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A Throughput-Optimized Array System for Multiple-Mouse MRI

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Abstract

MRI is a versatile tool for systematically assessing anatomical and functional changes in small animal models of human disease. Its noninvasive nature makes MRI an ideal candidate for longitudinal evaluations of disease progression, but relatively long scan times limit the number of observations that can be made in a given interval of time, imposing restrictions on experiment design and potentially compromising statistical power. Methods that reduce the overall time that is required to scan multiple cohorts of animals in distinct experimental groups are therefore highly desirable. Multiple-mouse MRI, in which several animals are simultaneously scanned in a common MRI system, has been successfully used to improve study throughput. However, to best utilize the next generation of small-animal MRI systems that will be equipped with an increased number of receive channels, a paradigm shift from simultaneously scanning as many animals as possible to scanning a more manageable number, at a faster rate, must be considered. This work explores the tradeoffs between the number of animals to scan at once and the number of array elements dedicated to each animal, to maximize throughput in systems with 16 receive channels. An array system consisting of 15 receive and five transmit coils allows acceleration by a combination of multi-animal and parallel imaging techniques. The array system was designed and fabricated for use on a 7.0-T/30-cm Bruker Biospec MRI system, and tested for high-throughput imaging performance in phantoms and live mice. Results indicate that up to a ninefold throughput improvement of a single sequence is possible compared to an unaccelerated single-animal acquisition. True data throughput of a contrast-enhanced anatomical study is estimated to be improved by just over six-fold.

Introduction

A common goal of MRI research involves exploration of new methods to reduce data acquisition time without sacrificing image quality. Progress towards this goal has been made through efficient encoding strategies and advances in radiofrequency (RF) detector design. Arrays of surface coils can be used to increase the signal-to-noise (SNR) of the measurement (1) compared to a larger, more lossy coil, and arrays can be used in combination with parallel imaging (PI) encoding schemes (2–5) to improve acquisition speed. The promise of faster image acquisition using arrays and efficient data reduction schemes has prompted manufacturers to supply MR systems with an ever increasing number of receiver channels.

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In preclinical research involving small animals, the goal of minimizing the duration that an animal spends in the scanner becomes part of a larger effort to reduce the overall time that is required to scan multiple cohorts of animals in distinct experimental groups. Since measurements from a large number of animals are often required to achieve the desired level of statistical power, challenges associated with the cost of scan time and the complexity of synchronizing instrument access with multi-stage animal preparation procedures often discourage the use of MRI in routine preclinical research.

The small size of a mouse, in relation to the bore of many MRI systems, offers significant flexibility for the efficient utilization of multi-channel receiver systems to improve overall throughput. For instance, multiple animals can be simultaneously scanned with a field of view (FOV) and acquisition time appropriate for a single mouse (6,7). The use of multiple-mouse MRI has permitted dramatic improvements in animal throughput for both anatomical (6,8–10) and functional (11–13) applications, while reducing imaging cost and enabling studies with high statistical power to be performed (14).

A modest but nontrivial investment in infrastructure is required to implement and support multiple-mouse MRI. Efficient workflow necessitates that at least some additional personnel may be necessary to enable animal preparation and scanning to proceed in parallel. A system for distributing anesthesia to multiple animals can be assembled from readily available components. Systems for monitoring the physiological status of multiple animals at once in an MR environment are now commercially available, as are RF coil systems developed expressly for this purpose. Investment in such infrastructure must be made with care to maximize the payoff in terms of image quality and throughput.

Optimal utilization of available receiver channels for multi-animal imaging depends on the target application. For high-resolution phenotyping acquisitions, which can take several hours to perform, it makes sense to simultaneously scan as many animals as possible (15). To accomplish this, an array of several volume coils that are each connected to a distinct receiver channel can be used. However, the burden of simultaneously preparing, monitoring, and scanning as many animals as possible can also be unnecessary, particularly for routine screening protocols of a short duration or for dynamic imaging protocols that require careful and lengthy animal preparation (13). For such applications, a multi-animal imaging paradigm in which a more manageable and optimized number of mice are simultaneously scanned at a faster rate should be considered. Arrays of coils dedicated to each animal enable PI acceleration in a multi-animal imaging system. The feasibility of scanning with multiple arrays of receive coils (MARCs) to improve throughput without sacrificing SNR in the target anatomy, compared to conventional imaging methods, was recently demonstrated (16). Two-element surface coil arrays placed against the chests of two mice improved the baseline SNR in the heart by 60% more than that measured using a standard mouse birdcage coil. Parallel imaging strategies were used to reduce data acquisition time.

