Reproducibility of the apparent diffusion coefficient in liver metastases of colorectal cancer and assessment of correlation with FDG-PET.

L. Heijmen[1], A. Heerschap[2], E. ter Voert[2], W. Oyen[3], H. de Wilt[4], C. Punt[5], L-F. de Geus- Oei[3], and H. van Laarhoven[1]

[1]Medical Oncology, Radboud University Nijmegen, Medical Centre, Nijmegen, Gelderland, Netherlands, [2]Radiology, Radboud University Nijmegen, Medical Centre, Nijmegen, Netherlands, [3]Nuclear Medicine, Radboud University Nijmegen, Medical Centre, [4]Surgery, Radboud University Nijmegen, Medical Centre, [5]Medical Oncology, Radboud University Nijmegen, Medical Centre

Introduction: Approximately 50% of primary colorectal cancers disseminates, predominantly to the liver. Irresectable metastatic colorectal cancer is treated with systemic therapy. Since only 40%-60% of patients responds to this potentially toxic treatment, early response monitoring is desirable. Several studies have shown promising results using diffusion weighted imaging (DWI) [1-3]. However, to the best of our knowledge, no reproducibility studies have been performed for DWI in liver metastases. Data on reproducibility are essential to ascertain the magnitude of changes detectable in the apparent diffusion coefficient (ADC). This is especially important for early response evaluation, since changes shortly after start of treatment may be small.

As ADC values are assumed to reflect cell (membrane) density a correlation with FDG uptake in PET is expected as been shown in breast cancer and rectal cancer [4;5].

Aim: to assess the reproducibility of DWI and the correlation between DWI and FDG-PET in liver metastases of colorectal cancer.

Methods: Patients with one or more liver metastases of colorectal cancer, who were scheduled for metastasectomy, were approached for participation in this study. So far 16 patients have been included and analyzed. Updated results will be presented. DWI was performed on a Siemens 1.5T scanner with three gradients (b-values: 50-300-600 sec/mm^2.) A 3-dimensional region of interest (ROI) was drawn around each tumor. Voxel values were exported to excel and analyzed in a histogram (comparing p10, p25, p75, p90, mean and area under curve (AUC). [Fig. 1] Reproducibility was assessed using a Bland Altman analyses for the AUC, mean ADC, the p10, p25, p75 and p90 value. Coefficient of reproducibility and limits of agreement were calculated.

Before surgery also FDG-PET-CT was performed on a hybrid PET/CT scanner (Biograph Duo, Siemens Medical Solutions USA, Inc., Knoxville, TN, USA). For PET analyses, ROI's were drawn around the lesions that were 41% of the maximum standardized uptake value (SUV) above the background value. Maximum and average SUV were recorded. The correlation between the average ADC and SUV values was assessed using the Pearson correlation coefficient.

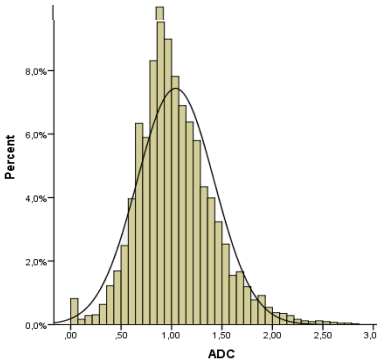

Fig. 1 Typical histogram of ADC values in a tumor. The curve in black shows the normal distribution curve.

Results: For all characteristics of the histogram diffusion weighted imaging showed similar reproducibility. Coefficient of reproducibility was just below 0.3 (0.27) x10^{-3} mm^2/sec for mean ADC values, and around 0.3 x10^{-3} mm^2/sec (range 0.28-0.33 x10^{-3} mm^2/sec) for p10, p25, p75, p90 and AUC. Mean ADC value of the tumors was 1.2x10^{-3} mm^2/sec.

In fig. 3 limits of agreement are shown in red and are consistently close to +0.3 and -0.3 x10^{-3} mm^2/sec. In gray, around zero, the mean difference is shown, indicating that there is no systemic anomaly between the first and second scan. [fig.3]

A trend towards a negative correlation between mean ADC and SUVmean was observed (-0.44, p=0.10).

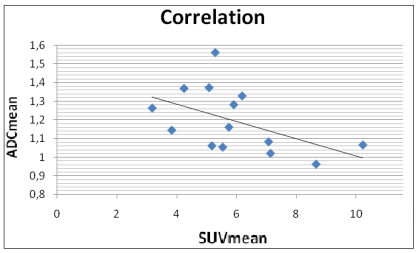

Fig. 2 Correlation between the mean apparent diffusion coefficient (Y-ax) and mean uptake of FDG in the tumors (X-as). Averages between first and second scans were taken.

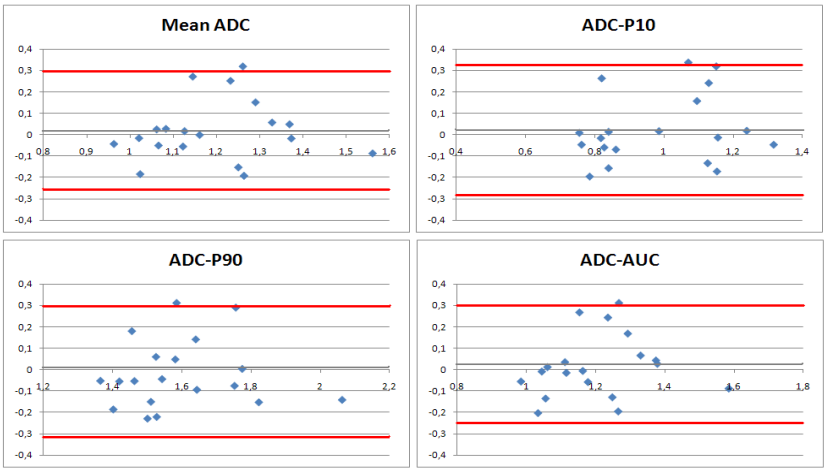

Fig. 3 Bland Altman analyses of different characteristics of the ADC histogram. On the Y-axis the difference in the measured parameter between the first and second scan is shown, on the X-axis the mean value of the measured parameter of the first and second scan. In red the limits of agreement are shown.

Discussion and conclusion: DWI showed a good reproducibility. Variability within one patient seemed smaller than changes in the parameters that can be expected from treatment. Not only the mean ADC value, but also the distribution of ADC values showed a good reproducibility, enabling the use of histograms to assess treatment effects on ADC. Changes larger than 0.3 x10^{-3} mm^2/sec in ADC value can be confidently detected in all ranges of the histogram. A significant correlation between ADC values and SUV, as described in breast cancer and rectal cancer, was not observed in our study of colorectal liver metastases, although a trend towards a negative correlation was seen. This could be explained by the shared effect of dense cellularity and cell turnover; giving both a high metabolism and uptake of FDG and a low ADC value.

References

[1] Cui Y et al. Radiology 2008;248:894-900. [2] Findlay Met al. J Clin Oncol 1996;14:700-708. [3] Koh DM et al. AJR Am J Roentgenol 2007;188:1001-1008. [4] Gu J et al. Mol Imaging Biol 25-9-2010. [5] Nakajo M et al. Eur J Nucl Med Mol Imaging 7-7-2010.