Tumor probability model for focal salvage strategies in recurrent prostate cancer patients after radiotherapy

C.D. Fernandes1*, G. Ghobadi1, P.J. van Houdt1, H.G. van der Poel1, J. de Jong1, S.W. Heijmink1, M. Smolic1, F.J. Pos1, U.A. van der Heide1
1The Netherlands Cancer Institute, Amsterdam, The Netherlands

ABSTRACT

Purpose: Focal salvage strategies may provide a curative option for locally recurrent prostate cancer (PCa), with decreased toxicity compared to whole gland approaches by delivering a tumor targeted treatment. Accurate tumor localization is crucial to ensure an appropriate target coverage with minimal toxicity. Magnetic resonance imaging (MRI), with anatomical and functional possibilities and increased spatial resolution in relation to PET, may prove a valuable tool for target definition. Prostate and tumor MRI characteristics are different for recurrent PCa after RT, with overall signal intensity reduction in T2w and decreased ADC values1. Here we aim to investigate the performance of a published primary PCa tumor probability (TP) model2 in the setting of local recurrence after RT.

Materials & Methods: The model was trained using T2w, ADC and K\text{trans} maps of primary PCa, prior knowledge provided by prevalence and biopsy maps, and validated with histopathology. Here we tested it in a cohort of 17 salvage radical prostatectomy patients with local recurrence after RT (13 after EBRT and 4 after low-dose rate brachytherapy), who received multi-parametric MRI prior to surgery. Histopathology slides were deformably registered to the best matching T2w slice and tumor ground truth (GT) contours were propagated to imaging. As recurrence usually occurs at the site of the primary PCa3, the tumor prevalence map4 was considered applicable. Biopsies obtained to ascertain recurrence were used to create a biopsy map, using the ratio positive biopsies / total number of biopsies taken per side (Fig.1). To generate tumor delineations from the TP maps, the optimal point on the training data ROC curve, i.e. the closest point to the top left corner, was used as a threshold. Distance was calculated between GT and TP map contours. Tumor detection was visually assessed.

Results: Voxel-wise AUC for the pooled test set was 0.82, with a median AUC=0.79 (0.43-0.95) when calculated on a patient level. The threshold resulted in a median sensitivity of 74% (0-100%) and...
specificity 79% (3–99%) in the test set. All 11 tumor foci ≥ 0.5 cm³ were correctly detected, but only 20 of the 45 foci <0.5 cm³ were found. The median 95% Hausdorff distance between TP and GT contours was 1.68 (0.45–2.26) cm. Brachytherapy seeds were often misclassified as tumor voxels.

**Conclusions:** A TP model originally trained in primary PCa was able to detect recurrent cancer with an AUC comparable to reported in primary PCa (AUC=0.78)². Smaller foci were often missed, and tumor detection was complicated after brachytherapy. The threshold defined based on primary PCa data was not optimal for recurrence detection, frequently resulting in false positives. The use of TP maps can aid in target definition for the design of focal salvage strategies.

¹ Barchetti and Panebianco 2014; ²CV Dinh et al. 2017; ³Pucar et al. 2007; ⁴Ou et al. 2009

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**Fig 1** – MRI images (T2w, ADC and K\text{trans}) and prior knowledge (tumor prevalence and biopsy maps). Tumor probability map with in red the GT tumor delineation and in green the regions identified by thresholding the TP map.