Published in final edited form as:

Pract Radiat Oncol. 2018 ; 8(3): e159–e165. doi:10.1016/j.prro.2017.10.004.

Use of 5-alpha-reductase inhibitors as alternatives to luteinizing-hormone releasing hormone (LHRH) analogues or anti-androgens for prostate downsizing prior to brachytherapy

Hee Joon Bae, BS¹, Omar Mian, MD, PhD², Dhananjay Vaidya, PhD³, Theodore L. DeWeese, MD¹, and Daniel Y. Song, MD¹

¹Department of Radiation Oncology and Molecular Radiation Sciences, Johns Hopkins University, Baltimore, MD, USA

²Department of Translational Hematology and Oncology Research, Cleveland Clinic, Cleveland, OH, USA

³Department of Oncology - Biostatistics and Bioinformatics Division, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Abstract

Introduction—Prostate hypertrophy, median lobe hypertrophy (MLH) and pubic arch interference (PAI) are relative contraindications to brachytherapy due to potential morbidity and technical considerations. GnRH analogues or non-steroidal anti-androgens are currently utilized to achieve prostatic downsizing prior to brachytherapy. However, such agents have been associated with effects on body habitus, metabolism, and quality of life. In contrast, 5-alpha reductase inhibitors (5-ARI) are far less frequently associated with these morbidities.

Materials and Methods—Patients with large gland size, MLH or PAI were offered 5-ARI therapy. Repeat TRUS was performed at 3–4 months, followed by brachytherapy if resolution achieved. If downsizing was inadequate, then patients were offered continuation of 5-ARI for additional 3 months, or GnRH agonist or antiandrogen therapy, or other curative treatment.

Results—Of 59 patients with follow-up available, 42 (71%) were deemed to have adequate downsizing; 37 (63%) after 3–4 months of 5-ARI, and 5 (8%) after 7–8 months. Seventeen patients (29%) received other treatments due to inadequate effect. Median volume reduction was 20%.

Of 41 patients undergoing brachytherapy, 4 (9.7%) required temporary catheterization due to obstruction. Median follow-up after implantation was 25 months (1–64 months). Median time for

Corresponding author: Daniel Y. Song, MD, Johns Hopkins University School of Medicine, Department of Radiation Oncology and Molecular Radiation Sciences, 401 North Broadway, Suite 1440, Baltimore, MD 21287-5678, Phone: 410-955-6980, dsong2@jhmi.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflicts of interest: None

return to IPSS 5 of baseline score was 7 months (IQR 6–13 months). All but 1 patient who received brachytherapy remain biochemically controlled.

Discussion—5-ARI monotherapy is an alternative for downsizing in patients with hypertrophy or PAI, with over 70% achieving adequate downsizing without use of GnRH analogues or antiandrogens. Patients who received brachytherapy experienced typical rates of post-implant urinary morbidity.

Keywords

prostate; brachytherapy; downsizing; androgen suppression; alpha-reductase

Introduction

Prostate brachytherapy is a well-accepted and highly effective treatment for localized prostate cancer. However, not all patients are suitable candidates for brachytherapy due to the presence of anatomic features which are considered to be contraindications for brachytherapy, due to either increased risk for post-implant toxicity and urinary retention or because they present technical challenges for the procedure (1). These anatomic considerations are related to the presence of benign prostatic hypertrophy and increased gland size. Another relative contraindication is pubic arch interference, which causes difficulty with needle/source access to the anterior gland. While the definition of what constitutes an unacceptably large prostate volume varies, it is often considered that a prostate volume larger than approximately 50–60 cc is not optimal for brachytherapy (2). Even if a patient meets the prostate volume limit and does not have pubic arch interference, the presence of median lobe hypertrophy (MLH) has also been correlated with diminished quality of life post-procedure with increased urinary toxicity (3), and, therefore, is also considered a relative contraindication to treatment (4).

In order to allow for brachytherapy in patients who harbor such features, varying regimens which utilize hormonal manipulation to reduce the size of the prostate and/or MLH have been introduced. Two regimens which are commonly utilized include luteinizing hormone-releasing hormone (LHRH) agonist monotherapy (5), or a combination of a non-steroidal anti-androgen and a 5-alpha reductase inhibitor (5-ARI) (6). Petit et al. also described a regimen of non-steroidal anti-androgen (bicalutamide) alone for prostate downsizing prior to brachytherapy (7). Despite their effectiveness, there are documented negative effects associated with both classes of agents, and it has been shown that patients prefer to avoid these therapies if possible (8).

