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Original article

Stereotactic body re-irradiation therapy for locally recurrent prostate cancer after external-beam radiation therapy: Initial report

Ré-irradiation stéréotaxique robotisée de récidive locale de cancer de prostate après radiothérapie externe : résultats préliminaires

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ABSTRACT

Purpose. – Management of prostate cancer relapses after external-beam radiation therapy is still undefined. Re-irradiation schedules have been explored in different tumour sites. In this report, we present our preliminary experience of re-irradiation using stereotactic body radiotherapy for localized prostate cancer failure.

Material and methods. – Between March 2011 and October 2014, robotic stereotactic body radiation therapy was administered to patients previously treated with external-beam radiation therapy to a median dose of 71.1 Gy (range, 45–76.5 Gy) and with biochemical failure corresponding to a local in-field recurrence of prostate cancer. Ten patients had recurrences after postoperative external-beam radiotherapy. Patients underwent a pelvic MRI to confirm the recurrence and a total body staging using a (^{18}F)-fluorocholine PET/CT. The prescription dose consisted of five fractions of 7.25 Gy to a total dose of 36.25 Gy. Efficacy was evaluated based on biochemical response and toxicity was evaluated according to CTCAE v.4.0 questionnaires and International Prostate Symptom Score.

Results. – Twenty-one patients were treated and followed for a median time of 11.7 months (mean: 13.4 months; range: 2.5–46.5 months). Median time between the first external-beam radiation therapy of prostate cancer and the first day of CyberKnife® treatment was 111 months (range: 38–398 months). One-year biochemical recurrence-free survival rate was 83.3%, and only one in-field progression was reported. Two patients had a biochemical failure corresponding to metastatic progression without evidence of local recurrence. Treatment was well tolerated, with only one grade 2 acute genitourinary toxicity, no grade ≥ 2 acute gastrointestinal or late toxicities were reported.

Conclusion. – Stereotactic body re-irradiation therapy using CyberKnife® after failed external-beam radiation therapy showed favourable results in terms of in-field local and biochemical control. Toxicity was low and acceptable. Further prospective studies are needed to confirm these results to select patient and to evaluate the introduction of androgen-deprivation therapy.

Mots clés :
Cancer de prostate
Récidive
Radiothérapie stéréotaxique
CyberKnife®

RÉSUMÉ

Objectif de l'étude. – La prise en charge des récidives de cancer de la prostate après radiothérapie est encore indéfinie. Des protocoles de ré-irradiation ont été explorés dans des localisations tumorales. Nous présentons notre expérience préliminaire de ré-irradiation stéréotaxique de récidives localisées de cancer de la prostate.

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Contrôle local
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Matériel et méthodes. – Entre mars 2011 et octobre 2014, une irradiation stéréotaxique a été délivrée chez des patients qui avaient préalablement reçu une irradiation externe de dose médiane de 71,1 Gy (45–76,5 Gy) et en situation de récidive biochimique en rapport avec une récidive locale de cancer de la prostate. Dix cancers ont récidivé après une radiothérapie externe postopératoire. Une IRM pelvienne et une TEP-scanographie à la (^{18}F)-fluorocholine ont confirmé la récidive. La dose totale prescrite était de 36,25 Gy en cinq fractions de 7,25 Gy. L'efficacité a été évaluée selon la réponse biochimique et la toxicité selon la Common Terminology Criteria for Adverse Events, version (CTCAE) v.4.0 et l'International Prostate Symptom Score (IPSS).
Résultats. – Vingt et un patients ont reçu un traitement et été suivis pendant une durée médiane de 11,7 mois (moyenne : 13,4 mois ; extrêmes : 2,5–46,5 mois). Le temps médian écoulé entre la radiothérapie initiale du cancer de la prostate et le premier jour de traitement par CyberKnife® était de 111 mois (38–398 mois). Le taux de survie sans récidive biochimique à 1 an était de 83 %, et une seule récidive dans le territoire d'irradiation a été rapportée. Deux patients étaient en situation d'échec biochimique correspondant à une progression métastatique sans signe de récidive locale. Le traitement a été bien toléré, un seul cas de toxicité aiguë génito-urinaire de grade 2 a été observé, aucune toxicité aiguë gastro-intestinale de grade supérieur ou égal à 2 et aucune toxicité tardive n'ont été signalées.
Conclusion. – La ré-irradiation en conditions stéréotaxiques par CyberKnife® après échec de radiothérapie externe a donné des résultats favorables en termes de contrôle local et biochimique. La toxicité était faible et acceptable. D'autres études prospectives sont nécessaires pour confirmer ces résultats, sélectionner les patients et évaluer l'intérêt de l'association d'une hormonothérapie.

