The effect of spatial resolution on the correspondence between hematoxylin-eosin stained sections and MR images for prostate cancer

G. Groenendaal[1], M. R. Moman[1], J. G. Korporaal[1], P. J. van Diest[2], M. van Vulpen[1], M. E. Philippens[1], and U. A. van der Heide[1]
[1]Radiotherapy, University Medical Center Utrecht, Utrecht, Utrecht, Netherlands, [2]Pathology, University Medical Center Utrecht, Utrecht, Utrecht, Netherlands

Introduction

For Diffusion Weighted (DW) MRI and Dynamic Contrast-Enhanced (DCE) MRI, high sensitivies and specificities are reported for the diagnosis of prostate cancer. Often, these values are based on the correspondence of imaging and pathology within relatively large volumes inside the prostate. However, for prognosis, therapy selection and the application of focal therapy, the volume and extent of a tumor are relevant. Here, decisions on a voxel level are required. Therefore, we investigated at which spatial resolution a voxelwise validation of MR images with hematoxylin-eosin (H&E) stained sections is meaningful.

Methods

So far, 9 patients with biopsy proven prostate cancer were included. The study was approved by the institutional review board and all patients gave informed consent. Prior to prostatectomy, scans were acquired on a 3 Tesla MRI system. To prevent deformations we chose not to use an endorectal coil. The imaging protocol consisted of a T2w, a DW-MRI and a DCE-MRI exam. T2w: TR/TE = 8396/120 ms, echo train length 13, acquisition matrix 256x256, FOV = 20 cm, slice thickness 3 mm, intersection gap 1 mm. DW-MRI: TR/TE = 5000/54 ms, acquisition matrix = 152 x 107, FOV = 38 cm, 9 averages, EPI-factor = 47, slice thickness = 3 mm, intersection gap = 1 mm, b values = 500, 1000, 2000 s/mm^2. DW-MR images acquired with a b-value of 2000 s/mm^2 were inverted and used for tumor detection during further analysis. Apparent Diffusion Coefficient (ADC) values were calculated from scans made with b values of 500 and 1000 s/mm^2. DCE-MRI: 20 transverse partitions, 2.5 mm section thickness, TR/TE = 4/1 ms, acquisition matrix 160 x 160, FOV 40 cm, flip angle 8, contrast agent Gadovist, concentration 0.1 ml/kg. The DCE-MRI exam yielded 120 acquisitions at 2.4s time interval. Concentration-time curves were analyzed using the Tofts model, yielding 3D maps of the blood flow parameter K^{trans} [1].

Each voxel in the images was labeled as either tumor or non-tumor based on thresholding. We analyzed our data for a range of threshold values to reduce the sensitivity to a specific value.

After prostatectomy, carbon rods were inserted inside the prostate to facilitate registration and validation of the registration. The prostate was cut into slices of ~4 mm. Subsequently, whole mount microscopic sections were cut from the macroscopic paraffin-embedded slices and stained with H&E. The pathologist delineated tumor tissue on the H&E stained sections using a microscope. Both the macroscopic slices and the H&E stained sections including the delineations were digitized. The H&E stained sections were registered to the macroscopic slices using the carbon rods. A 3D reconstruction of the prostate specimen was obtained by stacking of the digitized macroscopic slices, using the carbon rods as landmarks. After this, the T2w MR images were registered to the 3D prostate reconstruction. Carbon rods which were not used for the registration process were used to calculate the errors created by the stacking and the errors created during the H&E-macroscopic slices registration. To calculate the error resulting from the registration of the 3D prostate specimen with the T2w images, delineations of the prostate contours were used. We determined the Dice coefficient representing the correspondence of the tumor as labeled on the H&E stained sections and the MR images. To investigate the spatial resolution at which pathological validation is meaningful, we repeated this procedure at a range of larger voxel sizes. A larger voxel was labeled a tumor-containing voxel if at least one of the subvoxels was labeled tumor.

Results

The complete registration and reconstruction procedure yielded an average error from 1.7 to 3 mm for the different patients. In figure 1 A-E, one of the H&E stained sections is shown, together with the corresponding MR images. The delineation created by the pathologist was copied to the registered MR images.

The Dice coefficient of the tumor on the H&E stained sections and on the MR images was determined for the three thresholds of each imaging modality. The threshold yielding the highest Dice coefficient for all patients was used further.

The Dice coefficient of the tumor on the H&E stained sections and on the MR images is shown in figure 2 for the same patient. Below a voxel size of 0.4 cc, the Dice similarity drops rapidly. This indicates that there is a only a small chance that matching tumor voxels are found on the MR images and on the H&E stained sections within a volume of less than 0.4 cc. Other patients exhibit similar results, with the steep decrease in Dice coefficient found below volumes of 0.4-1.0 cc.

Discussion

Given the small registration errors, the comparison between H&E stained sections and MR images was possible on small volumes inside the prostate. We found good correspondence between the H&E stained sections and the MR images, when we considered suspicious regions on the MR images and tumor on the H&E stained sections as the same pathology when they were located within volumes larger than 0.4-1 cc. For smaller volumes, the validation of our MR images with pathology is less reliable. This also puts a limitation on the accuracy at which tumor volume and extent can be determined.

References

[1] Tofts et al., *JMRI* 1999: 10:223-232
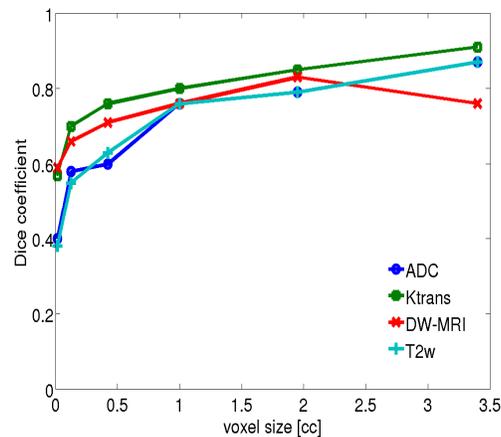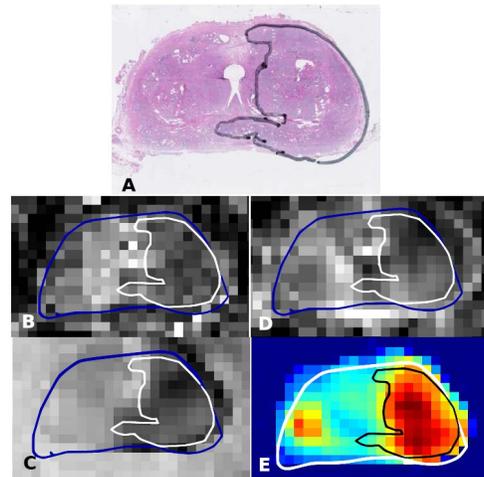
Figure 1: Comparison of the tumor delineated in an H&E stained section with the corresponding MR images **A**. H&E stained section with a delineation created by the pathologist. This delineation is copied to al the registered MR images **B**. T2w image **C**. DW-MRI image **D**. ADC map **E**. Ktrans map. Voxel size 0.016 cc.

Figure 2: Correspondence between suspicious regions on the MR images and tumor on the H&E stained sections given for different voxel sizes