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# Prostate-specific antigen bounce after curative brachytherapy for early-stage prostate cancer: A study of 274 African-Caribbean patients

N. Leduc[1,*], V. Atallah[1], M. Creoff[1], N. Rabia[2], T. Taouil[2], P. Escarmant[1], V. Vinh-Hung[1]

[1]*Department of Radiation Oncology, University Hospital of Martinique, France*
[2]*Department of Surgical Urology, University Hospital of Martinique, France*

**ABSTRACT**

**BACKGROUND:** Prostate cancer incidence in the African-Caribbean population ranks among the highest worldwide. We aim to evaluate the prostate-specific antigen (PSA) kinetics after brachytherapy, which so far remains unknown in this population.

**METHODS AND MATERIALS:** From 2005 to 2013, 371 patients received $^{125}$I brachytherapy of 145 Gy for early-stage prostate cancer. Eligibility criteria were cTNM ≤T2c, Gleason score ≤7, and initial PSA ≤15 ng/mL. Pretreatment androgen deprivation therapy was allowed. PSA bounce was defined as an increase of ≥0.4 ng/mL, lasting ≥6 months, followed by a decrease without any anticancer therapy. We examined PSA kinetics during followup.

**RESULTS:** For the 274 patients with at least 24 months followup, median age was 62 years old (range, 45–76). Initial PSA was <10 ng/mL in 244 and 10–15 ng/mL in 30 patients; 40 received androgen deprivation therapy. With a median followup of 50 months (range, 24–125), PSA declined continuously in 168 (61%) patients, bounced in 87 (31%), and initially declined and then rose in 22 (8%) patients. Among these latter patients, 18 presented clinical recurrence. Mean bounce intensity was 2.0 ng/mL (median, 1.2; range, 0.4–12.4). Bounces occurred in average 12 months after brachytherapy. Patients with bounce were significantly younger: mean age 59 vs. 63 years old in patients without bounce, $p$ <0.001. Bounce was also significantly associated with the immediate post-brachytherapy PSA, mean 4.0 among bounce cases vs. 2.9 among non-bounce cases, $p < 0.001$. Bounce was not associated with recurrence.

**CONCLUSIONS:** PSA bounce in our African-Caribbean population seemed earlier and was more intense than described in other populations. Early increase of PSA should not be ascribed to treatment failure. 

*Keywords:* Prostate cancer; PSA bounce; African-Caribbean

## Introduction

The incidence of prostate cancer in French West Indies (Martinique, Guadeloupe) ranks among the highest worldwide with a raw level of 268 to 259 of 100,000 and a standardized level of 163.7 of 100,000 from 2008 to 2010 (1). These numbers keep increasing and do not seem to plateau yet. Incidence and mortality for this pathology are significantly higher in the French Caribbean than in French mainland (2). In Martinique, all patients presenting with early-stage disease are treated according to French recommendations within our state-financed equal-access health care system. A wide range of curative treatments, including $^{125}$I brachytherapy, are available. Prostate permanent-implant brachytherapy is a widely used, efficient technique for the treatment of early-stage prostate cancer (3). Prostate-specific antigen (PSA) levels have been commonly used as a sensitive surrogate for the measurement of outcomes after brachytherapy and the detection of possible failure of treatment.

In contrast to PSA levels that can be measured after surgical removal of the gland, those after brachytherapy usually decrease over 2–5 years to their lowest detectable or undetectable level (nadir). It is of common knowledge among involved physicians that biochemical disease-free survival requires stable and low PSA levels (4, 5). As such,

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* Corresponding author. Department of Radiation Oncology, University Hospital of Martinique, BP 632, 97261 Fort-de-France, France. Tel.: +33-46-850-6750; fax: +596 596755060.

*E-mail address:* nicolas.leduc.mail@gmail.com (N. Leduc).

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noticeable increase of PSA level after treatment tend to be interpreted as a biochemical failure, leading physicians into increasing the frequency of clinical and biochemical followup and possibly the occurrence of additional invasive examinations or treatments.

However, it has been widely reported since the first observation by Wallner *et al.* (6) that patients can present a benign and transient elevation of PSA several months or years after brachytherapy. The etiology and predicting factors of this "bounce" or "spike" remain largely unknown.

