Mapping Contemporary Biopsy Zones to Traditional Prostatic Anatomy: The Key to Understanding Relationships Between Prostate Cancer Topography, MRI Conspicuity and Clinical Risk

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The traditional zonal approach to prostate anatomy devised by McNeal in 1981[1] was based on dividing the prostate into four histologically and anatomically distinct zones. Clinically, this zonal approach has proved to have utility in both benign and cancer-based urology, guiding both diagnostic and treatment decisions. However, this simplistic zonal approach risks conveying an overly reductive representation of prostate anatomy and may be partly responsible for the paucity of data examining differences in sub-zonal prostate cancer risk and prognosis, compared to the relative abundance of data comparing these features between simple tumour zones[2,3]. Furthermore, classical transrectal ultrasound (TRUS)-guided biopsy may have contributed to the lack of detailed understanding regarding the influence of tumour zone-of-origin, due to well-acknowledged under-sampling of the mid and anterior prostate[4].

In the PROMIS and PICTURE trials[5,6], a transperineal template mapping (TTPM) biopsy technique was employed as the diagnostic reference standard, where prostate tissue was exhaustively interrogated at 5mm intervals, providing a unique opportunity for sub-zonal analysis of prostate cancer topography.

The aim of this article is to map intricate biopsy information provided by modern transperineal biopsy protocols (e.g. Barzell, Ginsburg)[7,8] to the traditional McNeal anatomical zones, creating a bespoke tool designed to reveal important relationships between zones of tumour origin, to a wealth of other potential outcomes, including, tumour conspicuity on magnetic resonance imaging (MRI) and clinical risk, as derived from histopathological, genomic and longitudinal correlates.

We used traditional McNeal anatomical prostate zones as our ground truth, to which we mapped Barzell and Ginsburg biopsy zones (Fig. 1). Modified Barzell zones were plotted to apical and basal sections as previously described[9], while Ginsburg zones are aligned to the mid-gland alone, for simplicity.

Our proposed approach has additional factors and limitations to consider. The most important limitation is inter-patient variation, particularly given the close relationship between tumour volume and age. The transitional zone (TZ) demonstrably enlarges with age, due to progressive adenomatous growth from benign prostatic hyperplasia (BPH). As the TZ grows, the posterior peripheral zone (PZ) is compressed, which could conceivably alter the histopathological contents of posteriorly directed prostate biopsies (e.g. Barzell zones 13-20), to contain elements of both TZ and PZ, as opposed to pure PZ sampling in men with small-medium volume prostates. Indeed, these anatomical changes are also visible on MRI (e.g., moustache and tear-drop signs)[10]. This phenomenon may also occur in the antero-medial prostate (Barzell zones 1-4), where anterior fibromuscular stroma (AFMS) involvement may be dependent on TZ size. Clinician discretion is key, and in smaller prostates, it is not uncommon to limit zonal sampling, resulting in necessary recalibration of the TPM mapping protocol.

In tumours occupying multiple biopsy zones, it may be difficult to accurately ascertain the anatomical zone of origin. Nevertheless, known patterns of tumour growth may help address this challenge.[11] For example, a tumour detected in Barzell zones 1 and 7 (left anterior apex) is more likely to be of TZ origin, than a tumour found crossing zones 7 and 17 (anterior and posterior components of left apex), which is likely to be exclusively of PZ origin. When uncertainty of origin persists, the biopsy zone with the highest overall Gleason grade should be considered the index tumour (in accordance with the 2010 ISUP consensus conference). However, if the overall Gleason grades are identical across multiple biopsy zones, then the larger foci should be considered the index tumour[12], given the plausible biological rationale that the largest tumour focus is likely to be the most mature. Lastly, it is worth recalling that PZ tumours favour horizontal over vertical extension due to influence of perineural space, and the commonest location of PZ invasion by a TZ tumour is lateral to the AFMS, where the TZ-PZ stromal boundary is thinnest[13,14]. These oncological growth behaviours are useful to inform our understanding of tumour origin. However, for true determination of tumour origin, ratifying this estimation with genomic analysis of the tumour foci would be necessary, especially given the theory of clonal evolution, where origin cells may mutate, leading to a faster growing subclone which becomes larger/higher grade than the origin.

Here, we have mapped traditional zonal prostate anatomy to modern transperineal biopsy protocols, to provide a pragmatic research tool that enables sub-zonal data analysis of both mpMRI and histopathological-correlated outcomes. We hope our key will provide researchers with a valuable resource for elucidating effects of tumour location in prostate cancer diagnosis, management and prognosis.

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