

# The Oncological Outcome of HIFU for the Treatment of Localized Prostate Cancer

Francesco Ziglioli\* and Umberto Maestroni

*Department of Urology, University-Hospital of Parma, Parma, Italy*

**Abstract:** *Introduction:* Prostate cancer is considered one of the most important health problems. Due to the increased number of diagnosed patients and the inability to distinguish aggressive tumors, minimally-invasive procedures have become increasingly interesting. High-intensity focused ultrasound (HIFU) is an alternative option to radical surgery to treat prostate cancer. To date, however, no data are available on the efficacy of this technique in comparison to standard treatment.

*Methods and Results:* We reviewed the literature to concentrate on the oncological outcome of HIFU treatment of prostate cancer with the following key words: hifu, high intensity focused ultrasound, ultrasonic therapy, transrectal hifu, prostate ablation. MedLine and Embase via Ovid database were searched. Selection criteria were: English language, articles published between 2006 and 2013, case series including more than 150 participants and reported data on oncological outcome. Thirteen uncontrolled studies were identified. No randomized controlled trials (RCT) were found in the literature comparing HIFU to other routine approaches to prostate cancer treatment.

*Conclusion:* HIFU seems to be a promising minimally-invasive treatment for low- and intermediate-risk prostate cancer, especially for patients who are unfit for radical surgery. Prospective studies with longer follow-up periods and RCT are required to properly assess the benefits of HIFU and to compare this treatment with standard treatment.

**Keywords:** HIFU, high-intensity focused ultrasound, thermal ablation, prostate cancer, minimally-invasive procedures.

## INTRODUCTION

The advent of PSA testing more than two decades ago has improved early detection of prostate cancer, leading to more men being diagnosed and treated.

Interestingly, it is still controversial whether the increased detection and treatment of prostate cancer has led to increased overall survival rates. Data from two long-term screening studies were published in the last few years and reported conflicting results. The Prostate, Lung, Colorectal and Ovarian screening concluded that there is no difference between men who were screened and men who were not screened [1]. On the other hand, the European Randomized Study of Screening for Prostate Cancer found a 20% reduction in the mortality rate in screened men [2].

Moreover, we cannot distinguish between tumors that will progress and lead to mortality and tumors that will not cause complications and are clinically insignificant. For this reason, there has been recent interest in organ-sparing therapies able to control local cancer with low invasiveness and morbidity and low impact on the quality of life.

Over the last years, minimally invasive procedures have emerged as management techniques in-between

the surgical approach (Radical Prostatectomy) and watchful waiting. Different energy types and different methods of application have been developed to achieve the trifecta outcome (oncologic efficiency, continence and potency) [3], such as radiofrequency, cryotherapy, brachytherapy and high-intensity focused ultrasound (HIFU).

The aim of this review is to describe the principles of HIFU and to provide an overview of recent data on its efficacy and safety.

## MATERIALS AND METHODS

### Principles of HIFU

Lynn *et al.* proposed the focused ultrasound technique in 1942 [4,5], but it was firmly established in the 1950s, thanks to the work by Frank and William Fry, and initially used for ablating brain tissue [6,7]. One of the first investigators who conducted trials on this technique applied to human beings was S. Madersbacher [8].

The crucial impetus for the HIFU technique was the development of modern radiological imaging, such as diagnostic ultrasound (US) or magnetic resonance imaging (MRI), which allow non-invasive therapy guidance.

To date, only HIFU treatments of prostate cancer, uterine fibroids and, to some extent, the palliative

\*Address correspondence to this author at the Department of Urology, University-Hospital of Parma, Via Gramsci 14-43125 Parma, Italy; Tel: +39 0521 702182; Fax: +39 0521 702186; E-mail: ziglioli@hotmail.it

ablation of bone metastases have found clinical acceptance, while in other pathologies, such as tumors of breast, kidney or liver, the numbers of treated patients remain small.

