

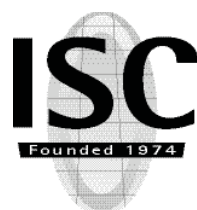
Prostate and Renal Cryoablation
CASE STUDY REVIEW

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**Focal Cryoablation:
Patient Selection and Case Study**

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International Society of Cryosurgery



Dear Reader,

The International Society of Cryosurgery is pleased to publish peer-reviewed case studies in urologic applications of cryosurgery.

In this issue Dr. Winston Barzell reviews a focal prostate cryoablation performed on patient Thomas Kabel. Dr. Barzell's international education and published research contribute to his standing as a respected urologist in a community setting. His clinical experience includes work with Memorial Sloan-Kettering Cancer Center and the Sloan-Kettering Institute for Cancer Research (NY), and with the Research Council of Canada (Montreal). He holds U.S. patents in device technology, and is the President/CEO of Barzell Whitmore Maroon Bells, a medical instrumentation company. He is in private practice with Urology Treatment Center (Sarasota, FL).

We are grateful to Dr. Barzell for providing the case parameters, clinical discussion and images, with special thanks to Mr. Thomas Kabel for permitting publication of his story. In addition to adding an element of human interest, Mr. Kabel's account illustrates a patient's experience choosing among therapeutic options and undergoing treatment. As a special section, Dr. Barzell shares his criteria for patient selection and his treatment protocol.

We acknowledge Endocare, Inc. (Irvine, CA, USA) for sponsorship of our series of cryoablation case studies.

Whether you are an experienced cryosurgeon, or a relative newcomer, I hope you find this case review to be of interest regarding the possibilities of focal prostate cryoablation.

Sincerely,

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INTRODUCTION

Selecting Patients for Focal Prostate Cryoablation Using 3D Mapping Biopsy

Focal treatment of prostate cancer (PCa) can be expected to remain controversial for the foreseeable future, despite pathology data suggesting that not all PCa is multifocal.¹ Early clinical studies of focal prostate cryoablation suggest excellent local disease control with minimal post-treatment morbidity, including 100% continence and 80% potency.²

If long-term results confirm the merits of a focal or conformal freeze of prostate tumors, the key question will be that of patient selection. A high degree of confidence in patient identification may require far more extensive tissue analysis than can be obtained by 10-14 TRUS-guided needles.

In the focal cryoablation presented by Dr. Winston Barzell, his decision followed diagnosis of unifocal disease using a “3D mapping” biopsy obtained transperineally, guided by a template similar to brachytherapy. Such a meticulous approach is especially mandated in qualifying candidates for focal treatment.

Dr. Barzell and his colleagues cited practical and theoretical reasons for the usefulness of a 3D mapping approach to biopsy (initially termed “saturation biopsy”). In their framework, TRUS biopsy has limitations in anterior and apical access, potentially greater risk of infection and rectal bleeding with larger numbers of sticks, and possible sampling error. The combination of these factors argued for a more systematic, reproducible technique to obtain comprehensive sampling.

Barzell, et al point out that bilateral 3D mapping biopsies are indicated when potentially high-risk patients have had three previously negative TRUS biopsies. In addition, they recommend use of this technique in two other situations:

1. Unilateral saturation biopsies are done solely on the contralateral side in patients with minimal one-sided prostate cancer and low PSA who are being considered for unilateral focal therapy (e.g. cryotherapy) to prove the absence of cancer on what will be the untreated side.
2. Bilateral saturation biopsies to define the extent of cancer are done in situations where low Gleason score and low volume disease are suspected and patients are being considered for expectant management.³

In the second instance, the purpose is to avoid possible TRUS under-sampling and underdiagnosis.

In the case presented here, Dr. Barzell performed a 3D mapping biopsy on patient Thomas Kabel prior to performing a focal freeze. The biopsy results gave him the confidence that Mr. Kabel was a candidate for the procedure detailed in this study.

1 Djavan, et al, Tech Urol Sep. 1999

2 Onik 2002, 2004; Bahn unpublished preliminary

3 Barzell, Whitmore et al. Urology Times, May 2003

CASE STUDY

Case History: Thomas Kabel

Urologic History and Presenting Symptoms

Mr. Thomas Kabel (DOB 04/11/39) was diagnosed with benign prostatic hyperplasia by his physician on 2/19/03. His slightly elevated PSA at that time was attributed to BPH and he was instructed to be re-tested in one month. His PSA had risen to 5.9 and he made an appointment with Dr. Barzell.

7/10/03 - Casodex prescribed

7/16/03 - Zoladex (3 mo. injection)

10/16/03 - Zoladex (3 mo. injection), continued on Casodex

Other Considerations

Patient age: 64

Lifestyle: Active

Patient was offered all standard

Target temperatures noted the first freeze included -25°C (Anterior), -58°C (LNVB) and +31°C (RNVB). During the second freeze temperatures included -26°C (Anterior), -86°C (LNVB) and +29°C (RNVB).

After the removal of the warming catheter, a Foley catheter was inserted.

