Radiation treatment of prostate cancers – the contemporary role of modern brachytherapy techniques

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Life expectancy is rising and the population is ageing in most countries [1]. Prostate cancer (PCa) is the second commonest diagnosed malignancy and it is the fifth leading cause of cancer mortality in men, representing a public health burden worldwide. Furthermore, the majority of PCa (around 62%) is diagnosed in men over 65 years [2].

The use of the prostatic specific antigen (PSA) as a tool for monitoring PCa progression was approved in 1986 by the US Food and Drug Administration, and later, in 1994, its use was accepted also for PCa screening among men aged more than fifty years [3]. With the introduction of PSA testing, there have been a dramatic change in the stage of the disease at the time of diagnosis, with early stages being actually more predominant than advanced stages. Also, a trend in declining mortality due to PCa has been seem, and the major reasons for it may be the progression in the treatment option that include radical prostatectomy in its modalities, hormonal therapy, and a variety of new techniques of radiation therapy, besides the early detection [4].

A recent study comparing the incidence and treatment outcomes of PCa in countries with higher levels of human development and GDP (gross domestic product) per capita, has shown high variations geographically and over time, revealing a greater PCa incidence, but not accompanied by a greater mortality rate due to the disease. A substantial reduction in mortality rates was reported in most countries, except in some Asian countries and Eastern Europe, where mortality increased [5]. Possible explanations for this could be the early diagnosis and easier access to new treatment modalities. Differences in records of incidence and mortality can also be a confounding factor.

Several studies have already provided evidence for the efficacy of dose-escalation on biochemical control (BC) of PCa. Mature results from randomized trials have shown a direct relation between increasing the radiation dose given to the prostate and/or seminal vesicles and BC; however, randomized data comparing different methods of dose escalation are sparse [6,7,8,9].

Traditionally, brachytherapy for the treatment of PCa has been performed using low-dose-rate (LDR) as an effective single modality treatment for low- and intermediate-risk disease, or as a boost to external beam radiation (EBRT) for intermediate and high-risk localized tumors, with excellent results reported by both single and multi-institutional studies [10].

Results of randomized trial ASCENDE-RT that was recently published, compared two methods of dose escalation for the treatment of intermediate- and high-risk PCa. Patients had EBRT – pelvic (46 Gy) followed by a boost with EBRT (78 Gy) or LDR, plus 12 months of androgen deprivation therapy in both arms. As a result, the LDR boost arm doubled the rate of BC, but no significant OS difference was observed between arms [11].

On the other hand, high-dose-rate brachytherapy (HDR) is less frequently used, and most often suggested to boost EBRT. This combination of HDR with EBRT has some advantages and, most of all, the reduction of overall treatment time and increased capability of work load of the linear accelerators, which are of special interest in developing countries, where waiting lists and lack of radiation oncology facilities are a reality. Furthermore, in locally advanced PCa, HDR is able to encompass at least two proximal thirds of the seminal vesicles, whenever necessary, with no risk of seeds discharge after the procedure. High-dose-rate has also a possibility of biological advantage through the delivery of higher doses per fraction, potentializing the biological effective dose given to the prostate, with excellent long terms results regarding BC [12], and low acute and late toxicity [13]. One prospective randomized trial with up to 10 years of follow-up has proved that HDR plus EBRT is more efficient than EBRT alone in terms of BC with less acute rectal toxicity and improved quality of life [14].

The use of HDR as a boost to EBRT and its indication as a sole treatment modality (even with a single dose) has already been reported as favorable by several institutions, but with short-term clinical outcomes [15,16]. The results of HDR use as monotherapy for early stage low-risk PCa are still missing in the literature, and furthermore, the outcomes from developing countries are practically inexistent, where the technique could be promising as HDR units are relative frequent, due the high incidence of cervix cancer.

Salvage therapy is another indication for prostate brachytherapy, using LDR or HDR, with promising results in

terms of efficiency and relative low cost when compared to other techniques [17,18].

In conclusion, PCa incidence is expected to increase in the near future, straining limited healthcare resources. Despite the fact that comparisons between published series are difficult due differences in the techniques and planning, an appropriate allocation of resources for cancer prevention, early diagnosis, and curative treatments is required worldwide, especially in developing countries.

