



Tina Sotis. *Awakening* ©2001. Oil on canvas, 34" × 46".

*Improved technology allows for delivery of therapeutic freezing to the prostate with protection of adjacent structures.*

# Image-Guided Prostate Cryosurgery: State of the Art

*Gary Onik, MD*

**Background:** Cryosurgery was first used to treat prostate cancer in the early 1970s but it was not until 1993, when the results from percutaneous ultrasound-guided cryosurgery were published, that the potential advantages of this treatment became apparent. Changes in equipment and techniques have improved the results of cryosurgery, in both tumor control and lower morbidity.

**Methods:** The author has reviewed data of his own and those of others concerning the changes in techniques employed and outcomes from prostate cryosurgery.

**Results:** Ultrasound-guided percutaneous transperineal placement of the cryoprobes allows monitoring of freezing in real time. Monitoring temperature at critical locations, separating the rectum and prostate by saline injection, and using argon gas rather than liquid nitrogen-based equipment have improved results and lowered complication rates. The technique produces outcomes similar to those obtained with brachytherapy and three-dimensional conformal radiation therapy.

**Conclusions:** Advantages of cryosurgery include the ability to re-treat patients without added morbidity and to treat salvage postradiation patients with acceptable results and morbidity. The recent demonstration that "nerve-sparing" cryosurgery is possible suggests that cryosurgery may be used more often.

## Introduction

With the decision of the Centers for Medicare and Medicaid Services (CMS), formerly the Health Care Financing Administration (HCFA), in 1999 to approve prostate cryosurgery for the treatment of primary prostate cancer, treatment options for patients were expanded.<sup>1</sup> Despite decades of investigation and incremental improvements in both radical prostatectomy (RP) and radiation therapy, neither treatment modality

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has distinguished itself as the procedure of choice for treating primary prostate cancer. Both modalities have limitations in treating patients with higher stage and Gleason grade disease. Also, the associated morbidities of RP and radiation therapy, while sometimes different in type, are not appreciably different in extent or incidence to clearly recommend one treatment over the other. As a result, each approach can be justifiably recommended as the procedure of choice. These options, along with “watchful waiting,” as possible strategies for prostate cancer management have led to patient confusion and consternation. Adding cryosurgery as still another treatment option to this already confusing environment further complicates patient choices.

The improvements in cryosurgical results gained in recent years due to the basic understanding of the thermal destruction of tissue, the advances in cryosurgical technique, and its unique inherent advantages may ultimately identify image-guided prostate cryosurgery (or perhaps another similarly image-guided ablative technology) as the treatment of first choice in treating all stages and grades of nonmetastatic prostate cancer.

Since the ultrasound-guided percutaneous transperineal approach for prostate cryosurgery is essentially identical to that of a radiation seed implantation, the potential advantages of cryosurgery can be well appreciated if freezing is viewed as another new implantable radiation source (Figs 1 and 2). Thus, the characteristics of the freezing probes are known and the freezing can be monitored and modulated in real time to ensure adequate therapy. There is no biological effect on structures adjacent to the frozen tissue, and the treatment is accomplished in a few minutes. There is no “dose threshold” for the freezing, and the

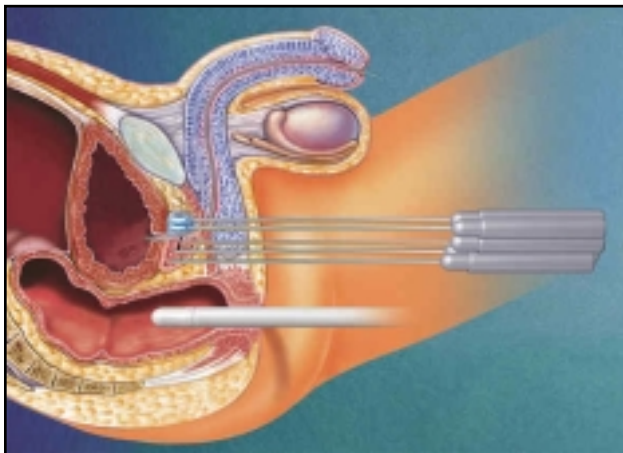


Fig 1. — Diagram showing the transperineal approach of prostate cryosurgery. The cryoprobes are placed percutaneously through the perineum using transrectal ultrasound for guidance. The approach is identical in concept to brachytherapy of the prostate. Reproduced with permission from Endocare, Inc, Irvine, California (1-888-236-3646; <http://www.endocare.com>).

treatment can be repeated. Full-dose external-beam radiation therapy can be incorporated into the therapy program, and since tissue planes are left intact, subsequent radical prostatectomy is a treatment option for local failure.<sup>2</sup>

Despite these advantages and the long history of thermal therapy (hyperthermia) in the field of radiation oncology, cryosurgery has been virtually ignored by the brachytherapy community. This review presents results suggesting that the advantages of freezing as a “radiation source” are finally being harnessed. This paper reviews the background of prostate cryosurgery, its lackluster early performance that created a negative perception of the procedure, the changes in instrumentation and technique that have improved prostate cryosurgery results, and the patient selection criteria for prostate cryosurgery.