HIFU uses high-power, highly-focused ultrasound beams that are targeted to converge on a specific point within the body. This technique is also referred to as ultrasonic ablation, sonablation or focal ultrasound surgery. The ultrasound beam causes vibration, thus creating heat [9]. An analogy has been made with focusing the sun's rays through a magnifying glass to start a fire [10].

The source of HIFU is a spherical piezoelectric transducer able to produce ultrasonic energy focused on a fixed point. The transducer has the property of changing its thickness in response to an applied voltage, thus creating an acoustic ultrasound wave with a frequency equal to that of the voltage applied. Frequencies used for HIFU therapy cover a 3-4 MHz range. Depending on the ultrasound frequency, site-intensity ranges between 1300 and 2200 W/cm<sup>3</sup> [11-13].

The thermal effect relies on the absorption of ultrasound energy by the tissue and its conversion into heat. A temperature of 75°C can be achieved with 1s treatment, well above the level to denature protein (41°C-43°C) and sufficient for coagulative necrosis [14].

The lesions produced by the HIFU technique are elliptical with a volume between 50-300 mm<sup>3</sup>. They have also been defined as "cigar-shaped" [15].

By combining single lesions, larger target volumes can be ablated without gaps. Between single shots, a pause time is needed in order to prevent tissue boiling and bubble formation, which might distort the US-targeted area.

Focused ultrasound allows a well-circumscribed lesion to be obtained in the focal point without damaging the intervening tissues. The tissue layers outside the ablated area remain unaffected. Since the sharpness of such induced tissue necrosis is comparable to a surgeon's sharp incision, the therapy has also been termed Focused Ultrasound Surgery (FUS) [16]. Therefore, this technique provides the advantage of a transrectal treatment with prostate destruction, minimizing the risk of rectal injury [17].

By increasing the intensity of the waves and focusing them on a single point, HIFU allows the

deposition of a large amount of energy into the targeted tissue, resulting in its destruction through cellular disruption and coagulative necrosis [18].

Two mechanisms of tissue damage are involved: thermal effect and cavitation [19].

The thermal effect is due to the conversion of ultrasound energy into heat. Tissue damage due to the thermal effect can be classified into three groups: hyperthermia that can destroy malignant cells with low temperatures (41-49 °C) during an extended period (>10 minutes); coagulation, consisting in necrosis of tumor tissue; and vaporization inducing tissue necrosis and charring (temperature >100°C) [20].

Cavitation is the result of the interaction of ultrasound and water microbubbles. This interaction leads to microbubbles vibration and their dissolution within prostate tissue. When the bubbles reach the size of resonance, they suddenly collapse and produce high-pressure shock waves, thus destroying adjacent tissue [21,22]. The dynamics of cavitation bubble clouds generated at the tissue boundary in continuous HIFU fields has been experimentally investigated by high-speed photography [23].

Two HIFU devices are currently available, the Ablatherm (EDAP TMS SA, Vaulx-en-Velin, France) and the Sonablate device (Focus Surgery Inc, Indianapolis, IN, USA), which have been in use since 1993 and 1995, respectively. The differences between Ablatherm and Sonablate mainly concern patient positioning, treatment algorithm, imaging and technical details.

### **The Ablation Procedure**

HIFU is performed through a computerized surgical device equipped with a treatment table, an ultrasound treatment system connected to an endorectal probe, a safety infrared ray detector, a refrigeration system keeping rectal mucosa below 14°C and a monitor to set and control the treatment procedure through echographic screening. The single piezoelectric crystal alternates between high-energy power for ablation and low-energy for ultrasound imaging [24].

The treatment is performed under spinal anaesthesia. The procedure can be personalized in order to obtain ideal treatment settings: ultrasound frequency, shot duration and waiting time between shots may be modified.

HIFU-induced lesions are visible using standard ultrasound as hyperechoic areas. To date, MRI is considered the gold standard for HIFU efficacy assessment as gadolinium enhanced T1-weighted images can clearly show the necrosis extent [25].