Although 5-ARIs also have known effects on reducing the size of the prostate, they have not been specifically studied with respect to use as a downsizing method prior to prostate brachytherapy. Studies comparing their utility vs LHRH agonists in terms of reducing urinary obstructive symptoms have suggested similar efficacy, while also showing fewer side-effects with respect to weight gain and erectile dysfunction (9). We evaluated a cohort of patients who were treated prior to brachytherapy using only 5-ARI (without LHRH agonists or anti-androgens) and report on the effectiveness of this approach on prostate downsizing and post-implant outcomes.

Materials and Methods

An IRB-approved database was utilized to identify any patient who had received 5-ARI immediately prior to planned brachytherapy due to large prostate volume, presence of median lobe hypertrophy, or pubic arch interference visualized on transrectal ultrasound (TRUS). Patients with severe pre-existing obstructive urinary symptoms were not considered suitable for 5-ARI therapy. All patients initially underwent baseline TRUS volume study; if one of the 3 criteria were identified, then they were offered the choices of 3 months of androgen deprivation (ADT) via LHRH agonist, androgen blockade with bicalutamide, or 5-ARI for 3–4 months, with discussion of the potential side effect profiles of each regimen. Large prostate volume was defined as >45cc on TRUS; we utilized 45cc as a cutoff rather than 50cc due to our experience of potential slight underestimation of volume on clinical TRUS vs intraoperative TRUS. All but 1 patient with 45–50cc volume also had another indication for downsizing. Patients were also advised that 5-ARI therapy would potentially achieve less reliable downsizing compared to LHRH agonist or bicalutamide. 5-ARI consisted of finasteride 5mg daily or 0.5 dutasteride daily, whichever was preferred within patient's insurance plan. In most instances, repeat TRUS was performed after 3–4 months; if adequate downsizing was achieved then the patient proceeded to brachytherapy. Some patients (n=4) with only one indication for downsizing did not have repeat TRUS prior to brachytherapy. Otherwise, patients were offered the possibility of continuing on 5-ARI for another 3–4 months, switching to LHRH agonist, or changing to another treatment modality altogether. Patients who continued to remain unsuitable following 7–8 months of 5-ARI were offered LHRH agonist or another treatment modality. For patients who underwent brachytherapy, 5-ARI treatment was discontinued the day prior to patient's brachytherapy procedure.

As part of routine clinical care, patients completed standardized International Prostate Symptom Score (IPSS, also known as AUA score) regarding urinary symptoms at time of initial consultation visit as well as at follow-up visits after brachytherapy. Prostate volumes were measured at baseline and following 5-ARI treatment using transrectal ultrasound, contoured on Variseed 9.0® (Varian, Palo Alto, CA). Presence of median lobe hypertrophy was determined by visual identification on axial and/or sagittal TRUS images (see example, Fig. 1); pubic arch interference was defined using previously described method on TRUS images (10). Patients were seen in follow-up visits at 1-month post-implantation and then every 6 months until 24 months, at which point they were seen every 12 months; PSA levels were obtained every 6 months continuously.

Results

Sixty-one patients seen for consideration of brachytherapy between November 2004 and June 2016 were identified who had been offered 5-ARI for prostate hypertrophy, MLH and/or PAI after undergoing TRUS volume study. One patient chose to receive ADT in order to ensure that his brachytherapy could be performed within a defined timeframe because of personal issues. None had history of prior use of 5-ARI or androgen deprivation. All 60 remaining patients presented with these options elected to take 5-ARI. Patients had either low- or intermediate-risk cancers; patient characteristics are shown in Table 1.

Figure 2 shows the pathways for evaluation and treatment outcomes for the group. One patient was started on finasteride but was subsequently diagnosed with pancreatic cancer and lost to follow up. Of the remaining 59 patients, 1 patient decided to not receive any treatment despite being deemed adequately downsized following 8 months of finasteride. Figure 1 shows an example of patient with MLH on TRUS before and after 5-ARI treatment.