## Cryosurgery Background

The treatment of localized prostate cancer remains controversial. Although pathologic studies have shown that the prevalence of prostate cancer is high, many of these cancers are not clinically significant.<sup>3</sup> In addition, even clinically significant cancers — generally accepted as those of a volume of 0.5 mL or greater — have a variable biologic behavior. On the other hand, the treatments for prostate cancer include a substantial risk of lifestyle-limiting morbidity. With some recent studies showing minimal survival benefit between no treatment and RP, the concept of “watchful waiting,” ie, not treating the primary tumor at all, has gained acceptance by some as a viable management alternative in certain patient populations.<sup>4</sup> The decision to treat prostate cancer with a particular ther-

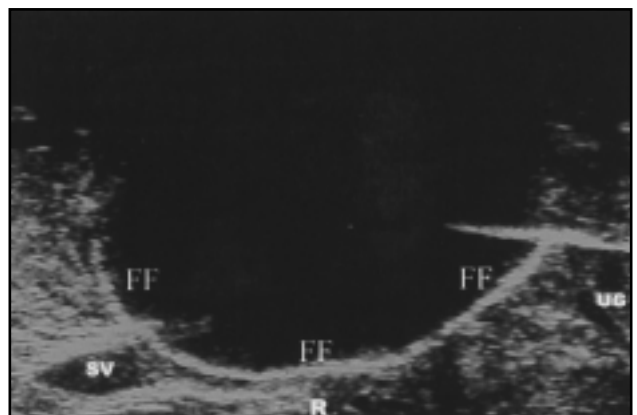


Fig 2. — Transrectal ultrasound showing the ice as it extends toward the rectum. The freezing front (FF) is exquisitely seen as a hyperechoic (white) line extending toward the rectum (R). The seminal vesicle (SV) and urogenital diaphragm (UG) can be identified. The ability to visualize the freezing as it encompasses the prostate and approaches the rectum gives a “freezing radiation source” greater control than traditional brachytherapy.

apy or with watchful waiting requires a careful assessment of the risk vs benefit for that patient. As the complications and lifestyle-limiting side effects of treatments are reduced, these decisions become easier. The reintroduction of prostate cryosurgery using a percutaneous approach under ultrasound guidance was consistent with this concept of trying to decrease the morbidity of prostate cancer treatment.

In 1966, Gonder et al<sup>5</sup> first reported the concept of a cryosurgery procedure for the treatment of prostate disease. Subsequently, an open transperineal cryosurgery procedure was developed in which the freezing was carried out on the surface of the prostate with visual monitoring. Using this same approach, Bonney et al<sup>6</sup> reported results of this procedure in 229 patients followed for up to 10 years. A comparison of these patients with those who underwent RP, radiation therapy, and other procedures showed equal survival among the treatment modalities. Although cryosurgery showed some advantages, such as being able to treat patients with large bulky tumors, poor monitoring of the freezing process resulted in major complications such as urethro-cutaneous and urethro-rectal fistula, thus limiting the acceptance of the procedure.

In 1993, the first series of percutaneous ultrasound-guided and monitored prostate cryosurgery was reported,<sup>7</sup> which stimulated a resurgence of interest in this treatment modality. As with any new procedure, ultrasound-guided prostate cryosurgery went through a significant learning curve in which the goals of the procedure looked attainable but the reported results, in both cancer control and complications, were variable. A negative perception of the procedure was compounded by the fact that most early series predominantly treated patients in whom radiation therapy had failed, and these patients have higher complication rates, particularly incontinence, than those without a history of radiation therapy (73% vs 3%).<sup>8,9</sup> The situation was also exacerbated by a high urethral complication rate caused by the use of an ineffective urethral warming catheter.<sup>10</sup> Despite these early obstacles, the long-term results from multiple institutions were examined, and in 1999 the CMS removed cryosurgery from the investigational category and included it with radiation and RP as a treatment for primary prostate cancer.

The quality of these results, taking into account the early technical variability of the procedure as well as the urethral warmer problems, is best reflected in the multi-institutional study recently published by Long et al.<sup>11</sup> When they compared cryosurgery vs radiotherapy using the same patient risk stratification and success criteria, the results from cryosurgery were comparable with both external-beam radiation therapy and

brachytherapy. For the low-risk group, the 5-year biochemical-free survival rate was 76% with cryosurgery for the low-risk group, 75%-87% for comparable brachytherapy in reported series, and 67%-81% for conformal radiotherapy. The results were comparable for medium- and high-risk groups. The incidence of rectal complications was greater for the radiation therapy group, while the rate of impotence was greater with cryosurgery. The results were remarkably similar despite the substantial disparity in resources and experience between the two therapies. When the latest advances in cryosurgical techniques are considered, the results and complication rates for cryosurgery reported in this study can be improved.

