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Original article

Assessment of the circumferential margins, extraprostatic extension and Gleason score in radical prostatectomy specimens: Comparison of a partial embedding method with supplemental total inclusion of peripheral tissues



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ABSTRACT

Background: Recent data suggest that up to 21% of positive circumferential margins (PCM) and 47% of extraprostatic extension (EPE) samples may be missed when partial embedding methods are employed. Kim and colleagues (2009) suggested that total inclusion of the periphery (3 mm rim) of the prostate prevented the failure to detect PCM and EPE.

Design: Radical prostatectomy specimen (n = 148) slides were reviewed after adoption of a protocol that included a ~3 mm rim of peripheral tissues. We evaluated whether the analysis of supplemental slides of prostate periphery changed margin status, presence of EPE, Gleason score and extent of PCM and EPE. *Results:* Partial sampling resulted in missing 29% of PCM and 20% of EPE without using data from the supplemental slides of prostate periphery. Changes from focal to extensive disease were found in 11/21 (52%) cases of positive circumferential margins and in 5/13 (38%) cases of extraprostatic extension. Changes in the Gleason score were uncommon.

Conclusions: These results indicate the importance of including all the prostate peripheral tissue for microscopic analysis when partial embedding methods are adopted.

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1. Introduction

The widespread use of prostate cancer screening based on digital rectal examination and serum specific prostatic antigen concentration in the last three decades has increased the number of minimal volume prostate adenocarcinoma detected in needle biopsies and, as a consequence, small volume carcinomas in prostatectomy specimens. In the current practice, most radical prostatectomy specimens show small tumors that are not grossly visible [4,13].

Acinar adenocarcinoma of the prostate is a major public health problem, and radical prostatectomy specimens are common in most laboratories dedicated to surgical pathology worldwide. Surprisingly, there is still no consensus on how such specimens

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should be handled even if some authorities are strong defenders of total embedding of prostatic tissues for all cases [4]. Based on the International Society of Urological Pathology (ISUP) consensus meeting, both total embedding and partial embedding are acceptable. It was consensual, however, to recommend that "if partial embedding is performed, a specific protocol should be followed, and the methodology should be documented in the pathology report [13]. Epstein and colleagues retrospectively studied 380 radical prostatectomy specimens from T1c (non-palpable, needle biopsy confirmed cancers) cases. The study population presumably contained small tumors that were likely to be grossly invisible. All specimens were processed in their entirety (mean of 34 slides). Adverse findings were defined as high Gleason score (≥ 7) , positive margins and extraprostatic extension. Nine alternative partial sampling strategies were compared with the entire embedding to determine the feasibility of detecting these adverse findings. The approaches were based on extensive sampling of the posterior regions with several different methods for the midanterior areas. The finding of high Gleason scores oscillated from 83% to

98% in the evaluated methods, while positive margins (71–100%) and extraprostatic extension (62-96%) had considerably broader ranges. The authors recommended two methods: embedding every posterior section plus one midanterior slice of each side (and all remaining anterior sections of one side if a sizable tumor was detected using microscopy) and a similar method that examined every posterior section that had been obtained only from the ipsilateral areas of previously positive needle biopsies. Using these two methods, high Gleason scores, positive margins and extraprostatic extensions were detected in 98, 100%, and 96% and 92%; 93% and 85% of cases for each method, respectively [14]. The asymmetric sampling of the prostate using these methods may possibly induce a potential bias in the calculation of either the tumor volume or the percentage of gland involvement [19]. It is an important issue because some assessment of the tumor extent is now part of the recommendations for the pathology reports of radical prostatectomy specimens [18]. The percentage of gland involvement and tumor volume are popular methods of estimation of the tumor size in radical prostatectomy specimens because they do not require whole mount sections as does the measurement of the linear extent of the index tumor [1].

Some reports disagree about the extent of relevant missed data by partial embedding methods. Vainer and colleagues reported that alternate slicing missed extraprostatic extension in two cases and positive margins in one case, from a case series of 238 prostatectomies [17]. Similar results were obtained by Llanos and colleagues in a smaller series of 48 specimens in which one case of extraprostatic extension and no case of positive circumferential margin were missed [10]. Recently, a large series of 618 specimens strongly discouraged partial sampling. Positive margins and extraprostatic extension were detected in 87% and 72% for the alternate slices, 79% and 53% for alternate posterior slices plus one midanterior section, and 95% and 93%, respectively, for the previously mentioned method recommended by Epstein and colleagues [8].