Overall, 42 of the remaining 59 patients (71.1%) were deemed to have adequate downsizing, with 37 (62.7%) adequately downsized after 3–4 months of 5-ARI, and 5 (8.5%) after 7–8 months of 5-ARI. Seventeen patients (28.8%) received other treatments due to inadequate downsizing effect from 5-ARI.

Effects of 5-ARI on prostate volume by duration of treatment and stratified by indication are summarized in Table 2. No patient with baseline volume >60cc (n=3) was able to achieve downsizing adequate to receive brachytherapy. Outcomes by indication (MLH, PAI, or volume) are shown in Table 3.

All patients were treated with Pd-103 brachytherapy to a dose of 125 Gy, with the exception of 4 patients who received 90 Gy followed by external beam radiation. Of the 41 patients undergoing brachytherapy, 4 patients (9.7%) required 1–3 weeks of post-implant catheterization due to temporary obstructive uropathy. Patients were seen in follow-up at 1-month post-implantation and then approximately every 6 months thereafter. Median follow-up after implantation was 25 months (range 1–64 months). With regard to patient-reported urinary function (IPSS), median time to return to IPSS score of within 5 of baseline score was 7 months (IQR 6–13, range 3–45 months). Three patients remained with IPSS >5 compared to baseline at last follow-up 6 months, at 11, 24, and 37 months, respectively. With the exception of one patient who developed biochemical failure (Phoenix definition) at 6 months post-implantation, all patients who received brachytherapy remain biochemically controlled at last follow-up, with all having stable or declining PSA values at last follow-up. No patient has required urologic or surgical intervention for urinary outflow tract issues.

Discussion

The presence of an enlarged prostate gland has long been recognized as a contributor to increased risk of post-implant morbidity, such that it is currently well accepted as a contraindication (4). Although Wallner et al initially reported that patients with median lobe hypertrophy did not experience worse outcomes than patients without MLH (11), in a follow-up paper evaluating a larger cohort they found that MLH was associated with significantly higher AUA scores at last follow-up compared to a control cohort of patients (3), and MLH is also considered a relative contraindication to brachytherapy (4). Pubic arch interference is also a well-recognized barrier to implantation. Although the use of extended lithotomy position can be helpful, it does not eliminate the concern for obstruction of anteriorly placed needles.

A recent systematic literature review by a task group of the American Brachytherapy Society found no demonstrated benefit from adding ADT to brachytherapy for patients with low- and favorable intermediate-risk prostate cancers (12). Therefore, the apparent utility of ADT

for such patients is limited to remediation of the technical conditions noted above. To date, all medication regimens reported in the literature for downsizing patients' prostate glands prior to brachytherapy include either LHRH agonists or non-steroidal anti-androgens, or combinations thereof. Unfortunately, side effects of LHRH agonists have been well-documented to include hot flashes, decreased libido and sexual function, weight gain, fatigue, anemia, decreased muscle mass, metabolic syndrome, and increased risk of diabetes mellitus (13,14). A meta-analysis of observational data has shown a consistent positive association between ADT and risk of cardiovascular disease (15). Furthermore, even short-term ADT prior to brachytherapy has been associated with increases in risk of overall mortality amongst prostate cancer patients. In an analysis of >11,000 men treated with brachytherapy with or without neoadjuvant ADT, Nanda et al. found that ADT was associated with a significantly increased risk of all-cause mortality in men with low-risk prostate cancer who had at least a single risk factor for coronary artery disease (16). Given the lack of proven benefit on disease control of ADT for low- and favorable intermediate-risk prostate cancers, combined with the negative effects on overall health, alternatives to currently utilized ADT regimens for patients who need reduction in gland size are needed.

