small number treated with the most advanced use of all modern features (two freeze cycles, approved urethral warming, thermocouple monitoring, and 6-8 cryoprobes). However despite the variations the experimental outcome was very comparable to outcomes after radiotherapy as the positive biopsy rate of cryotherapy matched results of radiotherapy. Significant differences appeared in rates of erectile dysfunction and rectal injury between the two treatments, with lower rates of rectal problems after cryotherapy but higher rates of potency after radiotherapy. Overall the data in this report indicates that cryotherapy can be performed with low morbidity and can produce results comparable to radiotherapy.

---

9. "QUALITY-OF-LIFE OUTCOMES FOR MEN TREATED WITH CRYOSURGERY FOR LOCALIZED PROSTATE CARCINOMA"

Authors: Robinson JW, Saliken JC, Donnelly BJ, Barnes P, Guyn L

Institution: University of Calgary in Calgary, Alberta, Canada

Date/Publication: November 1999, Cancer Vol. 86 (9)

Indication: Primary

Patient Selection: Biopsy-proven adenocarcinoma of the prostate, PSA level less than or equal to 30 ng/mL, a stage of T1 to T3 NO MO by clinical evaluation, bone scan, chest x-ray and TRUS guided biopsies

Number of Patients: 69

Length of Follow-up: 1 year

Efficacy: 68% PSA < 0.3, 32% PSA >0.3

Measure of Efficacy: PSA level

Key Words: quality-of-life (QOL), sexual function, cryosurgery, radiotherapy

Summary:
Since early use of cryotherapy was abandoned due to a high incidence of complications, this study aims to determine the quality of life of men after treatment of prostate cancer with modern-

ized cryotherapy procedures. Patients completed the Functional Assessment of Cancer Treatment-Prostate (FACT-P) before the procedure, 6 weeks, and 3, 6, and 12 months after the procedure. Despite a drop in FACT-P scores from pretreatment to 6 weeks, by 12 months there were no significant differences compared with pretreatment scores, with the exception of sexual function. There was a sharp decline in sexual function at 6 weeks and then only a small increase over the year. However, twelve months may not be sufficient time to observe the full degree to which erectile functioning will return subsequent to cryosurgery. The overall pattern of results suggests that cryosurgery has a minimal impact on QOL since most aspects of a patient's life prior to surgery will return after 1 year of cryotherapy.

---

10. "CRYOSURGERY FOR PROSTATE CANCER: IMPROVED GLANDULAR ABLATION BY USE OF 6 TO 8 CRYOPROBES"

Author: Lee F, Bahn DK, Badalament RA, Kumar AB, Klionsky D, Onik GM, Chinn DO, Greene C

Institution: Crittenton Hospital in Rochester, Michigan

Date/Publication: July 1999, Urology Vol. 54 (1)

Indication: Primary

Patient Selection: Patients in the two groups had to have similar PSA level, clinical stage, and Gleason score

Number of Patients: Total: 163, 5-probe: 82, 6 to 8-probe: 81

Length of Follow-up: 6 months

Efficacy: 5-probe: 39%, 6 to 8-probe: 53%

Measurement of Efficacy: complete glandular ablation

Key Words: 5-probe vs. 6 to 8-probe, probe complications, efficacy

Summary:
The objective of this study is to determine the efficacy for increased glandular destruction by using 6-8 cryoprobes in place of the traditional 5 probes. The results of the study demonstrate that using 6-8 cryoprobes has 3.5 times higher odds of obtaining near total destruction over the traditional use of 5 cryoprobes. While there was a concern that more probes would create more

PRIMARY CRYOABLATION

complications, the results disproved this concern as no complications appeared using 6-8 cryoprobes. Therefore, this study indicates that using 6-8 cryoprobes has an advantage over the use of 5 cryoprobes.

