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A Dialyzer-Based Flow System for Validating Dynamic Contrast Enhanced MR Image Acquisition

Sunder Rajan^{1,*}, Luke Herbertson¹, Marcelino Bernardo², and Peter Choyke³

¹Office of Science and Engineering Laboratories, Center for Devices and Radiological Health, FDA, Silver Spring, Maryland, USA.

²SAIC-Frederick, Frederick, Maryland, USA.

³Molecular Imaging Program, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA.

Abstract

Purpose: Dynamic contrast enhanced magnetic resonance imaging (MRI) has proven to be quite sensitive for the characterization of masses and early response to therapy. However, it is fraught with a number of procedural challenges as well as a lack of standardization. In this article, we describe the use of a simple dialyzer-based flow system to evaluate reproducibility of dynamic contrast enhanced MRI under active flow conditions.

Methods: The MR signal during a bolus injection of Gd-DTPA was analyzed to test the precision and variability of contrast agent kinetics during a typical dynamic contrast enhanced MRI sequence. A simple model allows an estimation of the washout rate constant of Gd-DTPA through the polysulfone tubules of the dialyzer.

Results: The simple flow phantom described here provided reproducible measurements of the washout rate constants. The washout rate increased from $0.20 \pm 0.005 \text{ min}^{-1}$ to $0.25 \pm 0.008 \text{ min}^{-1}$ over 32 weeks. Measurements were also made at week 24 using dynamic computed tomography and found to be $0.27 \pm 0.006 \text{ min}^{-1}$. Overall, the computed tomography derived rate constants results were found to be ~12% higher than the corresponding MRI values.

Conclusion: In this study, we show that a simple dialyzer-based flow phantom can be used for testing dynamic contrast enhanced MRI pulse sequences and also allows for short-term reproducibility testing of rate constants.

Keywords

flow-phantom; DCE-MRI; dialyzer; polysulfone

Conventional contrast enhanced magnetic resonance imaging (MRI), which involves the comparison of images obtained before, during, and after the administration of contrast agents, has been used for over 20 years. Improvements in temporal resolution now allow

*Correspondence to: Sunder Rajan, Ph.D., 10903 New Hampshire Ave., WO 62, Room 1113, Silver Spring, MD 20993. sunder.rajan@fda.hhs.gov.

time-resolved acquisition of post-contrast images during the vascular phase of the contrast agent. Dynamic contrast enhanced MRI (DCE-MRI) is a quantitative adaptation of contrast enhanced imaging and has been used to measure the properties of the microvasculature and the tissue using pharmacokinetic modeling (1–3). DCE-MRI has emerged as a versatile tool for the evaluation of tissue perfusion in cancer diagnosis and therapy monitoring (4). DCE-MRI involves the acquisition of rapid T_1 -weighted gradient echo images of the volume of interest, from which concentrations of the contrast agent are computed. The time-concentration changes are then used to derive vascular properties through pharmacokinetic modeling.

Although DCE-MRI has already proven to be quite sensitive for the characterization of masses and early response to therapy, it is fraught with a number of procedural challenges as well as a lack of standardization, resulting in confusion about how to interpret results among different centers (5). Sources of variability in DCE imaging occur along the entire imaging chain. Variability in injection rates and patient cardiovascular status influences the consistency of DCE-MRI. The reliability of image acquisition is influenced by trade-offs between temporal and spatial resolution, signal-to-noise ratio, and the imprecision in the conversion of the signal measured during the dynamic scan to the instantaneous concentration of contrast agent. The choice of pharmacokinetic model also contributes to the overall variability. In this report, we describe the use of a novel flow phantom to address the variability associated with image acquisition.

