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High-Intensity Focused Ultrasound for Localized Prostate Cancer: Ready for Prime Time?

Patrick J. Bastian

Department of Urology, Klinikum der Universität – Campus Großhadern, Ludwig-Maximilians-Universität München, Marchioninistr. 15, 81377 Munich, Germany

Since the introduction of prostate-specific antigen (PSA) testing, a well-recognized phenomenon of overdiagnosis and overtreatment of prostate cancer (PCa) has arisen [1]. In combination with improved imaging modalities, PCa is now detected at earlier stages [2]. Urologists have to base patient counseling on the current recommendations and guidelines to individualize treatment decisions as much as possible.

According to the current European Association of Urology guidelines, the treatment of low-risk, localized PCa consists of surgical removal of the prostate or radiation therapy [3]. To minimize the side effects of active treatment for low-risk PCa, numerous treatment modalities have been introduced. However, therapeutic options, such as cryosurgery or high-intensity focused ultrasound (HIFU), are considered experimental or investigational [3], and no study contains a long enough follow-up to assess the role of such treatments in the management in PCa. Another novel approach to reduce overtreatment of low-risk PCa is active surveillance, and large prospective trials in this area are currently ongoing [4].

In the study by Crouzet et al, 803 patients with PCa were treated using HIFU at six centers over a period of 17 yr [5]. Of that sample, 579 cases were treated at a single center, whereas three centers treated only 58 cases combined. Interestingly, only 40% of the cohort comprised low-risk PCa patients according to the d’Amico risk stratification; about 46% were intermediate-risk PCa patients, and 14% were high-risk patients. Furthermore, mean follow-up was only 42 mo—not very long for localized PCa—and median follow-up was never provided.

The results of overall and cancer-specific survival seem intriguing at first look. The control biopsy was negative in 85% of cases [5]. In contrast, a recent study by Biermann et al revealed that up to 44% still report a positive result for PCa in the control biopsy 6 mo after HIFU treatment [6]. Nevertheless, Crouzet et al report a clear difference in outcome among the different risk groups [5]. The conclusion in the paper is too strong and cannot be drawn from the data presented. The proposed equivalence of the oncologic effectiveness of HIFU compared with conformal external-beam radiation must withstand the test of a future prospective randomized trial.

Nevertheless, Crouzet et al have to be congratulated on starting a novel PCa treatment as early as 1993, when most urologists were still fascinated by the advances of surgical treatment for PCa [7]. During the first 7 yr of the study, a HIFU prototype was used, followed by two commercially available HIFU systems.

Several points in this paper [5] warrant further discussion. As previously mentioned, only one center has broad experience with the technique. It would be interesting to look at the individual results of each center. Furthermore, because treatment started in 1993, long-term data could be presented in a subanalysis. The HIFU inclusion criteria are very vague: Not all patients were candidates for radical surgery. This criterion is not very specific and is seriously affected by selection bias. Today it seems that HIFU is used more as a treatment for low-risk PCa than for advanced or high-grade PCa [8]. This factor has to be considered when offering HIFU to current PCa patients. In the search for optimal criteria for active surveillance, we have learned that strict inclusion criteria are very important to achieve the best possible outcome for patients [4].

Three different criteria were chosen to evaluate disease-free survival. Interestingly, the Stuttgart definition (PSA
The rates of incontinence and erectile dysfunction have to be functional outcome of patients. Besides oncologic outcome, bidities are potential candidates for HIFU. As reported, only PSA and biopsy Gleason score were independent predictors of disease progression. This finding underscores that only low-risk PCa patients with comorbidities are potential candidates for HIFU.

One major factor in the treatment of low-risk PCa is the functional outcome of patients. Besides oncologic outcome, the rates of incontinence and erectile dysfunction have to be considered; unfortunately, these data are not reported [5]. This aspect is important because the authors stress that repeated HIFU is possible. In a report by Blana et al, the incontinence rate was 13% and the erectile dysfunction rate was 55% [10]. Other complications such as bladder outlet obstruction, urethral stricture, and urethro-rectal fistula requiring surgical reintervention have to be assessed. HIFU is far from being a successful treatment without side effects. There is no doubt that we, as urologists, have to improve individual treatment planning for patients with low-risk PCa. However, because the diagnostic tools are far from perfect, one has to be careful about recommending treatment options that have not been studied thoroughly and tested against the recommended treatment options from our guidelines.

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References


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Sebastien Crouzet a,b,*, Albert Gelet a,b

a Department of Urology, Edouard Herriot Hospital, Lyon, France
b Therapeutic Ultrasound Research Laboratory, Inserm, U556, Lyon, France; Université de Lyon, Lyon, France

Bringing new treatment options into the urologic practice can be challenging. As discussed by Bastian in his editorial, urologists have to be careful about recommending new treatments [1]. Bastian raises several issues that need to be addressed. In our study, we presented the outcomes of high-intensity focused ultrasound (HIFU) for localized prostate cancer (PCa) from six urologic centers [2]. Despite the different number of patients treated in each center, the outcomes were quite similar. We compared the nadir prostate-specific antigen (PSA) after HIFU in each center and found no difference for four centers, with a mean nadir PSA ≤0.3 ng/ml in 52–59% of cases. In two centers the mean nadir PSA after treatment was ≤0.3 ng/ml in 26–31% of cases, with a significant difference compared to the other four centers.

Concerning the negative biopsy rate, the study of Biermann et al included only 25 patients over a 4-yr period (6 patients per year) and used a different device (Sonablate, Focus Surgery Inc, Indianapolis IN, USA) [3]. Those factors might explain the high positive control biopsy rate, which is far from our current practice. In a review paper of 37 articles/abstracts, Rebillard et al found a negative biopsy rate of 64–93% with the Ablatherm device.

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* Corresponding author. Urology and Transplantation Department, Edouard Herriot Hospital, 5 place d’Arsonval, 69437 Lyon Cedex 03, France. Tel. +33 4 722 110 583; Fax: +33 4 722 110 559. E-mail address: sebastien.crouzet@chu-lyon.fr (S. Crouzet).

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