---

11. "CRYOSURGICAL ABLATION OF THE PROSTATE: HIGH RISK PATIENT OUTCOMES"

Author: Prepelica KL, Okeke Z, Murphy A, Katz AE

Institution: Columbia-Presbyterian Medical Center in New York, New York

Date/Publication: April 2005, Cancer Vol. 103 (8)

Indication: Primary

Patient Selection: Patients with prehormone therapy high-risk features (high risk defined as either a PSA level greater than or equal to 10 ng/mL, Gleason sum score greater than or equal to 8, or both of these features)

Number of Patients: 65

Length of Follow-up: 35 months

Efficacy: 83.3%

Measurement of Efficacy: The American Society for Therapeutic Radiology and Oncology (ASTRO) definition of biochemical failure (3 consecutive increases in PSA level)

Morbidity: 3.1% Rectal pain, 3.1% urinary retention, 3.1% incontinence, 1.5% voiding complications, no perineal discomfort, rectourinary fistula, or disease progression

Measurement of Morbidity: Measured immediately after surgery and up to 77 months

Key Words: High Risk, efficacy

Summary:
This study focuses on men with high-risk features for prostate carcinoma who were unwilling to undergo radical surgery or radiation therapy. Using the modern system of cryotherapy which includes TRUS and urethral warmers, the high risk patients received efficacious results. The results from this study

are very comparable to similar studies using the same modality in high-risk patients. This reaffirmed data indicates that cryoablation is a feasible treatment option in patients with organ-confined prostate carcinoma who have high-risk features. Because the results of this study have a short follow-up, a longer follow-up is necessary to determine the durability of the treatment.

---

12. "CRYOABLATION OF PROSTATE: 10 YEAR EXPERIENCE WITH 249 CASES"

Author: Fletcher C Derrick, Jr., John J Britton, Alan W Fogle, Jonathon T Donaldson, Bonner Thomason, Ian Y Marshall, Stephen Bielsky, William H Holl, George B DelPorto, Paul W Sanders, Benjamin K McInnes, Raymond Rosenblum, James W Kellet, Alex Ramsay

Institution: Charleston, SC

Date/Publication: May 21-26, 2005, The 2005 Annual Meeting of the American Urological

Association Association, San Antonio, TX

Indication: Primary

Number of Patients: 249

Length of Follow-up: 10 years

Efficacy: 64%, 75%, and 84%

Measurement of Efficacy: 0.5, 1.0, and 2.0 PSA thresholds

Morbidity: 3.6% stricture or bladder neck contracture, 0.8% prostate abscess, 0.4% prostate-rectal fistula, 8% stress incontinence, 2% severe incontinence, and 90% impotent

Key Words: efficacy, long-term follow-up

Summary:
This objective of this study was to determine the efficacy of cryoablation of the prostate in cases of primary cancer (88.24% of patients) and radiation failure (11.76% of patients). Patients had Gleason scores ranging from 5-9 with 34.76% low risk patients, 38.09% moderate risk patients, and 27.17% high risk patients. Of the 249 patients, follow-up data was available for 230

PRIMARY CRYOABLATION

cases. At the 10 year follow-up, 64%, 75% and 84% of patients were disease free with 0.5, 1.0, and 2.0 PSA ng/mL thresholds. Overall morbidity rates were low with no operative deaths. 9 patients had a stricture or bladder neck contracture and 2 patients had a prostate abscess, most likely due to the large size of the gland. One patient had a prostate rectal fistula. 90% of the patients were continent post surgery and 10% retained some normal erectile dysfunction. However, 50% of patients had some return of normal function beginning in 6 months. The results of the study suggest that cryoablation of the prostate is a minimally invasive, alternative treatment of primary cancer of the prostate. The results also demonstrate that cryoablation of the prostate is the treatment of choice for radiation failure patients whose cancer is still confined to the prostate gland.

