"Does Higher r1 Relaxivity Transfer in Improved Vessel Enhancement of the Run-off Vasculature?" - Evaluation of Macrocylic Gadolinium Chelates for Peripheral MR-Angiography at 3 T by an Inter-individual Comparison of Gadobutrol vs Gadoterate Meglumine, Both Injected at the Same Dose Level of 0.07 mmol/kg BW

U. I. Attenberger[1], M. Voth[2], A. Luckscheiter[3], S. Haneder[1], S. O. Schoenberg[1], and H. J. Michaely[1]

[1]Department of Clinical Radiology and Nuclear Medicine, University Medical Center Manheim, Mannheim, Germany, [2]Bayer Schering AG, Berlin, Germany, [3]University of Heidelberg, Heidelberg, Germany

Purpose: Since nephrogenic systemic fibrosis (NSF) has been linked to gadolinium-chelate administration in patients with impaired renal function [1], contrast agent dose and chelate stability have attracted broad attention. Numerous studies have demonstrated linear compounds to be the least stable, whereas the macrocyclic compounds are the most stable [2]. Among the macrocyclic contrast agents gadobutrol is characterized by the highest R1-relaxiviy compared to gadoterate meglumine and gadoteridol [3] The aim of this study was to evaluate the enhancement characteristics and the image quality of gadobutrol and gadoterate meglumine for peripheral MR-angiography (MRA) with a low-dose regime of 0.07 mmol/kg body weight.

Material and Methods: Out of 172 patients with PAOD 2x21 age, sex and MDRD matched groups were drawn. Both groups (n=21 per each group) underwent a continuous table movement (TimCT) MRA (TR/TE 2.4/1.0 ms/ FA 21°, voxel size 1.2mm^3) for the entire run-off vessels on a 3 T MR scanner (Siemens Tim Trio). Gadobutrol, diluted with sodium 1:1 was injected at a dose level of 0.07 mmol/kg BW in group 1 and compared to gadoterate meglumine, injected at the same dose level and injection rate in group 2. Injection rate was 1.5 ml/sec followed by a 20ml saline flush injected at the same rate. Based on a subtraction technique SNR, CNR and CE ($SI_{post\text{-}contrast}$-$SI_{pre\text{-}constrast}/SD_{noise}$) were analyzed for 7 vessel segments in both groups and the results were compared by an unpaired student`s t-test. Image quality was assessed for 17 vessel segments by two readers, blinded to all data, on a four-point Likert-type scale (1 representing non-diagnostic, 2 moderate, 3 good visualization, 4 representing excellent visualization). Results were compared by an unpaired Wilcoxon test. A p<0.05 was chosen to indicate statistical significant difference. The interobserver agreement was quantified using kappa statistics.

Results: Gadobutrol revealed higher SNR and CNR values in all vessel segments, with a statistically significant different SNR in 5 out of 7 and CNR in 6 out of 7 vessel segments. The SNR values ranged from 38.8±33 to 14.7±11.3 for gadobutrol, and from 20.2 ±10.3 to 9.3±3.1 for gadoterate meglumine. The CNR values ranged from 35.5±30 to 11.5±8.8 for gadobutrol and from 18±9.9 to 6.3±2.7 for gadoterate meglumine. The overall CE was also statistically significant different with higher CE values for gadobutrol (p = 0.00044). For image quality analysis 714 judgements ([21x17]*2) were made in total by each reader; 326 vessel segments were assessed in group 1 (gadobutrol), 300 vessel segments were assessed in group 2 (gadoterate meglumine). In group 1, 29 vessel segments could not be assessed within the calf station whereas in the comparator group 41 vessel segments were not assessable. The median values for the thigh and calf station are given in Table 1. For both readers the overall median value was 4 for gadobutrol whereas gadoterate meglumine revealed a lower overall median value of 3. Image quality was assessed statistically significant different by both readers (reader 1 p < 0.0001, reader 2 p < 0.0001). The interobserver agreement was κ=0.935 for gadobutrol and κ=1 for gadoterate meglumine. Figure 1 illustrates an example for image quality revealed with gadoterate meglumine and gadobutrol respectively.

Table 1- Median values of both readers for the thigh and calf vessels are given. Gadobutrol revealed higher median values for every single vessel segment assessed, with a p value indicating statistically significant difference (p< 0.05).

		Profunda femoris artery	Superficial femoral artery	Truncus	Anterior tibial artery	Posterior tibial artery	Fibular artery
Reader 1	gadobutrol	4	4	4	4	4	4
	gadoterate meglumine	3	3	3	3	3	3
Reader 2	gadobutrol	4	4	4	4	4	4
	gadoterate meglumine	3	3	3	3	3	3

Conclusion: The results illustrate that gadobutrol, when applied at the same gadolinium dose per weight, provides markedly higher SNR and CNR values than gadoterate meglumine, which is most pronounced in the smaller vessels of the calf station. The preliminary results of this ongoing study suggest that low-dose MRA minimizing the risk of NSF can be best performed with gadobutrol.

References:
[1] Rydahl C et al, Invest Radiol 2008.
[2] Schmitt-Willich H, Br J Radiol 2007.
[3] Rohrer M et al, Invest Radiol 2005.

Figure 1 illustrates the image quality of gadoterate meglumine (a) *vs* gadobutrol (b). Especially the distal calf vessels could be depicted more clearly using gadobutrol, which was also reflected by the statistically significant higher median values for gadobutrol for both readers.