State-of-the-art small-animal MRI systems can currently be equipped with 16 parallel receive channels, offering new opportunities for throughput improvement. The optimal use of such capabilities requires careful evaluation of the tradeoffs between the number of mice to simultaneously scan and the number of array elements to dedicate to each mouse. The purpose of this work was to design and evaluate a throughput-optimized RF coil configuration for improving the throughput of short duration screening protocols on a four-channel 7.0-T/30-cm Biospec MRI (Bruker Biospin MRI, Ettlingen, Germany) system into which a broadband 16 channel receiver system will be installed. Results indicate such an approach can significantly improve throughput for routine imaging in biomedical research involving mouse models.

Experimental

Selection of Array Geometry

Several coil configurations were compared to investigate relative throughput that could be achieved as the number of animals and the number of coils per animal vary. The maximum number of mice was limited to five to maintain compatibility with the most commonly performed studies at our imaging facility: short routine screening protocols that leave little time for animal preparation in parallel with scanning, and drug development studies that utilize dynamic contrast-enhanced MRI, where complicated animal preparation procedures on five mice take about as long as the overall imaging protocol (13). Based on input from our veterinary staff and previous findings for practical 2D multi-mouse imaging (10), the array configurations shown in Figure 1 were chosen as candidate geometries. Configuration I represents single-mouse imaging with a 16-element array. Configurations II to V represent MARCs, where an individual coil array is dedicated to each animal. Configuration VI represents an unshielded array distributed over the multi-mouse volume.

To investigate the candidate geometries, the configurations were modeled in XFDTD 7.0 (Remcom, State College, PA, USA). The array elements were specified as thin copper traces that were placed around a cylinder with a 30-mm outer diameter (OD) and a 28-mm inner diameter (ID). The elements consisted of rectangular loops extending 2.0-cm along the main field axis, and were overlapped with neighbors to approximate critical overlap along the circumferential direction. B_1 coil sensitivity maps were generated and exported to Matlab to investigate PI performance. The sensitivity maps were pointwise multiplied with numerical mouse phantoms (homogeneous cylinders with a 27-mm OD) to generate individual coil images that covered the entire multi-mouse FOV. Sensitivity encoding (SENSE) geometry (g -) factor maps (4) were calculated for each of the coil configurations and for various reduction factors. Coil elements were assumed to be perfectly decoupled for this PI performance simulation.

To avoid confusion between throughput, parallel imaging acceleration, and changes to the image encoding matrix due to multi-animal imaging, total throughput T is defined as:

$$T = \frac{R \times N}{F}, \quad (1)$$

where R is the traditional PI reduction factor, N is the number of mice simultaneously scanned, and F is the matrix extension factor that accounts for enlarging the unaccelerated FOV to cover multiple animals compared to the traditional single-animal case (16). Thus, instead of considering what g -factor results from a particular reduction factor, the g -factor can be expressed as a function of overall throughput, T , allowing consistent criteria for comparing the performance of dissimilar array structures.

Array System Fabrication

Among the geometries considered, configuration V offered highest throughput acceleration with the lowest expected SNR penalty (see Results). The full array system consists of 20 total coils: 15 receive-only coils and five transmit birdcage coils. Circuit traces of the three-element subarrays, that extended 2.0 cm along the z -axis and 3.5 cm along the angular/circumferential direction, were milled from a flexible copper substrate using a ProtoMat C100/HF circuit prototyping system (LPKF Laser & Electronics, Wilsonville, OR, USA) and were then wrapped around a G10 tube with a 28-mm ID and a 30-mm OD. This coil dimension is appropriate for imaging a single organ or tumors with up to a 1.5-cm diameter. The overall size represents a compromise between accommodation of a range of animal sizes, close proximity of the receive array, and room for a surrounding shielded transmit

coil, while allowing for arrangement of multiple subarrays within the gradients. This system easily accommodates a typical 30-g mouse. The receive elements were populated with discrete components to achieve the desired tuning and matching with loading phantoms (30-mL, 25-mm OD syringes filled with 0.45% NaCl in distilled water, to mimic the loading characteristics of 30-g mice) in place and with the shielded transmit coils present but actively decoupled. A photograph and circuit schematic of a representative receive coil is shown in Figure 2.

