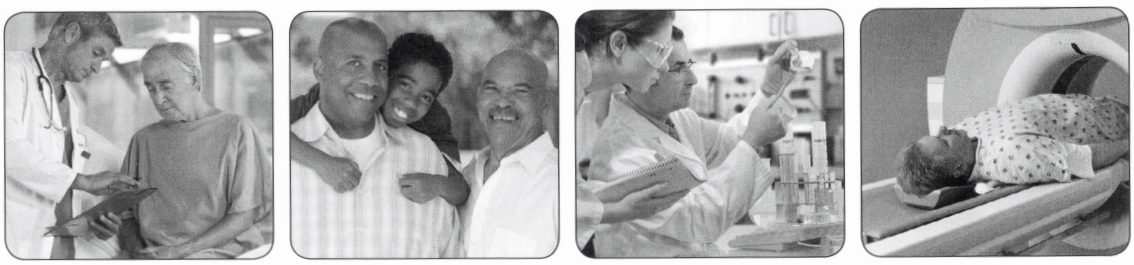
HARVARD MEDICAL SCHOOL

2016 *Annual Report on* PROSTATE DISEASES



Covering advances in the diagnosis and treatment of prostate cancer, benign prostatic hyperplasia, erectile dysfunction, prostatitis, and related conditions

HARVARD HEALTH PUBLICATIONS *Trusted advice for a healthier life*

A DOCTOR'S AND PATIENT'S PERSPECTIVE:

One man's experience with targeted focal therapy for low-risk prostate cancer

Men diagnosed with low-risk prostate cancers that grow slowly and may never become lethal face difficult choices. One option is to treat the whole prostate gland with surgery or radiation. However, radical treatments such as these can cause erectile dysfunction and other side effects. Another option is to monitor the cancer with active surveillance and to initiate treatment only when it gets worse. But since active surveillance leaves a cancer in place, men can find it unsettling.

A third option, called targeted focal therapy, can provide a compromise solution. With targeted focal therapy, doctors treat only cancerous portions of the prostate while leaving the rest of the gland—including the nerves that control erectile and bowel function and the muscles that control urinary continence—intact. Targeted focal therapy can be performed using several methods. Doctors can freeze tumor tissue with cryotherapy, for instance, or they can destroy it with high-intensity focused ultrasound (HIFU), which uses sound waves to selectively heat tumors to lethal temperatures while sparing normal tissue. (For more detailed discussion of these methods, see "Focal therapy," page 68.)

Harvard-affiliated hospitals do not currently offer targeted focal therapy for prostate cancer. Therefore, we spoke with an internationally recognized expert who does, along with one of his patients. Presented below, this discussion of his experience can help readers assess targeted focal therapy as a potential treatment.

The doctor: E. David Crawford, M.D., is a professor of surgery, urology, and radiation oncology, and head of the Section of Urologic Oncology at the University of Colorado Anschutz Medical Campus, in Denver. He is the recipient of more than 95 research grants and an author of more than 500 scientific publications concerning the diagnosis and treatment of prostate cancer, metastatic prostate cancer, hormone-refractory prostate cancer, benign prostatic hyperplasia (BPH), advanced bladder cancer, and other areas of urological infections and malignancies.

The patient: Brian Kols [not his real name; changed to protect his privacy] was treated with focal therapy by Dr. Crawford in 2010.

The interviewer: Marc B. Garnick, M.D., editor in chief of the Annual, moderated the discussion.

Q: Dr. Crawford, would you please introduce Brian Kols and describe his case?

Crawford: I first met Brian in March of 2010, when he sought us out for an opinion on his prostate cancer, which had been diagnosed a few months earlier. At the time, he was 59 years old. A biopsy had revealed Gleason 6 cancer in 10% of a single core on one side of his prostate. He didn't have a markedly elevated PSA level, and his prostate volume was 45 cubic centimeters. Other doctors had recommended radical prostatectomy, but Brian was newly married and concerned about the sexual side effects. And apart from his cancer, he was the picture of health and a nonsmoker. The rectal exam didn't raise any significant concerns, although there had been some urinary bleeding that was attributed to a separate bladder tumor.