### Literature Search and Selection

We reviewed the literature to concentrate on the oncological outcome of HIFU treatment for prostate cancer with the following key words: HIFU, high intensity focused ultrasound, ultrasonic therapy, transrectal HIFU, prostate ablation. MedLine and Embase via Ovid database were searched. Selection criteria were: English language, articles published between 2006 and 2013, case series including more than 150 participants and reporting data on oncological outcome. Data about side effects and QoL after treatment were not evaluated in this study. All studies that did not meet the inclusion criteria were excluded.

Recent publications were preferred. Literature search was conducted on 4<sup>th</sup> October 2013.

### RESULTS

We identified 13 case series assessing HIFU as a primary or salvage therapy option in prostate cancer [26-38]. Studies characteristics are shown in Table 1. The number of patients included in the case series ranged from 163 to 1002, giving a total of 5285 patients; however it was not possible to determine how many patients underwent redo-HIFU. Also, some reports seemed to refer to the same group of patients, with different follow-up duration. Whenever possible, double citations were eliminated. Most patients underwent one treatment.

The mean patient age was 68.23 (SD  $\pm 2.37$ ), ranging from 62.7 to 72 yr. Gleason score ranged from

**Table 1: Case Series of HIFU for Prostate Cancer: Oncological Outcome**

Author Study period	No. Patients	Age	Mean follow-up (wks)	PSA (ng/mL)	PSA nadir (wk)	Failure criterion	nADT (n)	TUR-P pre HIFU (n)	DFSR
Ganzer [26] 1997-2009	538	67.7	Not reported	11.2	19.9	Phoenix ASTRO	196(36.4%)	416 (77.3%)	61 (10y)
Chaussy[27] N.R.	96+175 <sup>1</sup>	65.8	18.7-10.9 <sup>2</sup>	Not reported	15	Phoenix ASTRO	None	175 (64.6%)	Not reported
Thuroff [28] 1995-2009	704	68.4	Not reported	9.9	8	Phoenix ASTRO	61 (4.2%)	528 (75%)	99 (10y)
Pfeiffer [29] 2002-2006	191	69.7	52.8	7.2	9.5	Stuttgart	81 (42.4%)	92+2(49.2%) <sup>3</sup>	62.8 (5y)
Pinthus [28] 2005-2010	447	62.7	24	6.6	12	Stuttgart, Horwitz	None	Not reported	Not reported
Poissonier [31] 1996-2003	227	68.8	27.5	6.99	Not reported	biopsy, PSA >1 ng/mL	76 (33.4%)	175 (77%)	66 (5y)
Blana [32] 1994-2009	356	69.6	32	6.8	14.4	Phoenix ASTRO	None	205(57.6%)	54 (7y)
Crouzet [33] 1997-2009	1002	71	76	7.7	7.9	Phoenix ASTRO	392(39.1%)	939(93.7%)	97 (10y)
Uchida [34] 1999-2007	517	68	24	9.2	Not reported	Phoenix ASTRO	343(66.3%)	Not reported	72 (5y)
Sumitomo [35] 1999-2006	530	68	24	10.4	within 4 wks	Phoenix ASTRO	270(50.9%)	Not reported	64.7 (3y)
Mearini [36] 2004-2007	163	72	24	7.3	11	Phoenix ASTRO	None	Not reported	78.1
Ahmed [37] 2005-2007	172	64.1	11.5	8.3	Not reported	PSA $\leq 0.5$ ng/mL	50 (29%)	None	Not reported
Murat [38] 1995-2006	167	68	18	6.9	Not reported	Phoenix ASTRO	95 (56.9%)	not reported	53 (3y)

<sup>1</sup>96 patients did not undergo TUR-P. 175 patients underwent TUR-P.

<sup>2</sup>Follow-up data were collected separately for patients who underwent TUR-P and patients who did not undergo TUR-P.