For RF excitation, five linear high-pass birdcage coils were fabricated by milling eight 6-cm long, 6-mm wide rungs and the tuning and matching circuit layout into the flexible copper substrate. The coil supports, including those for the birdcage rungs (OD = 51 mm) and the RF shield (OD = 64 mm), were cut from thin-wall G10 tubing. The shield was made by overlapping three copper sheets with breaks placed every 6 cm to reduce the potential for gradient-induced eddy currents. With the loading phantom and actively-decoupled receive array in place, nonmagnetic multi-layer capacitors (American Technical Ceramics, Huntington Station, NY, USA) were iteratively varied until the transmit coils were matched to 50 Ω at 300.3 MHz. A photograph and schematic of a representative unshielded birdcage coil is shown in Figure 2. Because only one transmit channel is available, a 5-way Wilkinson power divider must be used to simultaneously distribute power into all transmit coils.

A drawback of multi-mouse imaging is that gradients large enough to accommodate all mice and associated hardware must be used. For the 7-T 30-cm system, the largest available gradient coil (B-GA20; $G_{\text{max}} = 200$ mT/m; $t_{\text{rise,min}} = 200$ μ s) has a usable bore diameter of only 20 cm. Because of the tight bore space, the five coil assemblies had to be staggered when placed in a custom built multi-coil holder, as shown in Figure 3. This spatial offset is easily removed during image acquisition by assigning an offset in readout (RO) frequency according to mouse position (6).

Array Decoupling

Inductive coupling between coil elements is detrimental to image quality and limits the ability to use PI for acceleration. Inter-array coupling (i.e. coupling between elements dedicated to different mice) was minimized by RF shielding, and configuration V allowed intra-array (i.e. elements dedicated to a common mouse) overlap decoupling from all elements of a subarray. Coupling was measured with loading phantoms and all system components in place, but with the transmit coils actively detuned. Preamplifier decoupling was used to compensate for imperfect overlap (1,17). Commercial low-input impedance preamplifiers (Microwave Technology Inc., Fremont, CA, USA) were used for this task. As measured by the manufacturer, the 15 preamplifiers had an input impedance $Z_{\text{in}} = (4.6 \pm 0.2) + (0.4 \pm 0.2)\text{j}$, a noise figure = 0.4 dB, and a gain = 25.8 ± 0.6 dB. The effect of current reduction was measured with independent probes that were loosely coupled to each of the array elements with the matching circuitry alternatively terminated to 50 Ω and to the corresponding preamplifiers, while all other coils were deactivated. PIN diodes were placed in all birdcage legs to provide active decoupling from the receive coils. PIN diode traps were placed in the array element loops to actively-decouple receive from transmit coils (17). The schematics in Figure 2 illustrate these decoupling strategies.

Phantom Testing

Prior to use on animals, the performance of the array system and reference single-mouse imaging hardware (8-leg, 35-mm ID, high-pass birdcage coil; 1P T8102 Bruker Biospin) were tested with phantoms.

SNR Characterization—Five 30-mL, 25-mm OD homogeneous phantoms filled with 0.45% NaCl and 0.01% Magnevist in distilled water (with a measured conductivity of 8 mS/cm) were created to approximate the loading of five 30-g mice. To compare the consistency of subarray fabrication, each module was sequentially placed in the central position of the coil holder and spin echo (FOV = 3.4×3.4 cm, matrix = 256×256 , TE/TR = 15/500 ms, 3 1-mm slices) images of a common phantom were acquired. The acquisitions were repeated with the transmitter turned off to acquire noise only images that provided a measure of intra-array noise correlations. Based on these acquisitions, SNR was calculated as (1,18):

$$SNR = \sqrt{\frac{\mathbf{w}^H \mathbf{b} \mathbf{b}^H \mathbf{w}}{0.5 \mathbf{w}^H \mathbf{\Psi} \mathbf{w}}}, \quad (2)$$

where $\mathbf{\Psi}$ is the noise covariance matrix, $\mathbf{b}$ is the vector of complex coil sensitivities, and $\mathbf{w}$ contains the coil weighting coefficients:

$$\mathbf{w} = \frac{\mathbf{\Psi}^{-1} \mathbf{b}}{\mathbf{b}^T \mathbf{\Psi}^{-1} \mathbf{b}^*}. \quad (3)$$

To investigate SNR performance in the final multi-animal array configuration, the array system was assembled into the multi-coil holder and the spin-echo signal and noise acquisitions were repeated, shifting the RO center frequency for subarray modules 2 and 4, but keeping the FOV static along the phase encoding (PE) direction. Data from each subarray were acquired serially using three of the four receive channels available on our Biospec system. Phantoms were placed in all subarray modules, transmit power was individually calibrated and applied to each subarray individually, and all unused excitation coil ports were terminated to 50 Ω . SENSE (4) g -factor maps were estimated from the fully acquired data and the maps were used to estimate SNR performance with PI. The SNR acquisitions were repeated with the reference birdcage coil at isocenter and at the edge of the gradient interior.

