# DCE-MRI in Endometrial Carcinomas

Renate Gruner[1,2], Ingfrid Salvesen Haldorsen[1], Torfinn Taxt[1,2], and Helga Salvesen[2,3]

*[1]Dept of Radiology, Haukeland University Hospital, Bergen, Bergen, Norway, [2]University of Bergen, Bergen, Bergen, Norway, [3]Dept of Obstetrics and Gynecology, Haukeland University Hospital, Bergen, Bergen, Norway*

Objectives: Endometrial carcinoma is the most common gynecological malignancy in industrialized countries, and the incidence is increasing.Treatment and prognosis is influenced by surgical Federation of Gynecology and Obstetretics (FIGO) stage, histological subtype and grade. Markers for intra tumor angiogenesis such as micro vessel density and vascular proliferation have been reported as prognostic factors in endometrial cancer, and such markers may also be potential predictors for response to anti-angiogenic therapeutics. Advanced MRI methods like dynamic contrast enhanced perfusion weighted imaging (DCE-MRI) and diffusion weighted imaging (DW-MRI) may potentially provide new tools to characterize histopathological and angiogenic subtypes relevant for prognosis and individualization of treatment in endometrial carcinomas (1 - 3). However, no such data has to the best of our knowledge previously been reported in relation to DCE/DW-MRI in endometrial cancers. The purpose of this study was to explore the feasibility of perfusion MRI in endometrial carcinomas and investigate possible correlation between perfusion derived parameters and the apparent diffusion coefficient (ADC) derived from diffusion imaging.

Methods: Preoperative MRIs from ten women (62-84 yrs, mean 74) were analyzed in regions identified as healthy tissue (myometrium) and in tumor regions. All patients (FIGO stage IA through IIIC) were surgically staged according to the FIGO staging system (4). The patients were randomly selected from a larger ongoing study of MRI in endometrial carcinomas. Images were acquired on a 1.5T Avanto system using a 6 channel body coil (Siemens, Germany). In addition to conventional structural T1 and T2 weighted imaging, DCE-MRI and DW-MRI were acquired. DCE-MRI: 12 axial slices 3D FLASH (TE/TR= 1.05/2.64 ms, FA=12º, Matrix 256x256, FoV=30x30mm2, 5mm slice thickness). Multiple pre-contrast images (FA=4º, 8º, 12º, 15º) were used to transform the measured signal intensities to tissue contrast concentrations. Contrast agent (Dotarem) was administered acc.to body weight. DW-MRI: 2D axial (EPI, b=0 and 1000s/mm2, TE/TR= 79/3100ms, Matrix 128x128, FoV=30x30mm2, 5mm slice thickness, NA 12).

An experienced radiologist marked the two regions of interest in each patient, and one additional region of interest covering a blood-feeding vessel in the DCE-MRI (i.e. the arterial input function). However, the quality of the vessel signals was poor and differed substantially between patients. A population based vessel signal, which was individually optimized in each patient using a blind source separation technique (5), was therefore used instead. An in-house implementation of the adiabatic approximation model of Johnson and Wilson (aaJW) was used to analyze the contrast concentration curves in the myometrium and tumor regions in each patient. The aaJW model (6) allowed the estimation of more parameters than the common Tofts model (7), resulting in four independent parameters; blood flow (Fb), blood volume (vb), extraction fraction (E) and the volume of the extravascular extracellular space EES, (ve). ADC values were obtained from the DW-MRI. Statistical comparisons between the two tissue regions and correlation analysis between DCE-MRI and DW-MRI parameters were performed using a significance threshold of $p < 0.05$ (SPSS version18).

Results: The endometrial carcinomas typically displayed lower post contrast enhancement and had faster contrast wash-out compared to normal myometrium (DCE-MRI). There were significantly higher values of blood volume (vb), extraction fraction (E), EES volume (ve) and ADC in the normal myometrium compared to the tumor regions (Related Samples Wilcoxon Signed Rank test, p=0.008). No significant differences in blood flow (Fb) between the two tissue groups (p=0.11). Using a weighted input of ADC and EES volume in a k-means clustering algorithm, it was possible to automatically classify 9 (out of 10) tumor regions and 9 (out of 9; perfusion modeling failed in one case) regions in the myometrium. Combining all 19 regions of interest in one analysis showed that ADC values correlated with blood flow (Fb, p=0.01) and extraction fraction (E, p=0.014), and even stronger with the two volume parameters (vb and ve <0.001, Spearman rank correlation).

Discussion/ Conclusion: These preliminary results show that DCE-MRI acquisition and subsequent modeling are highly feasible in endometrial carcinomas. However, further analyses are needed to understand the large variability in the vessel signals using the current regional approach. Restricted diffusion (lower ADC) was seen in the tumors compared to the myometrium, in agreement with previous reports on mean tumor ADC values in endometrial carcinomas and in normal myometrium (2, 8). The estimated diffusion and perfusion parameters correlated, particularly when comparing all 19 regions in one analysis. It will be interesting to test in larger patient series for correlations between diffusion and perfusion parameters, clinical and histopathological data. To better identify heterogeneity and the underlying pathophysiology in these tumors, studies of the feasibility of voxel-wise analysis are in progress. Studies exploring the potential of DCE-MRI as a marker for angiogenesis and phenotype in endometrial carcinomas are warranted.

References: 1) Kinkel et al Eur Radiol 2009, 2) Shen et al AJR 2008, 3) Harry. Gynecol Onco 2010, 4) Pecorelli.Int J Gynaeco Obstet 2009, 5) Grüner, Taxt. MRM 2006, 6) Lawrence, Lee. J Cereb BF Metab 1998, 7) Tofts et al JMRI 1999, 8) Tamai et al. JMRI 2007