New approach of ultra-focal brachytherapy for low- and intermediate-risk prostate cancer with custom-linked I-125 seeds: A feasibility study of optimal dose coverage

Thomas Brun 1,*, Jean-Marc Bachaud 2, Pierre Graff-Cailleaud 2, Bernard Malavaud 3, Daniel Portalez 3,4, Christian Popotte 5, Richard Aziza 4, Amélie Lusque 6, Thomas Filleron 6, Soléakhéna Ken 1

ABSTRACT

PURPOSE: To present the feasibility study of optimal dose coverage in ultra-focal brachytherapy (UFB) with multiparametric MRI for low- and intermediate-risk prostate cancer.

METHODS AND MATERIALS: UFB provisional dose plans for small target volumes (<7 cc) were calculated on a prostate training phantom to optimize the seeds number and strength. Clinical UFB consisted in a contour-based nonrigid registration (MRI/Ultrasound) to implant a fiducial marker at the location of the tumor focus. Dosimetry was performed with iodine-125 seeds and a prescribed dose of 160 Gy. On CT scans acquired at 1 month, dose coverage of 152 Gy to the ultra-focal gross tumor volume was evaluated. Registrations between magnetic resonance and CT scans were assessed on the first 8 patients with three software solutions: VariSeed, 3D Slicer, and Mirada, and quantitative evaluations of the registrations were performed. Impact of these registrations on the initial dose matrix was performed.

RESULTS: Mean differences between simulated dose plans and extrapolated Bard nomogram for UFB volumes were 36.3% (26 to 56) for the total activity, 18.3% (10 to 30) for seed strength, and 22.5% (16 to 38) for number of seeds. Registration method implemented in Mirada performed significantly better than VariSeed and 3D Slicer (p = 0.0117 and p = 0.0357, respectively). For dose plan evaluation between Mirada and VariSeed, D100% (Gy) for ultra-focal gross tumor volume had a mean difference of 28.06 Gy, mean values being still above the objective of 152 Gy. D90% for the prostate had a mean difference of 1.17 Gy. For urethra and rectum, dose limits were far below the recommendations.

CONCLUSIONS: This UFB study confirmed the possibility to treat with optimal dose coverage target volumes smaller than 7 cc. © 2018 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords: I-125 seeds; Ultra-focal brachytherapy; Prostate cancer; Registration

Introduction

The conventional treatment of localized prostate cancer (PCa) is based on whole-gland approaches and drives a significant risk of adverse effects in terms of continence and sexuality (1, 2). However, surgical specimens showed that in a significant proportion of patients, the risk of cancer progression was entailed by a single focus of undifferentiated cancer (3–6). Addressing the index lesion would...
achieve both cancer control and preservation of quality of life. Although recent developments in imaging and biopsy technologies can outline the extent of the cancer, the challenge of focusing the required precision with the treatment agent remains a daunting task, and focal treatments proposed between active surveillance (AS) of low-risk PCa and definitive treatment of aggressive forms (7–15) are still options under assessment (16).

Indeed, focal treatments raise three questions for an optimal clinical setup: How to define precisely the target volume? How to focus the therapeutic agent on this target? And finally, how to monitor the rest of the gland after treatment?

This study assessed the feasibility of obtaining by ultra-focal brachytherapy (UFB) a prescribed dose of 160 Gy to the MRI tumor volume (ultra-focal gross tumor volume, UF-GTV) plus a 2-mm margin. Primary objective was fulfilled when, at 1-month post-UFB (D100), the dose delivered to 100% of the UF-GTV reached or exceeded 95% of the prescribed dose ($D_{100} \geq 152$ Gy).

In this article, we detail the technical workflow that was required to set up the present first registered UFB program (NCT01902680) for low- and intermediate-risk PCa.

First, the number and activity of iodine-125 ($^{125}$I) seeds used for conventional brachytherapy of the whole prostate are defined on the basis of the gland volume (approximately, 2 seeds/cc) (17). By definition, UFB addresses targets of complex shapes and smaller volumes, which spurred us to consider the implantation of multiple seeds of low activity.

Second, the objective of precision in the delivery of the seeds led us to implement the sequential use of three separate systems of imaging: multiparametric MRI (mpMRI) to inform on the position and volume of the target, 3D transrectal ultrasound (TRUS) to deliver a fiducial marker within the target taking advantage of nonrigid registration with mpMRI, and 2D biplanar US required for treatment planning.

Third, the assessment of the treatment quality— that is the dose delivered to the target, as opposed to the gland in conventional whole-gland brachytherapy—had to acknowledge the limitations of the systems used for registration between preoperative mpMRI and postoperative mpMRI and CT scan.

Methods and materials

Study design and patient selection

Patients referred for AS were offered to participate in the institutional review board—approved Phase II protocol (NCT01902680). All patients gave their written informed consent. Selection criteria were in accordance with European Association of Urology guidelines (1) for AS (prostate specific antigen <10 ng/mL, cT1c-cT2a, Gleason score on referring TRUS biopsies ≤6 [3 + 3], ≤3 positive cores, ≤50% of any core involved with cancer).

Simon’s (18) optimal two-stage design was selected in the present feasibility study, according to which at least 6 of the first 8 patients had to meet the primary objective of $D_{100} \geq 152$ Gy for the study to continue to full accrual (17 patients). We report on the 8 patients enrolled in the first stage of the study.

Provisional dose plan calculation for small target volumes

In whole-gland brachytherapy, manufacturer’s nomogram (Bard, Covington, GA) models the number and activity of the seeds required for the treatment on the basis of the prostate volume assessed on preoperative mpMRI (17). However, the seed strength for very low volumes (<7 cc) are extrapolated but did not correspond to homogeneous implantation in terms of activity (<0.393 mCi) and number of seeds (Fig. 1, right part).

To compensate for the nomogram’s lack of information for small volumes, predicted dose plans on an ultrasound prostate training phantom (CIRS053, Norfolk, VA) were performed for volumes ranging from 1 to 6 cc. For these volumes, the optimization of the implantation geometry was carried out by the same highly trained medical physicist to have homogeneous treatment plans. As a result, the number of needles respected a circumferential implantation, and the position of the needles was 2 mm inside the target with a spacing of 5 mm. The number of seeds was set for each volume according to the homogeneity in the dose distribution. A good compromise was found between the number of seeds with respect to the number of needles and an activity sufficiently weak to optimize the dose distribution. Once the implantation geometry was found for each volume, the seed activity was varied from 0.079 to 0.472 mCi (0.1–0.6 U) to obtain a correct coverage of the target and to have a margin of 2 mm between the prescribed dose and UF-GTV. Fig. 2 presents three simulated dose plans for small volumes on the CIRS053 phantom.

Workflow of UFB for low- to intermediate-risk PCa

The workflow of UFB for low- to intermediate-risk PCa is described on Fig. 3.

The first step consisted in the imaging protocol for the characterization of the focal tumor volume. All included patients underwent mpMRI acquired on a 1.5 T MAGNETOM Aera Siemens scanner (Siemens Healthcare, Erlangen, Germany) with 18-channel surface body coil. The imaging protocol (19) consisted in the acquisition of anatomic 3D fast spin echo T2-weighted MRI, functional diffusion-weighted MRI, dynamic contrast-enhanced MRI. PI-RADS-V2 was used for detection and localization of the targets. The Urostation Touch (KOELIS, La Tronche, France) was used to perform nonrigid mpMRI/3D-TRUS contour-based fusion (20) to guide and limit targeted core biopsy (21, 22).
دریافت فوری

متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات