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European Association of Urology



## Letter to the Editor

**Reply to Alessia Cimadamore, Marina Scarpelli, Liang Cheng, et al's Letter to the Editor, re: Maria Chiara Sighinolfi, Bernardo Rocco's Words of Wisdom re: EAU Guidelines: Prostate Cancer 2019. Mottet N, van den Bergh RCN, Briers E, et al. <https://uroweb.org/guideline/prostate-cancer/>. Eur Urol 2019, 76:871**

We read with interest the report from Cimadamore et al [1]. The authors describe a “traumatic neuroma” (TN) as a novel pathological finding. TN could be detected incidentally at the prostate surface during surgery; histologically, it is supposed to arise from a truncated nerve at the periprostatic tissue, maybe deriving—as an inflammatory reaction—from local anesthesia during prostate biopsy (PB) [1]. The occurrence seems rare but also under-reported, given the lack of symptoms and oncological drawbacks.

However, the finding of a TN can pose a surgical concern. The perception of a TN during the release of bundles could resemble tight adhesion of periprostatic tissue to the capsule. Therefore, it can be misinterpreted as extracapsular extension (ECE) of the tumor and can drive the surgeon toward a non-nerve-sparing strategy with a wider plane of dissection.

Some considerations may arise.

First, the possible relationship with PB should be recognized.

PB is one of the most frequent urological procedures, with 1 million PB performed yearly in the European Union [2]. The need for repeat biopsy is common and mandatorily scheduled as part of active surveillance (AS). Approximately one-third of men on AS are “reclassified” at follow-up and require a definitive treatment [3]. The impact of multiple PB rounds on radical prostatectomy has been evaluated in

terms of complications [4]; however, the impact of multiple PBs on surgical specimen represents an underaddressed issue. The novel finding described by Cimadamore et al [1] should be known by surgeons and diagnosed intraoperatively by pathologists, to avoid unnecessary non-nerve-sparing procedures.

How could a finding resembling ECE be clarified intraoperatively? As suggested by 2019 European Association of Urology guidelines [3], frozen section (FS) analysis is able to rule out the inadvertent excision into the tumor. However, prostate FS is limited by a number of factors, such as the absence of standard sampling [5] and the need for a fully equipped setup, consisting of cryostats, technicians, and pathologists on site, to prepare specimen and interpret glass slides with an analog microscope [6]. Thus, FS is hardly affordable at all institutions, especially in view of the contraction of pathologists' workforce.

Intraoperative analysis could be simplified with fluorescence confocal microscopy (FCM) [6]. FCM provides microscopic analysis of freshly excised tissues, with straight acquisition of digital images without conventional processing, dedicated setup, or an on-site pathologist, since images could be shared remotely.

The ability of FCM to discriminate between prostate and periprostatic soft tissues has been evaluated on samples retrieved during radical prostatectomy from suspicious periprostatic areas [6]. FCM agreement with hematoxylin-eosin for the interpretation of periprostatic components is almost perfect, and nerves could be distinguished with a rate of 97.14% of correct diagnosis (Fig. 1).

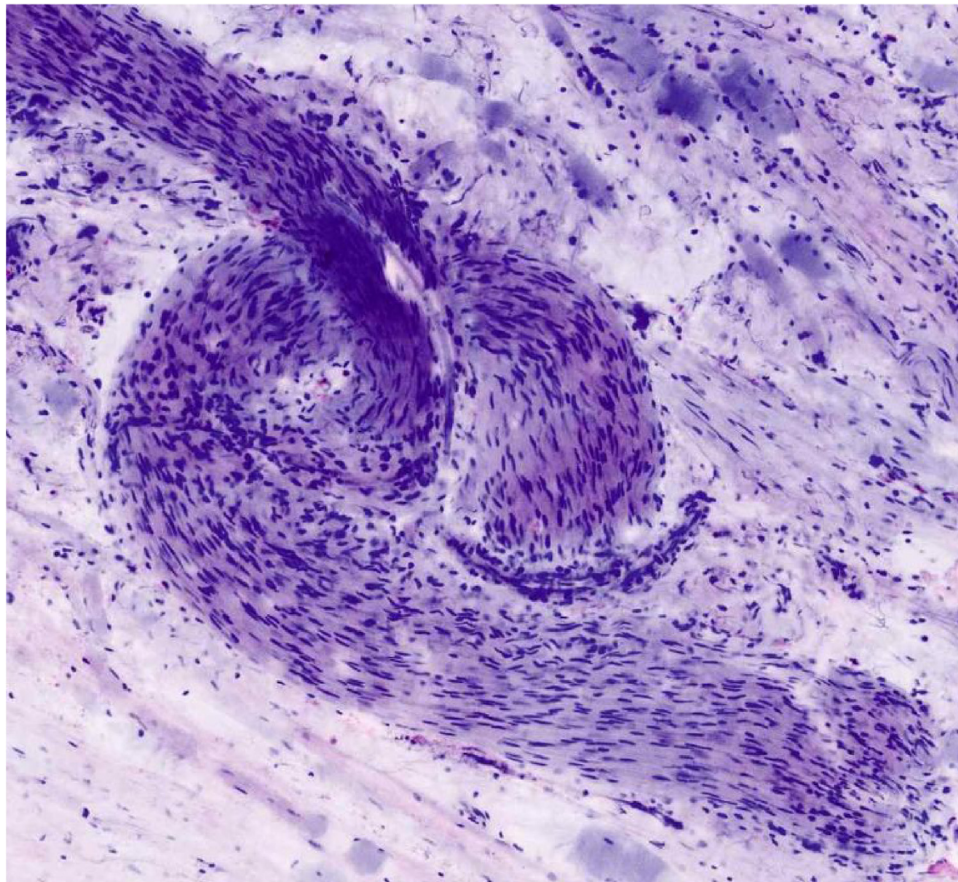
Whether FCM could depict a TN is still exploratory; efforts should be done to extend the range of tissues—and related inflammatory alterations—effectively interpreted with FCM.

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**Fig. 1 – Detection of a nerve with FCM. Note the HE appearance, with range of colors (purple to pink) similar to conventional pathology. The level of agreement with FCM for the detection of periprostatic soft tissue components (connective, muscular, fatty tissue, and vessels) has been described as “almost perfect” [6]. FCM = fluorescence confocal microscopy; HE = hematoxylin-eosin.**

Certainly, surgical strategy is moving towards a step-by-step tailored approach, in which the dissection is histologically driven and could be modified accordingly; a full nerve-sparing strategy together with secondary resection in case of tumor persisting at surgical margin could be the perspective to guarantee complete oncological excision, while sparing functional tissue as much as possible.

**Conflicts of interest:** The authors have nothing to disclose.

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