Quality Factor—To quantify sources of loss that contribute to SNR reductions, unloaded and loaded quality factor (Q) measurements on a representative receive element were performed. The element under test was disconnected from its associated preamplifier, and the three-element subarray module was reinserted back into the detuned shielded transmit volume coil. Two small loop probes were loosely coupled to the receive element, during which S_{21} current profiles were captured on a network analyzer. Q was estimated by dividing the resonance frequency by the -3 dB bandwidth.

Image Distortions—To characterize distortions due to scanning in the gradient periphery, a grid phantom consisting of coronal, sagittal, and axial plates with 0.9-mm holes placed every 1.9 mm along a Cartesian grid was filled with 0.1% Magnevist in distilled water and scanned in each subarray volume. Axial, sagittal, and coronal slices were sequentially positioned along the central slabs of the grid phantoms and spin-echo images were acquired with acquisition parameters identical to those used for SNR measurements. Worst-case geometric distortions were calculated along each of the three principal planes according to AAPM NMR Task Group 6:

$$\%GD = 100 \times \frac{\Delta_{actual} - \Delta_{measured}}{\Delta_{actual}}, \quad (4)$$

where the apparent hole spacing along the most distorted grid line $\Delta_{measured}$ was compared to the true physical spacing Δ_{actual} . A simple forward mapping procedure, in which

distorted grid locations were mapped to undistorted anchor locations (19), was implemented in Matlab to demonstrate geometric distortion correction. By applying the distortion correction along a coronal image from a peripheral subarray, the distortions to the slice profile could also be estimated. This was accomplished by comparing the profile of a 1-mm saturation slice at the center (position 3) with the slice profile in position 1 after distortion compensation.

B₀ Homogeneity—For single-animal imaging, an automated routine that iteratively varies first-order shims provides a straightforward methodology for generating a relatively homogeneous B₀ field. For multi-animal imaging, in which non-contiguous imaging volumes are positioned throughout the magnet bore, achieving a homogeneous B₀ field is a more difficult problem. In this work, seven shim settings were compared: results from A) automated first-order shimming over each of the five volumes individually, B) automated shimming of the sum of signals from all volume coils (10), and C) using a numerical average of the individual shims from A.

Shimming was performed over the entire sensitive region of the birdcage coils and analyzed over a small volume at the center of each subarray. To achieve a large homogeneous sensitivity, the transmit birdcage coils were operated in transmit/receive mode with receive coils deactivated. Point resolved spectroscopy (PRESS) on the homogeneous loading phantoms (described previously) was performed over a one-cm³ voxel within each of the five supported imaging volumes. Shim performance was measured as the full width at half max (FWHM) over each subarray volume and the maximum frequency difference between peak frequencies in different volumes.

Animal Imaging—Once imaging performance was evaluated in phantoms, the capabilities of the multi-animal imaging system were tested *in vivo*. All animal procedures were approved by our Institutional Animal Care and Use Committee, which is accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care International.

Two weeks prior to imaging, the right thyroid glands of six male Nu/Nu mice were orthotopically injected with 2.5×10^5 papillary thyroid carcinoma (BCPAP) cells (20). Prior to imaging, five of the six mice were anesthetized and placed supine on a custom-built multi-mouse sled distributing 2% isoflurane (IsoSol; VEDCO, St. Joseph, MO, USA) in oxygen through nose cones (Figure 4). For comparison, the sixth mouse was prepared and scanned with the conventional single-animal sled and imaging hardware.

