Three-dimensional computed tomography-guided monotherapeutic pararectal brachytherapy of prostate cancer with seminal vesicle invasion

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Abstract

Purpose: To treat patients with prostate cancer and seminal vesicle invasion with monotherapeutic three dimensional computed tomography (3-DCT)-guided posterior pararectal brachytherapy.

Methods and materials: Three hundred and sixty two patients with clinical stage T1 a,b or T2 a,b of prostate cancer were referred for 3-DCT-guided brachytherapy. Each underwent further staging with 3-D CT-guided pararectal biopsy of the seminal vesicles under local anesthesia during the pre-treatment CT-planning. Forty-three patients (12%) were upstaged to T3 cNoMo disease. In the set of 43 patients, eight had Gleason’s score ≤6, 24 Gleason’s score = 7, and 11 patients ≥ 8. Initial PSA was <10 ng/ml in 14 patients, 10–20 ng/ml in 11 patients, and >20 in 18 patients. Of the 43 patients, 37 patients were treated monotherapeutically with 3-D CT-guided brachytherapy. No patients received hormone therapy after the implant. The prescribed dosage to the seminal vesicles and prostate is 120 Gy with Pd-103 seeds and 144 Gy with 1±125 seeds.

Results: The prescribed dosage was achieved in all 37 patient’s throughout the seminal vesicles whose range of target radiation extended 5–10 mm outside the target in the adjacent fat as calculated with post-implant CT-dosimetry with Varian Brachy Vision or MMS software. Prostate Specific Antigen (PSA) outcome data were available in 34 patients treated with monotherapy and follow up ranged from 12–56 months (median, 24 months). Decreased PSA levels were stratified into six groups based on the presenting Gleason’s score and initial PSA. In the first group (with Gleason’s score ≤ 6 and initial PSA < 20 ng/ml), PSA levels decreased to less than 0.5 ng/ml in all seven patients (100%) after brachytherapy. In the second group (with Gleason’s = 7 and initial PSA < 20 ng/ml), PSA levels decreased to less than 1 ng/ml in 11 of 13 patients (85%); additionally PSA levels decreased to less than 0.5 ng/ml in ten patients (77% in this group). In the third group (with Gleason’s score = 7 and initial PSA > 20 ng/ml), PSA decreased to less than 0.5 ng/ml in four out of eight patients (50%). All of the patients in the fourth group (with Gleason’s score ≥ 8 and initial PSA < 20 ng/ml) decreased their PSA levels to less than 0.5 ng/ml in three of three patients. PSA decreased less than 0.5 ng/ml in two out of three patients (67% in the last group with Gleason’s score ≥ 8 and initial PSA > 20 ng/ml). There were no patients with Gleason’s score of 1–6 and greater than 20 ng/ml initial PSA. Patients, irrespective of the Gleason’s score and PSA, had an overall response of decreased PSA (less than 1 ng/ml) of 79%.

Conclusion: 3-D CT-guided brachytherapy delivers adequate dosage to the seminal vesicles. Clinical and biochemical results are encouraging in patients with low initial PSA levels regardless of their Gleason’s scores, but longer-term data in a greater number of patients is necessary. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Prostate; Cancer; Seminal vesicle; Brachytherapy

1. Introduction

The incidence of seminal vesicle invasion with localized prostate cancer reported after radical prostatectomy is 13-14% [11,18]. However, clinical staging with biopsy of the seminal vesicles is not routinely performed in all patients of prostatic adenocarcinoma during the initial transrectal ultrasound-guided biopsy of the prostate or prior to initiation of any treatment, surgical or radiation therapy.

In our protocol we include biopsy of seminal vesicles for clinical staging of adenocarcinoma of the prostate in all patients who are referred for 3-dimensional CT-guided posterior brachytherapy and have had no transrectal ultrasound-guided seminal vesicle biopsy performed prior to referral. The procedure is performed under local anesthesia during the pre-treatment CT planning. The 3-dimensional stereotactic system is adjusted to avoid the coccyx and spare
2. Methods and materials

Three-hundred and sixty-two patients staged at T1 a,b or T2 a,b prostate cancer were referred for 3-DCT-guided brachytherapy. Each underwent further staging with 3-DCT-guided pararectal biopsy of the seminal vesicles. Three biopsies were performed of each seminal vesicle.