So his case brings home the whole issue of overdiagnosis and overtreatment of prostate cancer. For 20 years patients have been asking me, "Hey Doc, why can't you just take out part of my prostate, or why can't I have a lumpectomy like some women with breast cancer?" We would explain that prostate cancer exists in multiple places in the gland, and that 20% to 30% of men diagnosed with low-grade disease actually harbor something worse that's been missed on biopsy. That's what got us to start doing mapping biopsies, which take dozens of cores from the prostate in a tight grid. We use the results to generate a three-dimensional model of the gland, and we don't miss any significant cancer that way—our assessment of the prostate is as good as if we had taken the gland out. We got some publicity for that, and this is how Brian found out about us. When we did a mapping biopsy on him, we found more cancer in his prostate than what was seen in the initial biopsy, and even a bit of Gleason pattern 4. But over all, he was in a very good position for a partial ablation [targeted tissue destruction] that would save his nerves and preserve his sexual potency.

Q: Brian, let's turn it over to you now. What led up to your diagnosis of prostate cancer?

Kols: It started with my PSA history. The first time I had it checked was in August of 2005, and the level was 2.1 [nanograms per milliliter, or ng/ml]. Then in 2007 it went up to 4.2, and in April 2009 it was 6.49. I also had microscopic amounts of blood in my urine, so my general practitioner recommended that I see a urologist. I had a biopsy at the urologist's office, and that's when we found the cancer.

Crawford: What sort of advice did you get?

Kols: Well, I was given three options: one would be to monitor the cancer with active surveillance, another was to have a radical prostatectomy, and the third option was radiation. Active surveillance didn't interest me because my PSA was changing so fast—I knew that I would always be wondering when the cancer was going to flare up. And the consequences of radical treatment worried me, especially radical prostatectomy and the possibility of erectile

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dysfunction. I kept thinking, "There has got to be a better option, something in between." And that's what brought me to you.

Crawford: We determined that the bleeding you had was from a superficial bladder tumor that we took care of. And there's been no problem with that.

Kols: Yes, that's right.

Q: Do you have a family history of prostate cancer, Brian?

Kols: Not that I'm aware of, no.

Q: Was your family involved in your decision to go with focal therapy?

Kols: Absolutely. My wife found Dr. Crawford on the Internet.

Q: What were your initial thoughts about focal therapy as opposed to the other options you were hearing about?

Kols: I was encouraged that it could have fewer side effects than radical treatment, and that we could always take the prostate out later if the cancer became more pervasive. The way I saw it, focal therapy kept my options open.

Crawford: Brian was eligible for active surveillance based on one biopsy containing Gleason 6 cancer. Then we performed a mapping biopsy that showed more extensive disease, including a bit of pattern 4 [which raised his overall Gleason score to 3+4, or Gleason 7].

Q: Dr. Crawford, how many places in the country have the same type of focal therapy program that you have? I know some centers no longer do mapping biopsies.

Crawford: No one does mapping biopsies to the extent that we do them. We mark the location of every snippet of tissue that we take so we know exactly where in the prostate it comes from. Then we use that information to generate a three-dimensional view of where the cancers are—allowing us to target tumors for treatment.

Q: Are the mapping biopsies all transperineal [taken through the skin between the scrotum and the anus], or do you do them transrectally [through the rectum] as well?

Crawford: We always do them transperineally, and so far haven't seen any infectious complications. However we do see infectious complications from the transrectal biopsies that are done in follow-up.

Q: What sort of antibiotic regimen do you use?

Crawford: We are seeing more serious antibiotic-resistant infections following transrectal prostate biopsies. So in the past 12 months we have intensified our antibiotic coverage to include drugs like Levaquin [levofloxacin], and we are also adding injections of gentamicin at the time of the biopsy.

Q: So, the mapping biopsy allows you to create a three-dimensional model of the prostate, so you can determine the actual volume of the cancer?

Crawford: That's right, and you can look at it from any angle you want.

Q: How do you select which tissues you're going to ablate?

Crawford: Well, we're still not able to identify the dominant cancer—what some people call the index lesion. So we treat all the cancer that we can see. The mapping biopsy gives us a precise reconstruction of where cancer is in the prostate, and we go after all of it.

Q: Is the procedure done under general, regional, or local anesthesia?

Crawford: We can do it either way, but we mostly do it under general anesthesia since we don't want our patients to move at all.

Q: What do you tell people to expect after the procedure?

Crawford: We tell them that in rare cases they might have some mild, reversible erectile dysfunction that generally lasts for a couple of months. Infections haven't been a problem. Some men have a bit of trouble urinating.

