Quantitative analysis of pharmacokinetic parameters using DCE-MRI of prostate from patients with prostate cancer before and after intensity-modulated radiotherapy.

P. Zamecnik[1], C. Zechmann[2], F. L. Giesel[3], C. Thieke[4], and S. Delorme[4]

[1]Radiology, German Cancer Research Center (DKFZ), Heidelberg, Baden-Württemberg, Germany, [2]Radiology, DKFZ, Heidelberg, Germany, [3]DKFZ, heidelberg, Germany, [4]DKFZ, Heidelberg, Germany

Introduction:

The intensity-modulated radiotherapy (IMRT) has been proven to be an effective therapeutic option to treat prostate cancer [2]. Nevertheless there is relatively high prevalence of biochemical progression after external beam therapy (20-50 %). To facilitate the patient management in such cases functional imaging techniques could be used. Dynamic contrast-enhanced MRI (DCE-MRI) has been proven to have better results for the primary localization of the tumor areas within the prostate and for the localization of the recurrent prostate cancer after external beam radiotherapy than T2-weighted images [1]. To establish DCE-MRI as a relevant tool for MRI-examinations after IMRT it is important to know, which pharmacokinetic parameters could be changed after radiotherapy of the prostate cancer. The aim of this work was to prove the changes of the very common perfusion pharmacokinetic parameters in the prostate using DCE-MRI of patients with prostate cancer after IMRT compared to the values prior radiotherapy in terms of definition of a relevant control parameter.

Material and Methods:

Twenty-four men (mean age 65.2 years) with histologically proved prostate cancer underwent a standardized MRI-examination before and after IMRT. All examinations were performed using a clinical 1.5 T MR imaging system; a surface coil was used. The control MRI followed between 4 and 9 months after the first MRI (mean: 5.8 months). The IMRT started approximately 1 week after the initial MRI (total dose 76 Gy). The imaging protocol comprised usual nonenhanced T2 TSE and T1 TSE sequences, dynamic contrast-enhanced T1-weighted and delayed T1-weigted contrast-enhanced sequences. Parameters of the DCE sequence: FLASH 2D (slice thickness 3 mm, TR 125, TE 3.11, 10-18 slices, 25 measurement repetitions, matrix 128 x 128,acquisition time 4 min 30 sec). As a contrast medium gadopentetate dimeglumine was used. The contrast medium was injected within 30 seconds in weight-adapted dosage 0.1 mmol/kg. The control MRI-examination was performed with an identical imaging protocol compared to the initial MRI, to ensure the intraindividual comparability of the results. The dynamic sequences were evaluated using DynaLab software (Mevis, Bremen, Germany). This software uses a two-compartment dynamic pharmakokinetic model as previously described [3]. to compile colour-coded maps, reflecting pharmacokinetic parameters A (amplitude) and k_{ep} (redistribution rate constant). On the basis of the histological findings (biopsy before radiotherapy), T2-weighted and dynamic contrast-enhanced sequences (colour maps) intraprostatic tumor areas in the initial MRI were identified. Within these areas one slice was chosen, where the tumor area showed the biggest diameter. In this slice a region of interest was drawn in the tumor area and around the whole intersection area of the prostate. The same regions of interest where then used on a similar section in the posttherapeutic images. The amplitude and k_{ep} values before and after IMRT were determined in the tumor areas and in the corresponding intersection area of the whole prostate.

Results:

After IMRT, the k_{ep} showed a significant decrease in the tumor areas and also in the corresponding intersection area of the whole prostate. Mean k_{ep} in the tumor areas prior to IMRT was 8.41± 7.74 min^{-1} , after IMRT was 5.93± 5.64 min^{-1} , p<0,036 (example: Fig. 1 and 2). In the corresponding intersection areas of the whole prostate was the mean k_{ep} prior IMRT 10.25 ± 4.22 min^{-1} , after was 7.60 ± 4.38 min^{-1}, p< 0,027. The amplitude showed a slightly, nonsignificant increase after IMRT, both in the tumor areas and in the corresponding intersection areas of the whole prostate: 1.68 ± 0.29 (prior IMRT) vs. 1.75 ± 0.55 (after) in the tumor areas; in the corresponding intersection area of the whole prostate 1.44 ± 0.37 vs. 1.49 ± 0.26 (significance level 0.05). Mean ratio: tumor volume/volume of the corresponding intersection area of the whole prostate was 18.6 %.

Discussion:

There are no available literature sources about intraindividual comparison of DCE-MRI-based pharmacokinetic parameters of the prostate in patients with prostate cancer prior to and after IMRT. In our study the k_{ep} showed a significant decrease after IMRT, i.e. this parameter is applicable for monitoring of intraprostatic changes after IMRT. On the contrary, the amplitude showed no significant changes after IMRT. One of the possible explanations for this is the nature of k_{ep} as a compound parameter, which depends on several parameters like interstitial space configuration, architecture of vessels, tumor blood flow, i.e. on the vessel permeability and perfusion, which can be influenced by radiotherapy in several ways. In this relation it seems to be important, that DCE-MRI showed in recent studies [1] better results in the localization of the recurrent prostate cancer after external beam radiotherapy then the T2-weighted images. This implies the general presumption, that the use of DCE-MRI as a standard aftercare MRI-examination tool could facilitates the management of the prostate cancer patient, in terms of more precise further diagnostic and therapeutic measures.

References:

1. **Haider MA et al.;** Dynamic Contrast-Enhanced Magnetic Resonance Imaging for Localization of Recurrent Prostate Cancer after External Beam Radiotherapy; Int J Radiat Oncol Biol Phys. 2007 Sep 17

2**. Livi L et al;** Localized prostate cancer treated with intensity-modulated radiotherapy; Tumori. 2006 May-Jun;92(3):197-201.

3. **Hoffmann U et al.** Pharmacokinetic mapping of the breast: a new method for dynamic MR mammography; Magn Reson Med 1995; 33:506–514

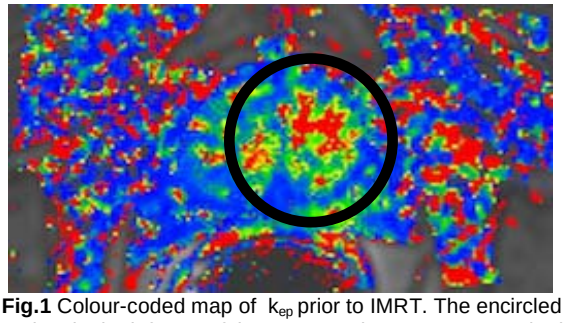

Fig.1 Colour-coded map of k_{ep} prior to IMRT. The encircled region in the left part of the prostate shows tumor area (red and yellow sector) with elevated k_{ep} values.

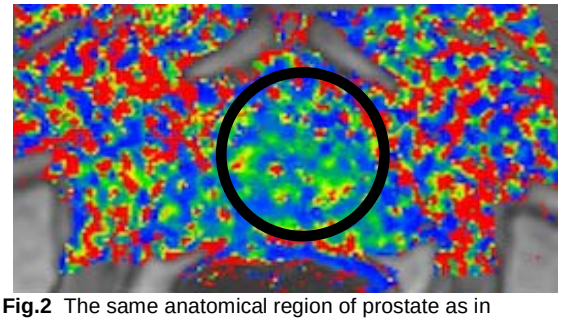

Fig.2 The same anatomical region of prostate as in Fig.1 five months after IMRT, color-coded map of k_{ep}. No elevated k_{ep} values in the initial tumor region.