Seminal vesicle invasion of prostate adenocarcinoma occurs through direct extension of the tumor through the ejaculatory ducts, through invasion of the capsule in the prostate base or through the perineural invasion in the peri-prostatic fat tissue (more often in the distal portion of seminal vesicles). Forty-three out of 362 patients (12%) had seminal vesicle invasion upstaged with 3-dimensional pararectal biopsy (T3cNoMo). Pathological seminal vesicle invasion has been reported after radical prostatectomy in 63 out of 375 patients (13%) T3cNoMo [18].

Seminal vesicle involvement is a poor prognostic feature in patients who have undergone radical prostatectomy in 3–5 years, particularly in patients with high grade tumor Gleason’s score ≥ 7, PSA > 10, and/or distal portion of seminal vesicle involvement [2,3,4,18]. The range of success after radical prostatectomy with seminal vesicle invasion at eight large centers is reported to be 5–60% [13].

External beam radiation (EBRT) has been used to treat patients with prostatic cancer and seminal vesicle invasion (T3cNoMo). Although EBRT may not be sufficient to provide long term control of stage T3c prostate cancer [1,5], large radiation field with EBRT to include seminal vesicles increases the dose to the rectum by 40–50% [6]. Because of the low risk of invasion of the seminal vesicles in the low risk patients (6% of 192 patients with PSA < 10 ng/ml and Gleason’s score ≤ 6) and because of the high dosage to the rectum with a large radiation field, monotherapeutic EBRT has not been recommended [6]. Furthermore, the Clinical Research Committee of the American Brachytherapy Society considers ultrasound guided, transperineal brachytherapy alone a relative contraindication for patients with poor prognosis prostate cancer (Stage T3, prostate >60 gm, previous transurethral resection, PSA > 10 ng/ml, Gleason’s score > 6, extensive intraprostatic calcification) [12].

The combined method of EBRT and booster with brachytherapy covering only the portion of seminal vesicles near the base of the prostate has been performed with transrectal ultrasound-guided transperineal approach [16]. Dosage of the seminal vesicles using combined treatment as calculated with dose volume histograms was not adequate [16]. We report 37 patients with prostate cancer and seminal vesicle invasion treated with monotherapeutic 3-dimen-sional stereotactic CT-guided pararectal brachytherapy with excellent coverage of the entire seminal vesicles.
performed with Varian Brachy Vision, and post-implant CT dosimetry is performed with Varian/MIVIS or Varian BrachyVision (Figs. 2 and 3).

3. Results

Follow-up was determined by office visits every 3 months during the first year, every 6 months during the second year, and yearly thereafter. In addition, data were collected from direct telephone contact and patient responses to written annual questionnaires.

Prescribed dosage (120 Gy using Palladium-103 seeds and 144 Gy using Iodine-125 seeds) to the entire seminal vesicles was achieved in all 37 patients treated with mono-therapeutic 3-D stereotactic CT-guided brachytherapy as calculated with postimplant CT-dosimetry with Varian Brachytherapy or Varian MMS. Follow-up PSA results were available 12–56 months (median, 24 months) in 34 patients treated with brachytherapy. We have established a PSA level less than 1 ng/ml as a nadir. PSA levels were stratified into six groups based on the presenting Gleason’s score and initial PSA. In the group (with Gleason’s score ~6 and initial PSA <20 ng/ml), PSA levels decreased to less than 0.5 ng/ml in all seven patients (100%) after brachytherapy. In the group with Gleason’s = 7 and initial PSA <20 ng/ml, PSA levels decreased to less than 1 ng/ml in 11 of 13 patients (85%) and PSA < 0.5 ng/ml in ten patients (77%). In the group with Gleason’s score = 7 and initial PSA > 20 ng/ml, PSA decreased to less than 0.5 ng/ml in four out of eight patients (50%). In the group with Gleason’s score ≥ 8 and initial PSA < 20 ng/ml PSA levels decreased to less than 0.5 ng/ml in three of three patients. PSA decreased less than 0.5 ng/ml in two out of three patients in the last group 67% with Gleason’s score ≥ 8 and initial PSA > 20 ng/ml. There were no patients with a Gleason score of 1–6 and greater then 20 ng/ml initial PSA. (Table 1). Patients (n = 34), irrespective of the Gleason’s score and PSA, had an overall response from CT guided brachytherapy of 79% (decreased PSA less than 1 ng/ml).