<sup>3</sup>92 patients underwent TUR-P and 2 patients underwent adenectomy.

2 to 10, the vast majority of patients being  $\leq 7$ . In most series, the D'Amico risk classification was used, with a prevalence of patients in the low-risk group.

PSA before treatment ranged from 6.6 ng/mL to 11.2 ng/mL. Mean pre-treatment PSA was 8.54 ng/mL (SD  $\pm 1.57$  ng/mL).

Between 0% and 56.9% received neoadjuvant androgen deprivation therapy (nADT) and between 49.2% and 93.7% underwent TUR-P (Trans-Urethral Resection – Prostate) before or in combination with HIFU. In some series, data about pre-HIFU TUR-P were not reported. In one case [29], 2 patients underwent adenomectomy before HIFU.

The vast majority of the case series used Phoenix criteria to define failure and to assess the oncological outcome of the treatment. In one case, Stuttgart criterion was used [33] and in one case, failure was defined according with Stuttgart and Horwitz criteria [30]. In one case, we found that the criterion used to define oncological failure consisted in finding two PSA  $\geq 0.5$  ng/mL [37] and, in another case, PSA  $\geq 1$  ng/mL [30].

Mean follow-up time ranged from 10.9 to 76 weeks.

PSA nadir and PSA nadir time were reported in most studies. PSA nadir time ranged from 7.9 to 19.9 weeks.

Disease-free survival rate (DFSR) was reported in 10 out of the 13 identified series, while it was not well defined or not reported at all in 3 series. Except for two studies, DFSR was reported at  $\geq 5$  years. When patient stratification in risk groups was reported, the highest DFSR was found in the low-risk group.

Prostate biopsies were taken at 3 or 6 months after HIFU in the vast majority of cases.

## DISCUSSION

Depending on tumor stage and life expectancy, the European Association of Urology (EAU) and the American Association of Urology (AUA) recommend radical prostatectomy, external beam radiation therapy (EBRT) and active surveillance as standard treatment options for patients with localized prostate cancer [39].

HIFU has emerged as an alternative therapeutic option in patients with clinically localized prostate cancer, who are not suitable for Radical Prostatectomy

[40]. Although the medical associations of France, United Kingdom and Italy approve HIFU as primary and salvage treatment for prostate cancer, the AUA and the EAU do not recommend its routine use [41-43]. This is due to the overall lack of data about long term follow-up and HIFU comparison to conventional therapy options.

However, because biopsy strategies and imaging techniques can detect a higher number of tumors, there is growing interest in minimally invasive therapies, especially for patients who are unsuitable for major surgical procedures.

Despite the fact that HIFU technique has been used for many years, data reported in the literature are still controversial and evidence of its routine use is not available. Moreover, there are no randomized controlled trials comparing the HIFU technique to radical prostatectomy or other minimally invasive techniques for the treatment of prostate cancer.

Our literature search identified 13 valuable studies but there is no common agreement about the methodology to measure treatment effectiveness or failure. Actually, there is no common criterion to define failure. In the vast majority of studies, failure was assessed according to the ASTRO criteria [44]. However, these criteria have been validated in PSA failure after radiotherapy. Interestingly, the Stuttgart definition, a PSA increase of 1.2 ng/mL above the PSA nadir value [45] is used to assess failure in a minority of studies, although it has been validated specifically for HIFU. When the ASTRO criteria were not used, the HIFU treatment effectiveness was assessed using surrogate outcomes, such as biochemical-free survival rate or negative prostate biopsy. However, it remains questionable whether surrogate outcomes correlate with patient-relevant outcomes.

The technique efficacy seems encouraging in terms of disease-free survival rate and in terms of number of failures in the 5y, 7y and 10y follow-up periods. However, the PSA outcomes reported in the series varied significantly, making comparisons difficult. Almost all studies used D'Amico classification for risk stratification of patients [46], thus providing evidence that the probability of PSA rising is higher in the high-risk group. Crouzet *et al.* reported the clearest difference in outcomes among the different risk groups [33].