Anti-androgens have been described as such a potential alternative to LHRH agonists. Petit et al. described their experience using bicalutamide (50mg/day) in 25 patients prior to brachytherapy, with a median reduction in volume of 26%; this was not statistically different from the 32% reduction observed in a comparison cohort of 56 patients receiving LHRH agonist. Decreased libido and erectile function were observed in 44% and 20% of bicalutamide-treated patients, respectively. Nine patients (36%) reported breast tenderness with bicalutamide (7). Although most detailed reports of gynecomastia associated with anti-androgen therapy have been based on high-dose (150mg/day) bicalutamide with a rate of ~70% reported at such doses (17), lower doses of bicalutamide have also been associated with gynecomastia. Specifically, Zanardi reported 42% of men developed gynecomastia on a relatively low-dose 100mg/week regimen of bicalutamide (18). Gaudet et al. reported a randomized trial comparing the combination of bicalutamide + dutasteride + tamoxifen vs LHRH agonist + bicalutamide in 60 patients. Relative reductions in prostate volume from baseline were 35.5% vs 31.7%, respectively, with the bicalutamide + dutasteride + tamoxifen group being non-inferior in effect. Presumably due to use of tamoxifen, rates of gynecomastia in the bicalutamide + dutasteride + tamoxifen group were lower than other reports with bicalutamide, at 19.4% pre-implant and declining to 7–8% by 1–6 months post-implant (19).

To our knowledge, ours is the first report of 5-ARI monotherapy for this purpose. 5-ARIs have been previously shown in randomized trials to reduce both total prostate volume as well as volume of the transition zone, with mean 19–26% reduction in prostate volume reported following 1–2 years of treatment (20). Our experience suggests that much of the volume reduction is achieved within the initial few months, with declining response thereafter. The median reduction observed in our study was 20%, similar to prior studies utilizing longer durations, but we cannot exclude that more protracted 5-ARI treatment may have achieved a slightly higher rate of patients being able to receive brachytherapy. However, we did not deem more prolonged deferral of definitive therapy justifiable, although our observed rates of biochemical control do not suggest any detrimental effect of

the modest delay in treatment while undergoing 5-ARI therapy. Indeed, 5-ARIs actually result in declines in PSA values and have also been shown to inhibit growth of low-grade prostate cancers (21). We utilized a lower and more stringent cutoff value for prostate size than most, and therefore some patients who we treated with 5-ARI would not have been considered in need of downsizing at other centers, e.g. those with volumes 45–50cc or 45–60cc. However, we do not have reason to believe this affected the observations made, nor our conclusion that 5-ARIs can be effective for prostatic size reduction as demonstrated herein.

Although we did not directly measure side effects of 5-ARIs, the side effect profile of these agents is well described and well-documented in large prospective trials and are favorable when compared to those of LHRH agonists or anti-androgens. In the Proscar Long-Term Efficacy and Safety Study, patients were administered either finasteride (5mg daily) or placebo and observed for 4 years. Differences in patient-reported sexual dysfunction were only significant during the first year (15% vs 7%), with no differences between the 2nd and 4th years (7% in both groups). Only 4% of patients treated with finasteride and 2% with placebo interrupted the study due to sexual adverse events (22). Furthermore, a blinded study by Mondaini et al strongly suggests that perceived sexual side effects related to 5-ARIs have more to do with patients' expectations (i.e. a 'nocebo' effect) than the medication itself (23). The North American Finasteride Trial found side effects of finasteride to occur at very low rates, with decreased libido (3.4%), ejaculatory disorder (2.7%), and erectile dysfunction (1.7%) being the most common and no difference in rates of subjects withdrawing due to adverse effects compared to the placebo arm. In addition, finasteride has not been found to decrease bone mineral density, and has a slightly favorable effect on body mass index (0.6 – 0.8 kg/m² reduction) (24).

Of the two currently available 5-ARIs, most patients within our cohort took finasteride, as the side effect profile is more robustly studied, as well as the fact that insurance coverage/preferred tier status and cost were also considerations. However, there is evidence that dutasteride may provide greater suppression of intraprostatic dihydrotestosterone (DHT) than does finasteride (94–97% vs. 68–85% reduction), likely due to its inhibition of both isoforms of DHT (type 1 and 2), whereas finasteride inhibits only isoform type 2 (25). Hence our results may have differed had a greater proportion taken dutasteride.

The majority of the existing literature on adverse effects of ADT is from patients receiving LHRH agonists. Degarelix is an LHRH antagonist which is also utilized in the treatment of prostate cancer, and some limited pre-clinical mouse data suggest potentially differing effects on atherosclerotic plaques compared to LHRH agonist (26). However, a randomized Phase III trial comparing the two classes of agents demonstrated similar acute clinical side effects, including cardiovascular effects such as cardiac failure and myocardial ischemia (27).

