Excretion rate and distribution volumes in common marmoset monkeys after slow and fast injection of Gadobutrol

Gunther Helms[1,2], Christina Schlumbohm[3], Enrique Garea-Rodriguez[4,5], and Eberhard Fuchs[5]

[1]*Medical Radiation Physics, Lund University, Lund, Scania, Sweden,* [2]*Cognitive Neurology, Göttingen University Medical Center, Göttingen, Lower Saxony, Germany,* [3]*Encepharm Inc., Göttingen, Lower Saxony, Germany,* [4]*Neuroanatomy, Albert-Ludwigs-University Freiburg, Freiburg, Badenia, Germany,* [5]*Clinical Neurobiology Group, German Primate Center, Göttingen, Lower Saxony, Germany*

Target audience

preclinical researchers

Introduction

The common marmoset monkey (*Callithrix jacchus*) is a small New World primate. It is increasingly used as a model for human neurodegenerative diseases (1,2). Acute inflammatory lesions are detected by MRI enhancement after intravenous application of gadolinium-based contrast agents. By serial measurements of the longitudinal relaxation rate R1=1/T1, we observed a significant increase in excretion half-time and distribution volume (DV) after rapid injection of Gadobutrol in marmosets.

Methods

Marmoset monkeys (3-17 yrs, 340-520 g) were scanned in supine position under general anesthesia [Diazepam (0,3mg/kg i.m.); Alfaxam®; (10mg/kg i.m); Robinul® (0.01mg/i.m. per animal)] in a clinical 3T MR scanner (Siemens TIM TRIO, Erlangen, Germany) using an 8 channel wrist coil (3). Injection anesthesia was followed by inhalation anesthesia with 1% isofluorane in a 30:70 O2:N2O mixture after intubation. The excretion of the gadolinium (Gd) contrast agent Gadovist® (triple dose 0.3 mM/kg body weight) was studied in three animals by consecutive R1 mapping on two occasions: after slow (during approx 2 min) and after more rapid injection into the sapheneous vein (approx. 15 sec). Ethics approval had been obtained from the authorities of the federal state of Lower Saxony.

MRI was performed at isotropic resolution in oblique axial orientation with a 128 mm field-of-view (FOV) in read-direction aligned to the body axis. With a phase FOV of 48 mm, fold-over artifacts were limited to the shoulders. T1-w(eighted) 3D MRI was performed using MP-RAGE (TI = 0.9 s, a = 9°, TR = 2.25 s, BW = 200 Hz/px, 4:19 min) (Fig. 1). Multi-echo FLASH was used for quantitative multi-parameter mapping at 0.5 mm resolution as in (4). Seven alternating gradient echoes were acquired at TE = 3.69, 7.38, … 25.83 ms (BW = 300°Hz/px, TR = 30 ms) with predominant T1-w (α = 28°) alternating with PD-w (α = 5°).

Dicom images were converted to 3D Nifti volumes in the neuroscience RL convention. Using a marmoset head template developed in house, the T1-w MP-RAGE volume was aligned to the intercommissural orientation and interpolated to 0.25 mm. It the served as an individual reference for the averaged T1-w and PD-w sets (FSL 4.1 lineal registration tool, FLIRT, www.fmrib.ox.ac.uk/fsl). Maps of R1 were calculated as described in (5) and evaluated over a region-of-interest (ROI) were placed in the straight sinus using MRIcro. A mono-exponential transition was fitted with the baseline R1 defining the endpoint and neglecting intial outliers The DV was calculated from the extrapolated R1 amplitude using a relaxivity of 3.6 1/s/mM (6).

Results

After slow injection an exponential time course of R1 was observed with an excretion halftime of 26±4 min as reported earlier (3). A rapid injection, however, resulted in initial high outliers within the first 15 min (Fig. 2). The following excretion was consistently slower (62±8 min) and of lower amplitude indication a larger DV (0.36±0.01 l/kg) as compared to slow injection (0.26±0.02 l/kg). The baseline R1 values were consistent (slow: 0.53±0.10 1/s; fast: 0.52±0.05 1/s). After 15 min of equilibration, similar values of R1 were measured in the sinus and in cortex (about 5-7% increase with only small effects on the GM-WM contrast).

Discussion

Using dual angle R1-mapping in marmosets we report bolus effects, slower excretion and increased distribution volume of Gadovist after rapid injection. Spatial B1 correction of R1 was not applied due to the small head size. A higher value of relaxitivity (5 1/s/mM obtained from (7)) yielded DV's of up to 0.5 l/kg. The study shows the limits of a single compartment model for Gd excretion. The strongest increase in distribution volume was observed in an obese animal, so it may be speculated on implication of fatty tissue. Slow injection is beneficial and an equilibration delay of at least 15 minutes is recommended when performing Gd-enhanced MRI in marmosets, as suggested earlier (2).

References

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Figure 1: sagittal view of T1-w MP-RAGE prior (A) and after (B) Gadovist

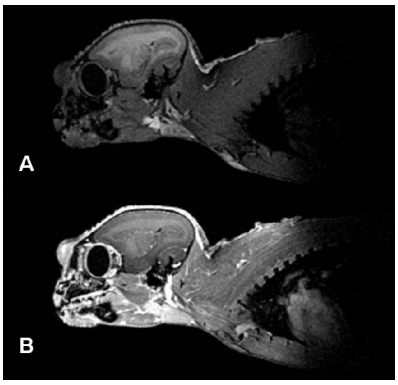

Figure 2: R1time course after fast and slow injection in one animal