## Patient Selection

The extent and pathologic character of the patient's disease are importance factors in choosing a proper therapy for prostate cancer. Treatments such as RP and brachytherapy (without external boosting) have higher recurrence rates as the extent and aggressiveness of the disease increases. One of the great advantages of cryosurgery is the flexibility of the procedure to be tailored to treat both high- and low-risk patients as well as patients in whom failed radiation therapy has failed.

### *Patients at High Risk for Local Recurrence*

The use of cryosurgery for the treatment of solid organ cancers made a resurgence with the advent of ultrasound monitoring of hepatic cryosurgery first proposed in 1984.<sup>12</sup> Hepatic cryosurgery filled a unique place in the armamentarium of liver cancer treatment in that it successfully treated patients with multiple tumors or tumors that were unresectable due to proximity to major vasculature that could not be sacrificed.<sup>13,14</sup> Due to its target patient population of previously untreatable patients with an expected mortality of virtually 100%, imaging-guided hepatic cryosurgery was readily embraced by some surgical oncologists.<sup>15</sup>

The situation with prostate cancer is similar to liver cancer in that a significant portion of prostate cancer patients are unresectable, based on the high proportion of patients who have capsular penetration at the time of definitive treatment. However, efforts at preoperative staging have been inadequate to identify this patient population. The difficulty is further compounded by the fact that at the time of RP, the surgeon's ability to appreciate capsular penetration and involvement of the neurovascular bundles is inadequate. Vaidya et al<sup>16</sup> recently reported virtually no correlation between the surgeon's determination of tumor pene-

tration into the periprostatic tissue with involvement of the neurovascular bundle and actual pathologic confirmation. The result is that in this study, as well as in other reports, positive margin rates of 30%-40% associated with nerve-sparing RP are not uncommon. Using various clinical parameters such as Gleason score, clinical stage, and prostate-specific antigen (PSA) level, the statistical chance for capsular penetration can be reasonably predicted preoperatively.<sup>17,18</sup> This approach can lower the positive margin rate when rigorously applied, as demonstrated by Eggleston et al.<sup>19</sup> In actual clinical practice, however, most urologists believe that RP is still the “gold standard” of treatment. This leads to a natural reluctance, based on a statistical analysis, for them to deny a treatment that may provide the best chance for cure.

Based on the success of cryosurgery in treating unresectable liver cancer, it was hoped that the ability to freeze into the periprostatic tissue and encompass tumor capsular penetration could improve the treatment of prostate cancer patients at high risk of positive surgical margins. The preliminary data seem to support the potential success of this primary goal of prostate cryosurgery — improved treatment outcomes in patients at high risk of local recurrence. Numerous studies on ultrasound-guided prostate cryosurgery have demonstrated the ability of the procedure to successfully treat patients with stage T3 prostate cancer with demonstrated gross extracapsular disease.<sup>20,21</sup> Demonstration of this concept in patients with a “high likelihood” of capsular penetration, based only on statistical analysis, is more problematic since the exact margin status of the patient is not known preoperatively or post operatively following a cryosurgical procedure. There is, however, some evidence to support excellent results in patients at high risk for positive margins.

Onik et al<sup>22</sup> have shown that aggressive periprostatic freezing was facilitated by separating the rectum from the prostate at the time of the operation by a saline injection into Denonvilliers’ fascia. No local recurrences were seen in 61 patients followed for up to 4 years despite the fact that 68% of the patients were considered at high risk of capsular penetration and local failure, based on the factors of Gleason score of 7 or greater, PSA >10 ng/mL, already failed radiation, or extensive bilateral disease based on preoperative biopsies.

When cryosurgery is performed aggressively to achieve a negligible detectable PSA level following cryosurgery, comparisons with RP should be possible. In the only published study comparing the outcomes between aggressive “total” cryosurgery and RP in one clinical practice,<sup>23</sup> cryosurgery had a 23% greater

chance of resulting in a PSA level of less than 0.2 ng/mL than did RP (96% vs 73%). When a 0.0 PSA was used as the success criteria, cryosurgery maintained its approximately 20% advantage over RP (66.9% vs 48.2%). As patients became at greater risk for positive margins based on a PSA of 20 ng/mL or greater, cryosurgery maintained its results while the results of RP deteriorated further (86% vs 36%). While this study was retrospective and included a relatively small number of patients, its results are consistent with the original cryosurgical treatment rationale of destroying extracapsular cancer by treating the periprostatic tissues. In addition, these findings are consistent with the other studies showing success in treating T3 disease and other high-risk patients, as well as the unequivocally successful results seen in treating unresectable liver tumors.