Our results suggest the 5-ARI monotherapy does not replace anti-androgens or LHRH analogues but provides a comparatively less morbid alternative for prostatic volume reduction. Although the percentage volume reduction observed is smaller than that seen with LHRH agonists, clinicians may consider it as another option, particularly for patients who

do not require a large degree of downsizing and wish to avoid the side effects associated with anti-androgens or LHRH analogues. Also, our findings may have broader relevance than for brachytherapy alone. Prostate size is a contributor to urinary outcomes after external beam radiotherapy as well, and therefore shrinkage of the prostate is helpful for men treated with these modalities also. The findings from this paper provide useful quantification of the expected degree of downsizing prior to any modality of treatment.

Acknowledgments

This work was supported by the National Center for Advancing Translational Sciences (grant UL1 TR001079), and the generosity of the Pembroke France and John Noble Oncology Research Fund.

References

1. Gelblum DY, Potters L, Ashley R, Waldbaum R, Wang XH, Leibel S. Urinary morbidity following ultrasound-guided transperineal prostate seed implantation. *Int J Radiat Oncol Biol Phys*. 1999; 45(1):59–67. [PubMed: 10477007]
2. Hinnen KA, Battermann JJ, van Roermund JGH, Moerland MA, Jurgenliemk-Schulz IM, Frank SJ, et al. Long-Term Biochemical and Survival Outcome of 921 Patients Treated With 1–125 Permanent Prostate Brachytherapy. *Int J Radiat Oncol* [Internet]. 2010 Apr; 76(5):1433–8. [cited 2017 Sep 12]. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S0360301609005161>.
3. Nguyen J, Wallner K, Han B, Sutlief S. Urinary morbidity in brachytherapy patients with median lobe hyperplasia. *Brachytherapy*. 2002; 1(1):42–7. [PubMed: 15062186]
4. Davis, BJ., Horwitz, EM., Lee, WR., Crook, JM., Stock, RG., Merrick, GS., et al. Brachytherapy [Internet]. Vol. 11. Elsevier Inc; 2012. American Brachytherapy Society consensus guidelines for transrectal ultrasound-guided permanent prostate brachytherapy; p. 6-19. Available from: <http://dx.doi.org/10.1016/j.brachy.2011.07.005>
5. Kucway R, Vicini F, Huang R, Stromberg J, Gonzalez J, Martinez A. Prostate volume reduction with androgen deprivation therapy before interstitial brachytherapy. *J Urol*. 2002; 167(6):2443–7. [PubMed: 11992054]
6. Merrick GS, Butler WM, Wallner KE, Galbreath RW, Allen ZA, Kurko B. Efficacy of neoadjuvant bicalutamide and dutasteride as a cytoreductive regimen before prostate brachytherapy. *Urology*. 2006; 68(1):116–20. [PubMed: 16844453]
7. Petit JH, Gluck C, Kiger WS, Henry DL, Karasiewicz C, Talcott J, et al. Bicalutamide alone prior to brachytherapy achieves cytoreduction that is similar to luteinizing hormone-releasing hormone analogues with less patient-reported morbidity. *Urol Oncol Semin Orig Investig*. 2008; 26(4):372–7.
8. Allan CA, Collins VR, Frydenberg M, McLachlan RI, Matthiesson KL. Androgen deprivation therapy complications. *Endocr Relat Cancer* [Internet]. 2014 Aug; 21(4):T119–29. [cited 2016 Mar 15]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24872511>.
9. Cindolo L, Alvarez-Maestro M, Castellucci R, Schips L. Efficacy and safety of dutasteride for the treatment of symptomatic benign prostatic hyperplasia (BPH): a systematic review and meta-analysis. *World J Urol*. 2015; 33(3):441–2. [PubMed: 24777253]
10. Henderson A, Laing RW, Langley SE. Identification of pubic arch interference in prostate brachytherapy: Brachytherapy [Internet]. 2003 Jan; 2(4):240–5. [cited 2017 Apr 27]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/15062132>.
11. Wallner K, Smathers S, Sutlief S, Ph D, Corman J, Ellis W. Prostate Brachytherapy in Patients with Median Lobe Hyperplasia. 2000; 156:152–6. August 1999.
12. Keyes M, Merrick G, Frank SJ, Grimm P, Zelefsky MJ. American Brachytherapy Society Task Group Report: Use of androgen deprivation therapy with prostate brachytherapy-A systematic literature review. *Brachytherapy* [Internet]. 2017 Mar; 16(2):245–65. [cited 2017 May 3]. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S1538472116306183>.
13. Tsai H-T, Keating NL, Van Den Eeden SK, Haque R, Cassidy-Bushrow AE, Ulcickas Yood M, et al. Risk of Diabetes among Patients Receiving Primary Androgen Deprivation Therapy for