The Quantitative Imaging Biomarkers Alliance has proposed static phantoms containing standard solutions of relaxation agents to study the fidelity of concentration measurements (http://qibawiki.rsna.org/index.php?title=DCE-MRI_tech_ctte#Reference_Materials). However, static phantoms do not address inaccuracies stemming from the use of accelerated k-t space sampling techniques, such as keyhole, k-t Broad-use Linear Acquisition Speed-up Technique (BLAST), and k-t SENSitivity Encoding (SENSE), caused by changing image contrast during the passage of the contrast agent. Static phantoms must also incorporate a wide range of concentrations in order to mimic the DCE-MRI conditions. Additionally, preparing and maintaining precise concentrations of contrast agent can be challenging. It is to be noted that in DCE-MRI, kinetic rate constants are ultimately used rather than absolute concentrations.

Flow phantoms can potentially address the shortcomings of static phantoms by allowing for the measurement of washout rates rather than absolute concentrations. In addition, flow phantoms can also allow for the implementation of pulse sequences with advanced K-space strategies. Flow phantoms for the validation of MRI flow and velocity measurements have been reported (6); however, these are not well suited for the evaluation of DCE-MRI due to the inherent differences between bulk flow and perfusion phenomena. A flow phantom for DCE-MRI has also been recently reported (7) using a plastic mold for modeling breast DCE-MRI. Although the authors have demonstrated the utility of this phantom for tracking changes in the concentration of contrast agent, this design has several limitations. The small compartments and port design used for mixing could lead to highly nonuniform flow profiles, and also the construction of the phantom requires machined components and specialized pumps.

In this article, we describe the use of a simple dialyzer-based flow system to evaluate DCE-MRI derived washout parameters. The dialyzer, which is composed of two compartments separated by semipermeable hollow fibers, lends itself to testing the precision and variability of contrast agent washout kinetics during a typical DCEMRI sequence. The bolus of contrast agent enters the hollow fibers and a part of it diffuses across their walls. During the washout phase, the residual contrast agent in the extra-luminal region is gradually washed away as it diffuses back into the intra-luminal space. It must be noted that this two-compartment construct does not model actual tissue compartments well as the relative compartment volumes are not physiologic. In addition, the two-compartment model does not mimic the water exchange effects observed in vivo. However, the measured washout rate constant serves as a surrogate for evaluating the performance of the imaging system and pulse sequence without the complications of kinetic modeling and input functions. In addition, to validate the DCEMRI results, the washout parameters were compared with the measurements from dynamic computed tomography (CT) imaging. Although, CT imaging is less sensitive to Gd-DTPA, it offers a more direct measure of the concentration.

METHODS

Description of the Dialyzer Flow System

The flow phantom consisted of a gravity flow system and a Fresenius™ Optiflux Dialyzer (Model # F200NR, kindly provided by Dr. Howard Austin, NIH) commonly used for hemodialysis treatments (Fig. 1). The dialyzer is a two-compartment tubular device, ~25 cm in length, with two inlet ports and two outlet ports. The two “blood-side” ports (arterial and venous) are connected by tightly packed polysulfone hollow fibers to make up the intra-tubular space. The hollow fibers have a 200 µm diameter and a wall thickness of 40 µm. The two “dialysate” ports connect to the outer compartment, which surrounds the polysulfone fibers.

A reservoir (10 L) containing degassed water (dissolved oxygen concentration of <2 ppm) was placed on the patient table during the scan. Tygon tubing (1/4'' ID) was used to deliver the flowing medium to the dialyzer and out to a waste container (Fig. 2). The flow rate was controlled by varying the height between the reservoir and the outlet of the system. A calibrated, nonmagnetic flow meter (Gilmont Instruments, Barrington, IL, Model #GF-1360) was used to monitor the flow rate through the test model. The water flow rates were adjusted between 50 and 180 mL/min, but a constant flow rate of 160 mL/min was used for the reproducibility studies. The first cross-sectional slice of the dialyzer only contained the tubules with no extra-luminal space (Fig. 3). The distal slice positions contained both intra- and extra-tubular space, which were imaged using the DCE pulse sequence to determine washout rate constants.

During the MRI scan, the dialysate ports of the dialyzer were closed so that water only flowed through the intra-tubular space at a known rate, and there is no flow through the extra-tubular space. In between experiments, all ports are opened to flush the system with degassed water. Contrast media entering the phantom from inside the polysulfone hollow fibers will partially diffuse into the outer compartment. Following the contrast media injection, degassed water was used to gradually flush out both compartments. A schematic

of the flow system is shown in Figure 2. The dialyzer was tested repeatedly over a 32-week period to study the long-term stability and performance of the phantom and DCE scan sequence. When not in use, the flow system was stored with degassed water in the system and flushed weekly. In most of the experiments, static tubes containing various known concentrations of contrast agent were arranged in close proximity to the dynamic flow phantom and imaged simultaneously. These static standards were used to confirm the temporal stability of the signal during the DCE scan.

Contrast Agent Bolus

Contrast medium was delivered to the flow system using a power injector (Medrad, Indianola, PA) via a T-junction valve placed near the reservoir. A bolus of 10–25 mL of 5 mM diethylenetriaminepentaacetate (Gd-DTPA) (Magnevist™, Bayer, Princeton, NJ) was injected at a rate of 1 mL/s, followed by a 10 mL flush of degassed water. The contrast agent mixed with the gravity-fed bulk flow of degassed water well upstream of the dialyzer. The concentration and volumes of Gd-DTPA were chosen empirically to generate an adequate signal during the dynamic scan.

MRI Scanning

A 3 T MRI clinical scanner (Achieva, Philips Medical Systems, Best, The Netherlands) along with a 6-channel receive-cardiac array coil was used for imaging. The dialyzer was positioned horizontally within the cardiac array coil, with the long axis of the dialyzer parallel to the z-axis. The entry slice was positioned approximately at the isocenter of the magnet. The use of a nonselective radiofrequency pulse for imaging ensured that steady-state magnetization was achieved for the flowing medium. The tubing upstream of the dialyzer was coiled into two loops, so that the flowing medium was subjected to the nonselective radiofrequency pulses of the DCE pulse sequence, which prevented any in-flow signal effects. This was confirmed by checking that the signal intensity in the dialyzer relative to a static phantom, during static and flow conditions were the same (0.965 ± 0.032 for static versus 0.952 ± 0.032 for flow). A DCE-MRI clinical scan protocol was used. The imaging protocol consisted of localizer images, followed by a dynamic scan during contrast bolus passage (pulse repetition time (TR)/echo time (TE)/flip angle (FA) = 7/2.2 ms/10°). A 3D-transverse slab of 60 mm, with 10 slices (with 20% oversampling), partition thickness of 6 mm and an approximate in-plane spatial resolution of 1.2 mm were used (matrix of 256 by 186, with a field of view of 260 × 260 mm). A total of 54 dynamic scans were obtained during each run, lasting ~10 min (11 s per dynamic scan). Coronal imaging was performed to evaluate the dynamic signal behavior as a function of distance from the entry point in the dialyzer. For coronal imaging, the temporal resolution was 5.5 s per scan because slice oversampling was not used.

In some of the experiments, the results from SENSE-based parallel imaging were compared with Keyhole-SENSE scan protocols on the Philips MRI system. For the Keyhole sequence, only a 25% k-space coverage was used on the dynamic scans, which allowed an improved temporal resolution of 5.73 s. The last dynamic scan provided the reference image. All the other parameters were the same except the total number of dynamic scans. The shorter scan time per time point (5.73 s), allowed 105 dynamic scans. SENSE and Keyhole processing

was performed by the built-in system software and exported to Medical Image Processing, Analysis and Visualization for region of interest (ROI) processing as for the standard DCE scans.

In addition, an inversion recovery pulse sequence was used to estimate the T_1 of the flow medium (degassed water) in a plastic tube. A slice selective inversion pulse was used along with echoplanar sampling of the magnetization, using the following acquisition parameters: TR/TE of 10 s/34 ms and inversion delay times of 50, 100, 350, 750, 1250, 2500, and 5000 ms. The ROI data was fitted to a nonlinear T_1 recovery curve using the solver functionality in Microsoft Excel.

CT Scanning

A Philips PET-CT Gemini system was used to obtain dynamic CT scans using the same flow system as described above. However, there were two key differences in the set up relative to MRI: (1) the concentration of the contrast agent was increased to 250 mM to compensate for the lower sensitivity of CT, and (2) the Phantom was placed ~15 degree from vertical position, to minimize the pooling and buoyancy effects of the contrast agent, which was observed when high concentrations of the contrast agent was used as a bolus. A total of 60 dynamic CT scans, covering four slices (slice thickness: 6 mm, field of view: 27×27 cm, Matrix 512×512 , tube current: 100 mAs, 90 kVp, 0.5 s rotation time) were recorded every 10 s.

Data Processing

The MR image data were exported as Philips PAR-REC files and imported into Medical Image Processing, Analysis and Visualization (Version 4.4.1, National Institutes of Health, Bethesda, MD). The CT data were exported as DICOM files and also imported into Medical Image Processing, Analysis and Visualization. For MRI data, the kinetic plots were derived by extracting ROIs from the dynamic images and fitted to an exponential curve in Microsoft Excel, using the built in trend-line fitting function. The ROI values from the first slice in the dialyzer, which contained only the fibers in potting material, was used to derive the ratio of signal contribution from the intra-luminal compartment for the slices in the dual compartment region. Only the ROIs from the first slice containing both intra- and extra-tubule region was used for all washout rate constants. The signal from the rest of the dialyzer was not used.

Washout Kinetic Model

Although, the two-compartment dialyzer could potentially serve as a model for tissue and, hence, lend itself to the use of previously described pharmacokinetic models, we chose to use a simple wash-in/wash-out model to derive the wash-out rate constant from the observed signal changes. This is because the relative sizes of the compartments were not comparable with actual tissue and the assumptions for physiologic models are not valid. In addition, the main objective of this phantom was to measure the reproducibility of the data acquisition part of the DCE method, independent of the pharmacokinetic model. Equations [1–3] describe a simple model for the washout of the contrast agent at the entry slice position within the dialyzer. $C_{out}(t)$ and $C_{in}(t)$ are the concentrations of Gd-DTPA at a given time, t ,

after the start of the bolus injection, for the regions outside and inside the hollow fiber compartments, respectively.

$$\frac{dC_{\text{out}}}{dt} = -k(C_{\text{out}} - C_{\text{in}}) \quad [1]$$

$$\ln \frac{C_{\text{out}}(t)}{C_{\text{out}}(0)} = -kt \quad [2]$$

$$C_{\text{out}}(t) = C_{\text{out}}(0)e^{-kt} \quad [3]$$

C_{in} is assumed to be zero when $t > 4$ min and the flow rate is >150 mL/min. As the bolus passes through the dialyzer, both C_{out} and C_{in} are changing due to the diffusion of the Gd-DTPA from the intra-luminal space to the extra-luminal space. During this phase, the concentration of Gd-DTPA in the outer compartment increases rapidly. After the passage of the bolus, the input concentration of the Gd-DTPA is close to zero (as seen from the signal behavior of the first slice where extra-luminal space is absent) and the concentration gradient of Gd-DTPA is reversed. This causes the washout of the Gd-DTPA from the outer to the intra-luminal compartment. In this model, the intra-luminal Gd-DTPA concentration is assumed to be zero in the high flow rate condition 4 min after the passage of the bolus through the slice.

The rate of change of C_{out} during the dynamic scan can be expressed in terms of a washout constant (k). The k term reflects the permeability-surface area product, which is the “leakiness” property of the polysulfone material for the Gd-DTPA complex. During this washout period, C_{in} is assumed to be negligible. This expression allows the estimation of k from an exponential fitting of C_{out} versus time.

Measurement of Post-Contrast T_1 and GD-DTPA Concentrations from Dynamic MRI

The signal intensity value from a ROI for each time point was extracted from the entry slice. This value contains components from both the extra- and intra-luminal compartments. Because it is assumed that the contrast agent concentration in the intra-luminal compartment is negligible after 4 min, the signal contribution from the intraluminal is constant and was subtracted from the total ROI value for each time point. The concentrations of Gd-DTPA were computed from its known values of T_1 relaxivity ($4.8 \text{ s}^{-1} \text{ Mm}^{-1}$ at 3.0 T) (8), the pre-contrast T_1 relaxation time of flow medium (measured value of degassed water of 3 s for all experiments using inversion recovery imaging), and the computed T_1 value for each post-contrast time point image.

The post-contrast T_1 values were computed from the ROI signal values using the previously described equations for spoiled gradient echo contrast behavior (9,10). Equation [4] relates the observed steady-state signal s to pulse sequence parameters (TR/TE/flip angle θ), the T_1 and T_2 values. In Eqs. [4] and [6], s_{pre} and s_{post} refer to the image signal values from an ROI; and $T_{1,\text{pre}}$ and $T_{1,\text{post}}$ refer to the T_1 values pre-contrast and post-contrast, respectively. It is also assumed that $e^{-(TE/T_2^*)}$ values are the same for pre- and post-contrast conditions, due to the short TE values used. Equation [5] allows the calculation of s'_{pre} from the pre-contrast images from measured or assumed values of $T_{1,\text{pre}}$. This in turn can be used to calculate $T_{1,\text{post}}$ from s_{post} , TR, and flip angle used in the dynamic scan as per Eqs. [6–8]. Equation [9] allows the calculation of the concentration of the contrast agent from the instantaneous value of $T_{1,\text{post}}$.

$$s_{\text{pre}} = s_0 \cdot \sin\theta \cdot e^{-\left(TE/T_2^*\right)} \frac{\left|1 - e^{-\text{TR}/T_{1,\text{pre}}}\right|}{\left|1 - \cos\theta \cdot e^{-\text{TR}/T_{1,\text{pre}}}\right|} \quad [4]$$

$$s_0 \cdot \sin\theta \cdot e^{-\left(TE/T_2^*\right)} = s_{\text{pre}} \frac{\left|1 - \cos\theta \cdot e^{-\text{TR}/T_{1,\text{pre}}}\right|}{\left|1 - e^{-\text{TR}/T_{1,\text{pre}}}\right|} = s'_{\text{pre}} \quad [5]$$

$$s_{\text{post}} = s'_{\text{pre}} \cdot \frac{\left|1 - e^{-\text{TR}/T_{1,\text{post}}}\right|}{\left|1 - \cos\theta \cdot e^{-\text{TR}/T_{1,\text{post}}}\right|} \quad [6]$$

$$e^{-\text{TR}/T_{1,\text{pre}}} = \frac{s'_{\text{pre}} - s_{\text{post}}}{s'_{\text{pre}} - s_{\text{post}} \cdot \cos\theta} \quad [7]$$

$$T_{1,\text{post}} = -\text{TR} / \ln \left[\frac{s'_{\text{pre}} - s_{\text{post}}}{s'_{\text{pre}} - s_{\text{post}} \cdot \cos\theta} \right] \quad [8]$$

$$[\text{GdDTPA}] = \frac{1}{\text{relaxivity}} \cdot \left[\frac{1}{T_{1,\text{post}}} - \frac{1}{T_{1,\text{pre}}} \right] \quad [9]$$

Measurement Gd-DTPA Concentrations from CT Dynamic Images

For CT data, ROI mean values of Hounsfield units from the four slices were added to improve the signal-to-noise ratio. Direct measures of concentration of the contrast agent were made by subtracting the post-contrast Hounsfield units from that of the average pre-contrast values. The last 4 min of the washout curve was fitted to an exponential decay to find the washout rate constant.

RESULTS

Figure 3 shows an example of images using the phantom for a typical dynamic scan. Figure 3a,b shows an example of the transverse and vertical (sagittal) slices of the phantom, respectively. Labels A–F point to the (A) dialysate port, (B) input for flow medium, (C) potted slice position which has no extra-tubular space, (D) slice position for dynamic imaging, (E) static tube with 5 mM solution of Gd-DTPA, and (F) a bag filled with degassed water, respectively. Figure 3c shows the changes in signal observed during the dynamic scan. The signals from the two-compartment region of the entry slice to the dialyzer (◆), potted slice (□), and a 5 mM Gd-DTPA standard solution (x) are shown. The signal from the potted slice was found to be 25% of that found inside the dialyzer, which is a measure of the relative intra-tubular volume and also reflects the shape of the bolus input. Figure 4 shows an example of washout curves obtained from a coronal scan that corresponds to signal changes from ROIs spaced 1 cm apart along the length of the dialyzer. A continuous drop in the peak wash-in signal and a prolongation of the washout was observed as a function of depth (along the z-axis). This behavior is consistent with the flattening of the input function over the length of the dialyzer, because the washout from each slice serves as an input for the following slice. The assumption that the intra-luminal Gd-DTPA concentration is negligible will therefore only hold true for the entry slice position, which was used to determine the washout constant (k).

In Figure 5, washout curves obtained for the axial and coronal data sets from an ROI position close to the entry slice is shown. In general, coronal imaging offers better resolution temporally and in the z -direction. The wash-out rate constants were not found to be significantly different ($0.239 \pm 0.0056 \text{ min}^{-1}$, $n = 5$ runs for transverse imaging versus $0.236 \pm 0.0080 \text{ min}^{-1}$, $n = 3$ for coronal imaging, $P = 0.8$ one-tailed t -test). The measured rate constant was found to increase as a function of flow rate up to 150 mL/min; no significant effect of flow rate was observed above 150 mL/min.

Transverse dynamic imaging was used to compare the washout constants obtained using accelerated scanning methods. No significant difference was found by using keyhole implementation using the central 25% of the k -space was acquired during the dynamic scans. The washout constants were not significantly different in one comparison (0.256 and 0.253 min^{-1} for SENSE and keyhole, respectively).

The sensitivity of the measured rate constant to the assumed pre-contrast T_1 value of the flowing medium (water) was assessed using one of the datasets. As shown in Figure 6, the rate constants only vary by ~5% over a range of 2–4 s for the assumed T_1 values.

One of the primary concerns with any phantom design is the need for long-term stability testing across sites or systems. This phantom was tested using the same controlled conditions over a period of 32 weeks. The results are summarized in Figure 7. The rate constant increased from 0.20 to 0.25 min⁻¹ over 32 weeks, with most of the change occurring between weeks 1 and 2.

Figure 8 shows the washout curves from a dynamic CT scan. The rate constant was found to be $0.273 \pm 0.006 \text{ min}^{-1}$ ($n = 3$). This compares with $0.242 \pm 0.004 \text{ min}^{-1}$ ($n = 3$) found using DCE MRI during the same 3-week period.

DISCUSSION

DCE MRI has been increasingly used for monitoring early response to cancer therapy. However, the adoption of DCE-MRI has been limited by a number of factors including a lack of an appropriate test model, lack of standardization of data acquisition protocols, availability of software, and differences in pharmacokinetic models. Here, we report the use of a novel flow phantom, which allows the investigation of the data quality in DCE-MRI. Although the phantom is based on two compartments separated by polysulfone material, it is not necessarily an appropriate surrogate for the intra- and extra-vascular compartments in tissue, primarily due to the rather low relative compartment volumes of the phantom compared with tissue (25% for intra-tubule in this dialyzer).

The conventional approach to the phantom testing of DCE pulse sequences has been to use static phantoms for the validation of T_1 measurements and hence concentration estimates. This static phantom approach will not allow the evaluation of novel pulse sequence methods, such as those that use k-space sharing, which could potentially be addressed using a suitable flow phantom. However, the use of static phantoms does allow for accurate T_1 measurements and the validation of flip angles.

The rate constants measured by DCE-MRI are somewhat lower but within 15% of the CT measured rate constants for three sample points. Because the CT measurements provide a more direct measure of the Gd⁺³ concentration, the CT results are considered a good validation of the MRI results. However, the experimental setup for MRI and CT were different and the concentration of Gd⁺³ bolus was higher for CT, which limits the comparison. There are many expected sources of error in the estimates of the washout rate constants during a DCE MR scan. These include: $T_{1\text{pre}}$ estimates, flip angle values, susceptibility effects, partial volume effects, non-negligible intra-luminal Gd-DTPA, water exchange effects, and temporal averaging caused by the limited temporal resolution of the 3D gradient echo scan. In addition, degradation of the polysulfone hollow-fibers over time may also contribute to a drift in the results. These aspects pertaining to the dialyzer flow phantom are discussed in greater detail below.

In this study, the correct pre-contrast T_1 measured from inversion recovery pulse sequence was used independently, thereby eliminating the confounding effects of the T_1 measurement conducted as a part of the DCE protocol. However, the effect of the imprecision in the estimates of pre-contrast T_1 on the measured rate constants was analyzed computationally as

shown in Figure 6. A 2-fold increase in $T_{1\text{pre}}$ (from 2 to 4 s) only decreases the value of the rate constant by 5% (from 0.245 to 0.235 min^{-1}). The main reason for this is that the underestimation of the pre-contrast T_1 results in a systematic overestimation of the post-contrast T_1 across all the time points as per Eq. [8], and the overall impact on the rate constant is not as strong. In addition, the high value of pre-contrast T_1 (3 s) converts to a very small concentration error.

The flip angle is also directly used in the expression for $T_{1,\text{post}}$ as a cosine term in the denominator and in the s'_{pre} term, and will therefore influence the precision of the results. However, the effect is expected to be small. For example, in one of the data sets, changing the value of the flip angle from 10° to 20° resulted in a 5% decrease in the value of the washout constant (from 0.239 to 0.229 min^{-1}). The use of B_1 correction which is now available in many MRI systems is expected to improve the precision.

There are other factors that could lead to signal changes during the dynamic scan within the dialyzer. Trapped air bubbles can lead to signal artifacts if not properly controlled. It was found that the use of degassed water and careful elimination of air bubbles in the flow system before imaging minimizes this concern. In addition, if signal voids are stationary, excluding them for the ROI measurements can minimize the effect of these regions. The presence of in-flow effects could also contribute to errors. However, the use of a nonselective 3D excitation with the body coil minimizes the in-flow effects as demonstrated by comparison of signal intensity under static and flow conditions.

The assumption of negligible intra-luminal concentrations of Gd-DTPA is central to accurately modeling the washout period (Eq. [1]). This condition is only met under certain conditions. The input function as seen in Figure 3c is sharp and shows that the Gd-DTPA concentration reaching baseline, at the entry point of the dialyzer within 3 min of the start of the dynamic scan (~ 1 min after the start of the concentration spike). Hence, a few minutes after the end of the bolus, no new Gd-DTPA is entering the slice region. At the slice position where the two compartments begin, the accumulated Gd-DTPA from the bolus is diffusing back into the intra-luminal compartment from the extra-luminal compartment, while also being flushed away by the flowing water. At a system flow rate exceeding 150 mL/min, and an internal diameter of 4 cm, each slice (6 mm) is replenished by fresh flowing medium approximately every 3 s. Under these conditions, the intra-luminal concentrations are negligible, even assuming an upper estimate of 0.5 min^{-1} for the washout constant. The dynamic data was fitted after 4 min from the end of the contrast agent spike to minimize this effect of residual intra-luminal concentration. Choosing a slice position as close to the entrance and as thin as possible can further minimize this effect. Results from imaging in the coronal plane and choosing a 2 mm thin ROI close to the entry position for curve fitting gave values of the washout constant not significantly different from axial imaging using 6 mm slices (0.236 versus 0.245 min^{-1} , respectively). Subtraction of the pre-contrast intraluminal component is only valid if water exchange effects are slow relative to the MR timescale. This is assumed to be the case given the rather large size of the compartments. Nonetheless, errors in the estimates of intraluminal signal contribution could influence the final value of the computed rate constants and could be one factor in the deviation of the MR from CT results.

