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Intra-surgical total and re-constructible pathological prostate examination for safer margins and nerve preservation (Istanbul preserve)

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A B S T R A C T

Purpose: To demonstrate a novel frozen section analysis technique during robot assisted radical prostatectomy with 2 distinct advantages: evaluation of the entire circumference and easier reconstruction for whole mount evaluation.

Material and methods: Istanbul Preserve was performed on patients who underwent robotic prostatectomy with nerve sparing between 10/2014 and 7/2016. Gland was sectioned at 3–4 mm intervals from apex to bladder neck. Entire tissue representing margins (except for the most anterior portion) was circumferentially excised and microscopically analyzed. In margin positivity, approach was individualized based on extent of positive margin and Gleason pattern. A matched cohort was established for comparison. Retrospective analysis of a prospectively maintained database was performed. Impact of FSA on PSM rate was primarily assessed.

Results: Data on 170 patients was analyzed. Positive surgical margin was reported in 56(33%) on frozen section. Neurovascular bundle was partially or totally resected in 79% and 18%. Conversion of positive margin to negative was achieved in 85%. Overall positive margin rate decreased from 22.5% to 7.5%. Nerve sparing increased from 87% to 93%. Location of positive margin at frozen was at the neurovascular bundle area in 39%; thus Istanbul Preserve detected 61% additional margin positivity compared to other techniques. Reconstruction for whole mount was easy.

Conclusion: Istanbul Preserve is a novel technique for intraoperative FSA during RARP allowing for microscopic examination of the entire prostate for margin status and easy re-construction for whole mount examination. It guarantees safer margins together with increased rate of nerve sparing.

1. Introduction

Precise local clinical staging is unlikely for many patients with prostate cancer (PCa). Patients with organ confined cancer may be noted to have disease beyond the capsule (pT3), and controversially, up to 50% with clinical T3 disease may prove to have localized disease at pathological examination of prostatectomy material [1]. Cancer foci are not visible during surgery, even with the magnification of robotic technology, representing a dilemma for the urologist in planning and executing dissection planes during radical prostatectomy (RP). The goal of surgery is to eliminate cancer, while preserving the quality of life of the patient. Preserving the neurovascular bundle (NVB) improves functional outcomes, such as maintenance of potency and continence [2]. When aiming for nerve sparing (NS) surgery, dissection plane needs to be in close proximity of the gland, potentially jeopardizing surgical margins. Thus NS approach has the inherent potential risk of leaving cancerous tissue behind.

Accumulating data suggests that frozen section analysis (FSA) during RP may allow for achieving lower positive surgical margin (PSM) rates while improving NS rates [3-6]. The systematic technique described from The Martini-Clinic Prostate Cancer Center has revolutionized this pathological approach [3]. However, their methodology is restricted to the FSA evaluation of tissue adjacent to the NVB, with a potential to miss PSM elsewhere in the gland. It involves multiple perpendicularly cut sections performed on the longitudinally dissected NVB adjacent tissue, possibly impairing perfect reconstruction for whole-mount evaluation. Herein, we describe a novel FSA technique, in which the entire prostate is examined for margins and perfect

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reconstruction for whole mount evaluation is easily conceivable with minimal tissue loss.

2. Method

2.1. Patient population

Data on patients who underwent **I**ntra-**S**urgical **T**otal **an**d *Re*-Constructi**bl**e Pathological **Pr**ostate **E**xamination for **S**afer Margins and N**erve** Preservation (Istanbul Preserve) during NS robot assisted radical prostatectomy (RARP) between 10/2014 and 7/2016 were retrospectively reviewed from a prospectively maintained database. All patients had a pre-operative multiparametric prostate MRI and patients with overt extracapsular extension did not undergo FSA.

2.2. Surgical technique

We attempt to preserve tissue surrounding the prostate as designated by the 'Veil of Aphrodite' technique in efforts to preserve the large network of nerves surrounding the prostate like a hammock [7]. Prostatectomies were performed using Da Vinci Robotic Systems with the AirSeal system (Conmed). Upon completion of prostatectomy and suture ligation of the dorsal venous complex, the specimen was bagged and removed via the extension (3 cm) of the camera port. Robotic arms were removed without undocking. The incision was re-tightened with suturing. Once the prostate was out, sutures were placed to depict apex, mid and base of the gland, before submitting to pathology. Surgery proceeded with hemostasis and lymph node dissection (LND) during FSA analysis. Anastomosis began after FSA was finalized.