Q: How long after the mapping biopsy did you have your procedure, Brian?

Kols: The biopsy was on March 25, 2010, and then I had my targeted therapy a few months later, on July 8.

Crawford: How did your procedure go, and what were your thoughts when it was over?

Kols: It went well, and I was relieved that my nerves were never cut. However, I did have some discomfort from the catheter, which was in for three or four days.

Crawford: Which was easier, the mapping biopsy or the focal therapy? Or were they about the same?

Kols: About the same—I'd say the focal therapy was a little easier. I was able to go right back to work.

Q: What was the most difficult aspect of the procedure for you?

Kols: Just the catheter, that's all.

Crawford: And how long was the catheter kept in after the focal therapy, as opposed to the biopsy?

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Kols: Four days after the biopsy, and three days after the focal therapy. But it was easier the second time around, since I knew what to expect.

Q: Did you have any side effects?
Kols: No, not really. My potency was reduced a little bit for the first three months. But Dr. Crawford said it would return, and sure enough, it did—I'm now as good as ever. I don't need drugs to help with my erections, and I don't have any urinary or bowel problems.
Crawford: Tell us about the changes in your PSA since we performed the procedure back in 2010.
Kols: My PSA level fell substantially. When I last had it recorded, on Dec. 13, 2014, it was 0.43 ng/ml.

Q: How much of the prostate gland was actually treated?
Crawford: I would say we took about half. So it's certainly smaller, but not so small that the reduction in size would explain why Brian's PSA level has fallen so low.

Q: What about additional follow-up?
Crawford: Our current approach—and this is subject to change—is to biopsy every year for at least the first couple of years. If patients are still negative, then we go to every other year. Brian is still negative at five years, and now we're asking if we need to do another biopsy if his PSA stays low. But this is uncharted territory.

Q: Do you biopsy the lesions that were ablated, or do you do general biopsies?
Crawford: General biopsies, usually 12 cores.

Q: What do the ablated tissues look like under the microscope?
Crawford: A lot of it looks like normal prostate, although we do see some scar tissue and inflammation. It would be worrisome to see atypical small acinar proliferation [lesions that are suspicious for malignancy], but that hasn't happened with Brian—his biopsies have been fine, there's no cancer. But I tell my patients, "You know, you might need another treatment later." And I've had men fail targeted focal therapy so that I have to go back and do a radical prostatectomy on them. But that's less than 6% of the men I've treated with focal therapy so far. We're pretty particular about who gets it.

Q: And what's the technical difficulty of doing a radical prostatectomy after focal therapy?
Crawford: I've only had to do a few of these cases, and they haven't been hard.

Q: So, Brian, has the treatment met your expectations?
Kols: Oh, I'm very pleased—everything is normal. I should point out that I am on Proscar [finasteride, a 5-alpha-reductase inhibitor used for the treatment of benign prostatic hyperplasia (BPH)]. And there's some evidence that it can help to prevent low-grade cancer.
Crawford: BPH can elevate PSA, so we use finasteride to control for that. If PSA levels rise while a patient is on the drug, it's usually because something significant is happening with his cancer. Also, a Canadian study of men with low-grade prostate cancer showed a reduction in positive biopsies at two to four years among those taking dutasteride [Avodart, also a 5-alpha-reductase inhibitor] compared with placebo.

Q: Who is and who is not a candidate for focal therapy?
Crawford: Well, that starts with defining who is a candidate for mapping biopsies. And that would be someone with small volumes of cancer, usually Gleason 6 or maybe Gleason 3+4 in no more than 20% of cores. It's not for somebody who has 4+3 cancer all around his prostate or bilaterally in a pattern 4—we're talking about low-grade risk. Our intent with the mapping biopsy is to isolate these Gleason 6 and 3+4 cancers and to make sure that there's nothing else there. But we will treat a Gleason 8 cancer if it's located in a small area. So this is really precision medicine. I would say 40 out of 100 patients who walk through our doors with prostate cancer might be eligible for mapping biopsies.

Q: Do you have the manpower to do all this and to process the biopsies in a cost-effective way?
Crawford: You have to be creative in how you approach it, but yes, we do.

Q: Brian, any parting comments?
Kols: Well, I'm extremely grateful. I have a great quality of life, and I want other men facing a similar situation to know about my experience.