

Pathological validation of a model based on diffusion weighted imaging and dynamic contrast-enhanced MRI for tumor delineation in the prostate peripheral zone

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Introduction

In standard prostate radiotherapy, the complete prostate is treated with a homogeneous dose. To further improve treatment outcome, several groups proposed to increase the dose to the visible tumor. To this end, the robustness of MR based tumor delineations needs to be improved. When it comes to tumor delineation, for each voxel inside the prostate one needs to decide whether or not it is part of the tumor. We developed a statistical model, which predicts tumor presence on a voxel level (voxel size 2.5x2.5x2.5 mm³) inside the peripheral zone (PZ). Furthermore, we show how this model can be used to derive a valuable input for radiotherapy treatment planning.

Methods

87 radiotherapy patients and 12 prostatectomy patients were included in this study. A T2 weighted (T2w), DWI and DCE-MRI exam were performed using a 3T Philips Achieva MR scanner. A 6-element phased array coil (sense cardiac) was used as receive coil during the scans. T2w images were acquired with a fast spin-echo sequence, TR/TE = 8396/120 ms, echo train length 13, acquisition matrix 256x256, FOV = 20 cm, slice thickness 3 mm, intersection gap 1 mm. DWI scans were performed using a multislice single shot SE-EPI sequence (FOV = 38 cm, slice thickness = 3 mm, EPI-factor = 47, intersection gap = 1 mm, TR/TE=5000/54 ms, acquisition matrix = 152 x 107, 9 averages, sense factor = 2 in AP direction, phase encoding direction = PA, b values 300, 500, 1000 s/mm²). The DCE-MRI protocol consisted of a 3D spoiled gradient echo sequence (20 transverse partitions, 2.5 mm slice thickness, TR/TE=4/1 ms, flip angle 8°, FOV = 40 cm, acquisition matrix = 160 x 160). Scans were repeated 120 times at 2.4s interval. A concentration of 0.1 ml/kg of Gadobutrol (1.0M)(Gadovist, Schering AG, Berlin, Germany) contrast was injected with 2 ml/s, followed by a saline flush. Concentration of the contrast agent was calculated from the MR signal using preceding small flip angle scans (6, 16 and 32°, TR/TE = 50/1.1 ms). For each voxel the Tofts Model[1] was fitted to the measured concentration time curves. This yielded 3D maps of the volume transfer constant K_{trans}. A generic arterial input function (AIF) was used for all patients.

To improve the robustness of MR based prostate radiotherapy we first created a validated logistic regression model, which predicts tumor presence on a voxel level. After this we translated model outcome into discrete risk levels for tumor presence, which can be used as target volumes for treatment planning.

In order to create a validated model, we performed two steps: 1. Model creation 2. Model validation. Creation of the model was performed on 87 radiotherapy patients. To create the model in each radiotherapy patient highly suspicious and highly non-suspicious regions were delineated. A logistic regression model was fitted through the data. This model was based on the voxel ADC and K_{trans} as well as the minimum and maximum ADC and K_{trans} in a 3x3x3 kernel around this voxel and the relative voxel position.

From radiotherapy patients, a ground truth for the tumor delineations is not available. Therefore, validation cannot be performed on this patient group. For the validation of the voxel-wise performance of the model an independent group of 12 prostatectomy patients was used. From a previous study we know that the registration error between the MR images and histopathology is on average about one voxel [2]. This error needs to be taken into account when validating the model. This was done by considering a voxel as true positive even if the tumor tissue was present in a neighbouring voxel. To make the model applicable in a radiotherapy setting, after model validation, the model was stratified to create three different risk levels for tumor presence: high-risk, intermediate and low risk.

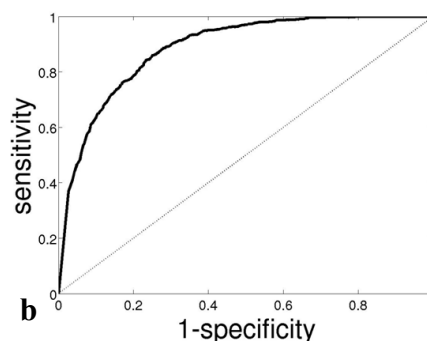
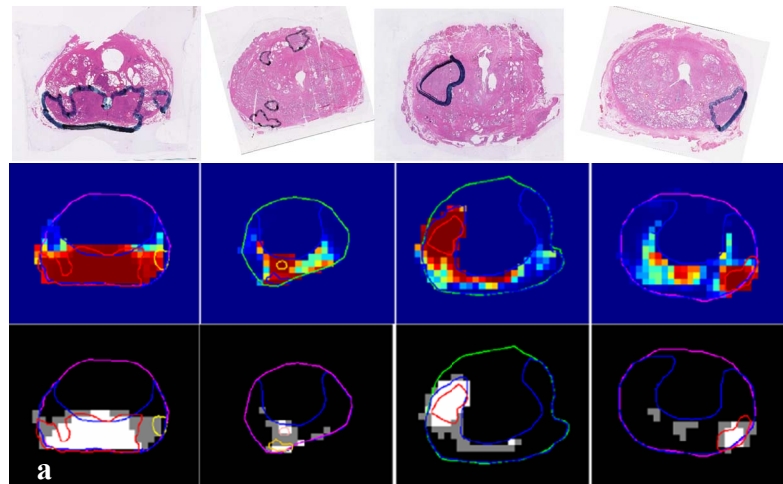
Results

The model gave an area under the receiver operating characteristic curve (AUC) of 0.70 for the prediction of tumor presence in the prostatectomy group. When the registration error between MR images and pathology was taken into account, the AUC further improved to 0.89. We propose that model outcome values with a high positive predictive value (PPV) can be used to define the high-risk regions. Model outcome values with a high negative predictive value (NPV) can be used to define low-risk regions. The intermediate outcome values can be used to define intermediate risk regions. In patients with advanced prostate cancer the complete prostate would be treated with the standard dose. High-risk regions could be treated with an extra boost dose to the tumor tissue. Extra safety margins could be used around the intermediate risk regions.

Discussion

We developed a logistic regression with a high diagnostic performance for voxel-wise prediction of tumor presence. The model output can be used to define different risk levels for tumor presence, which in turn could serve as an input for dose planning. In this way the robustness of tumor delineations for focal boost therapy can be greatly improved.

References [1]Tofts et al. JMRI 1999 10(3):223-32 [2] Groenendaal et al. Radiother Oncol. 2010 94(2):145-50.



a. Four patient examples. Upper row: hematoxylin and eosin stained slices with tumor delineations created by a pathologist. Delineations are copied to the MR images. Middle row: model prediction. Lower row: Stratified risk levels for treatment planning. white: high risk, grey: intermediate risk, black: low risk. b. ROC curve of model performance. AUC=0.89.