Results and Follow-up

2/10/04 - First post-treatment PSA <0.1

6/10/04 - PSA 0.1

10/22/04 - PSA 0.7

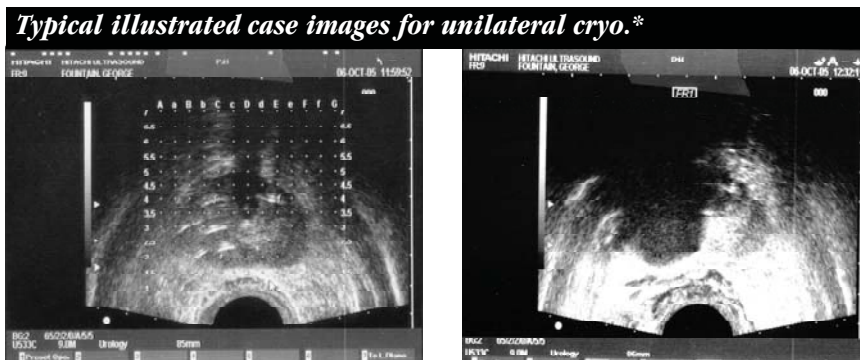
Urinary function post-treatment: noted as medium stream, no incontinence.

Sexual function post-treatment: 9/19/05 return to normal sexual function noted.

11/9/05 - Biopsy; 12 cores were taken, all samples were benign.

3/14/06 - PSA 1.04 (most recent)
NOTE: Inasmuch as the patient's PSA prior to treatment was 5.9, and given that only a hemi-freeze was done, it is anticipated that the patient's PSA will stabilize somewhere between 1.5 and 2.5.

* NOTE: Original Kabel case images were not available.



Ultrasonic transverse image of prostate after placement of cryoprobes and thermal monitors. Arrow indicates initial access to Denonvilliers space prior to saline injection.

Ultrasonic transverse view of right-sided iceball formation. Notice large space created between prostate and rectum by saline injection into Denonvilliers space.

4/23/03 - TRUS biopsy (12 needles)

Results - Left side of gland positive for adenocarcinoma, confirmed by Johns Hopkins; Gleason grade 3 + 3

5/12/03 - Bone scan (results: negative)

No other diagnostic scans were done

7/8/03 - 3D mapping biopsy on right (contralateral) side of gland

Results - All negative

treatment options for localized prostate cancer. Patient elected focal cryoablation per qualification by Dr. Barzell.

Treatment and Follow-Up

11/20/03

Focal prostate cryoablation performed by Dr. Barzell. Six probes were placed and a double freeze/thaw cycle was used to ablate the left side of the gland.

PHYSICIAN DIALOGUE

Interview with Winston Barzell, M.D. Urology Treatment Center, Sarasota, Florida, USA

What was your experience with your early cryo cases?

To satisfy myself that cryo was effective, I adversely selected my early patients. I chose high-risk cases with high-grade or locally advanced PCa (Gleason >7), patients who ordinarily have a high failure rate with other treatment modalities. Despite this, they all did well, and a lot of the patients with Gleason 8 or 9 scores still have unmeasurable PSAs. I'm not satisfied by a low or unmeasurable PSA alone, and therefore I biopsy every patient at 1-year post-cryo. The vast majority not only have negative biopsies, but the samples reveal either very little or no gland tissue. This suggests that the effects of cryo are likely to be long lasting.

I strongly believe in the Onik technique of separating the rectum from the prostate [injecting saline solution into Denonvilliers' fascia]. For example, I recently did a case of a patient with a bad cancer on one side, and I wanted to treat aggressively outside the gland on that side. The NVB thermocouple on that side registered -60°C. This would not have been safely possible without creating a space between the prostate and rectum, at least not in my hands. I tend to be conservative, and firmly believe in the dictum of "above all, do no harm." Without this separation I could end up potentially under-treating in my attempt to avoid a rectal injury. Once mastered, this technique is an easy matter, and I personally can't conceive of a reason why it shouldn't be done in each case.

What role do you now see for cryo?

I believe that cryo as a treatment option will become a strong contender at both extremes of PCa. On one hand, it's ideal for salvage and high grade/high stage cases,

where evidence exists that it is superior to other options. On the other, it will be suitable for some early cases. Until recently patients with minimal early PCa faced with whole gland treatment with potential for side effects, or a watchful waiting approach with the risk of cancer growth or spread. Focal cryotherapy offers an intermediate position of treating only the part of the gland involving cancer. Thus, cryo can be an excellent choice for: 1) patients with high grade/high stage cancer; 2) salvage therapy after failed radiation; and 3) some early cancer patients who fit the criteria for focal cryoablation, are uncomfortable with a watchful waiting approach, and don't want whole gland treatment.

What do you tell patients about cryo?

While we have medium, and long term data on the effectiveness of total gland cryotherapy, in cases where "focal" or unilateral cryotherapy is being considered, I tell patients that we don't have long term data supporting this modality, and therefore the treatment has to be considered somewhat "quasi-experimental". I don't want anyone saying they thought it was a widely accepted standard form of treatment. In other words patients should be fully informed.

How many focal cases have you performed and what are your results?