The global position of the custom sled was adjusted after execution of a coronal fast low angle shot (FLASH) 2D position scan (multi-animal: FOV = 20×10 cm, matrix = 256×128 , TE/TR = 4/25 ms, 1 10-cm slice; single-animal: FOV = 10×3.5 cm, matrix = 128×64 , TE/TR = 4/25 ms, 1 3.5-cm slice) and the position of each sled cradle was fine-tuned to align imaging volumes along the field axis. Automated scanner calibrations were performed prior to execution of a three-plane FLASH acquisition (multi-animal: FOV = 18×18 cm, matrix = 256×256 , TE/TR = 3/100 ms, 3 2-mm slices; single-animal: FOV = 4.5×4.5 cm, matrix = 64×64 , TE/TR = 3/100 ms, 3 2-mm slices). Coronal and axial T₂-weighted rapid acquisitions with refocused echoes (RARE) (multi-animal and single-animal: FOV = 3.42×3.42 cm, fully-encoded matrix = 256×256 , TE_{eff}/TR = 42.4/3500 ms, 18 1.0-mm slices, RARE factor = 8) and an axial T₁-weighted acquisition (multi-animal and single-animal: FOV = 3.42×3.42 cm, fully-encoded matrix = 256×256 , TE/TR = 15/1000 ms, 18 1.0-mm slices) acquired before and after administration of contrast were used to visualize tumors in these animals. Both unaccelerated ($R = 1$) and PI-accelerated ($R_{\text{eff}} = 1.8$) acquisitions were performed. The FOV was always prescribed over the central mouse, where data from all animals would alias in a true multi-animal experiment, and the RO frequency bandwidth

was offset according to the associated mouse position (Figure 3). Because all subarrays were highly shielded from one another and thus possessed localized sensitivities (2), PI reconstructions such as generalized autocalibrating partially parallel acquisitions (GRAPPA) (5) could be performed individually without contamination from other imaging volumes.

Results

The six candidate coil configurations shown in Figure 1 were analyzed by numerical simulation to determine the most desirable geometry for throughput-optimized small-animal MRI investigations on systems equipped with 16 receive channels. Based on g -factor maps from all configurations with accelerations from $T=1$ to $T=12$, the maximum g -factors observed over all numerical mouse phantoms are shown in Figure 5 as a function of throughput. In general, configuration V offered the highest throughput with the lowest maximum g -factor. Furthermore, the ease with which all three subarray elements can be intrinsically decoupled by geometry alone led to the selection of V as the best throughput-optimized configuration.

All 15 phantom-loaded receive elements achieved an average 50 Ω -match of $S_{11,\text{mean}} = -31$ dB (with $S_{11,\text{best}} = -40$ dB and $S_{11,\text{worst}} = -24$ dB) with the actively-decoupled volume coils in place. With the five loading phantoms in place and receive elements actively-decoupled, the transmit coils achieved a 50 Ω -match of $S_{11,\text{mean}} = -32$ dB, $S_{11,\text{best}} = -44$ dB, and $S_{11,\text{worst}} = -23$ dB. Critical coil overlapping minimized intra-array inductive coupling with average S_{21} of -17.8 dB, -19.3 dB, -21.8 dB, -22.3 dB, and -19.7 dB for subarrays one to five, respectively, with a minimum of -15.5 dB and maximum of -24.4 dB. Average inter-array decoupling was $S_{21} = -55.6$ dB ($S_{21,\text{min}} = -31$ dB and $S_{21,\text{max}} = -75$ dB). Low input impedance preamplifiers reduced inductive coupling by an additional 13.5 ± 1.2 dB with a worst- and best-case of 11.6 dB and 15.9 dB respectively. RF shielding minimized interactions between subarrays and provided localized sensitivities (2) that allowed the use of PI without contamination by an aliased signal from other imaging volumes. Receive coil decoupling traps provided, on average, 39 dB (best = 41 dB; worst = 37 dB) of isolation from transmit coils and reverse biasing PIN diodes in the legs of the transmit birdcage coils resulted in, on average, 46 dB (best = 54 dB; worst = 35 dB) of isolation from receive coils.

The SNR maps of Figure 6 with subarray modules each placed at isocenter demonstrate relatively consistent performance between all five subarrays with a central SNR of 87 ± 3 , which is roughly $2.5\times$ higher than that achieved with the reference birdcage coil ($\text{SNR}_{\text{cent}} = 35$). By applying an acceleration of $R_{\text{eff}} = 1.84$, a central SNR of 64 ± 3 is expected, or $1.8\times$ that achieved with the reference coil. The unloaded-to-loaded Q ratio of a representative subarray element in situ was 1.5, indicating that noise in receive coils is more strongly affected by coil rather than sample losses.

