Table 3. Approximate reconstruction times (10 iterations, 16 subsets and 1 million photons per projection) for different MC-based scatter compensation acceleration schemes. Reconstructions were performed using 2.33 GHz Pentium processor with 8 GB RAM.

Scatter compensation method	Acceleration method	Time (min)
No compensation		0.8
MC-based	No acceleration	55.6
	Coarse grid	53.4
	Intermittent	11.6
	Coarse grid + intermittent	11.2

The comparison studies for the scatter compensation methods were performed with $64 \times 64 \times 64$ matrix sizes and coarse-grid down-sampling factor of 2 was used, because larger down-sampling factors could not fully preserve the details of the scatter projections (figure 1). With larger matrix sizes than $64 \times 64 \times 64$ larger down-sampling factors could probably be used for higher acceleration. This was not studied in this work, because in the case of cardiac SPECT $64 \times 64 \times 64$ matrix size is usually considered the standard.

The acceleration achieved with the coarse grid scatter modelling depends also on the implementation of the MC simulator that is used in the forward-projection. As mentioned, our MC simulator is based on the delta scattering technique (Woodcock *et al* 1965), which allows calculation of the photon interaction points without time-consuming ray tracing. Therefore, the coarse-grid scatter modelling provided acceleration mainly because the collimator response and attenuation modelling were performed with the sparser matrix. In the case of 1 million simulated photons per projection the time needed to model the collimator response and attenuation is, however, only a small fraction of the time that is spent in sampling the various probability distributions in the MC calculations. Thus the speed-up provided by the coarse-grid scatter modelling is quite small, but can be much greater if a smaller number of simulated photons are used. In addition, if a ray-tracing-based MC algorithm is used instead of delta scattering, coarse-grid scatter modelling will probably increase the speed much more, because the efficiency of ray tracing depends heavily on the matrix size.

In this study the scatter projections were not noticed to change markedly after two iterations, and thus in the intermittent scatter modelling scheme scatter projections were updated only during the first two OS-EM iterations. The number of scatter iterations needed may, however, depend on the imaging situation as mentioned by Kadrmas *et al* (1998) and should therefore be checked before using intermittent scatter modelling as an acceleration method.

One important thing that was not considered in detail in this work is the number of simulated photons per projection. We chose the 1 million photons per projection according to our preliminary studies, where we compared the quality of images reconstructed using different number of simulated photons and noticed that using over 1 million photons per projection does not lead to a significant increase in image quality. The performance of MC-based scatter compensation is, however, quite complicated because it is not only influenced by the number of simulated photons but also by the interplay of noise in attenuation map/projection data and the number of simulated photons. Therefore, a detailed study of noise effects, e.g. similar to the one presented by de Wit *et al* (2005), is probably needed in the future. If different number of photons per projection are to be used the speed-up factors might not be the same as in table 2.

Faster reconstruction times with MC-based scatter compensation than those shown in table 3 have been presented in the literature (e.g. de Wit *et al* (2005) and Xiao *et al* (2006)). This speed difference is probably mainly related to algorithm implementation. Our reconstruction algorithm is not yet fully optimized, and we believe that we can greatly reduce the execution time of our reconstruction. In addition to direct code optimization, we are also planning to parallelize our code for multi-core processors. The acceleration methods presented in this work should be very suitable for different parallelization schemes, because they do not affect the general structure of the OS-EM reconstruction algorithm.

5. Conclusions

We conclude that both the coarse grid and the intermittent scatter modelling methods are suitable for accelerating MC-based scatter compensation, and with these methods MC-based scatter compensation is a promising alternative for clinical cardiac SPECT.

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Use of a Clinical MRI Scanner for Pre-clinical Research on Rats

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RUNNING HEAD: Use of a 3-Tesla MRI Scanner for rat brain imaging

Key Words:
Quantitative mapping; human whole-body 3-Tesla MRI scanner; single dose of Gd-DTPA; dynamic susceptibility contrast (DSC); pre-clinical research; rat brain

Abstract (150words)

This study focused on evaluating the feasibility of rat brain imaging by use of a human whole-body 3-Tesla magnetic-resonance-imaging (MRI) scanner with developed transmit-and-receive radiofrequency coils.