References

1. http://hdr.undp.org/en/2015-report%20
2. Global Burden of Disease Cancer Collaboration, Fitzmaurice C, Allen C, Barber RM et al. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 32 Cancer Groups, 1990 to 2015: A Systematic Analysis for the Global Burden of Disease Study. *JAMA Oncol* 2017; 3: 524-548.
3. Hankey BF, Feuer EJ, Clegg LX et al. Cancer surveillance series: interpreting trends in prostate cancer – part I: Evidence of the effects of screening in recent prostate cancer incidence, mortality, and survival rates. *J Natl Cancer Inst* 1999; 91: 1017-1024.
4. Fontes F, Severo M, Castro C et al. Model-based patterns in prostate cancer mortality worldwide. *Br J Cancer* 2013; 108: 2354-2366.
5. Wong MC, Goggins WB, Wang HH et al. Global Incidence and Mortality for Prostate Cancer: Analysis of Temporal Patterns and Trends in 36 Countries. *Eur Urol* 2016; 70: 862-874.
6. Al-Mamgani A, van Putten WL, Heemsbergen WD, et al. Update of Dutch multicenter dose-escalation trial of radiotherapy for localized prostate cancer. *Int J Radiat Oncol Biol Phys* 2008; 72: 980-988.
7. Dearnaley DP, Sydes MR, Graham JD et al.; RT01 collaborators. Escalated-dose versus standard-dose conformal radiotherapy in prostate cancer: first results from the MRC RT01 randomised controlled trial. *Lancet Oncol* 2007; 8: 475-487.
8. Kuban DA, Tucker SL, Dong L et al. Long-term results of the M. D. Anderson randomized dose-escalation trial for prostate cancer. *Int J Radiat Oncol Biol Phys* 2008; 70: 67-74.
9. Zietman AL, DeSilvio ML, Slater JD et al. Comparison of conventional-dose vs high-dose conformal radiation therapy in clinically localized adenocarcinoma of the prostate: a randomized controlled trial. *JAMA* 2005; 294: 1233-1239.
10. Grimm P, Billiet I, Bostwick D et al. Comparative analysis of prostate-specific antigen free survival outcomes for patients with low, intermediate and high risk prostate cancer treatment by radical therapy. Results from the Prostate Cancer Results Study Group. *BJU Int* 2012; 109 Suppl 1: 22-29.
11. Rodda S, Tyldesley S, Morris WJ et al. ASCENDE-RT: An Analysis of Treatment-Related Morbidity for a Randomized Trial Comparing a Low-Dose-Rate Brachytherapy Boost with a Dose-Escalated External Beam Boost for High- and Intermediate-Risk Prostate Cancer. *Int J Radiat Oncol Biol Phys* 2017; 98: 286-295.
12. Pellizzon ACA, Silva DA, Fogaroli RC et al. Long Term Results of High Dose Rate Brachytherapy and External Beam Radiotherapy for Local and Locally Advanced Prostate Cancer. *Cancer Stud Ther J* 2017; 2: 1-10.
13. Pellizzon AC, Salvajoli JV, Maia MA et al. Late urinary morbidity with high dose prostate brachytherapy as a boost to conventional external beam radiation therapy for local and locally advanced prostate cancer. *J Urol* 2004; 171: 1105-1108.
14. Hoskin PJ, Rojas AM, Bownes PJ et al. Randomized trial of external beam radiotherapy alone or combined with high-dose-rate brachytherapy boost for localized prostate cancer. *Radiother Oncol* 2012; 103: 217-222.
15. Prada PJ, Jimenez I, González-Suarez H et al. High-dose-rate interstitial brachytherapy as monotherapy in one fraction and transperineal hyaluronic acid injection into the perirectal fat for the treatment of favorable stage prostate cancer: treatment description and preliminary results. *Brachytherapy* 2012; 11: 105-110.
16. Hoskin P, Rojas A, Ostler P et al. High-dose-rate brachytherapy alone given as two or one fraction to patients for locally advanced prostate cancer: acute toxicity. *Radiother Oncol* 2014; 110: 268-271.
17. Gawkowska-Suwinska M, Fijałkowski M, Białas B et al. Salvage brachytherapy for local recurrences of prostate cancer treated previously with radiotherapy. *J Contemp Brachytherapy* 2009; 1: 211-215.
18. Peters M, Piena MA, Steuten LM et al. Comparative cost-effectiveness of focal and total salvage 125I brachytherapy for recurrent prostate cancer after primary radiotherapy. *J Contemp Brachytherapy* 2016; 8: 484-491.