HIFU: Definitely ready for prime time

Jack Barkin, MD, FICS, FACS, DABU, MHM, CCPE, FRCS

Department of Surgery, University of Toronto, ON

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n 1970, brachytherapy for the management of localized prostate cancer began at Memorial Sloan Kettering. In 1991, Whitmore and colleagues studied the probability of metastatic disease in early stage carcinoma of the prostate in 679 patients treated with retropubic 1251 implants.¹ These patients were studied between 1970 and 1985 after being staged by pelvic lymph node dissection. The mean follow-up was 97 months. The actuarial distant metastases free-survival (DMFS) for patients at risk at 15 years after initial therapy was only 37%. Rather than abandoning brachytherapy because these results did not compare to radical prostatectomy rates, others decided to modify the approach and test whether transrectal brachytherapy would produce better results with less morbidity.

Ten years later, Nickel wrote an editorial in response to the study by Crook and colleagues on brachytherapy in Canada.² According to Nickel, the authors did not compare these brachytherapy data with results obtained with conventional radical prostatectomy or modern external beam radiotherapy. The morbidity associated with brachytherapy is "disturbing" and Crook and colleagues could not "recommend brachytherapy for patients with localized prostate cancer on a solid "evidence-based" basis."² Again, even with these significantly inferior results and high morbidity rates they did not abandon the procedure. In 2010, brachytherapy, with considerable modifications, was considered a gold-standard relatively non-invasive, effective and attractive treatment option for localized prostate cancer.

There are three accepted outcome measurements that represent the "trifecta" of successful prostate cancer treat-

ment, by any modality: rate of erectile dysfunction, incidence and degree of incontinence and biochemical cure/ survival rates.

Today, certainly in the United States, over 80% of the radical prostatectomies are being performed as robot-assisted laparoscopic radical prostatectomies (RALP). Recently, there was another report on the trifecta rates of RALP. In this report, Shikanov and colleagues published open radical prostatectomy trifecta rates of about 60% at 1 to 2 years, but highlights the fact that there is no standardized reporting schemes for these studies.³ Their results demonstrated the potential huge discrepancies created by non-objective reporting. The authors concluded that the trifecta outcome rates for RALP were comparable to open surgery, but outcome rates vary significantly depending on the tools used for continence and potency evaluation.

As there is no procedure that guarantees 100% cure and no optimal way to guarantee the highest quality of life for younger men with localized prostate cancer treated with surgery, brachytherapy or external beam radiation, I was compelled to explore options other than the standard ones.

In December 2004, I was first introduced to HIFU (highintensity focused ultrasound). In January 2006, HIFU was approved, but not insured, in Canada, to treat prostate cancer. In March 2006, I treated our first patient in Canada using the Sonoblate 500 machine. Since the initial treatment, we have treated over 500 patients and have exposed over 75 other urologists from all over Canada, USA and the world, to the HIFU procedure.

HIFU is a non-invasive acoustic ablation technique that uses intersecting, precision- focused ultrasound waves. It targets tissue and heats the target to 100°C with 3-second bursts of energy. HIFU destroys the targeted tissues at the focal intersection of the ultrasound waves. It also provides rapid heat dissipation to any of the non-treated tissue. There are 2 different machines available in Toronto, Ontario, Canada (Sonoblate and Ablatherm). There are differences in the machines and the technique of performing this 3 hour, out –patient, spinal anesthetic, non-invasive, prostate cancer treatment, which have been discussed elsewhere.⁴

The critically different treatment feature provided by the Sonoblate machine is that during treatment there are four images on the screen. There are 2 (transverse and sagital) real-time treatment images to compare to the 2 corresponding reference images. The Ablatherm machine only offers 2 images. The earlier reports on the HIFU treatments provided some very encouraging results. In the Ablatherm European MultiCenter Trial, 559 consecutive patients between 1995 and 1999 were studied with 4 successive prototypes. Of these, 402 patients had T1 and T2 primary, hormone naïve prostate cancer, with mean follow-up of 13 months. The negative biopsy rates were 92.1% in the low-risk, 86.4 % in the moderate risk, 82.1% high-risk groups. The PSA nadirs were 75% with nadir <0.4 (with complete treatment).⁵

The most experienced Sonoblate user is Uchida in Japan, who reported significant results. He used the machine on 63 patients with T1c and T2b lesions. The mean follow-up was 23 months (range: 3-63 months); all patients had biopsy at 6 months. The 3-year BDFS rate (ASTRO) in all patients was 75% after 3 years.⁶ The BDFS by PSA nadir: PSA<0.2: 100%, PSA 0.21 – 1.0: 74%, PSA >1: 21%. There was a negative biopsy rate in 87% of patients. Incontinence and erectile dysfunction rates were 1% and 25%, respectively.

The intent of HIFU is that it can provide cancer control rates (BDFS or negative biopsies) comparable to the other approaches, with lower rates of erectile dysfunction and incontinence, as an outpatient, non-invasive, low morbidity procedure. The patient can fly or go back to work the next day.

One of the most common criticisms concerning HIFU was that there was no significant long-term data to confirm its effectiveness. HIFU can be effective for post brachytherapy, cryotherapy, external beam radiation or HIFU failures and is showing between a 56-85% overall salvage rates, regardless of the failed primary treatment modality. The morbidity rates for either a second HIFU or post primary treatment failure HIFU are quite low.⁷

Presently, there are a primary Sonoblate trial (comparing to brachytherapy) and a radiation failure trial being performed in USA for the FDA. We have already treated our allotted number of biopsy proven radiation failure patients, that will each have a one year post-salvage HIFU biopsy. Chin recently reported significant salvage rates (68% negative biopsy) with low morbidity in his 40, non-trial radiationfailure patients.⁸

It has now been widely accepted that the Stuttgart definition (PSA nadir plus 1.2 ng/mL) of biochemical failure post primary HIFU treatment is the most indicative of impending treatment failure and should be reported.⁹

The report of our first 97 patients has recently been published.¹⁰ However, even in the past 24 months with the TCM (Tissue Change Monitoring) software modification our PSA nadir rates of 0-.2 ng/mL at 6 months are over 90%.

The longest Sonoblate results (657 patients from 1999-2008) of between 2 and 8 years, which includes the evolution through 4 different machines (S200, S500, V4-S500, S500-TCM) was published by Uchida recently.¹¹ His results include: stricture at 16.7%; incontinence grade I at 1.5%; epididymitis at 5.7%; and erectile dysfunction at (IIEF 5 < 7) at 22% at 2 years. The negative biopsy rate with a minimum follow-up of 2 years was 97% in sonoblate 200, 79% in S500, 94% in V4-S500 and 100% in S500-TCM group.

With the new software, suprapubic catheters and some other treatment-technique innovations, the Sonoblate reported stricture rate is less than 4%, e.d. rate is < 15% and incontinence rate <1%.¹¹

I believe that for patients with low-volume, low-intermediate risk localized prostate cancer and a desire to achieve a high "trifecta" result, HIFU should be considered a viable and effective option.

Competing interests: Dr. Jack Barkin is Director at Can-Am HIFU.

This paper has been peer-reviewed.

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Correspondence: Dr. Jack Barkin, 960 Lawrence Ave West, Suite 404, Toronto, ON M6A 3B5; j.barkin@rogers.com