Twenty percent of patients treated with brachytherapy experience transient treatment-related symptoms of frequency of urination and burning sensation lasting 2–4 weeks and were treated with alpha-blockers and Pyridium and/or steroids. None of the 37 patients treated for seminal vesicle involvement required a catheter after the implant procedure. One patient of the 37 patients, who had transurethral prostatectomy (TURP) prior to implant, developed

Fig. 1. CT image of 3-D CT-guided stereotactic pararectal biopsy needle placement into the seminal vesicles. The rectum and coccyx is spared.
lower urinary-tract infection 2 years after the implant and his urologist performed a TURP resulting in grade 2 incontinence. Transient rectal symptoms of diarrhea and/or constipation occurred after implant in 20% of the patients lasting 1–4 weeks. Two patients experienced post-implant delayed effect of radiation with grade 3 rectal complications 12 months after the implant with rectal bleeding and pain.

4. Discussion

Under the 3-D CT-guided pararectal approach, brachytherapy delivers adequate dosage to the entire seminal vesicles as well to the adjacent fat tissue. Under combined ultrasound-guided transperineal brachytherapy and external beam radiation, the dosage to the seminal vesicles has been reported to be inadequate [16]. In addition, with CT-guided monotherapeutic brachytherapy, the dosage to the adjacent organs (bladder and rectum) is 20–40% of the prescribed dose. This is less than the dosage given under combined methods of treatment or radical EBRT.

Studies have reported extra capsular extension to range from 15–60% in patients with clinically organ-confined disease and may have local recurrence after radical prostatectomy [14,15,17]. Furthermore, patients who underwent radical prostatectomy with negative surgical margins and negative lymph nodes have a better prognosis in spite of seminal vesicle invasion. PSA of $>10$ ng/ml and Gleason’s score $>7$ had adverse prognostic failure [17].

Table 1

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<th>N</th>
<th>PSA &lt;1 ng/ml</th>
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<td>3</td>
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</tr>
<tr>
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<td>2</td>
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The afterloading needles are not preloaded. If bleeding results from placement of any of the needles, then adjustments to the needles are made to avoid seed placement in the venous plexus; therefore, little, if any, seed migration occurs. There is no significant seed migration with loose seeds outside the capsule of the prostate, however we prefer seeds in rapid strand. This is confirmed with CT of the pelvis and chest radiographs taken 3–6 months after implant in all patients.

In the absence of infection, high initial PSA (greater than 20) is a poor prognostic indicator without and with seminal vesicle invasion. Although these patients may have negative bone scan, negative CT and negative MRI of the upper and lower abdomen, they may have microscopic systemic disease. We perform pelvic lymph node resection and/or nuclear Prostascint scan for patients with seminal vesicle invasion and high PSA. If positive we recommend EBRT and hormone therapy rather than monotherapy with brachytherapy. However, high-risk patients with Gleason’s score ≥ 7 and PSA < 20 have had good results and have good coverage with radioactive seeds.

5. Conclusions

3-DCT-guided monotherapeutic brachytherapy delivers adequate dosage to the seminal vesicles. Clinical and biochemical results are encouraging in patients with low initial PSAs regardless of their Gleason’s scores, but longer-term data in a greater number of patients is necessary.

References