Evaluation of Benign Prostatic Hyperplasia treatment response using Dynamic Contrast-Enhanced MRI

H. Henry[1], H. Polzer[1], J. T. Heverhagen[1], K. T. Baudendistel[1], G. Jia[1], H. Chun[2], H. von Tengg-Kobligk[3], X. Yang[2], A. L. Levine[2], T. J. Rosol[4], M. V. Knopp[1]

[1]Department of Radiology, The Ohio State University, Columbus, OH, United States, [2]Department of Radiology, The Ohio State University, Columbus, Ohio, United States, [3]Department of Radiology, German Cancer Research Center (DKFZ), Heidelberg, Germany, [4]Department of Veterinary Biosciences, The Ohio State University, Columbus, OH, United States

Introduction:

Benign prostatic hyperplasia (BPH) is an age related disease in men as well as beagles [1]. Numerous approaches mostly on the basis of volume measurements were made to demonstrate changes in the gland [2-6]. However, investigations on the usefulness of dynamic contrast-enhanced (DCE) MRI to monitor changes occurring in the disease process or during treatment of BPH are missing. Since DCE-MRI offers functional imaging of microvascular changes of solid organs, the purpose of this study was to demonstrate these changes in the prostate during treatment of BPH. Thereby, the feasibility of therapy-monitoring should be evaluated.

Subjects and Methods:

The study was approved by the local animal care committee. 12 male beagle dogs (mean age ± standard deviation, 4.4 ± 0.9 years) with spontaneous age related BPH (prostates were >2cm on digital palpation) were divided into a treatment group and a control group. The control group received a sham treatment, while in the treatment group a daily dose of 1 mg/kg finasteride (5-α-reductase inhibitor) was administered. All dogs were imaged five times (week -3,0,+4,+8,+12) on a 1.5T clinical scanner (Twinspeed, GE, Milwaukee, WI) using a standard head coil. Besides three dimensional volume measurements in T_1- and T_2- weighted sequences, DCE-MRI measurements were performed in the axial plane using a T_1-weighted 3D SPGR sequence (TR: 7.6ms, TE: 2.6ms, FA: 25°, Matrix 192 x 256, FOV 140mm, 26 slices, slice thickness 2mm, NEX 0.5, acquisition time 24s per volume, 32 time points, total acquisition time 12min 48s). After three baseline acquisitions 0.2 mmol/kg contrast agent (gadoteridol, Prohance™, Bracco Diagnostics, Inc., Princeton, NJ) were administered with an injection rate of 0.2 ml/s followed by a flush of 15 ml saline. The contrast enhancement was evaluated by pharmacokinetic mapping with a two compartment model [7] using color overlay images as well as regional ROI analysis. Motion was assessed and corrected within the DCE images by manual adjustment of the ROI in the individual time points.

We measured the baseline signal intensity (S_0) prior to contrast injection, the maximum signal intensity (S_{max}) after contrast application and the time to reach S_{max} (T_{max}). Additionally, the ratio S_{max}/S_0 was determined.

Results:

Prior to treatment the pharmaco-dynamic analysis showed distinct differences of contrast enhancement characteristics between the periurethral, inner zone and the parenchymal, outer zone in both treatment and control group. For the two pretreatment studies the median values of S_{max}/S_0 in the periurethral zone were twice as large as in the parenchymal zone, whereas the median value of T_{max} was the same in both zones.

During treatment the volumetric measurements of the prostate showed an average volume reduction of approximately 50% in the finasteride group. In addition, pharmacological effects were also revealed by changes of the contrast enhancement characteristics (Fig. 1). While the intensity of contrast enhancement in the parenchymal zone increased after treatment (Fig.2), the slope of the enhancement curve decreased and thereby the T_{max} increased. Neither the periurethral zone of the finasteride group nor both zones of the control group showed notable changes in the contrast enhancement characteristics.

The increase in contrast enhancement of the parenchymal zone in course of the treatment made it more and more difficult to delineate it from the periurethral zone.