Regarding the association between nADT and oncological outcome of HIFU, all studies except

Sumitomo *et al.* [35] reported that the probability of PSA rising after HIFU treatment seems to be irrespective of whether nADT was administered.

Another point is redo-HIFU. Unfortunately, it is not possible to determine the number of patients who underwent retreatment. The reasons for repeating treatment were technical problems, large prostate and residual tumor or recurrence. Although the number of repeated HIFU certainly demonstrates the safety of the procedure, it also generates confusion when data of different studies are compared.

## CONCLUSIONS

High-intensity focused ultrasound is considered a promising minimally-invasive treatment for prostate cancer, especially in patients with low- and intermediate-risk disease. To date, the most proper indication to HIFU is for patients who are not fit for, or are unwilling to undergo, radical surgery.

Longer term follow-up is required, in a more systematic and prospective manner, as well as randomized controlled trials comparing HIFU to other therapeutic strategies, such as radical prostatectomy, external beam radiotherapy (EBRT) and active surveillance. Also, common agreement on the definitions of failure and positive outcome is of utmost importance.

## ACKNOWLEDGEMENTS

Many thanks to Mary for her precious support.

## REFERENCES

- [1] Andriole GL, Crawford ED, Grubb RL 3rd, Buys SS, Chia D, Church TL, *et al.* Mortality results from a randomized prostate cancer screening trial. *N Engl J Med* 2009; 360: 1310-9. <http://dx.doi.org/10.1056/NEJMoa0810696>
- [2] Schröder FH, Hugosson J, Roobol MJ, Tammela TL, Ciatto S, Nelen V, *et al.* Screening and prostate cancer mortality in a randomized European study. *N Engl J Med* 2009; 360: 1320-8. <http://dx.doi.org/10.1056/NEJMoa0810084>
- [3] Eastham JA, Scardino PT, Kattan MW. Predicting an optimal outcome after radical prostatectomy: the trifecta nomogram. *J Urol* 2008; 179: 2207-10. <http://dx.doi.org/10.1016/j.juro.2008.01.106>
- [4] Lynn JG, Zwerner RL, Chick AJ, Miller AE. A new method for the generation and use of focused ultrasound in experimental biology. *J Gen Physiol* 1942; 26: 179-93. <http://dx.doi.org/10.1085/jgp.26.2.179>
- [5] Lynn JG, Zwerner RL, Chick AJ. The biological application of focused ultrasound waves. *Science* 1942; 96: 119-20. <http://dx.doi.org/10.1126/science.96.2483.119>
- [6] Fry WJ, Barnard JW, Fry FJ, Krumins RF, Brennan JF. Ultrasonically produced localized selective lesions in the central nervous system. *Am J Phys Med* 1955; 34: 413-23.
- [7] Barnett SB, Ter Harr GR, Ziskin MC, Nyborg WL, Maeda K, Bang J. Current status of research on biophysical effect of ultrasound. *Ultrasound Med Biol* 1994; 20: 205-18. [http://dx.doi.org/10.1016/0301-5629\(94\)90060-4](http://dx.doi.org/10.1016/0301-5629(94)90060-4)
- [8] Madersbacher S, Pedevilla M, Vingers L, Susani M, Marberger M. Effect of high-intensity focused ultrasound on prostate cancer *in vivo*. *Cancer Res* 1995; 55: 3346-51.
- [9] Kennedy JR, Ter Haar GR, Cranston D. High intensity focused ultrasound: surgery of the future? *Br J Radiol* 2003; 76: 590-599. <http://dx.doi.org/10.1259/bjr/17150274>