These results, together with the relatively low morbidity of the procedure and its ability to be performed in older patients and repeated when needed, may make cryosurgery the procedure of choice in this patient population. Whether better local control of extracapsular disease will result in improved survival remains to be proven by long-term data. The prevailing thinking is that the high-risk patients described eventually fail because they already have metastatic disease at the time of the original treatment and therefore improvements in local control of disease will have little impact on the ultimate outcome for these patients. As yet no reliable method of diagnosing patients with microscopic metastatic disease is available. That all or most of these patients who ultimately get metastatic disease already have it at the time of their original treatment is conjectural. The possibility that some patients develop metastatic disease only due to inadequate treatment of their local disease has to be considered. Adjuvant hormone therapy in high-risk patient populations is an important strategy. When combined with radiation, short-term hormone therapy appears to improve local-regional control and distant metastatic in patients with bulky tumors (T2-T4).<sup>24</sup> Long-term adjuvant hormonal therapy in addition to radiation appears to significantly affect the survival of patients having a Gleason score of greater than 7.<sup>25</sup> Since adjuvant therapy in these studies also had a significant effect on local control of tumor, the question of the importance of local control of tumor on the incidence of subsequent metastatic disease still needs investigation.

### *Patients With Organ-Confined, Low-Volume Disease With Low Gleason Score*

When treating patients with organ-confined prostate cancer, low morbidity with limited effect on patient lifestyle becomes a major factor in selecting a

treatment option. Cryosurgery has low general surgical morbidity, and it can be performed on an outpatient basis, with no need for blood transfusions, and with no reported perioperative cardiovascular or pulmonary complications. Urethro-rectal fistula, a serious local complication of prostate cryosurgery that occurs due to rectal freezing, has been virtually eliminated by the technique of injecting saline into Denonvilliers' fascia at the time of surgery, thus creating a large buffer zone between the rectum and the prostate capsule. When patients who failed radiation and those treated without the original urethral warmer are excluded, cryosurgery has achieved incontinence rates of 2% or less.<sup>22,26,27</sup> A study published by Robinson et al,<sup>28</sup> which reported on the quality of life of patients following cryosurgery, showed return of urinary function to baseline status in all patients by 1 year following the procedure.

### *Nerve-Sparing Cryosurgery*

In an effort to establish cryosurgery as a viable cancer treatment, it has been aggressively aimed at total gland ablation. However, total gland ablation with freezing of both neurovascular bundles has a significant negative impact on sexual functioning.<sup>28</sup> The high rate of impotence with cryosurgery is a major disadvantage compared with nerve-sparing RP and brachytherapy in the management of patients who are interested in maintaining sexual functioning. In our experience, total cryosurgery has the same impotency rate as non-nerve-sparing RP, virtually 100% in the short and intermediate term. The same reason that cryosurgery has demonstrated an advantage in treating high-risk patients, however, contributes to this significant rate of impotence. When cryosurgery is properly carried into the periprostatic tissue to encompass any extracapsular tumor that preferentially invades the neurovascular bundles, both bundles are necessarily destroyed. Therefore, in patients at high risk of bilateral extracapsular disease, impotence is an expected side effect and actually a welcome sign that treatment has been properly performed. The original thought that sexual dysfunction secondary to cryosurgery would only be temporary, based on the well-known ability of peripheral nerves to regenerate after cryosurgery, was erroneous. The parasympathetic system critical to erection has its secondary cell bodies in relation to the prostatic capsule, and the destruction of these by cryosurgery is evidently irreversible.

However, cryosurgery may be used as a nerve-sparing procedure similar in concept to the approach with RP. In fact, the demonstrated ability of cryosurgery to be repeated would give it a major theoretical advantage over nerve-sparing RP. Temperature monitoring to pre-

vent freezing of the neurovascular bundle opposite the demonstrated tumor can readily be used to preserve this structure, thus preserving potency.

We have now followed for up to 6 years a group of 9 patients who underwent unilateral nerve-sparing cryosurgery. The potency rate (defined as erection sufficient to carry out intercourse to the satisfaction of the patient) was 78% (7 of 9 patients) with no patient having evidence for a local recurrence on PSA monitoring or biopsy. The common factors in our patient selection for nerve-sparing cryosurgery were the small volume of cancer demonstrated on biopsy and the presence of unilateral disease on staging procedures. Of particular interest is that the group included high-risk patients, with 5 of 9 having some risk factor for extracapsular disease (3 of 9 patients had a Gleason score of 7 or above). The potency results were surprising in that only one nerve bundle was spared, yet our results rivaled results seen with bilateral nerve-sparing RP. The high potency rate with sparing of only one neurovascular bundle by cryosurgery is better than that expected with RP, which has been reported as 13% to 41%<sup>29,30</sup> and is probably accounted for by the lack of manipulation of the opposite neurovascular bundle and its associated blood supply.