The T_1-, T_2- weighted images obtained showed reasonable contrast. Acquired contrast-free time-of-flight magnetic-resonance-angiography images clearly showed the cortical middle-cerebral-artery (MCA) branches, and inter-hemispheric differences could be observed.

Dynamic-susceptibility-contrast MRI at a 1.17 mm^3 voxel resolution, performed three times following administration of gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA, 0.1 mmol/kg), demonstrated that the arterial input function (AIF) can be obtained from the MCA region, yielding cerebral blood flow (CBF), cerebral blood volume, and mean transit time (MTT) maps. The parietal-cortex (Pt)-to-hypothalamus (HT) CBF ratio was 45.11±2.85 %, and the MTT was 1.29±0.40 sec in the Pt and 2.32±0.17 sec in the HT region. A single dose of Gd-DTPA enabled assessment of AIF within the MCA territory and of quantitative CBF in rats.

Introduction

Magnetic-resonance-imaging (MRI) has been widely used in pre-clinical research on experimental small animals. Studies have typically been aimed at understanding the pathophysiologic status and for evaluating the efficacy/side effects of newly developed treatments, such as pharmaceutical and regenerative medicine. Recently, a different idea has surfaced: the use of a human whole-body MRI scanner for small-animal imaging [1]. Although small-animal dedicated scanners are superior to clinical scanners in terms of providing a better signal-to-noise ratio, the available pulse sequences are different from those on clinical scanners, and the magnetic field strength is often much higher. Small-animal imaging with clinical scanners is important for directly addressing clinical questions and/or identifying the source of signal changes, including various disease conditions in a clinical setting.

Smith et al. [2] demonstrated that anatomic brain T_1- weighted (T_1W) images and T_2-weighted (T_2W) images can be obtained for healthy rats by use of a 1-Tesla clinical MRI scanner with a specially designed radiofrequency (RF) coil, given a reasonable spatial resolution ($0.1953 \times 0.1953 \times 2.5$ mm, 24 min of T_1W and 48 min of T_2W). The image contrast was sufficiently high for distinguishing the cortical gray matter from the white matter (corpus callosum (CC)), as well as the lateral ventricle (LV) and interpeduncular cistern (IPC) from the thalamus (Thal). Guzman et al. [3] employed a clinical 1.5-Tesla MRI scanner with a commercially available RF coil and demonstrated that both T_1W and T_2W images can be obtained with good contrast, a reasonable spatial resolution of $0.3125 \times 0.3125 \times 1.5$ mm, and an acquisition time of 19 min 51 sec, as well as $0.35156 \times 0.375 \times 1.5$ mm at 8 min 34 sec, corresponding to T_1W and T_2W images, respectively. Other investigators [4] applied a clinical 1.5-Tesla MRI scanner with a 3-inch-diameter circular receive-only surface coil to assess anatomic images. Their images can be of use in the evaluation of the pathophysiologic status of stroke [4] and cancer [5, 6], as well as the effects of neural excitotoxicity [3]. There were also several studies with a clinical 3-Tesla MRI scanner fitted with commercial and/or hand-made RF coils for investigating the pathophysiology of stroke [7, 8] and brain tumors in rats [6, 9, 10]. Generally speaking, anatomic images with better contrast can be obtained in a stronger magnetic field, although there are additional factors which may influence the signal-to-noise ratio (SNR) or spatial resolution of anatomic images. Contrast-free time-of-flight magnetic-resonance angiography (TOF-MRA) can also be obtained on rats with a reasonable spatial resolution by use of a clinical 3-Tesla MRI scanner with a single-turn solenoid coil [11].