- [10] Kim Y, Rhim H, Choi MJ, Lim HK, Choi D. High-intensity focused ultrasound therapy: an overview for radiologists. *Korean J Radiol* 2008; 9: 291-302. <http://dx.doi.org/10.3348/kjr.2008.9.4.291>
- [11] Foster RS, Bihlre R, Sanghvi NT, Fry FJ, Donohue JP. High-intensity focused ultrasound in the treatment of prostatic disease. *Eur Urol* 1993; 23 (S1): 29-33.
- [12] Ter Haar G, Coussios C. High-intensity focused ultrasound: physical principles and devices. *Int J Hyperthermia* 2007; 23: 89-104. <http://dx.doi.org/10.1080/02656730601186138>
- [13] Madersbacher S, Kratzik C, Marberger M. Prostatic tissue ablation by transrectal high intensity focused ultrasound: histological impact and clinical application. *Ultrasonic Sonochemistry* 1997; 4: 175-9. [http://dx.doi.org/10.1016/S1350-4177\(97\)00026-6](http://dx.doi.org/10.1016/S1350-4177(97)00026-6)
- [14] Vaezy S, Andrew M, Kaczkowski P, Krum L. Image-guided acoustic therapy. *Annu Rev Biomed Eng* 2001; 3: 375-90. <http://dx.doi.org/10.1146/annurev.bioeng.3.1.375>
- [15] Coleman JA, Scardino PT. Targeted prostate cancer ablation: energy options. *Curr Opin Urol* 2013; 23: 123-8. <http://dx.doi.org/10.1097/MOU.0b013e32835d9e94>
- [16] Wenne JW, Preusser T, Günther M. High-intensity focused ultrasound: Principles, therapy, guidance, simulations and applications. *Z Med Phys* 2012; 22: 311-22. <http://dx.doi.org/10.1016/j.zemedi.2012.07.001>
- [17] Crouzet S, Murat FJ, Pasticier G, Cassier P, Chapelon JY, Gelet A. High-intensity focused ultrasound (HIFU) for prostate cancer: current clinical status, outcome and future perspectives. *Int J Hyperthermia* 2010; 26: 796-803. <http://dx.doi.org/10.3109/02656736.2010.498803>
- [18] Beerlage HP, van Leenders GJ, Oosterhof GO, Witjes JA, Ruijter ET, van der Kaa CA, *et al.* High-intensity focused ultrasound (HIFU) followed after one to two weeks by radical retropubic prostatectomy. Results of a prospective study. *Prostate* 1999; 39: 41-6. [http://dx.doi.org/10.1002/\(SICI\)1097-0045\(19990401\)39:1<41::AID-PROS7>3.0.CO;2-5](http://dx.doi.org/10.1002/(SICI)1097-0045(19990401)39:1<41::AID-PROS7>3.0.CO;2-5)
- [19] Kennedy JE, Ter Haar GR, Cranston D. High intensity focused ultrasound: Surgery of the future? *Br J Radiol* 2003; 76: 590-9. <http://dx.doi.org/10.1259/bjr/17150274>
- [20] Bozzini G, Colin P, Nevoux P, Villers A, Mordon S, Betrouni N. Focal therapy of prostate cancer: energy and procedures. *Urol Oncol* 2013; 31: 155-167. <http://dx.doi.org/10.1016/j.urolonc.2012.05.011>
- [21] Susani M, Madersbacher S, Kratzik C, Vingers L, Margerger M. Morphology of tissue destruction induced by focused ultrasound. *Eur Urol* 1993; 23(Suppl. 1): 34-8.
- [22] Stride EP, Coussios CC. Cavitation and contrast: the use of bubbles in ultrasound images and therapy. *Proc Inst Mech Eng* 2010; 224: 171-91. <http://dx.doi.org/10.1243/09544119JEIM622>
- [23] Chen H, Li X, Wang S. High-speed observation of cavitation bubble clouds near a tissue boundary in high-intensity focused ultrasound fields. *Ultrasonics* 2009; 49: 289-92. <http://dx.doi.org/10.1016/j.ultras.2008.09.010>