2.3. Frozen section analysis technique

Once the specimen reached the pathology laboratory, right and left surgical margins were inked individually (black and blue). Three distinctive colors were used to illustrate the apex, mid and base of the gland (yellow-green-orange) (Fig. 1). Afterwards, the gland was sectioned at 3–4 mm intervals from apex to bladder neck. Subsequently, entire tissue representing the margins (except for the most anterior portion) was circumferentially excised at a width of 4–5 mm. (separately for right and left halves) (Fig. 2). This tissue was then embedded in freezing media on a chuck and frozen at − 25 °C. 5–7 μ cryosections were cut from each half border, stained with hematoxylin and eosin, and examined microscopically. A PSM was reported, when malignant tissue was in contact with the inked margin. Based on color, particular location of the PSM (right or left and apex vs. mid gland vs. basis) was designated. A genitourinary pathologist and 2–3 technicians were involved in the process.

2.4. Approach in the presence of a positive surgical margin

Extent of further resection was tailored to the individual patient. In cases of wide margin positivity and Gleason pattern ≥ 4, entire NVB was resected; whereas in cases in whom PSM was restricted to a small area, re-resection was limited to the corresponding area (partial resection). When PSM was extensive, further resection(s) was performed from the corresponding area in the resection bed, until negative margins were reached with repeat FSA. In patients whose priority was preserving potency and in whom PSM was restricted to a few glands with Gleason pattern 3, re-resection from the prostate bed was omitted in order not to jeopardize functional outcomes.

2.5. Analysis

Data was analyzed for the results of FSA. In efforts to evaluate the impact of FSA on operative time and rate of PSM, a matched cohort form the surgeon's series was established and compared. Serum PSA, Gleason score, age and performance of LND were used to inaugurate the matched cohort.

Statistical analysis was performed using GraphPad Prism version 6.00 for Machintosh, GraphPad Software, La Jolla California USA, (www.graphpad.com) When assumption of normal distribution was not provided, unpaired *t*-test was used to compare two independent groups for numerical variables. Pearson $\chi 2$ test was used for comparison of multiple groups for categorical variables, when the condition was met. The possible factors were defined as categorical values and the entry value was accepted as 0.05 and the removal value was accepted as 0.10. The level of statistical significance was considered as $p < 0.05$.

3. Results

The study received approval by the institutional ethics committee (2016–16/6). A total of 221 consecutive men with PCa underwent RARP by a single surgeon (ARK) between October 2014 and July 2016. FSA with Istanbul Preserve technique was performed on 170. Mean age

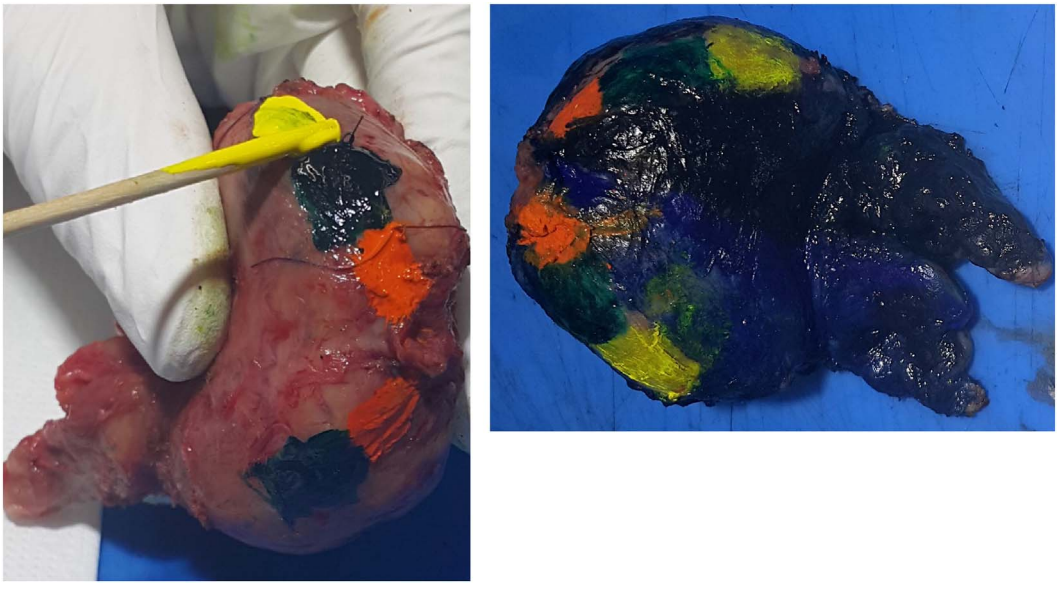

Fig. 1. Prostate is initially inked with individual colors to depict the right and left lobes and the apex, mid and base of the gland.