Dynamic-susceptibility-contrast MRI (DSC-MRI) [12] has been widely used in clinical diagnosis, particularly in patients with stroke [13-19] and tumors [20]. The application of clinical MRI scanners has been extended to DSC-MRI studies of small-animals with stroke [21, 22] and tumors [23] by use of a 1.5-Tesla MRI scanner. Up to now, small-animal studies have been performed on 1.5-Tesla MRI scanners only, and 3-Tesla scanners have not yet been employed. This is largely attributed to the fact that the susceptibility-induced inhomogeneous magnetic field may cause more serious distortion of the images at a higher static magnetic field. In DSC-MRI studies, the echo planar imaging (EPI) technique is mainly used because fast acquisition is required for accurate tracking of the bolus passage of MR contrast agents. The EPI technique, however, is very sensitive to magnetic field inhomogeneity, and thus the EPI images of small-animal brains may be severely distorted. The gradient slew rate (SR) is not high enough to support sufficiently short echo spacing period, when clinical scanners are used for high-spatial resolution imaging of small objects. Moreover, injected materials may cause further distortion [24]. Currently, it is unknown how severely dynamic EPI images of small-animal brains will become distorted on a 3-Tesla clinical scanner. The arterial input function (AIF) is also questionable. To the best of our knowledge, no DSC-MRI studies of small-animal brains on 3-Tesla clinical scanners have been reported.

This study was aimed at evaluating the feasibility of a human whole-body 3-Tesla MRI system developed for small animals, particularly for DSC-MRI with a single dose of gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA). The quality of various images, including the anatomic T_1W images, T_2W images, TOF-MRA images, and DSC images, was tested, and the availability of the AIF obtained from the rat brain was evaluated.

Materials and Methods

Subjects

The subjects were three healthy adult rats supplied by Japan SLC, Inc. (Shizuoka, Japan). All three rats were males, and they ranged in age from 20 to 24 weeks. Their weight range was between 400 to 600 grams. Anesthesia was administered with an intramuscular injection of ketamine (33 mg/kg; Daiichi-Sankyo Co., Ltd., Tokyo, Japan) and xylazine (6.6 mg/kg; Bayer Yakuhin, Ltd., Osaka, Japan). The first rat (Sprague-Dawley, SD) was used for T_1-W and T_2W imaging of the whole brain. The second rat, also a SD, was used for contrast-free TOF-MRA imaging. The third was a Wistar rat, which was used for a Gd-DTPA (0.1 mmol/kg; Bayer Yakuhin, Ltd., Osaka, Japan)-enhanced DSC-MRI sequence. Experiments were carried out according to the protocol approved by the Local Committee for Laboratory Animal Welfare, National Cardiovascular Center, Osaka, Japan.

MRI acquisition

A human whole-body 3-Tesla MRI scanner (Signa, GE Healthcare, Milwaukee, WI, USA) equipped with a 55-cm bore was employed in this study. The gradient coil system was capable of providing the maximum amplitude of the gradient at 40 mT/m, and at an SR of 150 T/m/s. All sequence programs employed in this study were designed for clinical studies.

Two solenoid coils designed for rats were specially developed to cover the whole brain, which are capable of both transmitting and receiving RF pulses. The three-turn solenoid coil, which had a diameter of 42 mm and a length along a cylindrical axis of 18 mm, was attached to an apparatus made of acrylic mold as shown in Fig. 1. All components of the stereotaxic apparatus consisted of non-magnetic materials that fixed the head position of the rats during data acquisition. The RF coil was designed to have an impedance of 50 Ω at a resonance frequency of 127.76 MHz. An additional single-turn surface coil of 62 mm diameter was also developed for better homogeneity, and was used for a single slice of DSC-MRI. The RF power had to be reduced in these coils below that of the standard human head coil because of the diameter of the small coil. The transmission signal was therefore attenuated to 20 dB, which allowed the use of automated scanner software including the calibration of the RF transmission power and receiver gains. All rats were fixed on the stereotaxic apparatus. They were placed at the center of the gantry and oriented with the cranio-caudal axis perpendicular to a static magnetic field. Their heads were positioned inside the coil toward the cranio-caudal direction.