- [24] Uchida T, Ohkusa H, Yamashita H, Shoji S, Nagata Y, Hyodo T, *et al.* Five years experience of transrectal high-intensity ultrasound using the Sonablate device in the treatment of localized prostate cancer. *Int J Urol* 2006; 13: 228-33. <http://dx.doi.org/10.1111/j.1442-2042.2006.01272.x>
- [25] Rouviere O, Lyonnet D, Raudrant A, Colin-Pangaud C, Chapelon JY, Bouvier R, *et al.* MRI appearance of prostate following transrectal HIFU ablation of localized cancer. *Eur Urol* 2001; 40: 265-74. <http://dx.doi.org/10.1159/000049786>
- [26] Ganzer R, Fritsche HM, Brandtner A, Bründl J, Coch D, Wieland WF, *et al.* Fourteen-year oncological and functional outcomes of high-intensity focused ultrasound in localized prostate cancer. *BJU Int* 2013; 112: 322-9. <http://dx.doi.org/10.1111/j.1464-410X.2012.11715.x>
- [27] Chaussy C, Thüroff S. The status of high-intensity focused ultrasound in the treatment of localized prostate cancer and the impact of a combined resection. *Curr Urol Rep* 2003; 4: 248-242. <http://dx.doi.org/10.1007/s11934-003-0077-0>
- [28] Thüroff S, Chaussy C. Evolution and outcomes of 3 MHz high intensity focused ultrasound therapy for localized prostate cancer during 15 years. *J Urol* 2013; 190: 702-10. <http://dx.doi.org/10.1016/j.juro.2013.02.010>
- [29] Pfeiffer D, Berger J, Gross AJ. Single application of high-intensity focused ultrasound as first line therapy for clinically localized prostate cancer: 5-year outcomes. *BJU Int* 2012; 110: 1702-7. <http://dx.doi.org/10.1111/j.1464-410X.2012.11375.x>
- [30] Pinthus JH, Farrokyar F, Hassouna MM, Woods E, Whelan K, Shayegan B, *et al.* Single-session primary high-intensity focused ultrasonography treatment for localized prostate cancer: biochemical outcomes using third generation-based technology. *BJU Int* 2012; 110: 1142-8. <http://dx.doi.org/10.1111/j.1464-410X.2012.10945.x>
- [31] Poissonier L, Chapelon JY, Rouvière O, Couvier L, Bouvier R, Martin X. Control of prostate cancer by transrectal HIFU in 227 patients. *Eur Urol* 2007; 51: 381-387. <http://dx.doi.org/10.1016/j.eururo.2006.04.012>
- [32] Blana A, Robertson CN, Brown SC, Chaussy C, Crouzet S, Gelet A, *et al.* Complete high-intensity focused ultrasound in prostate cancer: outcome from the @-registry. *Prostate Cancer Prostatic Dis* 2012; 15: 256-9. <http://dx.doi.org/10.1038/pcan.2012.10>
- [33] Crouzet S, Chapelon JY, Rouvière O, Mege-Lechevallier F, Colombel M, Tonoli-Catez H, *et al.* Whole-gland ablation of localized prostate cancer with high-intensity focused ultrasound: oncologic outcomes and morbidity in 1002 patients. *Eur Urol* 2013. Article in press. <http://dx.doi.org/10.1016/j.eururo.2013.04.039>
- [34] Uchida T, Shoji S, Nakano M, Hongo S, Masahiro N, Murota A, *et al.* Transrectal high-intensity focused ultrasound for the treatment of localized prostate cancer: eight-year experience. *Int J Urol* 2009; 16: 881-6. <http://dx.doi.org/10.1111/j.1442-2042.2009.02389.x>
- [35] Sumitomo M, Hayashi M, Watanabe T, Tsugawa M, Noma H, Yamaguchi A, *et al.* Efficacy of short-term androgen deprivation with high-intensity scuse ultrasound in the treatment of prostate cancer in Japan. *Urol* 2008; 72: 1335-40. <http://dx.doi.org/10.1016/j.urology.2007.12.041>