Nerve-sparing cryosurgery is a unique blend of an aggressive yet minimal procedure, which accounts for its combination of excellent cancer control and lack of complications. Extensive freezing of the periprostatic tissue is still carried out on the side of the demonstrated tumor. In patients with a high Gleason score or in those with cancer demonstrated at the base of the gland, prophylactic freezing of the confluence of the seminal vesicles can also be carried out. The expected incidence of urinary and rectal complications is lower than that of total cryosurgery, RP, or brachytherapy. No patient in our small series demonstrated persistent incontinence. Probably most important, however, is that an error in patient selection is correctable by retreatment without added morbidity, a situation unique to cryosurgery. Although a comparison is being made to results of RP, no conclusions can be drawn from this preliminary information except that further study is justified. A large, prospective, multi-institutional study is being planned to validate this treatment approach with a comparative group of RP patients.

### *Patients With Local Recurrence After Radiation Therapy*

Patients who received a maximal dose of radiation but suffer a local recurrence without evidence of metastatic disease are still theoretically curable. Unfortunately, radiation destroys the tissue planes needed for

a safe and effective attempt at salvage RP. RP in a salvage situation has demonstrated positive margins in 40% of patients<sup>31</sup> with prohibitive morbidity demonstrating a 58% incontinence rate and an incidence of rectal injury as high as 15%.<sup>32</sup> Consequently, salvage RP is rarely performed in this setting; most patients are placed on palliative hormone ablation therapy.

Based on the successful application of cryotherapy in patients with liver cancer, percutaneous prostate cryosurgery was immediately applied to this difficult-to-treat patient population. The treatment of patients for salvage after radiation therapy was not without difficulties, however. Early findings showed poor cancer control results with less than 25% of patients reaching PSA levels of 0.2 ng/mL<sup>33</sup> or less, with positive biopsy rates as high as 35%. Also, complications in this patient population could be significant. While the incontinence rate for nonsalvage cryosurgery patients is less than 2%, significant incontinence for radiation salvage patients can be as high as 42%.<sup>10</sup> Advances in cryosurgical technique have improved these results with a recent article by de la Taille et al<sup>34</sup> demonstrating a 60% success rate at providing an undetectable PSA. The associated incontinence rate was 9%.

Our results are consistent with this report. We recently examined 24 patients who had locally recurrent prostate cancer after radiation therapy and were treated with cryosurgery. The mean follow-up was 3 years, with a minimum of 1 year. The patient parameters indicated a group at extremely high risk of recurrence with 15 of 24 patients having a Gleason score of 7 or above and 4 patients having already failed hormone therapy. The median preoperative PSA level was 4.7 ng/mL (SD 3.4 ng/mL) and the postcryosurgery median PSA level was .01 ng/mL (SD 7.4 ng/mL). Nineteen patients have a stable PSA that is undetectable, and the 5 unstable patients have had negative biopsies. In these 24 high-risk patients, there is yet no evidence for a local recurrence. In addition, 3 of the 4 patients who have already failed hormone therapy have no evidence for recurrent disease. The incontinence rate in these patients was 33%, but this does not reflect the recent changes in freezing protocols and urethral warmer changes that has lowered this rate into the 10% range.<sup>34</sup> In addition, patients with severe incontinence that limited lifestyle were successfully treated with artificial sphincter placement.

Based on these results, cryosurgery was recently approved by the CMS as the only treatment specifically approved for the indication of recurrent local cancer after radiation failure. We believe that based on its potential for cure, cryosurgery has become the procedure of choice in this difficult-to-treat patient population.

## Technical Advances in Cryosurgery

### *Saline Injection Into Denonvilliers' Fascia*

A major theoretical criticism of prostate cryosurgery involves the anatomy of the pelvis with the close proximity of the prostate capsule to the rectal mucosa. Inadequate space between the prostate and the rectum can result in freezing the rectal mucosa with resultant urethro-rectal fistula. Subsequently, fear of causing urethro-rectal fistula may stop the freezing process prematurely (even if there is enough room for adequate freezing) and thus lead to a high incidence of tumor recurrence. Even for the experienced cryosurgeon, cryosurgery was at times a nerve-wracking balancing act between adequate treatment and rectal injury.

Probably the most important advance in the technique of prostate cryosurgery leading to the reproducibility of results involves the injection of saline into Denonvilliers' fascia at the time of freezing to tem-