---

13. "CRYOSURGERY OF THE PROSTATE: TECHNIQUES AND INDICATIONS"

Author: Cohen JK

Institution: Department of Urology, Allegheny General Hospital, Pittsburgh, Pennsylvania

Date/Publication: 2004, Reviews in Urology; 6:supplement 4): S20-S26

Indication: Primary & salvage

Number of patients: not stated

Length of follow-up: 10 years

Efficacy: Salvage 56% @ 10 years

Primary (without previous hormone therapy):
- Low risk: 68%
- Moderate risk: 63%
- High risk: 50%

Primary (without any previous therapy):
- Low risk: 63%
- Moderate risk: 62%
- High risk: 49%

Negative biopsy rate: 70% (not stated which population this applies to)

Measurement of efficacy: definition of biochemical failure: any patient who does not have a nadir < 0.4 ng/ml or who has two successive rises in PSA after treatment

Key words: efficacy, long term follow-up

Summary: This paper is largely intended as a technology review. It describes how the technologies have changed since the early days of liquid nitrogen cryomachines. It also documents the transient removal of the urethral warmer from the market by the FDA. The morbidity profile associated with modern cryoablation is significantly less than that of cryoablation in the 1990s. The paper also contains significant follow-up information although the matter in which it is presented makes it confusing. The number of patients in each group is not stated. The results are very good for salvage but less so for primary (in comparison to those of Bahn and Donnelly). It states that the best patients for cryoablation are those with bulky disease, high risk disease and those who have failed previous radiation therapy.

---

14. "TREATMENT OF ORGAN CONFINED PROSTATE CANCER WITH THIRD GENERATION CRYOSURGERY: PRELIMINARY MULTICENTER EXPERIENCE"

Author: Han KR, Cohen JK, Miller RJ, Pantuck AJ, Freitas DG, Cuevas CA, Kim HL, Lugg J, Childs SJ, Shuman B, Jayson MA, Shore ND, Moore Y, Zisman A, Lee JY, Ugarte R, Mynderse LA, Wilson TM, Sweat SD, Zincke H, Belldegrun AS.

Institution: Multicenter trial led by the UCLA Department of Urology

Date/Publication: October 2003, Journal of Urology. 170(4 Pt 1):1126-30.

Indication: Primary & salvage

Number of patients: 122 (106 with efficacy data)

Length of follow-up: 12 months

Efficacy: 81% immediately following procedure (nadir) 75% at 12 months: low risk: 78%, moderate and high risk: 71%

Measure of efficacy: PSA ≤ 0.4 ng/ml for both primary and salvage

Morbidity Primary:

Incontinence: 3% (requiring pads), impotency: 87% (of those previously potent), fistula: 0%

Salvage:

Incontinence: 11% (requiring pads), fistula: 0%

Key words: third generation, short term

Summary: This is an initial report of cryoablation using third technology equipment manufactured by Oncura. The study was conducted at 11 sites worldwide (average of 11 patients per site). Initial results are encouraging both in terms of efficacy and morbidity. The authors conclude that this technology has potential but further study which includes more follow-up is needed to prove the real morbidity and efficacy profile.

---

15. "SALVAGE CRYOSURGERY OF THE PROSTATE AFTER RADIATION FAILURE"

Author: Lim JS and Belldegrun AS

Institution: UCLA Department of Urology

Date/Publication: 2004, Reviews in Urology; 6(supplement 4): S27:S36

Indication: salvage

Key words: third generation, review

Summary: A review article of the technological advancements that have occurred in the past 10 years with salvage cryoablation. The morbidity profile associated with early salvage cryoablation can not be looked at a representative of modern salvage cryoablation. The efficacy of the modern treatment, along with the fact that it is repeatable makes it a preferred treatment modality for localized recurrent prostate cancer.

16. "PILOT EXPERIENCE WITH REAL-TIME ULTRASOUND GUIDED PERCUTENAOUS RENAL MASS CRYOABLATION"

Institution: Departments of Radiology, University of Virginia Health Sciences Center, Charlottesville, Virginia

Date/Publication: April 2004, Journal of Urology171(4):1620-3.

Indication: Renal

Number of patients: 3

Length of follow-up: 2 months

Efficacy: 100 %

Measure of efficacy: contrast enhancement

Morbidity: none

Key words: ultrathin, initial, pilot

Summary: Embryonic results from renal cryoablation using ultrathin 17 gauge cryoprobes are presented. The study population is extremely small (3 patients) but all were discharged the day following cryoablation. Post operative pain management was done with oral non-narcotic medications. In MRI scans preformed 6-7 weeks post cryoablation no patients had contrast enhancement. The procedure appears to be promising but more study is needed to definitively show that small probe cryoablation is equivalent to larger probe cryoablation.