- [36] Mearini L, D'urso L, Collura D, Zucchi A, Costantini E, Formiconi A, *et al.* Visually directed transrectal High Intensity Focused Ultrasound for the treatment of prostate cancer: a preliminary report on the Italian experience. *J Urol* 2009; 181: 105-112. <http://dx.doi.org/10.1016/j.juro.2008.09.024>
- [37] Ahmed HU, Zacharakis E, Dudderidge T, Armitage JN, Scott R, Callear J, *et al.* High-intensity focused ultrasound in the treatment of primary prostate cancer: the first UK series. *Br J Cancer* 2009; 101: 19-26. <http://dx.doi.org/10.1038/sj.bjc.6605116>
- [38] Murat FJ, Poissonier L, Rabilloud M, Belot A, Bouvier R, Rouvière O, *et al.* Mid-term results demonstrate salvage high-intensity focused ultrasound (HIFU) as an effective and acceptably morbid salvage treatment option for locally radiorecurrent prostate cancer. *Eur Urol* 2009; 55: 640-649. <http://dx.doi.org/10.1016/j.eururo.2008.04.091>
- [39] Hedenreich A, Bellmunt J, Bolla M, Joniau S, Mason M, Matveev V, *et al.* EAU Guidelines on prostate cancer. Part 1: Screening, diagnosis and treatment of clinically localized disease. *Eur Urol* 2011; 59: 61-71. <http://dx.doi.org/10.1016/j.eururo.2010.10.039>
- [40] Warmuth M, Johansson T, Mad P. Systematic review of efficacy and safety of high intensity focused ultrasound for the primary and salvage treatment of prostate cancer. *Eur Urol* 2010; 58: 803-15. <http://dx.doi.org/10.1016/j.eururo.2010.09.009>
- [41] Rebillard X, Soulié M, Chartier-Kastler E, Davin JL, Mignard JP, Moreau JL, *et al.* High-intensity focused ultrasound in prostate cancer; a systematic literature review of the French Association of Urology. *BJU Int* 2008; 101: 1205-13. <http://dx.doi.org/10.1111/j.1464-410X.2008.07504.x>
- [42] British Uro-oncology Group, British Association of Urological Surgeons, Section of Oncology, British Prostate Group. MDT (multidisciplinary team) guidance for managing prostate cancer. Second edition. British Association of Urological Surgeons. Website <http://www.baus.org.uk/AboutBAUS/publications/mdt-prostate>.
- [43] Guidelines on prostate cancer: diagnosis, staging and therapy [in Italian]. Associazione Urologi Italiani (Association of Italian Urologists). Website <http://auro.it/index.php/documenti-iniziativa/linee-guida>.
- [44] Roach M 3<sup>rd</sup>, Hanks G, Thames H Jr, *et al.* Defining biochemical failure following radiotherapy with or without hormonal therapy in men with clinically localized prostate cancer: recommendations of the RTOG-ASTRO Phoenix Consensus Conference. *Int J Radiat Oncol Biol Phys* 2006; 65: 965-974. <http://dx.doi.org/10.1016/j.ijrobp.2006.04.029>
- [45] Blana A, Brown SC, Chaussy C, *et al.* High-intensity focused ultrasound for prostate cancer: comparative definition of biochemical failure. *BJU Int* 2009; 104: 1058-62. <http://dx.doi.org/10.1111/j.1464-410X.2009.08518.x>
- [46] D'Amico AV, Whittington R, Malkowicz SB, Shultz D, Blank K, Broderick GA, *et al.* Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. *JAMA* 1998; 280: 969-74. <http://dx.doi.org/10.1001/jama.280.11.969>

Received on 11-12-2013

Accepted on 03-02-2014

Published on 13-02-2014

DOI: <http://dx.doi.org/10.6000/1929-2279.2014.03.01.7>

© 2014 Ziglioli and Maestroni; Licensee Lifescience Global.

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.