T_1W images were obtained with a conventional two-dimensional fast spin echo (2D-FSE) sequence. The repetition time (TR) was 1500 ms [10]. The echo time (TE) was fixed at 14 msec. The echo train length (ETL) was 3. The field of view (FOV) was set at 40×30 mm^2, the slice thickness at 1.5 mm, the slice gap at 0.5 mm, the number of excitations (NEX) at 10, and the band width (BW) at 31.3 kHz. The acquired matrix (256×160) was interpolated, and null pixels were added in k-space to produce square matrices of 256×256. The acquisition time was 10 min 3 sec.

T_2W images were obtained with a 2D-FSE and the following imaging parameters: TR 4100 ms, TE 128 ms, ETL 14, FOV 40×30 mm, slice thickness 1.5 mm, slice gap 0.5 mm, NEX 8, BW 31.3 kHz, acquired matrix 256×160, zero-filled to 256×256, phase direction ventral-dorsal, and an acquisition time of 11 min 2 sec.

TOF-MRA was performed by use of a three-dimensional flow-compensated spoiled gradient recalled (3D-SPGR) sequence prepared with magnetization transfer and with TR 53 ms, TE 5.5 ms, flip angle (FA) 45 degrees, BW 16 kHz, FOV 8×6 cm, slice thickness 0.2 mm, 1 acquired slab of 512×512×64, a voxel resolution 0.156 × 0.156 × 0.2 mm^3, NEX 1, and an acquisition time of 21 min 46 sec.

DSC images were obtained following the intravenous administration of Gd-DTPA to the T_2*-weighted gradient echo dynamic images. A bolus of Gd-DTPA (0.1 mmol/kg) was injected manually into the tail vein with a 22-gauge catheter via one meter of polyethylene tubing (PE50, internal diameter: 0.58 mm / outer diameter: 0.965 mm, Becton Dickinson and Company, Franklin Lakes, NJ, USA), and was followed by an additional administration of saline (1.0 ml). A multi-shot EPI with the number of shots at 2 was employed for improving EPI distortion and temporal resolution. Imaging parameters were TR 142 ms, TE 22.1 ms, FA 20°, FOV 40×40 mm, and a matrix size of 64×64, leading to a pixel size of 0.625×0.625 mm^2. The slice thickness was 3 mm in single slice around the hypothalamus (HT). The temporal resolution was 0.284 sec per image, and the acquisition time was 1 min 15 sec. This assessment was repeated three times at intervals of 40 min and 10 min, corresponding to the 1st-2nd and 2nd-3rd scans, respectively.

Data analysis

All MRI images were reconstructed on the same workstation provided for the GE Signa 3-Tesla scanner as used for the clinical programs. Then the images were transferred to a Linux workstation. Lastly, data analysis was carried out by use of in-house and commercial software program.

To evaluate the T_1W and T_2W image quality, we calculated the contrast-to-noise ratio (CNR) with an inter-tissue method [25-27] as follows: $CNR = (\pi/2)^{1/2} (SI_a - SI_b) / SI_{air}$, where SI_{air} represent air-mean-signal-intensity, SI_a and SI_b represent the signal intensities of tissue *a* and tissue *b*, respectively.

Angiograms were created by generation of the partial maximum intensity projection (MIP) with a commercial software programs (Virtual Place Liberty (VPL), AZE Co. Ltd. Tokyo, Japan). Visible middle cerebral artery (MCA) branches and left to right differences of MCA were carefully investigated.

For the DSC image slice section containing the internal carotid artery (ICA) and/or MCA, a series of images were carefully observed. A region of interest (ROI) was selected in the MCA region from which the AIF was obtained. Attention was paid, with the help of other anatomic information. For avoiding the susceptibility artifacts caused by air in the trachea, the area of the arterial circle of Willis was excluded in the definition of the AIF. The anterior cerebral artery was also excluded, because of possible susceptibility effects attributed to the venous blood. A Gaussian filter of 1.1 mm full width at half maximum (FWHM) was applied to all dynamic images. The time-versus-signal-intensity curves (TICs) were converted to the Gd-DTPA concentration according to Eq. (1) given in the Appendix. Functional mapping images of the mean transit time (MTT), cerebral blood volume (CBV), and cerebral blood flow (CBF) were carried out with the deconvolution method [28]. The theory is described in detail in the Appendix. For ROI analysis, images of 64×64 matrix size were converted to 256×256 with use of a sinc interpolation function.