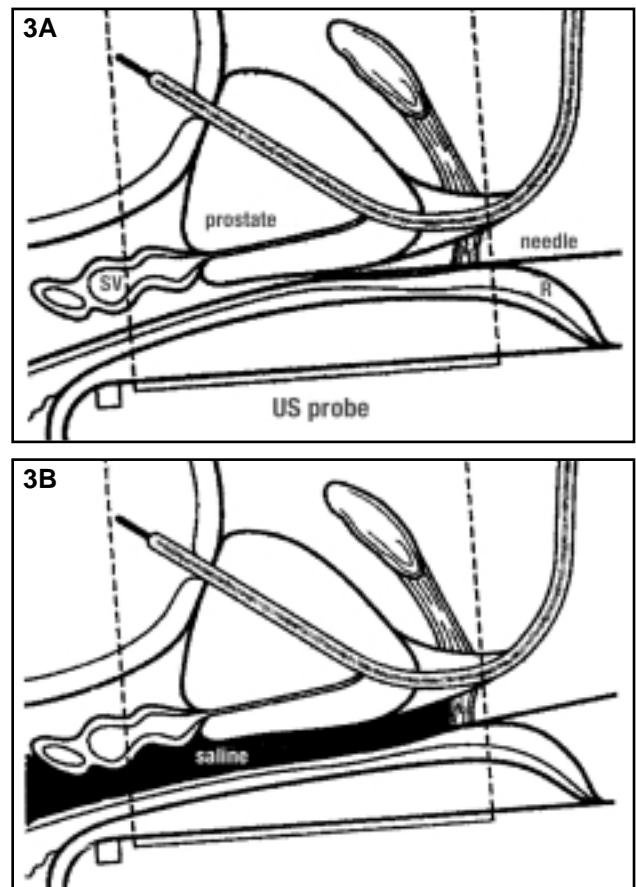


Fig 3A-B. — (A) This diagram shows a needle being placed into Denonvilliers' fascia at the time of cryosurgery. The rectum (R) is abutting the prostate capsule with Denonvilliers' fascia being a potential space. (B) Saline is injected into Denonvilliers' fascia and the space between the rectum and the prostate capsule has been artificially increased. This protects the rectum from freezing and allows adequate freezing beyond the prostate to encompass and cancer that has extended through the capsule.

porarily increase the space between the rectum and prostate (Fig 3). We have now utilized this saline injection technique in more than 200 patients, demonstrating that this maneuver virtually eliminates the risk of rectal freezing and the complication of urethro-rectal fistula without increasing morbidity. We have also demonstrated in more than 25 patients that the procedure can be successfully applied in patients in whom radiation therapy has failed.<sup>22</sup>

The elimination of the fear of rectal freezing has several consequences that improve the effect results of cryosurgery. First, with the rectum protected, freezing can be sufficiently extended outside the prostate to bring the  $-35^{\circ}\text{C}$  isotherm to the capsule of the prostate, thus ensuring adequate temperatures for cancer destruction everywhere within the prostate. The position of the  $-35^{\circ}\text{C}$  temperature isotherm changes in relation to the freezing margin as the iceball grows, being closer to the freezing margin with smaller ice volumes. With more freezing room, cryoprobes can be placed farther into the peripheral zone of the gland, where 80% of cancers reside, making the destructive temperature zone easier to reach the capsule with less freezing volume. This also exposes these cancers to faster freezing rates and colder temperatures, both of which improve the cancer destruction. Second, freezing can be extended far enough outside the prostate to also include extracapsular extension of cancer, thereby improving the local control of cancer in high-risk patients. The arrangement of the cryoprobes can be placed into the posterior urethral region to encompass the confluence of the seminal vesicle, thus preventing recurrence in this region. Third, with this move of cryoprobes into the peripheral zone, the freezing of the periurethral tissue is adequate but less intense, which may decrease over time the rate of urethral sloughing.

The potential benefit of the maneuver and its effect on cryosurgical results are indicated in our earlier study on the technique.<sup>22</sup> Ninety percent of patients had an undetectable PSA with no patient demonstrating a positive biopsy, despite the fact that more than two thirds of our patients were in a medium- to high-risk category. Currently, in more than 200 patients followed for up to 6 years, only 1 patient has had a local recurrence. Since our center is the only one that has applied this technique to any number of patients over time, these results will have to be confirmed by other centers.

### *Temperature Monitoring in Critical Areas and Improved Cryosurgical Protocols*

For reliable destruction of cancer by freezing, temperatures must reach certain critical limits. Recent *in vitro* and *in vivo* studies have shown that at least two

freeze-thaw cycles with temperatures reaching  $-35^{\circ}\text{C}$  are needed to reliably destroy prostate cancer cells.<sup>35</sup> Clinical studies have confirmed these parameters as well as the improvement that can occur in clinical results when temperature is monitored by thermocouples placed in critical areas in the prostate and two full freeze-thaw cycles are carried out. Wong et al<sup>9</sup> had 10 local failures in their first 12 cases with only ultrasound monitoring and six failures in the next 66 cases after thermocouple monitoring was carried out. They also demonstrated another major advantage of cryosurgery, ie, the ability to re-treat local failures. Using thermocouple monitoring to re-treat their previous failures, a negative biopsy rate of 94% (72 of 77 patients) was achieved at 30 months.

Saliken et al<sup>26</sup> reported a similar experience involving 69 patients. Ten patients initially had positive biopsies, with the majority of them occurring early in their cryosurgical experience. Ultimately, after re-treatment, 68 (98%) of 69 patients had negative biopsies.

### *Argon-Based Cryosurgical Equipment*

The original  $\text{LN}_2$ -based freezing equipment has now been replaced by Joule-Thompson argon gas systems. These systems allow faster freezing rates, which improves the reliability of cancer destruction. The more precise control of the freezing process by gas systems also adds to the safety of the procedure by allowing the freezing process to be stopped in a more timely fashion.

