INTRODUCTION: Prostate cancer (PCa) is the most common malignancy in the Western male population with an incidence of 648,000 and the third leading cause of death in developed countries in 2008 (1). Since not all prostate cancers are life-threatening, an accurate assessment of aggressiveness is essential to prevent overtreatment of indolent cancers. MRI plays an upcoming role in the diagnosis and management of prostate cancer. Next to T2-weighted imaging for detailed anatomical information (2), functional MRI techniques such as Diffusion Weighted Imaging and MR spectroscopic imaging have potential to assess aggressiveness (3;4;5). Dynamic contrast enhanced (DCE) MR imaging has already provided its usefulness in detecting and staging of prostate cancer (6;7). The purpose of this study is to retrospectively validate the performance of pharmacokinetic parameters derived from dynamic contrast enhanced MRI of the prostate at 3T for assessing PCa aggressiveness, with Gleason scores of cancer foci of whole mount section histopathology of resected prostates as the gold standard.

METHODS: The need for informed consent for retrospective use of anonymized clinical data was waived by the institutional review board. Fifty-three patients with histologically proven PCa who underwent multiparametric MR imaging with the use of an endorectal coil at 3T were enrolled in this study before prostatectomy. DCE-images were acquired by using turboflash 3D spoiled gradient echo images with a high temporal resolution, TR 2.4 or 2.9, TE 1.35 or 1.51, flip angle 14 or 10 and slice thickness 3 or 4 mm during a 15mL i. v. bolus injection of a gadolinium chelate (Dotarem®, Guerbet), which was administered with a power injector (Spectris Solaris, Medrad) and followed by a 20mL saline flush. For each patient a region of interest (ROI) was drawn within an area of PCa and a separate ROI was drawn within a non-cancer part of the peripheral zone (PZ) by a radiologist in consensus with a urogenital pathologist, based on the prostatectomy specimens (see fig.1). Calibration of the pharmacokinetic modeling was performed by using a ROI with histologically proven non-cancer PZ tissue as reference tissue to estimate the patient-dependent arterial input function in a method described earlier (8;9). Care was taken to choose the non-cancer tissue for calibration in a non-enhancing homogeneous area, excluding for example peri-prostatic blood vessels. For each ROI the mean, 25th and 75th percentile of the semi-quantitative parameters LateWash (Washout) and Relative Enhancement may be feasible metrics to investigate the potential to assess aggressiveness. According to the literature, there may be a correlation between microvessel density (MVD) and PCa aggressiveness, which could indicate that a lack of significance for DCE and PCa aggressiveness is inherent to a failure of the pharmacokinetic model; however, the current consensus about MVD is that it should not be implemented in routinely performed pathology reports due to for example different scoring techniques and inter-observer variability (11;12). Therefore we cannot make the assumption that the lack of correlation is model-based. The semi-quantitative parameters LateWash and Relative Enhancement showed a correlation with aggressiveness in the PZ for low and high aggressive PCa, but with considerable overlap between the different classes. Since other functional MR techniques also showed potential to assess aggressiveness with considerable overlap, a next step would be to combine these techniques to investigate their complementary value. In the TZ there was no correlation between aggressiveness classes for any of the parameters, probably due to the low number of lesions.

RESULTS: Two patients had to be excluded because their prostate did not contain any non-cancer PZ tissue. The remaining 51 patients had a total of 63 relevant PCa foci (with a minimum volume of 0.5cc), whereof 45 in the PZ, 16 in the transition zone (TZ) and two covering both zones. The ROIs covering both zones were excluded from analysis. In the PZ there were 18, 12 and 16 PCa foci for the low, intermediate and high grade respectively. All parameters were correlated with the thickest section with histologically proven PCa who underwent multiparametric MR imaging at 3T (see fig.1). Calibration of the pharmacokinetic modeling was performed by using a ROI with histologically proven non-cancer PZ tissue as reference tissue to estimate the patient-dependent arterial input function in a method described earlier (8;9). Care was taken to choose the non-cancer tissue for calibration in a non-enhancing homogeneous area, excluding for example peri-prostatic blood vessels. For each ROI the mean, 25th and 75th percentile of the semi-quantitative parameters LateWash (Washout) and Relative Enhancement may be feasible metrics to investigate the potential to assess aggressiveness. According to the literature, there may be a correlation between microvessel density (MVD) and PCa aggressiveness, which could indicate that a lack of significance for DCE and PCa aggressiveness is inherent to a failure of the pharmacokinetic model; however, the current consensus about MVD is that it should not be implemented in routinely performed pathology reports due to for example different scoring techniques and inter-observer variability (11;12). Therefore we cannot make the assumption that the lack of correlation is model-based. The semi-quantitative parameters LateWash and Relative Enhancement showed a correlation with aggressiveness in the PZ for low and high aggressive PCa, but with considerable overlap between the different classes. Since other functional MR techniques also showed potential to assess aggressiveness with considerable overlap, a next step would be to combine these techniques to investigate their complementary value. In the TZ there was no correlation between aggressiveness classes for any of the parameters, probably due to the low number of lesions.

DISCUSSION: For quantitative parameters our results were similar to previous reports showing higher Ktrans, Kep and Ve in prostate cancer of the PZ compared to non-prostate cancer tissue. However, these parameters did not show a significant correlation with aggressiveness. According to the literature, there may be a correlation between microvessel density (MVD) and PCa aggressiveness, which could indicate that a lack of significance for DCE and PCa aggressiveness is inherent to a failure of the pharmacokinetic model; however, the current consensus about MVD is that it should not be implemented in routinely performed pathology reports due to for example different scoring techniques and inter-observer variability (11;12). Therefore we cannot make the assumption that the lack of correlation is model-based. The semi-quantitative parameters LateWash and Relative Enhancement showed a correlation with aggressiveness in the PZ for low and high aggressive PCa, but with considerable overlap between the different classes. Since other functional MR techniques also showed potential to assess aggressiveness with considerable overlap, a next step would be to combine these techniques to investigate their complementary value. In the TZ there was no correlation between aggressiveness classes for any of the parameters, probably due to the low number of lesions.

CONCLUSION: In this retrospective study we found that the semi-quantitative parameters LateWash and Relative Enhancement may be feasible measures to assess the aggressiveness of PCa in the PZ, although due to the overlap between distinct classes further research is needed. Pharmacokinetic parameters Ktrans, Kep and Ve proved its usefulness for detection of PCa in the PZ, however, for the assessment of aggressiveness this study does not show any value in these parameters thus far. The future combination with other functional MR techniques might improve the distinction between the aggressiveness classes.


Acknowledgement ERC Grant agreement n° [243115]