Results

T_1W and T_2W images reconstructed with a spatial resolution of $0.156 \times 0.188 \times 1.5$ mm are shown in Fig. 2. White matter could be discriminated from cortical and deep-gray-matter regions. Locations of small anatomic features such as the caudate putamen (CPu); striatum, the CC, and the hippocampus (HC) could also be identified in both T_1-W and T_2-W anatomic images. The CNR between the HC and CC was 15.6 and 9.8, corresponding to the T_1W and T_2W images shown in Fig.2. The CNR between the HC and IC was 23.2 and 13.6 respectively, in which underestimation may exist in CNR attributed to the contamination of signal from the globus pallidus.

Results for MIP images obtained with contrast-free TOF-MRA are shown in Fig. 3. Coronal MIP images around the HT of 5 mm thickness are shown in Fig.3 (A). In this figure, the slice section contained ICAs and MCA. The MCA, the cortical branches in both the left and right hemispheres, can be identified. It is important to note that the anatomic structure of both cortical MCA arteries is different between the right and left hemispheres. The ROI for the AIF was selected in the MCA region indicated by the arrows in Fig.3 (A) and (B).

A typical example of a DSC-MRI image is shown in Fig.4. Distortion of the DSC-MRI images is visible in Fig.4(A) toward the phase direction. The magnified area in dynamic images around the MCA region, which is shown as a rectangle in Fig.4(A), is displayed in Fig.4(B). There were several pixels which indicated temporal changes in pixel contrast as a function of time, and these were reflected by Gd-DTPA negative enhancement. The pixel signal intensity varied as shown in Fig.4(C), and the curve shown was employed for estimating the AIF. Figure 5 shows the TIC in this area together with the TIC for the whole brain region, obtained from each of the three scans. The curves were visually reproducible in terms of shape, height and width of the curves around the peak, as well as the tail height at end of the scan. It should also be noted that the baseline before each injection of Gd-DTPA was consistent, even though the 2^{nd} and the 3^{rd} curves should have been affected by the previous injection of Gd-DTPA.

Functional mapping images of CBF, CBV, and MTT calculated according to the theory described in the Appendix are shown in Figure 6. Images obtained from this sequential assessment appeared to be reasonably clear, although slightly noisy, and were consistent among the scans. The absolute CBF (mean ± S.D.) in the cortical-gray-matter area (mainly the parietal cortex (Pt)) was 24.04±2.88, 17.75±3.34, and 31.87±7.27 ml/g/min, corresponding to the first, second, and third scans, respectively. The Pt-to-HT CBF ratio was 46.7%, 51.5%, and 43.0%, corresponding to the first, second, and third scans, respectively. The CBV was 0.49 (0.44), 0.50 (0.35), and 0.47 (0.41) ml/ml in the Pt (the HT) region, corresponding to the first, second, and third scans, respectively. The MTT in the same regions was 1.22 (2.51), 1.72 (2.29), and 0.92 (2.16) seconds, corresponding to each of the three scans. Among the three injections, the absolute MTTs (mean±S.D.) were 1.29±0.40 sec in the Pt and 2.32±0.17sec in the HT region.

Discussion

This study demonstrated that our system of a human whole-body 3-Tesla MRI, fitted with an in-house solenoid coil developed for small animals, can provide morphologic and functional images of the rat brain in vivo. The quality of T_1-W and T_2-W images obtained with a scan duration of approximately 10 min was better than those obtained in previous studies in which 1.5-Tesla clinical MRI scanners [3] were employed. The neocortex and large subcortical structures, such as the Thal and HC, are readily recognized in their topographic relationship to the CC, the ventricular system, and the subarachnoid space [2]. In T_1-W images, the cerebrospinal fluid (CSF)-containing spaces are visible as hypo-intense, and the arterial flow showed a signal loss caused by the so-called flow void effects, which is typically seen in spin echo sequence [2]. In T_2-W images, the CSF showed a bright white intensity (prolonged T_2 relaxation time), whereas the myelinated white matter showed black intensity (short T_2 relaxation time). The white-matter tracts such as the IC and CC were clearly visible in both T_1-W and T_2-W images, with better quality compared with previous reports employing 1.0- and 1.5-Tesla clinical MRI scanners [2, 3].