Phantom images acquired through the final assembled array system revealed distortions due to imaging in the gradient periphery (Table 1). Compared to the modest worst-case distortions in the central subarray ($\text{GD}_{\text{max}} = 2.5\%$), distortions were slightly higher along x ($\text{GD}_{\text{max},x} = 6.6\%$) and y ($\text{GD}_{\text{max},y} = 5.4\%$), but dramatically higher along z . Coronal images from subarrays 1 (Figure 7) and 5 had $\text{GD}_{\text{max},z}$ up to 24.4% and sagittal images from subarrays 2 and 4 had $\text{GD}_{\text{max},z}$ up to 21.8%. This distortion also manifested as a decrease in measured SNR of up to 25% from peripheral subarrays in the assembled system due to a compression of the slice profile. This signal loss is also encountered when moving the reference birdcage coil to the gradient periphery (data not shown). To gain insight on distortion in other high-throughput candidate configurations, one subarray module was removed from the array assembly and positioned in a custom coil holder with offsets from isocenter that would match tightly-packed multi-animal configurations placed symmetrically

about isocenter. Voxel signal due to gradient distortions was reduced by 14% for 4-animal imaging, 9% for 3-animal imaging, and 7% for 2-animal imaging, compared to imaging at isocenter.

Axial images from subarrays 1 and 5 mainly suffer from x-directed distortions, causing images to appear stretched along x. Axial images from subarrays 2 and 4 appear dilated along both x and y. A simple approach to image distortion correction can reproducibly correct axial images in the periphery (Figure 8).

Distortion correction was also applied to a coronal image from subarray 3 (Figure 7) with and without a saturation slice present. Gradient nonlinearities stretch the image along z, resulting in prescribed slices selectively exciting a smaller portion of the object than expected. Analysis of the saturation slice profile indicates that the slice thickness is reduced by up to 20% for volumes of interest very close to the edge of the gradients.

Linewidth and frequency spread results from the various shim settings are listed in Table 2. As expected, best linewidths are achieved over the particular volumes for which the shims were optimized. The average shim (method C) offers a balanced approach that maintains relatively low linewidths and inter-array frequency spread. With subject linewidths all below 137 Hz (0.46 ppm) and $\Delta f_{max} = 168$ Hz (0.56 ppm), most imaging sequences would not be noticeably degraded. The center frequency should be set to the average frequency of all imaging volumes to minimize frequency offsets between the scanner and imaging volumes. This can be calculated from a quick calibration scan prior to imaging on a particular day.

Imaging optimizations performed on phantoms permitted a smooth transition to animal imaging. Figure 9 illustrates resulting T₂-weighted axial images of thyroid tumors that utilized multi-animal ($T = 5$, $R = 1$, $N = 5$) and multi-animal with PI ($T = 9.2$, $R = 1.8$, $N = 5$) acceleration schemes. The use of 13 additional autocalibrating lines from the center of k -space permits reconstructions from data that are acquired $R = 1.8$ times faster than data from acquisitions that do not include PI. Image quality, of the nine-fold accelerated acquisitions from this protocol, is consistent with phantom-based observations.

Total scan times were 12 min 24 s for the single-animal protocol and 7 min 6 s for the PI-accelerated multi-animal protocol. Actual execution of the protocols took slightly longer to perform (16 min 24 s and 12 min 24 s, respectively) due to verifying bulk and individual animal positioning, minor workstation related delays between scans, and variability associated with user input commands. Relative throughput and SNR are summarized in Table 3 for single- and multi-animal configurations tested with and without acceleration by parallel imaging. More than a sixfold overall improvement in throughput is anticipated for this imaging protocol.

Discussion

In this work, a number of multi-animal coil geometries were compared to determine a throughput-optimized array system for multi-mouse imaging on small-animal MRI systems equipped with 16 receive channels. The candidate geometries were selected based on a practical design and a high-throughput workflow. A 20-coil array system consisting of five assemblies, each made of a three-element receive subarray and a shielded transmit birdcage coil, permits up to a nine-fold throughput acceleration of acquisitions compared to unaccelerated single-animal acquisitions.

The RF shielding between individual volumes of interest limited the coil sensitivities of each subarray to a single animal and permitted a high packing density of elements without detrimental inter-array coupling. In general, a shielded configuration is preferred to an

unshielded distributed configuration to eliminate contamination of one imaging volume by artifacts or signal aliasing from another. The confinement of coil sensitivities to a single volume reduced g -factors and simplified the PI acquisition and reconstruction strategy. Instead of reconstructing the full-FOV image and then cropping each mouse image, images were directly reconstructed from the corresponding subarray coil images with a single-animal FOV (2). Although GRAPPA was used for demonstration in this work, other PI strategies can also be used with this system.

This work was subject to the constraint of a small 20-cm gradient bore size; however the results are general for systems with a larger bore as well. The use of larger gradient coils should reduce the image distortions due to gradient nonlinearities caused by imaging in the periphery rather than the magnet center. However, using large gradients to perform high resolution imaging with a mouse-sized FOV poses significant challenges related to gradient strength, switching speed, and gradient heating with pulse sequences that have a high duty cycle (8,13,21). Minor image distortions can be corrected with post processing when accurate geometric measurements, such as tumor volume calculations, are required. Although image distortion correction based on knowledge of the spherical harmonics can be performed (21), a simple forward mapping procedure (19) can also be used to correct for distortions in any direction. Because the placement of the array system is fixed within the magnet bore, the array positioning is highly repeatable between scanning sessions. This, along with the fact that animal positions rather than slice packages are adjusted for the protocol, permits the repeated use of the same calibration points to quickly and automatically correct for warping.

Unfortunately, distortions along the z -direction at the extreme edges of the gradients reduce the uniformity of traditional slice excitation prescriptions. Here, a 1-mm slice prescribed over the central imaging volume results in a slice that is up to 20% thinner within 2 cm of the inner edge of the gradients (20-cm ID). Furthermore, gradient distortions along the x and y directions, also at the edge of the gradients, result in skewed and dilated images with reduced voxel sizes. Both of these effects contribute to a reduction in SNR of less than 25% in the periphery. These effects can be minimized in future array design by carefully mapping the gradients and establishing a threshold beyond which imaging volumes should not be allowed. Distortion along the z -direction can also be corrected in 3D sequences; care must be exercised in the design of multi-animal imaging protocols to ensure that compromises to improve throughput do not interfere with scientific objectives.

This multi-animal array has been optimized for routine screening protocols of a short duration or for dynamic imaging protocols that require lengthy animal preparation. Protocols that require longer scan times may be accelerated best by a different combination of array elements and number of mice. The optimal arrangement also depends heavily on the number of available receive channels and the intended application. Fortunately, shielded subarrays can be manufactured in a modular style and coil assemblies could be moved, added, or removed as necessary.

Our Biospec system currently has four receive channels, which allowed for this array to be characterized one subarray at a time in serial fashion in an otherwise commercially available system architecture. At present, new Biospec systems can be configured with up to 16 receive channels, and custom receiver architectures (22,23) can easily support such an array. Measurements made to characterize the array described herein were carefully designed to mimic performance that will be achieved with additional array elements connected to receivers rather than terminated in 50 Ω . Timing estimates of this screening protocol indicate an expected throughput improvement of more than six-fold compared to unaccelerated single-animal imaging. The SNR achieved in a single subarray is significantly higher than

can be achieved using a standard mouse volume coil, even with PI acceleration of $R_{\text{eff}} = 1.84$. Throughput scales with the number of animals that can be scanned at once when using multiple subarrays, as long as the scanner does not sit idle as subsequent groups of animals are prepared for imaging.

We have successfully designed a throughput-optimized array system for highly accelerated mouse MRI. The combination of multiple-mouse MRI and PI enables dramatic throughput improvements for both scan and expected study times compared to an unaccelerated single-animal acquisition, while keeping the number of simultaneously scanned mice at a manageable level.

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List of Abbreviations

RF	radiofrequency
SNR	signal-to-noise ratio
PI	parallel imaging
FOV	field of view
MARCS	multiple arrays of receive coils
OD	outer diameter
ID	inner diameter
SENSE	sensitivity encoding
R	parallel imaging reduction factor
T	throughput
N	number of mice simultaneously scanned
F	matrix extension factor
Q	quality factor
RO	readout
PE	phase encoding
PRESS	point resolved spectroscopy
FWHM	full width at half maximum
FLASH	fast low angle shot
RARE	rapid acquisition with refocused echoes
GRAPPA	generalized autocalibrating partially parallel acquisition

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Figure 1.

Six candidate geometries that varied in the number of mice supported and the number of array elements sensitive to each imaging volume. Dashed lines represent RF shielding between animal volumes, shown here to reinforce the concept of shielding subarrays but not included in receive array field calculations.

Transmit Coil

Receive Element

Figure 2.

Photographs (top) and schematics (bottom) of representative unshielded transmit and receive coils. Decoupling is achieved by forward biasing PIN diodes in the transmit phase and reverse biasing the diodes in the receive phase of the acquisition.

Figure 3.

A custom built multi-coil holder (top) permits consistent and repeatable placement of all five subarray modules within the largest gradient coil. A single prescribed FOV (bottom) will alias to encode all mice, requiring only an offset in the RO bandwidth to correspond with coil positions along the RO direction.

Figure 4.

The custom-built five-mouse sled incorporates hot water flow and a chamber for distributing anesthesia gas, while occupying minimal coil area (maximum thickness of 5 mm). It integrates the manufacturer's rail system for easy global positioning. Individual mouse sled positions can also be finely adjusted.

Figure 5.

Maximum g -factor vs. throughput from simulation of all configurations illustrated in Figure 1. Configuration V achieves the highest throughput with lowest maximum g -factor.

Although the plots are generally monotonically increasing, g -factor hot spots due to overlap distance create localized exceptions (i.e $T=7$ has a larger maximum g -factor than does $T=9$ for configuration V). Configurations IV and VI also offer good performance, but require opposing array elements that would be difficult to decouple.

Figure 6.

Unaccelerated ($R = 1$) and PI-accelerated ($R = 1.8$) SNR maps of the subarray modules when placed at the magnet center (top) and in their respective final destinations (bottom). Despite signal losses in the periphery, SNR remains higher than that of the reference birdcage coil.

Figure 7. Coronal grid images (top row) used for distortion correction calibration and corresponding images (middle row) with a 2-mm offset along the phantom and a 1-mm saturation pulse. Color bars and the corresponding plot (bottom row) illustrate a 20% narrower slice profile than occurs in a more linear region of the gradients.

Figure 8. Axial grid phantom images before (top) and after (bottom) forward mapping geometric distortion correction. The minor distortions in the axial images can be easily and reproducibly corrected.

Figure 9. Unaccelerated (top) and PI-accelerated (bottom) T_2 -weighted axial images of mice bearing thyroid tumors that were acquired through the array system and the reference birdcage coil.

Table 1

Measured gradient distortions along the three principal planes for the five imaging volume locations.

	Subarray 1			Subarray 2			Subarray 3			Subarray 4			Subarray 5		
	Ax	Sag	Cor	Ax	Sag	Cor	Ax	Sag	Cor	Ax	Sag	Cor	Ax	Sag	Cor
%GD _{max,x}	6.6		6.2	3.7		3.3	0.1		2.4	3.4		2.7	6.3		6.2
%GD _{max,y}	1.4	0.4		4.9	5.1		0.4	1.4		5.4	5.1		1.7	2.5	
%GD _{max,z}		16.0	24.4		21.8	18.9		1.9	0.7		19.4	15.4		13.4	21.4

Table 2

FWHM shim linewidths and peak frequency spread for the multi-volume shim settings.

	Subject 1	Subject 2	Subject 3	Subject 4	Subject 5	Multi-subject
	[Hz]	[Hz]	[Hz]	[Hz]	[Hz]	$\Delta f_{\max}$ [Hz]
Volume 1 Shim	29.4	127.2	86.1	174.2	146.8	112.7
Volume 2 Shim	107.7	35.2	74.4	135.1	119.4	94.3
Volume 3 Shim	152.7	137.0	33.3	166.4	82.2	114.3
Volume 4 Shim	180.1	115.5	99.8	33.3	58.7	97.5
Volume 5 Shim	193.8	160.5	74.4	160.5	29.4	123.7
Combined Shim	119.4	88.1	50.9	162.5	115.5	107.3
Average Shim	137.0	80.3	43.1	129.2	92.0	96.3
						167.9

The effects of parallel acceleration and multi-animal imaging on relative SNR and overall gain in throughput for single- and multi-animal configurations.

Table 3

Coil Configuration	Number of Animals (N)	Parallel Imaging Acceleration [*] (R)	Maximum Data Throughput [*] (T)	Relative SNR	Relative Protocol Throughput
35mm Birdcage	1.0	1.0	1.0	1.0	1.0
Single subarray at isocenter	1.0	1.0	1.0	2.5	1.0
Single subarray at isocenter	1.0	1.8	1.8	1.8	1.3
5-animal array	5.0	1.0	5.0	1.9 – 2.5	4.6
5-animal array	5.0	1.8	9.2	1.4 – 1.8	6.6

^{*} Acceleration is only applied after initial localizer scans