

DCE-MRI for the detection of patients with recurrent prostate cancer after radiotherapy; a matched case-control study.

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Introduction

Patients treated with radiotherapy for prostate cancer are at risk of developing recurrent disease during follow-up. Recurrence rates up to 60% are described in the literature depending on various risk factors, like tumor stage and tumor differentiation grade (1). It is important to detect these recurrences in an early stage, because then curative treatment may still be possible. Validation of dynamic contrast enhanced (DCE-)MRI and T2- weighted (T2w) MRI for the detection of prostate cancer recurrences with biopsy results, showed that this technique is a promising diagnostic tool (2).

However, the interpretation of the DCE-MRI in this population can be difficult because due to irradiation, changes occur in the microvasculature of both tumor and healthy prostate tissue. The goal of this study was therefore to assess the differences in DCE-MRI between patients with and without local recurrent prostate cancer after radiotherapy, to differentiate between radiation effects in prostate tissue and local recurrent tumor growth.

Methods and Materials

Subjects:

15 patients with biopsy-proven local recurrent prostate cancer were prospectively included in this institutional review board approved study. All patients had undergone an MRI exam prior to prostate biopsy, and are referred to as 'cases' in this study. For every case, a matched 'control', free from recurrent prostate cancer, was invited from the follow-up population of our radiotherapy department, and these controls underwent the same MRI exam. Matches were made based on primary radiotherapy modality, follow-up time, primary tumor differentiation grade and clinical tumor stage. For respectively case and controls, mean \pm SD age was 69.1 ± 5.7 and 70.6 ± 4.4 years and mean \pm SD follow-up time 65.4 ± 21.7 and 66.2 ± 23.0 months. In both groups, 6 patients had been treated with external beam radiotherapy and 9 patients with I-125 brachytherapy.

MRI exams:

MRI examinations were performed on a 3 Tesla MRI scanner (Achieva Philips Medical Systems, Best, the Netherlands). The DCE protocol consisted of a 3D spoiled gradient echo sequence (TR/TE 4.0/1.0 ms, flip angle 6°). Scans were repeated 120 times at 2.4s interval. A single acquisition consisted of 20 axial slices of 2.5 mm. The field of view was 40x40 cm², the reconstruction matrix 160x160. For contrast enhancement, 0.1 ml/kg body weight gadobutrol (1.0 M) (Gadovist, Schering) was injected intravenously. Tracer-kinetics modelling was done using the Tofts model resulting in 3D maps of the transfer constant K_{tr}, the extravascular extracellular space (EES) fractional volume v_e and the rate constant k_{ep} (3). In addition, the exam includes 2 anatomical scans: a multislice T2 weighted turbo spin echo (TSE) sequence (TR/TE 8400/120 ms) and a balanced turbo field echo (TFE) sequence (TR/TE 2.8/1.4 ms).

Based on the anatomical scans, the prostate gland and the peripheral zone (PZ) of the prostates were delineated. Furthermore, in cases, 'tumor suspected regions', with increased contrast enhancement based on the DCE parameter K_{tr}, were delineated. In controls, regions of equal volume, containing the highest K_{tr} values outside the urethral area, were delineated within the PZ as a comparison. The K_{tr} data within all delineated volumes were extracted for statistical analysis. The MR images and the extracted K_{tr} statistics were compared between the cases and controls.

Results and discussion

In all 15 cases, regions with elevated K_{tr} were present (1, 2 and 3 locations in resp. 5, 6 and 4 patients) as well as in 14 out of 15 controls (1 and 2 r in resp. 10 and 4 patients) (Fig.1). In 14 controls and in 14 cases a region with elevated K_{tr} was located around the urethra. This may reflect the presence of benign prostate hypertrophy. For the cases, outside the urethral area 9 out of 15 locations with elevated K_{tr} corresponded well with hypo-intense areas on the T2w MR images. However, for controls, locations outside the urethral area (4 locations, n=4) did not match with hypo-intense regions on the T2w images.

Statistical analysis: The mean, mean highest 10% and mean highest 25% (Fig. 2) of K_{tr} in the prostate, PZ and suspected regions were calculated. Differences between cases and controls were tested using the t-test or, if necessary, a non-parametrical test. For the total prostate and PZ, the mean highest 10% and 25% K_{tr} for cases were significantly higher than for controls (resp. p=0.000 and 0.007 for the prostate and p=0.003 and 0.034 for the PZ). The mean K_{tr} did not differ significantly between cases and controls. For the 'suspected region', all of the described statistical measures were significantly higher in cases compared to controls (resp. p=0.000, p=0.003 and p=0.001).

Conclusion

Even though radiotherapy of the prostate is likely to change perfusion characteristics of tissue, DCE-MRI shows a shift towards higher K_{tr} values in cases with recurrent cancer compared to controls. These differences can be used for detection purposes in the follow-up after radiotherapy for prostate cancer. Controls often show an elevated K_{tr}, but this is predominantly located around the urethra, and therefore seems to reflect benign prostate hypertrophy.

References

(1) Agarwal PK et al. *Cancer* 2008;112:307-14. (2) Haider MA et al. *Int J Radiat Oncol Biol Phys* 2008;70:425-30. (3) Tofts PS et al. *J Magn Reson Imaging* 1999;10:223-32.

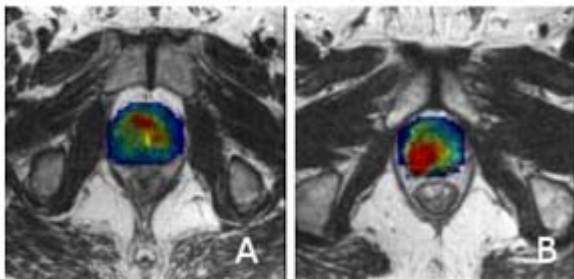


Figure 1: Transversal slice of T2 weighted MR with K_{tr} colour map overlay in a control patient (A) and case with recurrent tumour (B).

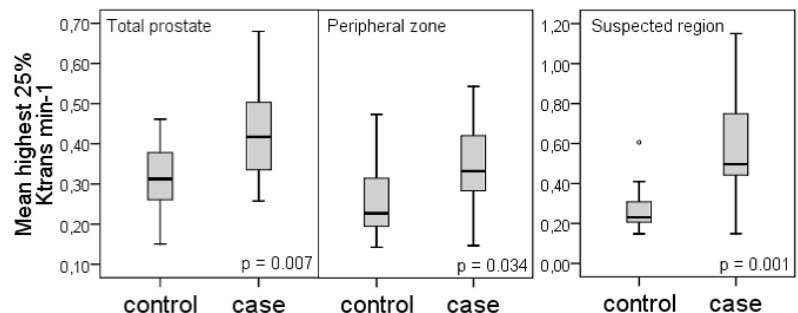


Figure 2: Distribution of the mean highest 25% K_{tr} for the total prostate, PZ and suspected regions in cases and controls.