■ ■ ■

Focal Cryoablation

1. "THE MALE LUMPECTOMY: RATIONALE FOR A CANCER TARGETED APPROACH FOR PROSTATE CRYOABLATION. A REVIEW"

Author: Onik G

Institution: Division of Surgical Imaging, Center for Surgical Advancement, Department of Surgery and Urology, Celebration Health in Celebration, Florida

Date/Publication: Aug. 2004, Technology in Cancer Research and Treatment Vol.3 (4)

Indication: Focal

Patient Selection: Patient must be potent prior to treatment and the prostate cancer had to be confined to a single prostate lobe

Number of Patients: 9

Length of Follow-up: 36 months

Efficacy: 100%

Measurement of Efficacy: Stability of PSA

Morbidity: 22% impotent, no instances of other complications previously described with cryosurgery such as obstruction, incontinence, penile numbness or fistula formation

Measurement of Morbidity: measured 1 year after surgery and up to 36 months

Key Words: focal, male lumpectomy, potency

Summary:
Since impotence and incontinence affect the male self image as much as the loss of a breast does in a woman, it is worthwhile to investigate the feasibility of a male lumpectomy. The lumpectomy shows that quality of life can be successfully integrated into cancer treatment. While the majority of prostate cancer cases are multi-focal, pathological literature indicates that 35% of prostate cancer is solitary and unilateral. This presents an opportunity for focal treatment. There has been little prior mention of focal treatment since it had little clinical significance with treatments aimed at total gland removal or destruction (such as surgery or radiation). Through improved gland sampling and biopsies, the chances of missing a significant multi-focal tumor have been diminished. With uni-focal cases identified, cryoablation can be

used as a safe and effective treatment with its inherent ability to be tailored to the extent of the patients' disease. The results of this study confirm cryoablation's efficacy as all patients were disease free and the majority maintained potency. The results demonstrate cryolumpectomy superiority over bilateral nerve sparing RP, brachytherapy, and external beam radiotherapy. In conclusion, preliminary results have shown that a procedure which effectively targets the cancerous portion of the prostate gland while limiting the patient morbidity is possible.

---

2. "FOCAL "NERVE-SPARING" CRYOSURGERY FOR TREATMENT OF PRIMARY PROSTATE CANCER: A NEW APPROACH TO PRESERVING POTENCY"

Author: Onik G, Narayan P, Vaughan D, Dineen M, Brunelle R

Institution: Division of Surgical Imaging, Center for Surgical Advancement, Department of Surgery and Urology, Celebration Health in Celebration, Florida

Date/Publication: July 2002, Urology Vol. 60 (1)

Indication: Focal

Patient Selection: Patient must be potent prior to treatment and the prostate cancer confined to a single prostate lobe

Number of Patients: 9

Length of Follow-up: ranging from 6 to 72 months (mean 36)

Efficacy: 100%

Measurement of Efficacy: Stability of PSA

Morbidity: 22% impotent (2 of 9), no instances of other complications previously described with cryosurgery such as obstruction, incontinence, penile numbness or fistula formation

Measurement of Morbidity: measured 1 year after surgery and up to 36 months

Key Words: focal, potency, nerve-sparing RP

Summary:
Focal "nerve-sparing" prostate cryosurgery is a unique combination of an aggressive treatment on the side of the cancer, yet a

"minimal" procedure on the side opposite the cancer. The results demonstrate that the approach is successful in local cancer control, with no evidence of local cancer recurrence in any patients. This has great significance since the patient population was not selected to ensure success as many of the patients had moderate to high risk features. A major concern for focal cryosurgery is the biopsy since focal cryoablation leaves some prostate tissue untreated. The results indicate that the procedure has extremely low morbidity. Focal cryosurgery is advantageous over RP nerve-sparing since it has the ability to be repeated, has a higher rate of potency when preserving one nerve bundle, and the rate of potency returns faster with cryotherapy. While a longer follow-up is needed, if the results are continually confirmed nerve-sparing cryosurgery could have a significant impact on the treatment of prostate cancer.

■ ■ ■