Title: PSMA PET for the identification of intra-prostatic tumors: investigating targeting guidelines for focal therapy and guided biopsy

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Structured Abstract:

Introduction: Accurate, non-invasive delineation of areas of highest suspicion for biologically significant prostate cancer (PCa) is necessary for proper risk stratification and further treatment planning. This would enable many aspects of cancer care for men with primary PCa including: biopsy guidance to enable accurate grading and disease monitoring (for active surveillance cases), guiding focal therapy treatments with ablative therapies, and design of radiation treatments incorporating focal boosting strategies. Prostate specific membrane antigen positron emission tomography (PSMA PET) is emerging as a clinically useful tool for imaging prostate cancer but there is a need, addressed in this study, to investigate the ability of PSMA PET to delineate dominant intra-prostatic lesion (DIL) boundaries for guided biopsy and focal therapy planning.

Methods: Using a prostatectomy cohort of 12 patients, we registered whole-mount mid-gland histology sections to in-vivo PSMA PET imaging. PET volumes were thresholded from 1—100% max standard uptake value (SUVmax) in 1% intervals. At each interval, we applied a margin of 0—30 voxels at one voxel increments, for a total of 3,000 segmentations for each patient. We calculated sensitivity and specificity on the 2D oblique histologic planes that intersect with the 3D segmentation for each patient for each DIL. We determined the percent threshold and margin combination that satisfied the following criteria: 95% sensitivity with maximal specificity (supporting focal therapy) and 95% specificity with maximal sensitivity (supporting guided biopsy).

Results: For the application of focal therapy, a threshold of 67% SUVmax with an 8.4 mm margin achieved a (mean ± std.) sensitivity of 95.0 ± 7.8% and specificity of 76.4 ± 14.7%. Qualitatively, we found our segmentations converge on the lesions defined by histology with minimal healthy tissue involvement. For the application of guided biopsy, a threshold of 81% SUVmax with a 5.1 mm margin achieved sensitivity of 65.1 ± 28.4% and specificity of 95.1 ± 5.2%. Previous literature indicates that all tumours would be targeted in multiple biopsy attempts given the size of the segmentations.

Conclusion: This study used accurate co-registration of PSMA PET/MRI and surgical histology to determine SUV thresholds and margin expansions having high sensitivity, supporting focal therapy, and high specificity, supporting guided biopsy. The thresholds and margin expansions determined by this study can be used in a larger validation study supporting clinical translation.