1. Introduction

For more than 2 decades, conventionally fractionated external-beam radiation therapy has been considered standard practice for the radical treatment of patients with localized prostate cancer. Consequently, this technique has evolved significantly [1]. Technological advances have been progressively introduced, from two-dimensional (2D) to three-dimensional intensity-modulated radiation therapy (3D-IMRT) and image-guided radiation therapy (IGRT). In parallel with this technological evolution, a progressive increase in prescribed and delivered radiation doses to the prostate has been observed [2,3]. Despite these strategic efforts to optimize outcomes of external-beam radiation therapy, the rate of biochemical failure after primary radiation therapy of prostate cancer is still not negligible. In a large study of 3839 patients with prostate cancer treated with external-beam radiation therapy, Kuban et al. have reported a biochemical failure rate of 33% [4]. In the literature, published rates of biochemical recurrence are in the range 22–69% after curative radiation therapy with or without androgen-deprivation therapy [5,6]. Management of prostate cancer relapses after external-beam radiation therapy is still unestablished and no consensus regarding the most appropriate treatment option exists [7]. Re-irradiation schedules have been explored in different localizations, such as the chest wall, head and neck, liver and pelvis cancer, with varying results and low toxicity [8–11]. Stereotactic body radiation therapy and hypofractionated radiation therapy for the primary treatment of localized prostate cancer have been recently evaluated, showing prostate specific antigen (PSA)-relapse-free survival rates similar to radical prostatectomy, conventional external-beam radiation therapy, or permanent brachytherapy, with low rates of late rectal and bladder toxicities [12–15]. Advances in treatment planning, radiation delivery, and conformity and precision due to image guidance, as in robotic stereotactic body radiotherapy, have made extreme hypofractionation possible and safe, without significant morbidity [16]. In this report, we present our preliminary experience of re-irradiation using stereotactic body radiotherapy, for local recurrence of prostate cancer, focusing one early rectal and bladder toxicities, as well as the initial patterns of PSA response.

2. Methods and materials

2.1. Patients

Between March 2011 and October 2014, robotic stereotactic body radiotherapy using the CyberKnife® System (Accuray Incorporated, Sunnyvale, California) was administered to patients with biochemical failure corresponding to a localized, in-field recurrence of prostate cancer, previously treated by external-beam radiation therapy. All of the patients treated at our center and meeting the selection criteria are reported in this retrospective study.

Selection criteria for inclusion in the study were as follows: at least 18 years of age; informed consent; presence of a single recurrence within the prostate gland, seminal vesicles, or anastomosis, previously treated with conventional radiotherapy; and presentation to and approval of the case by the multidisciplinary uro-oncology board.

Biochemical failure was defined according to the new ASTRO Phoenix criteria: "A serum PSA levels rise of at least 2 ng/mL above the nadir was considered the standard definition of biochemical failure after external-beam radiation therapy with or without androgen-deprivation therapy." [17].

Clinical diagnosis of a prostate cancer recurrence was based on biochemical failure confirmed by imaging studies. All patients underwent a pelvis MRI to confirm the recurrence within the prostate, seminal vesicles, or anastomosis, and therefore, in the field of the previous external radiation therapy. Total body staging was required to exclude any metastases using a (^{18}F)-fluorocholine positron emission tomography.

2.2. Planning and treatment

For patients with a prostate in place, fiducial markers were used to deliver image-guided stereotactic body radiotherapy. Three or four gold fiducial markers were placed in the prostate prior to treatment planning, under transrectal ultrasound guidance, with local anesthesia. One week later, a noncontrast CT scan was obtained, with 1.5-mm slice thickness, including the testes, which were contoured as organs at risk. For patients with a history of radical prostatectomy, image guidance was achieved using Xsight® Spine