Discussion:

During treatment with finasteride the parenchymal zone shrinks and the intensity of contrast enhancement increases which reflects an increase in blood volume per unit of tissue volume. This can be explained by the decrease in tissue volume while the number of blood vessels remains the same. Furthermore, the time to maximum signal intensity is prolonged in the parenchymal zone which demonstrates a longer accumulation period of the contrast agent in the tissue. Since the periurethral zone showed only minimal to no change the results indicate that finasteride is primarily effecting the parenchymal zone.

While our study is a prospectively designed experimental study, it is limited by the number of subjects. Nevertheless, we could demonstrate distinct changes in the perfusion parameters of the parenchymal zone in addition to the volume reduction. Therefore we conclude that DCE-MRI is capable to characterize benign tissue changes in the prostate as well as to monitor the effects of treatment in BPH more accurately than volume measurements alone.

References:

1. Berry et al. Am.J.Physiol 1986; 250: R1039-R1046
2. Murakoshi et al. Acta Pathol.Jpn. 1990; 40: 871-879
3. de la Rosette et al. Eur.Urol. 2003; 44: 346-351
4. Brierly et al. BJU.Int. 2003; 91: 360-364
5. Hoffmann et al. Eur.Urol. 2003; 43: 181-187
6. Tubaro et al. Curr.Opin.Urol. 2003; 13: 17-22
7. Hoffman et al. Magn.Reson.Med. 1995; 33: 506-514

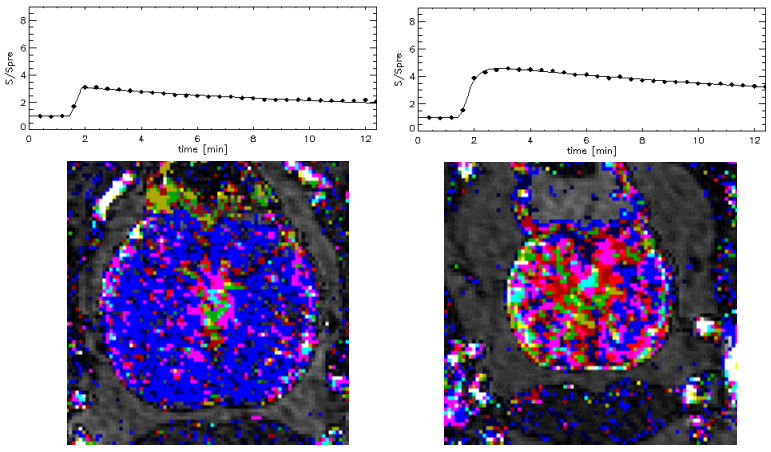

Fig. 1: Evaluation curve of the parenchymal zone with the corresponding color overlay underneath. The left curve shows the time intensity of one dog before treatment which shows moderate contrast enhancement compared to the right curve of the last treatment study which is also resembled by the color overlay image below each curve.

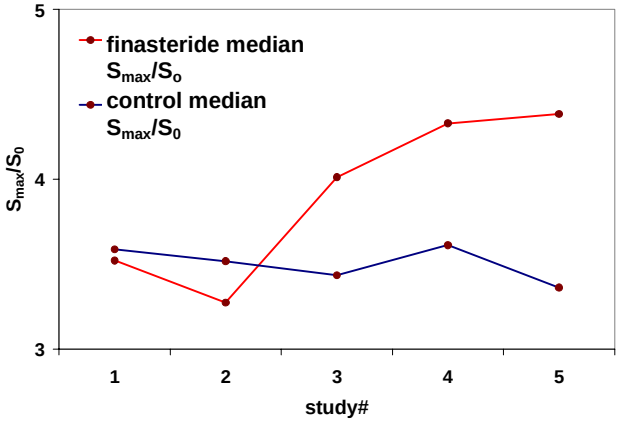

Fig. 2: Median ratio of maximum signal intensity and baseline signal intensity of the parenchymal zone over the five study dates. Study 1 and 2 are before and studies 3 to 5 are during treatment. The increase of the S_{max}/S_{base} ratio in the finasteride group demonstrates the increasing contrast enhancement in the parenchymal zone in course of the treatment.