In a series of 148 specimens, Kim and colleagues evaluated five different methods. Positive margins and extraprostatic extension were detected in the following rates: 83% and 84% for the alternate slicing; 87% and 88% for the alternate slicing with the complete embedding of the biopsy-positive posterior quarters; 89% and 88% for every posterior half; 91% and 90% for every posterior half plus one midanterior section; and 100% and 100% for the alternate slicing with 3 mm of the peripheral rim of the remaining prostate, respectively. Importantly, the fourth method when used as the same protocol proposed by Epstein and colleagues (adding the remaining ipsilateral anterior section with the detection of a sizeable tumor) could also allow the detection of all cases of extraprostatic extension and positive margins; however, the number of blocks was similar to that of entire sampling [9].

Since the start of 2013, we have adopted the suggestion by Kim and colleagues of supplemental inclusion of 3 mm peripheral tissues of the prostate. Such change was implemented both at an academic and private laboratories in Salvador, Brazil. The aim of this study was to compare our standard method of partial embedding (representing two slides of each of 12 regions of the prostate) [1] with additional examination of supplemental sections of margins and extraprostatic tissues (SSMEPT). It may be useful for practicing pathologists to estimate how much relevant data are missed when using the currently adopted partial embedding methods and how much extra work is required to adopt the inclusion of SSMEPT.

2. Materials and methods

2.1. Patients and protocols

All consecutive radical prostatectomy specimens examined in the Laboratory of Pathology IMAGEPAT (Salvador, Brazil) between

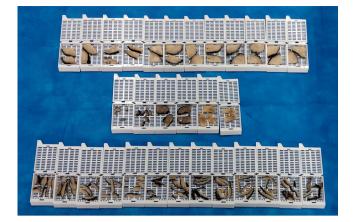


Fig. 1. Partial sampling method of the gross specimen. Upper cassettes contain samples of twelve different regions of the prostate (separated into apical, intermediate and basal regions/right and left/posterior and anterior). Central cassettes contain samples from the apical and basal regions.

January 2013 (the date on which the proposed protocol was adopted) and December 2014 were included in the study. The project was approved by the Research Ethics Committee of Hospital Universitário Professor Edgard Santos (number 679163) located in Salvador, Brazil.

All radical prostatectomy specimens were examined using the same protocol as described in detail elsewhere [1]. Briefly, both the apical and basal margins were sectioned according to the cone method and sliced in the sagittal plane. The remnant prostate was transversally sectioned into three thirds of comparable thickness, representing an apical, an intermediary and a basal third sections. Each region was sectioned into quadrants (resulting in twelve zones). Each zone was further sliced, alternating one slice for the gross specimen archive and one slice to be processed. Two slices were processed for each region, skipping one slice (24 slices in the quadrant shape, including the circumferential margin). In most prostates, this approach was equivalent to embedding alternate slices. However, it could range from total embedding in cases of small specimens to large volumes sent to gross archive in cases of larger glands. Since January 2013, we have prospectively evaluated the results of this method with examination of SSMEPT, which were processed in independent blocks. A representative case is illustrated in Fig. 1.

In the academic institution (Hospital Universitário Professor Edgard Santos), the Pathology residents were trained, and performed the gross examination and handling of specimens. In the private laboratory (Imagepat), all procedures were performed by the same pathologist experienced in urologic pathology. A peripheral 3 mm rim of peripheral prostate tissue was processed in its entirety for all cases as suggested by Kim and colleagues [9]. When grossly visible adipose extraprostatic tissue was detected, all that material (even if thicker than 3 mm) was processed to ensure detection of the transition between prostate and extraprostatic tissue. Inked margins of the two distal thirds of the seminal vesicles and deferent ducts were not processed routinely. At the first institution, residents included all SSMEPT in additional cassettes without a standard pattern of distribution. At the second institution, all SSMEPT sections were processed in the pattern of six slices per cassette (Fig. 1). As a result, we used only the data from the latter to calculate how many additional blocks and slides were required to ensure examination of all SSMEPT.

Positive margins and the presence of extraprostatic extension were detected and reported as recommended [11]. For both the quantification of positive circumferential margins and extraprostatic extension, we used the criteria suggested by Wheeler and Download English Version:

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