I've performed about 20-25. I have very strict selection criteria so to date I have no recurrences. Here I've stacked the deck in favor of focal cryo, since I include only ideal focal treatment candidates. The late Dr. W. F. Whitmore Jr. used to say, "Selection is the silent partner

of the successful oncologic surgeon." I've done about half of the cases conformally, where I expand the freeze to include potential precancerous regions outside the index cancer. What I don't want is a failure.

Continence is 100%. I'm not as impressed with the preservation of potency. One possibility is it might take a while for patients to regain potency, thus it is too early to tell for sure.

Who came up with the term "3D mapping"?

We did. In the first paper I wrote with my partner Dr. W. F. Whitmore III, we called it saturation biopsy but that term was confusing. It was used by many who were doing more than 12 TRUS biopsies. We prefer the term 3D pathologic mapping since the technique not only provides for a more comprehensive sampling of the prostate, but more importantly a reproducible coordinate system of mapping that can be translated into a treatment plan. This is what distinguishes it from other saturation biopsies.

Are patients initiating the request for focal?

While some patients are referred specifically for consideration of focal therapy, the majority are patients with minimal disease who are considering expectant management. I perform the 3-D mapping and if it shows only a focal area of cancer, I offer focal cryo as one option. Some like that idea, but I don't guarantee potency.

The ideas and opinions expressed herein are strictly those of the interviewee.

PATIENT EXPERIENCE

My Story

By Mr. Tom Kabel

I'm a retired high school math teacher; I also coached golf and bowling. I'm 67 years old as of April 2006. I have six children, three grandchildren, and another on the way. I work part-time at a golf course.

During a January 2003 insurance physical, the blood test revealed a PSA of 5.2. My doctor told me it could be due to an enlarged prostate, so I got retested in a month and it was 5.9. I had heard about Dr. Barzell, and I scheduled to see him. He did an in-office biopsy that showed a small amount of cancer on the left side only. He recommended a book by Patrick Walsh, M.D.

I began an internet search, including a specific search for cryoablation, and I attended "Man to Man" prostate cancer support group meetings. I was looking for everything. I made lists comparing the advantages and disadvantages of the four basic options. I ruled out beam radiation because of the number

of treatments, the temporary side effects, and the possibility it might not get all the cancer.

I asked if brachytherapy could treat one side only and the response was vague. I narrowed it down to radical prostatectomy (RP) and cryo.

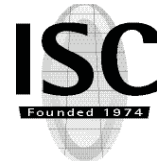
When I considered RP, I felt it would get all the cancer, but with the long recovery and the care I'd need at home, cryo became more appealing. I wanted to get back to my kids and the golf course as soon as possible. The cryo success statistics at that time were promising, plus in my case only half of my prostate would be frozen. I was confident of maintaining urinary control. Added to that, Dr. Barzell said if it didn't work, I could have the other side treated with cryo.

He did a 3D mapping biopsy two months later, confirming cancer on the left side only.

I delayed treatment until November 20 to visit my son in

London. When I went for my cryo they kept me overnight due to my diabetes and high blood pressure. For the first day or two at home I took oral analgesics, but there was hardly any pain. The following Monday, Dr. Barzell was giving a talk at "Man to Man", and he asked me attend, which I did. When the catheter came out, I had no trouble urinating—complete continence from the beginning. My kids came for Thanksgiving, and Dr. Barzell cleared me to play golf 10 days after my treatment. I played all 18 holes.

Dr. Barzell told me to expect detectable PSA since he didn't do a total freeze. My most recent is 1.04. I had biopsies on both sides a couple of months ago, and they were all negative. He has me on a list to talk to other patients. I tell them to look at all the options, but with my experience and recovery I do recommend cryo.



ISC Overview

The International Society of Cryosurgery was founded in 1974 to promote continuing medical education in the field of cryosurgery from an experimental and clinical point of view. The overall aim of the ISC is to continue to develop and expand membership of the society.

The headquarters of the Society are based in Casa di Cura Salus, Trieste, Italy. The Society corresponds with around 700 members worldwide. Membership is open to anyone who has a professional interest in research and education in the fields of Cryosurgery, Cryobiology, Cryopreservation, and other disciplines related to the use of low temperature in medicine.

ISC Activities: To learn more please visit our website

<http://www.societyofcryosurgery.org/futMeetings/index.htm>

ISC Publication:

The Society produces a biannual publication 'Cryosurgery'

<http://www.societyofcryosurgery.org/publications/index/htm>

which covers all aspects of Cryosurgery and Cryobiology.

ISC Officers and Board of Directors:

Please visit our website for a complete listing:

<http://www.societyofcryosurgery.org/officers/index/htm>

The case study presented here reflects the outcomes for a single physician and patient. Outcomes for other physicians and patients may vary so choice of treatment is best determined between a physician and patient where the risks can be evaluated specific to the individual patient. Cryoablation of the prostate, like all prostate procedures, involves certain risks including risk of incontinence, impotence and rectal injury. Physicians and patients interested in cryoablation as a treatment for prostate cancer should familiarize themselves with the risks and long term outcomes as documented in recent published clinical data. For a bibliography of cryoablation published data please contact the International Society of Cryosurgery.

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