This unexpected PSA bounce can be a cause of anxiety for the patient and his physician and could be the source of undue subsequent local or general treatment (7). This is all the more true that the patients in our care are almost exclusively of African descent. Indeed, it has often been argued that prostate cancer in African-American population has a poorer prognosis. Whether the disparities come from the differences of socioeconomic status and access to health care or from a physiological cause has been much discussed, and both phenomena are probably intricate (8–12). As a consequence, and despite the equal-access system our patients enjoy, we still consider our patients to be at high risk of recurrence, and it is still in our habit to scrutinize PSA levels after brachytherapy, especially when a PSA elevation is noted. Therefore, establishing the incidence and levels of PSA bounce compared with biochemical failure is a question of importance for adequate management of our population. In this study, we evaluated the biochemical outcome and successive PSA levels of 274 consecutive patients treated by permanent-implant brachytherapy to determine the rate of occurrence of PSA bounce and its predictive factors and differentiating factors from biochemical failure.

## Materials and Methods

### *Patients*

We reviewed the records of all 371 consecutive patients who received $^{125}$I brachytherapy as a curative treatment for early-stage (localized) disease from 2005 to 2014 in the University Hospital of Martinique, France. All patients were treated according to the French Urology Association guidelines (13, 14). Selected patients presented with low risk, early-stage disease: initial PSA (iPSA) $<$10 ng/mL, clinical stage $\leq$T2c, and Gleason $<$7. Patients with intermediate risk of recurrence were also included on a case-to-case basis with PSA $<$15 or Gleason 7 (3 + 4).

All patients were clinically staged by medical history, clinical examination (including digital rectal examination), and initial PSA level determination. All patients received a systematic pretreatment endorectal MRI to detect local and regional extension. Patients with intermediate risk were also prescribed a bone scintigraphy and thoracic, abdominal, and pelvic CT scans. Patients with capsular or seminal extension found on the MRI, and patients with systemic extension found on CT scans or bone scintigraphy, were excluded from brachytherapy. Pretreatment androgen deprivation therapy was allowed for 3 months for patients with high prostate volume ($>$50 cm$^3$) or altered urinary functions (IPS score $>$ 19).

### *Brachytherapy technique*

Thirty patients from 2005 to 2007 received linked seeds $^{125}$I brachytherapy (IMC7000 RAPID Strand seed; Oncura, Amersham, Buckinghamshire, UK). For all other subsequent patients, a real-time, ultrasound-guided planning technology with loose radioactive permanent implants of isotope $^{125}$I was used (BEBIG Isoseed I125; Eckert & Ziegler BEBIG GmbH, Berlin, Germany). The prescribed dose was systematically 145 Gy. Intraoperative $D_{90}$ was $>$145 Gy for all patients and mean $V_{100}$ was 99.1%. Planning, treatment, and dosimetric calculation techniques were identical for all patients.

### *Followup*

All patients received long-term followup in accordance to the French recommendations: a first consultation 2 months after treatment, then every 6 months for 3 years, and once a year afterward. PSA level determination was prescribed for each consultation. A post-planning MRI was prescribed 1 month after brachytherapy. Followup was performed in our radiation therapy ward. We restricted the statistical analysis to the patients with $>$24 months of followup.

### *Statistical analysis*

All data were obtained from an institutional registry. The insularity of Martinique provides low rates for patients lost to followup. Besides, the limited amount of laboratories provides consistent data for PSA values. We assessed the ethnicity of our patients using their phototype and place of birth.

To this day, there is no consensual definition for PSA bounce. A variety have been used in scientific literature with threshold values from 0.1 ng/mL (15) to 0.4 ng/mL (7, 16), followed by a decrease of any value or a decrease to PSA values lower than pre-bounce levels. As the standard deviation of PSA test is usually measured around 0.1 ng/mL, considered threshold values should not be lower (17). As a consequence, we identified three PSA bounce definitions that seem more commonly used:

- a 0.4 ng/mL bounce for $>$6 months, followed by any decrease (Definition 1) (7, 16).
- a 0.2 ng/mL bounce for $>$6 months, followed by any decrease (Definition 2) (18).
- 0.2 ng/mL bounce followed by a subsequent decrease to lower value than previous PSA nadir (Definition 3) (19–21).