Increasing the number of probes from 5 to 8 has allowed a more uniform freezing temperature to be achieved throughout the gland, which also improves results. Lee et al<sup>36</sup> showed an advantage to using 6-8 argon gas probes over 5 liquid nitrogen probes. Using re-treatment as an option, they achieved a negative biopsy rate of 96% (157 of 163 patients). Even with normal glands and residual PSA remaining after cryosurgery, this does not necessarily equate with treatment failure. Pisters et al<sup>2</sup> reported on 7 patients with locally advanced cancer who had cryosurgery followed by RP. In 4 patients who had no evidence of cancer in the gland, some normal glands were still identified.

Increasing the number of probes beyond 8 could have a potentially negative effect. A "cryoseed system" (Galil Medical Inc, Haifa, Israel) that utilizes 17-gauge needle probes to create a 1-cm diameter iceball was not able to totally ablate the prostate gland based on reported PSA results.<sup>37</sup> These poor results are probably the result of the short freezing length of these probes and the difficulty in accurately overlapping the freezing zones along the length of the gland. All of the data cur-

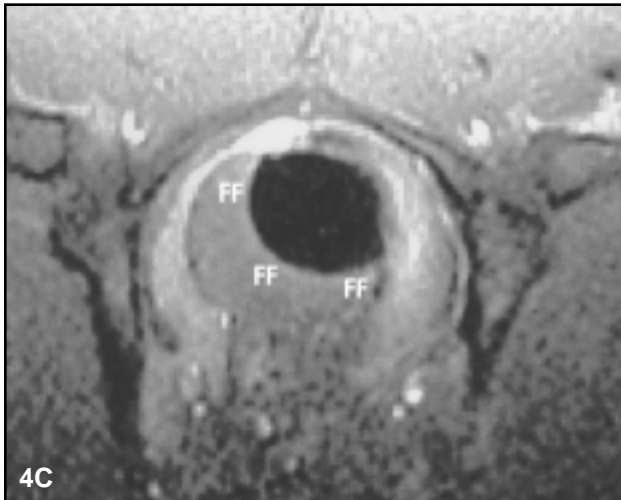
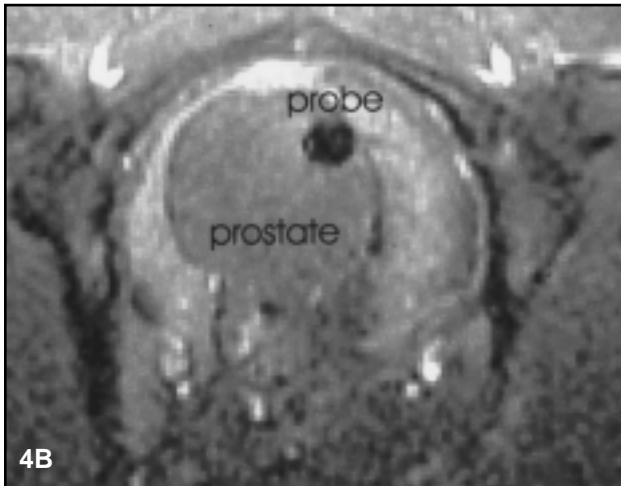
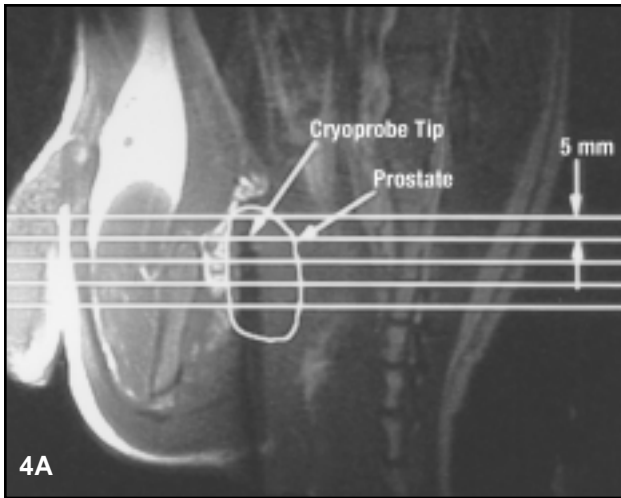


Fig 4 A-C. — (A) Sagittal MRI of a dog prostate. The cryoprobe extends from the perineum of the dog into the anterior portion of the prostate. (B) Axial MRI of the dog prostate prior to freezing. The probe is seen as a dark circle in the anterior portion of the prostate. (C) Axial MRI of the dog during freezing. The freezing appears on the MRI as a dark signal void the freezing front (FF) extends into the prostate. Note that anterior margin of the freezing can also be seen and that the freezing is asymmetric with less freezing extending anteriorly due to the large amount of blood flow in the anterior venous complex. These details cannot be appreciated on ultrasound due to shadowing that occurs beyond the freezing front.

rently used to gain acceptance of cryosurgery was developed with cryosurgical probes that freeze the length of the gland in one freeze; departing from this concept jeopardizes much of what has been learned about how to obtain consistent results using cryosurgery.

### Future Technical Improvements

With the recent approval by the CMS for reimbursement of cryosurgery, there is finally an incentive for commercial interests to make the investment to technically improve prostate cryosurgery. At the present time, the greatest improvements being made are those that have already been well established in the area of brachytherapy. Since the freezing capabilities of cryoprobes are predictable, planning software is already being developed to direct proper cryoprobe placement based on gland size and shape. Planning software will shortly be coupled to guidance software and hardware, which will simplify what now is a totally freehand approach to cryoprobe placement.

While ultrasound is inexpensive and readily available, it still is highly operator dependent and difficult to use by novices. Other cross-sectional imaging techniques such as magnetic resonance imaging (MRI) have the potential to simplify and standardize cryosurgical procedures. As opposed to ultrasound, where ice causes shadowing and shows only the leading edge of the iceball, both MRI and computed tomography (CT)

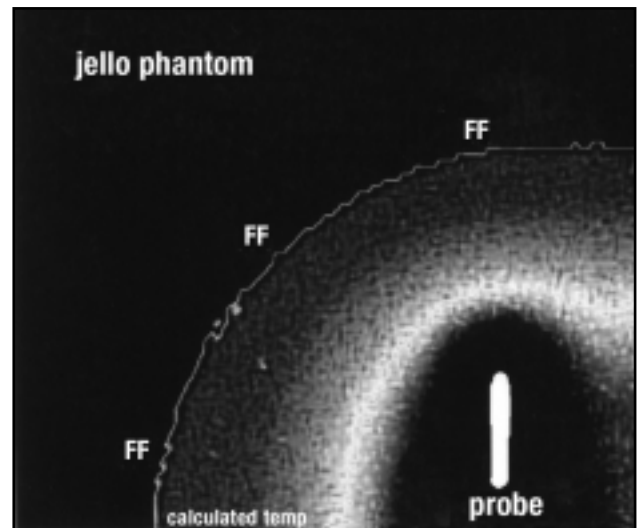


Fig 5. — MRI of a jello phantom showing calculated temperatures within the iceball. The freezing has extended out from the probe with the edge of the freezing (FF) noted by the white line. The different shades of gray within the iceball represent the calculated temperatures within the iceball. The temperatures are calculated on a computer by knowing the position of the freezing front and cryoprobe from the MRI and the temperature of the cryoprobe tip. The temperatures can be represented on the image also as isothermal lines. Alternatively, a cursor can be placed before the freeze on a structure of interest, and the temperature at that point can be continuously displayed.

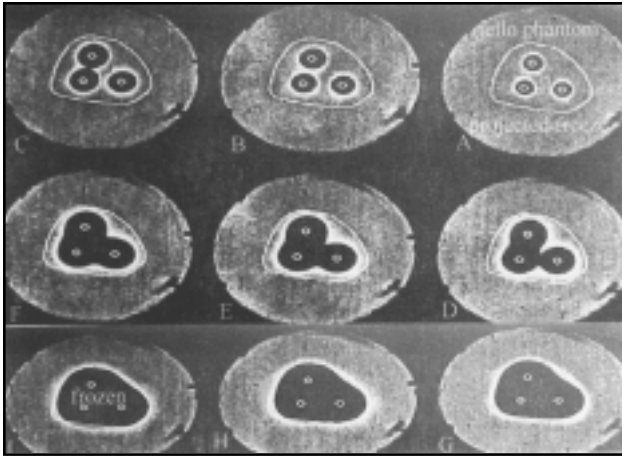


Fig 6. — Computer control of freezing based on MRI imaging. In this diagram, freezing is followed in a jello phantom over time proceeding from image A through image I. The phantom is imaged as the white circle on the gray background. Three cryoprobes, the dark circles, have been placed within the phantom and are being imaged in cross-section in a triangular arrangement. The cryoprobes have been circled with an oddly shaped line, which represents the shape and extent of freezing that the computer will try to reproduce by turning the cryoprobes on and off appropriately. The computer modulates the ice shape based on feedback on the extent of freezing from the MRI image. As the iceball grows over time, the freezing from each probe eventually coalesces and reproduces as closely as possible the shape that was specified.

show the full extent of the freezing (Fig 4). Using thermodynamic equations, these images can then be used to noninvasively calculate temperatures within the iceball (Fig 5) and automatically control the cryoprobes to create a specific freezing shape and profile (Fig 6).

We believe as the inherent advantages of freezing as a “brachytherapy radiation source” are appreciated, investment in technical developments will accelerate. At the present time, we are seeing only the tip of the “iceberg” of the technical potential of prostate cryosurgery.

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