MRA images also clearly showed the structure of distal MCA branches. The MRA findings of inter–hemispheric differences with regards to MCA in the SD rat were also consistent with a previous report on Wistar rats [29], which indicated the left-to-right asymmetrical structure in three out of 10 Wistar rats using a 7-Tesla MRI scanner dedicated to the small animal imaging [29]. Our MRA images are superior to those in previous work [11] that employed a clinical 3-Tesla MRI scanner and that only showed the major cerebral arteries and the carotid arteries because they focused mainly on validating occlusion models [11]. The superior quality of our MRA images can largely be attributed to the type of RF coil we used. Ours is a three-turn solenoid coil that covers only the cerebral area, whereas the previous work [11] employed a single-turn coil (diameter of 6.4 cm and length of 10 cm) that covered the whole head, including the brain and the neck. Additionally, the prolonged acquisition period in our study (almost twenty minutes) versus the significantly shorter acquisition period in the previous study [11] (almost four minutes) may have been a factor that led to higher-quality MRA images.

An important point with regard to this study is that DSC-MRI images of reasonable quality can also be obtained with a clinical MRI scanner at 3 Teslas on rats. In addition, we were able to extract the AIF from the rat brain, which is an important accomplishment. Selection of an ROI in the MCA region successfully provided the AIF. Spatial distortion or a susceptibility artifact was not visible in our observation. Signal changes were obtained during DSC-MRI following a single dose of Gd-DTPA. During this study, the dedicated transmitting and receiving RF coils were considered essential for obtaining a reasonable SNR. Our study was performed with the same sequence and the same dose rate (0.1 mmol/kg) of Gd-DTPA that are commonly used in clinical examinations. Moreover, it was performed with high (1.17 mm^3)-resolution dynamic imaging.

The quantitative images of CBF were consistent with a previous report on the use of [^{14}C] iodoantipyrine [30]. Namely, the Pt-to-HT contrast in CBF was 43-52 % in this study, which is close to the values reported by Bloom et al. [30] of 44-58 %. Although the absolute CBF and CBV values in our study were different from previous ones [13, 30, 31], unsure scaling factors of each ones were canceled out in calculating the MTT with Eq.(5) [32] (shown also in the Appendix). An analogous value for the MTT was represented in previous work [31, 33]. In the theoretical deconvolution step, the level of plasma gadolinium which was not influenced after previous injection by calculated subtraction with peak to base line with *(S(0)/S(t))* of Eq.(1) (Appendix).

We noticed that the absolute CBF and CBV values were overestimated, which suggests that some limitations apply, such as the partial volume effect (PVE) caused by insufficient spatial resolution as compared with the anatomic structure of the MCA. Detection of AIF with repeat injection was performed (Fig.5, right row). The major MCA diameter was approximately 0.5 mm at the maximum as evaluated from Fig.3, which suggested that the measured AIF is largely influenced by the PVE [24]. Also, the differences of absolute value may be reflected by the fact that a non-linear relationship exists between the signal intensity and the contrast agent concentration. Previous reports proposed methods for the non-linearity correction for brain tissue [34] and AIF [35]. Further studies are needed to confirm the accuracy and the reproducibility [36]. Image distortion caused by dielectric effects [37] and/or EPI distortion [38] are also additional error sources, and should be investigated systematically.

Along with the improved quality of acquired original dynamic images, the mapping image quality would also improve. For better detection of the dynamic susceptibility contrast that is caused by T_2* signals, the optimization of TE, FA, and the acquisition matrix should be investigated. We speculate that the multi-channel phased array coil and parallel imaging techniques would reduce the level of distortion. The DSC-MRI in this study was obtained only for a single slice. Further careful attention is needed to multi-slice imaging in order to minimize the inflow effects [35]. In our study, the contrast concentration *C(t)* curves including AIF's varied slightly among the three injections. A sophisticated injector system which need to be MR-compatible, may improve the variation.