- Clinically Localized Prostate Cancer. J Urol [Internet]. 2015 Jun; 193(6):1956–62. [cited 2017 May 3]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25524243>.
14. Pagliarulo V, Bracarda S, Eisenberger MA, Mottet N, Schröder FH, Sternberg CN, et al. Contemporary Role of Androgen Deprivation Therapy for Prostate Cancer. Eur Urol [Internet]. 2012 Jan; 61(1):11–25. [cited 2017 May 3]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/21871711>.
 15. Bosco C, Bosnyak Z, Malmberg A, Adolfsson J, Keating NL, Van Hemelrijck M. Quantifying Observational Evidence for Risk of Fatal and Nonfatal Cardiovascular Disease Following Androgen Deprivation Therapy for Prostate Cancer: A Meta-analysis. Eur Urol [Internet]. 2015 Sep; 68(3):386–96. [cited 2017 Sep 12]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25484142>.
 16. Nanda A, Chen M-H, Moran BJ, Braccioforte MH, Dosoretz D, Salenius S, et al. Neoadjuvant Hormonal Therapy Use and the Risk of Death in Men with Prostate Cancer Treated with Brachytherapy Who Have No or at Least a Single Risk Factor for Coronary Artery Disease. Eur Urol [Internet]. 2014 Jan; 65(1):177–85. [cited 2017 May 3]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22981136>.
 17. Fagerlund A, Cormio L, Palangi L, Lewin R, Santanelli di Pompeo F, Elander A, et al. Gynecomastia in Patients with Prostate Cancer: A Systematic Review. PLoS One [Internet]. 2015 Jan.10(8):e0136094. [cited 2016 Mar 15]. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4550398&tool=pmcentrez&rendertype=abstract>.
 18. Zanardi S, Puntoni M, Maffezzini M, Bandelloni R, Mori M, Argusti A, et al. Phase I–II trial of weekly bicalutamide in men with elevated prostate-specific antigen and negative prostate biopsies. Cancer Prev Res (Phila) [Internet]. 2009 Apr; 2(4):377–84. [cited 2016 Mar 15]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19336728>.
 19. Gaudet M, Vigneault É, Foster W, Meyer F, Martin A-G. Randomized non-inferiority trial of Bicalutamide and Dutasteride versus LHRH agonists for prostate volume reduction prior to 1–125 permanent implant brachytherapy for prostate cancer. Radiother Oncol [Internet]. 2016 Jan; 118(1):141–7. [cited 2017 Jun 2]. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S0167814015006428>.
 20. Gormley GJ, Stoner E, Bruskewitz RC, Imperato-McGinley J, Walsh PC, McConnell JD, et al. The Effect of Finasteride in Men with Benign Prostatic Hyperplasia. N Engl J Med [Internet]. 1992 Oct 22; 327(17):1185–91. [cited 2017 May 3]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/1383816>.
 21. Thompson, IM., Goodman, PJ., Tangen, CM., Parnes, HL., Minasian, LM., Godley, PA., et al. N Engl J Med [Internet]. Vol. 369. Massachusetts Medical Society; 2013. Aug 15. Long-Term Survival of Participants in the Prostate Cancer Prevention Trial; p. 603–10.[cited 2017 Sep 12]Available from: <http://www.nejm.org/doi/10.1056/NEJMoa1215932>
 22. Wessells H, Roy J, Bannow J, Grayhack J, Matsumoto AM, Tenover L, et al. Incidence and severity of sexual adverse experiences in finasteride and placebo-treated men with benign prostatic hyperplasia. Urology [Internet]. 2003 Mar; 61(3):579–84. [cited 2016 Mar 15]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/12639651>.
 23. Mondaini N, Gontero P, Giubilei G, Lombardi G, Cai T, Gavazzi A, et al. Finasteride 5 mg and sexual side effects: how many of these are related to a nocebo phenomenon? J Sex Med [Internet]. 2007 Nov; 4(6):1708–12. [cited 2016 Mar 15]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/17655657>.
 24. Roehrborn CG, Lee M, Meehan A, Waldstreicher J. Effects of finasteride on serum testosterone and body mass index in men with benign prostatic hyperplasia. Urology [Internet]. 2003 Nov; 62(5):894–9. [cited 2016 Mar 15]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/14624915>.
 25. Evans HC, Goa KL. Dutasteride. Drugs Aging [Internet]. 2003; 20(12):905–16-8. [cited 2017 May 3]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/14565784>.
 26. Hopmans SN, Duivenvoorden WCM, Werstuck GH, Klotz L, Pinthus JH. GnRH antagonist associates with less adiposity and reduced characteristics of metabolic syndrome and atherosclerosis compared with orchiectomy and GnRH agonist in a preclinical mouse modelContributed equally and share first authorship. Urol Oncol Semin Orig Investig [Internet].