No significant difference in washout rates was found using keyhole-SENSE compared with the SENSE (11). The interpretation of this result is limited by the fact that the phantom only allows for homogeneous ROIs. Hence, any k-space sampling artifacts would not necessarily be visualized. However, the effect of temporal resolution can be studied and shows that in this kinetic regime, the higher temporal resolution of keyhole does not significantly alter the values of the measured rate constants.

This study does not address the variability issues associated with the pharmacokinetic modeling. Such modeling is not applicable to the two-compartment system in this dialyzer cartridge because the compartment volume fractions and the input functions are quite different compared with typical tissue models. However, it provides the basis to design suitable phantoms using polysulfone tubules to model the entire DCE method.

A key positive attribute of this phantom is reliable short-term performance. Although, this dialyzer is sold as a single use device, the phantom was repeatedly used over a period of ~32 weeks. During this period, there was an upward drift of ~25% observed in the washout rate constant. This increase in the permeability over time is perhaps a reflection of the mild degradation of the polysulfone material and needs to be confirmed. Also, the long-term changes in the measured rate constant will still allow short-term comparisons of pulse sequence testing. One of the key findings is that the standard deviations of the washout rate constant using this simple reproducible phantom is between 5% and 10%. This may reflect the best-case result for typical in vivo DCEMRI measurements and serial comparisons. Such a phantom could also be useful for quality control of DCE-MRI. In this report, we have used the publicly available Medical Image Processing, Analysis and Visualization image processing application to extract signal values and performed the data processing using formulae in Microsoft Excel to make it easy to reproduce the results.

In conclusion, we have shown that it is feasible to design a multicompartment flow phantom for DCE-MRI using commercially available components. The phantom shows acceptable short-term reproducibility using a single MR scanner. It enables sources of variability during dynamic sequences to be evaluated across different pulse sequences by measuring the well-defined washout rate constant, which is associated with the contrast agent and membrane.

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FIG. 1.
Two-compartment flow phantom for studying washout kinetics.

FIG. 2.

Schematic of the flow phantom. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

FIG. 3.

The images (a) and (b) show sample axial and coronal images of the dialyzer. Labels A–F indicate the (A) dialysate port, (B) input for flow medium, (C) potted slice position which has no extra-tubular space, (D) slice position for dynamic imaging, (E) static tube with 5 mM solution of Gd-DPTA, and (F) a bag filled with degassed water, respectively. c: The changes in signal observed during the dynamic scan. The signals from the two-compartment region of the entry slice of the dialyzer (◆), slice through the plug region (□), and a 5 mM

Gd-DTPA standard solution (×) are shown. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

FIG. 4. Example of the dynamic signal behavior as a function of ROI distance from the entry position as seen in by coronal DCE data acquisition.

FIG. 5. Examples of exponential fits for the washout rate of the Gd-DTPA bolus for (a) a coronal measurement, and (b) an axial measurement.

FIG. 6.
Plot of the change in the washout rate constant “ k ” as a function of the assumed T_1 value of the pre-contrast medium.

FIG. 7.

Measured values of the washout rate constants using a single dialyzer as a function of storage time over 32 weeks. The error bars represent the spread in the values (SD) for three separate DCE scans.

FIG. 8. Example of (a) a dynamic CT image of an oblique slice CT image and (b) its corresponding exponential fit depicting the washout of Gd-DTPA.