A dedicated high-magnetic-field scanner equipped with a dedicated small bore is the optimal device for small-animal imaging. However, such systems are not commonly available. The system developed in this study might serve as a low-cost solution or an alternative. The use of the present system provides an opportunity for using the same imaging platform available for clinical studies for small-animal imaging [7]. This would allow us understanding the pathophysiological status from MRI signals using animal models with various diseases. More importantly, optimizing several scan parameters which have been limited in clinical patients may be performed easily on small animals with this system. In particular, the reproducibility of CBF assessment with DSC-MRI, which has been reported the limitation in clinical studies [19, 36], may be improved by performance of a systematic evaluation of each scan parameter when this system is used on small animals rather than clinical patients. With the addition of a high strength insert gradient coil [39] which allow for thinner slices and much faster read-out, the system performance can be enhanced and the spatial resolution with an acceptable SNR can be improved. The use of adapting coils can be an effective solution for those who operate MR scanners for human subjects and intend to gain experience [40] in pre-clinical research.

Conclusion

In this pre-clinical study on rats, reasonable image quality for morphologic information was obtained with T_1-W, T_2-W, and contrast-free TOF-MRA images, accomplished by use of a human whole-body 3-Tesla MRI scanner and newly developed solenoid coil. In DSC-MRI, it visualized transient signal changes with a single dose of Gd-DTPA, and with the same sequences which have been commonly used in clinical examinations. A human whole-body 3-Tesla MRI scanner and dedicated coil make it possible to detect the AIF in the MCA region of Wistar rats. High-resolution DSC-MRI was accomplished with a clinical scanner, but the spatial resolution with an acceptable SNR was insufficient for the rat brain. Although there might be some remaining issues with regard to AIF, we have shown the potential of DSC-MRI in our study.

Appendix

Calculation of functional mapping images from DSC-MRI

The observed TIC $S(t)$ was converted to a time–versus-concentration curve (TCC) $C(t)$ by the following equation [16, 36]

$$C(t) = k \cdot \Delta R2^*(t) = -k \cdot \ln(S(0)/S(t)) / TE, \qquad (1)$$

where $\Delta R2^*$ is the change in the T_2^* relaxation rate and k is a constant. In this study, it was assumed that k=1. $S(0)$ is the precontrast (baseline) signal and $S(t)$ is the measured signal at time t. The next step was to fit this first-pass period of TCC to a gamma-variate function;

$$C(t)=a(t-b)^c \exp(-(t-b)/d), \qquad (2)$$

where a, b, c, and d were determined by a nonlinear least-square fitting. To minimize the effects of the re-circulation of the contrast agent, data were neglected in the fit if these concentrations were less than 50 % of the maximum after the peak of the TCC. The fitted tissue TCC $Ct(t)$ was deconvolved by the fitted AIF $C_{AIF}(t)$ by use of a singular value decomposition with a block-circulant deconvolution matrix (b-SVD) method [28] and according to the equation

$$CBF \cdot R(t) = Ct(t) \otimes^{-1} C_{AIF}(t), \qquad (3)$$

where $\otimes^{-1}$ represents the deconvolution operator, and $R(t)$ is a residue function representing the tissue response to an instantaneous bolus. $CBF \cdot R(t)$ was estimated by deconvolving $Ct(t)$ by $C_{AIF}(t)$ using b-SVD, and then CBF was determined as the maximum value of the obtained $CBF \cdot R(t)$.

The CBV was calculated as follows:

$$CBV = \int_0^\infty C_t(t)dt \Big/ \int_0^\infty C_{AIF}(t)dt. \qquad (4)$$

Lastly, the MTT is calculated from CBF and CBV, applying the central volume principle [32]: $MTT=CBV/CBF$. $\qquad (5)$