2014 Nov; 32(8):1126–34. [cited 2017 May 3]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25242517>.

27. Klotz L, Boccon-Gibod L, Shore ND, Andreou C, Persson B-E, Cantor P, et al. The efficacy and safety of degarelix: a 12-month, comparative, randomized, open-label, parallel-group phase III study in patients with prostate cancer. *BJU Int* [Internet]. 2008 Dec; 102(11):1531–8. [cited 2017 May 3]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19035858>.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Summary

Androgen suppression in the form of luteinizing-hormone releasing hormone analogues or anti-androgens are currently utilized prior to brachytherapy for patients who have prostate hypertrophy or pubic arch interference. However, these agents have undesirable side effect profiles and have been associated with increased risk of cardiac mortality. We describe our experience with utilizing 5-alpha-reductase inhibitors alone as an alternative for this indication.

Figure 1a–b.

a) TRUS image at prostatic base of patient at baseline with median lobe hypertrophy (prostate outlined in red dashes); b) TRUS image of same patient after 4 months of 5-ARI therapy

Figure 2.
Flowchart showing clinical pathways and outcomes for all patients treated with 5-ARI.

Table 1

Pretreatment patient characteristics (n=60)

	Median (range or %)
Age	65 (50–78)
Gleason score	
3+2	1 (1%)
3+3	45 (75%)
3+4	12 (20%)
4+3	2 (3%)
T-stage	
T1c	53 (88%)
T2a	5 (8%)
T2b	2 (3%)
PSA (ng/mL)	5.2 (2.4 – 13.3)
Prostate volume (cc)	44.2 (20.2 – 68.1)
IPSS	6 (0 – 16)

Table 2

Prostate volume reduction vs 5-ARI duration: number of patients reflects those who had both baseline and follow-up TRUS volume measurements available for analysis

	Pre- treatment	After 3–4 months 5-ARI (% of baseline)	
Patients receiving 3–4 months 5-ARI (n=54)			
Prostate volume (cc, IQR)	44.2 (36.8 – 52.7)	37.1 (24.5 – 42.0)	
Ratio post-5-ARI vs pre- volume (IQR)	–	0.80 (0.71 – 0.85)	
	Pre- treatment	After 3–4 months 5-ARI (% of baseline)	After 7–8 months 5-ARI (% of baseline)
Patients receiving 7–8 months 5-ARI (n=9)			
Prostate volume (cc, IQR)	49.4 (43.7 – 53.4)	39.9 (36.1 – 45.4)	38.0 (35.0 – 43.9)
Ratio post-5-ARI vs pre- volume (IQR)	–	0.83 (0.90 – 0.68)	0.81 (0.70 – 0.86)

Table 3

Outcomes by indication for downsizing

	# of patients with indication	# receiving brachy	# of patients with single/sole indication	# receiving brachy
Median lobe	46 *	35 (76%)	24	23 (96%)
Large volume (>47–50cc)	24 *	13 (57%)	4	2 (50%)
Pubic arch interference	20 *	13 (65%)	6	3 (50%)
2 indications	26	15 (58%)	–	–

* totals include patients with single/sole indication and those with stated indication plus 1–2 others